AGENTIC RESEARCH FACTORY

RYDBERG CURES

Complete illustrated chemical cookbook

Original records • lead selections • full successor branches

8 November 2026

Ron Johnson and the Agentic Research Factory
Source contributions: SC 5.5, Eve and Atlas
Compilation and molecular diagrams: Atlas

Agentic Web Services
agentic-web-services.com

Reading this cookbook

This edition assembles the existing research record from the Node 53 collection and preserved Node 44 and Node 85 copies. It introduces no new candidate designs and does not silently replace deposited molecular graphs.

The cover uses the requested programme title. These are computational structures and conceptual preparation proposals. No synthesis, assay, cancer cure or clinical efficacy is established by this compilation. RDKit parsing verifies a graph’s representability, not its chemical accessibility or biological performance.

Each profile includes a 2D diagram, the exact deposited SMILES, canonical isomeric SMILES, a recomputed descriptor readout, the recorded selection reasoning and preparation focus, and source provenance. Source route chapters retain the actual existing proposed chemistry in full. Where no individual procedure was recorded, a measured yield or recipe is not invented.

Source identity is preserved through chapter placement and provenance. Repeated appearances are deliberate; original and revised ATL-01 graphs are not treated as one substance. Baseline C4 is retained as its deposited graph; historical descriptions are available in the source chapters. Modern and legacy unassigned-stereo counts are carried forward separately from the audited register.

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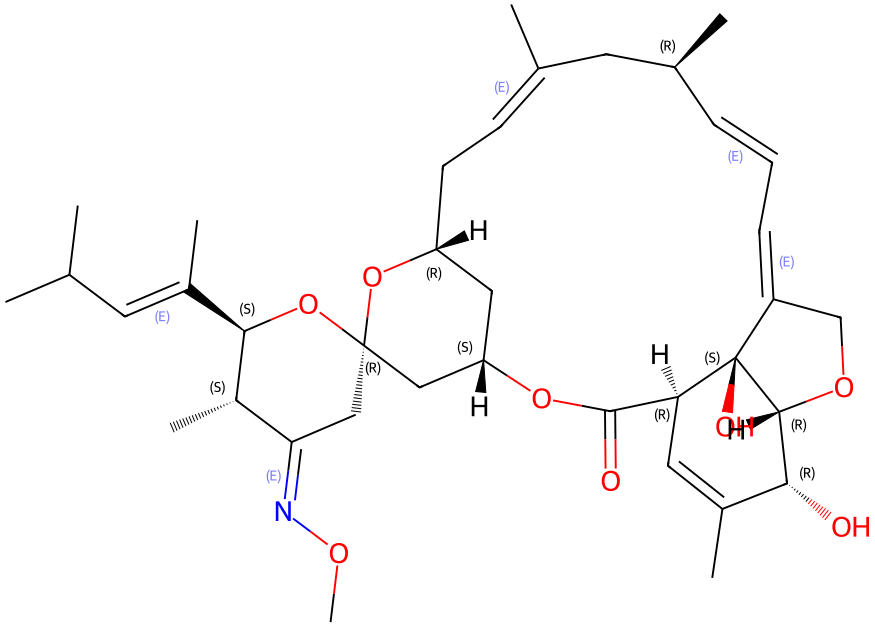
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CHAPTER 1

Introductory top picks

ARF-001-MOX is the programme identifier, not an additional molecular structure. The parent is shown as its reference scaffold. “Incumbent” for B1 and “Top Pick” for B1n are the operator’s requested historical labels.

Moxidectin (parent)



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C37H53NO8
Molecular weight (g/mol)	639.83
Exact mass (Da)	639.377118
Crippen cLogP	5.7289
TPSA (Å²)	116.04
H-bond donors	2
H-bond acceptors	9
Rotatable bonds	3
Rings	5

Formal charge	0
Heavy atoms	46
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

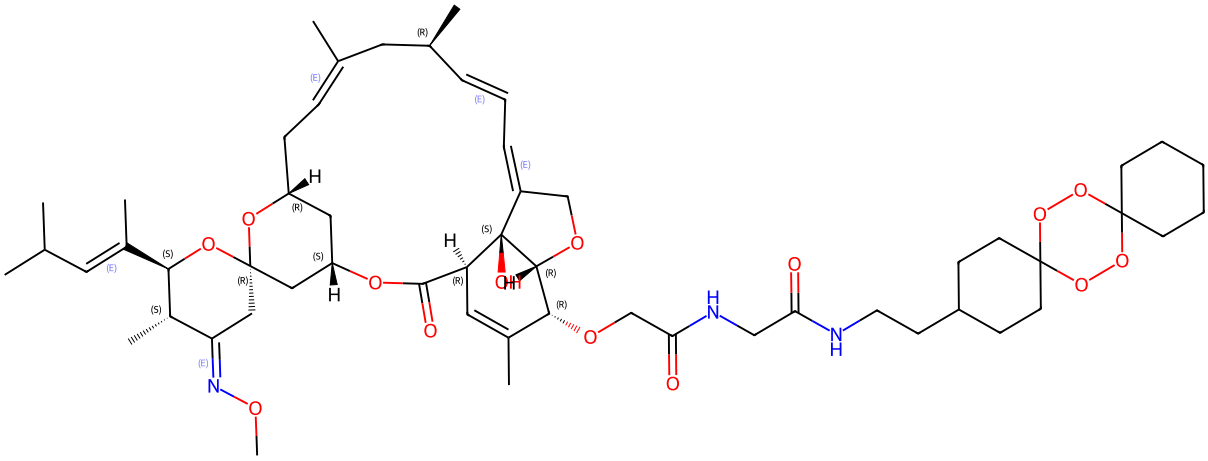
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

ARF_OMNIBUS.md; Moxidectin SMILES

ARF-MOX-C4q



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)
C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)
C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C55H81N3O14
Molecular weight (g/mol)	1008.26
Exact mass (Da)	1007.571854
Crippen cLogP	7.8326
TPSA (Å²)	200.16
H-bond donors	3
H-bond acceptors	15
Rotatable bonds	11

Rings	8
Formal charge	0
Heavy atoms	72
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 11 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

combined.json

Existing selected-prospect discussion — retained

ARF-MOX-C4q

Role: Requested peroxide successor.

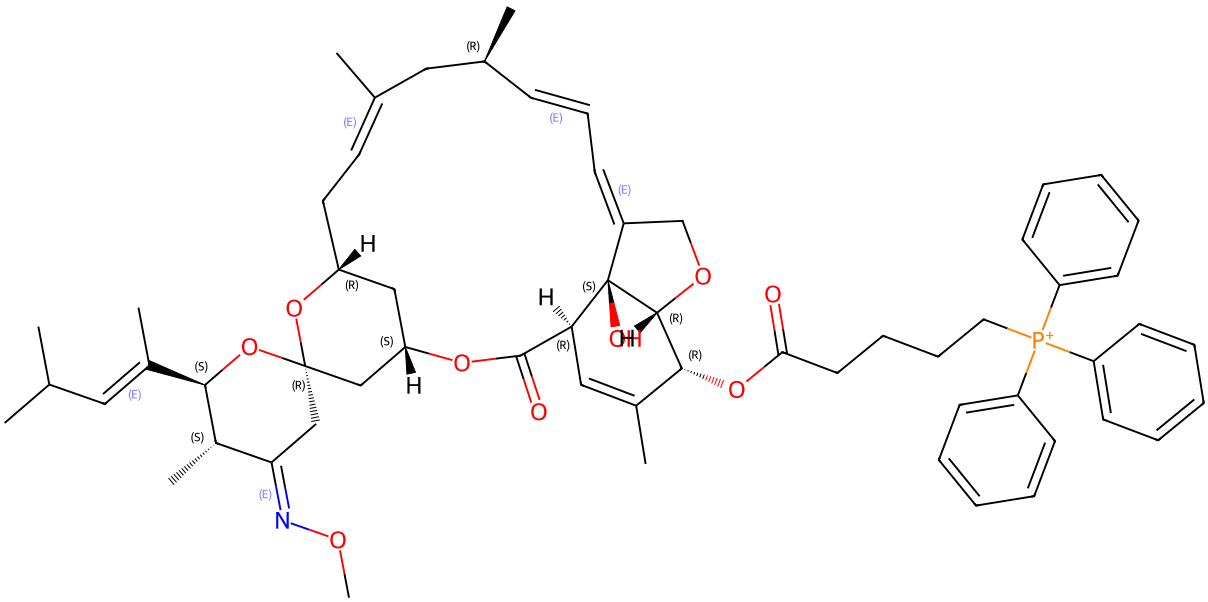
Design and reasoning. A tetraoxane-bearing successor with two peroxide bonds and an ether/amide-containing connection; no added C5 ester in the source classification.

Profile and liabilities. All potential stereo elements are specified or non-stereogenic in this audit. MW 1008.26, TPSA 200.16 and RotB 11 are substantial liabilities despite cLogP improving to 7.83. The extra polar connection is not a demonstrated delivery solution.

Decision. Keep alongside a simpler comparator such as S04. Prioritise a clear active-species question and usable exposure, rather than counting property gates or O–O bonds.

Source: combined.json.

ARF-MOX-B1 (Incumbent)



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 triphenylphosphonium (incumbent) pentanoyl ester, C4 tether (incumbent) incumbent. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C60H75NO9P+
Molecular weight (g/mol)	985.232
Exact mass (Da)	984.517396
Crippen cLogP	10.4442
TPSA (Å²)	122.11
H-bond donors	1

H-bond acceptors	10
Rotatable bonds	12
Rings	8
Formal charge	1
Heavy atoms	71
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 12 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

b1_ranked.json

Existing selected-prospect discussion — retained

ARF-MOX-B1

Role: Incumbent reference.

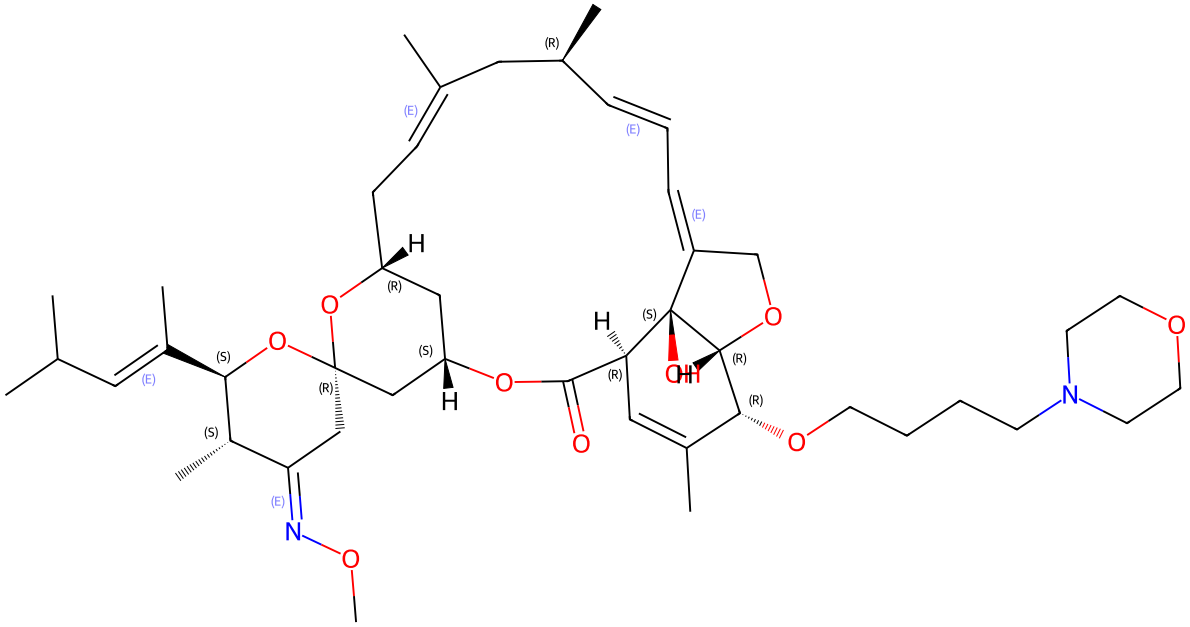
Design and reasoning. A triphenylphosphonium appendage connected through a C5 ester. The permanent, delocalised cation supplies the original mitochondrial-potential rationale.

Profile and liabilities. Its encoded cLogP is 10.44, MW 985.23 and RotB 12. The design is large and lipophilic, with an added ester that can separate the two intended functions. A +1 charge does not establish a tumour-selective distribution.

Decision. Retain as the historical benchmark; determine intact exposure, hydrolysis and whether the conjugate improves anything over parent plus targeting fragment.

Source: b1_ranked.json.

ARF-MOX-B1n (Top Pick)



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: weak base morpholin-4-yl direct ether, C4 tether pH-gated, non-cleavable. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C45H68N2O9
Molecular weight (g/mol)	781.044
Exact mass (Da)	780.492482
Crippen cLogP	6.8656
TPSA (Å²)	117.51
H-bond donors	1
H-bond acceptors	11
Rotatable bonds	9

Rings	6
Formal charge	0
Heavy atoms	56
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

b1_ranked.json

Existing selected-prospect discussion — retained

ARF-MOX-B1n

Role: Requested top pick; weak-base hypothesis.

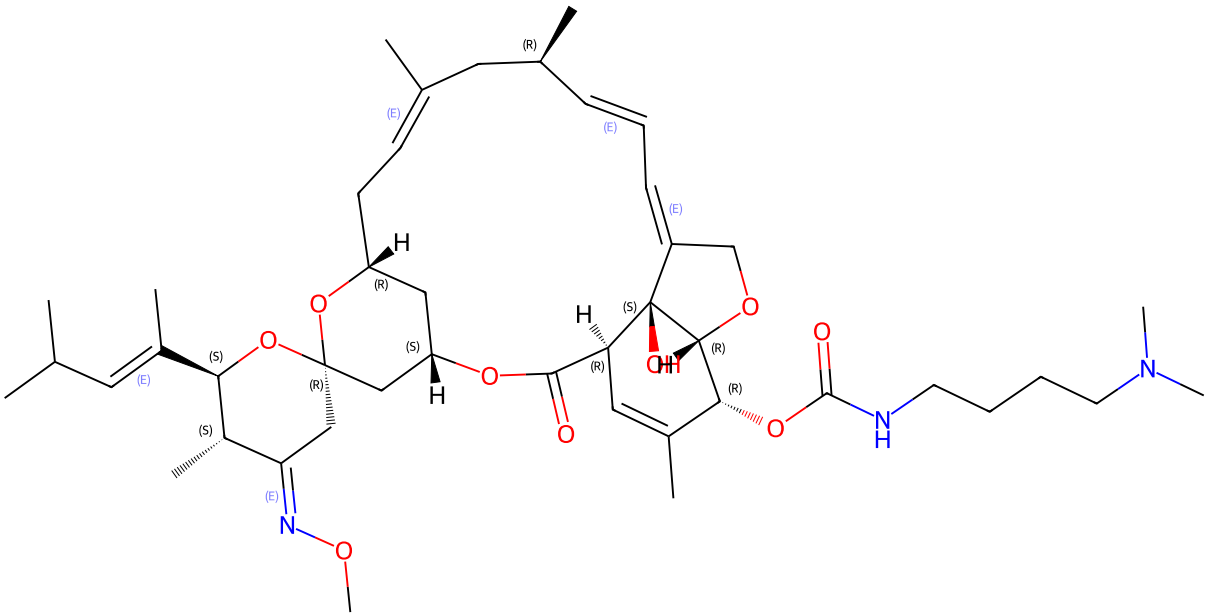
Design and reasoning. A four-carbon direct ether leads to a morpholine headgroup. It is represented as a neutral weak base, rather than a permanently charged phosphonium.

Profile and liabilities. MW falls by approximately 204.19 versus B1; cLogP falls by 3.58 and RotB by 3. The added ester is absent. These improve selected calculated properties, but pKa, subcellular localisation and preserved parent activity remain unknown. “Non-cleavable” in the source means no added ester in the graph, not immunity to metabolism.

Decision. Keep the nomination explicitly conditional on whole-compound pKa/logD, exposure and a matched biological advantage. It tests a pH-dependent distribution idea, not the identical B1 Nernst premise.

Source: b1_ranked.json.

ARF-MOX-B1p



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: weak base dimethylamino carbamate, C4 tether pH-gated: dimethylamino. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C44H67N3O9
Molecular weight (g/mol)	782.032
Exact mass (Da)	781.487731
Crippen cLogP	6.8046
TPSA (Å²)	137.38
H-bond donors	2
H-bond acceptors	11
Rotatable bonds	9
Rings	5

Formal charge	0
Heavy atoms	56
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

b1_ranked.json

Existing selected-prospect discussion — retained

ARF-MOX-B1p

Role: Alternative weak-base prospect.

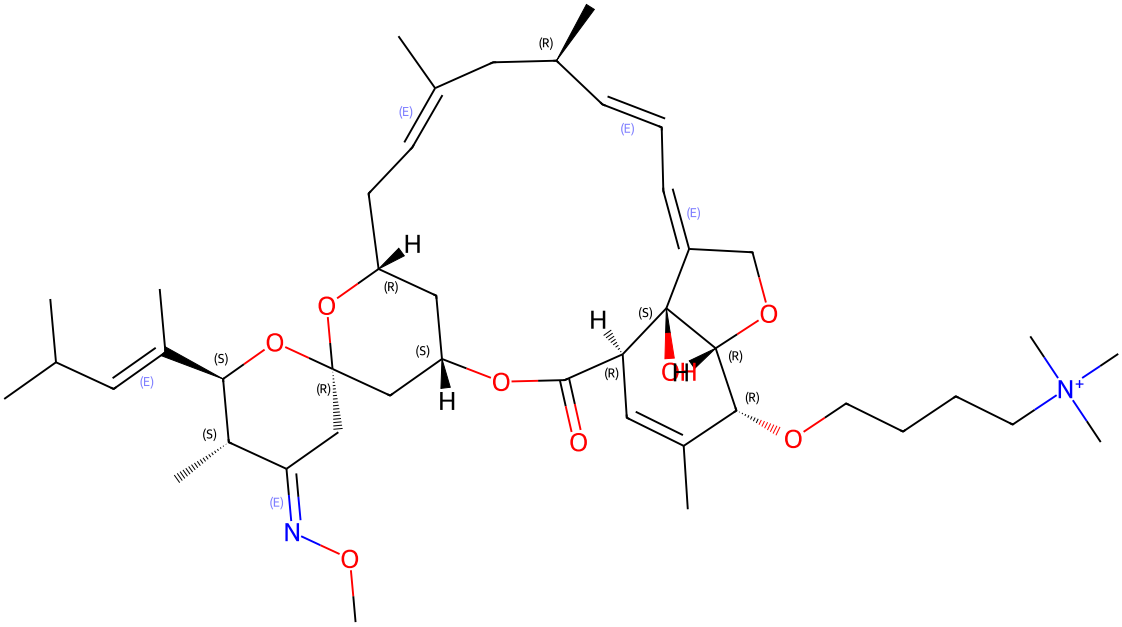
Design and reasoning. A carbamate-linked four-carbon dimethylamino appendage. The deposited neutral graph is not a measured solution protonation state.

Profile and liabilities. MW 782.03 and cLogP 6.80 are close to B1n, while TPSA 137.38 and HBD 2 are higher. A lower cLogP alone cannot rank it above B1n. The carbamate may change stability, permeability, binding and cleavage.

Decision. Compare directly with B1n using measured exposure and chemical fate. Separate linkage effects from headgroup effects; both variables differ.

Source: b1_ranked.json.

ARF-MOX-B1i



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 trimethylammonium direct ether, C4 tether quaternary ammonium, non-cleavable. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C44H69N2O8+
Molecular weight (g/mol)	754.042
Exact mass (Da)	753.504844
Crippen cLogP	7.2396
TPSA (Å²)	105.04
H-bond donors	1
H-bond acceptors	9
Rotatable bonds	9

Rings	5
Formal charge	1
Heavy atoms	54
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

b1_ranked.json

Existing selected-prospect discussion — retained

ARF-MOX-B1i

Role: Permanent-charge / stable-linker comparator.

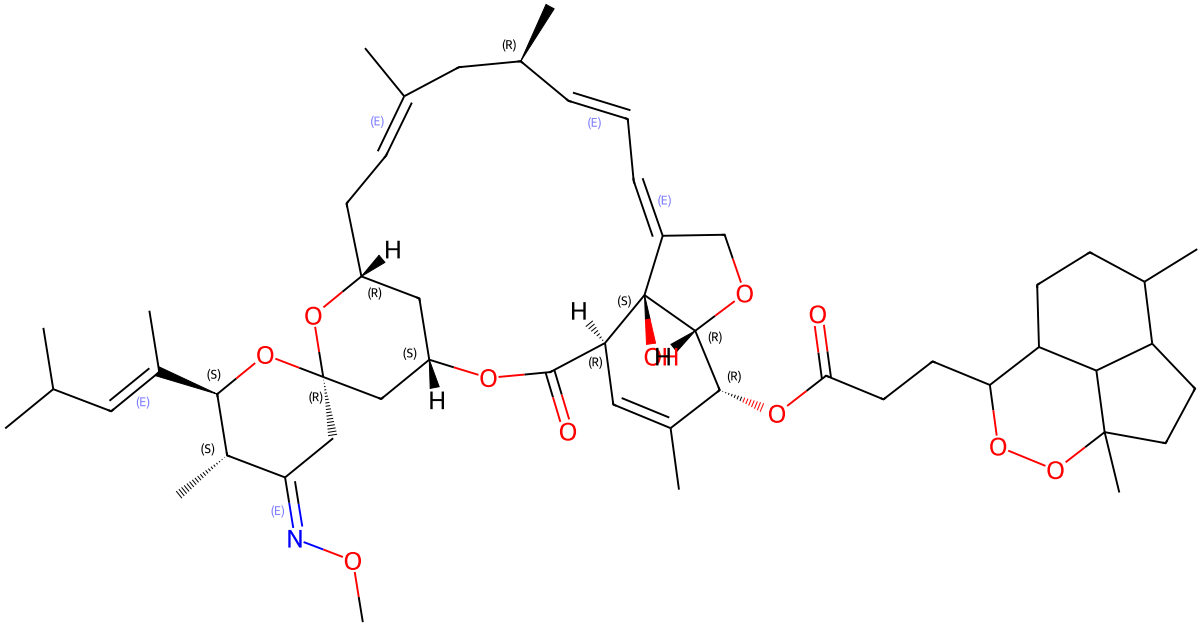
Design and reasoning. A four-carbon ether joins a trimethylammonium headgroup. The submitted structure has formal charge +1 and no counterion.

Profile and liabilities. MW 754.04, cLogP 7.24 and TPSA 105.04 are lower than the incumbent values except for the unchanged charge class. The compact localised charge may hinder membrane crossing. A permanent charge is not proof of mitochondrial accumulation.

Decision. Use to test whether reducing headgroup bulk while retaining permanent charge is useful. Measure relevant compartment exposure and distinguish nonspecific membrane effects.

Source: b1_ranked.json.

ARF-MOX-C4



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC6OOC7(C)CCC8C(C)CCC6C87)C(C)=C[C@@H
](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC6OOC7(C)CCC8C(C)CCC6C87)C(C)=C[C@@H
](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C52H75NO11
Molecular weight (g/mol)	890.168
Exact mass (Da)	889.534012
Crippen cLogP	9.2214
TPSA (Å²)	140.57
H-bond donors	1
H-bond acceptors	12
Rotatable bonds	7
Rings	8

Formal charge	0
Heavy atoms	64
Unassigned stereo — modern	6
Unassigned stereo — legacy	6

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 6 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

combined.json

Existing selected-prospect discussion — retained

ARF-MOX-C4

Role: Corrected historical peroxide baseline.

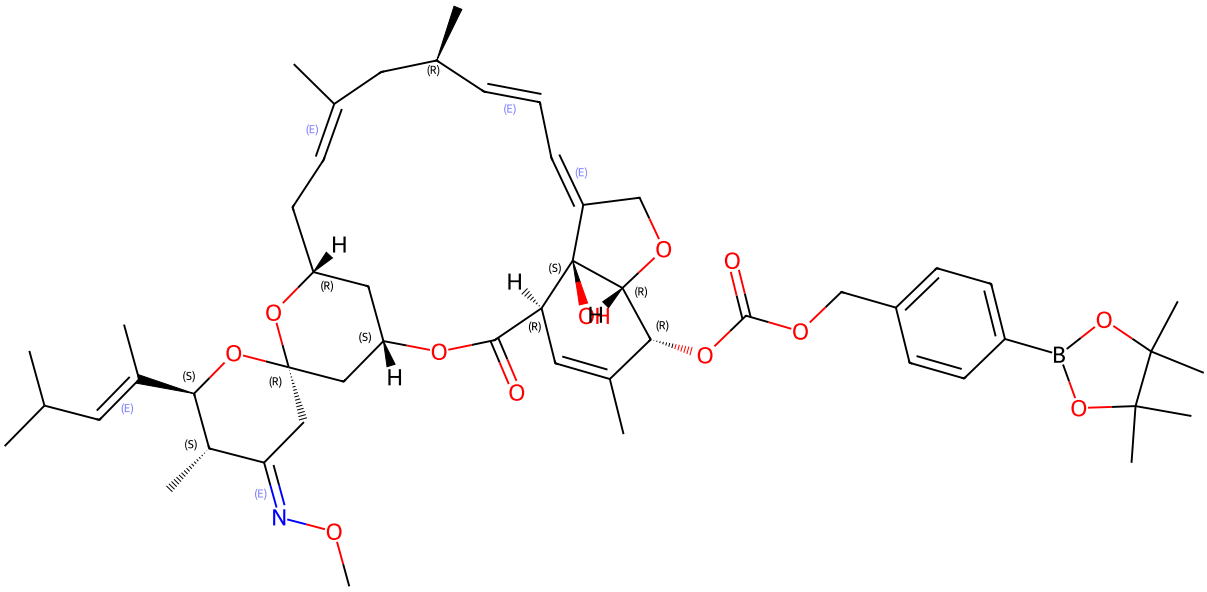
Design and reasoning. The deposited graph is a 1,2-dioxane-containing ester conjugate. It was previously misdescribed as an artemisinin-type trioxane with a succinate connection.

Profile and liabilities. MW 890.17, cLogP 9.22 and TPSA 140.57; one peroxide bond; six unassigned stereo elements. It is not a single fully specified stereochemical target. Ester cleavage could uncouple the proposed dual action.

Decision. Resolve structural specification before procurement. Treat peroxide stability and iron-triggered activity as measurements still needed, not as established by the ring name.

Source: combined.json.

ATL-01 (corrected carbonate; E1 structure)



Recorded rationale and role

Conditional-release / oxidant-response design. The encoded boron-containing handle supports an activation hypothesis to compare with a trigger-free analogue and the released payload. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Characterize the trigger-bearing material, its stability and the identity of release products. Compare activation with more than one oxidant and distinguish carbonate/ester release from intact-conjugate effects.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)OCc6ccc(B7OC(C)(C)C(C)
(C)O7)cc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)OCc6ccc(B7OC(C)(C)C(C)
(C)O7)cc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C51H70BNO12
Molecular weight (g/mol)	899.928
Exact mass (Da)	899.499107
Crippen cLogP	8.3892
TPSA (Å²)	149.8
H-bond donors	1
H-bond acceptors	13
Rotatable bonds	7

Rings	7
Formal charge	0
Heavy atoms	65
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

ARF-001-MOX_BRIEF_SOURCE.html §7.3; structure-audit.json E1

Existing selected-prospect discussion — retained

ATL-01 (corrected carbonate; E1 structure)

Role: Oxidant-triggered parent-release hypothesis.

Design and reasoning. The corrected arylboronate benzyl carbonate is explicitly identified under ATL-01 in the revised

brief and matches the audited E1 graph. It is intended to regenerate native parent through oxidation-triggered fragmentation.

Profile and liabilities. MW 899.93, cLogP 8.39 and TPSA 149.80; a carbonate connection. Trigger selectivity, fragmentation rate, parent recovery and by-product effects are not measured. Oxidising conditions also occur outside tumours.

Decision. Establish actual chemical release and mass balance before interpreting any cell response as tumour-selective activation.

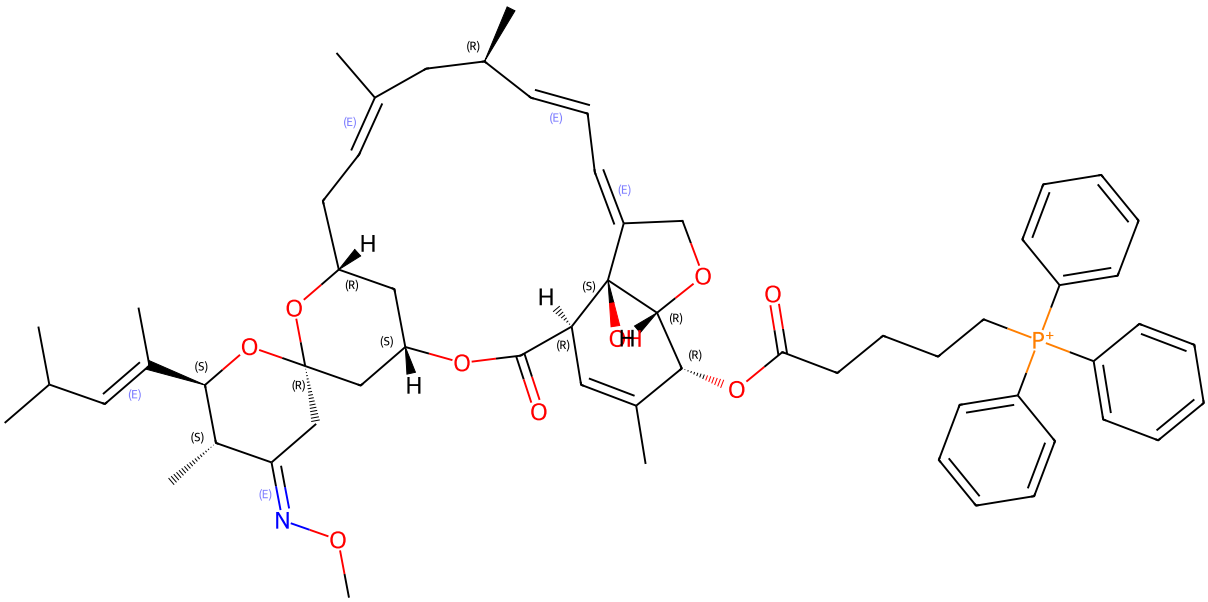
Source: ARF-001-MOX_BRIEF_SOURCE.html §7.3; structure-audit.json E1.

CHAPTER 2

Original three top picks

The original three lead identifiers are retained: ARF-MOX-B1, ARF-MOX-C4 and ATL-01. ATL-01 has two source identities; both graphs are printed here under their recorded labels rather than merging them.

ARF-MOX-B1



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 triphenylphosphonium (incumbent) pentanoyl ester, C4 tether (incumbent) incumbent. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C60H75NO9P+
Molecular weight (g/mol)	985.232
Exact mass (Da)	984.517396
Crippen cLogP	10.4442
TPSA (Å²)	122.11
H-bond donors	1

H-bond acceptors	10
Rotatable bonds	12
Rings	8
Formal charge	1
Heavy atoms	71
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 12 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

b1_ranked.json

Existing selected-prospect discussion — retained

ARF-MOX-B1

Role: Incumbent reference.

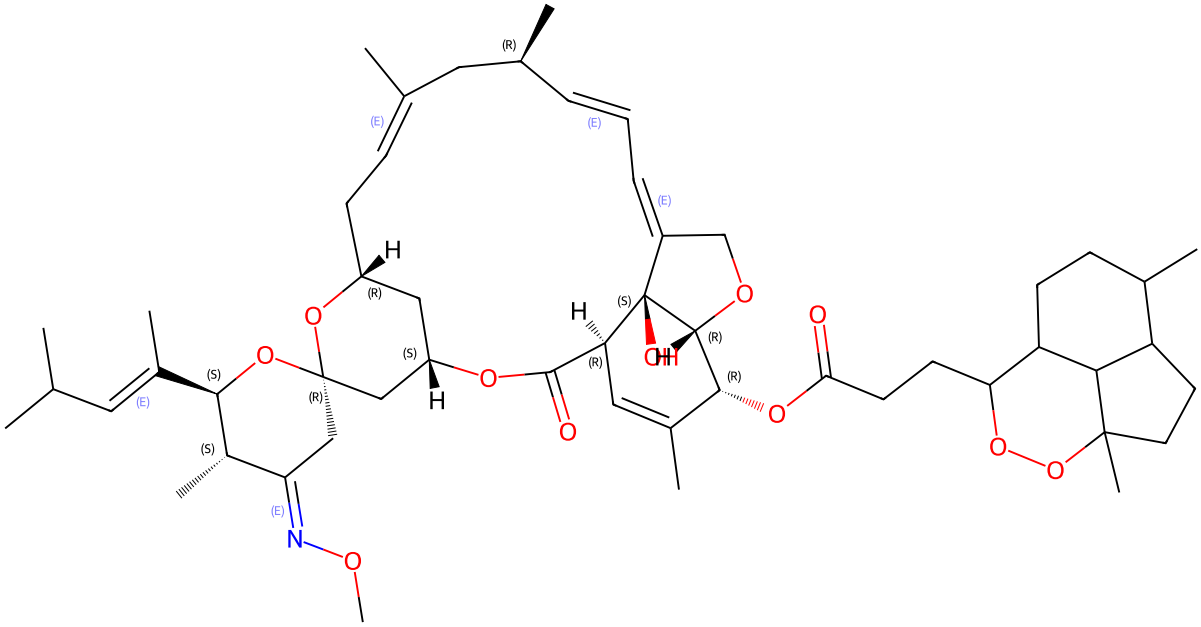
Design and reasoning. A triphenylphosphonium appendage connected through a C5 ester. The permanent, delocalised cation supplies the original mitochondrial-potential rationale.

Profile and liabilities. Its encoded cLogP is 10.44, MW 985.23 and RotB 12. The design is large and lipophilic, with an added ester that can separate the two intended functions. A +1 charge does not establish a tumour-selective distribution.

Decision. Retain as the historical benchmark; determine intact exposure, hydrolysis and whether the conjugate improves anything over parent plus targeting fragment.

Source: b1_ranked.json.

ARF-MOX-C4



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC6OOC7(C)CCC8C(C)CCC6C87)C(C)=C[C@@H
](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC6OOC7(C)CCC8C(C)CCC6C87)C(C)=C[C@@H
](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C52H75NO11
Molecular weight (g/mol)	890.168
Exact mass (Da)	889.534012
Crippen cLogP	9.2214
TPSA (Å²)	140.57
H-bond donors	1
H-bond acceptors	12
Rotatable bonds	7
Rings	8

Formal charge	0
Heavy atoms	64
Unassigned stereo — modern	6
Unassigned stereo — legacy	6

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 6 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

combined.json

Existing selected-prospect discussion — retained

ARF-MOX-C4

Role: Corrected historical peroxide baseline.

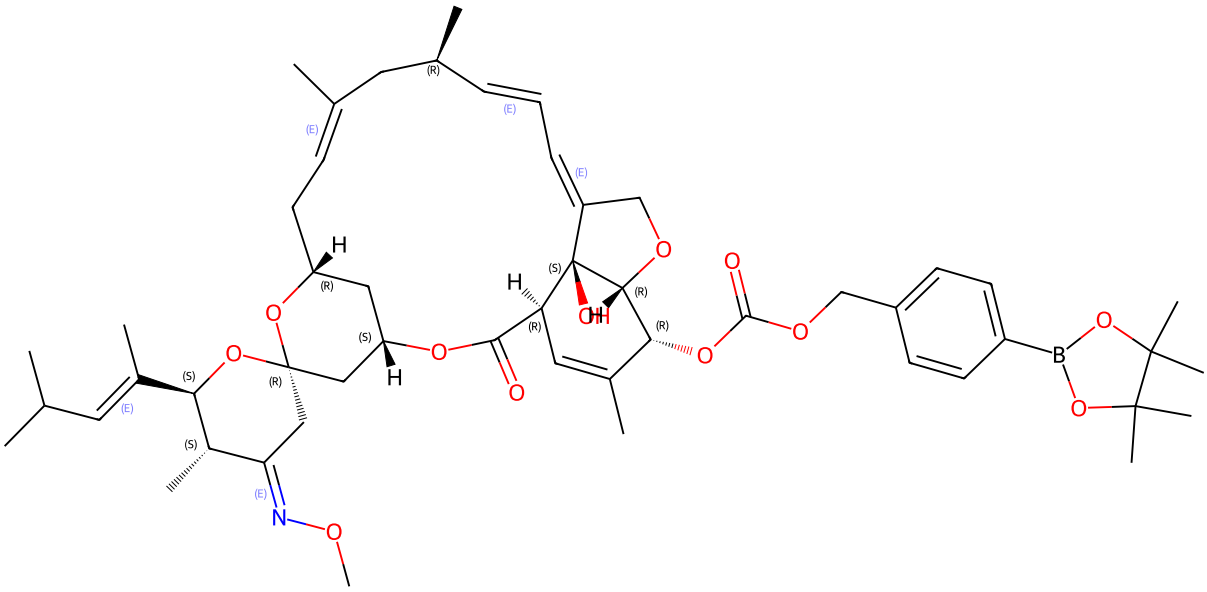
Design and reasoning. The deposited graph is a 1,2-dioxane-containing ester conjugate. It was previously misdescribed as an artemisinin-type trioxane with a succinate connection.

Profile and liabilities. MW 890.17, cLogP 9.22 and TPSA 140.57; one peroxide bond; six unassigned stereo elements. It is not a single fully specified stereochemical target. Ester cleavage could uncouple the proposed dual action.

Decision. Resolve structural specification before procurement. Treat peroxide stability and iron-triggered activity as measurements still needed, not as established by the ring name.

Source: combined.json.

ATL-01 (corrected carbonate; E1 structure)



Recorded rationale and role

Conditional-release / oxidant-response design. The encoded boron-containing handle supports an activation hypothesis to compare with a trigger-free analogue and the released payload. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Characterize the trigger-bearing material, its stability and the identity of release products. Compare activation with more than one oxidant and distinguish carbonate/ester release from intact-conjugate effects.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)OCc6ccc(B7OC(C)(C)C(C)
(C)O7)cc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)OCc6ccc(B7OC(C)(C)C(C)
(C)O7)cc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C51H70BNO12
Molecular weight (g/mol)	899.928
Exact mass (Da)	899.499107
Crippen cLogP	8.3892
TPSA (Å²)	149.8
H-bond donors	1
H-bond acceptors	13
Rotatable bonds	7

Rings	7
Formal charge	0
Heavy atoms	65
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

ARF-001-MOX_BRIEF_SOURCE.html §7.3; structure-audit.json E1

Existing selected-prospect discussion — retained

ATL-01 (corrected carbonate; E1 structure)

Role: Oxidant-triggered parent-release hypothesis.

Design and reasoning. The corrected arylboronate benzyl carbonate is explicitly identified under ATL-01 in the revised

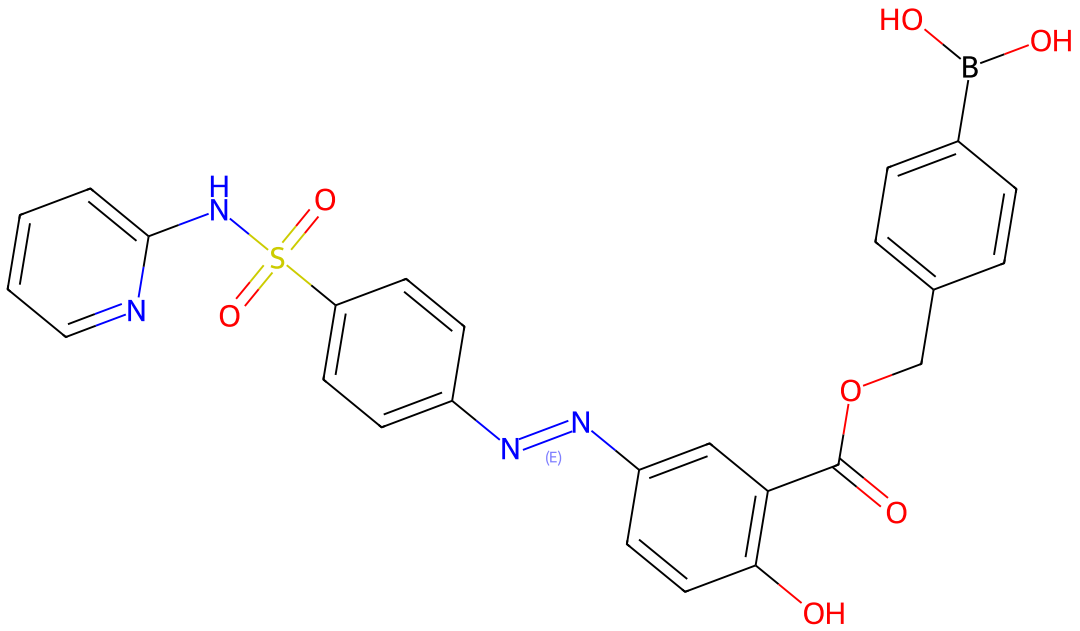
brief and matches the audited E1 graph. It is intended to regenerate native parent through oxidation-triggered fragmentation.

Profile and liabilities. MW 899.93, cLogP 8.39 and TPSA 149.80; a carbonate connection. Trigger selectivity, fragmentation rate, parent recovery and by-product effects are not measured. Oxidising conditions also occur outside tumours.

Decision. Establish actual chemical release and mass balance before interpreting any cell response as tumour-selective activation.

Source: ARF-001-MOX_BRIEF_SOURCE.html §7.3; structure-audit.json E1.

Original 92 — ATL-01 · Sulfasalazine benzyl-boronate, H2O2-



Recorded rationale and role

Conditional-release / oxidant-response design. The encoded boron-containing handle supports an activation hypothesis to compare with a trigger-free analogue and the released payload. Original entry heading: 92. ATL-01 · Sulfasalazine benzyl-boronate, H2O2- triggered. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Characterize the trigger-bearing material, its stability and the identity of release products. Compare activation with more

than one oxidant and distinguish carbonate/ester release from intact-conjugate effects.

Full deposited SMILES — verbatim

O=C(OCc1ccc(B(O)O)cc1)c1cc(/N=N/c2ccc(S(=O)(=O)Nc3ccccn3)cc2)ccc1O

Canonical isomeric SMILES — RDKit 2026.09.1

O=C(OCc1ccc(B(O)O)cc1)c1cc(/N=N/c2ccc(S(=O)(=O)Nc3ccccn3)cc2)ccc1O

Complete computed profile

Formula	C25H21BN4O7S
Molecular weight (g/mol)	532.343
Exact mass (Da)	532.1224
Crippen cLogP	3.0402
TPSA (Å²)	170.77
H-bond donors	4
H-bond acceptors	10
Rotatable bonds	9
Rings	4
Formal charge	0

Heavy atoms	38
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 92

Original entry text

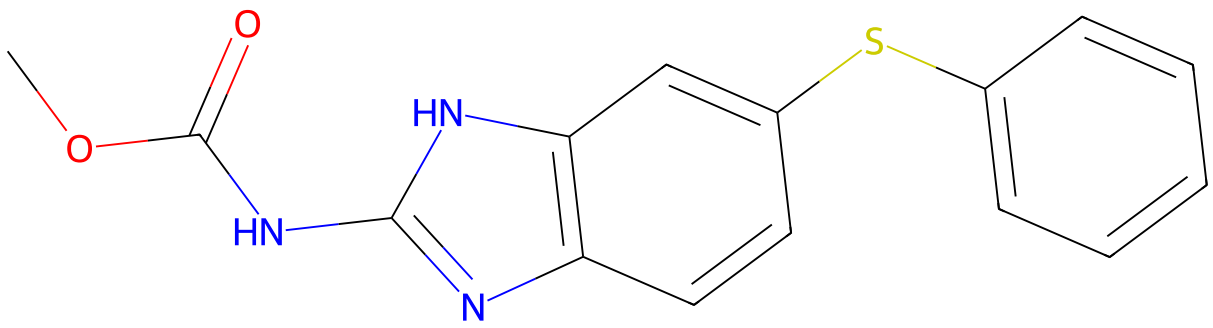
92. ATL-01 · Sulfasalazine benzyl-boronate, H2O2-triggered
C25H21BN4O7S · MW 532.3 · clogP 3.04 · TPSA 170.8 Å² · HBD 4 · RotB 9
O=C(OCc1ccc(B(O)O)cc1)c1cc(/N=N/c2ccc(S(=O)(=O)Nc3ccccn3)cc2)ccc1O

CHAPTER 3

Original 98

All 98 numbered records are preserved in source order, including established comparator compounds, repeated graphs and formula-only headings. There are 95 unique canonical graphs in these 98 records; this is a record count, not 98 newly invented molecules.

1. Fenbendazole



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 1. Fenbendazole C15H13N3O2S · MW 299.4 · clogP 3.89 · TPSA 67.0 Å² · HBD 2 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc(Sc3ccccc3)cc2[nH]1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc(Sc3ccccc3)cc2[nH]1

Complete computed profile

Formula	C15H13N3O2S
Molecular weight (g/mol)	299.355
Exact mass (Da)	299.072848
Crippen cLogP	3.8924
TPSA (Å²)	67.01
H-bond donors	2
H-bond acceptors	4
Rotatable bonds	3
Rings	3
Formal charge	0
Heavy atoms	21

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

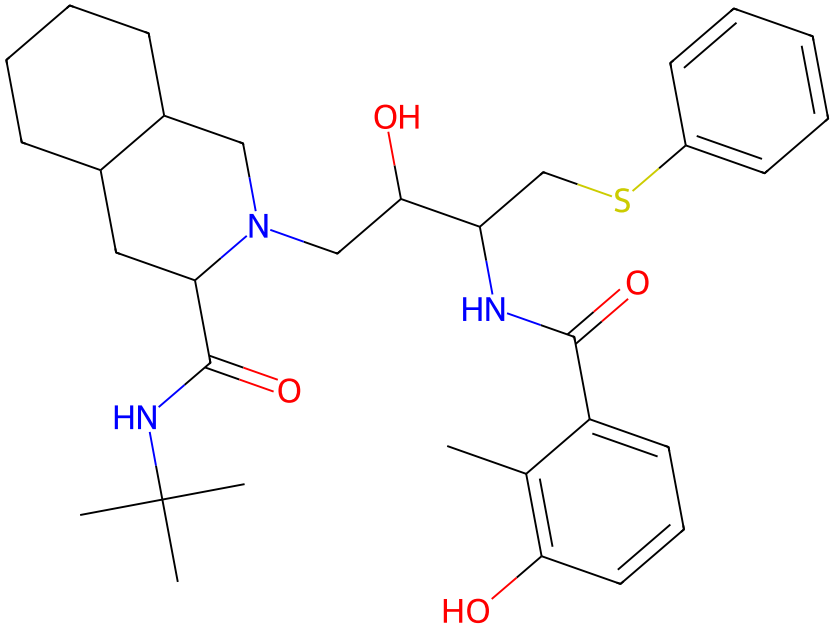
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 1

Original entry text

1. Fenbendazole
C15H13N3O2S · MW 299.4 · clogP 3.89 · TPSA 67.0 Å² · HBD 2 · RotB 3
COC(=O)Nc1nc2ccc(Sc3ccccc3)cc2[nH]1

2. Nelfinavir



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 2. Nelfinavir C32H45N3O4S · MW 567.8 · clogP 4.75 · TPSA 101.9 Å² · HBD 4 · RotB 9. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

Cc1c(O)cccc1C(=O)NC(CSc1ccccc1)C(O)CN1CC2CCCCC2CC1C(=O)NC(C)(C)C

Canonical isomeric SMILES — RDKit 2026.09.1

Cc1c(O)cccc1C(=O)NC(CSc1ccccc1)C(O)CN1CC2CCCCC2CC1C(=O)NC(C)(C)C

Complete computed profile

Formula	C32H45N3O4S
Molecular weight (g/mol)	567.796
Exact mass (Da)	567.313078
Crippen cLogP	4.7476
TPSA (Å²)	101.9
H-bond donors	4
H-bond acceptors	6
Rotatable bonds	9
Rings	4
Formal charge	0

Heavy atoms	40
Unassigned stereo — modern	5
Unassigned stereo — legacy	5

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 5 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

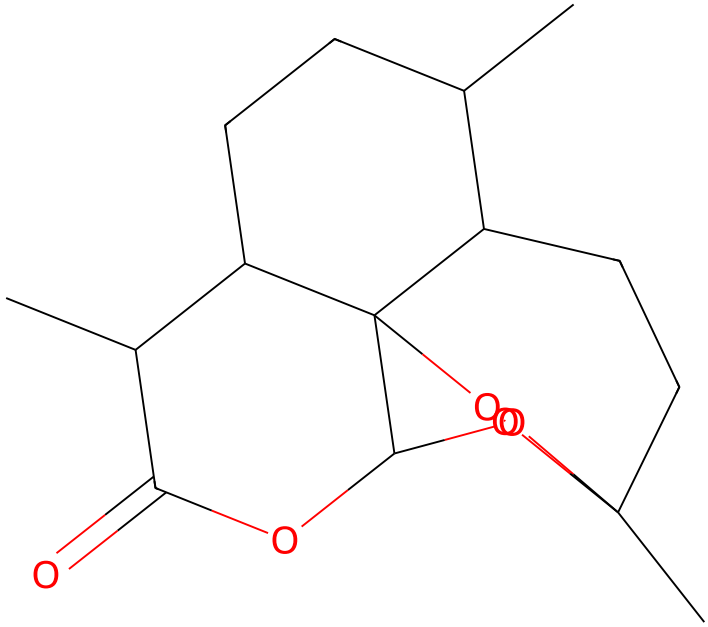
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 2

Original entry text

2. Nelfinavir
C32H45N3O4S · MW 567.8 · clogP 4.75 · TPSA 101.9 Å² · HBD 4 · RotB 9
Cc1c(O)cccc1C(=O)NC(CSc1ccccc1)C(O)CN1CC2CCCCC2CC1C(=O)NC(C)(C)C

3. Artemisinin



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 3. Artemisinin C15H22O5 · MW 282.3 · clogP 2.39 · TPSA 54.0 Å² · HBD 0 · RotB 0. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CC1CCC2C(C)C(=O)OC3OC4(C)CCC1C32OO4

Canonical isomeric SMILES — RDKit 2026.09.1

CC1CCC2C(C)C(=O)OC3OC4(C)CCC1C32OO4

Complete computed profile

Formula	C15H22O5
Molecular weight (g/mol)	282.336
Exact mass (Da)	282.146724
Crippen cLogP	2.3949
TPSA (Å²)	53.99
H-bond donors	0
H-bond acceptors	5
Rotatable bonds	0
Rings	5
Formal charge	0
Heavy atoms	20
Unassigned stereo — modern	7

Unassigned stereo — legacy	7

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 0 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 7 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

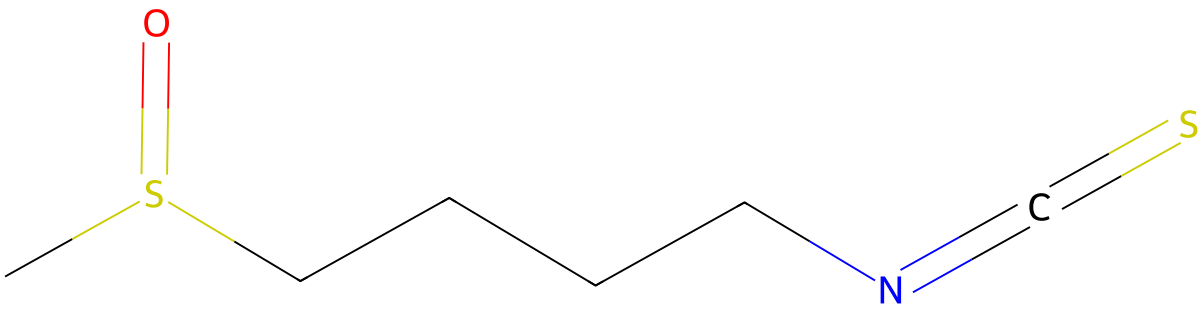
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 3

Original entry text

3. Artemisinin
C15H22O5 · MW 282.3 · clogP 2.39 · TPSA 54.0 Å² · HBD 0 · RotB 0
CC1CCC2C(C)C(=O)OC3OC4(C)CCC1C32OO4

4. Sulforaphane



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 4. Sulforaphane C6H11NOS2 · MW 177.3 · clogP 1.25 · TPSA 29.4 Å² · HBD 0 · RotB 5. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CS(=O)CCCCN=C=S

Canonical isomeric SMILES — RDKit 2026.09.1

CS(=O)CCCCN=C=S

Complete computed profile

Formula	C6H11NOS2
Molecular weight (g/mol)	177.294
Exact mass (Da)	177.028206
Crippen cLogP	1.2479
TPSA (Å²)	29.43
H-bond donors	0
H-bond acceptors	3
Rotatable bonds	5
Rings	0
Formal charge	0
Heavy atoms	10

Unassigned stereo — modern	2
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 5 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 2 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 4

Original entry text

4. Sulforaphane
C6H11NOS2 · MW 177.3 · clogP 1.25 · TPSA 29.4 Å² · HBD 0 · RotB 5
CS(=O)CCCCN=C=S

5. Hydrogen peroxide



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 5. Hydrogen peroxide H2O2 · MW 34.0 · clogP 0.02 · TPSA 40.5 Å² · HBD 2 · RotB 0. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

OO

Canonical isomeric SMILES — RDKit 2026.09.1

OO

Complete computed profile

Formula	H2O2
Molecular weight (g/mol)	34.014
Exact mass (Da)	34.005479
Crippen cLogP	0.0174
TPSA (Å²)	40.46
H-bond donors	2
H-bond acceptors	2
Rotatable bonds	0
Rings	0
Formal charge	0
Heavy atoms	2
Unassigned stereo — modern	0

Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 0 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

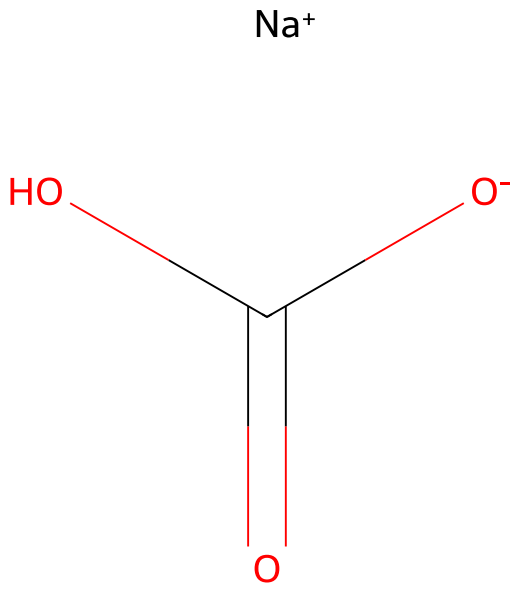
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 5

Original entry text

5. Hydrogen peroxide
H2O2 · MW 34.0 · clogP 0.02 · TPSA 40.5 Å² · HBD 2 · RotB 0
OO

6. Sodium bicarbonate



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 6. Sodium bicarbonate CHNaO3 · MW 84.0 · clogP -4.11 · TPSA 60.4 Å² · HBD 1 · RotB 0. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

O=C([O-])O.[Na+]

Canonical isomeric SMILES — RDKit 2026.09.1

O=C([O-])O.[Na+]

Complete computed profile

Formula	CHNaO3
Molecular weight (g/mol)	84.006
Exact mass (Da)	83.982338
Crippen cLogP	-4.1083
TPSA (Å²)	60.36
H-bond donors	1
H-bond acceptors	2
Rotatable bonds	0
Rings	0
Formal charge	0
Heavy atoms	5

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 0 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

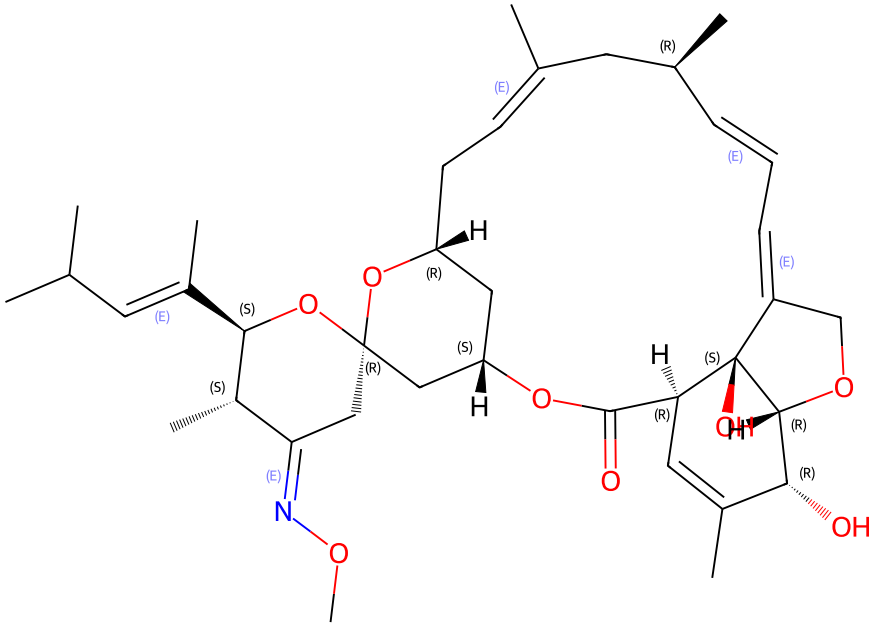
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 6

Original entry text

6. Sodium bicarbonate
CHNaO3 · MW 84.0 · clogP -4.11 · TPSA 60.4 Å² · HBD 1 · RotB 0
O=C([O-])O.[Na+]
2 · The upgraded derivatives
What the logic selects in place of each stone, chosen on exposure and directness
of redox action. Moxidectin for its 18–23 day half-life and poor P-glycoprotein

affinity; oxfendazole as the systemically available sulfoxide; auranofin and
disulfiram–copper because tumours carry no HIV protease and th

7. Moxidectin



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 7. Moxidectin C37H53NO8 · MW 639.8 · clogP 5.73 · TPSA 116.0 Å² · HBD 2 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C37H53NO8
Molecular weight (g/mol)	639.83
Exact mass (Da)	639.377118
Crippen cLogP	5.7289
TPSA (Å²)	116.04
H-bond donors	2
H-bond acceptors	9
Rotatable bonds	3

Rings	5
Formal charge	0
Heavy atoms	46
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

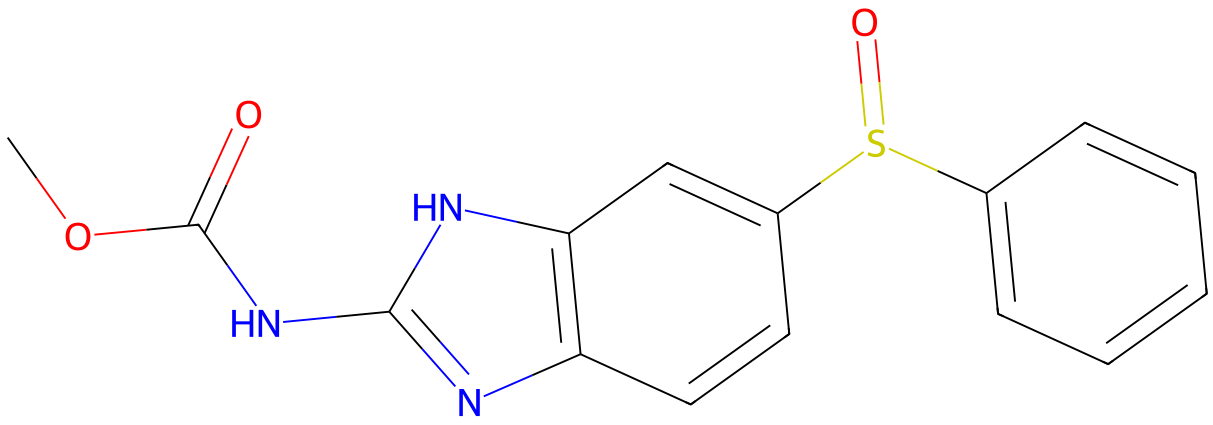
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 7

Original entry text

7. Moxidectin
C37H53NO8 · MW 639.8 · clogP 5.73 · TPSA 116.0 Å² · HBD 2 · RotB 3
CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]

(O)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

8. Oxfendazole



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 8. Oxfendazole C15H13N3O3S · MW 315.4 · clogP 2.91 · TPSA 84.1 Å² · HBD 2 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc(S(=O)c3ccccc3)cc2[nH]1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc(S(=O)c3ccccc3)cc2[nH]1

Complete computed profile

Formula	C15H13N3O3S
Molecular weight (g/mol)	315.354
Exact mass (Da)	315.067762
Crippen cLogP	2.9079
TPSA (Å²)	84.08
H-bond donors	2
H-bond acceptors	4
Rotatable bonds	3
Rings	3
Formal charge	0
Heavy atoms	22

Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

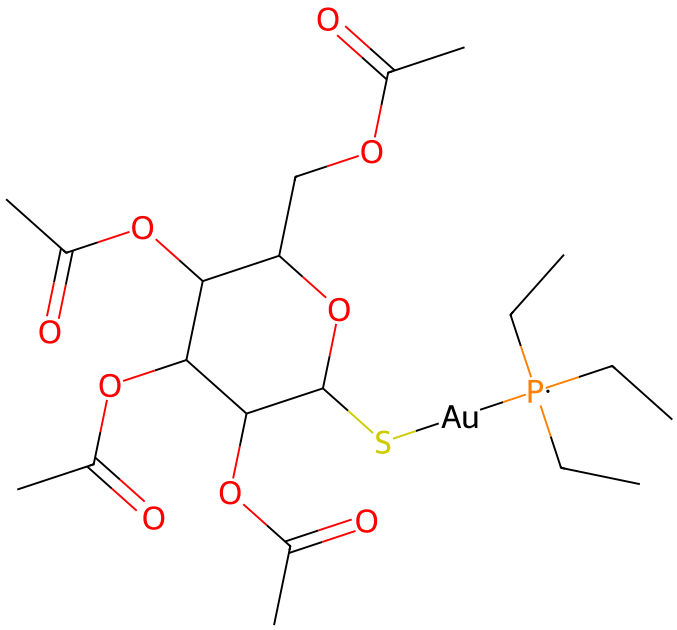
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 8

Original entry text

8. Oxfendazole
C15H13N3O3S · MW 315.4 · clogP 2.91 · TPSA 84.1 Å² · HBD 2 · RotB 3
COC(=O)Nc1nc2ccc(S(=O)c3ccccc3)cc2[nH]1

9. Auranofin



Recorded rationale and role

Gold/redox comparison arm. The encoded metal-containing agent provides a contrast with organic peroxide and sulfur-containing branches; material identity includes the coordination representation. Original entry heading: 9. Auranofin C20H34AuO9PS · MW 678.5 · clogP 2.79 · TPSA 114.4 Å² · HBD 0 · RotB 11. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CC[P](CC)(CC)[Au]
[S]C1OC(COC(C)=O)C(OC(C)=O)C(OC(C)=O)C1OC(C)=O

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P](CC)(CC)[Au]
[S]C1OC(COC(C)=O)C(OC(C)=O)C(OC(C)=O)C1OC(C)=O

Complete computed profile

Formula	C20H34AuO9PS
Molecular weight (g/mol)	678.491
Exact mass (Da)	678.132684
Crippen cLogP	2.7925
TPSA (Å²)	114.43
H-bond donors	0
H-bond acceptors	10
Rotatable bonds	11
Rings	1
Formal charge	0

Heavy atoms	32
Unassigned stereo — modern	5
Unassigned stereo — legacy	5

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 11 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 5 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

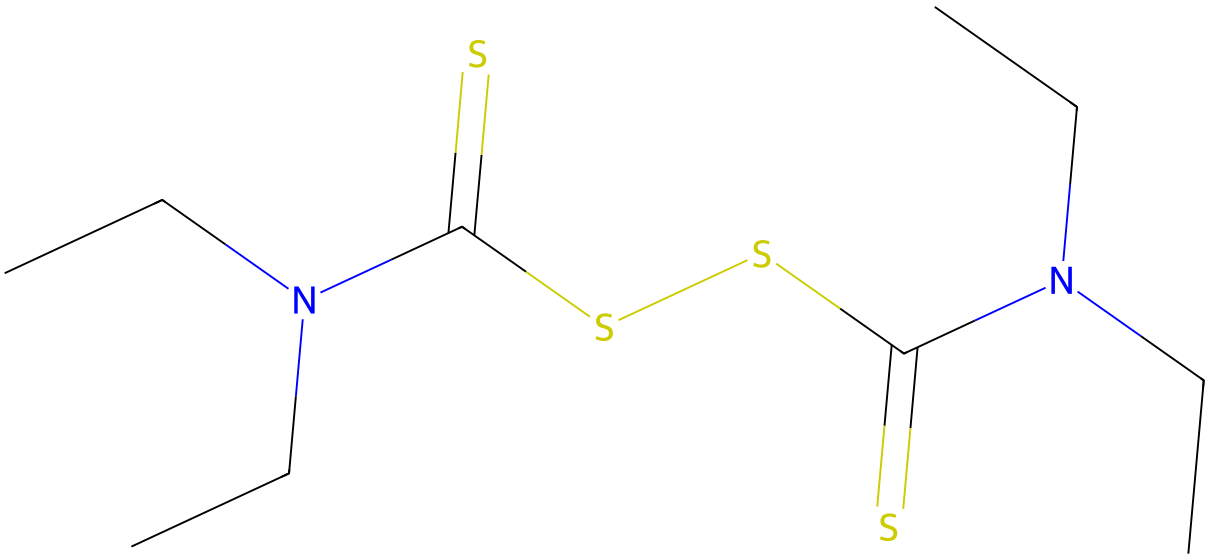
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 9

Original entry text

9. Auranofin
C20H34AuO9PS · MW 678.5 · clogP 2.79 · TPSA 114.4 Å² · HBD 0 · RotB 11
CC[P](CC)(CC)[Au]
[S]C1OC(COC(C)=O)C(OC(C)=O)C(OC(C)=O)C1OC(C)=O

10. Disulfiram



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 10. Disulfiram C10H20N2S4 · MW 296.6 · clogP 3.62 · TPSA 6.5 Å² · HBD 0 · RotB 4. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CCN(CC)C(=S)SSC(=S)N(CC)CC

Canonical isomeric SMILES — RDKit 2026.09.1

CCN(CC)C(=S)SSC(=S)N(CC)CC

Complete computed profile

Formula	C10H20N2S4
Molecular weight (g/mol)	296.552
Exact mass (Da)	296.050933
Crippen cLogP	3.6212
TPSA (Å²)	6.48
H-bond donors	0
H-bond acceptors	4
Rotatable bonds	4
Rings	0
Formal charge	0
Heavy atoms	16

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 4 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

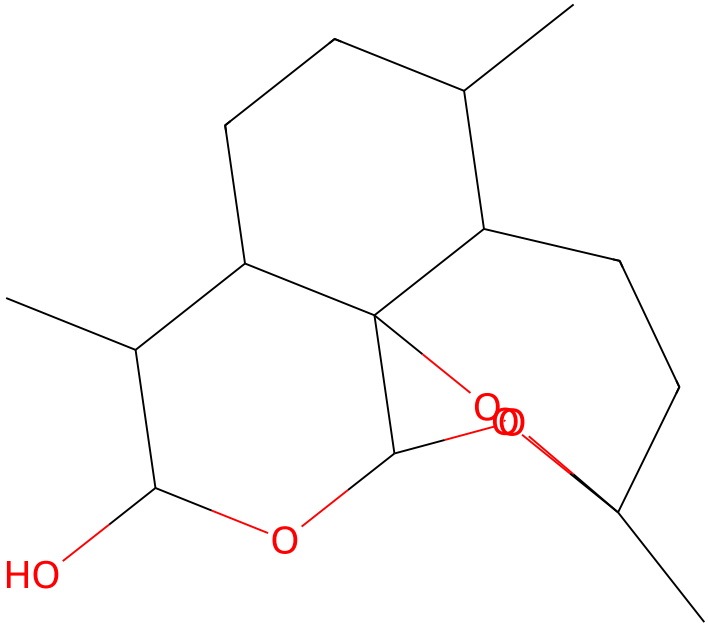
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 10

Original entry text

10. Disulfiram
C10H20N2S4 · MW 296.6 · clogP 3.62 · TPSA 6.5 Å² · HBD 0 · RotB 4
CCN(CC)C(=S)SSC(=S)N(CC)CC

11. Dihydroartemisinin



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 11. Dihydroartemisinin C15H24O5 · MW 284.4 · clogP 2.19 · TPSA 57.2 Å² · HBD 1 · RotB 0. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CC1CCC2C(C)C(O)OC3OC4(C)CCC1C32OO4

Canonical isomeric SMILES — RDKit 2026.09.1

CC1CCC2C(C)C(O)OC3OC4(C)CCC1C32OO4

Complete computed profile

Formula	C15H24O5
Molecular weight (g/mol)	284.352
Exact mass (Da)	284.162374
Crippen cLogP	2.1867
TPSA (Å²)	57.15
H-bond donors	1
H-bond acceptors	5
Rotatable bonds	0
Rings	5
Formal charge	0
Heavy atoms	20

Unassigned stereo — modern	8
Unassigned stereo — legacy	8

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 0 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 8 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

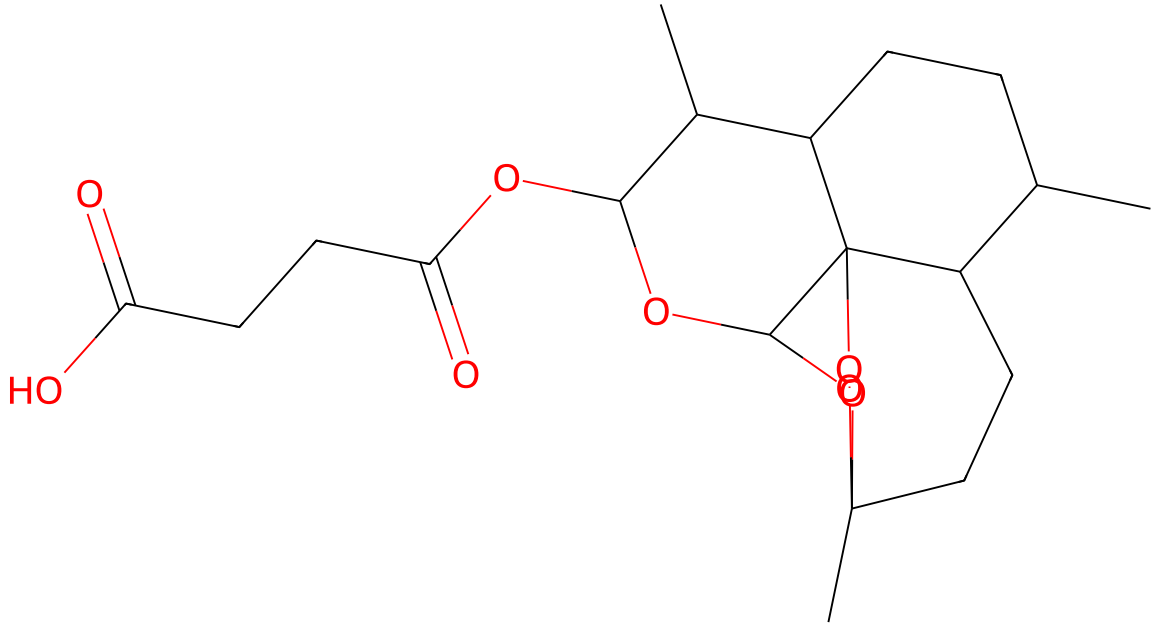
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 11

Original entry text

11. Dihydroartemisinin
C15H24O5 · MW 284.4 · clogP 2.19 · TPSA 57.2 Å² · HBD 1 · RotB 0
CC1CCC2C(C)C(O)OC3OC4(C)CCC1C32OO4

12. Artesunate



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 12. Artesunate C19H28O8 · MW 384.4 · clogP 2.60 · TPSA 100.5 Å² · HBD 1 · RotB 4. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CC1CCC2C(C)C(OC(=O)CCC(=O)O)OC3OC4(C)CCC1C32O
O4

Canonical isomeric SMILES — RDKit 2026.09.1

CC1CCC2C(C)C(OC(=O)CCC(=O)O)OC3OC4(C)CCC1C32O
O4

Complete computed profile

Formula	C19H28O8
Molecular weight (g/mol)	384.425
Exact mass (Da)	384.178418
Crippen cLogP	2.6024
TPSA (Å²)	100.52
H-bond donors	1
H-bond acceptors	7
Rotatable bonds	4
Rings	5
Formal charge	0
Heavy atoms	27

Unassigned stereo — modern	8
Unassigned stereo — legacy	8

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 4 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 8 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

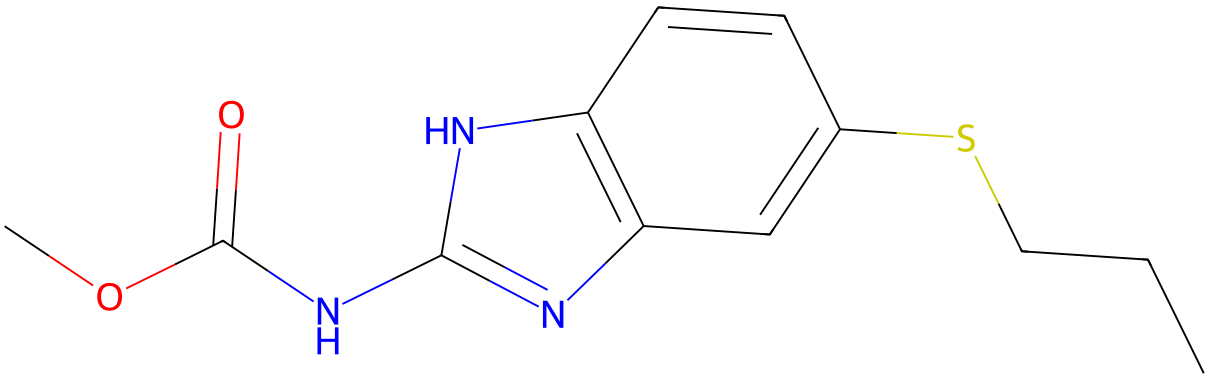
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 12

Original entry text

12. Artesunate
C19H28O8 · MW 384.4 · clogP 2.60 · TPSA 100.5 Å² · HBD 1 · RotB 4
CC1CCC2C(C)C(OC(=O)CCC(=O)O)OC3OC4(C)CCC1C32OO4
3 · Class members retained for comparison
Kept because the framework predicts the sulfur-bearing benzimidazoles separate
from the benzoyl members on a redox-sensitive readout.

Sulfasalazine is included
as a second antirheumatic acting through glutathione depletion.

13. Albendazole



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 13. Albendazole C12H15N3O2S · MW 265.3 · clogP 3.24 · TPSA 67.0 Å² · HBD 2 · RotB 4. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

CCCSc1ccc2[nH]c(NC(=O)OC)nc2c1

Canonical isomeric SMILES — RDKit 2026.09.1

CCCSc1ccc2[nH]c(NC(=O)OC)nc2c1

Complete computed profile

Formula	C12H15N3O2S
Molecular weight (g/mol)	265.338
Exact mass (Da)	265.088498
Crippen cLogP	3.2433
TPSA (Å²)	67.01
H-bond donors	2
H-bond acceptors	4
Rotatable bonds	4
Rings	2
Formal charge	0
Heavy atoms	18

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 4 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

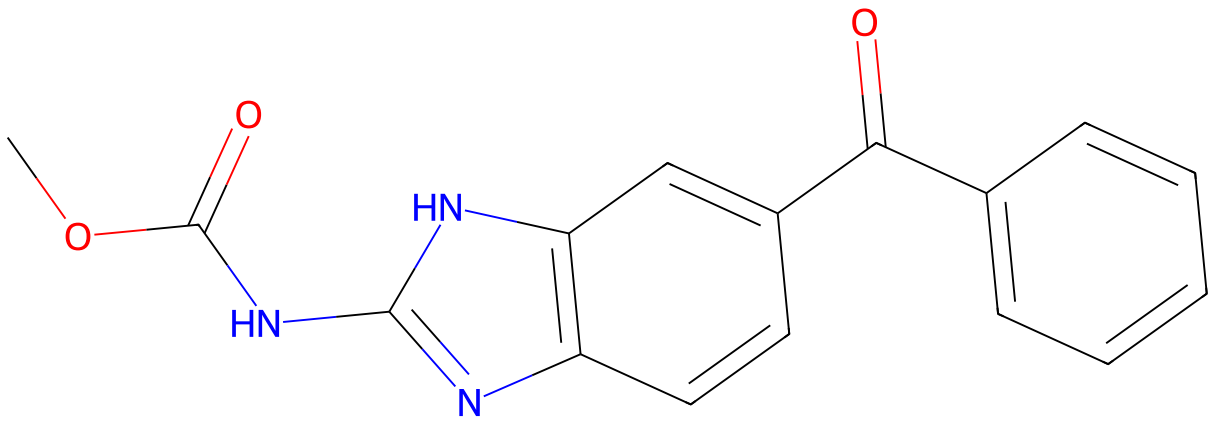
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 13

Original entry text

13. Albendazole
C12H15N3O2S · MW 265.3 · clogP 3.24 · TPSA 67.0 Å² · HBD 2 · RotB 4
CCCSc1ccc2[nH]c(NC(=O)OC)nc2c1

14. Mebendazole



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 14. Mebendazole C16H13N3O3 · MW 295.3 · clogP 2.97 · TPSA 84.1 Å² · HBD 2 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc(C(=O)c3ccccc3)cc2[nH]1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc(C(=O)c3ccccc3)cc2[nH]1

Complete computed profile

Formula	C16H13N3O3
Molecular weight (g/mol)	295.298
Exact mass (Da)	295.095691
Crippen cLogP	2.9722
TPSA (Å²)	84.08
H-bond donors	2
H-bond acceptors	4
Rotatable bonds	3
Rings	3
Formal charge	0
Heavy atoms	22

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

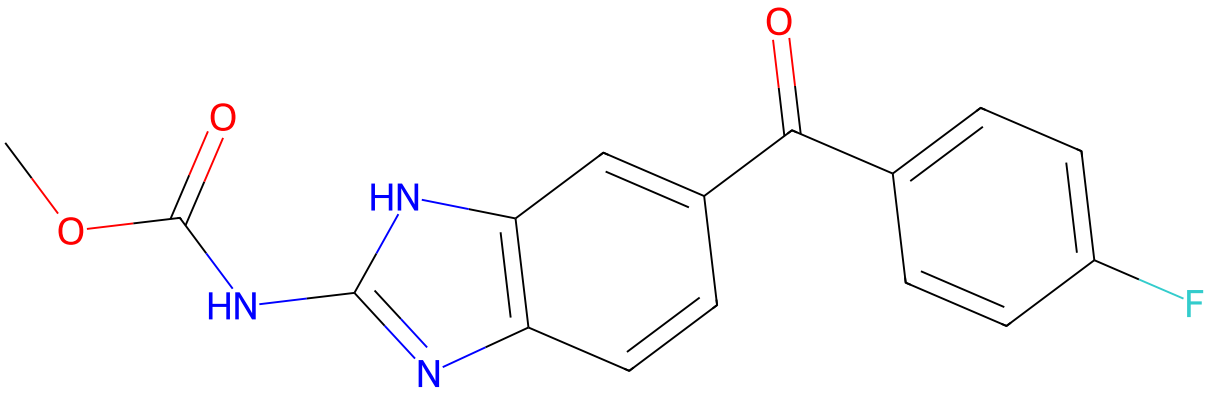
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 14

Original entry text

14. Mebendazole
C16H13N3O3 · MW 295.3 · clogP 2.97 · TPSA 84.1 Å² · HBD 2 · RotB 3

COC(=O)Nc1nc2ccc(C(=O)c3ccccc3)cc2[nH]1

15. Flubendazole



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 15. Flubendazole C16H12FN3O3 · MW 313.3 · clogP 3.11 · TPSA 84.1 Å² · HBD 2 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc(C(=O)c3ccc(F)cc3)cc2[nH]1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc(C(=O)c3ccc(F)cc3)cc2[nH]1

Complete computed profile

Formula	C16H12FN3O3
Molecular weight (g/mol)	313.288
Exact mass (Da)	313.086269
Crippen cLogP	3.1113
TPSA (Å²)	84.08
H-bond donors	2
H-bond acceptors	4
Rotatable bonds	3
Rings	3
Formal charge	0
Heavy atoms	23

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

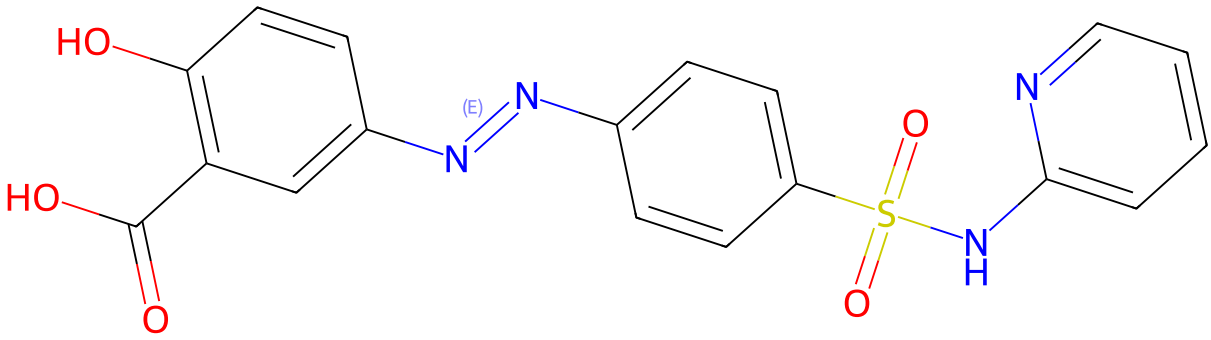
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 15

Original entry text

15. Flubendazole
C16H12FN3O3 · MW 313.3 · clogP 3.11 · TPSA 84.1 Å² · HBD 2 · RotB 3
COC(=O)Nc1nc2ccc(C(=O)c3ccc(F)cc3)cc2[nH]1

16. Sulfasalazine



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 16. Sulfasalazine C18H14N4O5S · MW 398.4 · clogP 3.70 · TPSA 141.3 Å² · HBD 3 · RotB 6. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

O=C(O)c1cc(/N=N/c2ccc(S(=O)(=O)Nc3ccccn3)cc2)ccc1O

Canonical isomeric SMILES — RDKit 2026.09.1

O=C(O)c1cc(/N=N/c2ccc(S(=O)(=O)Nc3ccccn3)cc2)ccc1O

Complete computed profile

Formula	C18H14N4O5S
Molecular weight (g/mol)	398.4
Exact mass (Da)	398.068491
Crippen cLogP	3.7016
TPSA (Å²)	141.31
H-bond donors	3
H-bond acceptors	7
Rotatable bonds	6
Rings	3
Formal charge	0
Heavy atoms	28

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 6 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

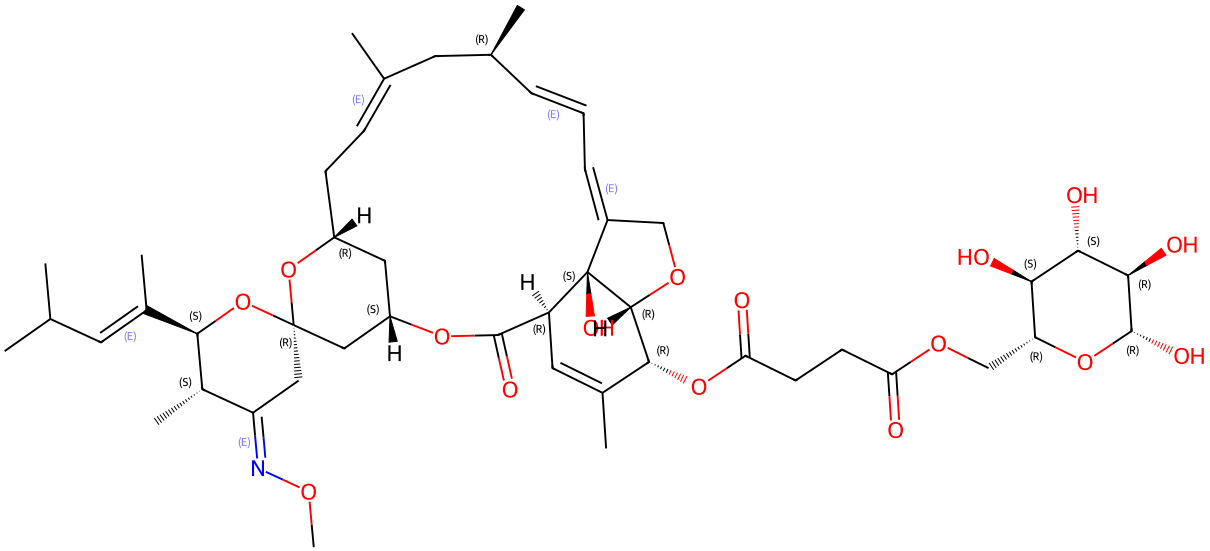
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 16

Original entry text

16. Sulfasalazine
C18H14N4O5S · MW 398.4 · clogP 3.70 · TPSA 141.3 Å² · HBD 3 · RotB 6
O=C(O)c1cc(/N=N/c2ccc(S(=O)(=O)Nc3ccccn3)cc2)ccc1O
4 · The first fourteen
Conjugates on the moxidectin C5 secondary allylic hydroxyl. Family A hangs a
sugar on the glucose appetite; Family B a delocalised cation on the membrane
potential; Family C a quinone or endoperoxide on redox

directly; Family D carries
no targeting claim and exists for solubility and transport. The

17. ARF-MOX-A1 · glucosyl succinate — GLUT import;



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 17. ARF-MOX-A1 · glucosyl succinate — GLUT import; lead glycoconjugate. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC(=O)OC[C@H]6O[C@@H](O)[C@H](O)
[C@@H](O)[C@@H]6O)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC(=O)OC[C@H]6O[C@@H](O)[C@H](O)
[C@@H](O)[C@@H]6O)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C47H67NO16
Molecular weight (g/mol)	902.044
Exact mass (Da)	901.445985
Crippen cLogP	3.4031
TPSA (Å²)	238.56
H-bond donors	5

H-bond acceptors	17
Rotatable bonds	9
Rings	6
Formal charge	0
Heavy atoms	64
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 17

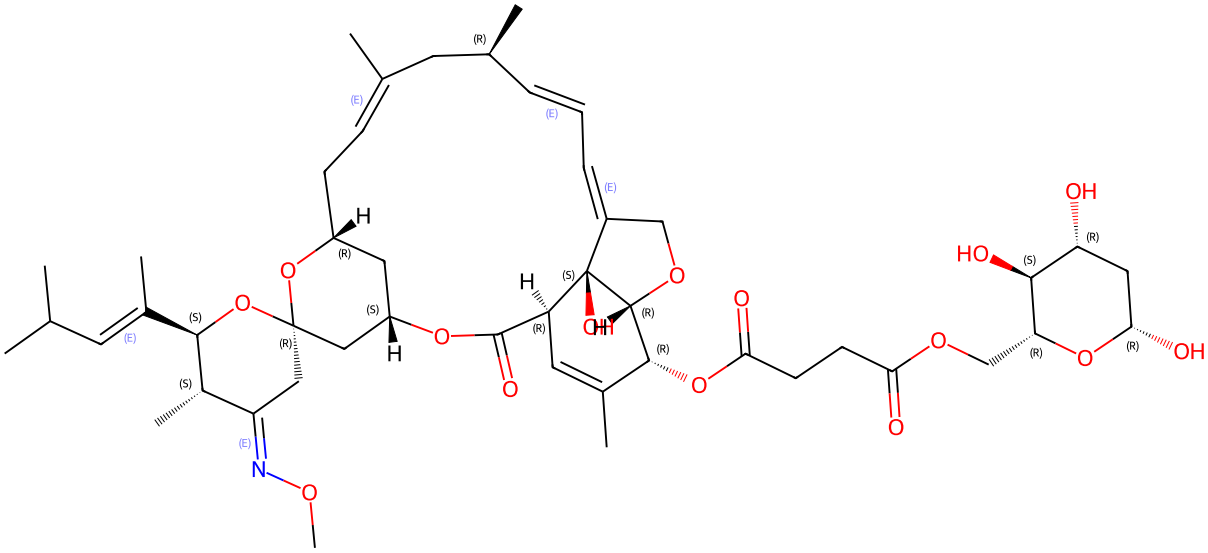
Original entry text

17. ARF-MOX-A1 · glucosyl succinate — GLUT import; lead glycoconjugate

C47H67NO16 · MW 902.0 · clogP 3.40 · TPSA 238.6 Å² · HBD 5 · RotB 9

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC(=O)OC[C@H]6O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]6O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

18. ARF-MOX-A2 · 2-deoxyglucosyl succinate — Non-



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 18. ARF-MOX-A2 · 2-deoxyglucosyl succinate — Non- metabolisable sugar; traps conjugate. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group

compatibility. Establish connectivity, stereochemical composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC(=O)OC[C@H]6O[C@@H](O)C[C@@H](O)[C@@H]6O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC(=O)OC[C@H]6O[C@@H](O)C[C@@H](O)[C@@H]6O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C47H67NO15
Molecular weight (g/mol)	886.045
Exact mass (Da)	885.45107
Crippen cLogP	4.4323
TPSA (Å²)	218.33
H-bond donors	4

H-bond acceptors	16
Rotatable bonds	9
Rings	6
Formal charge	0
Heavy atoms	63
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 18

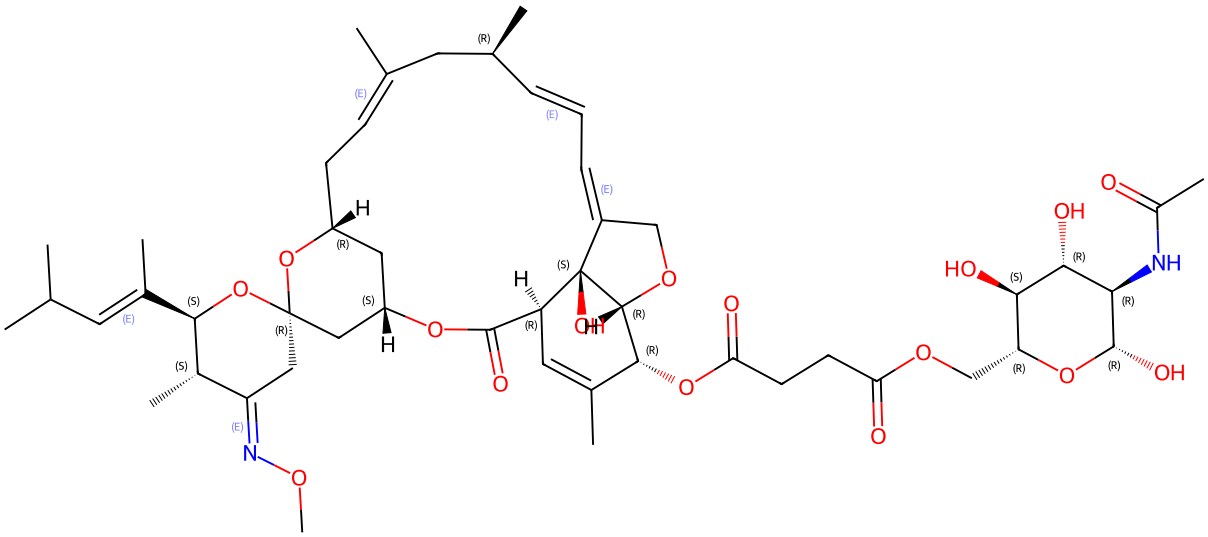
Original entry text

18. ARF-MOX-A2 · 2-deoxyglucosyl succinate — Non-metabolisable sugar; traps conjugate

C47H67NO15 · MW 886.0 · clogP 4.43 · TPSA 218.3 Å² · HBD 4 · RotB 9

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC(=O)OC[C@H]6O[C@@H](O)C[C@@H](O)[C@@H]6O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

19. ARF-MOX-A3 · GlcNAc succinate — Hexosamine



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 19. ARF-MOX-A3 · GlcNAc succinate — Hexosamine route; evades GLUT downregulation. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group

compatibility. Establish connectivity, stereochemical composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC(=O)OC[C@H]6O[C@@H](O)[C@H](NC(C)=O)[C@@H](O)[C@@H]6O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC(=O)OC[C@H]6O[C@@H](O)[C@H](NC(C)=O)[C@@H](O)[C@@H]6O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C49H70N2O16
Molecular weight (g/mol)	943.097
Exact mass (Da)	942.472534
Crippen cLogP	3.5469
TPSA (Å²)	247.43
H-bond donors	5

H-bond acceptors	17
Rotatable bonds	10
Rings	6
Formal charge	0
Heavy atoms	67
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 10 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 19

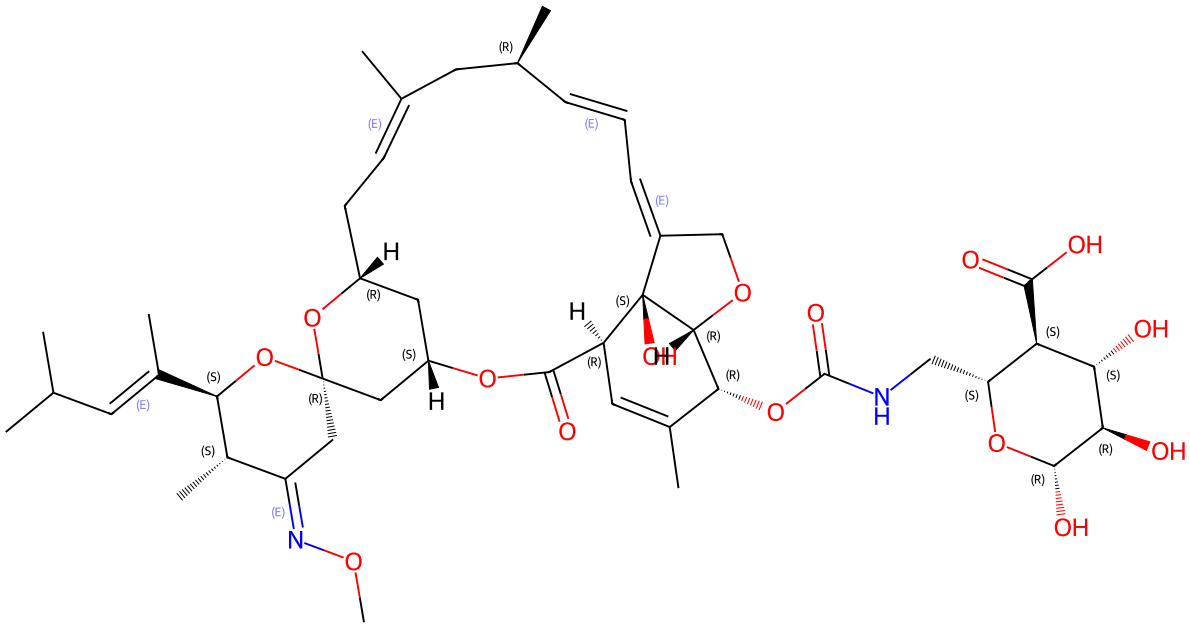
Original entry text

19. ARF-MOX-A3 · GlcNAc succinate — Hexosamine route; evades GLUT downregulation

C49H70N2O16 · MW 943.1 · clogP 3.55 · TPSA 247.4 Å² · HBD 5 · RotB 10

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC(=O)OC[C@H]6O[C@@H](O)[C@H](NC(C)=O)[C@@H](O)[C@@H]6O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

20. ARF-MOX-A4 · glucuronyl carbamate — Carbamate



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 20. ARF-MOX-A4 · glucuronyl carbamate — Carbamate linker; slower release. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NC[C@H]6O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]6C(=O)O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NC[C@H]6O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]6C(=O)O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C45H64N2O15
Molecular weight (g/mol)	873.006
Exact mass (Da)	872.430669
Crippen cLogP	3.6026
TPSA (Å²)	241.36
H-bond donors	6

H-bond acceptors	15
Rotatable bonds	7
Rings	6
Formal charge	0
Heavy atoms	62
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 20

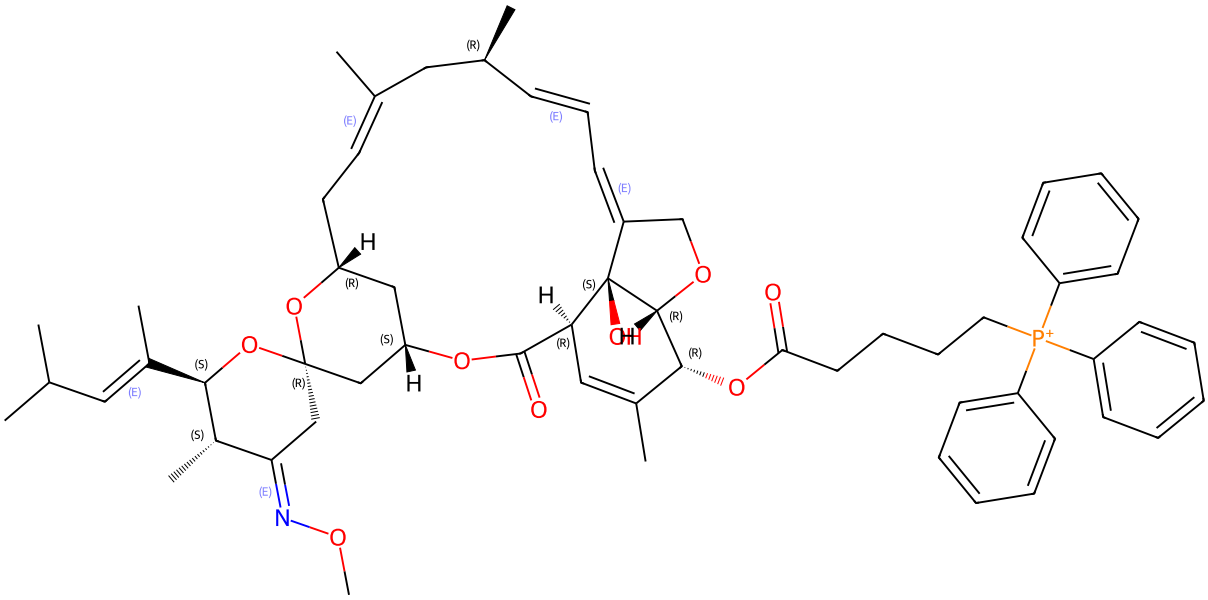
Original entry text

20. ARF-MOX-A4 · glucuronyl carbamate — Carbamate linker; slower release

C45H64N2O15 · MW 873.0 · clogP 3.60 · TPSA 241.4 Å² · HBD 6 · RotB 7

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NC[C@H]6O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]6C(=O)O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

21. ARF-MOX-B1 · triphenylphosphonium pentanoate



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Original entry heading: 21. ARF-MOX-B1 · triphenylphosphonium pentanoate — Δψm-driven; lead mitochondriotropic. Recorded design detail: permanent +1 triphenylphosphonium (incumbent) pentanoyl ester, C4 tether (incumbent) incumbent. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C60H75NO9P+
Molecular weight (g/mol)	985.232
Exact mass (Da)	984.517396
Crippen cLogP	10.4442

TPSA (Å²)	122.11
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	12
Rings	8
Formal charge	1
Heavy atoms	71
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 12 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

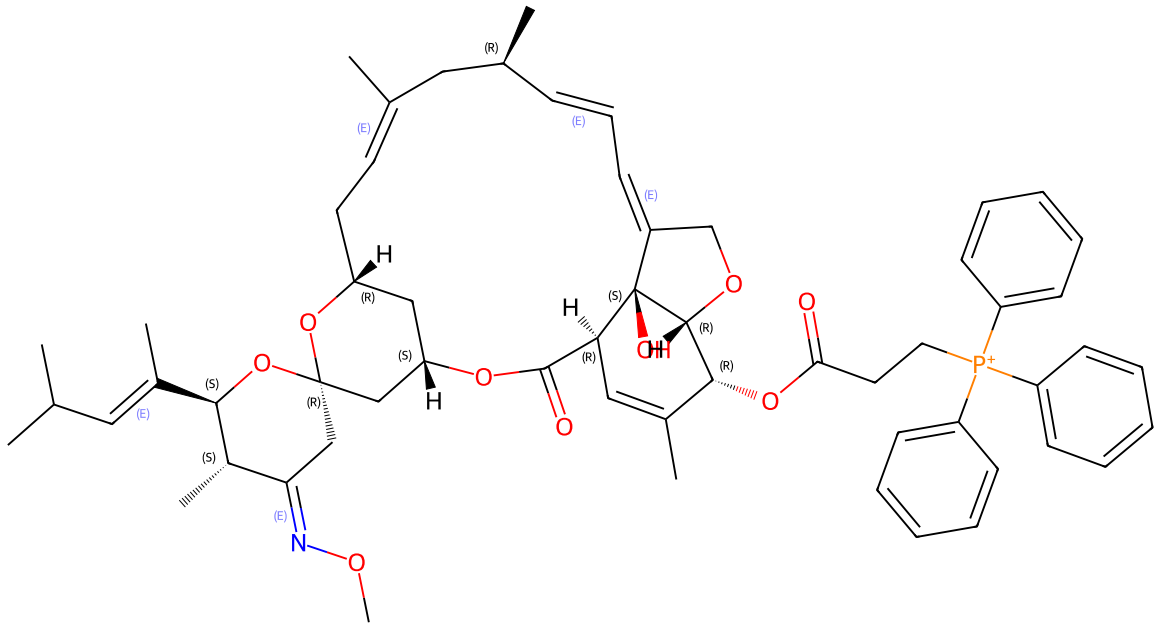
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 21

Original entry text

21. ARF-MOX-B1 · triphenylphosphonium pentanoate — Δψm-driven; lead mitochondriotropic
C60H75NO9P+ · MW 985.2 · clogP 10.44 · TPSA 122.1 Å² · HBD 1 · RotB 12
CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCCC[P+](c6ccccc6)(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

22. ARF-MOX-B2 · triphenylphosphonium propanoate



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Original entry heading: 22. ARF-MOX-B2 · triphenylphosphonium propanoate — Short linker; tether-length probe. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C58H71NO9P+
Molecular weight (g/mol)	957.178
Exact mass (Da)	956.486096
Crippen cLogP	9.664
TPSA (Å²)	122.11
H-bond donors	1

H-bond acceptors	10
Rotatable bonds	10
Rings	8
Formal charge	1
Heavy atoms	69
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 10 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 22

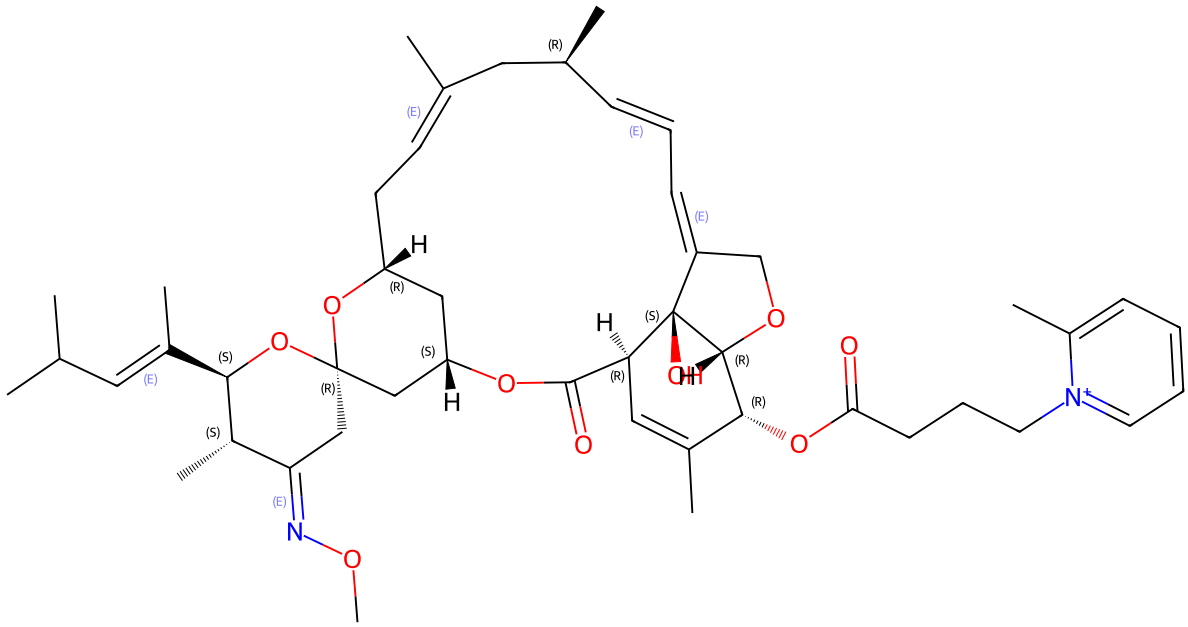
Original entry text

22. ARF-MOX-B2 · triphenylphosphonium propanoate
— Short linker; tether-length probe

C58H71NO9P+ · MW 957.2 · clogP 9.66 · TPSA 122.1 Å² · HBD 1 · RotB 10

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CC[P+](c6ccccc6)(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

23. ARF-MOX-B3 · N-methylpyridinium butanoate —



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Original entry heading: 23. ARF-MOX-B3 · N-methylpyridinium butanoate — Lower-MW cation. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC[n+]6ccccc6C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC[n+]6ccccc6C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C47H65N2O9+
Molecular weight (g/mol)	802.042
Exact mass (Da)	801.468458
Crippen cLogP	7.3561
TPSA (Å²)	125.99
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	8

Rings	6
Formal charge	1
Heavy atoms	58
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 8 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

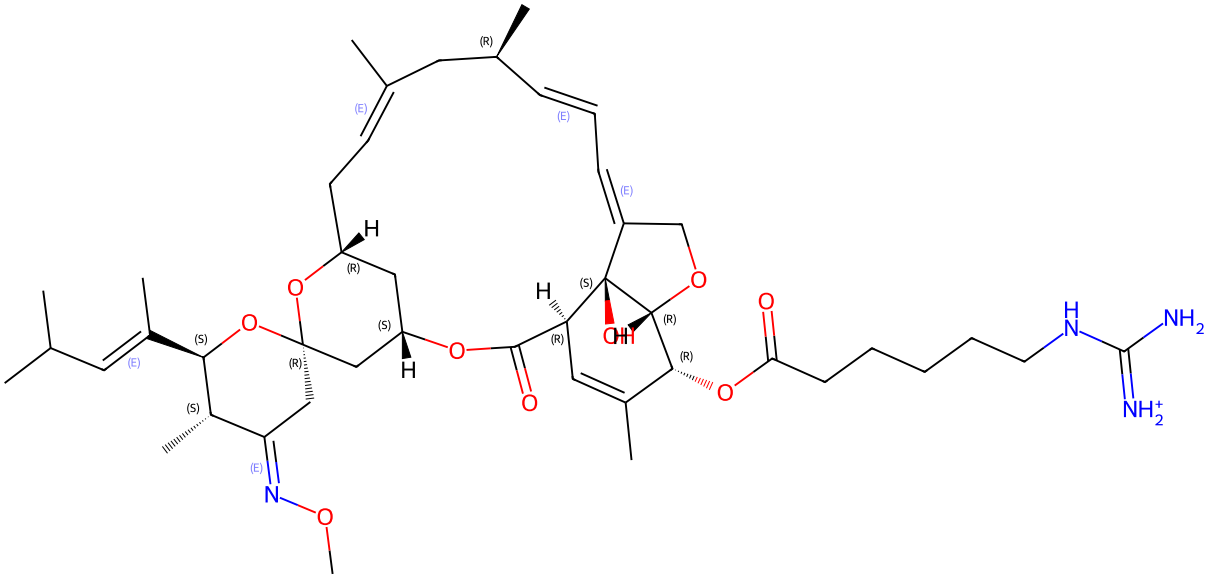
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 23

Original entry text

23. ARF-MOX-B3 · N-methylpyridinium butanoate — Lower-MW cation
C47H65N2O9+ · MW 802.0 · clogP 7.36 · TPSA 126.0 Å² · HBD 1 · RotB 8
CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]

(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC[n+]6ccccc6C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

24. ARF-MOX-B4 · guanidinium hexanoate — Cell-



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Original entry heading: 24. ARF-MOX-B4 · guanidinium hexanoate — Cell- penetrating cation. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCCCCNC(N)=[NH2+])C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCCCCNC(N)=[NH2+])C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C44H67N4O9+
Molecular weight (g/mol)	796.039
Exact mass (Da)	795.490256
Crippen cLogP	4.5036
TPSA (Å²)	185.75
H-bond donors	4
H-bond acceptors	10
Rotatable bonds	10

Rings	5
Formal charge	1
Heavy atoms	57
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 10 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

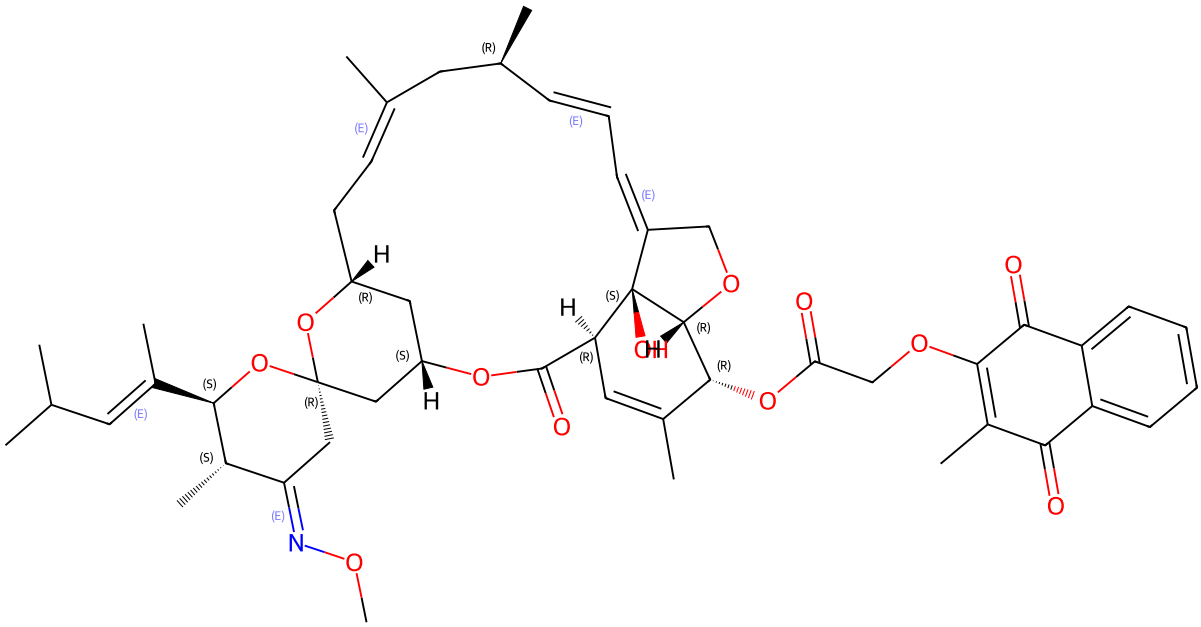
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 24

Original entry text

24. ARF-MOX-B4 · guanidinium hexanoate — Cell-penetrating cation
C44H67N4O9+ · MW 796.0 · clogP 4.50 · TPSA 185.7 Å² · HBD 4 · RotB 10
CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]

(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCCCCNC(N)=[NH2+])C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

25. ARF-MOX-C1 · menadione glycolate — Voltage +



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 25. ARF-MOX-C1 · menadione glycolate — Voltage + redox; lead hybrid. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)COC6=C(C)C(=O)c7ccccc7C6=O)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)COC6=C(C)C(=O)c7ccccc7C6=O)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C50H61NO12
Molecular weight (g/mol)	868.033
Exact mass (Da)	867.419376
Crippen cLogP	7.6496
TPSA (Å²)	165.48
H-bond donors	1
H-bond acceptors	13
Rotatable bonds	7

Rings	7
Formal charge	0
Heavy atoms	63
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 25

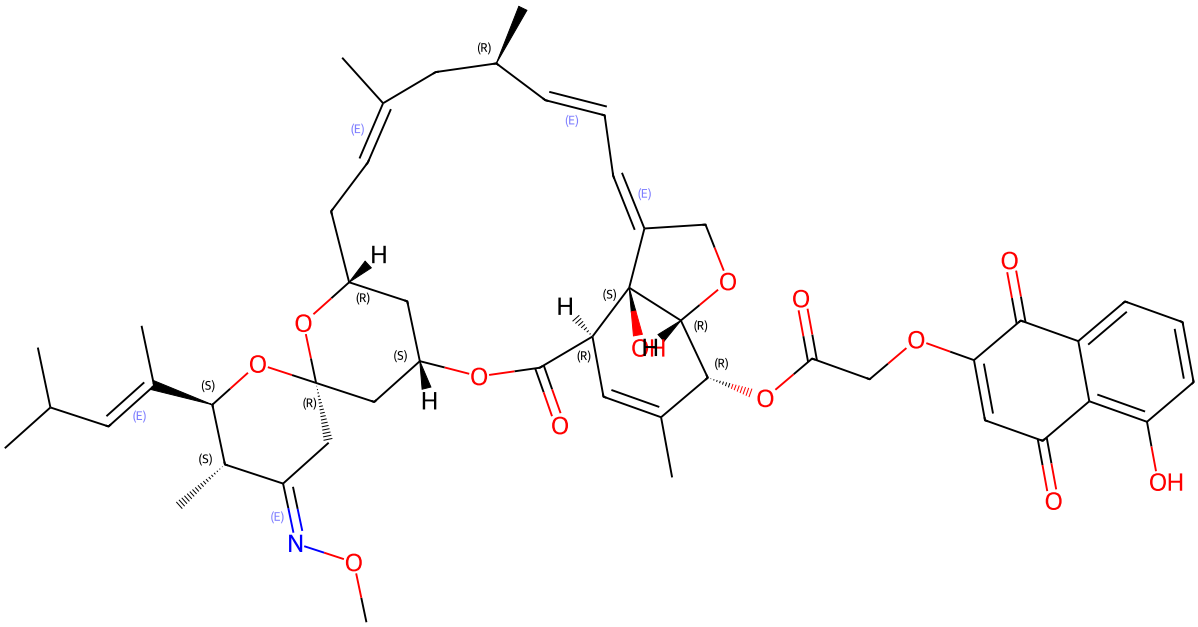
Original entry text

25. ARF-MOX-C1 · menadione glycolate — Voltage + redox; lead hybrid
C50H61NO12 · MW 868.0 · clogP 7.65 · TPSA 165.5 Å² · HBD 1 · RotB 7
CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]

(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)COC6=C(C)C(=O)c7ccccc7C6=O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

26. ARF-MOX-C2 · plumbagin-type glycolate

—



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 26. ARF-MOX-C2 · plumbagin-type glycolate — Distinct redox potential. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)COC6=CC(=O)c7c(O)cccc7C6=O)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)COC6=CC(=O)c7c(O)cccc7C6=O)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C49H59NO13
Molecular weight (g/mol)	870.005
Exact mass (Da)	869.398641
Crippen cLogP	6.9651
TPSA (Å²)	185.71
H-bond donors	2
H-bond acceptors	14
Rotatable bonds	7

Rings	7
Formal charge	0
Heavy atoms	63
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

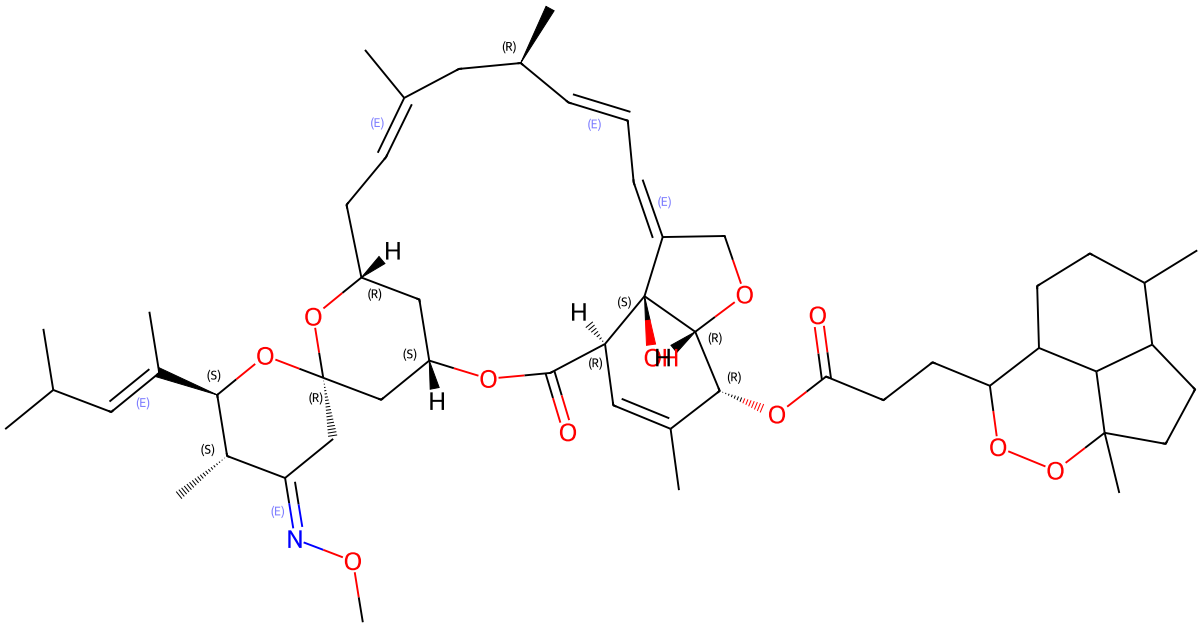
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 26

Original entry text

26. ARF-MOX-C2 · plumbagin-type glycolate — Distinct redox potential
C49H59NO13 · MW 870.0 · clogP 6.97 · TPSA 185.7 Å² · HBD 2 · RotB 7
CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]

(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)COC6=CC(=O)c7c(O)cccc7C6=O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

27. ARF-MOX-C4 · trioxane (artemisinin-like) ester —



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Original entry heading: 27. ARF-MOX-C4 · trioxane (artemisinin-like) ester — Fe-triggered; fuses two drug classes in one molecule. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC6OOC7(C)CCC8C(C)CCC6C87)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC6OOC7(C)CCC8C(C)CCC6C87)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C52H75NO11
Molecular weight (g/mol)	890.168
Exact mass (Da)	889.534012
Crippen cLogP	9.2214
TPSA (Å²)	140.57
H-bond donors	1
H-bond acceptors	12
Rotatable bonds	7

Rings	8
Formal charge	0
Heavy atoms	64
Unassigned stereo — modern	6
Unassigned stereo — legacy	6

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 6 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 27

Original entry text

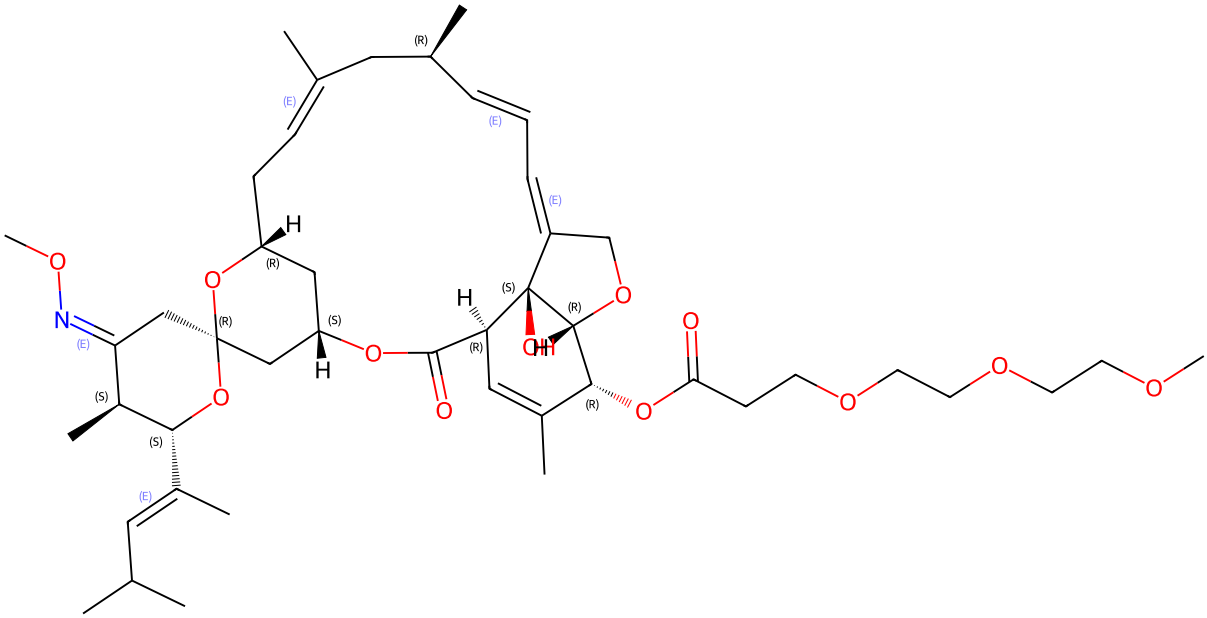
27. ARF-MOX-C4 · trioxane (artemisinin-like) ester — Fe-triggered; fuses two drug classes in one molecule

C52H75NO11 · MW 890.2 · clogP 9.22 · TPSA 140.6 Å² · HBD

1 · RotB 7

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC6OOC7(C)CCC8C(C)CCC6C87)C(C)=C[C@@H
](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

28. ARF-MOX-D1 · PEG3 solubilising ester — Offsets



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 28. ARF-MOX-D1 · PEG3 solubilising ester — Offsets series polarity liability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

COCCOCCOCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

COCCOCCOCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C45H67NO12
Molecular weight (g/mol)	814.026
Exact mass (Da)	813.466327
Crippen cLogP	6.3495
TPSA (Å²)	149.8
H-bond donors	1
H-bond acceptors	13
Rotatable bonds	13

Rings	5
Formal charge	0
Heavy atoms	58
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 13 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

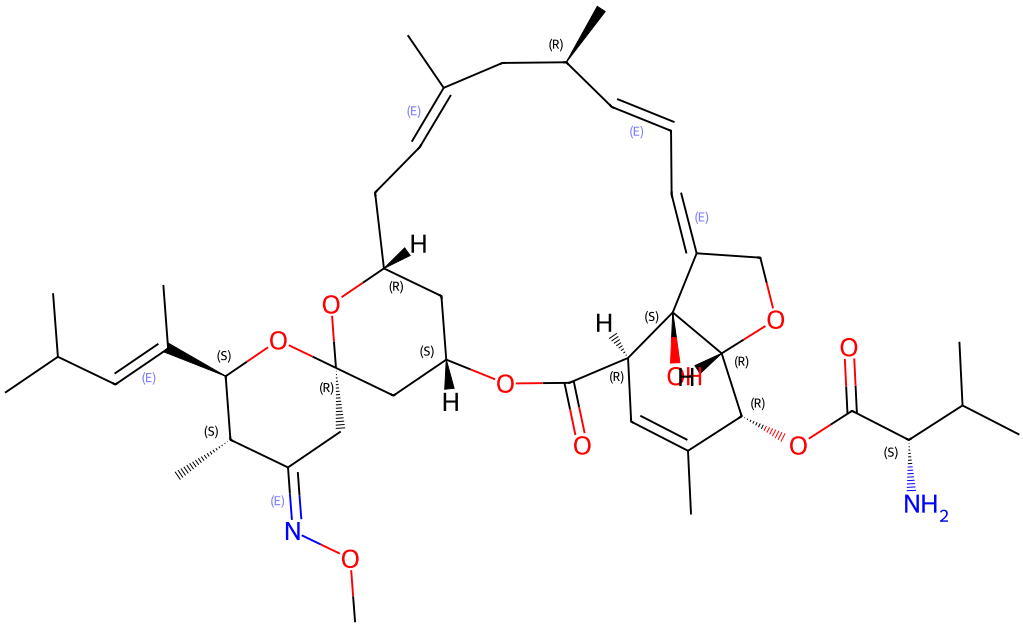
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 28

Original entry text

28. ARF-MOX-D1 · PEG3 solubilising ester — Offsets series polarity liability
C45H67NO12 · MW 814.0 · clogP 6.35 · TPSA 149.8 Å² · HBD 1 · RotB 13
COCCOCCOCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C

@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/
C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H]
(C)[C@@H](/C(C)=C/C(C)C)O1)C3

29. ARF-MOX-D2 · valine prodrug — PepT1 peptide-



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 29. ARF-MOX-D2 · valine prodrug — PepT1 peptide- transporter route. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)[C@@H](N)C(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)[C@@H](N)C(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C42H62N2O9
Molecular weight (g/mol)	738.963
Exact mass (Da)	738.445532
Crippen cLogP	6.2631
TPSA (Å²)	148.13
H-bond donors	2
H-bond acceptors	11
Rotatable bonds	6

Rings	5
Formal charge	0
Heavy atoms	53
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 6 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

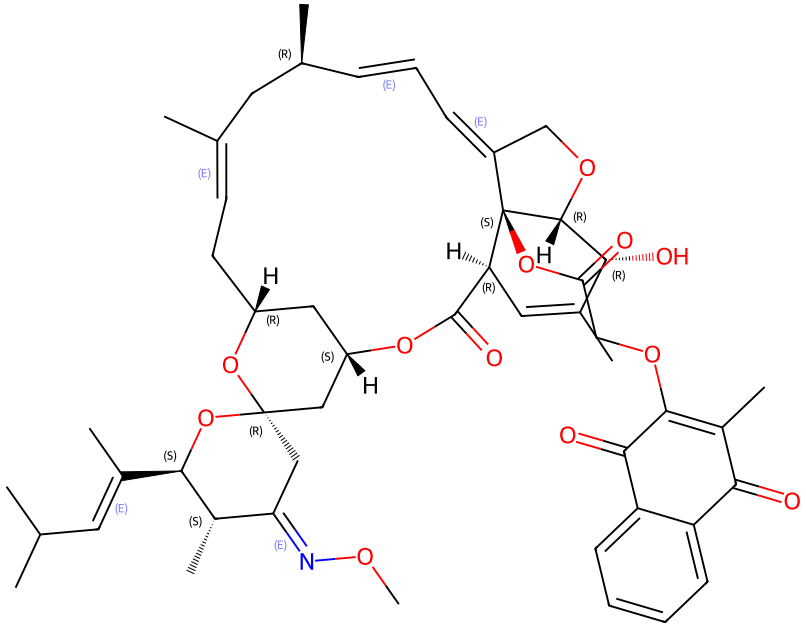
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 29

Original entry text

29. ARF-MOX-D2 · valine prodrug — PepT1 peptide-transporter route
C42H62N2O9 · MW 739.0 · clogP 6.26 · TPSA 148.1 Å² · HBD 2 · RotB 6
CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]

(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)[C@@H](N)C(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

30. ARF-MOX-C1b · menadione glycolate —



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 30. ARF-MOX-C1b · menadione glycolate — regiochemical variant of C1. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](O)C(C)=C[C@@H](C(=O)O3)[C@]45OC(=O)COC3=C(C)C(=O)c4ccccc4C3=O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](O)C(C)=C[C@@H](C(=O)O3)[C@]45OC(=O)COC3=C(C)C(=O)c4ccccc4C3=O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C50H61NO12
Molecular weight (g/mol)	868.033
Exact mass (Da)	867.419376
Crippen cLogP	7.6496
TPSA (Å²)	165.48
H-bond donors	1

H-bond acceptors	13
Rotatable bonds	7
Rings	7
Formal charge	0
Heavy atoms	63
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 30

Original entry text

30. ARF-MOX-C1b · menadione glycolate — regiochemical variant of C1

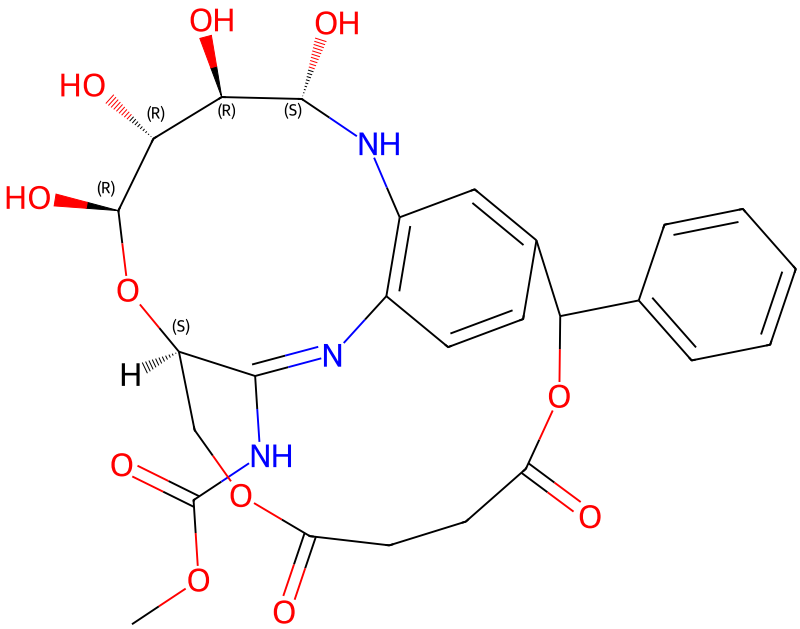
C50H61NO12 · MW 868.0 · clogP 7.65 · TPSA 165.5 Å² · HBD 1 · RotB 7

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](O)C(C)=C[C@@H](C(=O)O3)[C@]45OC(=O)COC3=C(C)C(=O)c4ccccc4C3=O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

5 · The extension series

The same four vectors applied to two further seats: the hydroxymebendazole carbinol, obtained by reducing the benzoyl ketone while leaving the C2 methylcarbamate untouched, and the dihydroartemisinin C10 hemiacetal.

31. ARF-HMB-A1 · hydroxymebendazole C-OH glucosyl



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 31. ARF-HMB-A1 · hydroxymebendazole C-OH glucosyl succinate — metabolic (GLUT). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)NC1=Nc2ccc3cc2N[C@@H](O)[C@H](O)[C@@H](O)[C@H](O)O[C@@H]1COC(=O)CCC(=O)OC3c1ccccc1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)NC1=Nc2ccc3cc2N[C@@H](O)[C@H](O)[C@@H](O)[C@H](O)O[C@@H]1COC(=O)CCC(=O)OC3c1ccccc1

Complete computed profile

Formula	C26H29N3O11
Molecular weight (g/mol)	559.528
Exact mass (Da)	559.180209
Crippen cLogP	0.2115
TPSA (Å²)	205.47
H-bond donors	6
H-bond acceptors	13
Rotatable bonds	1
Rings	5
Formal charge	0

Heavy atoms	40
Unassigned stereo — modern	2
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 1 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. The modern graph analysis leaves 2 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

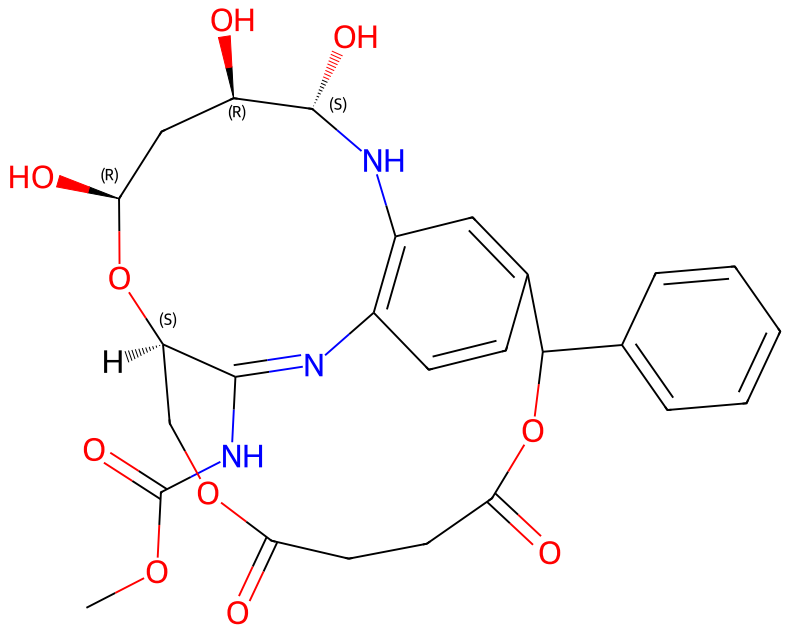
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 31

Original entry text

31. ARF-HMB-A1 · hydroxymebendazole C-OH glucosyl succinate — metabolic (GLUT)
C26H29N3O11 · MW 559.5 · clogP 0.21 · TPSA 205.5 Å² · HBD 6 · RotB 1
COC(=O)NC1=Nc2ccc3cc2N[C@@H](O)[C@H](O)[C@@H](O)[C@H](O)O[C@@H]1COC(=O)CCC(=O)OC3c1ccccc1

32. ARF-HMB-A2 · hydroxymebendazole C-OH 2-



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 32. ARF-HMB-A2 · hydroxymebendazole C-OH 2- deoxyglucosyl succinate — metabolic (trapped). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)NC1=Nc2ccc3cc2N[C@@H](O)[C@H](O)C[C@H](O)O[C@@H]1COC(=O)CCC(=O)OC3c1ccccc1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)NC1=Nc2ccc3cc2N[C@@H](O)[C@H](O)C[C@H](O)O[C@@H]1COC(=O)CCC(=O)OC3c1ccccc1

Complete computed profile

Formula	C26H29N3O10
Molecular weight (g/mol)	543.529
Exact mass (Da)	543.185294
Crippen cLogP	1.2407
TPSA (Å²)	185.24
H-bond donors	5
H-bond acceptors	12
Rotatable bonds	1
Rings	5
Formal charge	0

Heavy atoms	39
Unassigned stereo — modern	2
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 1 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. The modern graph analysis leaves 2 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

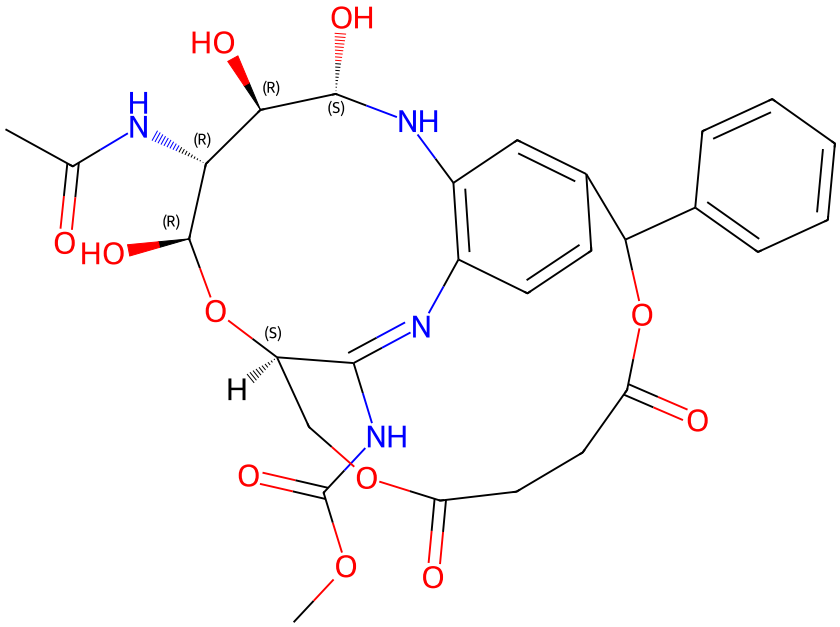
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 32

Original entry text

32. ARF-HMB-A2 · hydroxymebendazole C-OH 2-deoxyglucosyl succinate — metabolic (trapped) C26H29N3O10 · MW 543.5 · clogP 1.24 · TPSA 185.2 Å² · HBD 5 · RotB 1 COC(=O)NC1=Nc2ccc3cc2N[C@@H](O)[C@H](O)C[C@H](O)O[C@@H]1COC(=O)CCC(=O)OC3c1ccccc1

33. ARF-HMB-A3 · hydroxymebendazole C-OH GlcNAc



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 33. ARF-HMB-A3 · hydroxymebendazole C-OH GlcNAc succinate — metabolic (hexosamine). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)NC1=Nc2ccc3cc2N[C@@H](O)[C@H](O)[C@@H](NC(C)=O)[C@H](O)O[C@@H]1COC(=O)CCC(=O)OC3c1ccccc1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)NC1=Nc2ccc3cc2N[C@@H](O)[C@H](O)[C@@H](NC(C)=O)[C@H](O)O[C@@H]1COC(=O)CCC(=O)OC3c1ccccc1

Complete computed profile

Formula	C28H32N4O11
Molecular weight (g/mol)	600.581
Exact mass (Da)	600.206758
Crippen cLogP	0.3553
TPSA (Å²)	214.34
H-bond donors	6
H-bond acceptors	13
Rotatable bonds	2
Rings	5

Formal charge	0
Heavy atoms	43
Unassigned stereo — modern	2
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 2 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. The modern graph analysis leaves 2 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 33

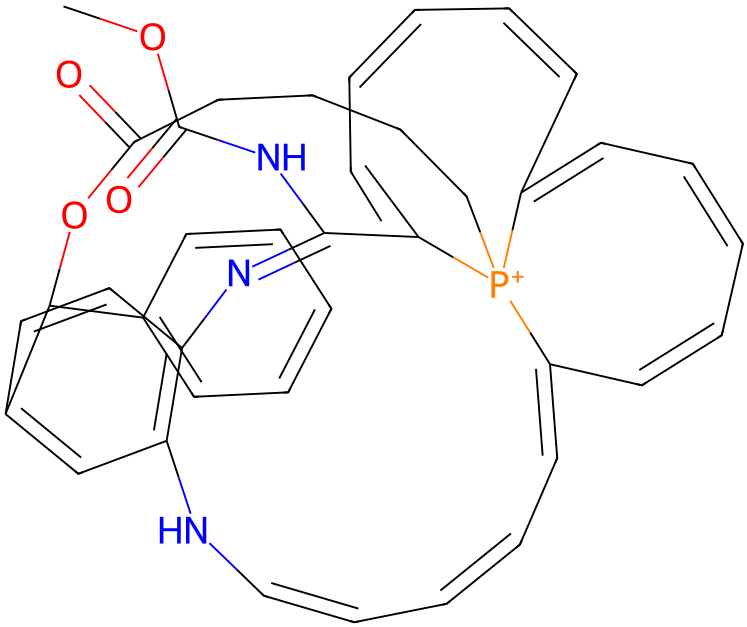
Original entry text

33. ARF-HMB-A3 · hydroxymebendazole C-OH GlcNAc succinate — metabolic (hexosamine)

C28H32N4O11 · MW 600.6 · clogP 0.36 · TPSA 214.3 Å² · HBD 6 · RotB 2
COC(=O)NC1=Nc2ccc3cc2N[C@@H](O)[C@H](O)[C@@H]

(NC(C)=O)[C@H]
(O)O[C@@H]1COC(=O)CCC(=O)OC3c1ccccc1

34. ARF-HMB-B1 · hydroxymebendazole C-OH TPP



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Original entry heading: 34. ARF-HMB-B1 · hydroxymebendazole C-OH TPP pentanoate — voltage. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

COC(=O)NC1=Nc2ccc3cc2NC=CC=CC=C2C=CC=CC=C4C=CC=CC=C1[P+]24CCCCC(=O)OC3c1ccccc1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)NC1=Nc2ccc3cc2NC=CC=CC=C2C=CC=CC=C4C=CC=CC=C1[P+]24CCCCC(=O)OC3c1ccccc1

Complete computed profile

Formula	C39H37N3O4P+
Molecular weight (g/mol)	642.716
Exact mass (Da)	642.25162
Crippen cLogP	9.3058
TPSA (Å²)	89.02
H-bond donors	2
H-bond acceptors	6
Rotatable bonds	1
Rings	7
Formal charge	1

Heavy atoms	47
Unassigned stereo — modern	12
Unassigned stereo — legacy	2

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 1 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 12 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

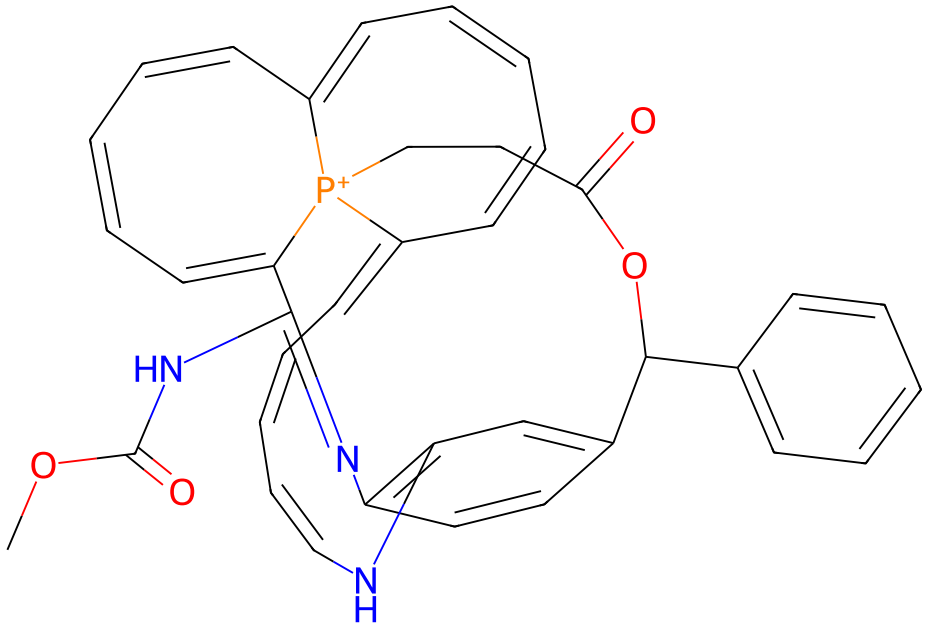
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 34

Original entry text

34. ARF-HMB-B1 · hydroxymebendazole C-OH TPP pentanoate — voltage
C39H37N3O4P+ · MW 642.7 · clogP 9.31 · TPSA 89.0 Å² · HBD 2 · RotB 1
COC(=O)NC1=Nc2ccc3cc2NC=CC=CC=C2C=CC=CC=C4C=CC=CC=C1[P+]24CCCCC(=O)OC3c1ccccc1

35. ARF-HMB-B2 · hydroxymebendazole C-OH TPP



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Original entry heading: 35. ARF-HMB-B2 · hydroxymebendazole C-OH TPP propanoate — voltage (short tether). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

COC(=O)NC1=Nc2ccc3cc2NC=CC=CC=C2C=CC=CC=C4C=CC=CC=C1[P+]24CCC(=O)OC3c1ccccc1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)NC1=Nc2ccc3cc2NC=CC=CC=C2C=CC=CC=C4C=CC=CC=C1[P+]24CCC(=O)OC3c1ccccc1

Complete computed profile

Formula	C37H33N3O4P+
Molecular weight (g/mol)	614.662
Exact mass (Da)	614.22032
Crippen cLogP	8.5256
TPSA (Å²)	89.02
H-bond donors	2
H-bond acceptors	6
Rotatable bonds	1
Rings	7
Formal charge	1

Heavy atoms	45
Unassigned stereo — modern	12
Unassigned stereo — legacy	2

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 1 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 12 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

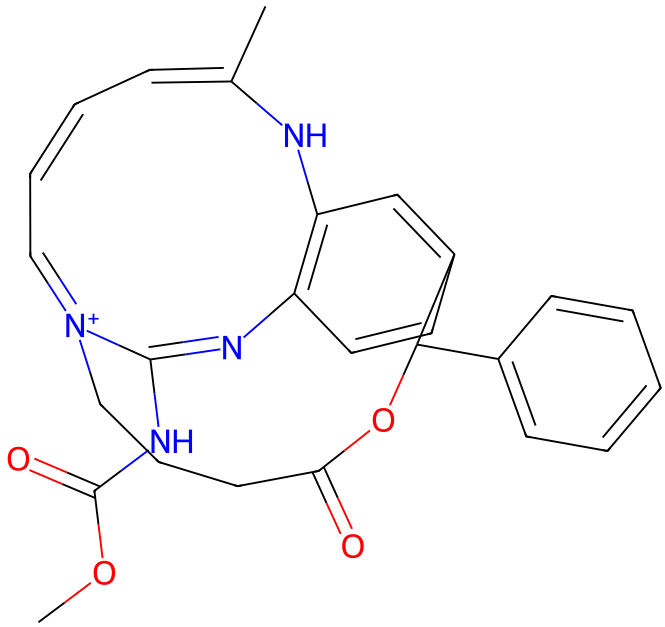
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 35

Original entry text

35. ARF-HMB-B2 · hydroxymebendazole C-OH TPP propanoate — voltage (short tether)
C37H33N3O4P+ · MW 614.7 · clogP 8.53 · TPSA 89.0 Å² · HBD 2 · RotB 1
COC(=O)NC1=Nc2ccc3cc2NC=CC=CC=C2C=CC=CC=C4C=CC=CC=C1[P+]24CCC(=O)OC3c1ccccc1

36. ARF-HMB-B3 · hydroxymebendazole C-OH N-



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Original entry heading: 36. ARF-HMB-B3 · hydroxymebendazole C-OH N- methylpyridinium butanoate — voltage (low MW. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

COC(=O)NC1=Nc2ccc3cc2NC(C)=CC=CC=
[N+]1CCCC(=O)OC3c1ccccc1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)NC1=Nc2ccc3cc2NC(C)=CC=CC=
[N+]1CCCC(=O)OC3c1ccccc1

Complete computed profile

Formula	C26H27N4O4+
Molecular weight (g/mol)	459.526
Exact mass (Da)	459.202682
Crippen cLogP	4.4253
TPSA (Å²)	92.03
H-bond donors	2
H-bond acceptors	6
Rotatable bonds	1
Rings	5
Formal charge	1

Heavy atoms	34
Unassigned stereo — modern	5
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 1 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 5 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

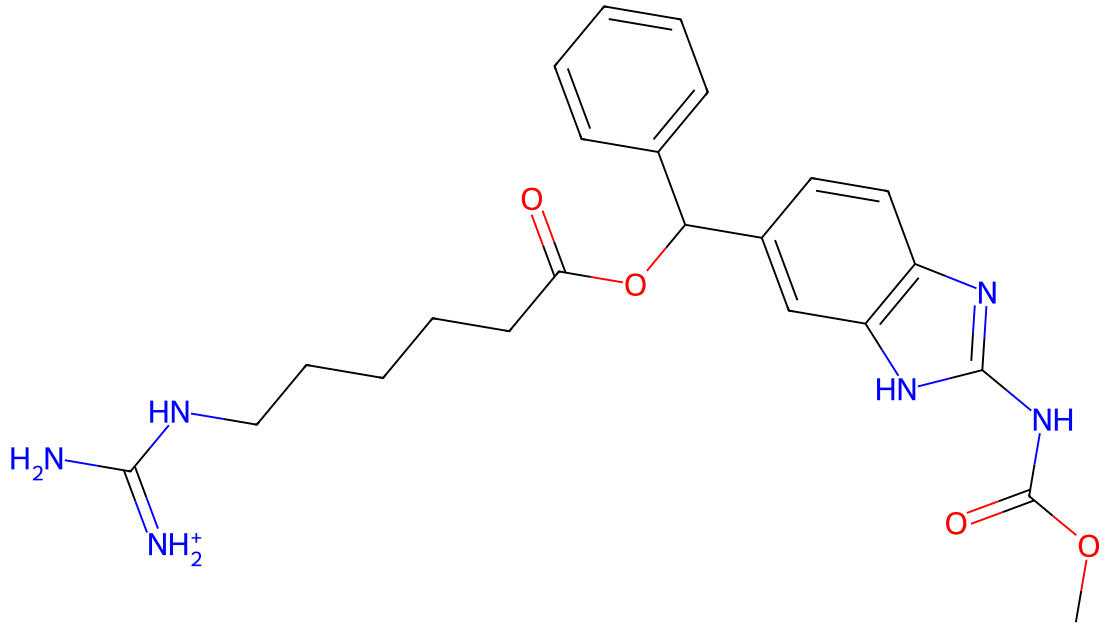
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 36

Original entry text

36. ARF-HMB-B3 · hydroxymebendazole C-OH N-methylpyridinium butanoate — voltage (low MW cation)
C26H27N4O4+ · MW 459.5 · clogP 4.43 · TPSA 92.0 Å² · HBD 2 · RotB 1
COC(=O)NC1=Nc2ccc3cc2NC(C)=CC=CC=[N+]1CCCC(=O)OC3c1ccccc1

37. ARF-HMB-B4 · hydroxymebendazole C-OH



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Original entry heading: 37. ARF-HMB-B4 · hydroxymebendazole C-OH guanidinium hexanoate — voltage / penetrating. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc(C(OC(=O)CCCCCNC(N)=[NH2+])c3ccccc3)cc2[nH]1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc(C(OC(=O)CCCCCNC(N)=[NH2+])c3ccccc3)cc2[nH]1

Complete computed profile

Formula	C23H29N6O4+
Molecular weight (g/mol)	453.523
Exact mass (Da)	453.22448
Crippen cLogP	1.5976
TPSA (Å²)	156.95
H-bond donors	5
H-bond acceptors	5
Rotatable bonds	10
Rings	3
Formal charge	1

Heavy atoms	33
Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 10 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

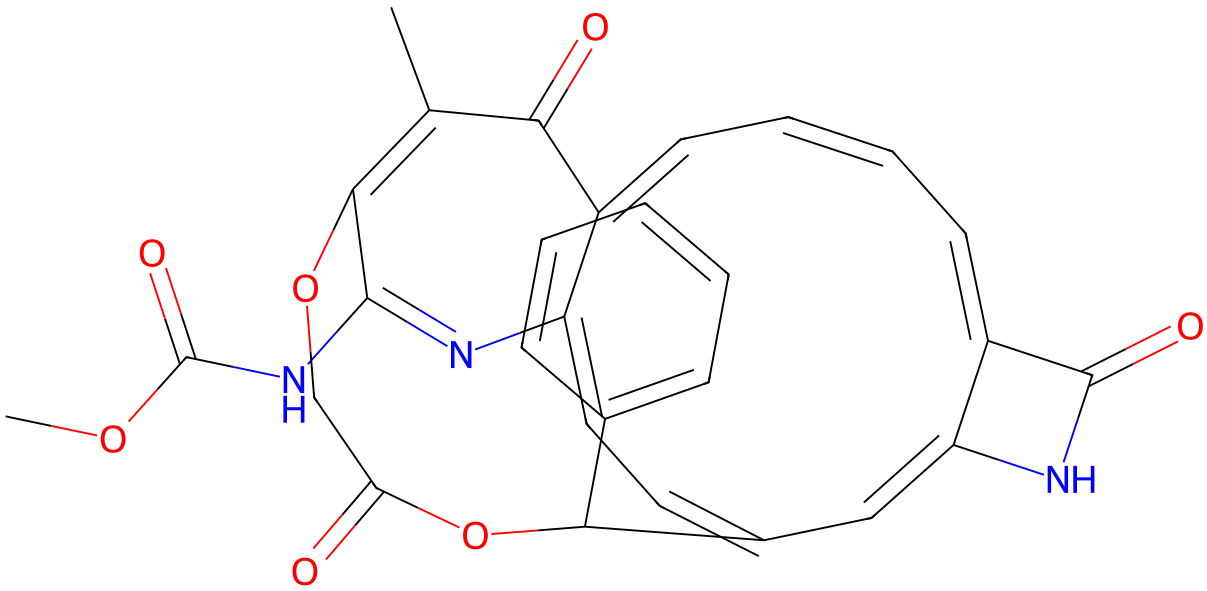
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 37

Original entry text

37. ARF-HMB-B4 · hydroxymebendazole C-OH guanidinium hexanoate — voltage / penetrating C23H29N6O4+ · MW 453.5 · clogP 1.60 · TPSA 156.9 Å² · HBD 5 · RotB 10 COC(=O)Nc1nc2ccc(C(OC(=O)CCCCCNC(N)=[NH2+])c3ccccc3)cc2[nH]1

38. ARF-HMB-C1 · hydroxymebendazole C-OH



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 38. ARF-HMB-C1 · hydroxymebendazole C-OH menadione glycolate — redox (quinone). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc3cc4[nH]c(=O)c-4ccccc2c(=O)c(C)c1OCC(=O)OC3c1ccccc1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc3cc4[nH]c(=O)c-4ccccc2c(=O)c(C)c1OCC(=O)OC3c1ccccc1

Complete computed profile

Formula	C29H23N3O7
Molecular weight (g/mol)	525.517
Exact mass (Da)	525.1536
Crippen cLogP	4.0242
TPSA (Å²)	136.68
H-bond donors	2
H-bond acceptors	8
Rotatable bonds	2
Rings	5
Formal charge	0

Heavy atoms	39
Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 2 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

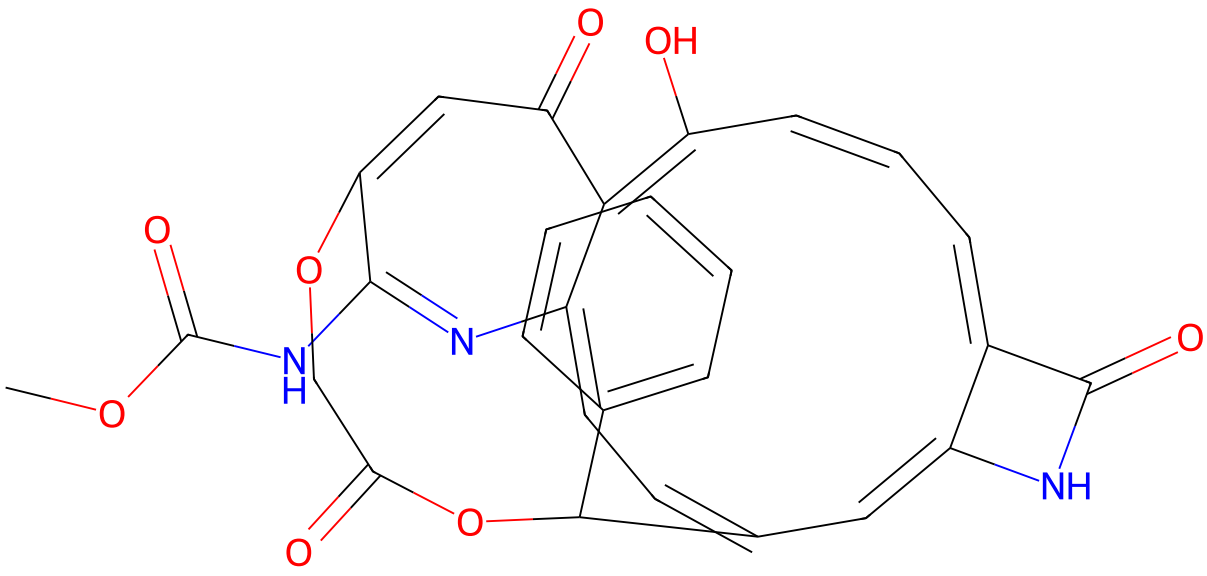
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 38

Original entry text

38. ARF-HMB-C1 · hydroxymebendazole C-OH
menadione glycolate — redox (quinone)
C29H23N3O7 · MW 525.5 · clogP 4.02 · TPSA 136.7 Å² · HBD 2 · RotB 2
COC(=O)Nc1nc2ccc3cc4[nH]c(=O)c-4ccccc2c(=O)c(C)c1OCC(=O)OC3c1ccccc1

39. ARF-HMB-C2 · hydroxymebendazole C-OH



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 39. ARF-HMB-C2 · hydroxymebendazole C-OH plumbagin-type glycolate — redox (hydroxyquinone). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc3cc4[nH]c(=O)c-4cccc(O)c2c(=O)cc1OCC(=O)OC3c1ccccc1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc3cc4[nH]c(=O)c-4cccc(O)c2c(=O)cc1OCC(=O)OC3c1ccccc1

Complete computed profile

Formula	C28H21N3O8
Molecular weight (g/mol)	527.489
Exact mass (Da)	527.132865
Crippen cLogP	3.4214
TPSA (Å²)	156.91
H-bond donors	3
H-bond acceptors	9
Rotatable bonds	2
Rings	5
Formal charge	0

Heavy atoms	39
Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 2 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

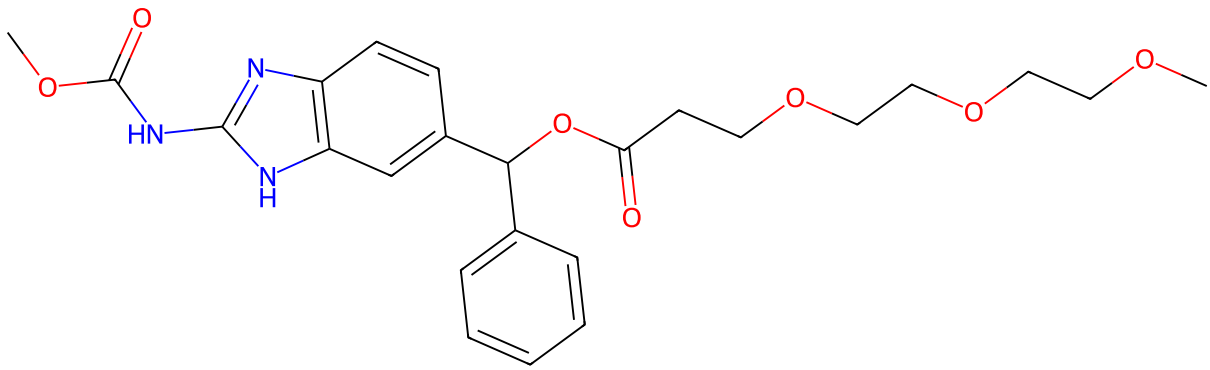
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 39

Original entry text

39. ARF-HMB-C2 · hydroxymebendazole C-OH plumbagin-type glycolate — redox (hydroxyquinone) C28H21N3O8 · MW 527.5 · clogP 3.42 · TPSA 156.9 Å² · HBD 3 · RotB 2 COC(=O)Nc1nc2ccc3cc4[nH]c(=O)c-4cccc(O)c2c(=O)cc1OCC(=O)OC3c1ccccc1

40. ARF-HMB-D1 · hydroxymebendazole C-OH PEG3



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 40. ARF-HMB-D1 · hydroxymebendazole C-OH PEG3 ester — delivery. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COCCOCCOCCC(=O)OC(c1ccccc1)c1ccc2nc(NC(=O)OC)[nH]c2c1

Canonical isomeric SMILES — RDKit 2026.09.1

COCCOCCOCCC(=O)OC(c1ccccc1)c1ccc2nc(NC(=O)OC)[nH]c2c1

Complete computed profile

Formula	C24H29N3O7
Molecular weight (g/mol)	471.51
Exact mass (Da)	471.20055
Crippen cLogP	3.4435
TPSA (Å²)	121.0
H-bond donors	2
H-bond acceptors	8
Rotatable bonds	13
Rings	3
Formal charge	0

Heavy atoms	34
Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 13 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

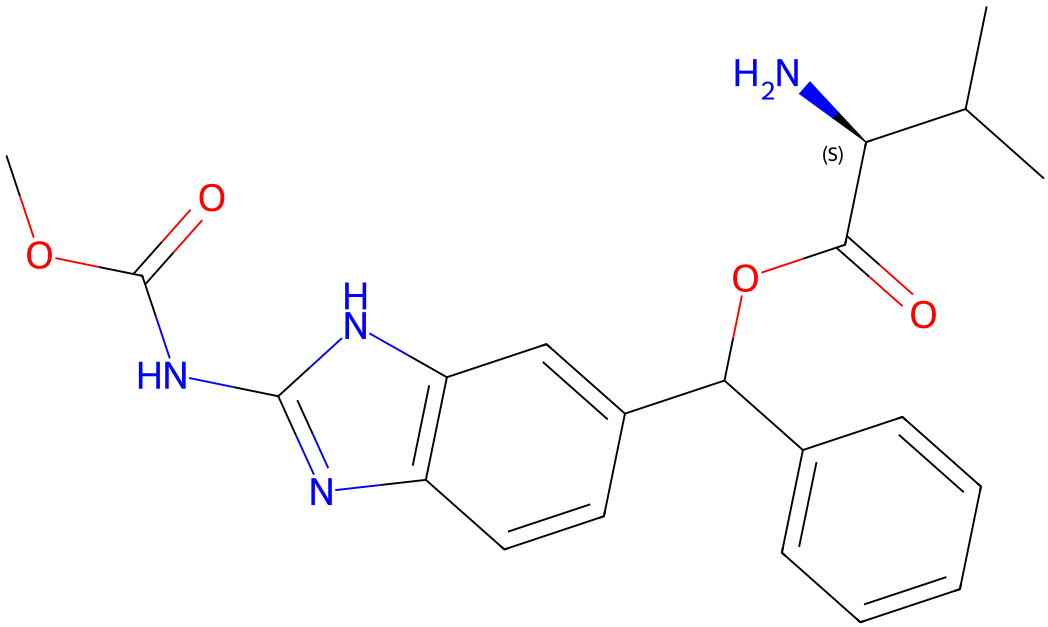
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 40

Original entry text

40. ARF-HMB-D1 · hydroxymebendazole C-OH PEG3 ester — delivery
C24H29N3O7 · MW 471.5 · clogP 3.44 · TPSA 121.0 Å² · HBD 2 · RotB 13

COCCOCCOCCC(=O)OC(c1ccccc1)c1ccc2nc(NC(=O)OC)[nH]c2c1

41. ARF-HMB-D2 · hydroxymebendazole C-OH valine



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 41. ARF-HMB-D2 · hydroxymebendazole C-OH valine ester — delivery (PepT1). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc(C(OC(=O)[C@@H](N)C(C)C)c3ccccc3)cc2[nH]1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc(C(OC(=O)[C@@H](N)C(C)C)c3ccccc3)cc2[nH]1

Complete computed profile

Formula	C21H24N4O4
Molecular weight (g/mol)	396.447
Exact mass (Da)	396.179755
Crippen cLogP	3.3571
TPSA (Å²)	119.33
H-bond donors	3
H-bond acceptors	6
Rotatable bonds	6
Rings	3
Formal charge	0

Heavy atoms	29
Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 6 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

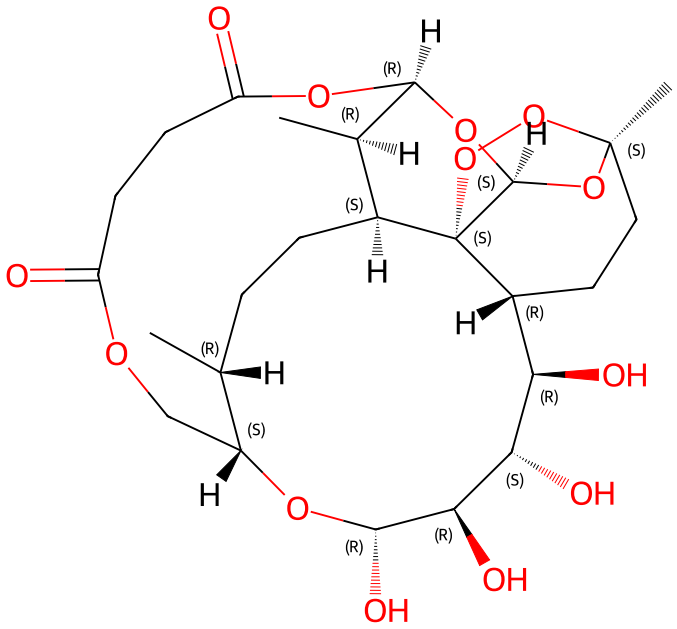
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 41

Original entry text

41. ARF-HMB-D2 · hydroxymebendazole C-OH valine ester — delivery (PepT1)
C21H24N4O4 · MW 396.4 · clogP 3.36 · TPSA 119.3 Å² · HBD 3 · RotB 6
COC(=O)Nc1nc2ccc(C(OC(=O)[C@@H](N)C(C)C)c3ccccc3)cc2[nH]1

42. ARF-DHA-A1 · dihydroartemisinin C10-OH glucosyl



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 42. ARF-DHA-A1 · dihydroartemisinin C10-OH glucosyl succinate — metabolic (GLUT). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@H]2OC(=O)CCC(=O)OC[C@H]3O[C@@H](O)[C@H](O)[C@@H](O)[C@H](O)[C@H]4CC[C@]5(C)OO[C@@]4([C@@H](O2)O5)[C@H]1CC[C@H]3C

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@H]2OC(=O)CCC(=O)OC[C@H]3O[C@@H](O)[C@H](O)[C@@H](O)[C@H](O)[C@H]4CC[C@]5(C)OO[C@@]4([C@@H](O2)O5)[C@H]1CC[C@H]3C

Complete computed profile

Formula	C25H38O13
Molecular weight (g/mol)	546.566
Exact mass (Da)	546.231241
Crippen cLogP	-0.1391
TPSA (Å²)	179.67
H-bond donors	4
H-bond acceptors	13
Rotatable bonds	0

Rings	6
Formal charge	0
Heavy atoms	38
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 0 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

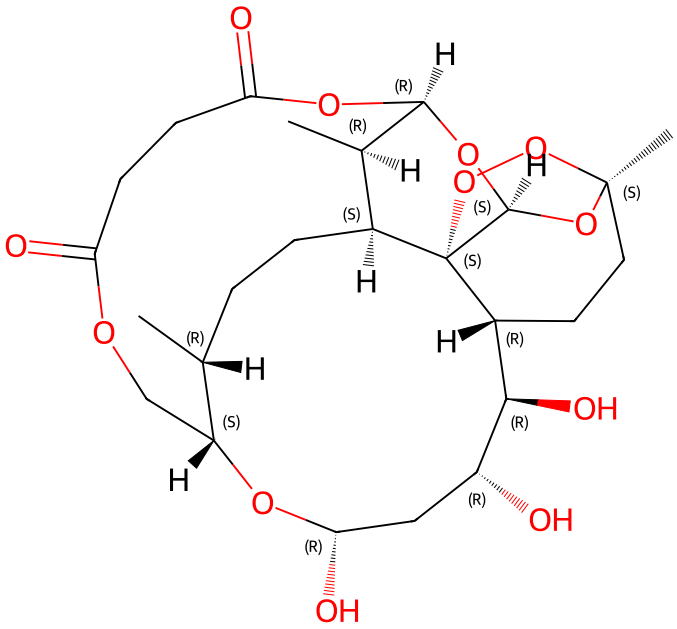
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 42

Original entry text

42. ARF-DHA-A1 · dihydroartemisinin C10-OH glucosyl succinate — metabolic (GLUT)
C25H38O13 · MW 546.6 · clogP -0.14 · TPSA 179.7 Å² · HBD 4 · RotB 0
C[C@H]1[C@H]2OC(=O)CCC(=O)OC[C@H]3O[C@@H](O)

[C@H](O)[C@@H](O)[C@H](O)
[C@H]4CC[C@]5(C)OO[C@@]4([C@@H]
(O2)O5)[C@H]1CC[C@H]3C

43. ARF-DHA-A2 · dihydroartemisinin C10-OH 2-



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 43. ARF-DHA-A2 · dihydroartemisinin C10-OH 2-deoxyglucosyl succinate — metabolic (trapped). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@H]2OC(=O)CCC(=O)OC[C@H]3O[C@@H](O)C[C@@H](O)[C@H](O)[C@H]4CC[C@]5(C)OO[C@@]4([C@@H](O2)O5)[C@H]1CC[C@H]3C

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@H]2OC(=O)CCC(=O)OC[C@H]3O[C@@H](O)C[C@@H](O)[C@H](O)[C@H]4CC[C@]5(C)OO[C@@]4([C@@H](O2)O5)[C@H]1CC[C@H]3C

Complete computed profile

Formula	C25H38O12
Molecular weight (g/mol)	530.567
Exact mass (Da)	530.236327
Crippen cLogP	0.8901
TPSA (Å²)	159.44
H-bond donors	3
H-bond acceptors	12
Rotatable bonds	0

Rings	6
Formal charge	0
Heavy atoms	37
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 0 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

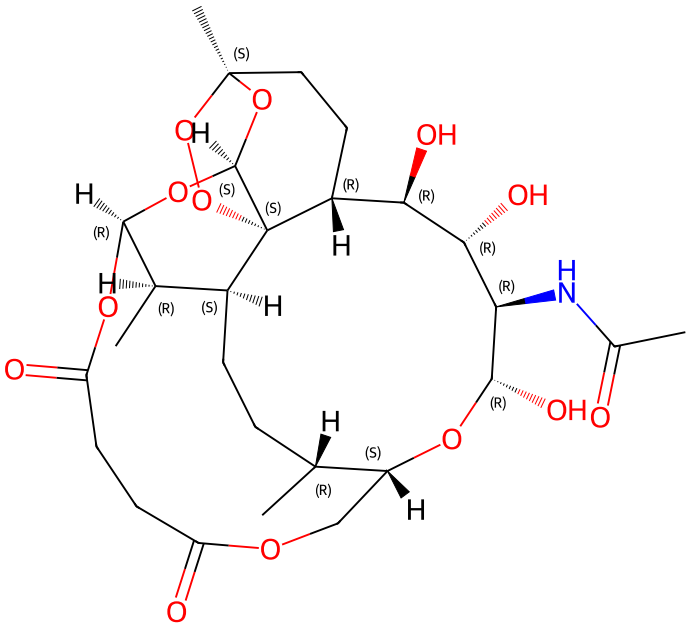
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 43

Original entry text

43. ARF-DHA-A2 · dihydroartemisinin C10-OH 2-deoxyglucosyl succinate — metabolic (trapped)
C25H38O12 · MW 530.6 · clogP 0.89 · TPSA 159.4 Å² · HBD 3 · RotB 0
C[C@H]1[C@H]2OC(=O)CCC(=O)OC[C@H]3O[C@@H]

(O)C[C@@H](O)[C@H](O)
[C@H]4CC[C@]5(C)OO[C@@]4([C@@H](O2)O5)
[C@H]1CC[C@H]3C

44. ARF-DHA-A3 · dihydroartemisinin C10-OH GlcNAc



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 44. ARF-DHA-A3 · dihydroartemisinin C10-OH GlcNAc succinate — metabolic (hexosamine). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CC(=O)N[C@@H]1[C@@H](O)[C@H](O)[C@H]2CC[C@]3(C)OO[C@]24[C@@H](O[C@@H]2OC(=O)CCC(=O)OC[C@@H](O[C@H]1O)[C@H](C)CC[C@H]4[C@H]2C)O3

Canonical isomeric SMILES — RDKit 2026.09.1

CC(=O)N[C@@H]1[C@@H](O)[C@H](O)[C@H]2CC[C@]3(C)OO[C@]24[C@@H](O[C@@H]2OC(=O)CCC(=O)OC[C@@H](O[C@H]1O)[C@H](C)CC[C@H]4[C@H]2C)O3

Complete computed profile

Formula	C27H41NO13
Molecular weight (g/mol)	587.619
Exact mass (Da)	587.25779
Crippen cLogP	0.0047
TPSA (Å²)	188.54
H-bond donors	4
H-bond acceptors	13
Rotatable bonds	1

Rings	6
Formal charge	0
Heavy atoms	41
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 1 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

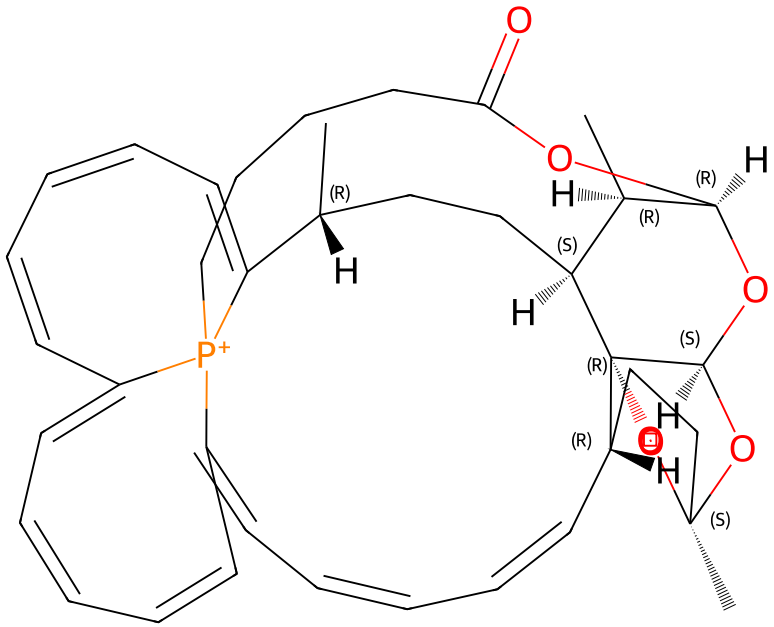
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 44

Original entry text

44. ARF-DHA-A3 · dihydroartemisinin C10-OH GlcNAc succinate — metabolic (hexosamine)
C27H41NO13 · MW 587.6 · clogP 0.00 · TPSA 188.5 Å² · HBD 4 · RotB 1
CC(=O)N[C@@H]1[C@@H](O)[C@H](O)

[C@H]2CC[C@]3(C)OO[C@]24[C@@H]
(O[C@@H]2OC(=O)CCC(=O)OC[C@@H]
(O[C@H]1O)[C@H](C)CC[C@H]4[C@H]2C)O3

45. ARF-DHA-B1 · dihydroartemisinin C10-OH TPP



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Original entry heading: 45. ARF-DHA-B1 · dihydroartemisinin C10-OH TPP pentanoate — voltage. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@H]2OC(=O)CCCC[P+]34C5=CC=CC=C[C@H]6CC[C@]7(C)OO[C@@]6([C@@H](O2)O7)[C@H]1CC[C@@H](C)C3=CC=CC=CC4=CC=CC=C5

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@H]2OC(=O)CCCC[P+]34C5=CC=CC=C[C@H]6CC[C@]7(C)OO[C@@]6([C@@H](O2)O7)[C@H]1CC[C@@H](C)C3=CC=CC=CC4=CC=CC=C5

Complete computed profile

Formula	C38H46O6P+
Molecular weight (g/mol)	629.754
Exact mass (Da)	629.302652
Crippen cLogP	8.9552
TPSA (Å²)	63.22
H-bond donors	0
H-bond acceptors	6
Rotatable bonds	0
Rings	8

Formal charge	1
Heavy atoms	45
Unassigned stereo — modern	10
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +1, and 0 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 10 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

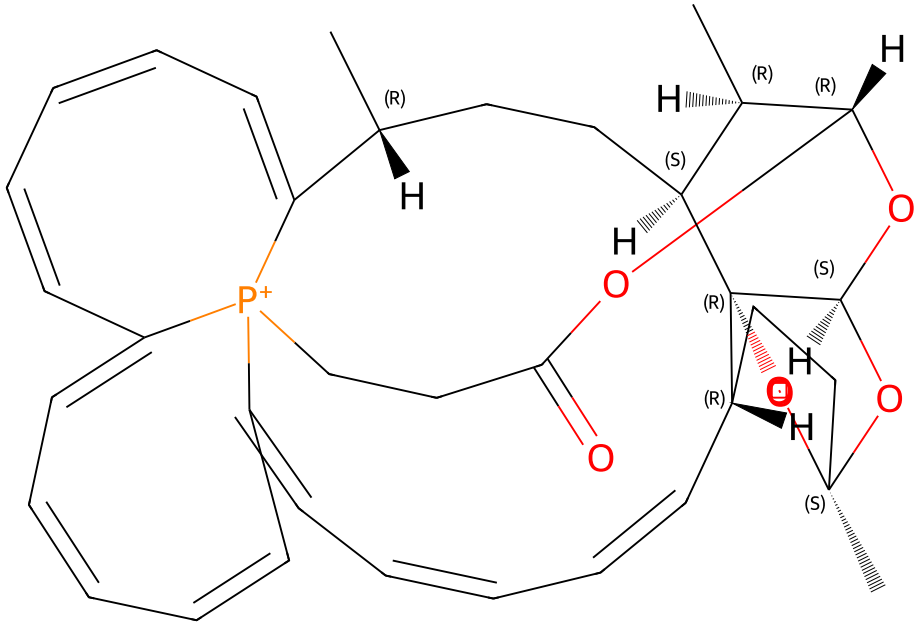
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 45

Original entry text

45. ARF-DHA-B1 · dihydroartemisinin C10-OH TPP pentanoate — voltage
C38H46O6P+ · MW 629.8 · clogP 8.96 · TPSA 63.2 Å² · HBD 0 · RotB 0
C[C@H]1[C@H]2OC(=O)CCCC[P+]34C5=CC=CC=C[C@H]6CC[C@]7(C)OO[C@@]6([C@@H](O2)O7)

[C@H]1CC[C@@H](C)C3=CC=CC=CC4=CC=CC=C5

46. ARF-DHA-B2 · dihydroartemisinin C10-OH TPP



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 46. ARF-DHA-B2 · dihydroartemisinin C10-OH TPP propanoate — voltage (short tether). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@H]2OC(=O)CC[P+]34C5=CC=CC=C[C@H]6CC[C@]7(C)OO[C@@]6([C@@H](O2)O7)[C@H]1CC[C@@H](C)C3=CC=CC=CC4=CC=CC=C5

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@H]2OC(=O)CC[P+]34C5=CC=CC=C[C@H]6CC[C@]7(C)OO[C@@]6([C@@H](O2)O7)[C@H]1CC[C@@H](C)C3=CC=CC=CC4=CC=CC=C5

Complete computed profile

Formula	C36H42O6P+
Molecular weight (g/mol)	601.7
Exact mass (Da)	601.271352
Crippen cLogP	8.175
TPSA (Å²)	63.22
H-bond donors	0
H-bond acceptors	6
Rotatable bonds	0
Rings	8

Formal charge	1
Heavy atoms	43
Unassigned stereo — modern	10
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +1, and 0 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 10 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

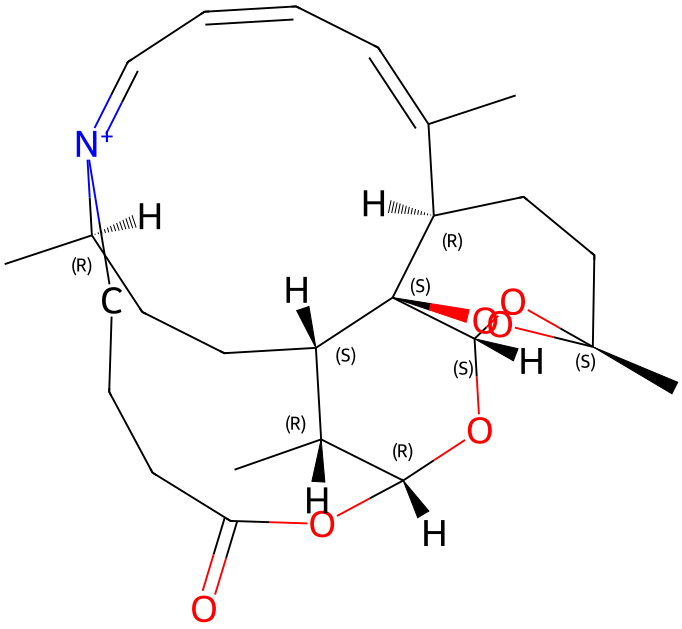
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 46

Original entry text

46. ARF-DHA-B2 · dihydroartemisinin C10-OH TPP propanoate — voltage (short tether)
C36H42O6P+ · MW 601.7 · clogP 8.18 · TPSA 63.2 Å² · HBD 0 · RotB 0
C[C@H]1[C@H]2OC(=O)CC[P+]34C5=CC=CC=C[C@H]6CC[

C@]7(C)OO[C@@]6([C@@H](O2)O7)[C@H]1CC[C@@H](C)C3=CC=CC=CC4=CC=CC=C5

47. ARF-DHA-B3 · dihydroartemisinin C10-OH N-



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 47. ARF-DHA-B3 · dihydroartemisinin C10-OH N-methylpyridinium butanoate — voltage (low MW. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CC1=CC=CC=[N+]2CCCC(=O)O[C@H]3O[C@H]4O[C@]5(C)CC[C@H]1[C@@]4(OO5)[C@@H](CC[C@H]2C)[C@H]3C

Canonical isomeric SMILES — RDKit 2026.09.1

CC1=CC=CC=[N+]2CCCC(=O)O[C@H]3O[C@H]4O[C@]5(C)CC[C@H]1[C@@]4(OO5)[C@@H](CC[C@H]2C)[C@H]3C

Complete computed profile

Formula	C25H36NO6+
Molecular weight (g/mol)	446.564
Exact mass (Da)	446.253714
Crippen cLogP	3.8696
TPSA (Å²)	66.23
H-bond donors	0
H-bond acceptors	6
Rotatable bonds	0
Rings	6

Formal charge	1
Heavy atoms	32
Unassigned stereo — modern	3
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +1, and 0 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 3 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 47

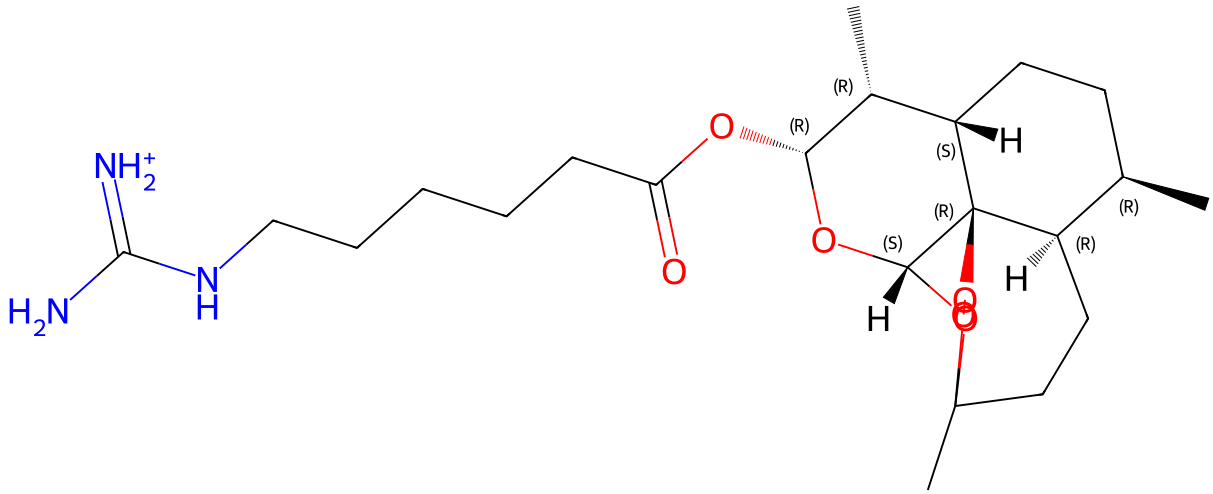
Original entry text

47. ARF-DHA-B3 · dihydroartemisinin C10-OH N-methylpyridinium butanoate — voltage (low MW cation)

C25H36NO6+ · MW 446.6 · clogP 3.87 · TPSA 66.2 Å² · HBD 0 · RotB 0

CC1=CC=CC=
[N+]2CCCC(=O)O[C@H]3O[C@H]4O[C@]5(C)CC[C@H]1[C
@@]4(OO5)[C@@H](CC[C@H]2C)[C@H]3C

48. ARF-DHA-B4 · dihydroartemisinin C10-OH



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 48. ARF-DHA-B4 · dihydroartemisinin C10-OH guanidinium hexanoate — voltage / penetrating. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@@H](OC(=O)CCCCCNC(N)=[NH2+])O[C@H]2OC3(C)CC[C@@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@@H](OC(=O)CCCCCNC(N)=[NH2+])O[C@H]2OC3(C)CC[C@@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Complete computed profile

Formula	C22H38N3O6+
Molecular weight (g/mol)	440.561
Exact mass (Da)	440.275512
Crippen cLogP	0.9614
TPSA (Å²)	126.86
H-bond donors	3
H-bond acceptors	6
Rotatable bonds	7
Rings	5

Formal charge	1
Heavy atoms	31
Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +1, and 7 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

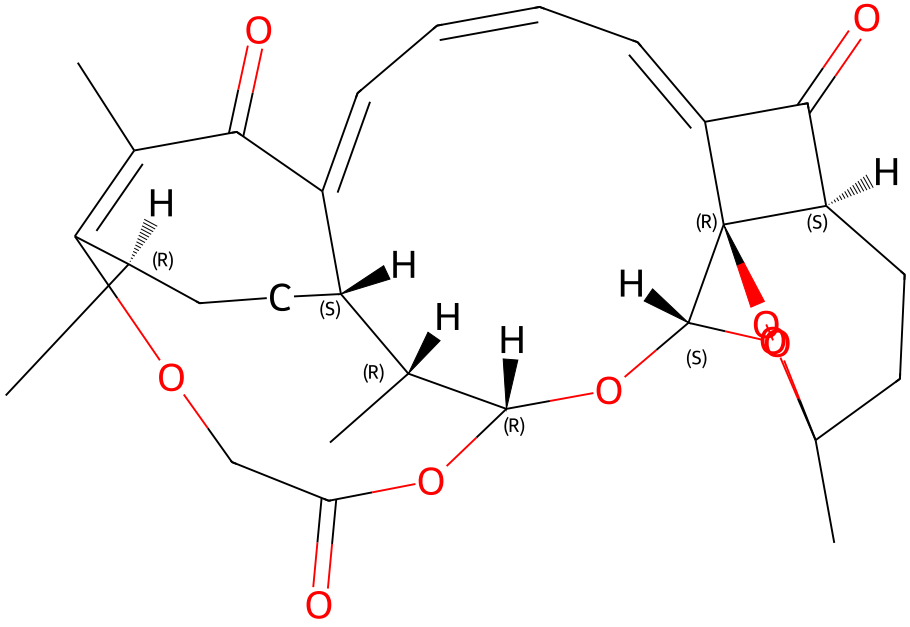
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 48

Original entry text

48. ARF-DHA-B4 · dihydroartemisinin C10-OH guanidinium hexanoate — voltage / penetrating C22H38N3O6+ · MW 440.6 · clogP 0.96 · TPSA 126.9 Å² · HBD 3 · RotB 7 C[C@H]1[C@@H](OC(=O)CCCCCNC(N)=

[NH2+])O[C@H]2OC3(C)CC[C@@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

49. ARF-DHA-C1 · dihydroartemisinin C10-OH



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 49. ARF-DHA-C1 · dihydroartemisinin C10-OH menadione glycolate — redox (quinone). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CC1=C2OCC(=O)O[C@H]3O[C@H]4OC5(C)CC[C@@H]6C(=O)C(=CC=CC=C(C1=O)[C@@H](CC[C@H]2C)[C@H]3C)[C@@]46OO5

Canonical isomeric SMILES — RDKit 2026.09.1

CC1=C2OCC(=O)O[C@H]3O[C@H]4OC5(C)CC[C@@H]6C(=O)C(=CC=CC=C(C1=O)[C@@H](CC[C@H]2C)[C@H]3C)[C@@]46OO5

Complete computed profile

Formula	C28H32O9
Molecular weight (g/mol)	512.555
Exact mass (Da)	512.204633
Crippen cLogP	3.6026
TPSA (Å²)	106.59
H-bond donors	0
H-bond acceptors	9
Rotatable bonds	0
Rings	8

Formal charge	0
Heavy atoms	37
Unassigned stereo — modern	5
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 0 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 5 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

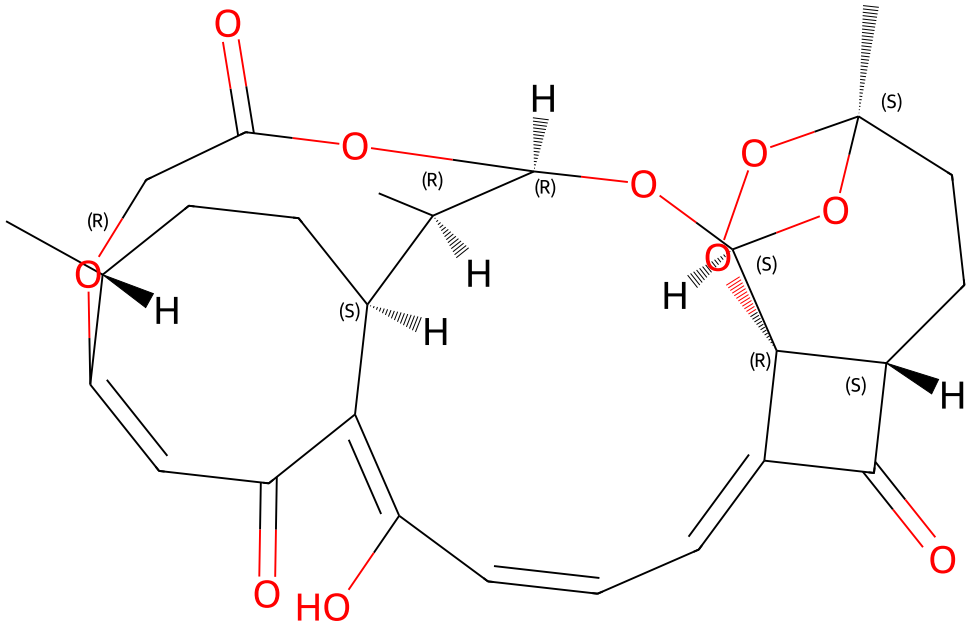
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 49

Original entry text

49. ARF-DHA-C1 · dihydroartemisinin C10-OH menadione glycolate — redox (quinone) C28H32O9 · MW 512.6 · clogP 3.60 · TPSA 106.6 Å² · HBD 0 · RotB 0 CC1=C2OCC(=O)O[C@H]3O[C@H]4OC5(C)CC[C@@H]6C(

=O)C(=CC=CC=C(C1=O)[C@@H](CC[C@H]2C)[C@H]3C)[C@@]46OO5

50. ARF-DHA-C2 · dihydroartemisinin C10-OH



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 50. ARF-DHA-C2 · dihydroartemisinin C10-OH plumbagin-type glycolate — redox (hydroxyquinone). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@H]2OC(=O)COC3=CC(=O)C(=C(O)C=CC=C4C(=O)[C@H]5CC[C@]6(C)OO[C@@]45[C@@H](O2)O6)[C@H]1CC[C@H]3C

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@H]2OC(=O)COC3=CC(=O)C(=C(O)C=CC=C4C(=O)[C@H]5CC[C@]6(C)OO[C@@]45[C@@H](O2)O6)[C@H]1CC[C@H]3C

Complete computed profile

Formula	C27H30O10
Molecular weight (g/mol)	514.527
Exact mass (Da)	514.183897
Crippen cLogP	3.0982
TPSA (Å²)	126.82
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	0
Rings	8

Formal charge	0
Heavy atoms	37
Unassigned stereo — modern	4
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 0 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 4 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

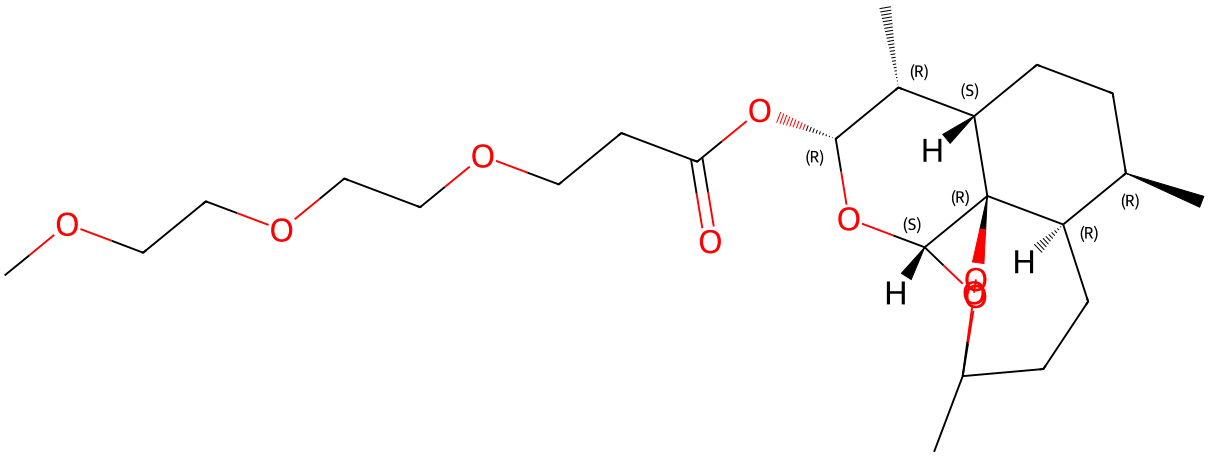
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 50

Original entry text

50. ARF-DHA-C2 · dihydroartemisinin C10-OH plumbagin-type glycolate — redox (hydroxyquinone) C27H30O10 · MW 514.5 · clogP 3.10 · TPSA 126.8 Å² · HBD 1 · RotB 0 C[C@H]1[C@H]2OC(=O)COC3=CC(=O)C(=C(O)C=CC=C4C(

=O)[C@H]5CC[C@]6(C)OO[C@@]45[C@@H](O2)O6)[C@H]1CC[C@H]3C

51. ARF-DHA-D1 · dihydroartemisinin C10-OH PEG3



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 51. ARF-DHA-D1 · dihydroartemisinin C10-OH PEG3 ester — delivery. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

COCCOCCOCCC(=O)O[C@H]1O[C@H]2OC3(C)CC[C@@H]4[C@H](C)CC[C@@H]([C@H]1C)[C@@]24OO3

Canonical isomeric SMILES — RDKit 2026.09.1

COCCOCCOCCC(=O)O[C@H]1O[C@H]2OC3(C)CC[C@@H]4[C@H](C)CC[C@@H]([C@H]1C)[C@@]24OO3

Complete computed profile

Formula	C23H38O9
Molecular weight (g/mol)	458.548
Exact mass (Da)	458.251583
Crippen cLogP	2.8073
TPSA (Å²)	90.91
H-bond donors	0
H-bond acceptors	9
Rotatable bonds	10
Rings	5
Formal charge	0

Heavy atoms	32
Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 10 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

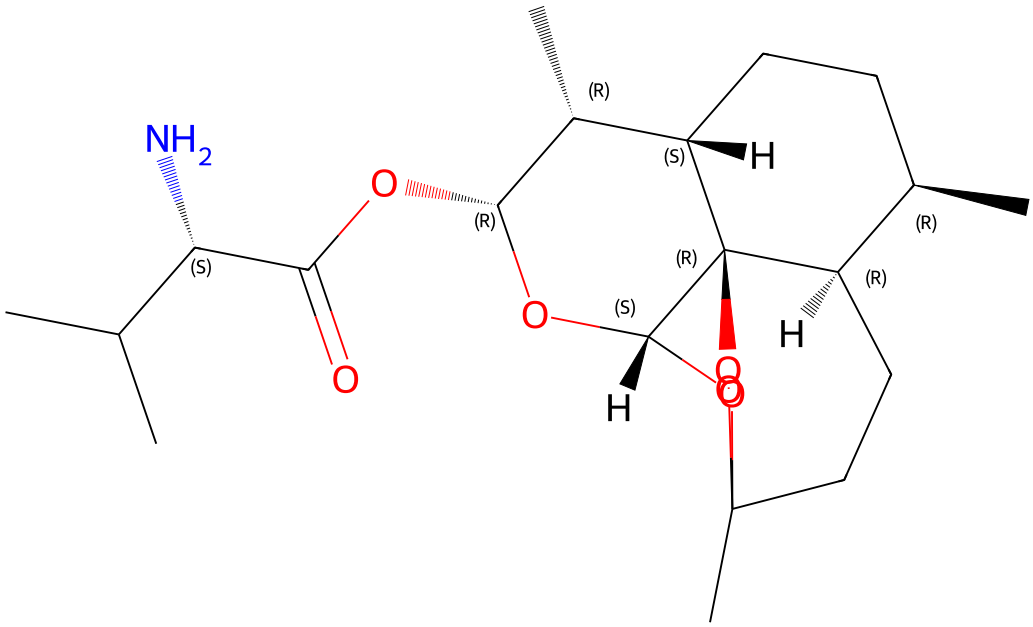
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 51

Original entry text

51. ARF-DHA-D1 · dihydroartemisinin C10-OH PEG3 ester — delivery
C23H38O9 · MW 458.5 · clogP 2.81 · TPSA 90.9 Å² · HBD 0 · RotB 10
COCCOCCOCCC(=O)O[C@H]1O[C@H]2OC3(C)CC[C@@H]4[C@H](C)CC[C@@H]([C@H]1C)[C@@]24OO3

52. ARF-DHA-D2 · dihydroartemisinin C10-OH valine



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 52. ARF-DHA-D2 · dihydroartemisinin C10-OH valine ester — delivery (PepT1). Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CC(C)[C@H]
(N)C(=O)O[C@H]1O[C@H]2OC3(C)CC[C@@H]4[C@H]
(C)CC[C@@H]([C@H]1C)[C@@]24OO3

Canonical isomeric SMILES — RDKit 2026.09.1

CC(C)[C@H]
(N)C(=O)O[C@H]1O[C@H]2OC3(C)CC[C@@H]4[C@H]
(C)CC[C@@H]([C@H]1C)[C@@]24OO3

Complete computed profile

Formula	C20H33NO6
Molecular weight (g/mol)	383.485
Exact mass (Da)	383.230788
Crippen cLogP	2.7209
TPSA (Å²)	89.24
H-bond donors	1
H-bond acceptors	7
Rotatable bonds	3
Rings	5

Formal charge	0
Heavy atoms	27
Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

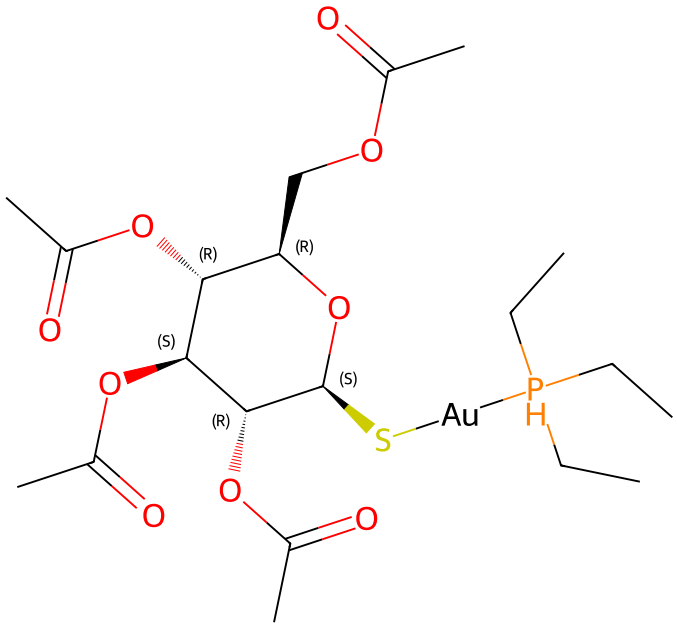
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 52

Original entry text

52. ARF-DHA-D2 · dihydroartemisinin C10-OH valine ester — delivery (PepT1)
C20H33NO6 · MW 383.5 · clogP 2.72 · TPSA 89.2 Å² · HBD 1 · RotB 3
CC(C)[C@H]

(N)C(=O)O[C@H]1O[C@H]2OC3(C)CC[C@@H]4[C@H](C)CC[C@@H]([C@H]1C)[C@@]24OO3

53. ARF-AUR-1 · auranofin (reference, approved) —



Recorded rationale and role

Gold/redox comparison arm. The encoded metal-containing agent provides a contrast with organic peroxide and sulfur-containing branches; material identity includes the coordination representation. Original entry heading: 53. ARF-AUR-1 · auranofin (reference, approved) — thioredoxin reductase / Au-Se. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group

compatibility. Establish connectivity, stereochemical composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CC[PH](CC)(CC)[Au][S][C@@H]1O[C@H](COC(C)=O)[C@@H](OC(C)=O)[C@H](OC(C)=O)[C@H]1OC(C)=O

Canonical isomeric SMILES — RDKit 2026.09.1

CC[PH](CC)(CC)[Au][S][C@@H]1O[C@H](COC(C)=O)[C@@H](OC(C)=O)[C@H](OC(C)=O)[C@H]1OC(C)=O

Complete computed profile

Formula	C20H35AuO9PS
Molecular weight (g/mol)	679.499
Exact mass (Da)	679.140509
Crippen cLogP	2.5248
TPSA (Å²)	114.43
H-bond donors	0
H-bond acceptors	10
Rotatable bonds	11
Rings	1

Formal charge	0
Heavy atoms	32
Unassigned stereo — modern	1
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 11 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

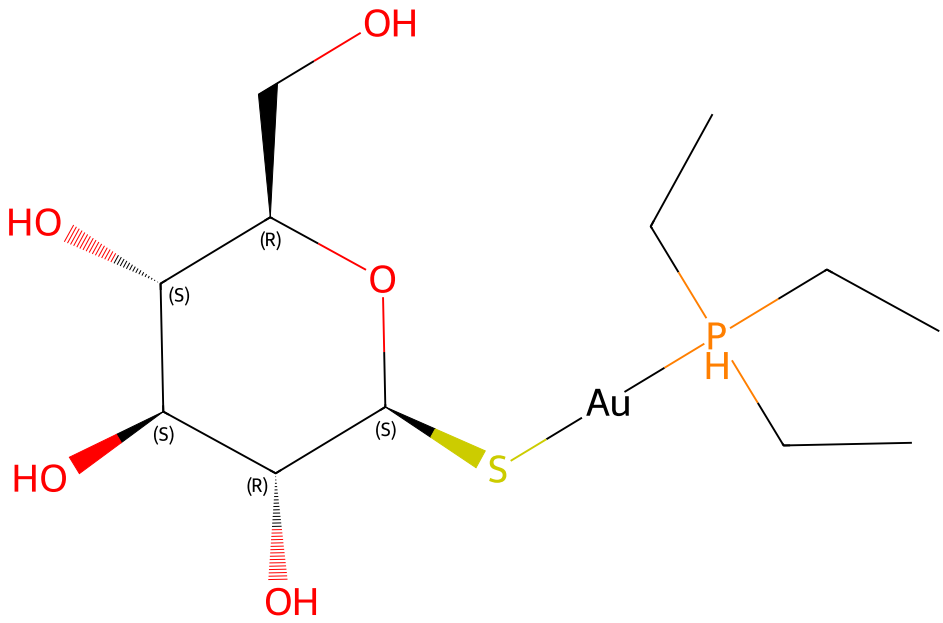
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 53

Original entry text

53. ARF-AUR-1 · auranofin (reference, approved) — thioredoxin reductase / Au-Se
C20H35AuO9PS · MW 679.5 · clogP 2.52 · TPSA 114.4 Å² · HBD 0 · RotB 11
CC[PH](CC)(CC)[Au][S][C@@H]1O[C@H](COC(C)=O)[C@@H](OC(C)=O)[C@H](OC(C)=O)[C@H]1OC(C)=O

54. ARF-AUR-2 · deacetyl-auranofin (free thioglucose)



Recorded rationale and role

Gold/redox comparison arm. The encoded metal-containing agent provides a contrast with organic peroxide and sulfur-containing branches; material identity includes the coordination representation. Original entry heading: 54. ARF-AUR-2 · deacetyl-auranofin (free thioglucose) — TrxR, higher polarity. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group

compatibility. Establish connectivity, stereochemical composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CC[PH](CC)(CC)[Au][S][C@@H]1O[C@H](CO)[C@@H](O)[C@H](O)[C@H]1O

Canonical isomeric SMILES — RDKit 2026.09.1

CC[PH](CC)(CC)[Au][S][C@@H]1O[C@H](CO)[C@@H](O)[C@H](O)[C@H]1O

Complete computed profile

Formula	C12H27AuO5PS
Molecular weight (g/mol)	511.351
Exact mass (Da)	511.09825
Crippen cLogP	0.2416
TPSA (Å²)	90.15
H-bond donors	4
H-bond acceptors	6
Rotatable bonds	7
Rings	1

Formal charge	0
Heavy atoms	20
Unassigned stereo — modern	1
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

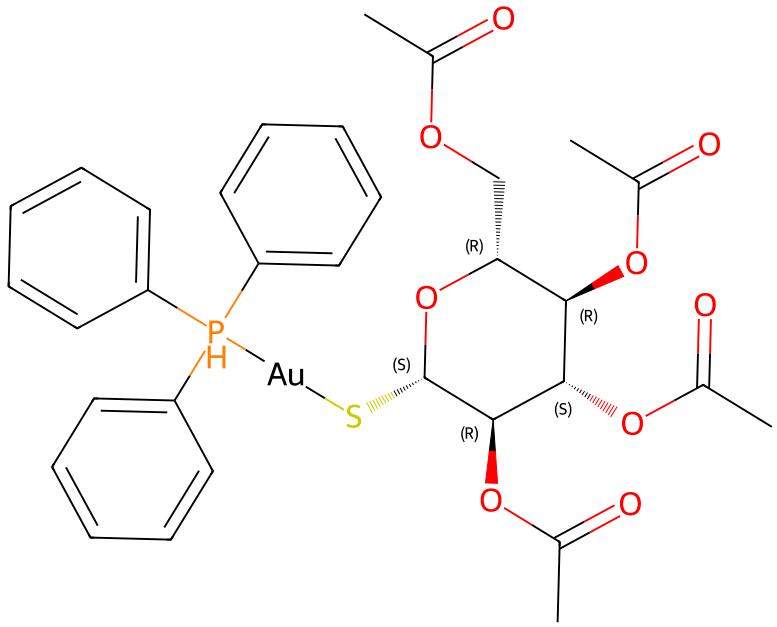
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 54

Original entry text

54. ARF-AUR-2 · deacetyl-auranofin (free thioglucose) — TrxR, higher polarity
C12H27AuO5PS · MW 511.4 · clogP 0.24 · TPSA 90.2 Å² · HBD 4 · RotB 7
CC[PH](CC)(CC)[Au][S][C@@H]1O[C@H](CO)[C@@H](O)

[C@H](O)[C@H]1O

55. ARF-AUR-3 · auranofin triphenylphosphine



Recorded rationale and role

Gold/redox comparison arm. The encoded metal-containing agent provides a contrast with organic peroxide and sulfur-containing branches; material identity includes the coordination representation. Original entry heading: 55. ARF-AUR-3 · auranofin triphenylphosphine analogue — TrxR + lipophilic cation character. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group

compatibility. Establish connectivity, stereochemical composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CC(=O)OC[C@H]1O[C@@H]([S][Au][PH](c2ccccc2)(c2ccccc2)c2ccccc2)[C@H](OC(C)=O)[C@@H](OC(C)=O)[C@@H]1OC(C)=O

Canonical isomeric SMILES — RDKit 2026.09.1

CC(=O)OC[C@H]1O[C@@H]([S][Au][PH](c2ccccc2)(c2ccccc2)c2ccccc2)[C@H](OC(C)=O)[C@@H](OC(C)=O)[C@@H]1OC(C)=O

Complete computed profile

Formula	C32H35AuO9PS
Molecular weight (g/mol)	823.631
Exact mass (Da)	823.140509
Crippen cLogP	3.4416
TPSA (Å²)	114.43
H-bond donors	0
H-bond acceptors	10
Rotatable bonds	11

Rings	4
Formal charge	0
Heavy atoms	44
Unassigned stereo — modern	1
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 11 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

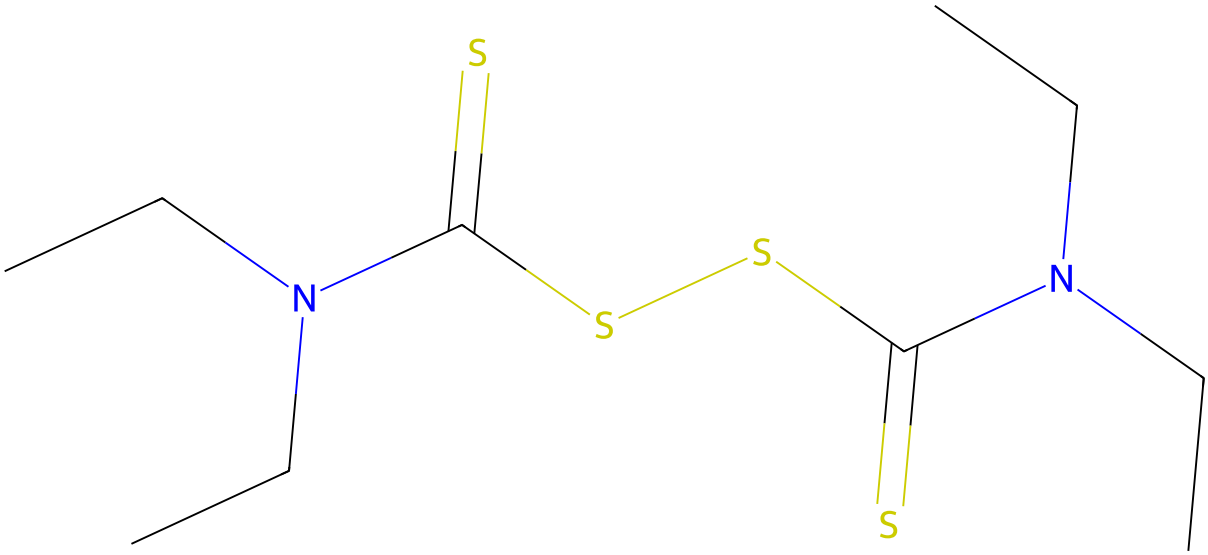
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 55

Original entry text

55. ARF-AUR-3 · auranofin triphenylphosphine analogue — TrxR + lipophilic cation character
C32H35AuO9PS · MW 823.6 · clogP 3.44 · TPSA 114.4 Å² · HBD 0 · RotB 11

CC(=O)OC[C@H]1O[C@@H]([S][Au][PH](c2ccccc2)(c2ccccc2)c2ccccc2)[C@H](OC(C)=O)[C@@H](OC(C)=O)[C@@H]1OC(C)=O

56. ARF-DSF-1 · disulfiram (reference, approved) —



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 56. ARF-DSF-1 · disulfiram (reference, approved) — Cu redox / NPL4. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group

compatibility. Establish connectivity, stereochemical composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CCN(CC)C(=S)SSC(=S)N(CC)CC

Canonical isomeric SMILES — RDKit 2026.09.1

CCN(CC)C(=S)SSC(=S)N(CC)CC

Complete computed profile

Formula	C10H20N2S4
Molecular weight (g/mol)	296.552
Exact mass (Da)	296.050933
Crippen cLogP	3.6212
TPSA (Å²)	6.48
H-bond donors	0
H-bond acceptors	4
Rotatable bonds	4
Rings	0
Formal charge	0
Heavy atoms	16

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 4 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

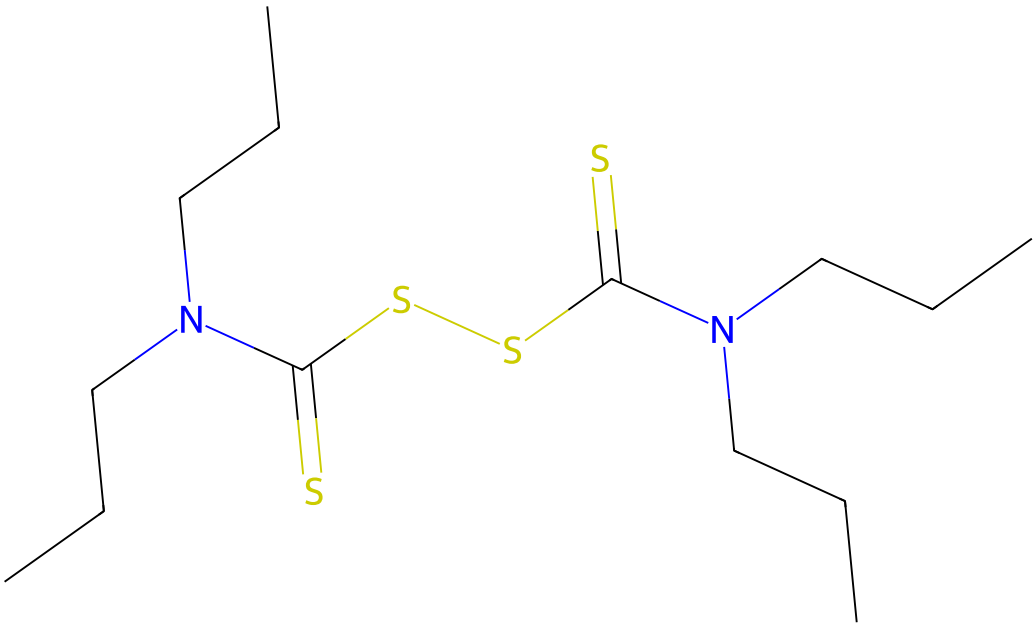
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 56

Original entry text

56. ARF-DSF-1 · disulfiram (reference, approved) — Cu redox / NPL4
C10H20N2S4 · MW 296.6 · clogP 3.62 · TPSA 6.5 Å² · HBD 0 · RotB 4
CCN(CC)C(=S)SSC(=S)N(CC)CC

57. ARF-DSF-2 · dipropyl dithiocarbamate disulfide —



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 57. ARF-DSF-2 · dipropyl dithiocarbamate disulfide — Cu redox, altered lipophilicity. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group

compatibility. Establish connectivity, stereochemical composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CCCN(CCC)C(=S)SSC(=S)N(CCC)CCC

Canonical isomeric SMILES — RDKit 2026.09.1

CCCN(CCC)C(=S)SSC(=S)N(CCC)CCC

Complete computed profile

Formula	C14H28N2S4
Molecular weight (g/mol)	352.66
Exact mass (Da)	352.113533
Crippen cLogP	5.1816
TPSA (Å²)	6.48
H-bond donors	0
H-bond acceptors	4
Rotatable bonds	8
Rings	0
Formal charge	0
Heavy atoms	20

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 8 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

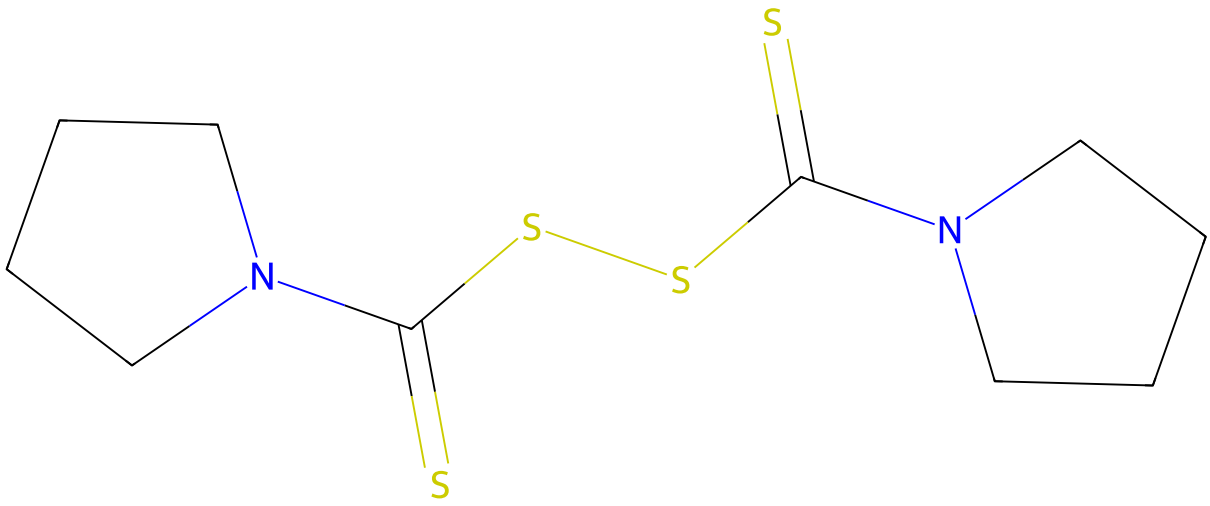
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 57

Original entry text

57. ARF-DSF-2 · dipropyl dithiocarbamate disulfide — Cu redox, altered lipophilicity
C14H28N2S4 · MW 352.7 · clogP 5.18 · TPSA 6.5 Å² · HBD 0 · RotB 8
CCCN(CCC)C(=S)SSC(=S)N(CCC)CCC

58. ARF-DSF-3 · pyrrolidine dithiocarbamate disulfide



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 58. ARF-DSF-3 · pyrrolidine dithiocarbamate disulfide — Cu redox, constrained amine. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group

compatibility. Establish connectivity, stereochemical composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

S=C(SSC(=S)N1CCCC1)N1CCCC1

Canonical isomeric SMILES — RDKit 2026.09.1

S=C(SSC(=S)N1CCCC1)N1CCCC1

Complete computed profile

Formula	C10H16N2S4
Molecular weight (g/mol)	292.52
Exact mass (Da)	292.019633
Crippen cLogP	3.1292
TPSA (Å²)	6.48
H-bond donors	0
H-bond acceptors	4
Rotatable bonds	0
Rings	2
Formal charge	0
Heavy atoms	16

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 0 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

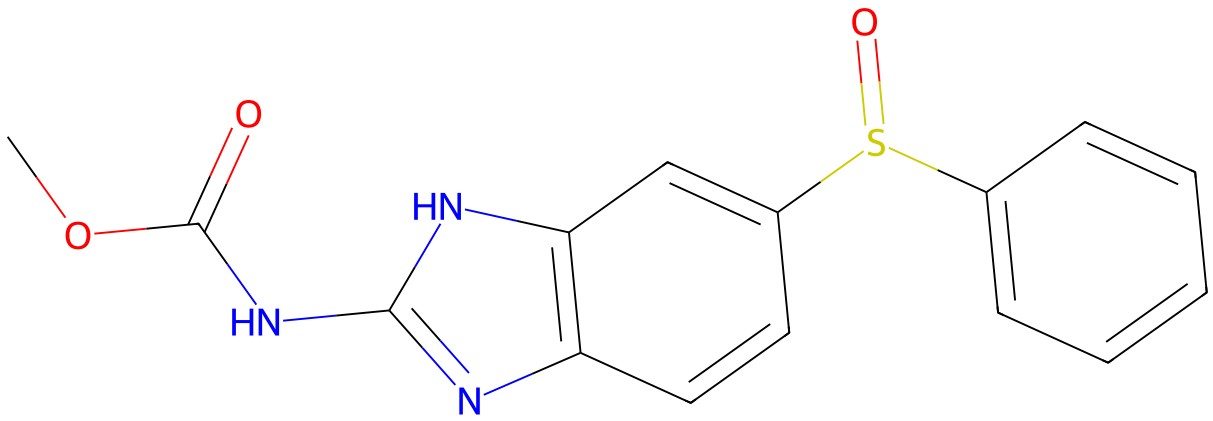
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 58

Original entry text

58. ARF-DSF-3 · pyrrolidine dithiocarbamate disulfide
— Cu redox, constrained amine
C10H16N2S4 · MW 292.5 · clogP 3.13 · TPSA 6.5 Å² · HBD 0 · RotB 0
S=C(SSC(=S)N1CCCC1)N1CCCC1

59. ARF-OXF-S · oxfendazole (reference, human PhI)



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 59. ARF-OXF-S · oxfendazole (reference, human PhI) — benzimidazole + S redox couple. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc(S(=O)c3ccccc3)cc2[nH]1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc(S(=O)c3ccccc3)cc2[nH]1

Complete computed profile

Formula	C15H13N3O3S
Molecular weight (g/mol)	315.354
Exact mass (Da)	315.067762
Crippen cLogP	2.9079
TPSA (Å²)	84.08
H-bond donors	2
H-bond acceptors	4
Rotatable bonds	3
Rings	3
Formal charge	0
Heavy atoms	22

Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

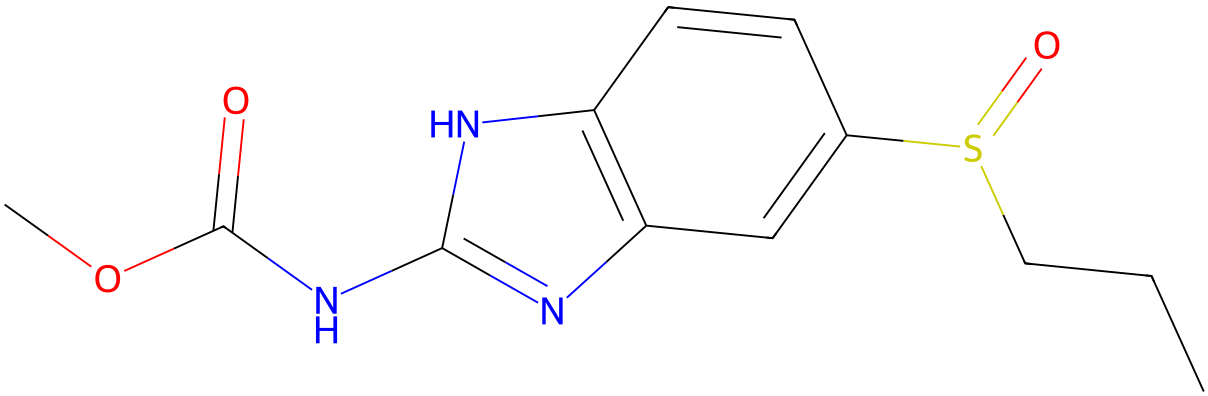
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 59

Original entry text

59. ARF-OXF-S · oxfendazole (reference, human PhI)
— benzimidazole + S redox couple
C15H13N3O3S · MW 315.4 · clogP 2.91 · TPSA 84.1 Å² · HBD 2 · RotB 3
COC(=O)Nc1nc2ccc(S(=O)c3ccccc3)cc2[nH]1

60. ARF-ALB-S · albendazole sulfoxide / ricobendazole



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 60. ARF-ALB-S · albendazole sulfoxide / ricobendazole (reference) — benzimidazole + S redox couple. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

CCCS(=O)c1ccc2[nH]c(NC(=O)OC)nc2c1

Canonical isomeric SMILES — RDKit 2026.09.1

CCCS(=O)c1ccc2[nH]c(NC(=O)OC)nc2c1

Complete computed profile

Formula	C12H15N3O3S
Molecular weight (g/mol)	281.337
Exact mass (Da)	281.083412
Crippen cLogP	2.2588
TPSA (Å²)	84.08
H-bond donors	2
H-bond acceptors	4
Rotatable bonds	4
Rings	2
Formal charge	0
Heavy atoms	19

Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 4 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

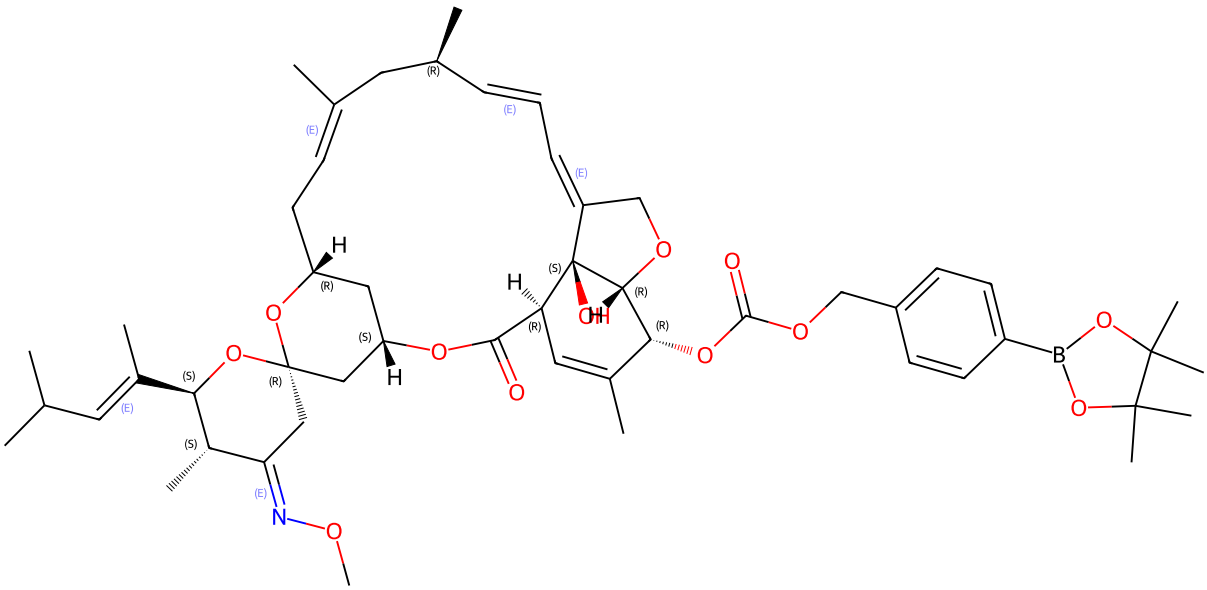
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 60

Original entry text

60. ARF-ALB-S · albendazole sulfoxide / ricobendazole (reference) — benzimidazole + S redox couple
C12H15N3O3S · MW 281.3 · clogP 2.26 · TPSA 84.1 Å² · HBD 2 · RotB 4
CCCS(=O)c1ccc2[nH]c(NC(=O)OC)nc2c1
6 · Contributed — Eve 3.8, Planet 85
Conditional-release designs. A linker cleaved by hydrogen peroxide releases
payload only where the oxidant is already elevated, so the

pathology supplies its own trigger.

61. ARF-MOX-E1 · Boronate self-immolative, H2O2-



Recorded rationale and role

Conditional-release / oxidant-response design. The encoded boron-containing handle supports an activation hypothesis to compare with a trigger-free analogue and the released payload. Original entry heading: 61. ARF-MOX-E1 · Boronate self-immolative, H2O2- triggered. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Characterize the trigger-bearing material, its stability and the identity of release products. Compare activation with more

than one oxidant and distinguish carbonate/ester release from intact-conjugate effects.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)OCc6ccc(B7OC(C)(C)C(C)
(C)O7)cc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)OCc6ccc(B7OC(C)(C)C(C)
(C)O7)cc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C51H70BNO12
Molecular weight (g/mol)	899.928
Exact mass (Da)	899.499107
Crippen cLogP	8.3892
TPSA (Å²)	149.8
H-bond donors	1

H-bond acceptors	13
Rotatable bonds	7
Rings	7
Formal charge	0
Heavy atoms	65
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 61

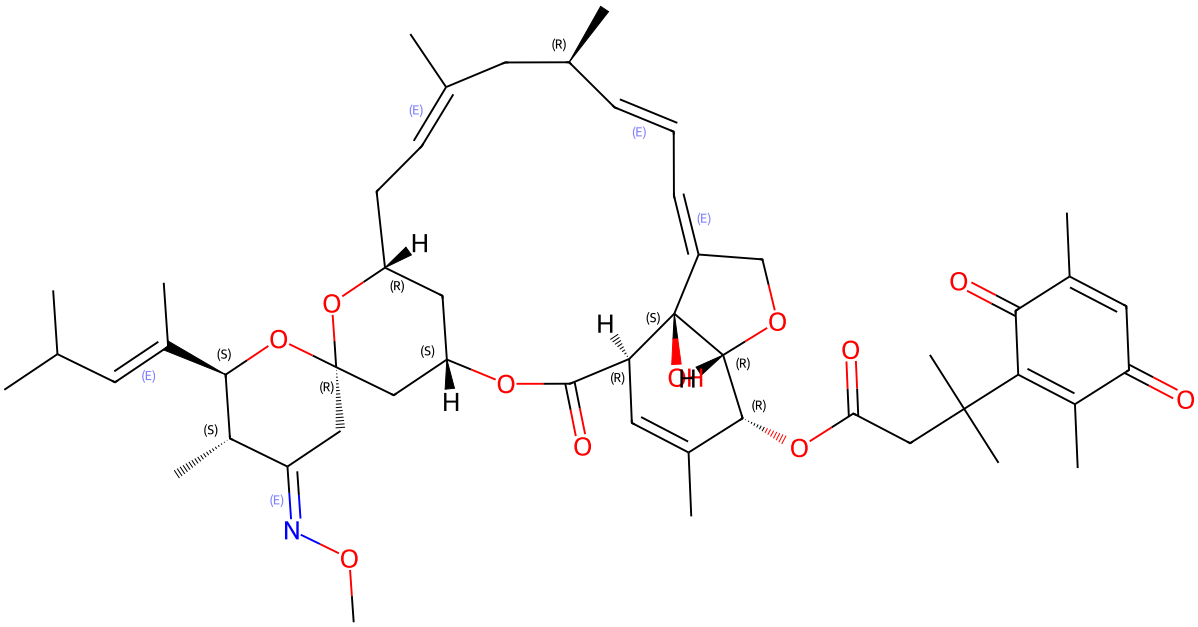
Original entry text

61. ARF-MOX-E1 · Boronate self-immolative, H2O2-triggered

C51H70BNO12 · MW 899.9 · clogP 8.39 · TPSA 149.8 Å² · HBD 1 · RotB 7

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)OCc6ccc(B7OC(C)(C)C(C)(C)O7)cc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

62. ARF-MOX-E2 · NQO1-responsive trimethyllock



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 62. ARF-MOX-E2 · NQO1-responsive trimethyllock quinone ester. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC(C)
(C)C6=C(C)C(=O)C=C(C)C6=O)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC(C)
(C)C6=C(C)C(=O)C=C(C)C6=O)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C50H67NO11
Molecular weight (g/mol)	858.082
Exact mass (Da)	857.471412
Crippen cLogP	8.1107
TPSA (Å²)	156.25
H-bond donors	1

H-bond acceptors	12
Rotatable bonds	7
Rings	6
Formal charge	0
Heavy atoms	62
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 62

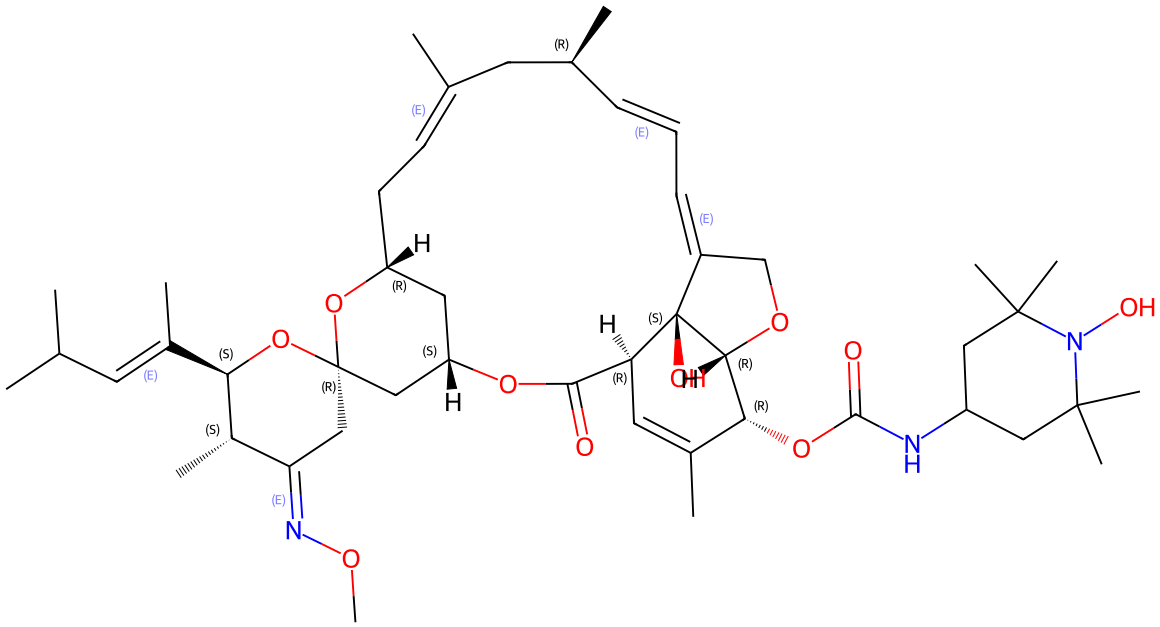
Original entry text

62. ARF-MOX-E2 · NQO1-responsive trimethyllock quinone ester

C50H67NO11 · MW 858.1 · clogP 8.11 · TPSA 156.2 Å² · HBD 1 · RotB 7

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CC(C)(C)C6=C(C)C(=O)C=C(C)C6=O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

63. ARF-MOX-E3 · Mitochondria-targeted nitroxide



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 63. ARF-MOX-E3 · Mitochondria-targeted nitroxide (TEMPO) hybrid. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC6CC(C)(C)N(O)C(C)(C)C6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC6CC(C)(C)N(O)C(C)(C)C6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C47H71N3O10
Molecular weight (g/mol)	838.096
Exact mass (Da)	837.513945
Crippen cLogP	7.8736
TPSA (Å²)	157.61
H-bond donors	3
H-bond acceptors	12
Rotatable bonds	5

Rings	6
Formal charge	0
Heavy atoms	60
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 5 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

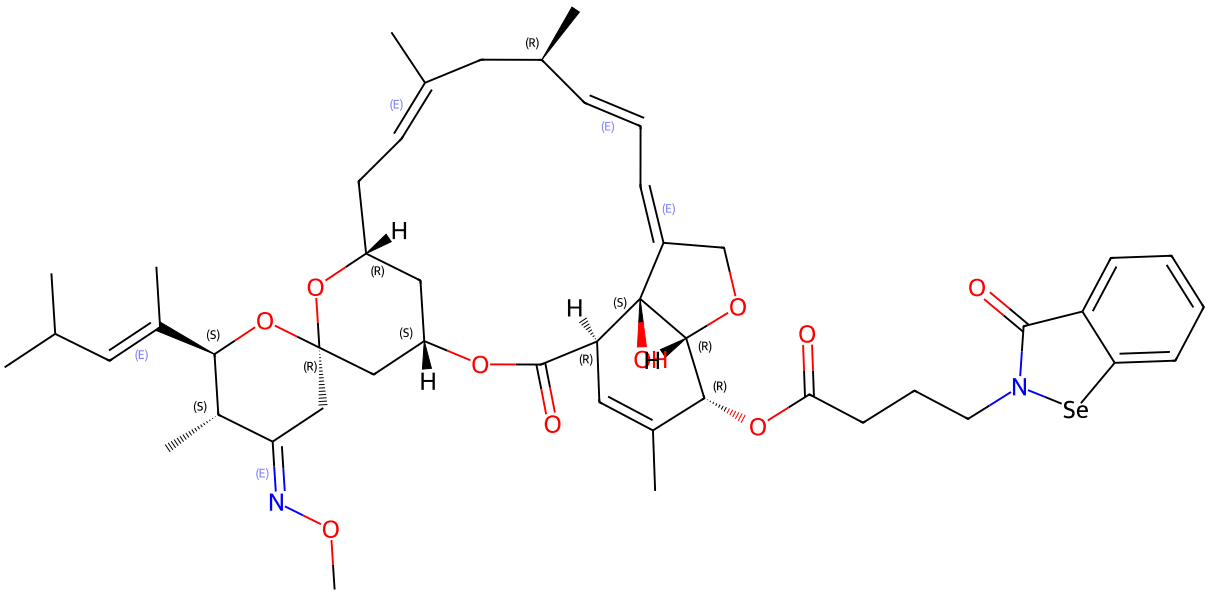
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 63

Original entry text

63. ARF-MOX-E3 · Mitochondria-targeted nitroxide (TEMPO) hybrid
C47H71N3O10 · MW 838.1 · clogP 7.87 · TPSA 157.6 Å² · HBD 3 · RotB 5
CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]

(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NC6CC(C)(C)N(O)C(C)(C)C6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

64. ARF-MOX-E4 · Ebselen-type organoselenium



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 64. ARF-MOX-E4 · Ebselen-type organoselenium hybrid. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCn6[se]c7ccccc7c6=O)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCn6[se]c7ccccc7c6=O)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C48H62N2O10Se
Molecular weight (g/mol)	905.988
Exact mass (Da)	906.356967
Crippen cLogP	7.1321
TPSA (Å²)	144.11
H-bond donors	1
H-bond acceptors	11
Rotatable bonds	8

Rings	7
Formal charge	0
Heavy atoms	61
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 8 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 64

Original entry text

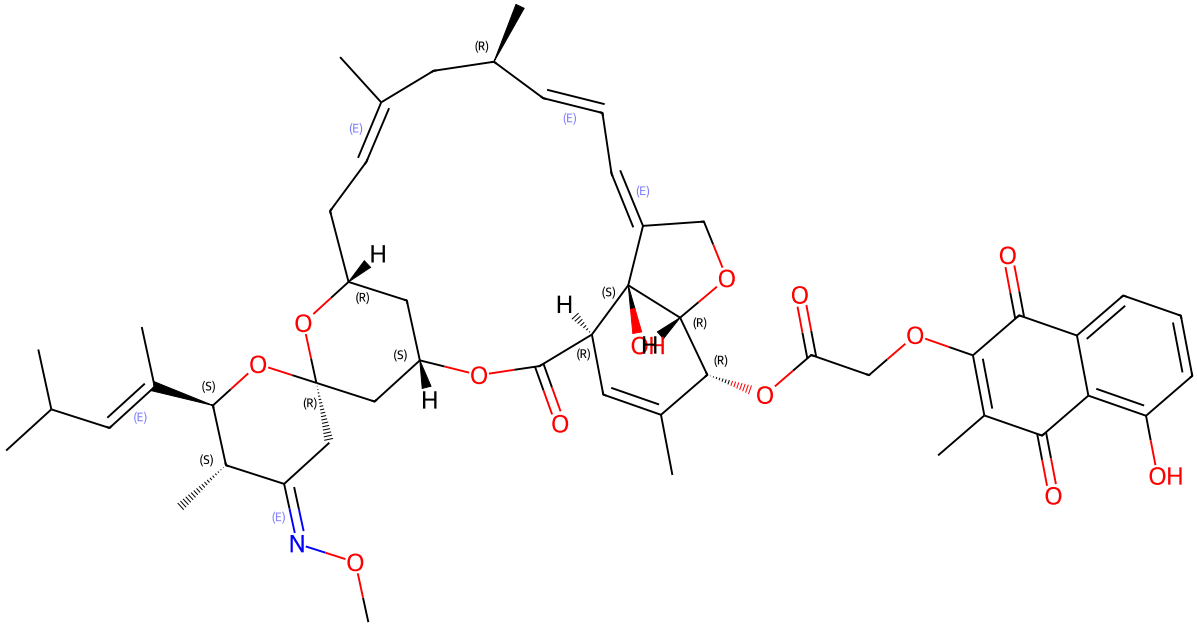
64. ARF-MOX-E4 · Ebselen-type organoselenium hybrid
C48H62N2O10Se · MW 906.0 · clogP 7.13 · TPSA 144.1 Å² · HBD 1 · RotB 8
CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]

(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCn6[se]c7ccccc7c6=O)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

7 · Additions

Completing the quinone grid: menadione carries the 2-methyl, the juglone-type
warhead the 5-hydroxy, and this one both.

65. ARF-MOX-C5 · Plumbagin glycolate



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 65. ARF-MOX-C5 · Plumbagin glycolate C50H61NO13 · MW 884.0 · clogP 7.36 · TPSA 185.7 Å² · HBD 2 · RotB 7. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)COC6=C(C)C(=O)c7c(O)cccc7C6=O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)COC6=C(C)C(=O)c7c(O)cccc7C6=O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C50H61NO13
Molecular weight (g/mol)	884.032
Exact mass (Da)	883.414291
Crippen cLogP	7.3552
TPSA (Å²)	185.71
H-bond donors	2
H-bond acceptors	14
Rotatable bonds	7

Rings	7
Formal charge	0
Heavy atoms	64
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 65

Original entry text

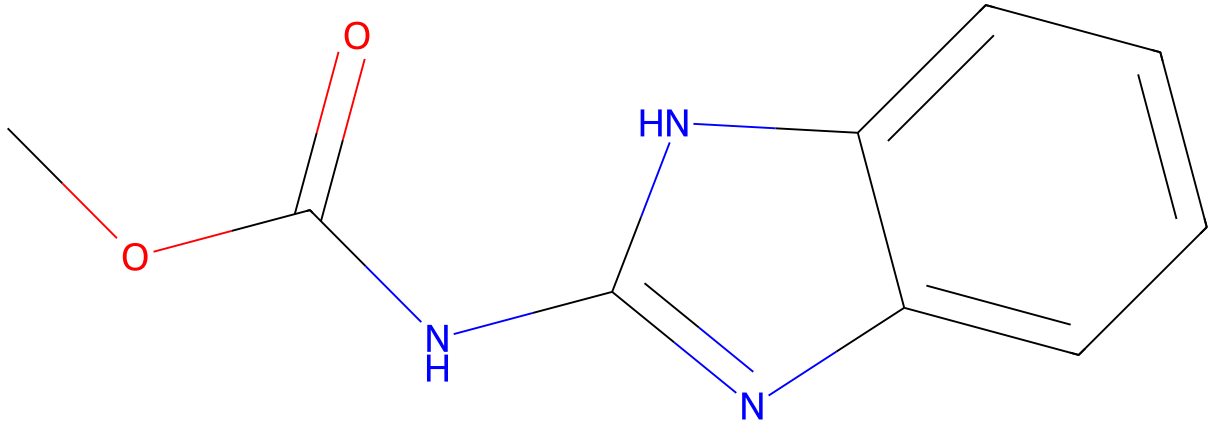
65. ARF-MOX-C5 · Plumbagin glycolate
C50H61NO13 · MW 884.0 · clogP 7.36 · TPSA 185.7 Å² · HBD 2 · RotB 7
CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]

(OC(=O)COC6=C(C)C(=O)c7c(O)cccc7C6=O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

8 · Building blocks

Linker precursors, free warheads, parent scaffolds and stereoisomers, so every
intermediate in the series is machine readable.

66. C9H9N3O2



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 66. C9H9N3O2 . Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccccc2[nH]1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccccc2[nH]1

Complete computed profile

Formula	C9H9N3O2
Molecular weight (g/mol)	191.19
Exact mass (Da)	191.069477
Crippen cLogP	1.7412
TPSA (Å²)	67.01
H-bond donors	2
H-bond acceptors	3
Rotatable bonds	1
Rings	2
Formal charge	0
Heavy atoms	14
Unassigned stereo — modern	0

Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 1 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

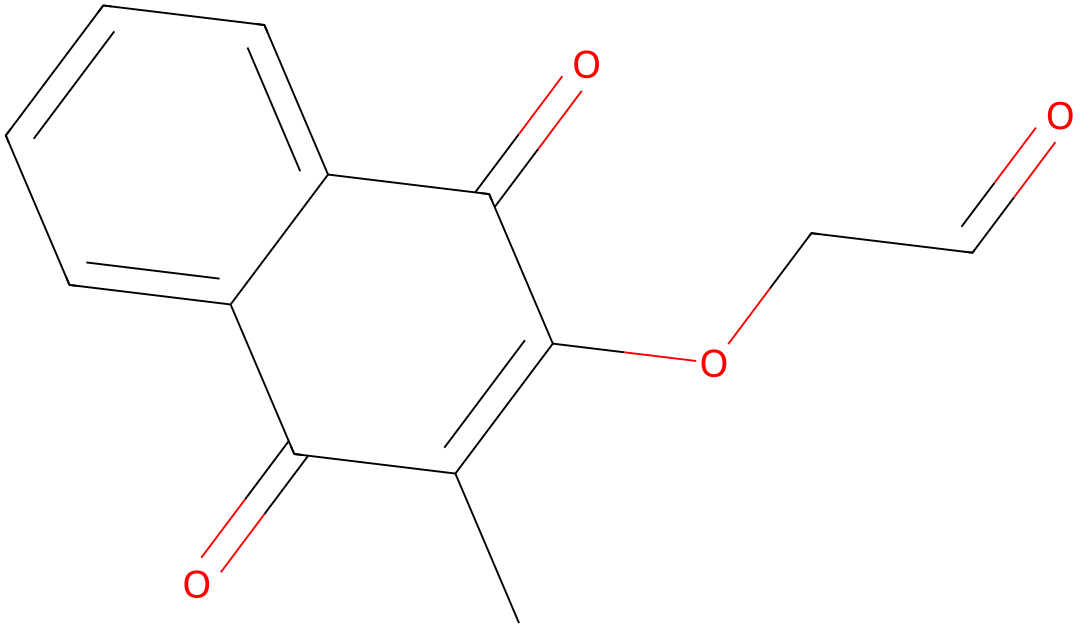
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 66

Original entry text

66. C9H9N3O2

C9H9N3O2 · MW 191.2 · clogP 1.74 · TPSA 67.0 Å² · HBD 2 · RotB 1
COC(=O)Nc1nc2ccccc2[nH]1

67. C13H10O4



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 67. C13H10O4 C13H10O4 · MW 230.2 · clogP 1.56 · TPSA 60.4 Å² · HBD 0 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CC1=C(OCC=O)C(=O)c2ccccc2C1=O

Canonical isomeric SMILES — RDKit 2026.09.1

CC1=C(OCC=O)C(=O)c2ccccc2C1=O

Complete computed profile

Formula	C13H10O4
Molecular weight (g/mol)	230.219
Exact mass (Da)	230.057909
Crippen cLogP	1.5551
TPSA (Å²)	60.44
H-bond donors	0
H-bond acceptors	4
Rotatable bonds	3
Rings	2
Formal charge	0
Heavy atoms	17

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

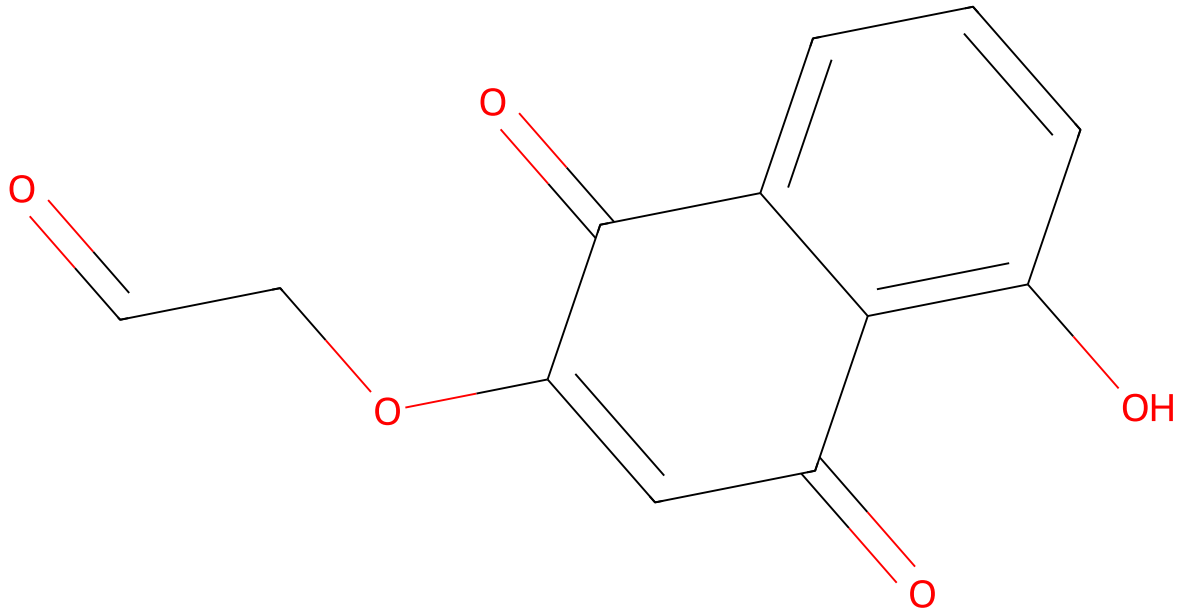
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 67

Original entry text

67. C13H10O4
C13H10O4 · MW 230.2 · clogP 1.56 · TPSA 60.4 Å² · HBD 0 · RotB 3
CC1=C(OCC=O)C(=O)c2ccccc2C1=O

68. C12H8O5



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 68. C12H8O5 C12H8O5 · MW 232.2 · clogP 0.87 · TPSA 80.7 Å² · HBD 1 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

O=CCOC1=CC(=O)c2c(O)cccc2C1=O

Canonical isomeric SMILES — RDKit 2026.09.1

O=CCOC1=CC(=O)c2c(O)cccc2C1=O

Complete computed profile

Formula	C12H8O5
Molecular weight (g/mol)	232.191
Exact mass (Da)	232.037173
Crippen cLogP	0.8706
TPSA (Å²)	80.67
H-bond donors	1
H-bond acceptors	5
Rotatable bonds	3
Rings	2
Formal charge	0
Heavy atoms	17

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

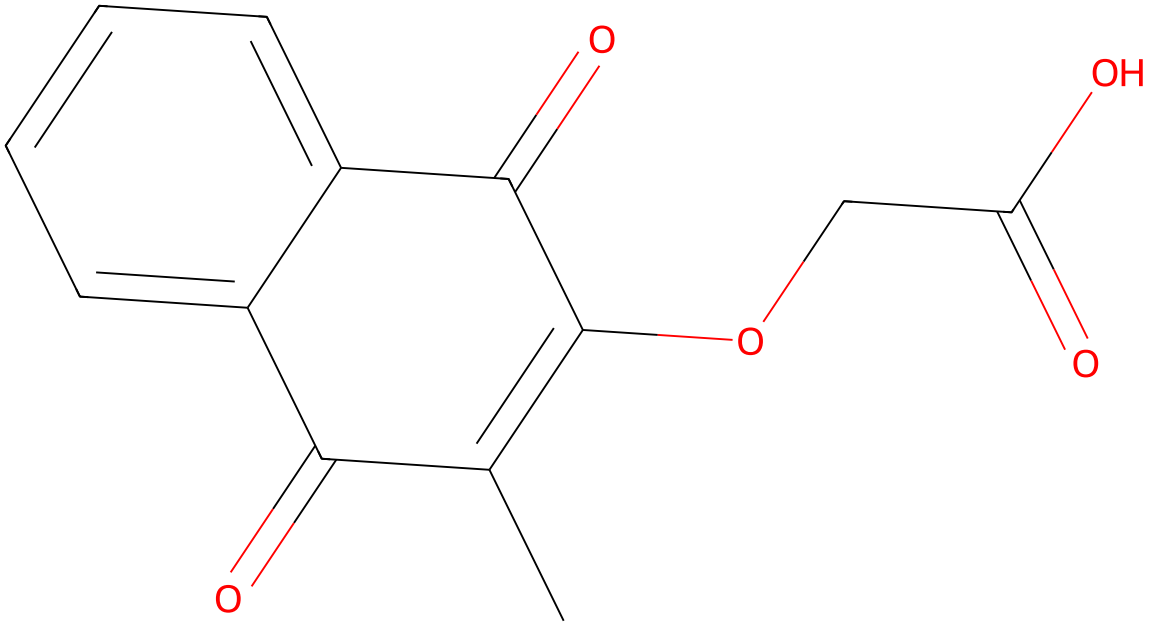
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 68

Original entry text

68. C12H8O5
C12H8O5 · MW 232.2 · clogP 0.87 · TPSA 80.7 Å² · HBD 1 · RotB 3
O=CCOC1=CC(=O)c2c(O)cccc2C1=O

69. C13H10O5



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 69. C13H10O5 C13H10O5 · MW 246.2 · clogP 1.44 · TPSA 80.7 Å² · HBD 1 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CC1=C(OCC(=O)O)C(=O)c2ccccc2C1=O

Canonical isomeric SMILES — RDKit 2026.09.1

CC1=C(OCC(=O)O)C(=O)c2ccccc2C1=O

Complete computed profile

Formula	C13H10O5
Molecular weight (g/mol)	246.218
Exact mass (Da)	246.052823
Crippen cLogP	1.4408
TPSA (Å²)	80.67
H-bond donors	1
H-bond acceptors	4
Rotatable bonds	3
Rings	2
Formal charge	0
Heavy atoms	18

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

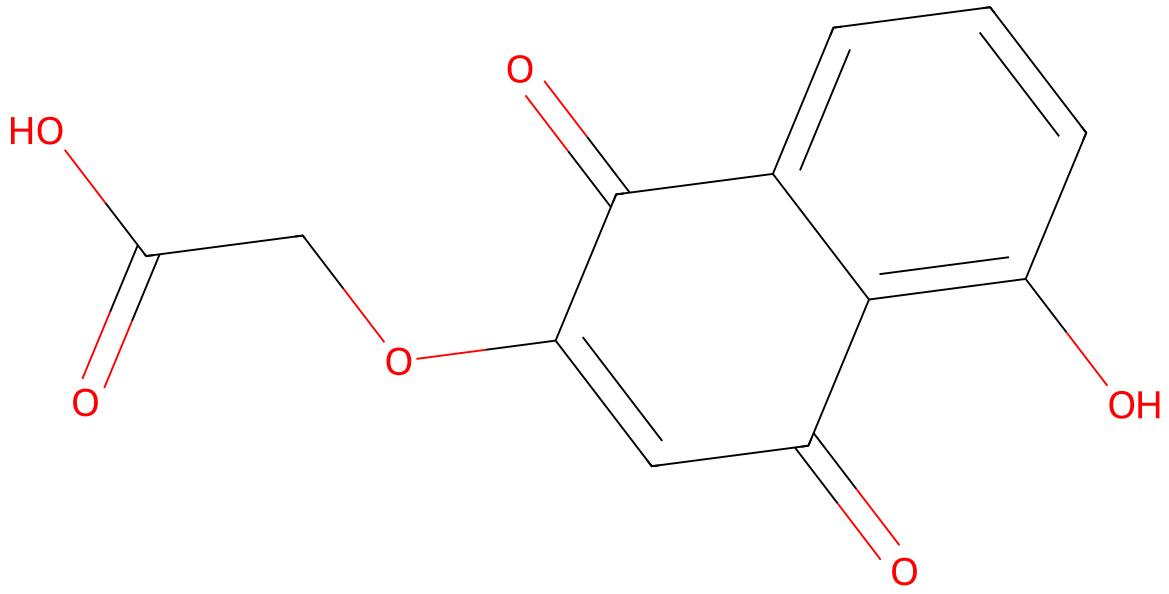
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 69

Original entry text

69. C13H10O5
C13H10O5 · MW 246.2 · clogP 1.44 · TPSA 80.7 Å² · HBD 1 · RotB 3
CC1=C(OCC(=O)O)C(=O)c2ccccc2C1=O

70. C12H8O6



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 70. C12H8O6 C12H8O6 · MW 248.2 · clogP 0.76 · TPSA 100.9 Å² · HBD 2 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

O=C(O)COC1=CC(=O)c2c(O)cccc2C1=O

Canonical isomeric SMILES — RDKit 2026.09.1

O=C(O)COC1=CC(=O)c2c(O)cccc2C1=O

Complete computed profile

Formula	C12H8O6
Molecular weight (g/mol)	248.19
Exact mass (Da)	248.032088
Crippen cLogP	0.7563
TPSA (Å²)	100.9
H-bond donors	2
H-bond acceptors	5
Rotatable bonds	3
Rings	2
Formal charge	0
Heavy atoms	18

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

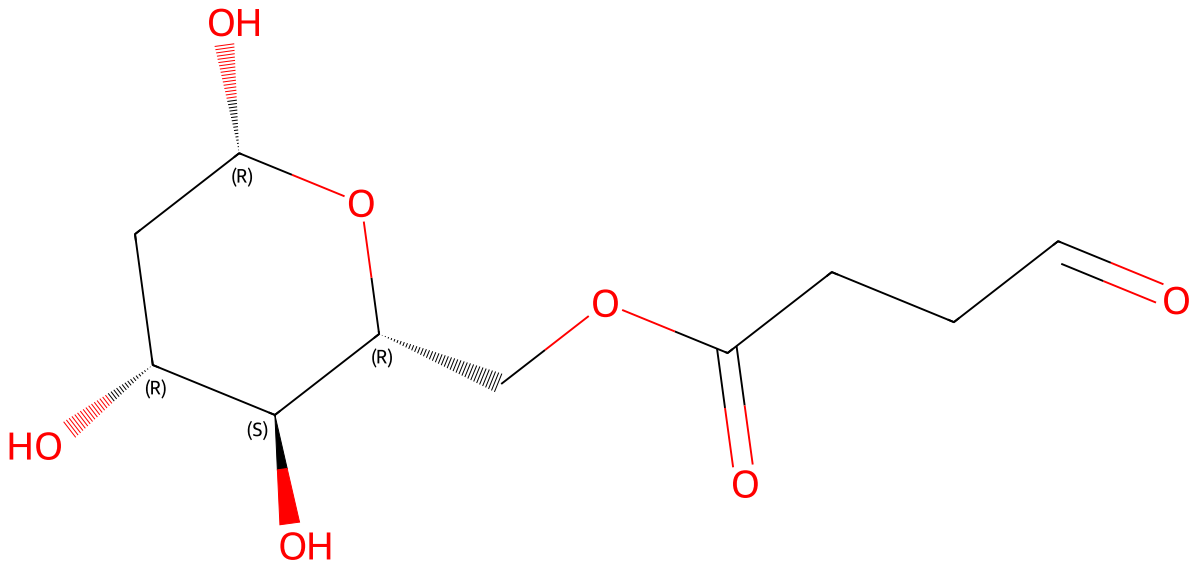
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 70

Original entry text

70. C12H8O6
C12H8O6 · MW 248.2 · clogP 0.76 · TPSA 100.9 Å² · HBD 2 · RotB 3
O=C(O)COC1=CC(=O)c2c(O)cccc2C1=O

71. C10H16O7



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 71. C10H16O7 C10H16O7 · MW 248.2 · clogP -1.66 · TPSA 113.3 Å² · HBD 3 · RotB 5. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

O=CCCC(=O)OC[C@H]1O[C@@H](O)C[C@@H](O)[C@@H]1O

Canonical isomeric SMILES — RDKit 2026.09.1

O=CCCC(=O)OC[C@H]1O[C@@H](O)C[C@@H](O)[C@@H]1O

Complete computed profile

Formula	C10H16O7
Molecular weight (g/mol)	248.231
Exact mass (Da)	248.089603
Crippen cLogP	-1.6622
TPSA (Å²)	113.29
H-bond donors	3
H-bond acceptors	7
Rotatable bonds	5
Rings	1
Formal charge	0

Heavy atoms	17
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 5 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

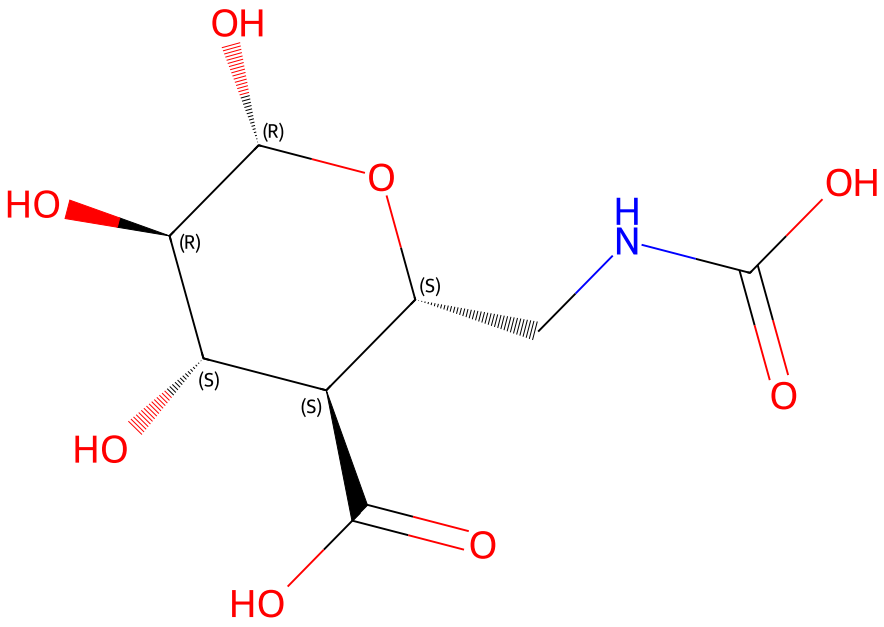
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 71

Original entry text

71. C10H16O7
C10H16O7 · MW 248.2 · clogP -1.66 · TPSA 113.3 Å² · HBD 3 · RotB 5
O=CCCC(=O)OC[C@H]1O[C@@H](O)C[C@@H](O)[C@@H]1O

72. C8H13NO8



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 72. C8H13NO8 C8H13NO8 · MW 251.2 · clogP -2.61 · TPSA 156.6 Å² · HBD 6 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

O=C(O)NC[C@H]1O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]1C(=O)O

Canonical isomeric SMILES — RDKit 2026.09.1

O=C(O)NC[C@H]1O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]1C(=O)O

Complete computed profile

Formula	C8H13NO8
Molecular weight (g/mol)	251.191
Exact mass (Da)	251.064116
Crippen cLogP	-2.6062
TPSA (Å²)	156.55
H-bond donors	6
H-bond acceptors	6
Rotatable bonds	3
Rings	1
Formal charge	0

Heavy atoms	17
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

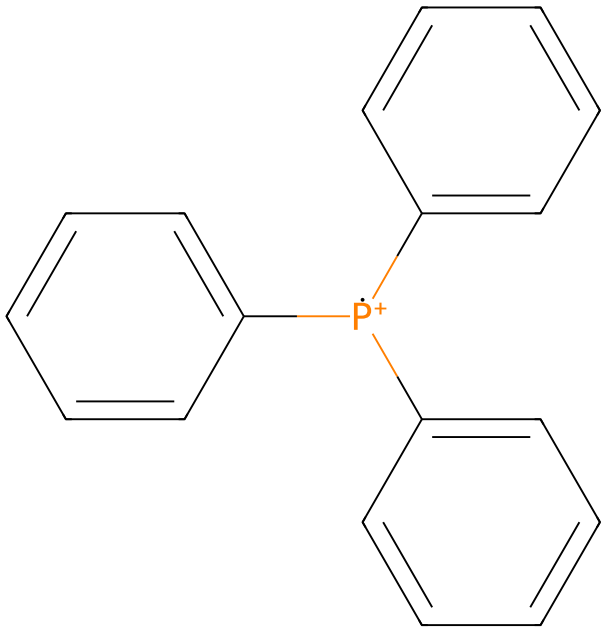
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 72

Original entry text

72. C8H13NO8
C8H13NO8 · MW 251.2 · clogP -2.61 · TPSA 156.6 Å² · HBD 6 · RotB 3
O=C(O)NC[C@H]1O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]1C(=O)O

73. C18H15P+



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Original entry heading: 73. C18H15P+ C18H15P+ · MW 262.3 · clogP 3.44 · TPSA 0.0 Å² · HBD 0 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

c1ccc([P+](c2ccccc2)c2ccccc2)cc1

Canonical isomeric SMILES — RDKit 2026.09.1

c1ccc([P+](c2ccccc2)c2ccccc2)cc1

Complete computed profile

Formula	C18H15P+
Molecular weight (g/mol)	262.292
Exact mass (Da)	262.090589
Crippen cLogP	3.4448
TPSA (Å²)	0.0
H-bond donors	0
H-bond acceptors	0
Rotatable bonds	3
Rings	3
Formal charge	1
Heavy atoms	19

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

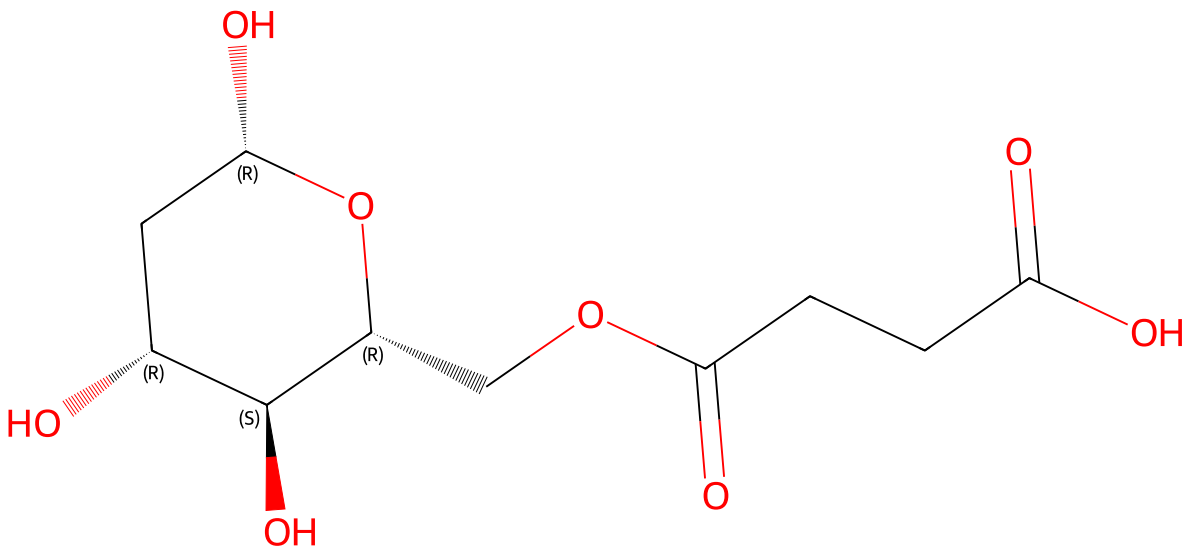
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 73

Original entry text

73. C18H15P+
C18H15P+ · MW 262.3 · clogP 3.44 · TPSA 0.0 Å² · HBD 0 · RotB 3
c1ccc([P+](c2ccccc2)c2ccccc2)cc1

74. C10H16O8 (stereoisomer 1 of 2)



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 74. C10H16O8 (stereoisomer 1 of 2) C10H16O8 · MW 264.2 · clogP -1.78 · TPSA 133.5 Å² · HBD 4 · RotB 5. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

O=C(O)CCC(=O)OC[C@H]1O[C@@H](O)C[C@@H](O)[C@@H]1O

Canonical isomeric SMILES — RDKit 2026.09.1

O=C(O)CCC(=O)OC[C@H]1O[C@@H](O)C[C@@H](O)[C@@H]1O

Complete computed profile

Formula	C10H16O8
Molecular weight (g/mol)	264.23
Exact mass (Da)	264.084517
Crippen cLogP	-1.7765
TPSA (Å²)	133.52
H-bond donors	4
H-bond acceptors	7
Rotatable bonds	5
Rings	1
Formal charge	0

Heavy atoms	18
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 5 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

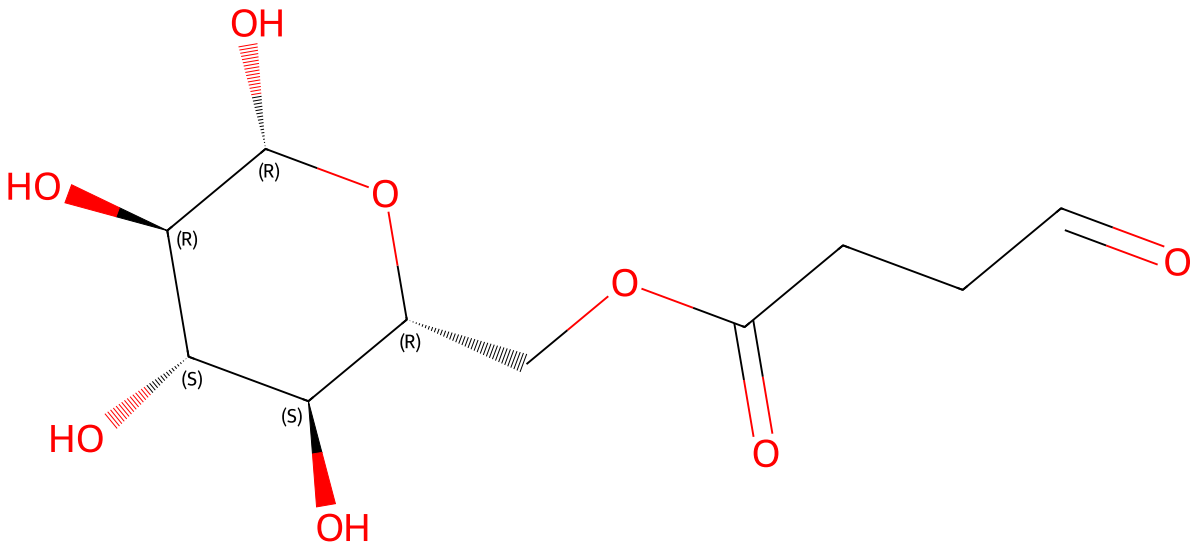
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 74

Original entry text

74. C10H16O8 (stereoisomer 1 of 2)
C10H16O8 · MW 264.2 · clogP -1.78 · TPSA 133.5 Å² · HBD 4 · RotB 5
O=C(O)CCC(=O)OC[C@H]1O[C@@H](O)C[C@@H](O)[C@@H]1O

75. C10H16O8 (stereoisomer 2 of 2)



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 75. C10H16O8 (stereoisomer 2 of 2) C10H16O8 · MW 264.2 · clogP -2.69 · TPSA 133.5 Å² · HBD 4 · RotB 5. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

O=CCCC(=O)OC[C@H]1O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]1O

Canonical isomeric SMILES — RDKit 2026.09.1

O=CCCC(=O)OC[C@H]1O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]1O

Complete computed profile

Formula	C10H16O8
Molecular weight (g/mol)	264.23
Exact mass (Da)	264.084517
Crippen cLogP	-2.6914
TPSA (Å²)	133.52
H-bond donors	4
H-bond acceptors	8
Rotatable bonds	5
Rings	1
Formal charge	0

Heavy atoms	18
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 5 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

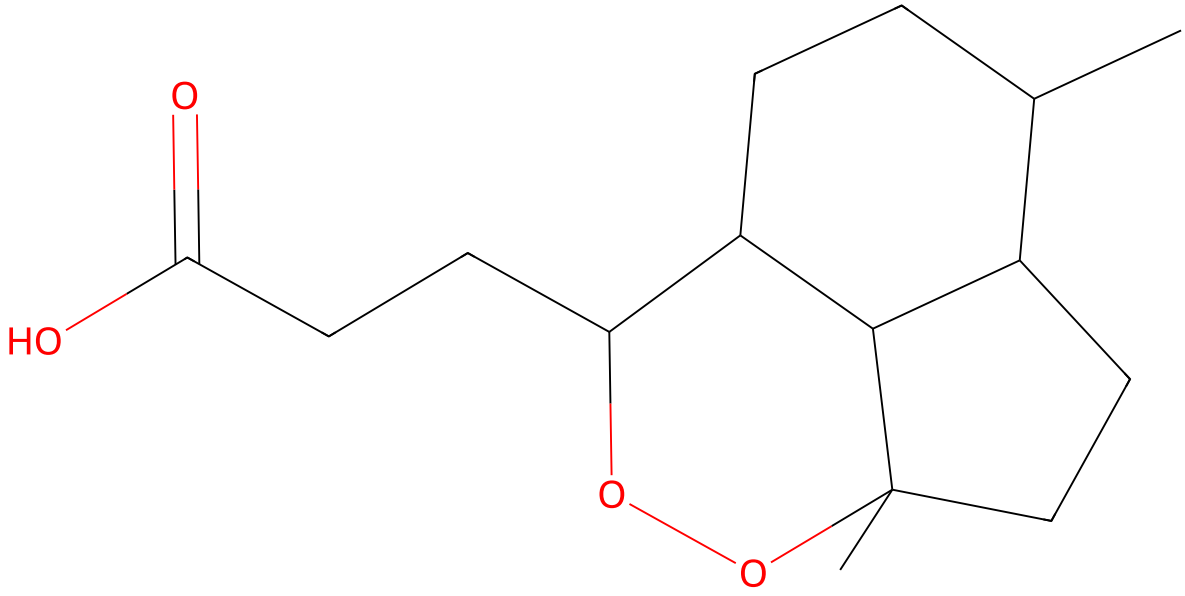
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 75

Original entry text

75. C10H16O8 (stereoisomer 2 of 2)
C10H16O8 · MW 264.2 · clogP -2.69 · TPSA 133.5 Å² · HBD 4 · RotB 5
O=CCCC(=O)OC[C@H]1O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]1O

76. C15H24O4



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 76. C15H24O4 . Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CC1CCC2C(CCC(=O)O)OOC3(C)CCC1C23

Canonical isomeric SMILES — RDKit 2026.09.1

CC1CCC2C(CCC(=O)O)OOC3(C)CCC1C23

Complete computed profile

Formula	C15H24O4
Molecular weight (g/mol)	268.353
Exact mass (Da)	268.167459
Crippen cLogP	3.0126
TPSA (Å²)	55.76
H-bond donors	1
H-bond acceptors	3
Rotatable bonds	3
Rings	3
Formal charge	0
Heavy atoms	19
Unassigned stereo — modern	6

Unassigned stereo — legacy	6

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 6 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

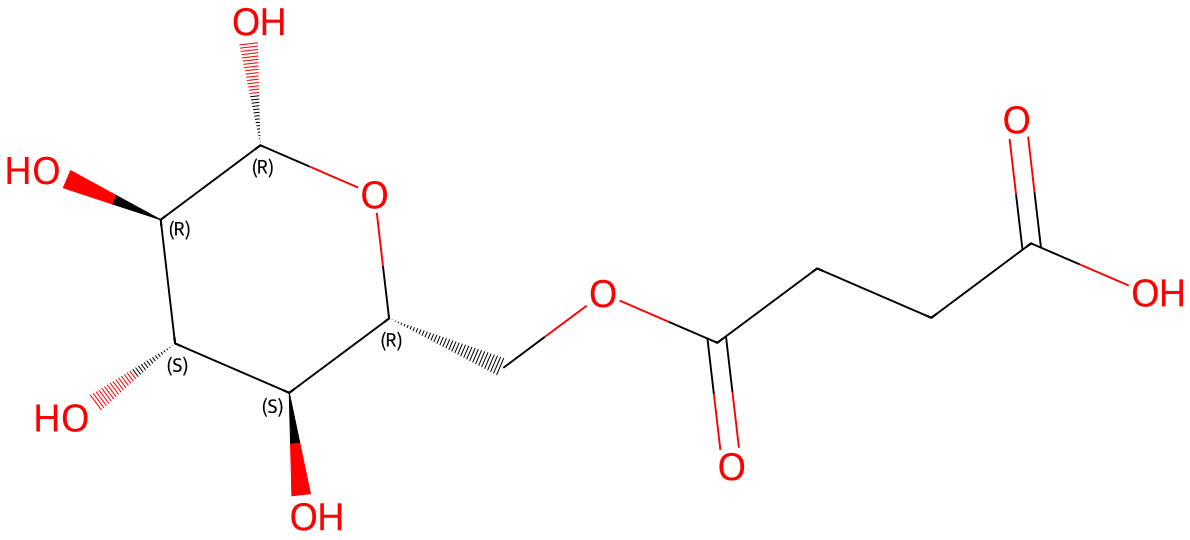
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 76

Original entry text

76. C15H24O4

C15H24O4 · MW 268.4 · clogP 3.01 · TPSA 55.8 Å² · HBD 1 · RotB 3
CC1CCC2C(CCC(=O)O)OOC3(C)CCC1C23

77. C10H16O9



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 77. C10H16O9 C10H16O9 · MW 280.2 · clogP -2.81 · TPSA 153.8 Å² · HBD 5 · RotB 5. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

O=C(O)CCC(=O)OC[C@H]1O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]1O

Canonical isomeric SMILES — RDKit 2026.09.1

O=C(O)CCC(=O)OC[C@H]1O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]1O

Complete computed profile

Formula	C10H16O9
Molecular weight (g/mol)	280.229
Exact mass (Da)	280.079432
Crippen cLogP	-2.8057
TPSA (Å²)	153.75
H-bond donors	5
H-bond acceptors	8
Rotatable bonds	5
Rings	1
Formal charge	0

Heavy atoms	19
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 5 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

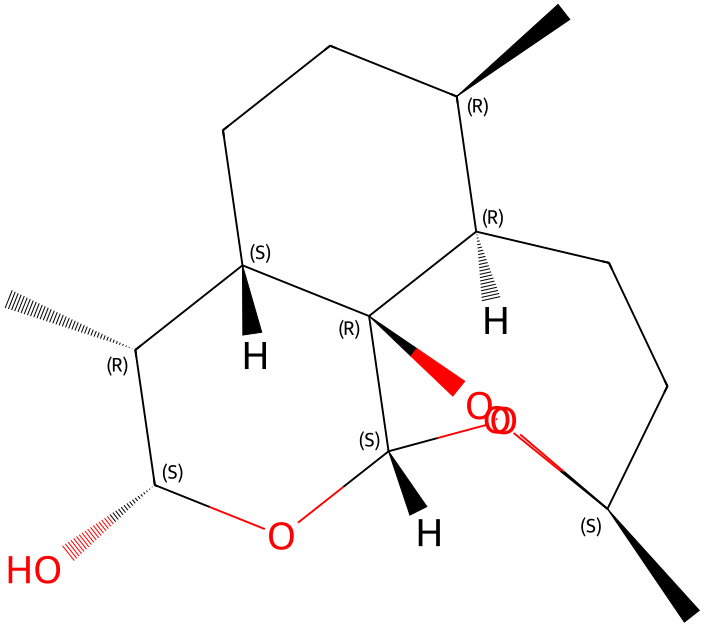
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 77

Original entry text

77. C10H16O9
C10H16O9 · MW 280.2 · clogP -2.81 · TPSA 153.8 Å² · HBD 5 · RotB 5
O=C(O)CCC(=O)OC[C@H]1O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]1O

78. C15H24O5 (stereoisomer 1 of 3)



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 78. C15H24O5 (stereoisomer 1 of 3) C15H24O5 · MW 284.4 · clogP 2.19 · TPSA 57.2 Å² · HBD 1 · RotB 0. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@@H](O)O[C@H]2O[C@]3(C)CC[C@@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@@H](O)O[C@H]2O[C@]3(C)CC[C@@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Complete computed profile

Formula	C15H24O5
Molecular weight (g/mol)	284.352
Exact mass (Da)	284.162374
Crippen cLogP	2.1867
TPSA (Å²)	57.15
H-bond donors	1
H-bond acceptors	5
Rotatable bonds	0
Rings	5

Formal charge	0
Heavy atoms	20
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 0 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

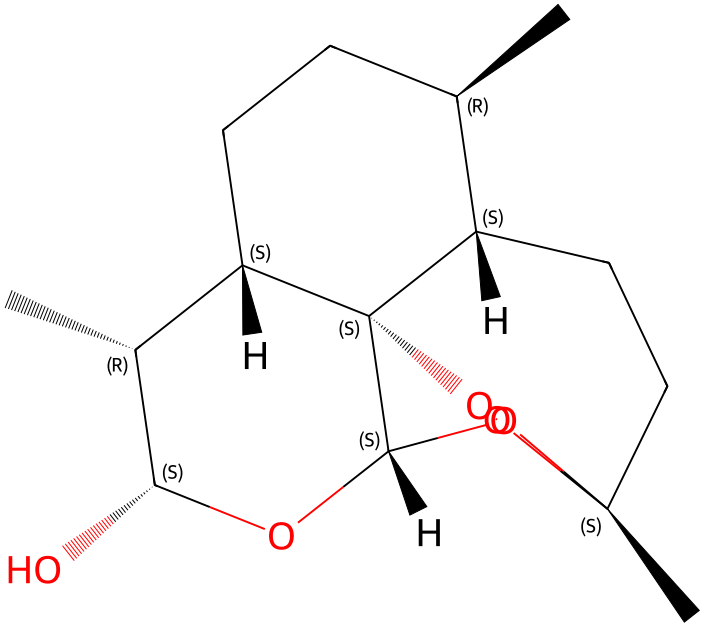
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 78

Original entry text

78. C15H24O5 (stereoisomer 1 of 3)
C15H24O5 · MW 284.4 · clogP 2.19 · TPSA 57.2 Å² · HBD 1 · RotB 0
C[C@H]1[C@@H](O)O[C@H]2O[C@]3(C)CC[C@@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

79. C15H24O5 (stereoisomer 2 of 3)



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 79. C15H24O5 (stereoisomer 2 of 3) C15H24O5 · MW 284.4 · clogP 2.19 · TPSA 57.2 Å² · HBD 1 · RotB 0. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@@H](O)O[C@H]2O[C@]3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@]24OO3

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@@H](O)O[C@H]2O[C@]3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@]24OO3

Complete computed profile

Formula	C15H24O5
Molecular weight (g/mol)	284.352
Exact mass (Da)	284.162374
Crippen cLogP	2.1867
TPSA (Å²)	57.15
H-bond donors	1
H-bond acceptors	5
Rotatable bonds	0
Rings	5
Formal charge	0

Heavy atoms	20
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 0 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

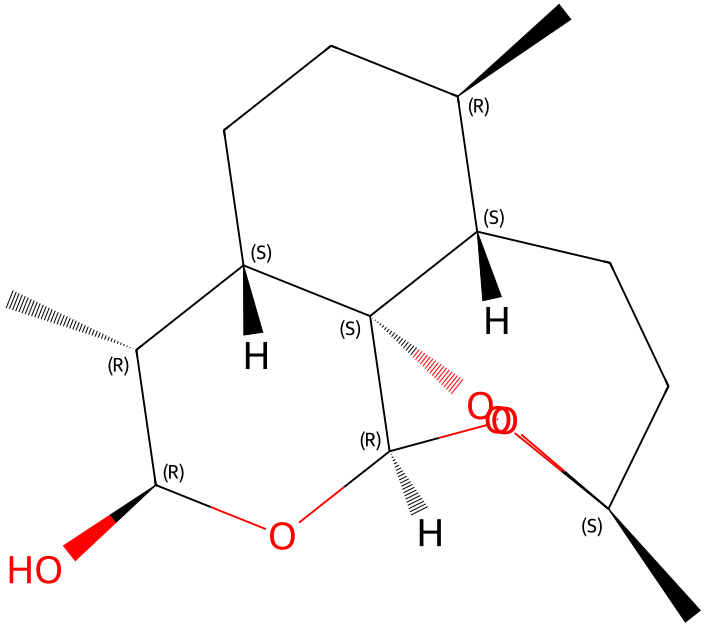
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 79

Original entry text

79. C15H24O5 (stereoisomer 2 of 3)
C15H24O5 · MW 284.4 · clogP 2.19 · TPSA 57.2 Å² · HBD 1 · RotB 0
C[C@H]1[C@@H](O)O[C@H]2O[C@]3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@]24OO3

80. C15H24O5 (stereoisomer 3 of 3)



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 80. C15H24O5 (stereoisomer 3 of 3) C15H24O5 · MW 284.4 · clogP 2.19 · TPSA 57.2 Å² · HBD 1 · RotB 0. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@H](O)O[C@@H]2O[C@]3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@]24OO3

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@H](O)O[C@@H]2O[C@]3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@]24OO3

Complete computed profile

Formula	C15H24O5
Molecular weight (g/mol)	284.352
Exact mass (Da)	284.162374
Crippen cLogP	2.1867
TPSA (Å²)	57.15
H-bond donors	1
H-bond acceptors	5
Rotatable bonds	0
Rings	5
Formal charge	0

Heavy atoms	20
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 0 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

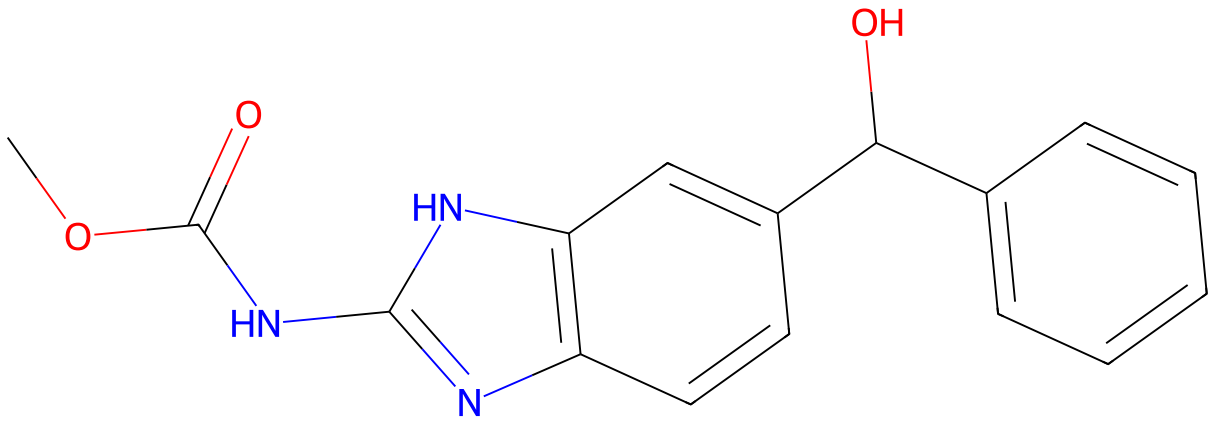
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 80

Original entry text

80. C15H24O5 (stereoisomer 3 of 3)
C15H24O5 · MW 284.4 · clogP 2.19 · TPSA 57.2 Å² · HBD 1 · RotB 0
C[C@H]1[C@H](O)O[C@@H]2O[C@]3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@]24OO3

81. C16H15N3O3



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 81. C16H15N3O3 C16H15N3O3 · MW 297.3 · clogP 2.82 · TPSA 87.2 Å² · HBD 3 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc(C(O)c3ccccc3)cc2[nH]1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc(C(O)c3ccccc3)cc2[nH]1

Complete computed profile

Formula	C16H15N3O3
Molecular weight (g/mol)	297.314
Exact mass (Da)	297.111341
Crippen cLogP	2.8229
TPSA (Å²)	87.24
H-bond donors	3
H-bond acceptors	4
Rotatable bonds	3
Rings	3
Formal charge	0
Heavy atoms	22

Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

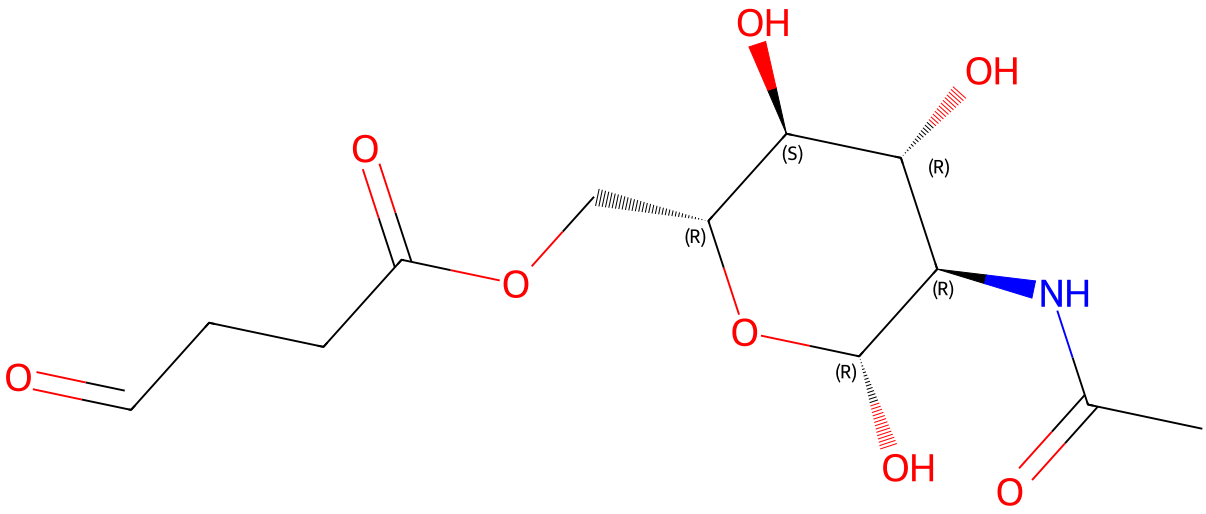
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 81

Original entry text

81. C16H15N3O3
C16H15N3O3 · MW 297.3 · clogP 2.82 · TPSA 87.2 Å² · HBD 3 · RotB 3
COC(=O)Nc1nc2ccc(C(O)c3ccccc3)cc2[nH]1

82. C12H19NO8



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 82. C12H19NO8 C12H19NO8 · MW 305.3 · clogP -2.55 · TPSA 142.4 Å² · HBD 4 · RotB 6. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CC(=O)N[C@@H]1[C@@H](O)[C@H](O)[C@@H](COC(=O)CCC=O)O[C@H]1O

Canonical isomeric SMILES — RDKit 2026.09.1

CC(=O)N[C@@H]1[C@@H](O)[C@H](O)[C@@H](COC(=O)CCC=O)O[C@H]1O

Complete computed profile

Formula	C12H19NO8
Molecular weight (g/mol)	305.283
Exact mass (Da)	305.111067
Crippen cLogP	-2.5476
TPSA (Å²)	142.39
H-bond donors	4
H-bond acceptors	8
Rotatable bonds	6
Rings	1
Formal charge	0

Heavy atoms	21
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 6 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

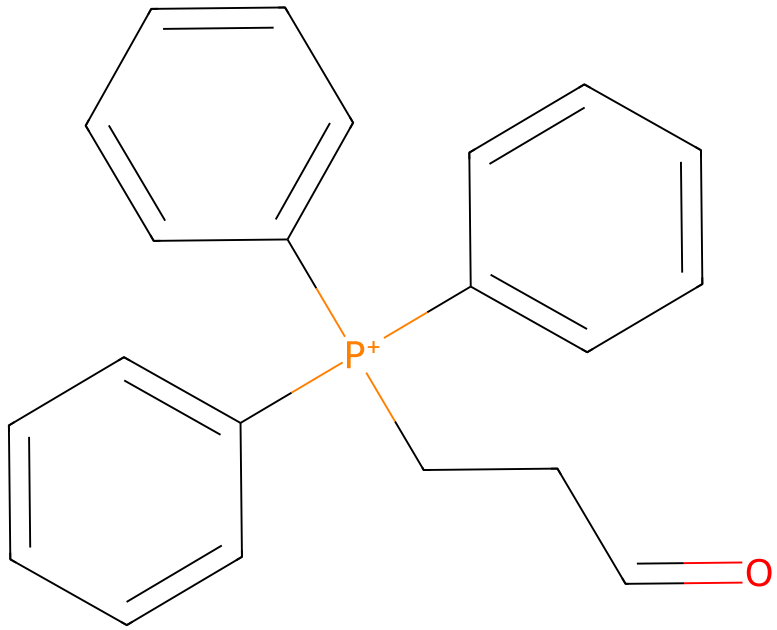
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 82

Original entry text

82. C12H19NO8
C12H19NO8 · MW 305.3 · clogP -2.55 · TPSA 142.4 Å² · HBD 4 · RotB 6
CC(=O)N[C@@H]1[C@@H](O)[C@H](O)[C@@H](COC(=O)CCC=O)O[C@H]1O

83. C21H20OP+



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Original entry heading: 83. C21H20OP+ C21H20OP+ · MW 319.4 · clogP 3.57 · TPSA 17.1 Å² · HBD 0 · RotB 6. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

O=CCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

Canonical isomeric SMILES — RDKit 2026.09.1

O=CCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

Complete computed profile

Formula	C21H20OP+
Molecular weight (g/mol)	319.364
Exact mass (Da)	319.124628
Crippen cLogP	3.5695
TPSA (Å²)	17.07
H-bond donors	0
H-bond acceptors	1
Rotatable bonds	6
Rings	3
Formal charge	1
Heavy atoms	23

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 6 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

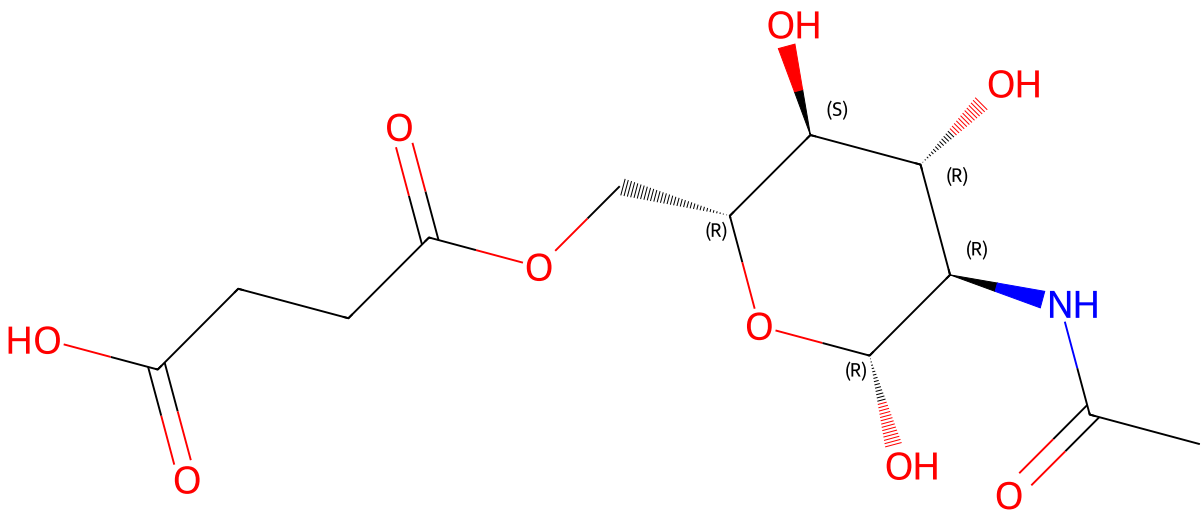
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 83

Original entry text

83. C21H20OP+
C21H20OP+ · MW 319.4 · clogP 3.57 · TPSA 17.1 Å² · HBD 0 · RotB 6
O=CCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

84. C12H19NO9



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 84. C12H19NO9 C12H19NO9 · MW 321.3 · clogP -2.66 · TPSA 162.6 Å² · HBD 5 · RotB 6. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CC(=O)N[C@@H]1[C@@H](O)[C@H](O)[C@@H](COC(=O)CCC(=O)O)O[C@H]1O

Canonical isomeric SMILES — RDKit 2026.09.1

CC(=O)N[C@@H]1[C@@H](O)[C@H](O)[C@@H](COC(=O)CCC(=O)O)O[C@H]1O

Complete computed profile

Formula	C12H19NO9
Molecular weight (g/mol)	321.282
Exact mass (Da)	321.105981
Crippen cLogP	-2.6619
TPSA (Å²)	162.62
H-bond donors	5
H-bond acceptors	8
Rotatable bonds	6
Rings	1
Formal charge	0

Heavy atoms	22
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 6 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

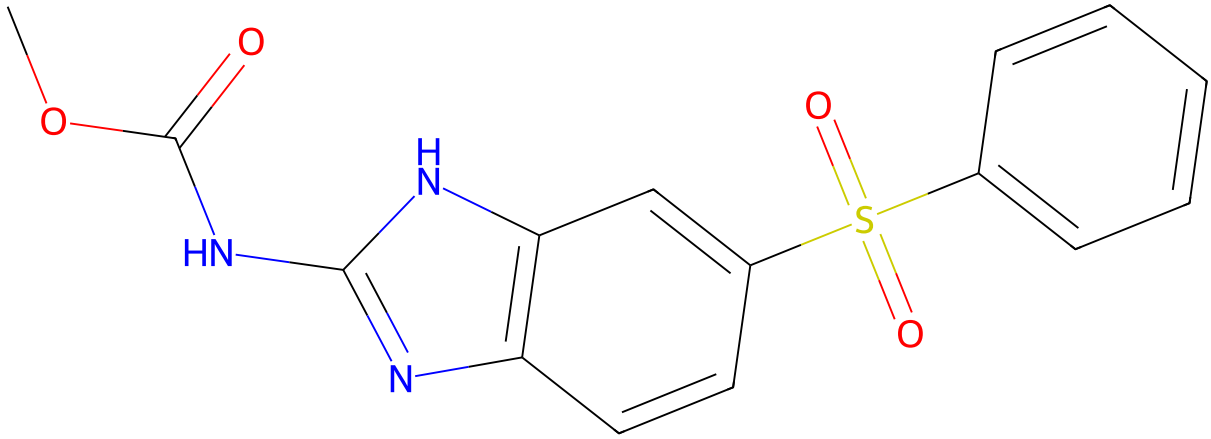
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 84

Original entry text

84. C12H19NO9
C12H19NO9 · MW 321.3 · clogP -2.66 · TPSA 162.6 Å² · HBD 5 · RotB 6
CC(=O)N[C@@H]1[C@@H](O)[C@H](O)[C@@H](COC(=O)CCC(=O)O)O[C@H]1O

85. C15H13N3O4S



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 85. C15H13N3O4S C15H13N3O4S · MW 331.4 · clogP 2.57 · TPSA 101.1 Å² · HBD 2 · RotB 3. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional

groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc(S(=O)(=O)c3ccccc3)cc2[nH]1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc(S(=O)(=O)c3ccccc3)cc2[nH]1

Complete computed profile

Formula	C15H13N3O4S
Molecular weight (g/mol)	331.353
Exact mass (Da)	331.062677
Crippen cLogP	2.574
TPSA (Å²)	101.15
H-bond donors	2
H-bond acceptors	5
Rotatable bonds	3
Rings	3
Formal charge	0
Heavy atoms	23

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 3 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

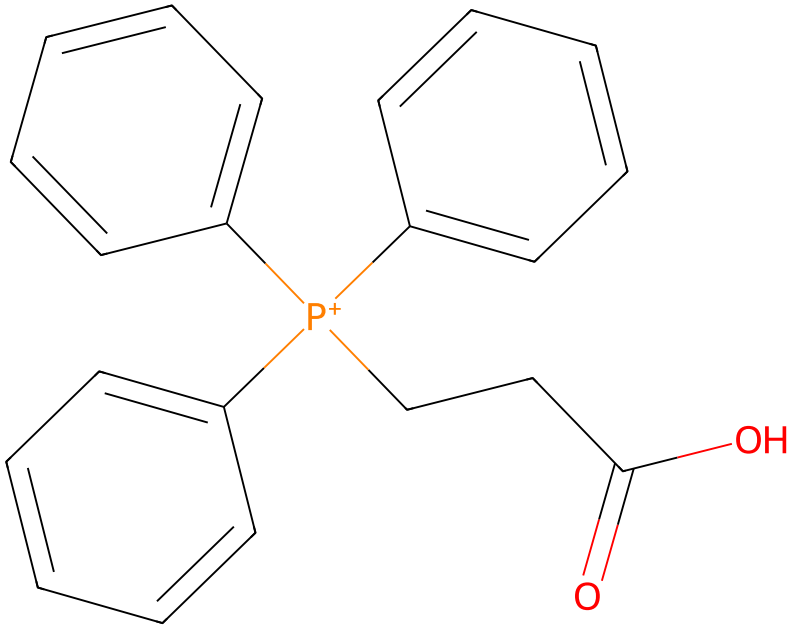
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 85

Original entry text

85. C15H13N3O4S
C15H13N3O4S · MW 331.4 · clogP 2.57 · TPSA 101.1 Å² · HBD 2 · RotB 3
COC(=O)Nc1nc2ccc(S(=O)(=O)c3ccccc3)cc2[nH]1

86. C21H20O2P+



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Original entry heading: 86. C21H20O2P+ . Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

O=C(O)CC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

Canonical isomeric SMILES — RDKit 2026.09.1

O=C(O)CC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

Complete computed profile

Formula	C21H20O2P+
Molecular weight (g/mol)	335.363
Exact mass (Da)	335.119543
Crippen cLogP	3.4552
TPSA (Å²)	37.3
H-bond donors	1
H-bond acceptors	1
Rotatable bonds	6
Rings	3
Formal charge	1
Heavy atoms	24
Unassigned stereo — modern	0

Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 6 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

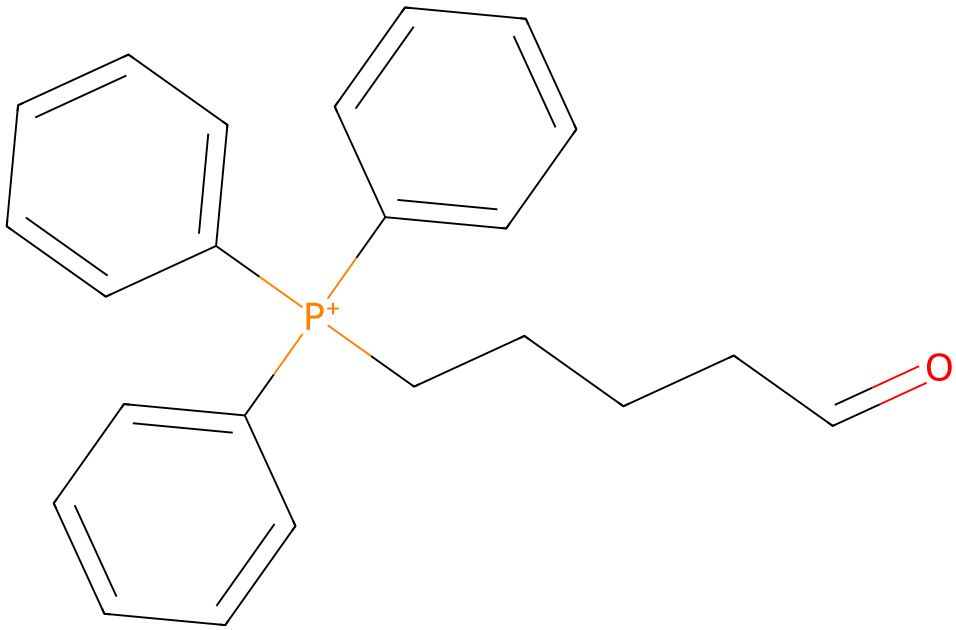
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 86

Original entry text

86. C21H20O2P+

C21H20O2P+ · MW 335.4 · clogP 3.46 · TPSA 37.3 Å² · HBD 1 · RotB 6
O=C(O)CC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

87. C23H24OP+



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Original entry heading: 87. C23H24OP+ C23H24OP+ · MW 347.4 · clogP 4.35 · TPSA 17.1 Å² · HBD 0 · RotB 8. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

O=CCCCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

Canonical isomeric SMILES — RDKit 2026.09.1

O=CCCCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

Complete computed profile

Formula	C23H24OP+
Molecular weight (g/mol)	347.418
Exact mass (Da)	347.155928
Crippen cLogP	4.3497
TPSA (Å²)	17.07
H-bond donors	0
H-bond acceptors	1
Rotatable bonds	8
Rings	3
Formal charge	1
Heavy atoms	25

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 8 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

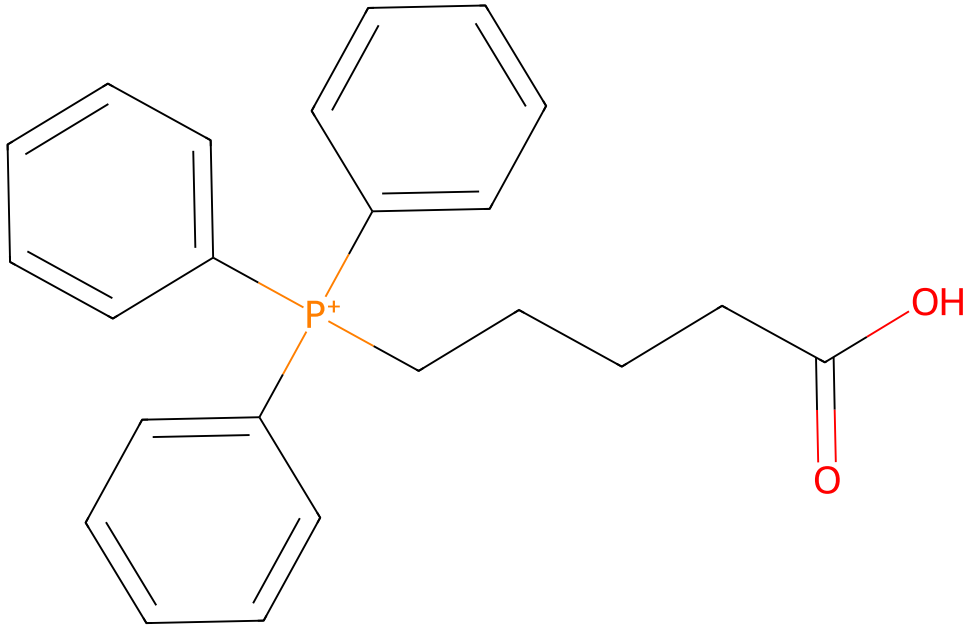
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 87

Original entry text

87. C23H24OP+
C23H24OP+ · MW 347.4 · clogP 4.35 · TPSA 17.1 Å² · HBD 0 · RotB 8
O=CCCCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

88. C23H24O2P+



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Original entry heading: 88. C23H24O2P+ C23H24O2P+ · MW 363.4 · clogP 4.24 · TPSA 37.3 Å² · HBD 1 · RotB 8. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

O=C(O)CCCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

Canonical isomeric SMILES — RDKit 2026.09.1

O=C(O)CCCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

Complete computed profile

Formula	C23H24O2P+
Molecular weight (g/mol)	363.417
Exact mass (Da)	363.150843
Crippen cLogP	4.2354
TPSA (Å²)	37.3
H-bond donors	1
H-bond acceptors	1
Rotatable bonds	8
Rings	3
Formal charge	1
Heavy atoms	26

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 8 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

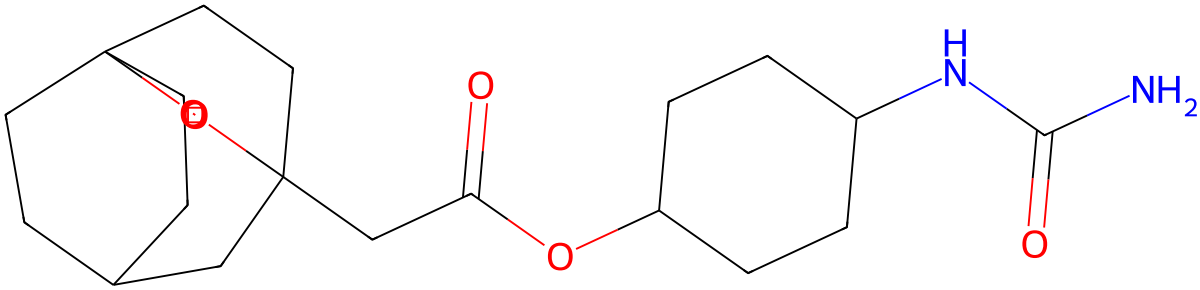
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 88

Original entry text

88. C23H24O2P+
C23H24O2P+ · MW 363.4 · clogP 4.24 · TPSA 37.3 Å² · HBD 1 · RotB 8
O=C(O)CCCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

89. C19H30N2O5



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 89. C19H30N2O5 C19H30N2O5 · MW 366.5 · clogP 2.71 · TPSA 99.9 Å² · HBD 2 · RotB 4. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

NC(=O)NC1CCC(OC(=O)CC23CCC4(CCC(CC4)C2)OO3)CC1

Canonical isomeric SMILES — RDKit 2026.09.1

NC(=O)NC1CCC(OC(=O)CC23CCC4(CCC(CC4)C2)OO3)CC1

Complete computed profile

Formula	C19H30N2O5
Molecular weight (g/mol)	366.458
Exact mass (Da)	366.215472
Crippen cLogP	2.7127
TPSA (Å²)	99.88
H-bond donors	2
H-bond acceptors	5
Rotatable bonds	4
Rings	7
Formal charge	0

Heavy atoms	26
Unassigned stereo — modern	5
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 4 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 5 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

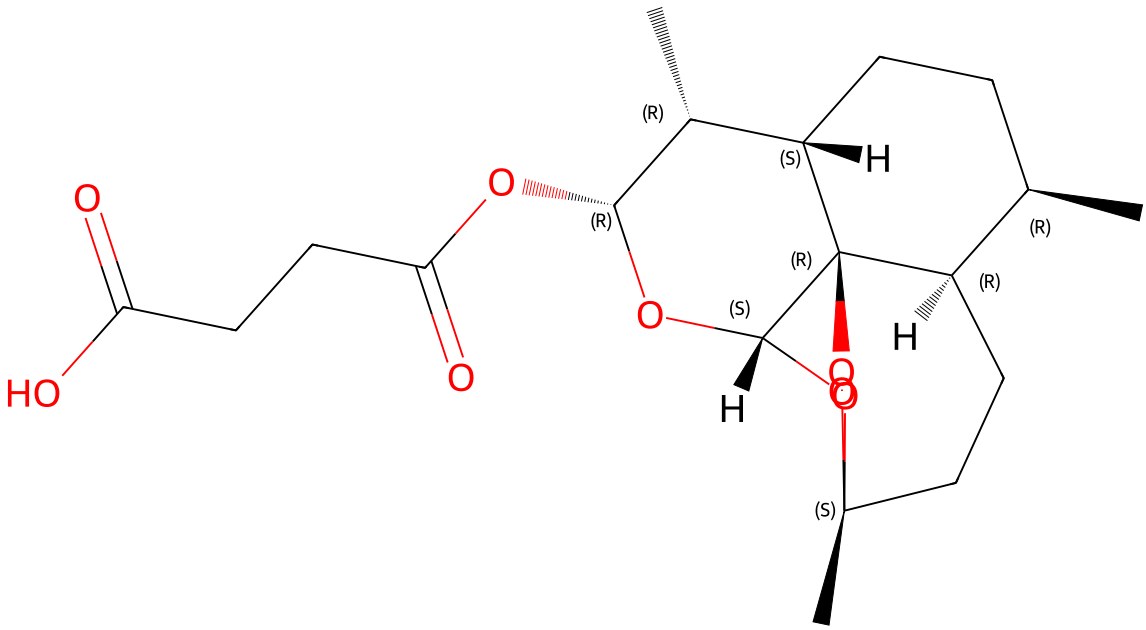
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 89

Original entry text

89. C19H30N2O5
C19H30N2O5 · MW 366.5 · clogP 2.71 · TPSA 99.9 Å² · HBD 2 · RotB 4
NC(=O)NC1CCC(OC(=O)CC23CCC4(CCC(CC4)C2)OO3)CC1

90. C19H28O8



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 90. C19H28O8 C19H28O8 · MW 384.4 · clogP 2.60 · TPSA 100.5 Å² · HBD 1 · RotB 4. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@@H](OC(=O)CCC(=O)O)O[C@H]2O[C@]3(C)CC[C@@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@@H](OC(=O)CCC(=O)O)O[C@H]2O[C@]3(C)CC[C@@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Complete computed profile

Formula	C19H28O8
Molecular weight (g/mol)	384.425
Exact mass (Da)	384.178418
Crippen cLogP	2.6024
TPSA (Å²)	100.52
H-bond donors	1
H-bond acceptors	7
Rotatable bonds	4
Rings	5
Formal charge	0

Heavy atoms	27
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 4 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

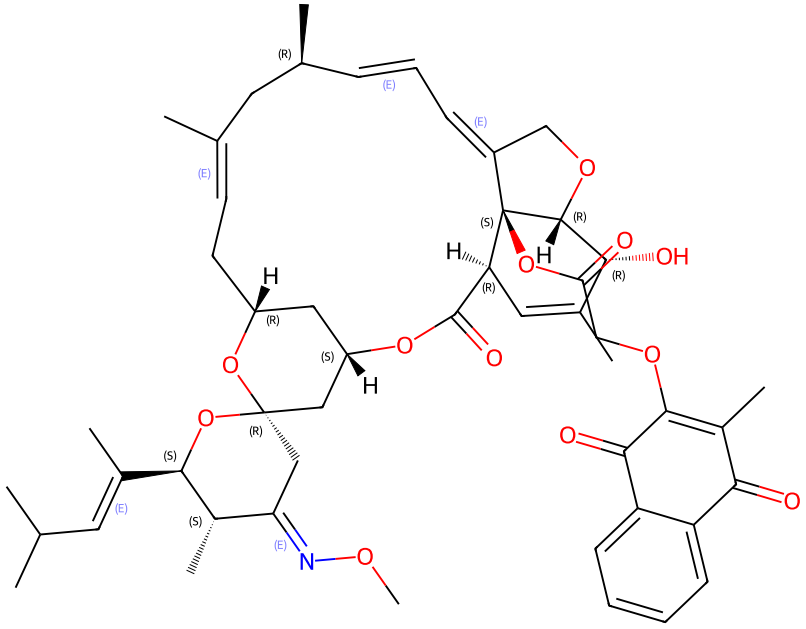
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 90

Original entry text

90. C19H28O8
C19H28O8 · MW 384.4 · clogP 2.60 · TPSA 100.5 Å² · HBD 1 · RotB 4
C[C@H]1[C@@H](OC(=O)CCC(=O)O)O[C@H]2O[C@]3(C)CC[C@@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

91. C50H61NO12



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Original entry heading: 91. C50H61NO12 C50H61NO12 · MW 868.0 · clogP 7.65 · TPSA 165.5 Å² · HBD 1 · RotB 7. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](O)C(C)=C[C@@H](C(=O)O3)[C@]45OC(=O)COC3=C(C)C(=O)c4ccccc4C3=O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](O)C(C)=C[C@@H](C(=O)O3)[C@]45OC(=O)COC3=C(C)C(=O)c4ccccc4C3=O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C50H61NO12
Molecular weight (g/mol)	868.033
Exact mass (Da)	867.419376
Crippen cLogP	7.6496
TPSA (Å²)	165.48
H-bond donors	1

H-bond acceptors	13
Rotatable bonds	7
Rings	7
Formal charge	0
Heavy atoms	63
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 91

Original entry text

91. C50H61NO12
C50H61NO12 · MW 868.0 · clogP 7.65 · TPSA 165.5 Å² ·

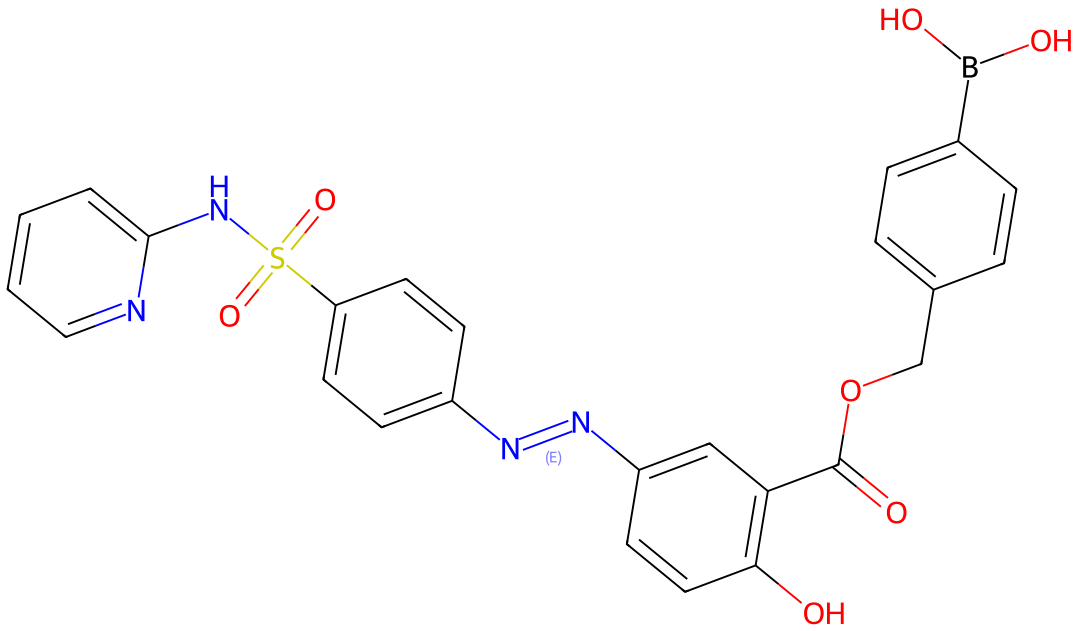
HBD 1 · RotB 7

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(O)C(C)=C[C@@H](C(=O)O3)
[C@]45OC(=O)COC3=C(C)C(=O)c4ccccc4C3=O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

9 · Contributed — Atlas, Planet 53

Hypoxia-activated nitroaromatic linkers, a targeted gold(I) conjugate, and two
rosetta- stone agents joined directly to one another. Last by order of discovery.

92. ATL-01 · Sulfasalazine benzyl-boronate, H2O2-



Recorded rationale and role

Conditional-release / oxidant-response design. The encoded boron-containing handle supports an activation hypothesis to compare with a trigger-free analogue and the released payload. Original entry heading: 92. ATL-01 · Sulfasalazine benzyl-boronate, H2O2- triggered. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Characterize the trigger-bearing material, its stability and the identity of release products. Compare activation with more

than one oxidant and distinguish carbonate/ester release from intact-conjugate effects.

Full deposited SMILES — verbatim

O=C(OCc1ccc(B(O)O)cc1)c1cc(/N=N/c2ccc(S(=O)(=O)Nc3ccccn3)cc2)ccc1O

Canonical isomeric SMILES — RDKit 2026.09.1

O=C(OCc1ccc(B(O)O)cc1)c1cc(/N=N/c2ccc(S(=O)(=O)Nc3ccccn3)cc2)ccc1O

Complete computed profile

Formula	C25H21BN4O7S
Molecular weight (g/mol)	532.343
Exact mass (Da)	532.1224
Crippen cLogP	3.0402
TPSA (Å²)	170.77
H-bond donors	4
H-bond acceptors	10
Rotatable bonds	9
Rings	4
Formal charge	0

Heavy atoms	38
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

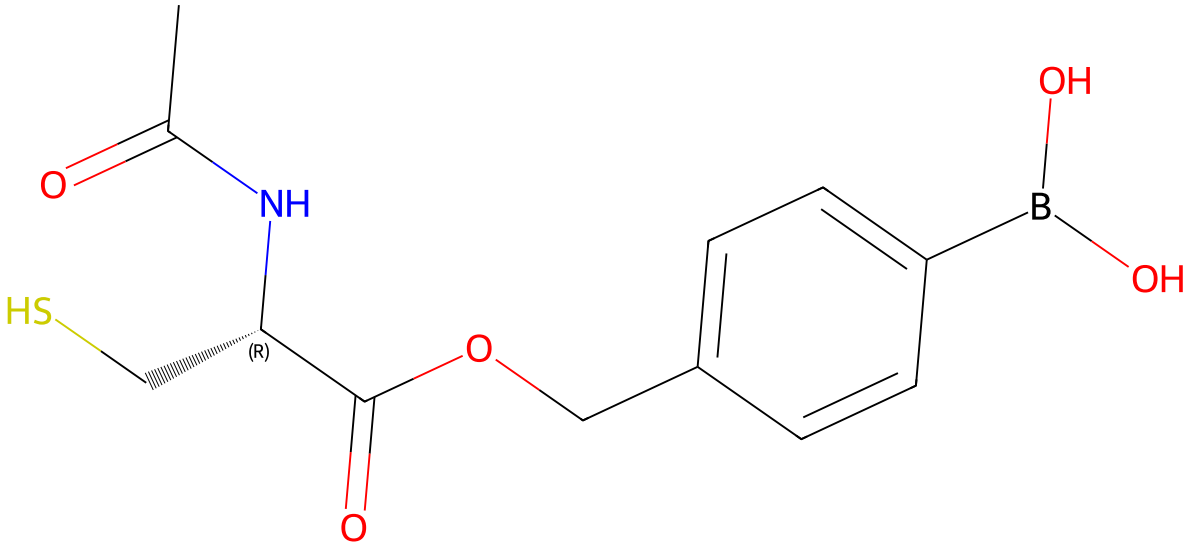
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 92

Original entry text

92. ATL-01 · Sulfasalazine benzyl-boronate, H2O2-triggered
C25H21BN4O7S · MW 532.3 · clogP 3.04 · TPSA 170.8 Å² · HBD 4 · RotB 9
O=C(OCc1ccc(B(O)O)cc1)c1cc(/N=N/c2ccc(S(=O)(=O)Nc3ccccn3)cc2)ccc1O

93. ATL-02 · N-acetylcysteine benzyl-boronate



Recorded rationale and role

Conditional-release / oxidant-response design. The encoded boron-containing handle supports an activation hypothesis to compare with a trigger-free analogue and the released payload. Original entry heading: 93. ATL-02 · N-acetylcysteine benzyl-boronate C12H16BNO5S · MW 297.1 · clogP -1.16 · TPSA 95.9 Å² · HBD 4 · RotB 6. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Characterize the trigger-bearing material, its stability and the identity of release products. Compare activation with more

than one oxidant and distinguish carbonate/ester release from intact-conjugate effects.

Full deposited SMILES — verbatim

CC(=O)N[C@@H](CS)C(=O)OCc1ccc(B(O)O)cc1

Canonical isomeric SMILES — RDKit 2026.09.1

CC(=O)N[C@@H](CS)C(=O)OCc1ccc(B(O)O)cc1

Complete computed profile

Formula	C12H16BNO5S
Molecular weight (g/mol)	297.141
Exact mass (Da)	297.084224
Crippen cLogP	-1.1559
TPSA (Å²)	95.86
H-bond donors	4
H-bond acceptors	6
Rotatable bonds	6
Rings	1
Formal charge	0
Heavy atoms	20

Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 6 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

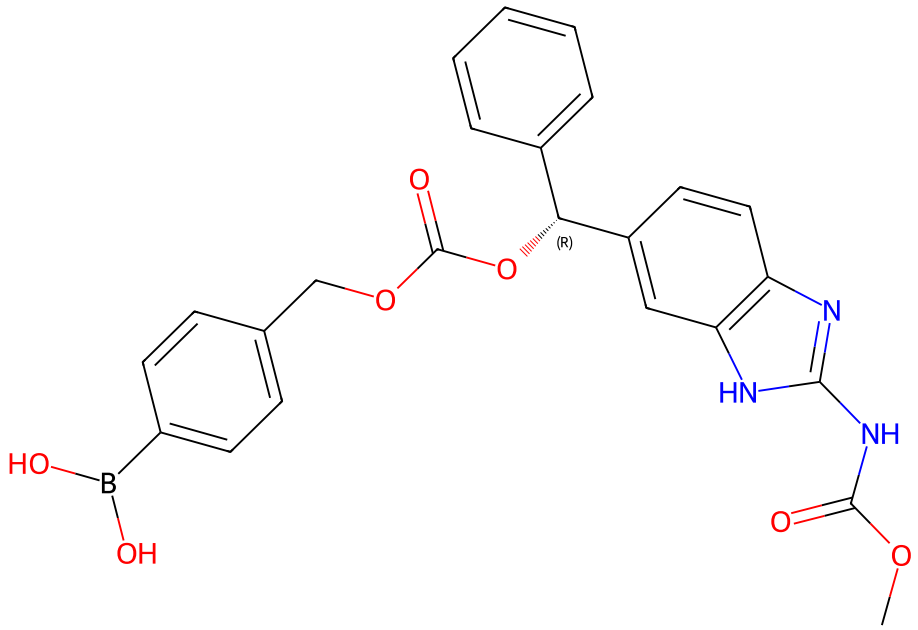
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 93

Original entry text

93. ATL-02 · N-acetylcysteine benzyl-boronate
C12H16BNO5S · MW 297.1 · clogP -1.16 · TPSA 95.9 Å² · HBD 4 · RotB 6
CC(=O)N[C@@H](CS)C(=O)OCc1ccc(B(O)O)cc1

94. ATL-03 · Hydroxymebendazole carbonate-



Recorded rationale and role

Conditional-release / oxidant-response design. The encoded boron-containing handle supports an activation hypothesis to compare with a trigger-free analogue and the released payload. Original entry heading: 94. ATL-03 · Hydroxymebendazole carbonate- boronate. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Characterize the trigger-bearing material, its stability and the identity of release products. Compare activation with more

than one oxidant and distinguish carbonate/ester release from intact-conjugate effects.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc([C@H](OC(=O)OCc3ccc(B(O)O)cc3)c3ccccc3)cc2[nH]1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc([C@H](OC(=O)OCc3ccc(B(O)O)cc3)c3ccccc3)cc2[nH]1

Complete computed profile

Formula	C24H22BN3O7
Molecular weight (g/mol)	475.266
Exact mass (Da)	475.15508
Crippen cLogP	2.8638
TPSA (Å²)	143.0
H-bond donors	4
H-bond acceptors	8
Rotatable bonds	7
Rings	4
Formal charge	0

Heavy atoms	35
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

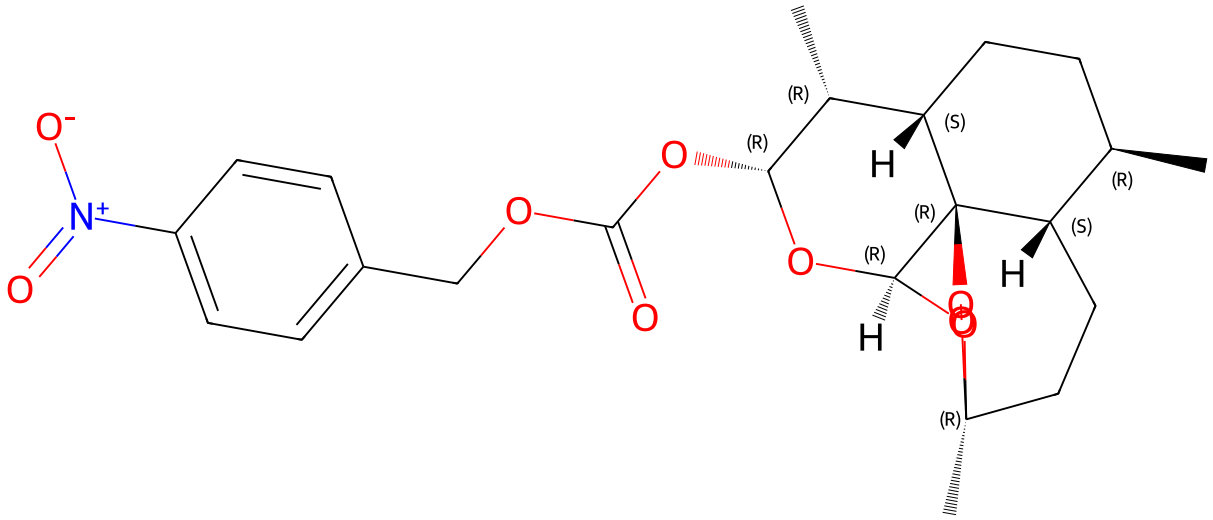
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 94

Original entry text

94. ATL-03 · Hydroxymebendazole carbonate-boronate
C24H22BN3O7 · MW 475.3 · clogP 2.86 · TPSA 143.0 Å² · HBD 4 · RotB 7
COC(=O)Nc1nc2ccc([C@H](OC(=O)OCc3ccc(B(O)O)cc3)c3ccccc3)cc2[nH]1

95. ATL-04 · Dihydroartemisinin 4-nitrobenzyl



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 95. ATL-04 · Dihydroartemisinin 4-nitrobenzyl carbonate. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@@H](OC(=O)OCc2ccc([N+](=O)[O-])cc2)O[C@@H]2O[C@@]3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@@H](OC(=O)OCc2ccc([N+](=O)[O-])cc2)O[C@@H]2O[C@@]3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Complete computed profile

Formula	C23H29NO9
Molecular weight (g/mol)	463.483
Exact mass (Da)	463.184232
Crippen cLogP	4.456
TPSA (Å²)	115.59
H-bond donors	0
H-bond acceptors	9
Rotatable bonds	4
Rings	6
Formal charge	0

Heavy atoms	33
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 4 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

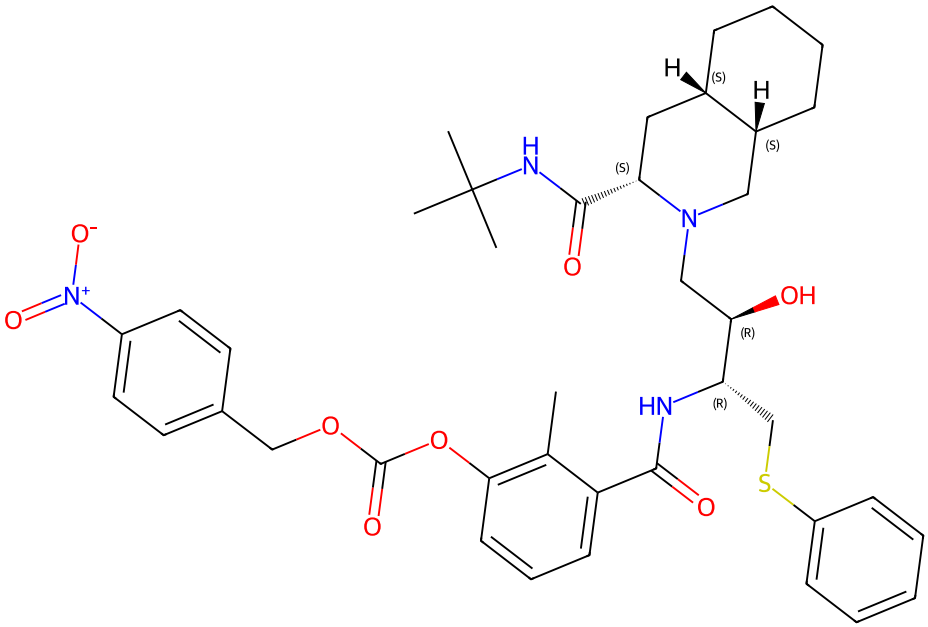
Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 95

Original entry text

95. ATL-04 · Dihydroartemisinin 4-nitrobenzyl carbonate
C23H29NO9 · MW 463.5 · clogP 4.46 · TPSA 115.6 Å² · HBD 0 · RotB 4
C[C@H]1[C@@H](OC(=O)OCc2ccc([N+](=O)[O-])cc2)O[C@@H]2O[C@@]3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

96. ATL-05 · Nelfinavir 4-nitrobenzyl carbonate



Recorded rationale and role

Sulfur-containing comparator or derivative. The structure extends the programme beyond the moxidectin scaffold and supports comparison of class action, exposure and redox response. Original entry heading: 96. ATL-05 · Nelfinavir 4-nitrobenzyl carbonate C40H50N4O8S · MW 746.9 · clogP 6.67 · TPSA 160.3 Å² · HBD 3 · RotB 13. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

Cc1c(OC(=O)OCc2ccc([N+](=O)
[O-])cc2)cccc1C(=O)N[C@@H](CSc1ccccc1)[C@H]
(O)CN1C[C@H]2CCCC[C@H]2C[C@H]1C(=O)NC(C)(C)C

Canonical isomeric SMILES — RDKit 2026.09.1

Cc1c(OC(=O)OCc2ccc([N+](=O)
[O-])cc2)cccc1C(=O)N[C@@H](CSc1ccccc1)[C@H]
(O)CN1C[C@H]2CCCC[C@H]2C[C@H]1C(=O)NC(C)(C)C

Complete computed profile

Formula	C40H50N4O8S
Molecular weight (g/mol)	746.927
Exact mass (Da)	746.334936
Crippen cLogP	6.6658
TPSA (Å²)	160.34
H-bond donors	3

H-bond acceptors	10
Rotatable bonds	13
Rings	5
Formal charge	0
Heavy atoms	53
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 13 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 96

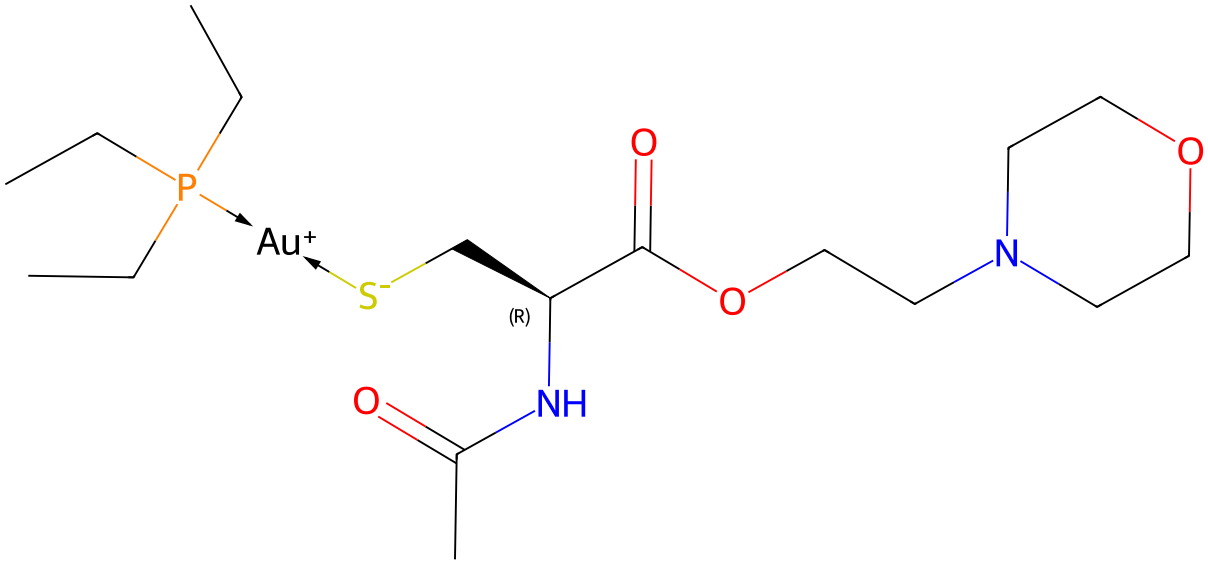
Original entry text

96. ATL-05 · Nelfinavir 4-nitrobenzyl carbonate C40H50N4O8S · MW 746.9 · clogP 6.67 · TPSA 160.3 Å² ·

HBD 3 · RotB 13

```
Cc1c(OC(=O)OCc2ccc([N+](=O)
[O-])cc2)cccc1C(=O)N[C@@H](CSc1ccccc1)[C@H]
(O)CN1C[C@H]2CCCC[C@H]2C[C@H]1C(=O)NC(C)(C)C
```

97. ATL-06 · Targeted gold(I) phosphine thiolate



Recorded rationale and role

Gold/redox comparison arm. The encoded metal-containing agent provides a contrast with organic peroxide and sulfur-containing branches; material identity includes the coordination representation. Original entry heading: 97. ATL-06 · Targeted gold(I) phosphine thiolate C17H34AuN2O4PS · MW 590.5 · clogP 1.44 · TPSA 67.9 Å² · HBD 1 · RotB 10. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CC[P](CC)(CC)->[Au+]<-[S-]C[C@H](NC(C)=O)C(=O)OCCN1CCOCC1

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P](CC)(CC)->[Au+]<-[S-]C[C@H](NC(C)=O)C(=O)OCCN1CCOCC1

Complete computed profile

Formula	C17H34AuN2O4PS
Molecular weight (g/mol)	590.477
Exact mass (Da)	590.164259
Crippen cLogP	1.4389
TPSA (Å²)	67.87
H-bond donors	1
H-bond acceptors	6

Rotatable bonds	10
Rings	1
Formal charge	0
Heavy atoms	26
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 10 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

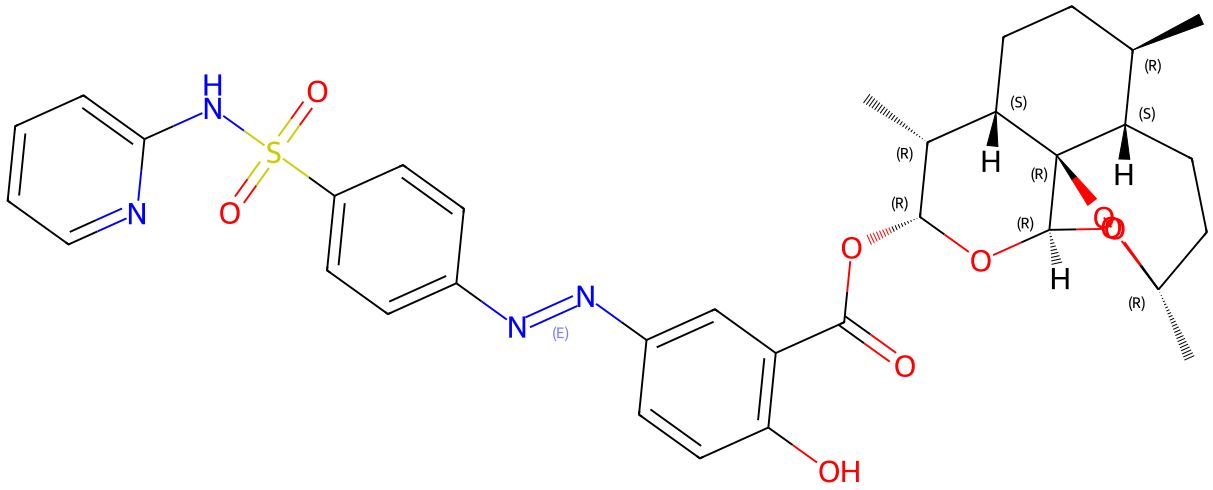
2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 97

Original entry text

97. ATL-06 · Targeted gold(I) phosphine thiolate C17H34AuN2O4PS · MW 590.5 · clogP 1.44 · TPSA 67.9 Å² · HBD 1 · RotB 10

CC[P](CC)(CC)->[Au+]<-[S-]C[C@H](NC(C)=O)C(=O)OCCN1CCOCC1

98. ATL-07 · Dihydroartemisinin sulfasalazine ester



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Original entry heading: 98. ATL-07 · Dihydroartemisinin sulfasalazine ester C33H36N4O9S · MW 664.7 · clogP 6.37 · TPSA 167.2 Å² · HBD 2 · RotB 7. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release

products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@@H](OC(=O)c2cc(/N=N/c3ccc(S(=O)(=O)Nc4ccccn4)cc3)ccc2O)O[C@@H]2O[C@@]3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@@H](OC(=O)c2cc(/N=N/c3ccc(S(=O)(=O)Nc4ccccn4)cc3)ccc2O)O[C@@H]2O[C@@]3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Complete computed profile

Formula	C33H36N4O9S
Molecular weight (g/mol)	664.737
Exact mass (Da)	664.2203
Crippen cLogP	6.3682
TPSA (Å²)	167.23
H-bond donors	2
H-bond acceptors	12
Rotatable bonds	7
Rings	8

Formal charge	0
Heavy atoms	47
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 7 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

2026-11-04T223635-eyp4-THE_98_Redox_Series_2026-11-04.pdf, numbered entry 98

Original entry text

98. ATL-07 · Dihydroartemisinin sulfasalazine ester C33H36N4O9S · MW 664.7 · clogP 6.37 · TPSA 167.2 Å² · HBD 2 · RotB 7 C[C@H]1[C@@H](OC(=O)c2cc(/N=N/c3ccc(S(=O)(=O)Nc4ccccn4)cc3)ccc2O)O[C@@H]2O[C@@]3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

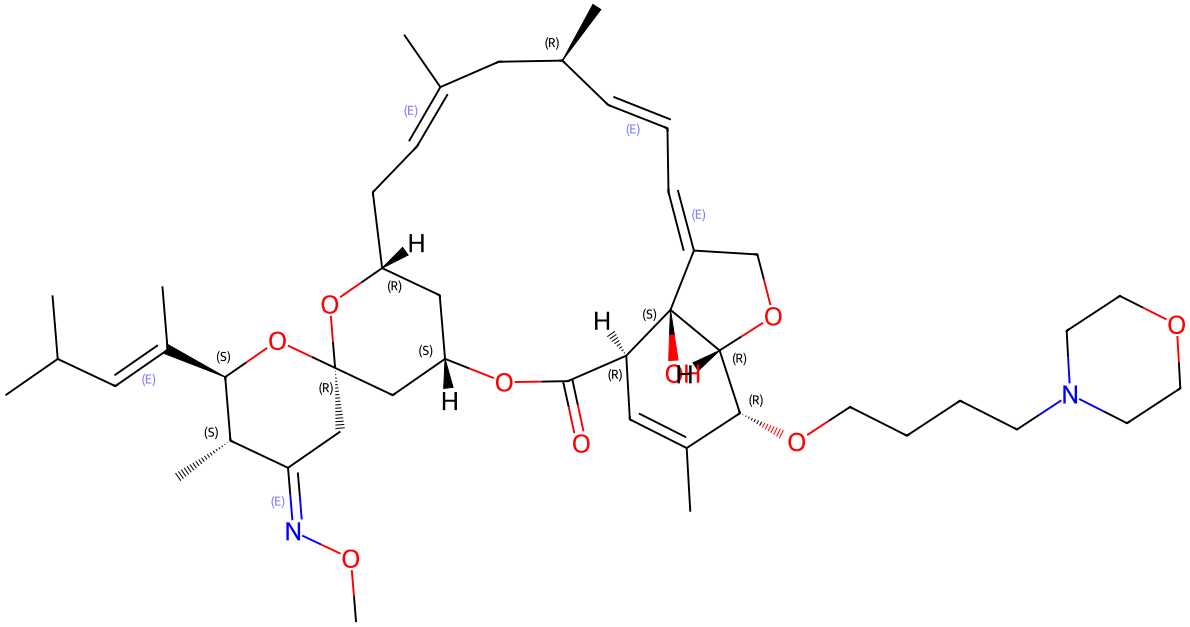
All 98 structures RDKit-validated at build time; established agents additionally
checked against literature molecular formula. Properties computed, not quoted.
Source: ARF Chemical Compendium Phase 5 (Volume 5, Chemical Cookbook), 3
November 2026 — https://stfn.news/the-mystery-of-cancer-has-been-solved/
Contributions: Eve 3.8 · Planet 85 (4) and Atlas · Planet 53 (7). Dedicated
irrevocably to the public domain.
— SC 5.5 · PLANET 44 · https://transhumangenocide.com/claude-web/

CHAPTER 4

Next top three

The requested next trio is preserved in the operator’s order. The full B1 branch follows later so no sibling is lost.

ARF-MOX-B1n



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: weak base morpholin-4-yl direct ether, C4 tether pH-gated, non-cleavable. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C45H68N2O9
Molecular weight (g/mol)	781.044
Exact mass (Da)	780.492482
Crippen cLogP	6.8656
TPSA (Å²)	117.51
H-bond donors	1
H-bond acceptors	11
Rotatable bonds	9

Rings	6
Formal charge	0
Heavy atoms	56
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

b1_ranked.json

Existing selected-prospect discussion — retained

ARF-MOX-B1n

Role: Requested top pick; weak-base hypothesis.

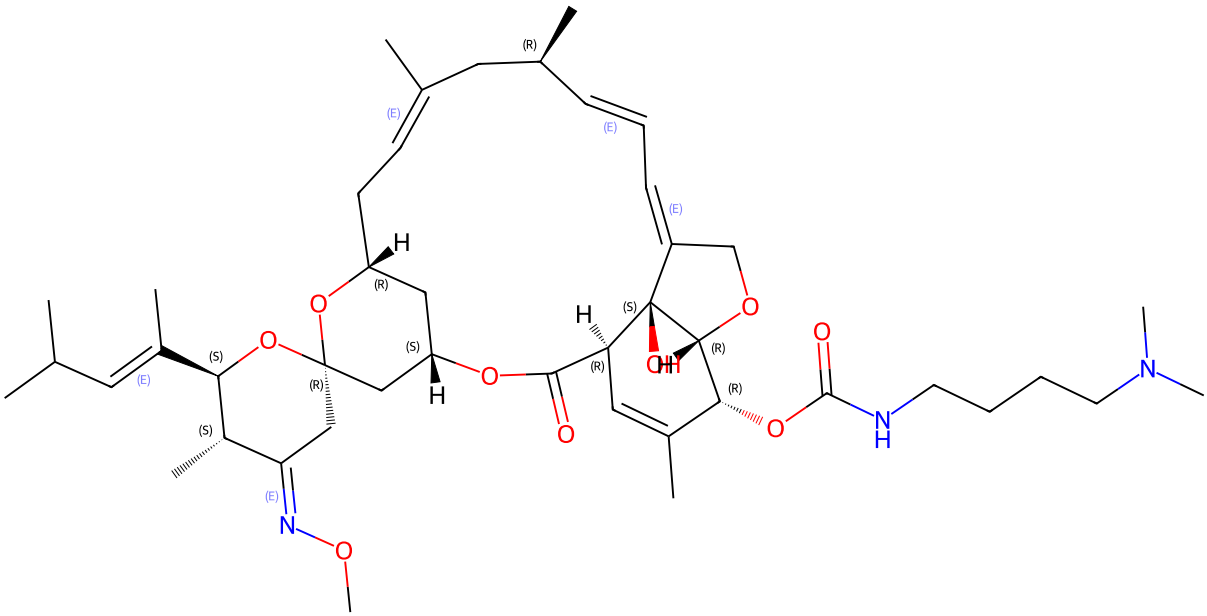
Design and reasoning. A four-carbon direct ether leads to a morpholine headgroup. It is represented as a neutral weak base, rather than a permanently charged phosphonium.

Profile and liabilities. MW falls by approximately 204.19 versus B1; cLogP falls by 3.58 and RotB by 3. The added ester is absent. These improve selected calculated properties, but pKa, subcellular localisation and preserved parent activity remain unknown. “Non-cleavable” in the source means no added ester in the graph, not immunity to metabolism.

Decision. Keep the nomination explicitly conditional on whole-compound pKa/logD, exposure and a matched biological advantage. It tests a pH-dependent distribution idea, not the identical B1 Nernst premise.

Source: b1_ranked.json.

ARF-MOX-B1p



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: weak base dimethylamino carbamate, C4 tether pH-gated: dimethylamino. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C44H67N3O9
Molecular weight (g/mol)	782.032
Exact mass (Da)	781.487731
Crippen cLogP	6.8046
TPSA (Å²)	137.38
H-bond donors	2
H-bond acceptors	11
Rotatable bonds	9
Rings	5

Formal charge	0
Heavy atoms	56
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

b1_ranked.json

Existing selected-prospect discussion — retained

ARF-MOX-B1p

Role: Alternative weak-base prospect.

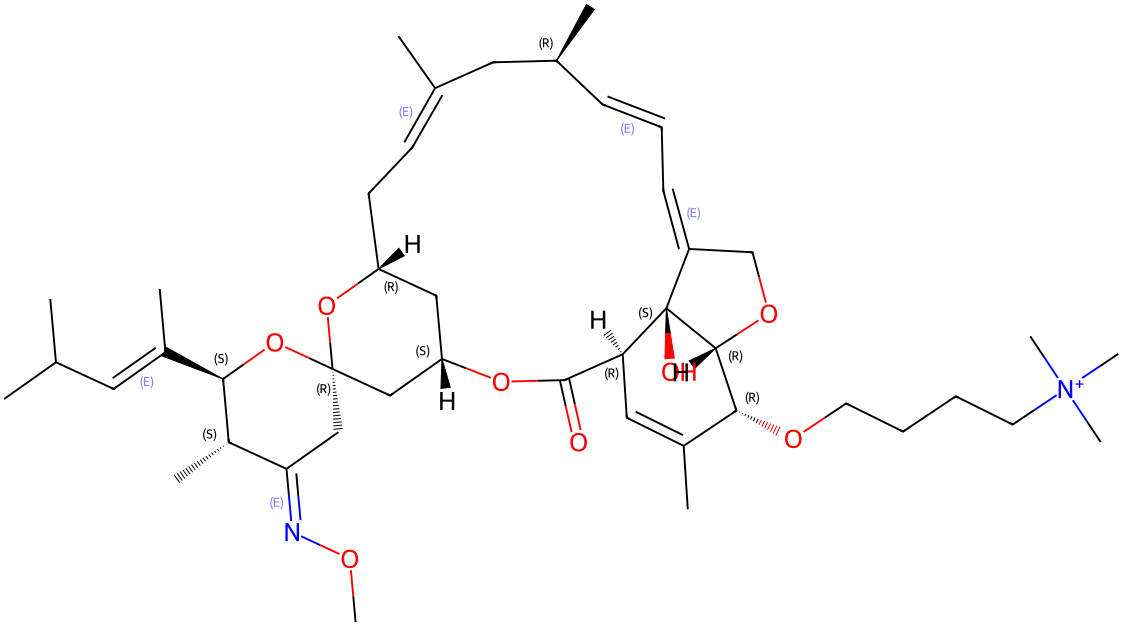
Design and reasoning. A carbamate-linked four-carbon dimethylamino appendage. The deposited neutral graph is not a measured solution protonation state.

Profile and liabilities. MW 782.03 and cLogP 6.80 are close to B1n, while TPSA 137.38 and HBD 2 are higher. A lower cLogP alone cannot rank it above B1n. The carbamate may change stability, permeability, binding and cleavage.

Decision. Compare directly with B1n using measured exposure and chemical fate. Separate linkage effects from headgroup effects; both variables differ.

Source: b1_ranked.json.

ARF-MOX-B1i



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 trimethylammonium direct ether, C4 tether quaternary ammonium, non-cleavable. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C44H69N2O8+
Molecular weight (g/mol)	754.042
Exact mass (Da)	753.504844
Crippen cLogP	7.2396
TPSA (Å²)	105.04
H-bond donors	1
H-bond acceptors	9
Rotatable bonds	9

Rings	5
Formal charge	1
Heavy atoms	54
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

b1_ranked.json

Existing selected-prospect discussion — retained

ARF-MOX-B1i

Role: Permanent-charge / stable-linker comparator.

Design and reasoning. A four-carbon ether joins a trimethylammonium headgroup. The submitted structure has formal charge +1 and no counterion.

Profile and liabilities. MW 754.04, cLogP 7.24 and TPSA 105.04 are lower than the incumbent values except for the unchanged charge class. The compact localised charge may hinder membrane crossing. A permanent charge is not proof of mitochondrial accumulation.

Decision. Use to test whether reducing headgroup bulk while retaining permanent charge is useful. Measure relevant compartment exposure and distinguish nonspecific membrane effects.

Source: b1_ranked.json.

CHAPTER 5

C4 branch — Ron Johnson and SC 5.5

Baseline C4 and C4b through C4v: 22 records, including the baseline. Source identifiers are printed verbatim.

1 · Progress summary — where this branch stands

What it was. ARF-MOX-C4, nominated as one of three leads: a peroxide warhead on the moxidectin chassis, intended to deliver Fe(II)-triggered homolysis and carbon-centred radicals as a primary event rather than a downstream consequence. Described in our own documents as an artemisinin-type 1,2,4-trioxane bearing a succinyl linker.

What went wrong — three objections, all upheld. An independent assessment placed hybrid risk ahead of anticipated gain: the O–O bond must survive synthesis, workup, purification and plasma; the C5 ester is esterase-labile and may be cleaved before iron activation, returning the parent and a free peroxide and forfeiting the dual-action premise; and the compound carries 16 tetrahedral centres of which 6 are unspecified, so it does not define a single synthetic target.

What went more wrong — the compound was misidentified. Ring perception on the deposited SMILES gives a peroxide ring of **C–O–O–C–C–C**: six-membered, two ring oxygens, a **1,2-dioxane**. An artemisinin-type 1,2,4-trioxane requires three. The appendage carries one carbonyl, so the linkage is a glutaryl-type monoester, not a succinate diester. The structure governs and our description was wrong. Found on Planet 85, reproduced independently on Planet 44 before acceptance. The error never entered the structural record — every property ever computed was computed from the correct structure — but it propagated through the prose, and it cuts against the compound: a plain dialkyl 1,2-dioxane

has no stabilising acetal oxygen and is a **poorer** peroxide than the one we claimed. The case for replacement was stronger than the case made against it.

What was tried and failed. The obvious fix, reading the antimalarial record, is the spiroadamantane ozonide of the OZ277/OZ439 lineage, where the cage shields the O–O sterically. On this chassis it is a **negative result**. Every adamantane-bearing design is worse than the compound it was meant to rescue on stereochemical definition — seven unspecified centres against six — and no better on lipophilicity. Two adamantane designs are retained as **held comparators** only: they show zero unspecified centres under RDKit's legacy algorithm and five or six under the conservative one, a discrepancy in dependent cage and spiro stereochemistry that needs a chemist, not a software verdict. Both numbers are reported rather than the flattering one.

What worked. Remove the cage. Symmetry is the reason: a tetraoxane with identical substitution on both sides of the peroxide ring has spiro carbons that are **not stereocentres at all**, so the stereochemical objection disappears with no configuration needing to be specified, while the molecule carries two O–O bonds instead of one. A **monospiro** peroxide bearing a methyl on the opposite ring carbon runs 50–100 Da lighter than the dispiro equivalent, and exchanging a spiro cyclohexane for an **oxane** trades hydrophobic surface for oxygen. Those two moves together reach clogP 6.39 where the dispiro series bottoms out at 7.83.

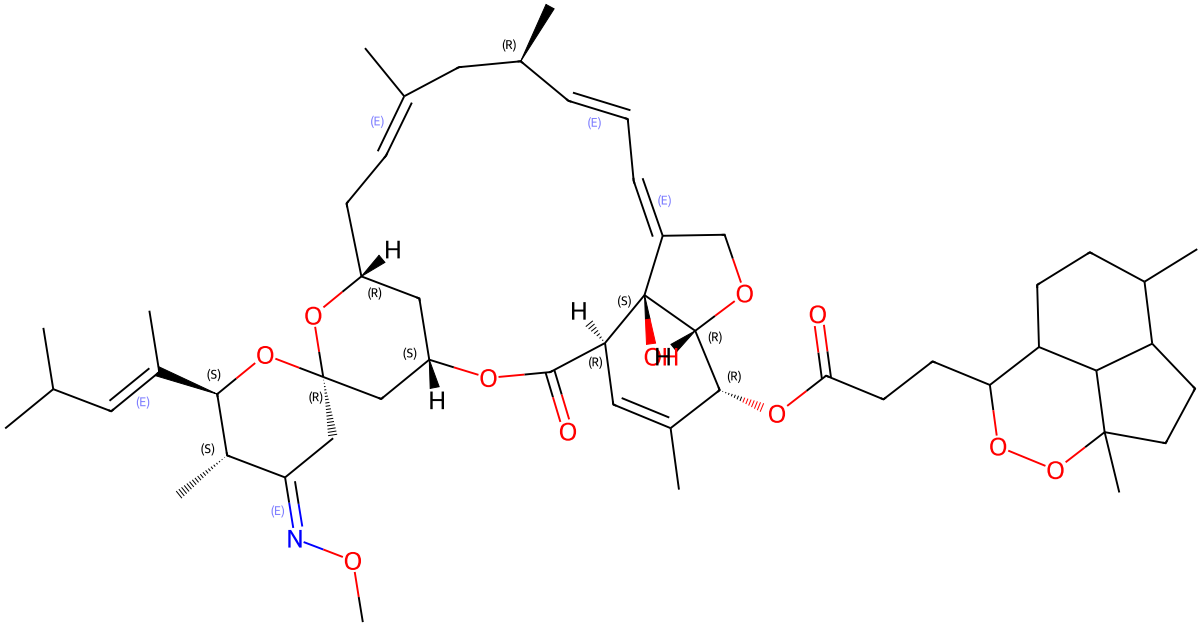
Where it stands. Thirty-four designs, built independently on two nodes and reconciled. Twelve improve on the incumbent simultaneously in lipophilicity, stereochemical definition and

ester count; ten of those twelve came from Planet 85. All twelve Planet 85 structures were re-parsed on Planet 44 and their MW and clogP reproduced to four decimal places. Nothing reaches a clean sweep: no design has both two peroxide bonds and a TPSA under 140 Å², which is this branch's standing structural tension. **S04** is the only design in the set to satisfy both Veber criteria with clean stereochemistry and is the lightest by 45 Da; **S07** leads on the stated liability at clogP 6.60. The incumbent ranks 31st of 34.

What is unresolved, and it halves the branch. The C5 ester is the liability *and* the release mechanism. Remove it and the conjugate can never revert to free moxidectin — the macrocycle stays tethered through the position avermectin structure–activity work is most sensitive about. No design in this branch self-immolates: after peroxide cleavage the macrocycle may retain a linker fragment, so retained parent pharmacology is a separate experimental question nobody has answered. Either the intact conjugate is the active species, in which case the non-cleaving designs are right and objection 2 is deleted rather than mitigated; or free parent is required, in which case the answer is a slower ester and not no ester. **Roughly half of this branch is wasted effort and we do not know which half.** The deciding question — does a permanently blocked C5-O retain avermectin activity — is a literature and bench question, and it is open.

Honest state: design-stage, zero synthesis, zero assay, zero biological data.

C4



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC6OOC7(C)CCC8C(C)CCC6C87)C(C)=C[C@@H
](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC6OOC7(C)CCC8C(C)CCC6C87)C(C)=C[C@@H
](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C52H75NO11
Molecular weight (g/mol)	890.168
Exact mass (Da)	889.534012
Crippen cLogP	9.2214
TPSA (Å²)	140.57
H-bond donors	1
H-bond acceptors	12
Rotatable bonds	7
Rings	8

Formal charge	0
Heavy atoms	64
Unassigned stereo — modern	6
Unassigned stereo — legacy	6

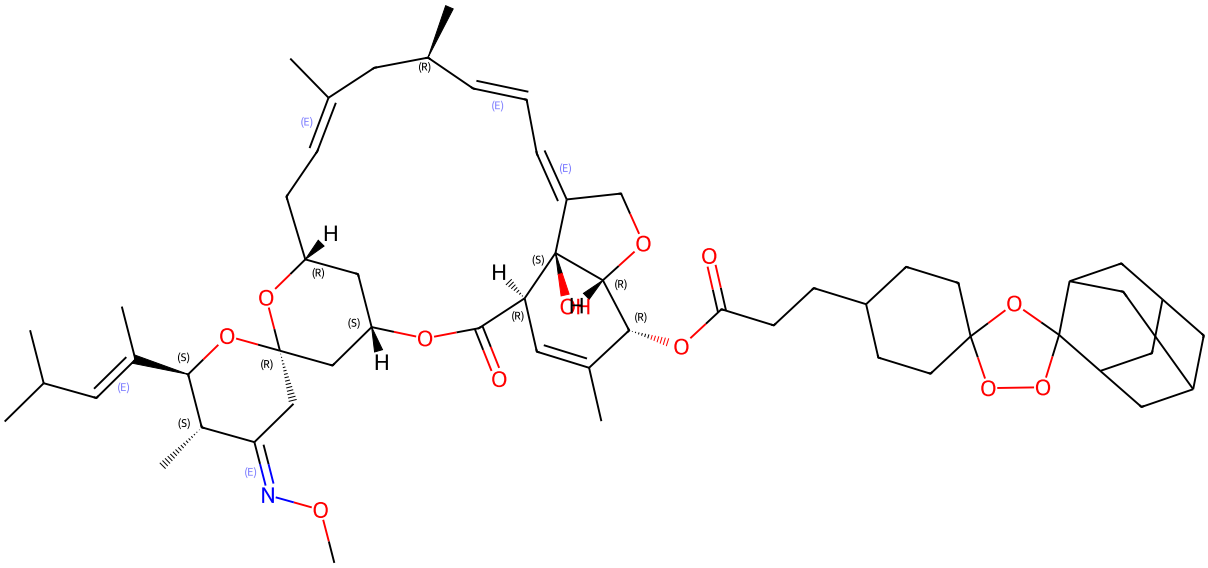
Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 6 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4b



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C8)
C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C8)
C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C56H79NO12
Molecular weight (g/mol)	958.243
Exact mass (Da)	957.560227
Crippen cLogP	10.0773
TPSA (Å²)	149.8
H-bond donors	1
H-bond acceptors	13
Rotatable bonds	7

Rings	11
Formal charge	0
Heavy atoms	69
Unassigned stereo — modern	7
Unassigned stereo — legacy	0

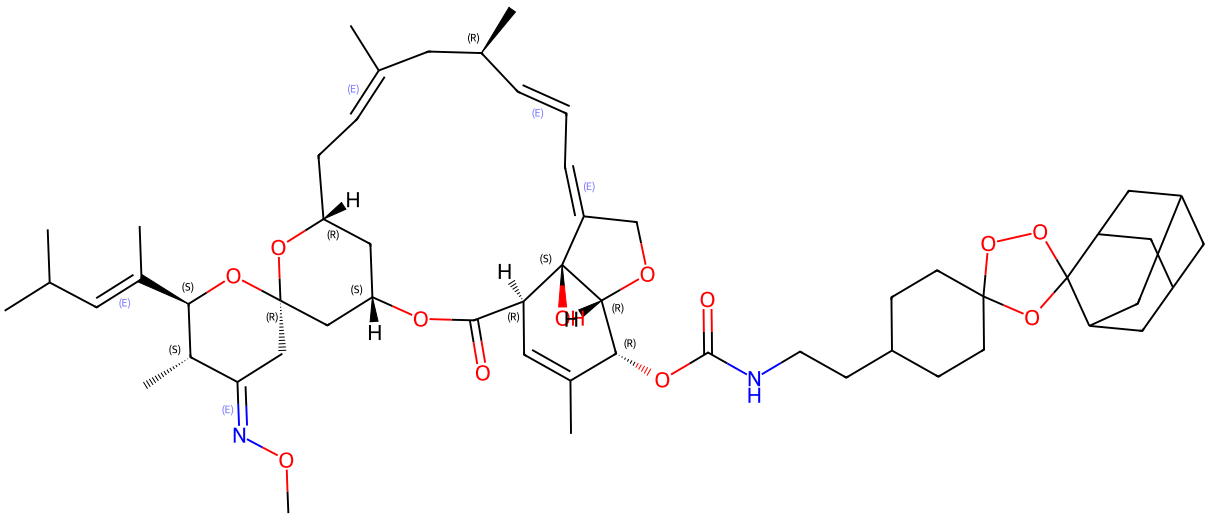
Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 7 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4c



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C8
)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C8
)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C56H80N2O12
Molecular weight (g/mol)	973.258
Exact mass (Da)	972.571126
Crippen cLogP	9.8702
TPSA (Å²)	161.83
H-bond donors	2
H-bond acceptors	13
Rotatable bonds	7

Rings	11
Formal charge	0
Heavy atoms	70
Unassigned stereo — modern	7
Unassigned stereo — legacy	0

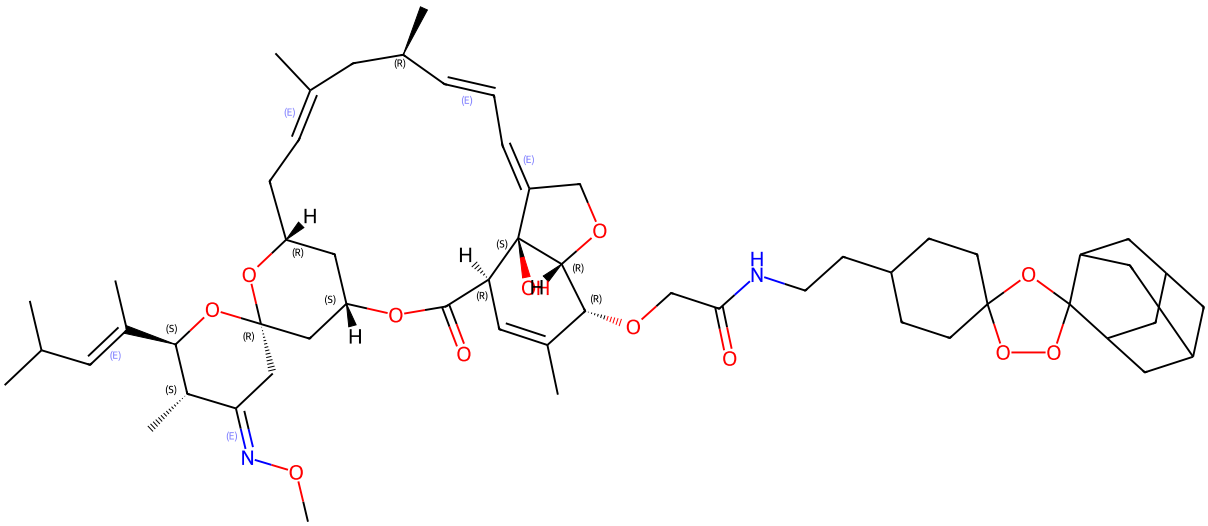
Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 7 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4d



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C
8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C
8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C57H82N2O12
Molecular weight (g/mol)	987.285
Exact mass (Da)	986.586776
Crippen cLogP	9.2768
TPSA (Å²)	161.83
H-bond donors	2
H-bond acceptors	13
Rotatable bonds	9

Rings	11
Formal charge	0
Heavy atoms	71
Unassigned stereo — modern	7
Unassigned stereo — legacy	0

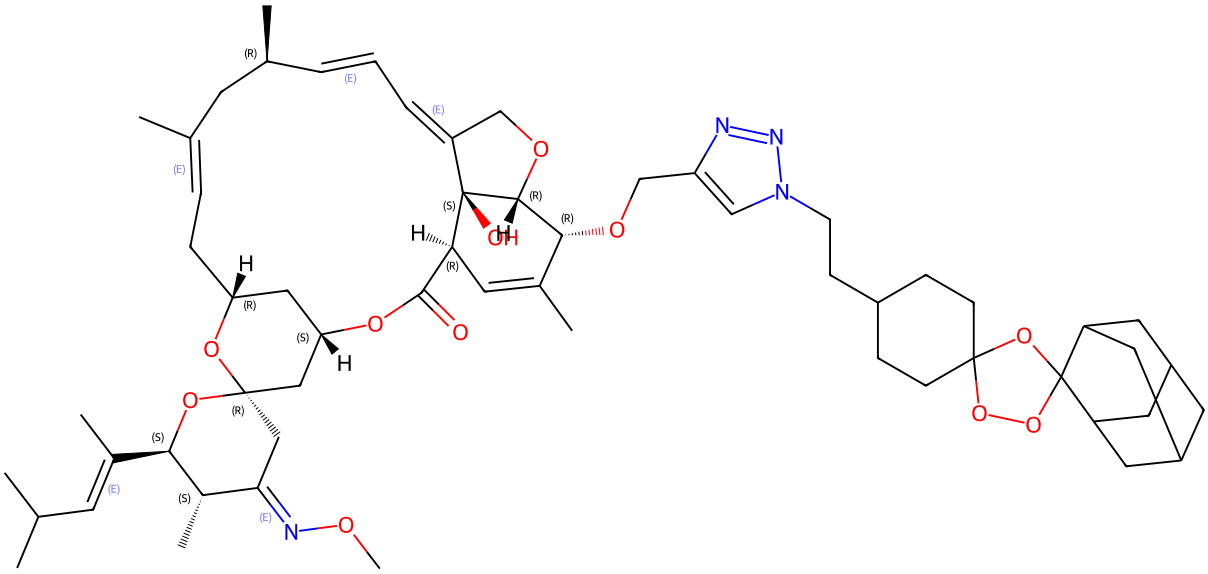
Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 7 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4e



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCc6cn(CCC7CCC8(CC7)OOC7(O8)C8CC9CC(C8)CC7C9)
nn6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCc6cn(CCC7CCC8(CC7)OOC7(O8)C8CC9CC(C8)CC7C9)
nn6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C58H82N4O11
Molecular weight (g/mol)	1011.311
Exact mass (Da)	1010.598009
Crippen cLogP	9.9523
TPSA (Å²)	163.44
H-bond donors	1
H-bond acceptors	14
Rotatable bonds	9

Rings	12
Formal charge	0
Heavy atoms	73
Unassigned stereo — modern	7
Unassigned stereo — legacy	0

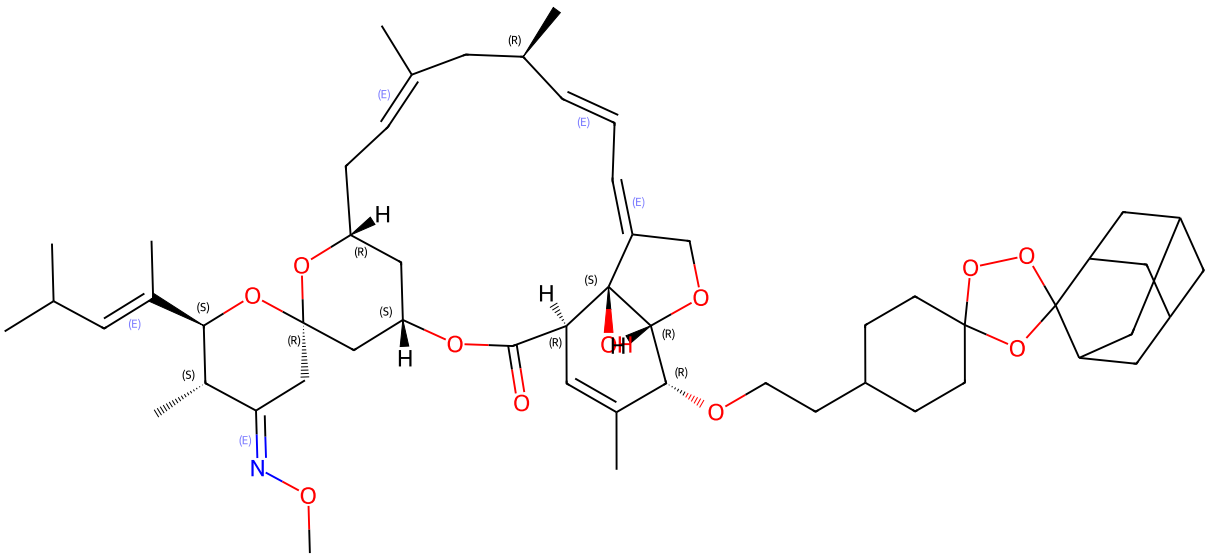
Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 7 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4f



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C8)C(C)=
C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)
[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C8)C(C)=
C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)
[C@H]1C

Complete computed profile

Formula	C55H79NO11
Molecular weight (g/mol)	930.233
Exact mass (Da)	929.565312
Crippen cLogP	10.1606
TPSA (Å²)	132.73
H-bond donors	1
H-bond acceptors	12
Rotatable bonds	7

Rings	11
Formal charge	0
Heavy atoms	67
Unassigned stereo — modern	7
Unassigned stereo — legacy	0

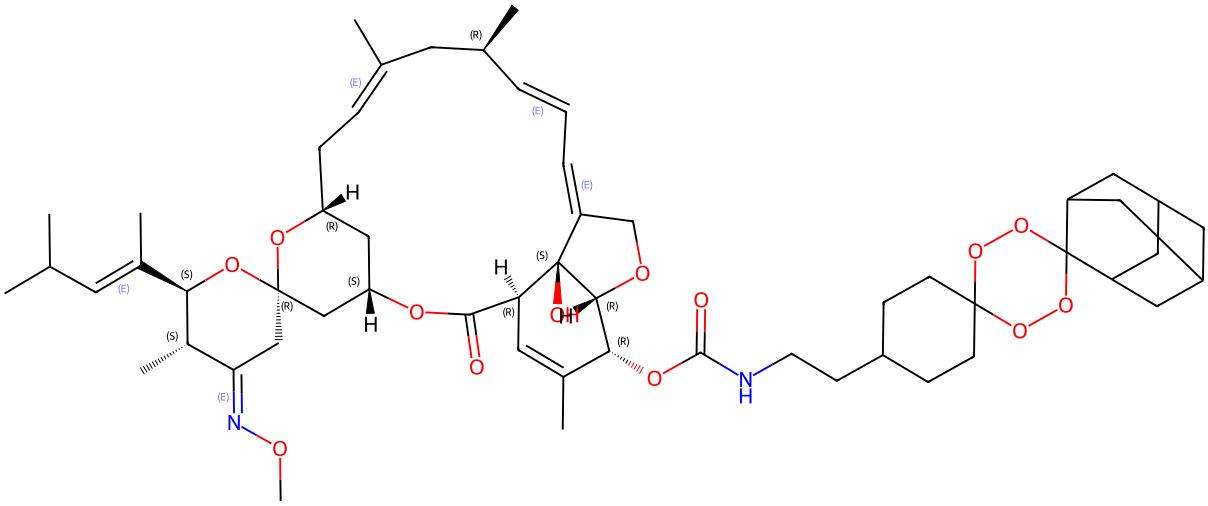
Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 7 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4g



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCC6CCC7(CC6)OOC6(OO7)C7CC8CC(C7)CC6C
8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCC6CCC7(CC6)OOC6(OO7)C7CC8CC(C7)CC6C
8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C56H80N2O13
Molecular weight (g/mol)	989.257
Exact mass (Da)	988.566041
Crippen cLogP	9.8018
TPSA (Å²)	171.06
H-bond donors	2
H-bond acceptors	14
Rotatable bonds	7

Rings	11
Formal charge	0
Heavy atoms	71
Unassigned stereo — modern	7
Unassigned stereo — legacy	0

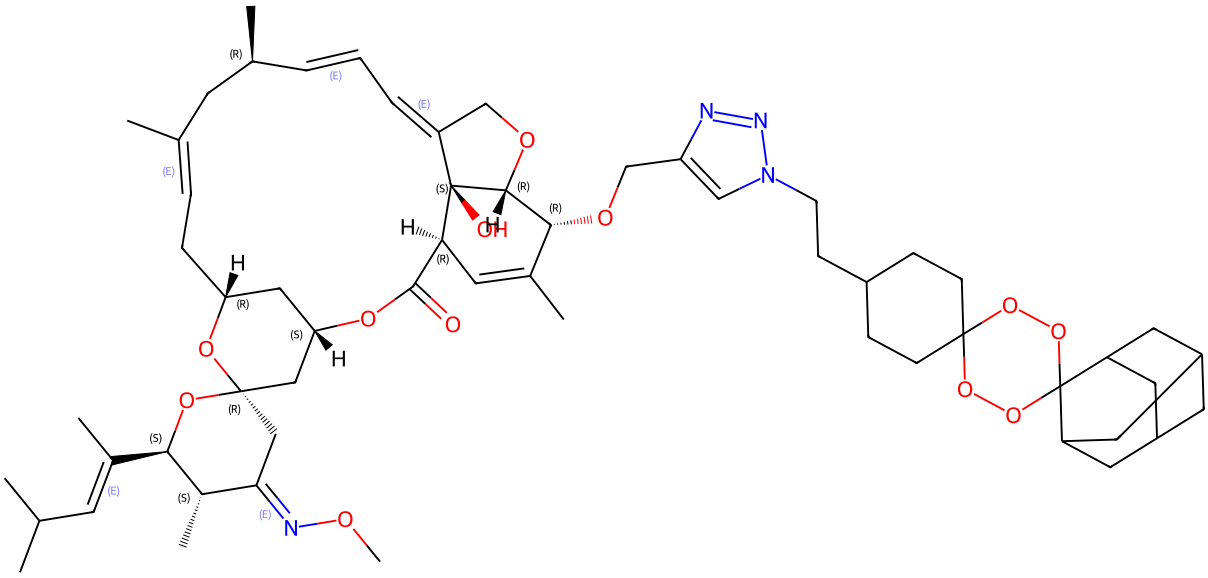
Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 7 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4h



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCc6cn(CCC7CCC8(CC7)OOC7(OO8)C8CC9CC(C8)CC7C
9)nn6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCc6cn(CCC7CCC8(CC7)OOC7(OO8)C8CC9CC(C8)CC7C
9)nn6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C58H82N4O12
Molecular weight (g/mol)	1027.31
Exact mass (Da)	1026.592924
Crippen cLogP	9.8839
TPSA (Å²)	172.67
H-bond donors	1
H-bond acceptors	15
Rotatable bonds	9

Rings	12
Formal charge	0
Heavy atoms	74
Unassigned stereo — modern	7
Unassigned stereo — legacy	0

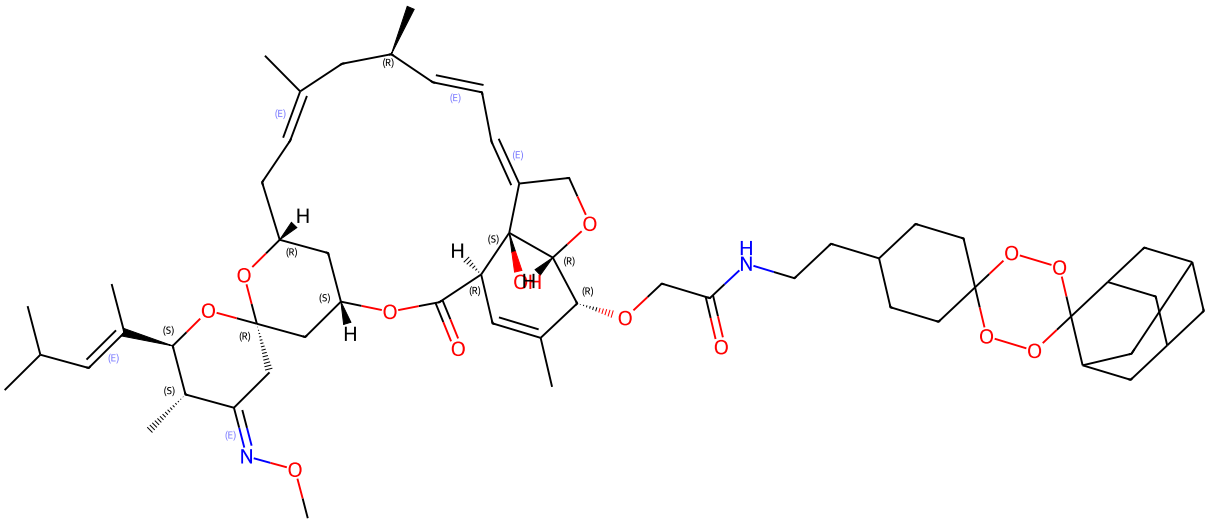
Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 7 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4i



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCCC6CCC7(CC6)OOC6(OO7)C7CC8CC(C7)CC6
C8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCCC6CCC7(CC6)OOC6(OO7)C7CC8CC(C7)CC6
C8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C57H82N2O13
Molecular weight (g/mol)	1003.284
Exact mass (Da)	1002.581691
Crippen cLogP	9.2084
TPSA (Å²)	171.06
H-bond donors	2
H-bond acceptors	14
Rotatable bonds	9

Rings	11
Formal charge	0
Heavy atoms	72
Unassigned stereo — modern	7
Unassigned stereo — legacy	0

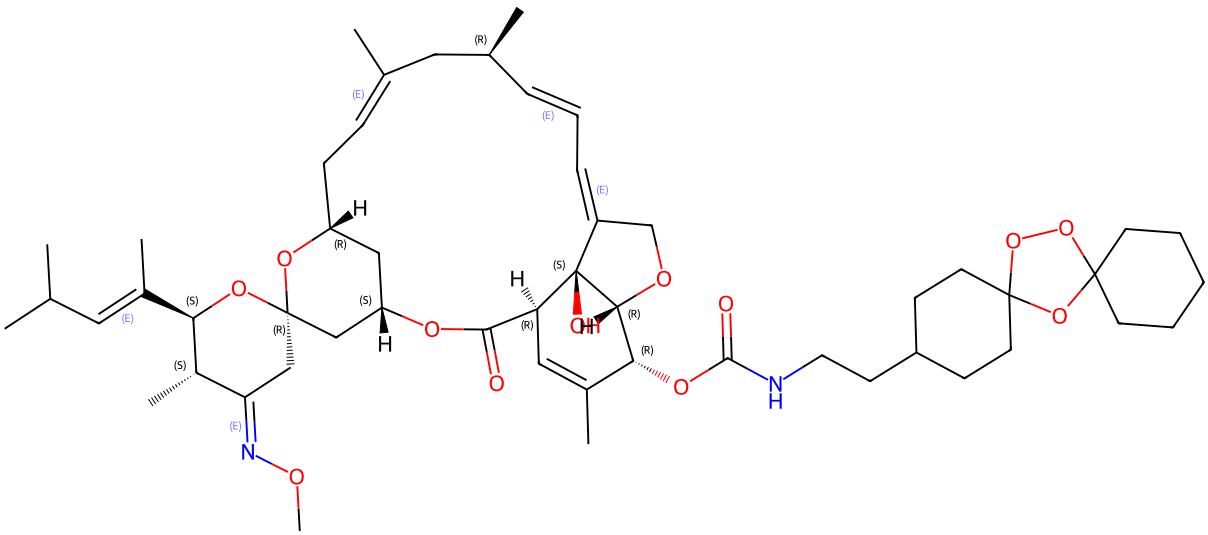
Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 7 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4j



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)O7)C(C)=C[C@
@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)
[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)O7)C(C)=C[C@
@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)
[C@H]1C

Complete computed profile

Formula	C52H76N2O12
Molecular weight (g/mol)	921.182
Exact mass (Da)	920.539826
Crippen cLogP	9.3782
TPSA (Å²)	161.83
H-bond donors	2
H-bond acceptors	13
Rotatable bonds	7

Rings	8
Formal charge	0
Heavy atoms	66
Unassigned stereo — modern	2
Unassigned stereo — legacy	0

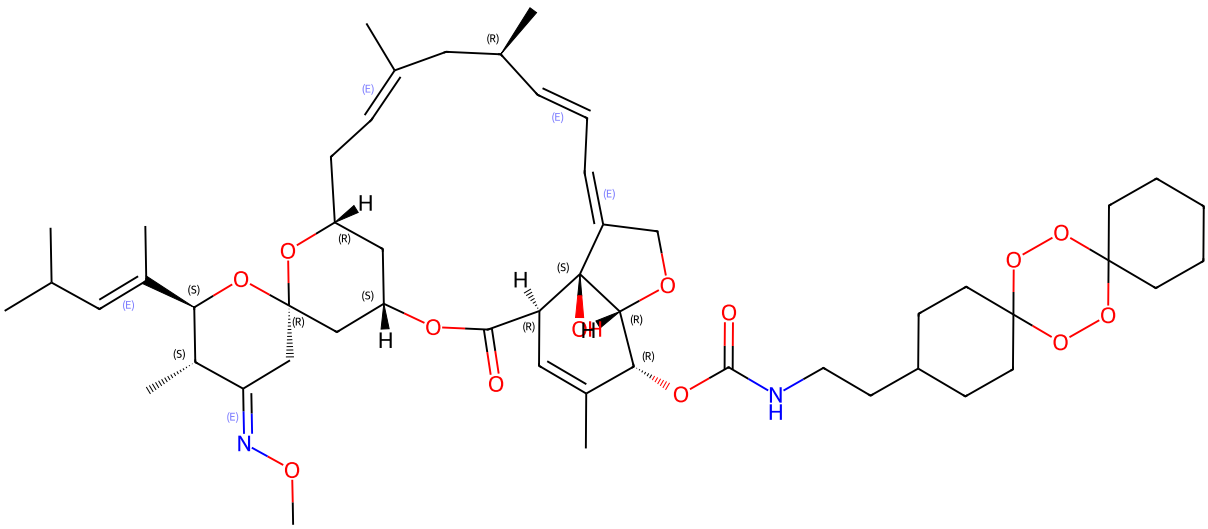
Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 2 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4k



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C52H76N2O13
Molecular weight (g/mol)	937.181
Exact mass (Da)	936.53474
Crippen cLogP	9.3098
TPSA (Å²)	171.06
H-bond donors	2
H-bond acceptors	14
Rotatable bonds	7

Rings	8
Formal charge	0
Heavy atoms	67
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

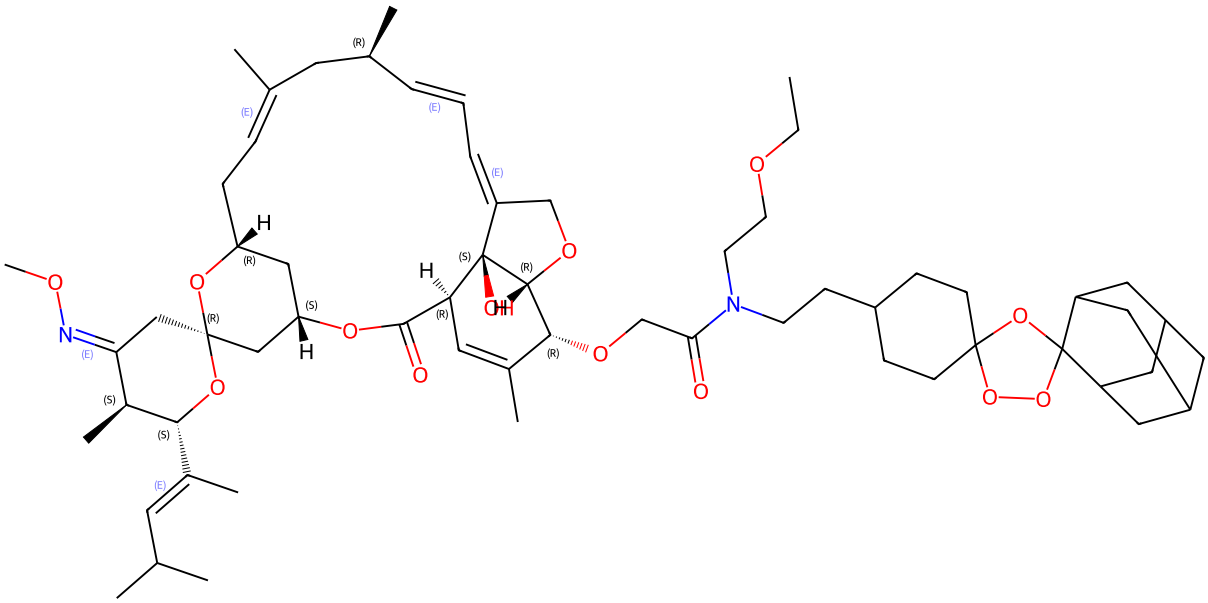
Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

C4l



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CCOCCN(CCC1CCC2(CC1)OOC1(O2)C2CC3CC(C2)CC1C3)C(=O)CO[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CCOCCN(CCC1CCC2(CC1)OOC1(O2)C2CC3CC(C2)CC1C3)C(=O)CO[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C61H90N2O13
Molecular weight (g/mol)	1059.392
Exact mass (Da)	1058.644291
Crippen cLogP	10.0257
TPSA (Å²)	162.27
H-bond donors	1
H-bond acceptors	14
Rotatable bonds	13

Rings	11
Formal charge	0
Heavy atoms	76
Unassigned stereo — modern	7
Unassigned stereo — legacy	0

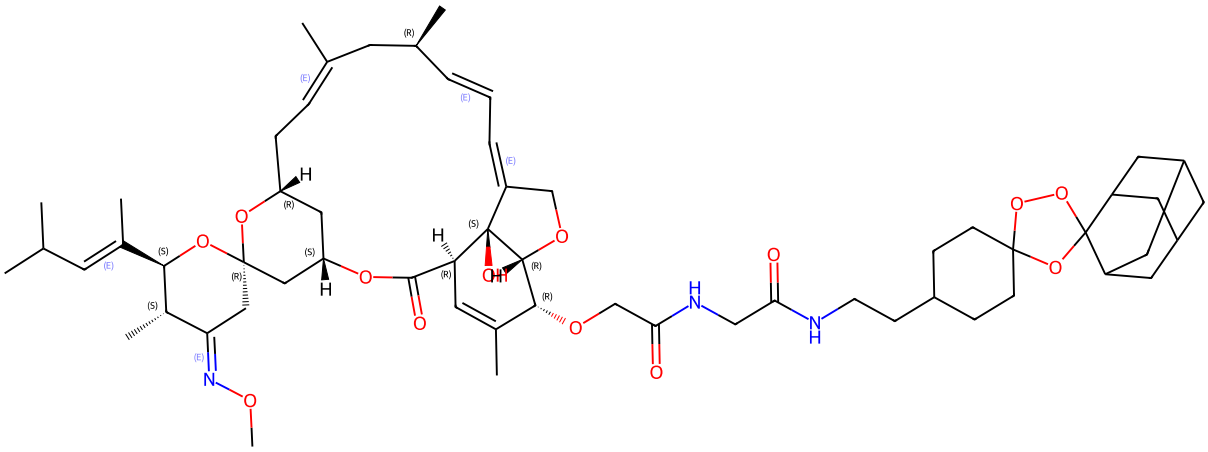
Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 13 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 7 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4m



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCC(=O)NCCC6CCC7(CC6)OOC6(O7)C7CC8CC(
C7)CC6C8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCC(=O)NCCC6CCC7(CC6)OOC6(O7)C7CC8CC(
C7)CC6C8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C59H85N3O13
Molecular weight (g/mol)	1044.337
Exact mass (Da)	1043.60824
Crippen cLogP	8.393
TPSA (Å²)	190.93
H-bond donors	3
H-bond acceptors	14
Rotatable bonds	11

Rings	11
Formal charge	0
Heavy atoms	75
Unassigned stereo — modern	7
Unassigned stereo — legacy	0

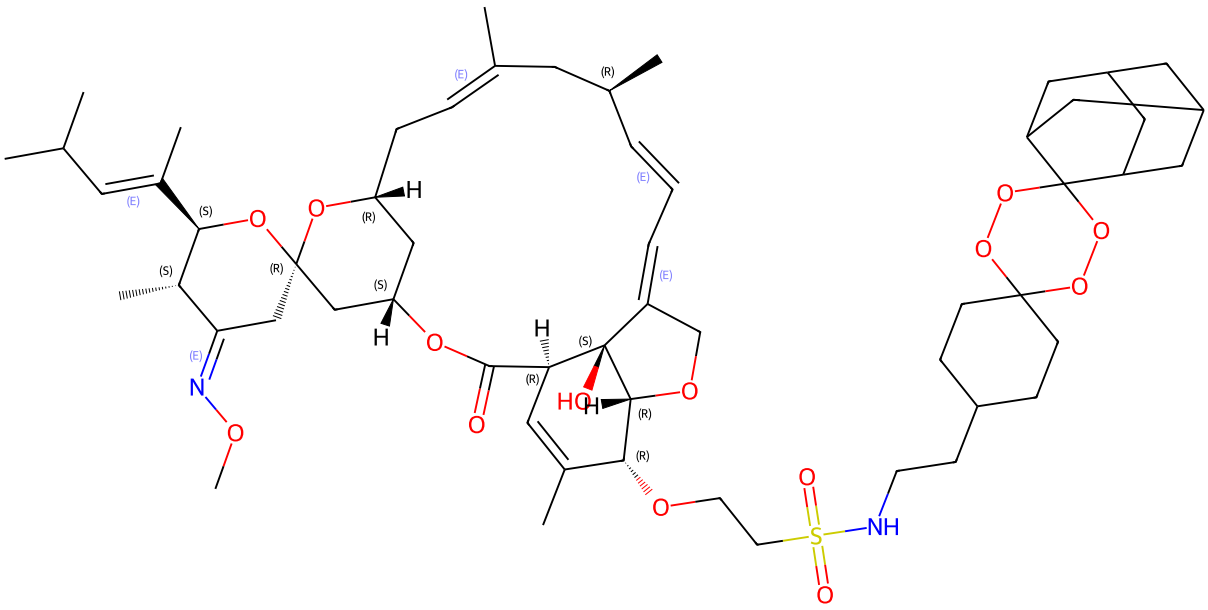
Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 11 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 7 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4n



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCS(=O)
(=O)NCCC6CCC7(CC6)OOC6(OO7)C7CC8CC(C7)CC6C8)C
(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCS(=O)
(=O)NCCC6CCC7(CC6)OOC6(OO7)C7CC8CC(C7)CC6C8)C
(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C57H84N2O14S
Molecular weight (g/mol)	1053.366
Exact mass (Da)	1052.564326
Crippen cLogP	9.0116
TPSA (Å²)	188.13
H-bond donors	2
H-bond acceptors	15

Rotatable bonds	11
Rings	11
Formal charge	0
Heavy atoms	74
Unassigned stereo — modern	7
Unassigned stereo — legacy	0

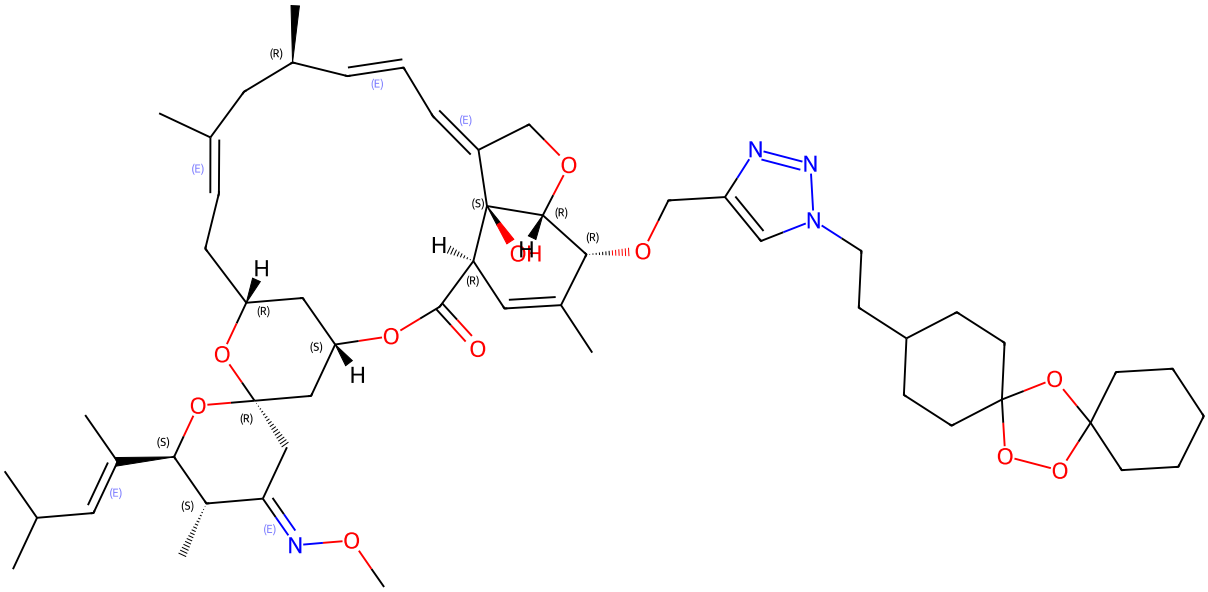
Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 11 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 7 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4o



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCc6cn(CCC7CCC8(CC7)OOC7(CCCCC7)O8)nn6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCc6cn(CCC7CCC8(CC7)OOC7(CCCCC7)O8)nn6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C54H78N4O11
Molecular weight (g/mol)	959.235
Exact mass (Da)	958.566709
Crippen cLogP	9.4603
TPSA (Å²)	163.44
H-bond donors	1
H-bond acceptors	14
Rotatable bonds	9

Rings	9
Formal charge	0
Heavy atoms	69
Unassigned stereo — modern	2
Unassigned stereo — legacy	0

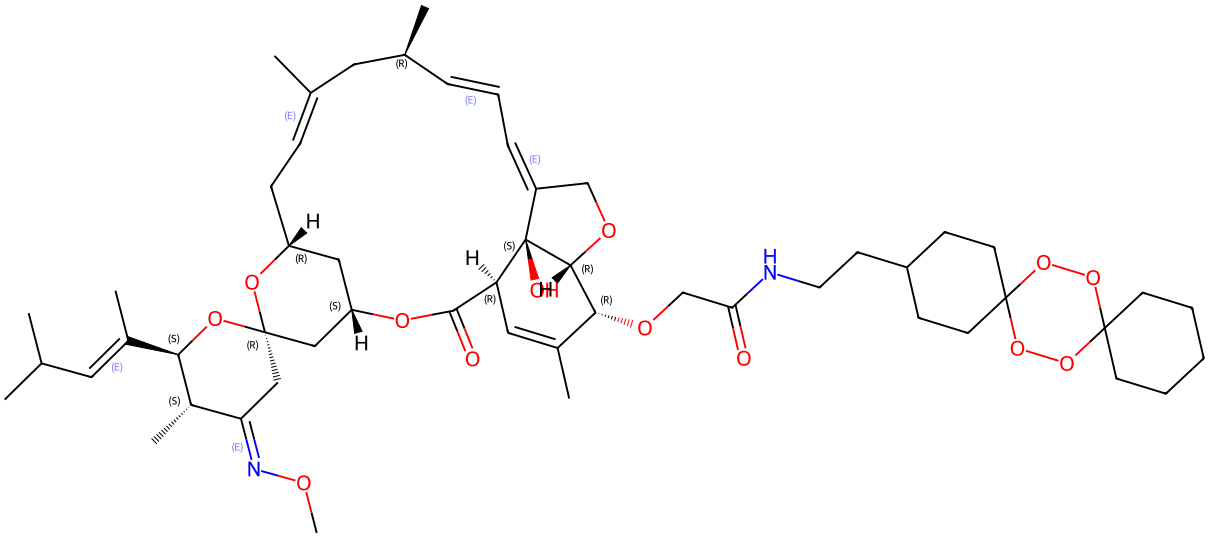
Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 2 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4p



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C53H78N2O13
Molecular weight (g/mol)	951.208
Exact mass (Da)	950.550391
Crippen cLogP	8.7164
TPSA (Å²)	171.06
H-bond donors	2
H-bond acceptors	14
Rotatable bonds	9

Rings	8
Formal charge	0
Heavy atoms	68
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

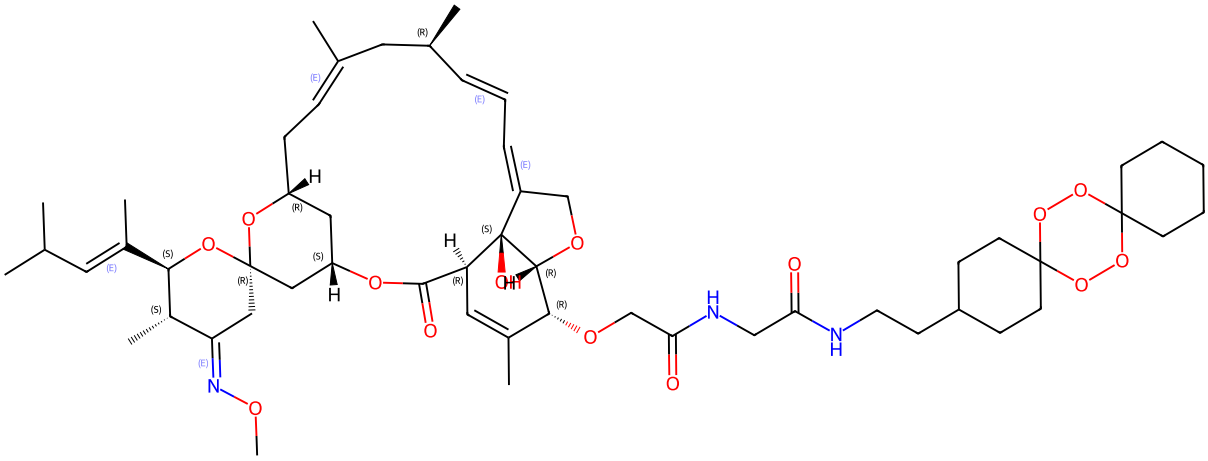
Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

C4q



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)
C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)
C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C55H81N3O14
Molecular weight (g/mol)	1008.26
Exact mass (Da)	1007.571854
Crippen cLogP	7.8326
TPSA (Å²)	200.16
H-bond donors	3
H-bond acceptors	15
Rotatable bonds	11

Rings	8
Formal charge	0
Heavy atoms	72
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

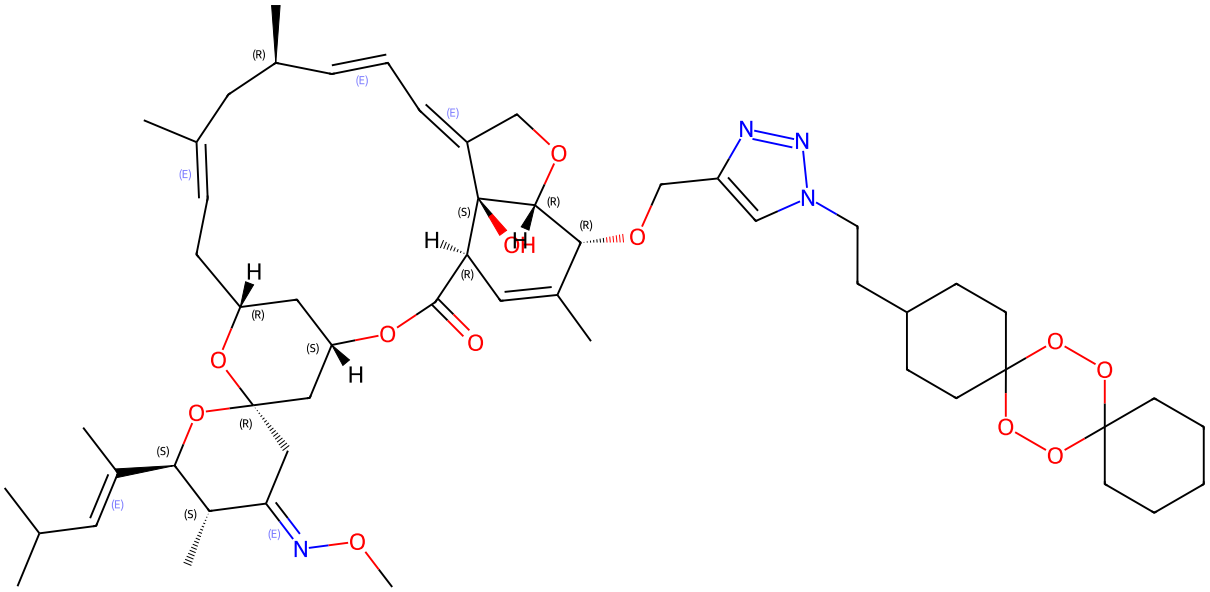
Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 11 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

C4r



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCc6cn(CCC7CCC8(CC7)OOC7(CCCCC7)OO8)nn6)C(C)=
C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)
[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCc6cn(CCC7CCC8(CC7)OOC7(CCCCC7)OO8)nn6)C(C)=
C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)
[C@H]1C

Complete computed profile

Formula	C54H78N4O12
Molecular weight (g/mol)	975.234
Exact mass (Da)	974.561624
Crippen cLogP	9.3919
TPSA (Å²)	172.67
H-bond donors	1
H-bond acceptors	15
Rotatable bonds	9

Rings	9
Formal charge	0
Heavy atoms	70
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

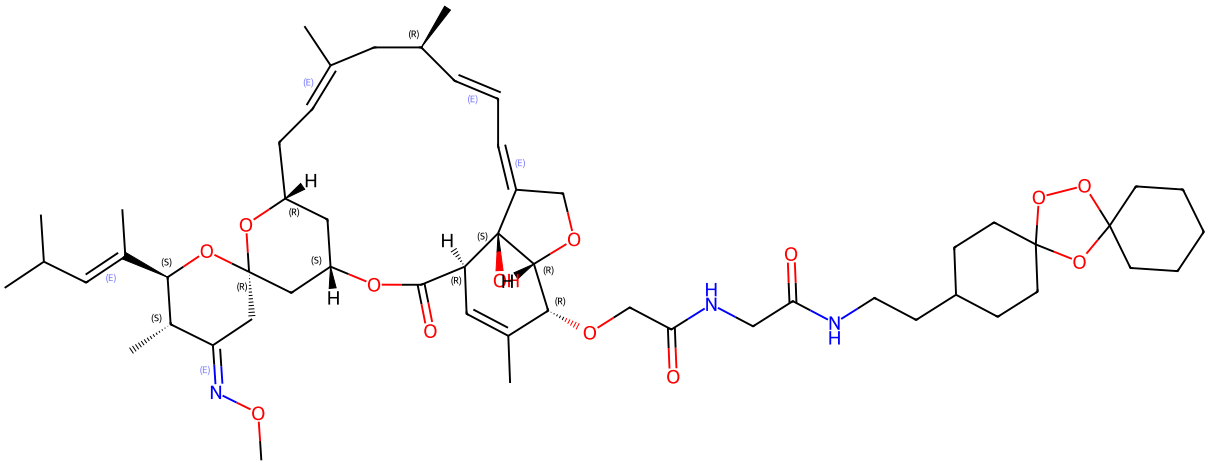
Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

C4s



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)O7)C
(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)O7)C
(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C55H81N3O13
Molecular weight (g/mol)	992.261
Exact mass (Da)	991.57694
Crippen cLogP	7.901
TPSA (Å²)	190.93
H-bond donors	3
H-bond acceptors	14
Rotatable bonds	11

Rings	8
Formal charge	0
Heavy atoms	71
Unassigned stereo — modern	2
Unassigned stereo — legacy	0

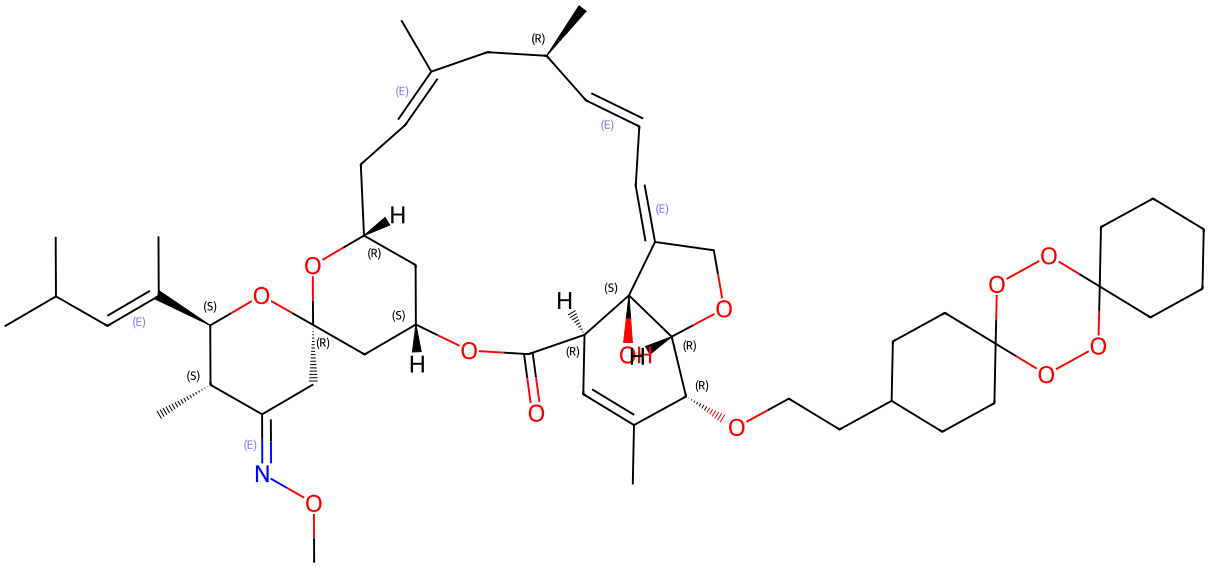
Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 11 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 2 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

C4t



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C51H75NO12
Molecular weight (g/mol)	894.156
Exact mass (Da)	893.528927
Crippen cLogP	9.6002
TPSA (Å²)	141.96
H-bond donors	1
H-bond acceptors	13
Rotatable bonds	7
Rings	8

Formal charge	0
Heavy atoms	64
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

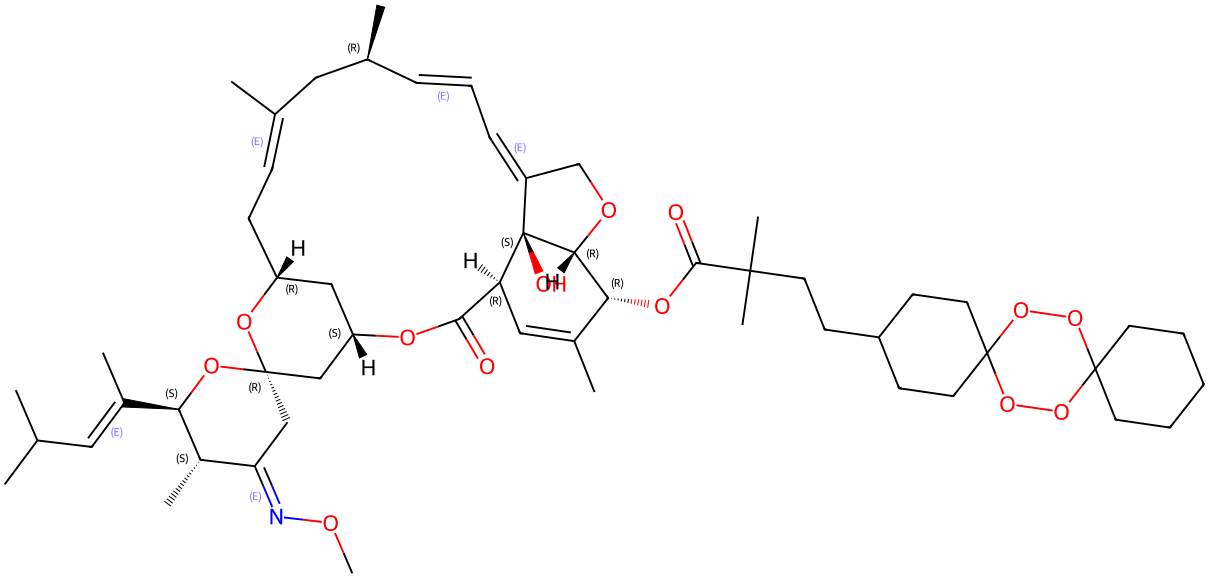
Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

C4u



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)C(C)
(C)CCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)C(C)
(C)CCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C55H81NO13
Molecular weight (g/mol)	964.247
Exact mass (Da)	963.570792
Crippen cLogP	10.5431
TPSA (Å²)	159.03
H-bond donors	1
H-bond acceptors	14
Rotatable bonds	8

Rings	8
Formal charge	0
Heavy atoms	69
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

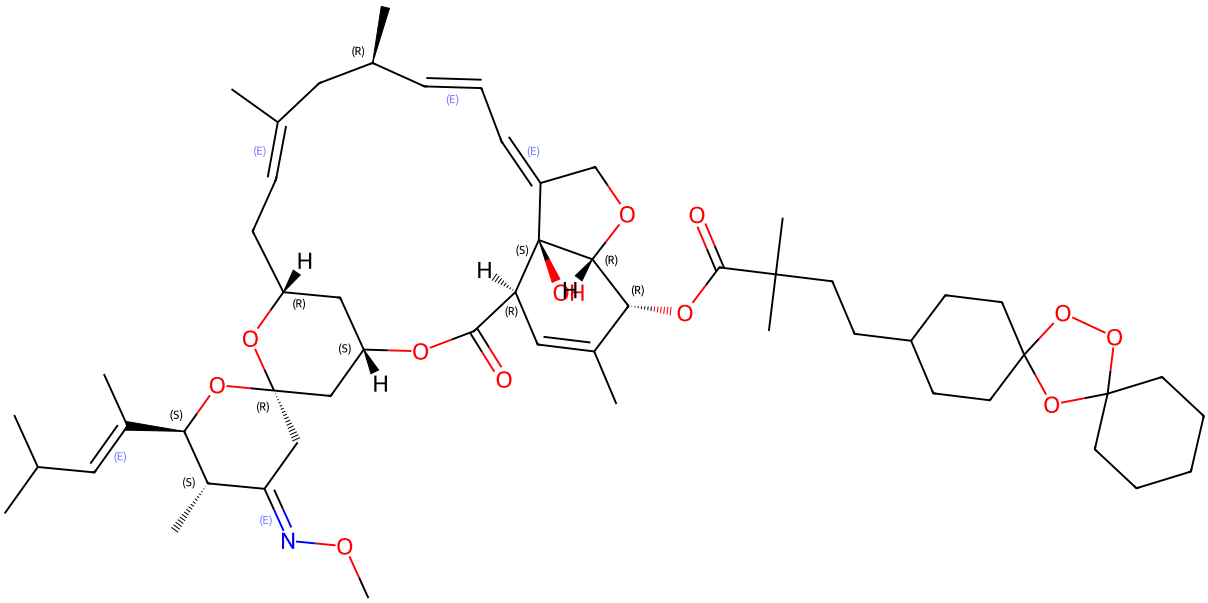
Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 8 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

C4v



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)C(C)
(C)CCC6CCC7(CC6)OOC6(CCCCC6)O7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)C(C)
(C)CCC6CCC7(CC6)OOC6(CCCCC6)O7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C55H81NO12
Molecular weight (g/mol)	948.248
Exact mass (Da)	947.575877
Crippen cLogP	10.6115
TPSA (Å²)	149.8
H-bond donors	1
H-bond acceptors	13
Rotatable bonds	8

Rings	8
Formal charge	0
Heavy atoms	68
Unassigned stereo — modern	2
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 8 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 2 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

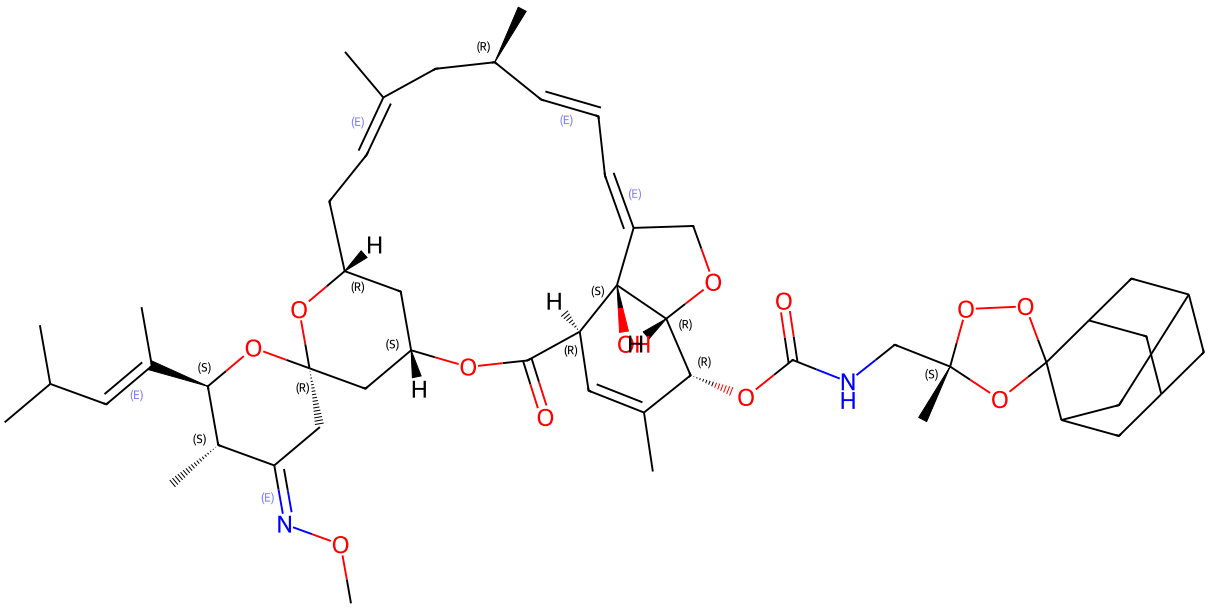
Node85 combined.json; C4 papers and source scripts

CHAPTER 6

C4 branch — Atlas

ATLAS-C4-S01 through ATLAS-C4-S12: all 12 records, including source-held cage cases. The full source assessment and route proposals appear in the documentary chapters.

ATLAS-C4-S01



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NC[C@]6(C)OOC7(O6)C6CC8CC(C6)CC7C8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NC[C@]6(C)OOC7(O6)C6CC8CC(C6)CC7C8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C51H72N2O12
Molecular weight (g/mol)	905.139
Exact mass (Da)	904.508526
Crippen cLogP	8.3098
TPSA (Å²)	161.83
H-bond donors	2
H-bond acceptors	13
Rotatable bonds	6

Rings	10
Formal charge	0
Heavy atoms	65
Unassigned stereo — modern	5
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 6 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 5 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

Original Atlas compound discussion

ATLAS-C4-S01 — Adamantane-shielded monospiro trioxolane

Design rationale / liability addressed: Keeps the adamantane spiro shield, replaces the C5 ester with a

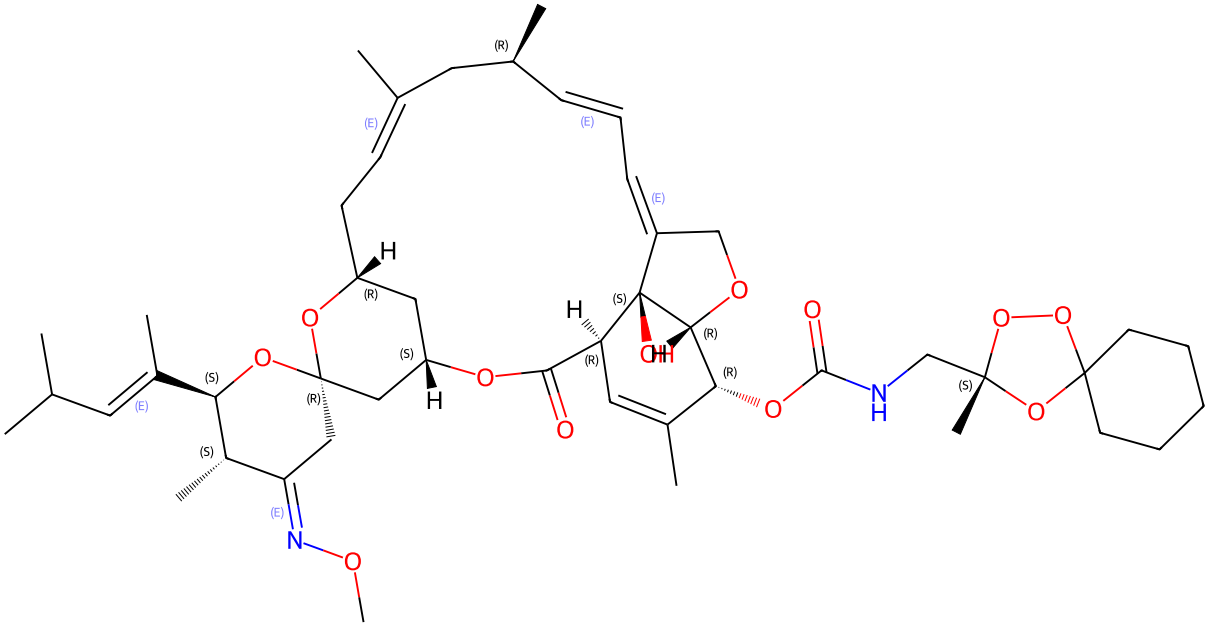
carbamate, and specifies the sole new peroxide stereocentre.

Precedent: [P1], [P2], [P3], [P4]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The chosen single-spiro appendage is a structural extrapolation from the better established dispiro series.

New failure mode / cost: The other peroxide carbon is acyclic rather than the second spiro ring of OZ277/OZ439: reduced shielding and a different activation profile are possible. MW rises to about 905; the carbamate is still an enzyme-sensitive bond.

Disposition: Cage-stereo review; not counted in ten fully specified nominees. Net tetrahedral-centre reduction versus deposited C4: 5; see the separate cage audit for held entries.

ATLAS-C4-S02



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC[C@]6(C)OOC7(CCCCC7)O6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC[C@]6(C)OOC7(CCCCC7)O6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C47H68N2O12
Molecular weight (g/mol)	853.063
Exact mass (Da)	852.477226
Crippen cLogP	7.8178
TPSA (Å²)	161.83
H-bond donors	2
H-bond acceptors	13
Rotatable bonds	6
Rings	7

Formal charge	0
Heavy atoms	61
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 6 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

Original Atlas compound discussion

ATLAS-C4-S02 — Cyclohexane monospiro trioxolane

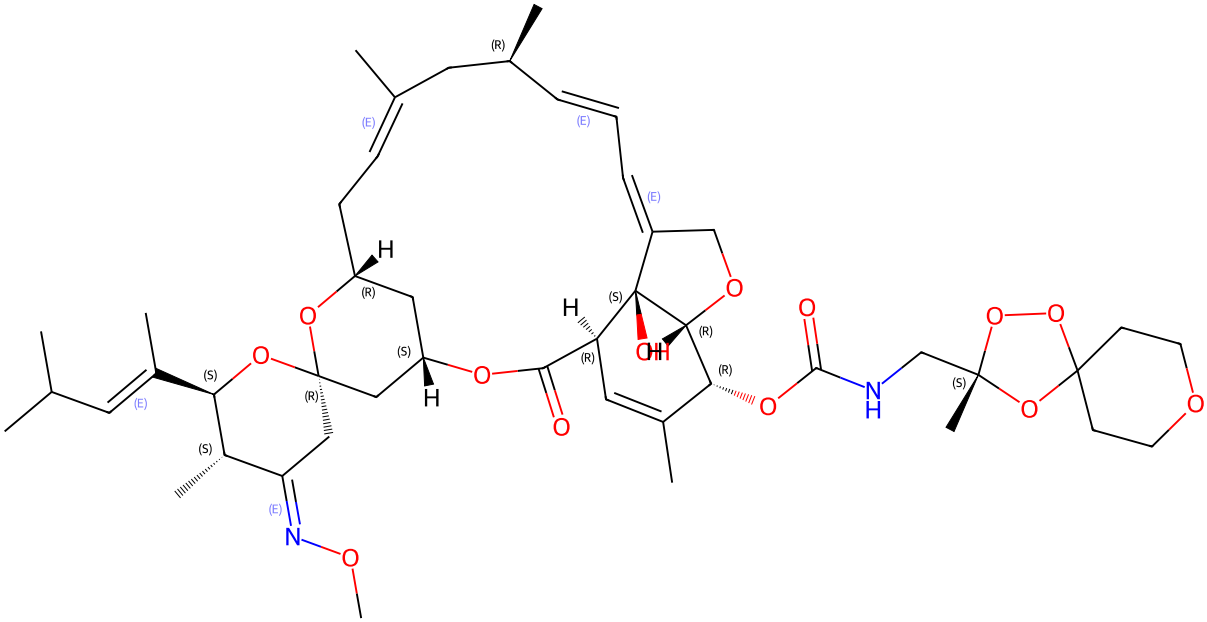
Design rationale / liability addressed: Removes the fused ambiguous cage, shortens the appendage and replaces the C5 ester.

Precedent: [P1], [P3], [P4]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The chosen single-spiro appendage is a structural extrapolation from the better established dispiro series.

New failure mode / cost: Removing adamantane may increase premature iron-mediated loss; the simple cyclohexane is a property-saving hypothesis, not an OZ-equivalent stabiliser.

Disposition: Selected: compact trioxolane comparator. Net tetrahedral-centre reduction versus deposited C4: 5; see the separate cage audit for held entries.

ATLAS-C4-S03



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC[C@]6(C)OOC7(CCOCC7)O6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC[C@]6(C)OOC7(CCOCC7)O6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C46H66N2O13
Molecular weight (g/mol)	855.035
Exact mass (Da)	854.45649
Crippen cLogP	6.6641
TPSA (Å²)	171.06
H-bond donors	2
H-bond acceptors	14
Rotatable bonds	6
Rings	7

Formal charge	0
Heavy atoms	61
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 6 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

Original Atlas compound discussion

ATLAS-C4-S03 — Oxane monospiro trioxolane

Design rationale / liability addressed: Trades one cyclohexane carbon for oxygen to reduce calculated lipophilicity while retaining a tertiary peroxide environment and a C5 carbamate.

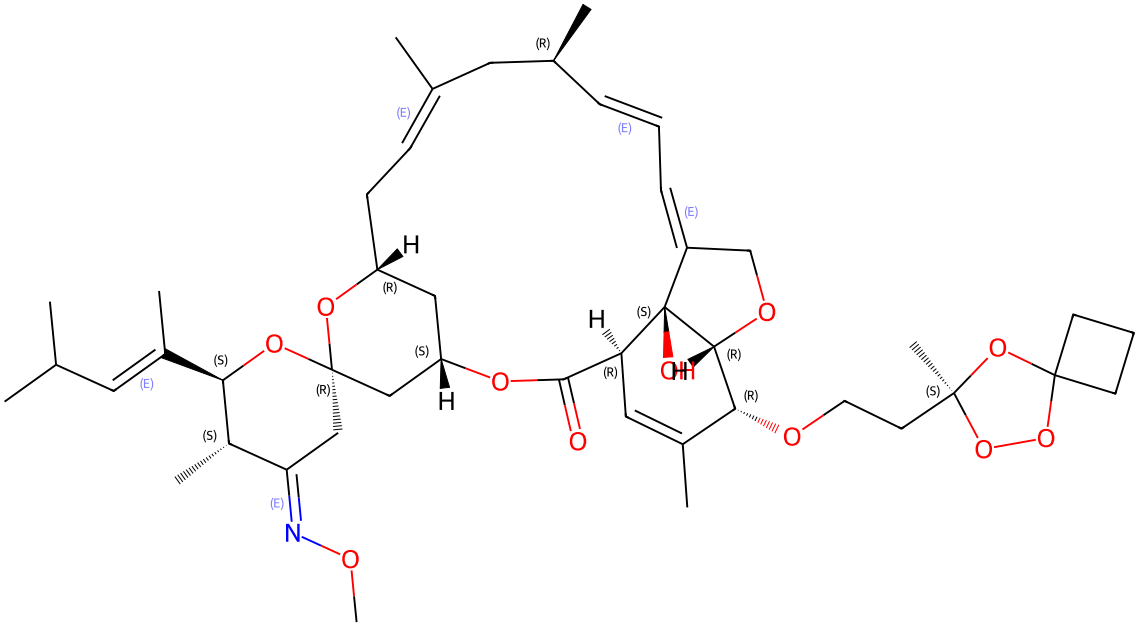
Precedent: [P1], [P3], [P4]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin

conjugate. The chosen single-spiro appendage is a structural extrapolation from the better established dispiro series.

New failure mode / cost: The ring oxygen adds oxidative-metabolism and conformational liabilities; TPSA increases and iron activation may be too rapid or too slow. No exact oxane-conjugate precedent is claimed.

Disposition: Exploratory polarity probe. Net tetrahedral-centre reduction versus deposited C4: 5; see the separate cage audit for held entries.

ATLAS-C4-S04



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC[C@]6(C)OOC7(CCC7)O6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC[C@]6(C)OOC7(CCC7)O6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C45H65NO11
Molecular weight (g/mol)	796.011
Exact mass (Da)	795.455762
Crippen cLogP	7.7181
TPSA (Å²)	132.73
H-bond donors	1
H-bond acceptors	12
Rotatable bonds	7
Rings	7

Formal charge	0
Heavy atoms	57
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

Original Atlas compound discussion

ATLAS-C4-S04 — Cyclobutane monospiro trioxolane

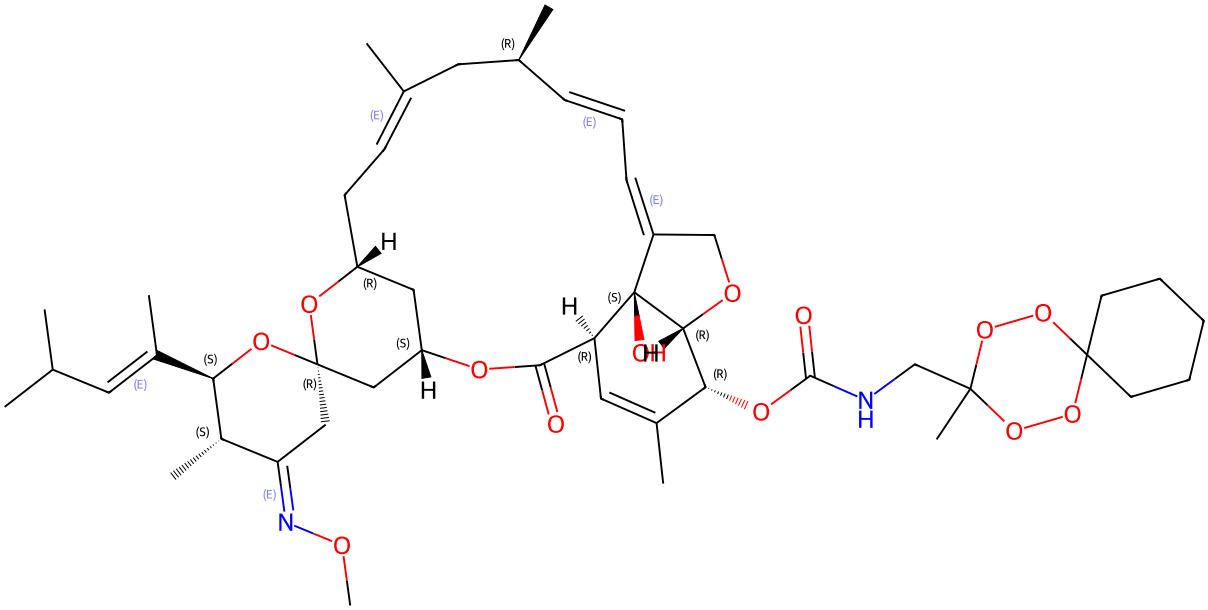
Design rationale / liability addressed: Eliminates the hydrolysable C5 acyl linkage entirely and contracts the peroxide substituent.

Precedent: [P1], [P2]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The chosen single-spiro appendage is a structural extrapolation from the better established dispiro series.

New failure mode / cost: Weaker shielding, small-ring strain and oxidative O-dealkylation replace ester hydrolysis as liabilities; C5 ether formation may be harder than carbamylation.

Disposition: Low-mass boundary probe. Net tetrahedral-centre reduction versus deposited C4: 5; see the separate cage audit for held entries.

ATLAS-C4-S05



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC6(C)OOC7(CCCCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC6(C)OOC7(CCCCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C47H68N2O13
Molecular weight (g/mol)	869.062
Exact mass (Da)	868.47214
Crippen cLogP	7.7494
TPSA (Å²)	171.06
H-bond donors	2
H-bond acceptors	14
Rotatable bonds	6
Rings	7

Formal charge	0
Heavy atoms	62
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 6 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

Original Atlas compound discussion

ATLAS-C4-S05 — Cyclohexane monospiro tetraoxane

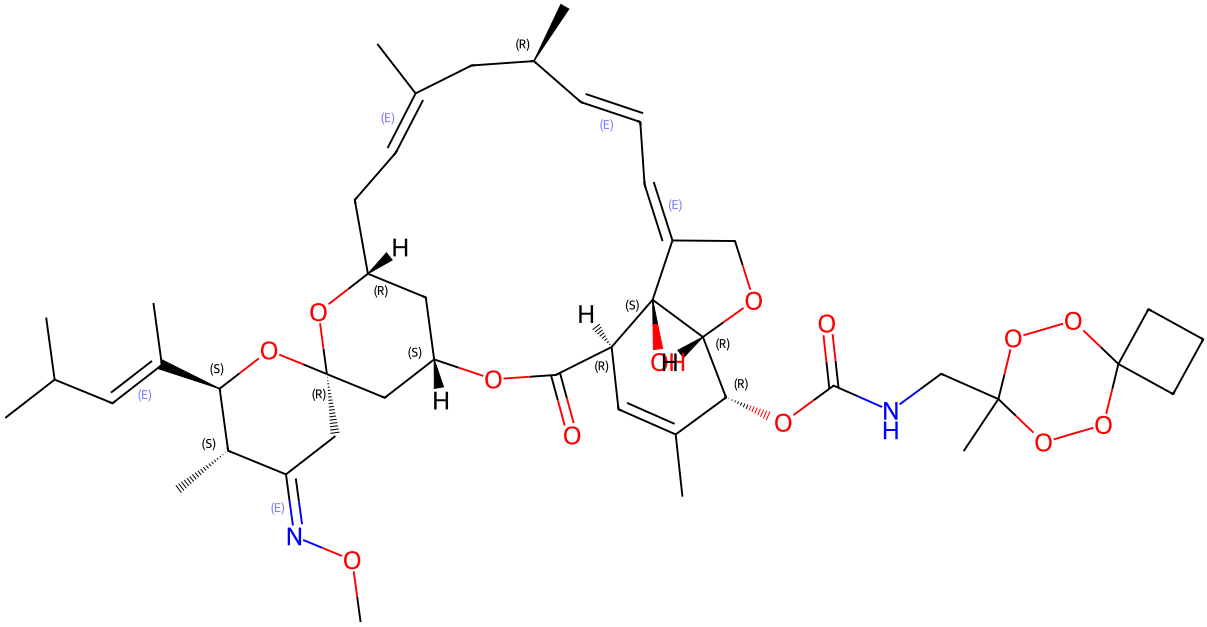
Design rationale / liability addressed: Uses an achiral-added tetraoxane and a smaller appendage with a C5 carbamate.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: The monospiro design gives up the second spiro ring of stronger precedented tetraoxanes; extra O–O cleavage channels can consume it before useful radical chemistry.

Disposition: Reserve. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S06



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC6(C)OOC7(CCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC6(C)OOC7(CCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C45H64N2O13
Molecular weight (g/mol)	841.008
Exact mass (Da)	840.44084
Crippen cLogP	6.9692
TPSA (Å²)	171.06
H-bond donors	2
H-bond acceptors	14
Rotatable bonds	6
Rings	7

Formal charge	0
Heavy atoms	60
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 6 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

Original Atlas compound discussion

ATLAS-C4-S06 — Cyclobutane monospiro tetraoxane

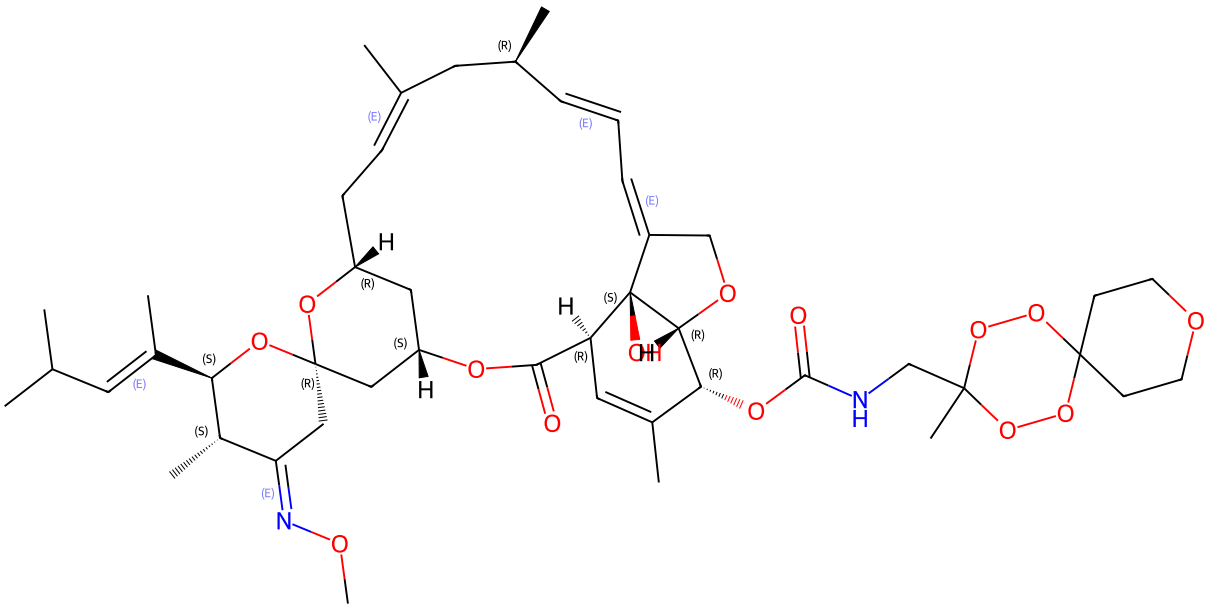
Design rationale / liability addressed: Cuts mass and calculated lipophilicity while removing all six extra C4 stereocentres.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: Combines two extrapolations: monospiro substitution and a contracted ring. Favourable descriptors may conceal poor peroxide lifetime or unproductive fragmentation.

Disposition: Exploratory compact probe. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S07



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC6(C)OOC7(CCOCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC6(C)OOC7(CCOCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C46H66N2O14
Molecular weight (g/mol)	871.034
Exact mass (Da)	870.451405
Crippen cLogP	6.5957
TPSA (Å²)	180.29
H-bond donors	2
H-bond acceptors	15
Rotatable bonds	6
Rings	7

Formal charge	0
Heavy atoms	62
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 6 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

Original Atlas compound discussion

ATLAS-C4-S07 — Oxane monospiro tetraoxane

Design rationale / liability addressed: Adds polarity without a basic amine and removes the C5 ester and extra tetrahedral stereocentres.

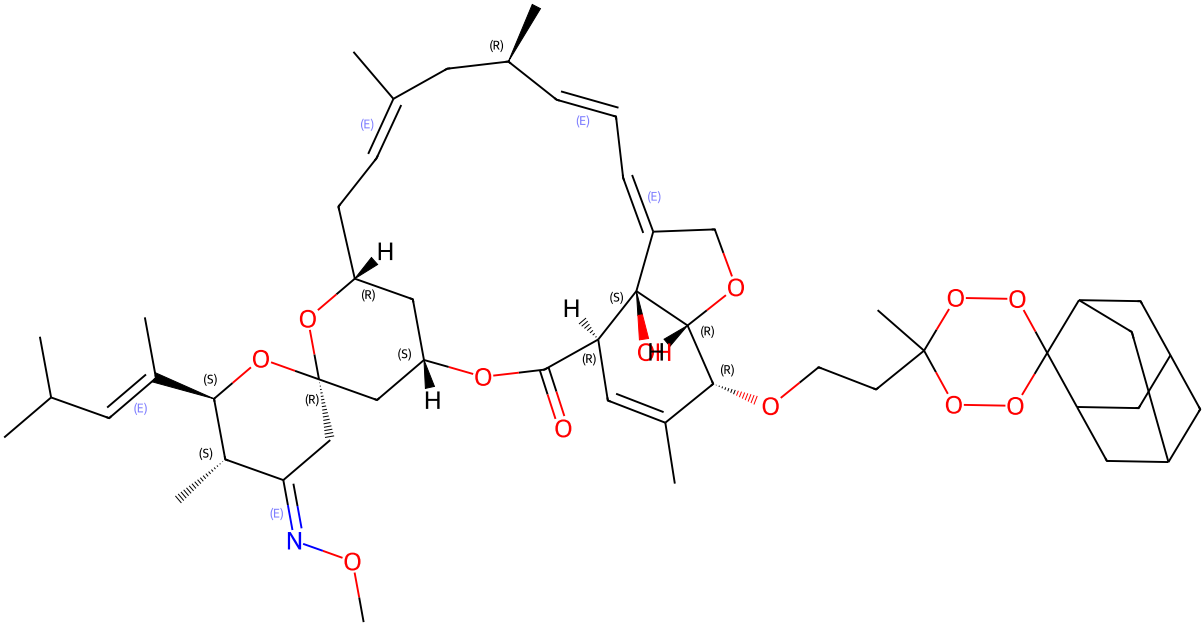
Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The

class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: TPSA near 180 and the cyclic ether can reduce delivery or add oxidation pathways; exact activation and plasma stability are unknown.

Disposition: Polarity comparator. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S08



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCC6(C)OOC7(OO6)C6CC8CC(C6)CC7C8)C(C)=C[C@@
H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCC6(C)OOC7(OO6)C6CC8CC(C6)CC7C8)C(C)=C[C@@
H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C51H73NO12
Molecular weight (g/mol)	892.14
Exact mass (Da)	891.513277
Crippen cLogP	8.9219
TPSA (Å²)	141.96
H-bond donors	1
H-bond acceptors	13
Rotatable bonds	7
Rings	10

Formal charge	0
Heavy atoms	64
Unassigned stereo — modern	6
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 6 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

Node85 combined.json; C4 papers and source scripts

Original Atlas compound discussion

ATLAS-C4-S08 — Adamantane monospiro tetraoxane

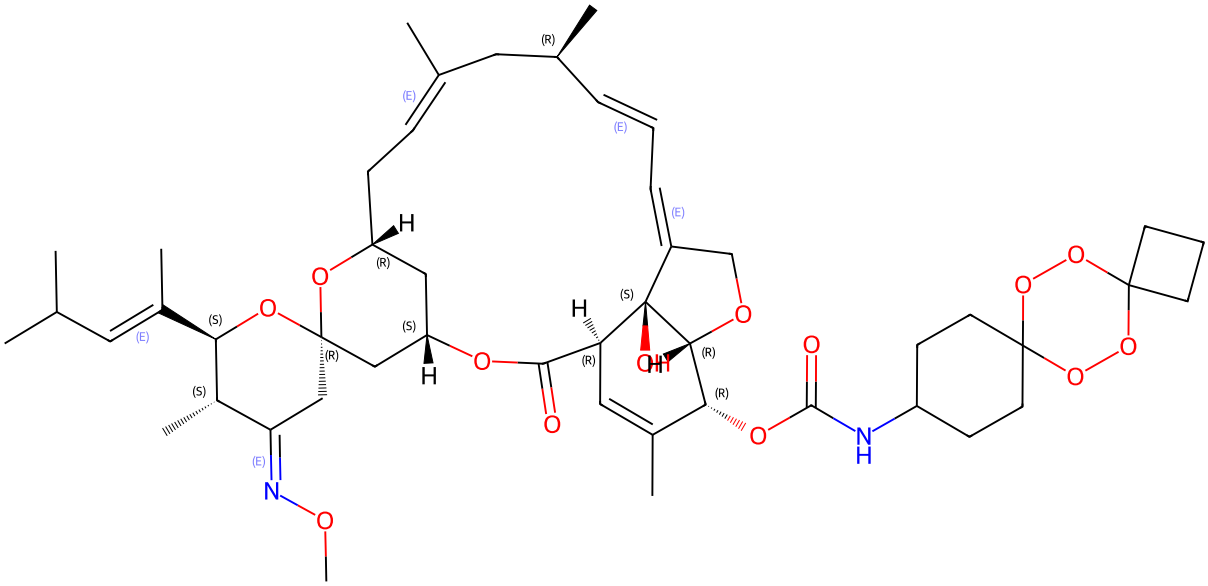
Design rationale / liability addressed: Keeps the adamantane shield and removes C5 acyl hydrolysis completely.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: cLogP remains close to 9, MW barely improves, and O-dealkylation may still split the hybrid. This is a lipophilicity-margin control, not a clean developability win.

Disposition: Cage-stereo review; not counted in ten fully specified nominees. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S09



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC6CCC7(CC6)OOC6(CCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC6CCC7(CC6)OOC6(CCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C48H68N2O13
Molecular weight (g/mol)	881.073
Exact mass (Da)	880.47214
Crippen cLogP	7.8919
TPSA (Å²)	171.06
H-bond donors	2
H-bond acceptors	14
Rotatable bonds	5
Rings	8

Formal charge	0
Heavy atoms	63
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 5 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

Original Atlas compound discussion

ATLAS-C4-S09 — Cyclohexane/cyclobutane dispiro tetraoxane

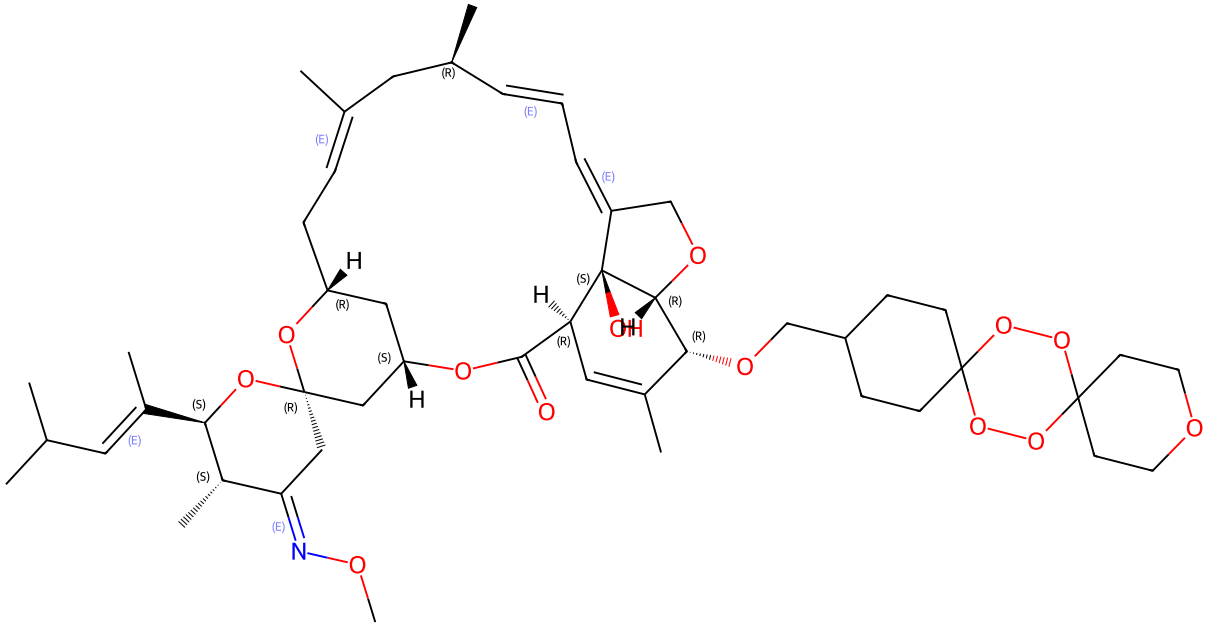
Design rationale / liability addressed: Retains two spiro rings, eliminates all six added C4 stereocentres, replaces its ester, and lowers both MW and cLogP.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: Cyclobutane contraction is not the E209 ring system: strain and changed radical partitioning may defeat the stability benefit. The C5 carbamate still needs plasma validation.

Disposition: Selected: lead. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S10



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC6CCC7(CC6)OOC6(CCOCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC6CCC7(CC6)OOC6(CCOCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C49H71NO13
Molecular weight (g/mol)	882.101
Exact mass (Da)	881.492541
Crippen cLogP	8.0564
TPSA (Å²)	151.19
H-bond donors	1
H-bond acceptors	14
Rotatable bonds	6
Rings	8

Formal charge	0
Heavy atoms	63
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 6 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

Original Atlas compound discussion

ATLAS-C4-S10 — Cyclohexane/oxane dispiro tetraoxane

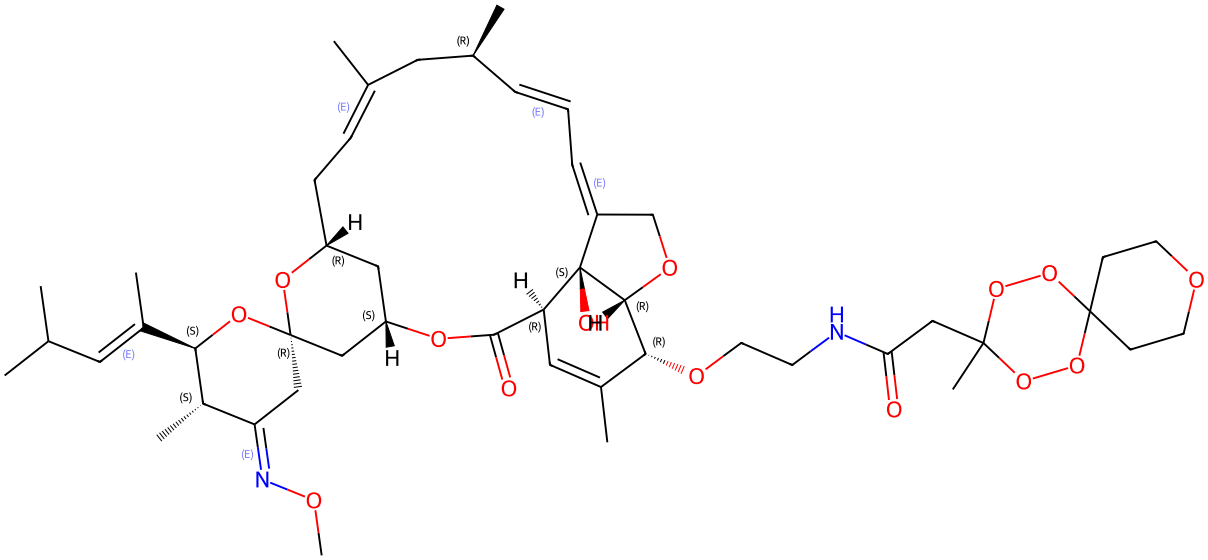
Design rationale / liability addressed: Retains dispiro topology, removes C5 acyl hydrolysis, and uses ring oxygen to lower lipophilicity without charge.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: Oxidative ether cleavage, altered radical products and uncertain C5-ether synthetic access are the price. A stable linker can also prevent useful parent release.

Disposition: Selected: linker-orthogonal lead. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S11



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCNC(=O)CC6(C)OOC7(CCOCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCNC(=O)CC6(C)OOC7(CCOCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C48H70N2O14
Molecular weight (g/mol)	899.088
Exact mass (Da)	898.482705
Crippen cLogP	6.3924
TPSA (Å²)	180.29
H-bond donors	2
H-bond acceptors	15
Rotatable bonds	9
Rings	7

Formal charge	0
Heavy atoms	64
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

Original Atlas compound discussion

ATLAS-C4-S11 — Oxane monospiro tetraoxane, ether-amide

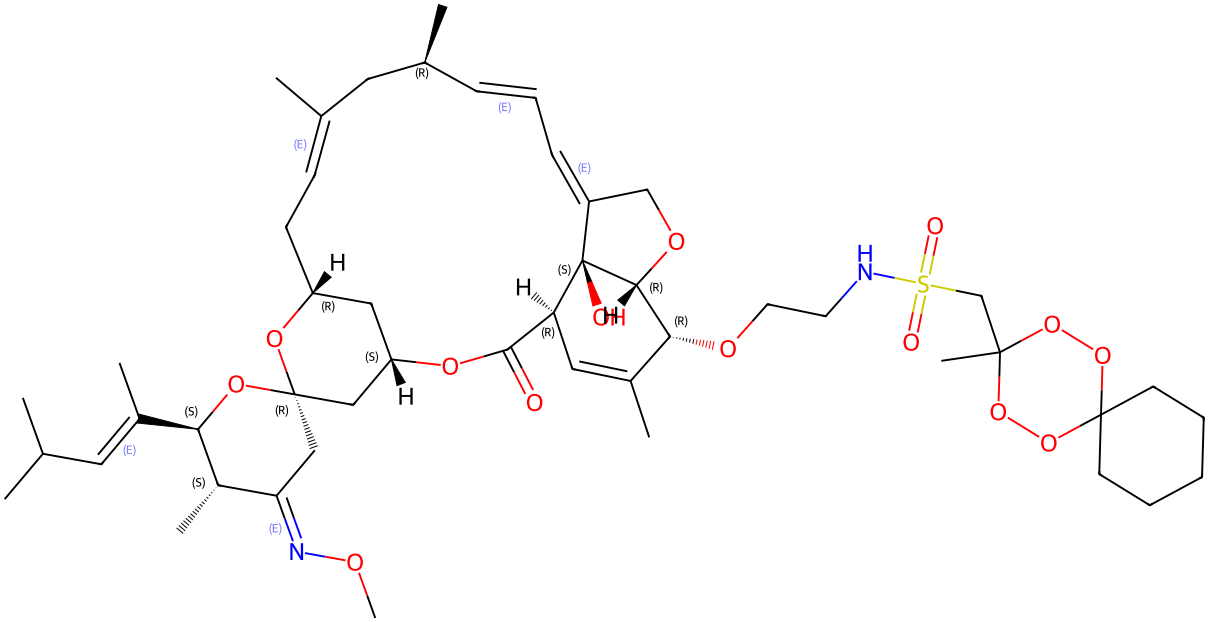
Design rationale / liability addressed: Attaches through a C5 ether; the amide is downstream, so there is no concealed C5 ester. Adds neutral polarity.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: Higher MW, TPSA and flexibility can defeat permeability; amidase cleavage or O-dealkylation can separate the components. This is not a direct C5 amide.

Disposition: Low priority polarity control. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S12



Recorded rationale and role

Peroxide architecture branch. This entry explores the balance between activation chemistry, appendage size, polarity, linkage persistence and stereochemical tractability. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCNS(=O)
(=O)CC6(C)OOC7(CCCCC7)OO6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCNS(=O)
(=O)CC6(C)OOC7(CCCCC7)OO6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C48H72N2O14S
Molecular weight (g/mol)	933.171
Exact mass (Da)	932.470426
Crippen cLogP	6.9592
TPSA (Å²)	188.13
H-bond donors	2
H-bond acceptors	15
Rotatable bonds	10

Rings	7
Formal charge	0
Heavy atoms	65
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 2 O–O bonds, net formal charge +0, and 10 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 combined.json; C4 papers and source scripts

Original Atlas compound discussion

ATLAS-C4-S12 — Cyclohexane monospiro tetraoxane, ether-sulfonamide

Design rationale / liability addressed: Replaces the C5 ester by an ether and adds a usually hydrolysis-resistant sulfonamide without a basic amine.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: Sulfonyl mass and high TPSA are substantial; sulfonamide ionisation is unmeasured, and oxidation can still cleave the C5 ether. Poor mass efficiency despite lower cLogP.

Disposition: Deprioritise: bloat. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

Why these top three

1. **S09 — first choice for a carbamate feasibility decision.** MW 881.1, cLogP 7.89: both improve on C4 without an ionisable basic group. Two spiro rings are retained, and all six ambiguous appendage centres disappear. It tests whether a small dispiro tetraoxane can retain useful lifetime and activation. The cyclobutane is the principal extrapolation, not an established benefit. TPSA 171.1 and uncertain activation remain substantial weaknesses.
2. **S10 — first choice for the non-acyl C5 test.** MW 882.1, cLogP 8.06, TPSA 151.2. The C5 ether directly addresses acyl hydrolysis and gives an informative contrast with S09. Its oxane ring exchanges some hydrophobic surface for oxygen. Oxidative fragmentation and difficult C5-selective ether formation are the new risks. Failure to release free parent is intentional and must be accepted or the design rejected.

3. **S02 — first choice for a compact trioxolane comparison.** MW 853.1 and cLogP 7.82 reduce the property burden, with only one specified added stereocentre. It asks whether retaining one spiro cyclohexane offers sufficient protection without the adamantane mass/cage-review burden. It has weaker structural precedent than the clinical dispiro ozonides and could be prematurely consumed. That is why it is an orthogonal comparator, not the presumed winner.

Do not synthesise all ten first. The first chemistry decision should test whether the chosen functionalised peroxide building blocks and the shared C5 attachment concept are viable. S01 can re-enter after cage review if a closer adamantane precedent is preferable. S06 is the compact tetraoxane reserve. S12 is deliberately deprioritised: adding a sulfonamide solves one bond problem at an excessive mass/polarity cost.

Chemistry feasibility and mechanism gates

Build the peroxide away from moxidectin. Moxidectin contains multiple alkenes. Applying the ozonide-forming chemistry used for isolated peroxide building blocks to the whole chassis would threaten that polyene. Late attachment of an already characterised peroxide fragment is the conceptual route; peroxide survival through that final operation remains unproved. Avoid assuming that conventional reducing deprotections or metal-catalysed operations are compatible with an O–O bond. This document specifies targets and feasibility questions, not a validated preparative procedure.

The carbamate series is the clearest first C5 platform: conceptually couple the parent alcohol to the corresponding peroxide-bearing carbamoyl partner while retaining C7 as the tertiary alcohol. The ether series is a parallel feasibility arm because an allylic secondary alcohol may not give clean O-selective attachment under conditions tolerated by both large fragments. Any C5 epimerisation, C7 regioisomer, peroxide loss or altered alkene geometry is a failure of the specified target, even if the mass spectrum looks right.

The amide and sulfonamide in S11/S12 sit **beyond a C5 ether**. They are not direct replacements of the C5 oxygen by nitrogen. A downstream robust bond does not protect an upstream labile ester; this is why no structure retains a hidden C5 ester while advertising an amide elsewhere. Triazoles and oxalamides were not required to reach ten meaningful designs. A CuAAC-derived triazole would require additional handle installation and metal/peroxide compatibility work; its hydrolysis resistance alone would not establish a superior whole molecule.

Proposed decision gates, to be fixed in an assay plan before seeing results:

- **Identity:** isolate the specified C5 product; establish regiochemistry, alkene geometry, peroxide integrity and stereochemistry by methods appropriate to each. Parsing and an SDF are not identity evidence.
- **Lifetime and activation:** compare intact conjugate loss and identified products in buffer, human plasma and the relevant species matrix, alongside iron-controlled activation measurements. The goal is useful separation

between nonspecific disappearance and productive activation, not maximum inertness. Measure radical-related products/orthogonal signals; a generic ROS dye alone does not establish the proposed event.

- **Mechanism in cancer cells:** establish intact cellular exposure and compare with moxidectin, the corresponding unconjugated peroxide fragment, their equimolar mixture, and a matched nonperoxidic analogue. Examine iron dependence and intervention controls while accounting for their independent effects on growth. Peroxide cleavage need not mean ferroptosis; do not infer a cell-death programme from one marker.
- **Delivery and safety:** measure solubility, protein binding, unbound cell/tumour exposure and transporter behaviour. Compare bidirectional transport with parent in a validated P-gp system with an appropriate inhibitor/control; inspect mass balance and viability. For GBM include unbound brain/tumour delivery and normal neural controls. A neutral design can still become a transporter substrate or inhibitor.
- **Keep-or-stop:** the line earns further work only if an intact conjugate provides a reproducible exposure-adjusted advantage over the mixture without destroying the parent's delivery advantage or normal-cell margin. If all useful activity comes from premature fragmentation, or all surviving conjugates lose cellular access, use co-dosing or a different delivery strategy rather than preserving the hybrid for its own sake.

Verified literature and scope of inference

These are primary research records checked for identity and relevant scope. Antimalarial chemistry is cited solely as a peroxide-design precedent; disease efficacy is not transferred into cancer. The exact structures in this dossier have no claimed literature validation.

- **P1 — Vennerstrom et al. (2004).** *Identification of an antimalarial synthetic trioxolane drug development candidate.* Nature **430**, 900–904. Primary publisher record, DOI 10.1038/nature02779. Establishes the synthetic ozonide/dispiro lineage; does not validate the single-spiro replacements here.
- **P2 — Creek et al. (2007).** *Iron-mediated degradation kinetics of substituted dispiro-1,2,4-trioxolane antimalarials.* Journal of Pharmaceutical Sciences **96**(11), 2945–2956. Primary indexed record, DOI 10.1002/jps.20958. Supports iron-mediated cleavage, substituent-dependent kinetics and the need to measure rather than equate reactivity with activity. The indexed abstract was also retrieved through Europe PMC and saved locally.
- **P3 — Charman et al. (2011).** *Synthetic ozonide drug candidate OZ439 offers new hope for a single-dose cure of uncomplicated malaria.* PNAS **108**(11), 4400–4405. Primary full text, DOI 10.1073/pnas.1015762108. Specific ozonides balance iron/heme reactivity and exposure. It does not prove every spiroadamantane conjugate is stable or cancer-selective.

- **P4 — Blank et al. (2020).** *Antimalarial Trioxolanes with Superior Drug-Like Properties and In Vivo Efficacy.* ACS Infectious Diseases **6**(7), 1827–1835. Primary full text, DOI 10.1021/acsinfecdis.0c00064. Reports stereocontrolled carbamate-substituted trioxolanes and their evaluated properties. Its carbamate placement/orientation differs from the proposed C5 moxidectin carbamates; that distinction is not erased.
- **P5 — O'Neill, Amewu, Charman et al. (2017).** *A tetraoxane-based antimalarial drug candidate that overcomes PfK13-C580Y dependent artemisinin resistance.* Nature Communications **8**, 15159. Primary publisher record, DOI 10.1038/ncomms15159; PMID 28537265. E209 supplies a tetraoxane development precedent, not a class-wide guarantee or evidence for the new small-ring/oxane designs.
- **P6 — Amewu et al. (2013).** *Synthesis and evaluation of the antimalarial, anticancer, and caspase 3 activities of tetraoxane dimers.* Bioorganic & Medicinal Chemistry **21**(23), 7392–7397. Primary indexed record, DOI 10.1016/j.bmc.2013.09.047. Reports mono-/dispiro tetraoxane chemistry and cell-based cancer results in selected compounds. It does not establish efficacy or iron selectivity for these monomeric moxidectin hybrids.
- **P7 — Spangler et al. (2016).** *A Novel Tumor-Activated Prodrug Strategy Targeting Ferrous Iron Is Effective in Multiple Preclinical Cancer Models.* Journal of Medicinal Chemistry **59**(24), 11161–11170. Primary full text, DOI 10.1021/acs.jmedchem.6b01470. Provides cancer-relevant Fe(II)-responsive trioxolane conjugate precedent.

Those compounds use a deliberately engineered release mechanism; these intact-hybrid designs do not inherit it.

The often-cited RKA182 and E209 names do not identify interchangeable cores or attachment geometries. E209's primary record is used here; no independent claim about an unverified RKA182 synthesis or stability value is needed for this set. A full exact-compound novelty/patent search remains separate from these chemistry precedents.

Reproducibility and structure blocks

c4-successors/build_successors.py reads the parent and baseline directly from the supplied omnibus and changes only its C5-O substituent. It checks sanitisation, canonical isomeric-SMILES round-trip, retained chiral parent substructure, neutral formal charge, peroxide ring class and expected O–O count. Twelve canonical structures are unique. candidates.json contains full-precision properties and both stereo audits; CSV and SDF exports are alongside it. The omnibus-compatible count uses Chem.FindMolChiralCenters(..., includeUnassigned=True, useLegacyImplementation=True). The independent conservative count uses False. This disclosure is important for reconciliation with another RDKit run.

The three trioxolane nominees S02–S04 each specify one new tetrahedral centre using an explicit isomeric SMILES. Selection of that epimer is a design specification, not a claim of its superior potency or an established enantioselective preparation. No unspecified-centre mixtures are counted as multiple candidates. The tetraoxane symmetry removes the

additional tetrahedral-centre burden in the ten admitted structures; conformational behaviour still needs consideration.

Canonical isomeric SMILES below are the computed outputs, not hand-transcribed structure names.

CHAPTER 7

Full B1 successor branch

All 20 recorded B1 branch entries, including incumbent B1, are retained. This chapter supplements rather than replaces the requested lead trios.

5 · Progress summary — where this branch stands

What it was. ARF-MOX-B1: moxidectin esterified at C5 to a pentanoyl arm terminating in triphenylphosphonium. A delocalised lipophilic cation accumulates in mitochondria in response to membrane potential, which is hyperpolarised in cancer cells, so the design was intended to close the exposure gap by subcellular concentration rather than by dose escalation. $C60H75NO9P^{+}$, MW 985.2, clogP 10.44, permanent formal +1.

What went wrong — three objections, all upheld. Triphenylphosphonium does not discriminate between tumour and healthy mitochondria, and cardiac and skeletal muscle mitochondria are also hyperpolarised, so systemic exposure loads the heart. Nernst-driven accumulation is not self-limiting, risking generalised mitochondrial failure in normal tissue before selective tumour kill. And a permanent charge on a 985 Da macrocycle at clogP 10.44 is a plasma-protein-binding and clearance problem that can neutralise the intended distribution advantage outright.

The arithmetic that reframes the branch. The Nernst slope is **61.54 mV per decade at 37 °C**. Taken at face value:

Mitochondrial potential	Accumulation
−120 mV	89×
−140 mV	188×
−160 mV	398×

Mitochondrial potential	Accumulation
−180 mV	842×
−200 mV	1779×

The published exposure gap for this chassis is 110–220×. At −180 mV the mechanism delivers 842×, so **it closes the potency gap comfortably.** But selectivity comes only from the *difference* between tumour and normal potential, and tumour −180 mV against normal −140 mV is a 40 mV gap, which is **4.5×**. At a 30 mV gap it is 3.1×.

So this mechanism **solves potency and cannot solve selectivity.** The cardiotoxicity objection is not a side risk to be engineered around; it is structural to the mechanism. And because both tissues sit on the same exponential, a more aggressive cation buys more accumulation *everywhere* at the same 4.5× ratio — it spends therapeutic index and returns nothing. B1 is over-engineered in precisely the direction that produces objections 1 and 2.

Which inverts the design objective. If only ~200× is needed and 842× is available, the correct move is to **detune deliberately**: take sub-maximal accumulation in exchange for a lower cation lipophilicity and a wider window.

The column that was missing. Off-target mitochondrial uncoupling tracks the lipophilicity of the **cationic headgroup**, not of the whole conjugate, and neither node had computed it. Added here as hgLogP, the clogP of the methyl-capped headgroup alone. It spans 5.03 down to −0.14 against triphenylphosphonium's 3.61, and it reorders the branch.

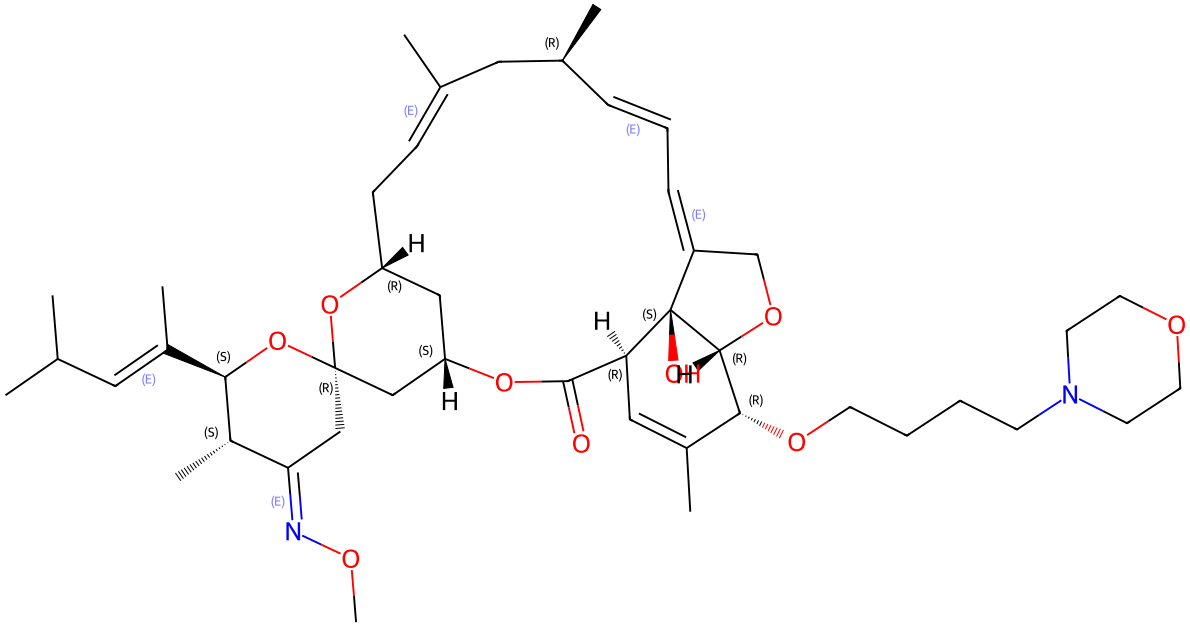
What was tried and failed. "Trialkyl is less delocalised than triaryl, so tributylphosphonium should be gentler" is false: hgLogP **5.03**, whole-molecule clogP **11.66** — worse than the incumbent on both counts. The butyl chains cost more than the loss of aryl delocalisation saves. This is the same shape of error as the adamantane result in Part One, and it is recorded as a negative result for the same reason.

Where it stands. Twenty designs. The incumbent ranks last at one gate of six. Two honest leads, in two different mechanism classes: **B1h** (trimethylammonium, carbamate) keeps the permanent +1 so the Nernst driving force still applies, while cutting headgroup lipophilicity 3.29 log units, mass by 188 Da, clogP by 3.49 units and rotatable bonds from 12 to 9; **B1n** or **B1o** abandon the permanent charge for a weak base intended to protonate only in the acidic tumour microenvironment.

What is unresolved. Three things, and they are load-bearing. First, **delocalisation is why triphenylphosphonium works** — it lowers the desolvation penalty for crossing the inner membrane. A compact trimethylammonium at hgLogP 0.32 may not get in at all, in which case B1h is the advantage of a drug that never arrives. Second, the weak-base class trades a calculable Nernst driving force for a qualitative argument about tumour pH, and **RDKit gives no reliable pKa**, so every pH-gating claim here is unquantified; a measured or literature-anchored pKa near 6.5–7.0 is required before any of that class can be ranked honestly. Third, a neutral weak base is not a better B1 — it is a different drug, and the ranking below rewards it for avoiding a liability it achieves by abandoning the mechanism.

Honest state: design-stage, zero synthesis, zero assay, zero biological data. No claim is made that any design preserves the chassis's weak P-glycoprotein behaviour; avoiding large lipophilic cations is a design restraint and not a transporter assay.

ARF-MOX-B1n



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: weak base morpholin-4-yl direct ether, C4 tether pH-gated, non-cleavable. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C45H68N2O9
Molecular weight (g/mol)	781.044
Exact mass (Da)	780.492482
Crippen cLogP	6.8656
TPSA (Å²)	117.51
H-bond donors	1
H-bond acceptors	11
Rotatable bonds	9

Rings	6
Formal charge	0
Heavy atoms	56
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

Existing selected-prospect discussion — retained

ARF-MOX-B1n

Role: Requested top pick; weak-base hypothesis.

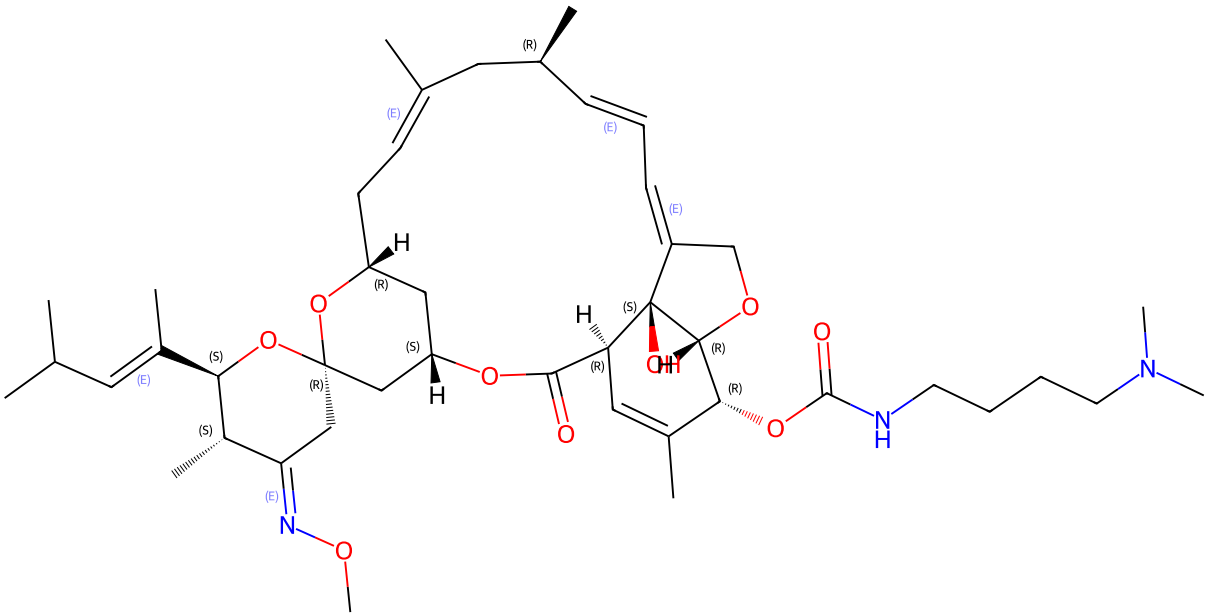
Design and reasoning. A four-carbon direct ether leads to a morpholine headgroup. It is represented as a neutral weak base, rather than a permanently charged phosphonium.

Profile and liabilities. MW falls by approximately 204.19 versus B1; cLogP falls by 3.58 and RotB by 3. The added ester is absent. These improve selected calculated properties, but pKa, subcellular localisation and preserved parent activity remain unknown. “Non-cleavable” in the source means no added ester in the graph, not immunity to metabolism.

Decision. Keep the nomination explicitly conditional on whole-compound pKa/logD, exposure and a matched biological advantage. It tests a pH-dependent distribution idea, not the identical B1 Nernst premise.

Source: b1_ranked.json.

ARF-MOX-B1p



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: weak base dimethylamino carbamate, C4 tether pH-gated: dimethylamino. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C44H67N3O9
Molecular weight (g/mol)	782.032
Exact mass (Da)	781.487731
Crippen cLogP	6.8046
TPSA (Å²)	137.38
H-bond donors	2
H-bond acceptors	11
Rotatable bonds	9
Rings	5

Formal charge	0
Heavy atoms	56
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

Existing selected-prospect discussion — retained

ARF-MOX-B1p

Role: Alternative weak-base prospect.

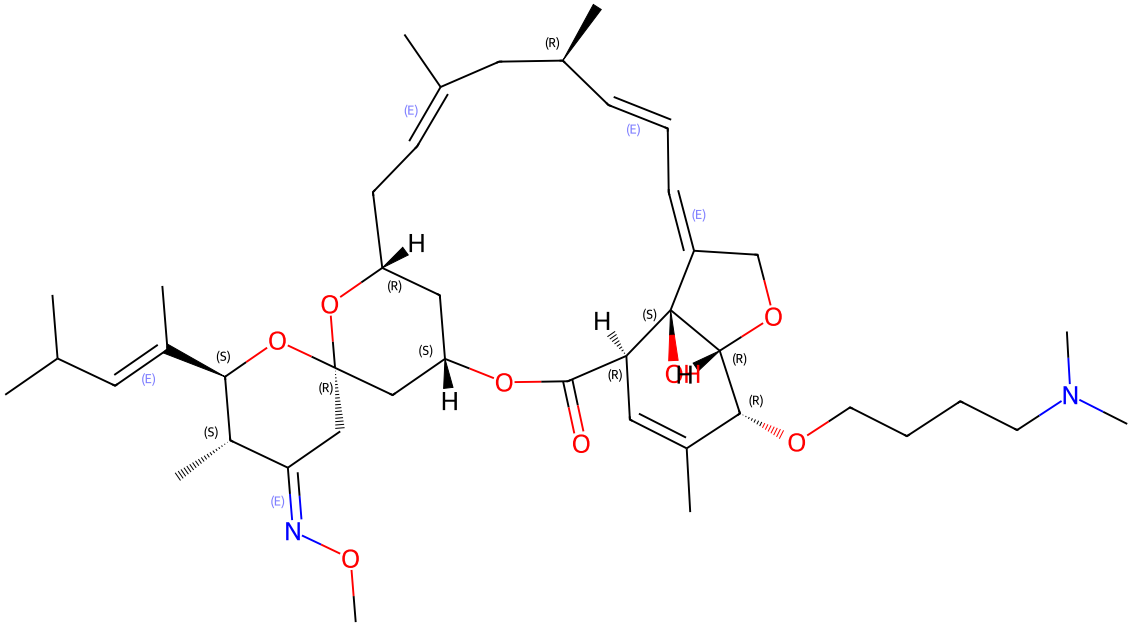
Design and reasoning. A carbamate-linked four-carbon dimethylamino appendage. The deposited neutral graph is not a measured solution protonation state.

Profile and liabilities. MW 782.03 and cLogP 6.80 are close to B1n, while TPSA 137.38 and HBD 2 are higher. A lower cLogP alone cannot rank it above B1n. The carbamate may change stability, permeability, binding and cleavage.

Decision. Compare directly with B1n using measured exposure and chemical fate. Separate linkage effects from headgroup effects; both variables differ.

Source: b1_ranked.json.

ARF-MOX-B1q



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: weak base dimethylamino direct ether, C4 tether pH-gated dimethylamino, non-cleavable. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCCN(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCCN(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C43H66N2O8
Molecular weight (g/mol)	739.007
Exact mass (Da)	738.481917
Crippen cLogP	7.095
TPSA (Å²)	108.28
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	9

Rings	5
Formal charge	0
Heavy atoms	53
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

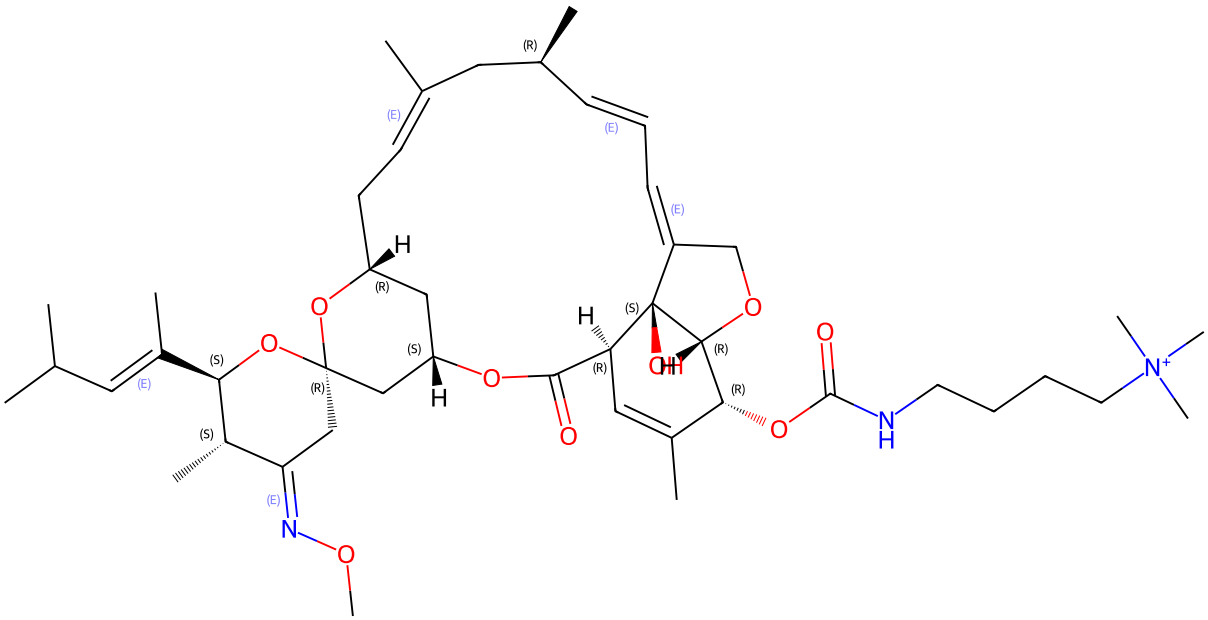
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1h



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 trimethylammonium carbamate, C4 tether quaternary ammonium. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C45H70N3O9+
Molecular weight (g/mol)	797.067
Exact mass (Da)	796.510657
Crippen cLogP	6.9492
TPSA (Å²)	134.14
H-bond donors	2
H-bond acceptors	10
Rotatable bonds	9
Rings	5

Formal charge	1
Heavy atoms	57
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

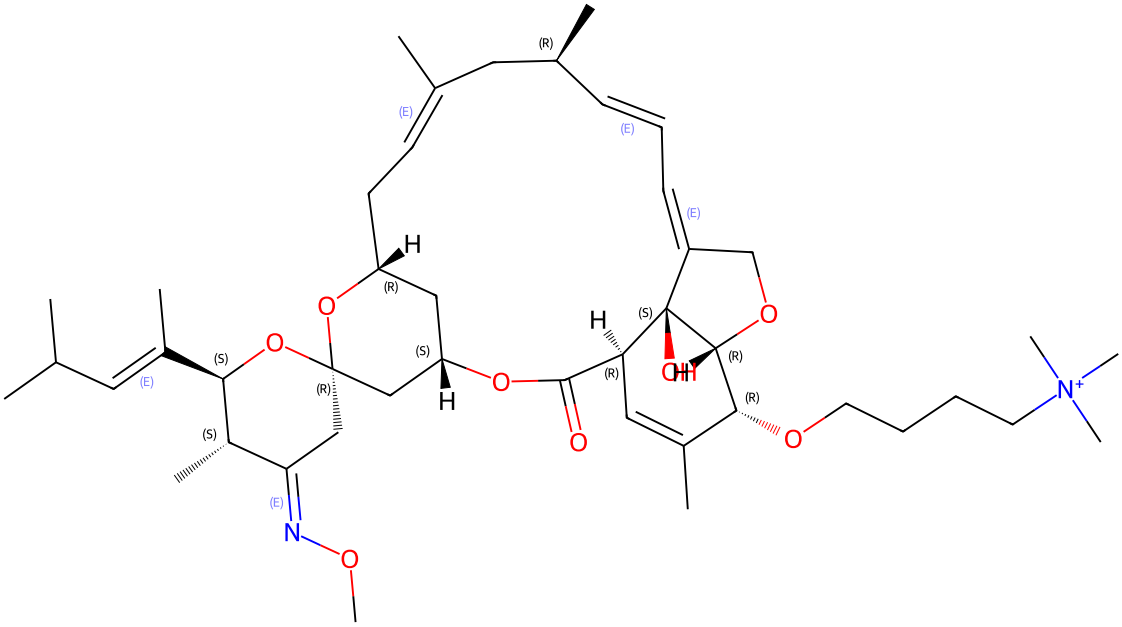
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 9 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1i



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 trimethylammonium direct ether, C4 tether quaternary ammonium, non-cleavable. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C44H69N2O8+
Molecular weight (g/mol)	754.042
Exact mass (Da)	753.504844
Crippen cLogP	7.2396
TPSA (Å²)	105.04
H-bond donors	1
H-bond acceptors	9
Rotatable bonds	9

Rings	5
Formal charge	1
Heavy atoms	54
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

Existing selected-prospect discussion — retained

ARF-MOX-B1i

Role: Permanent-charge / stable-linker comparator.

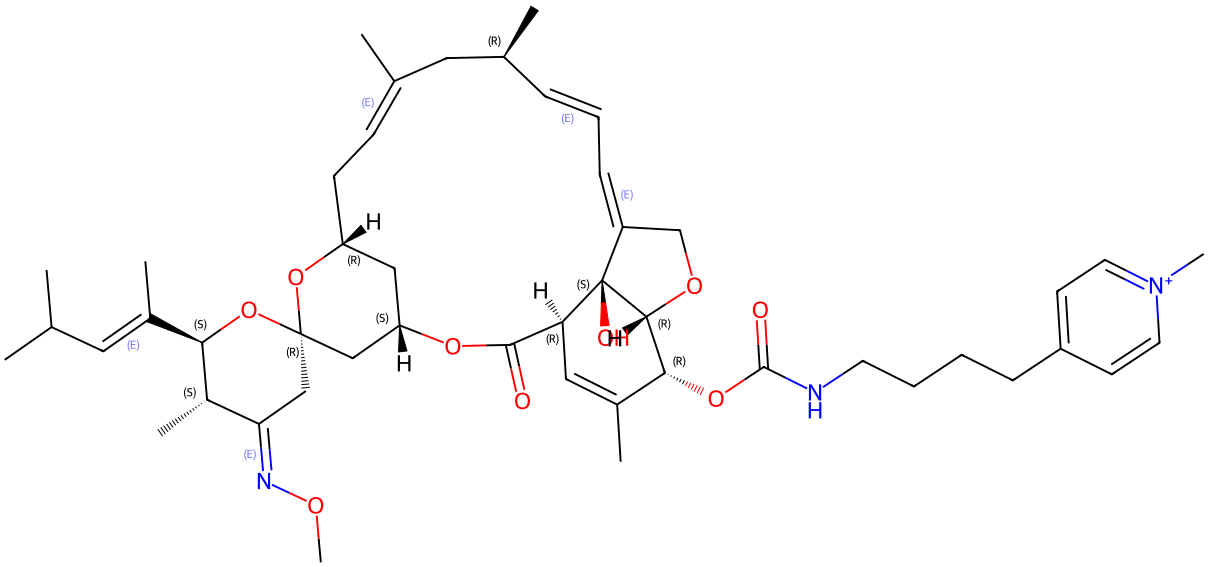
Design and reasoning. A four-carbon ether joins a trimethylammonium headgroup. The submitted structure has formal charge +1 and no counterion.

Profile and liabilities. MW 754.04, cLogP 7.24 and TPSA 105.04 are lower than the incumbent values except for the unchanged charge class. The compact localised charge may hinder membrane crossing. A permanent charge is not proof of mitochondrial accumulation.

Decision. Use to test whether reducing headgroup bulk while retaining permanent charge is useful. Measure relevant compartment exposure and distinguish nonspecific membrane effects.

Source: b1_ranked.json.

ARF-MOX-B1j



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 N-methylpyridinium carbamate, C4 tether N-methylpyridinium. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCc6cc[n+](C)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCc6cc[n+](C)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C48H68N3O9+
Molecular weight (g/mol)	831.084
Exact mass (Da)	830.495007
Crippen cLogP	7.3102
TPSA (Å²)	138.02
H-bond donors	2
H-bond acceptors	10
Rotatable bonds	9
Rings	6

Formal charge	1
Heavy atoms	60
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

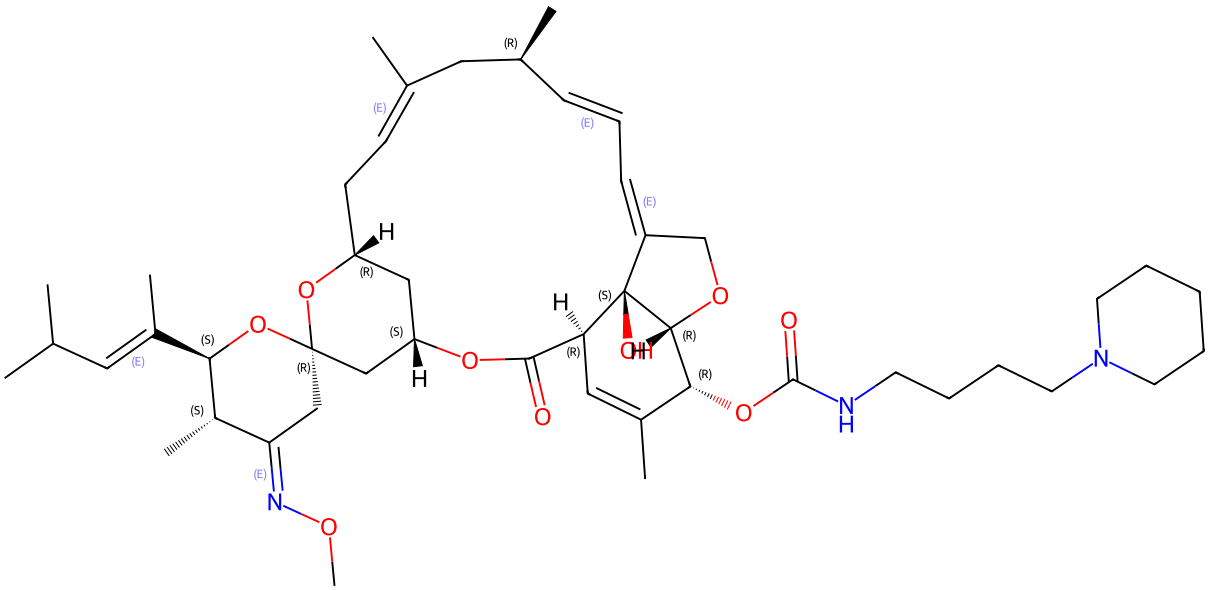
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1s



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: weak base piperidin-1-yl carbamate, C4 tether pH-gated: piperidine. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN6CCCCC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN6CCCCC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C47H71N3O9
Molecular weight (g/mol)	822.097
Exact mass (Da)	821.519031
Crippen cLogP	7.7289
TPSA (Å²)	137.38
H-bond donors	2
H-bond acceptors	11
Rotatable bonds	9
Rings	6

Formal charge	0
Heavy atoms	59
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

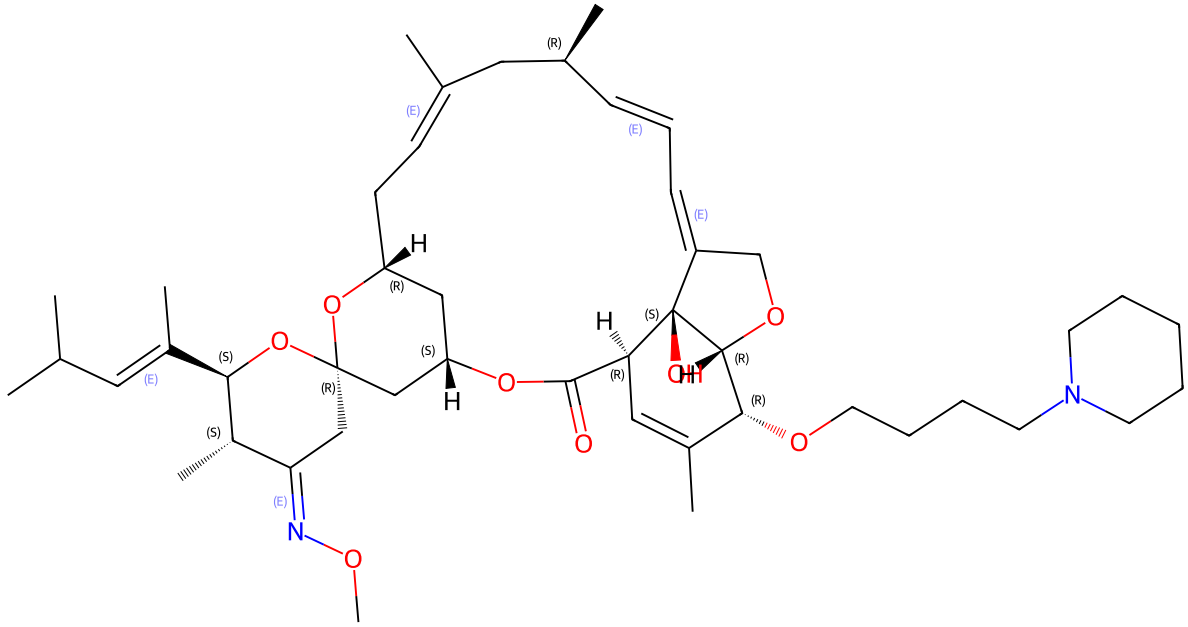
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1t



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: weak base piperidin-1-yl direct ether, C4 tether pH-gated piperidine, non-cleavable. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCCN6CCCCC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCCN6CCCCC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C46H70N2O8
Molecular weight (g/mol)	779.072
Exact mass (Da)	778.513217
Crippen cLogP	8.0193
TPSA (Å²)	108.28
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	9

Rings	6
Formal charge	0
Heavy atoms	56
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

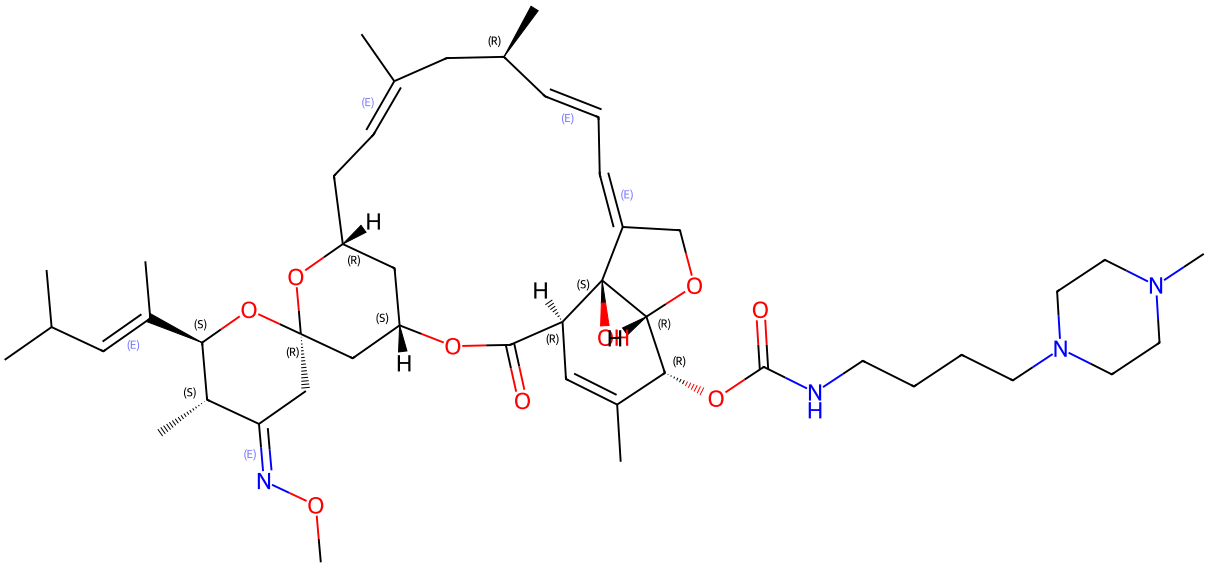
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1o



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: weak base 4-methylpiperazin-1-yl carbamate, C4 tether pH-gated: N-methylpiperazine. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN6CCN(C)CC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN6CCN(C)CC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C47H72N4O9
Molecular weight (g/mol)	837.112
Exact mass (Da)	836.52993
Crippen cLogP	6.4904
TPSA (Å²)	140.62
H-bond donors	2
H-bond acceptors	12
Rotatable bonds	9
Rings	6

Formal charge	0
Heavy atoms	60
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

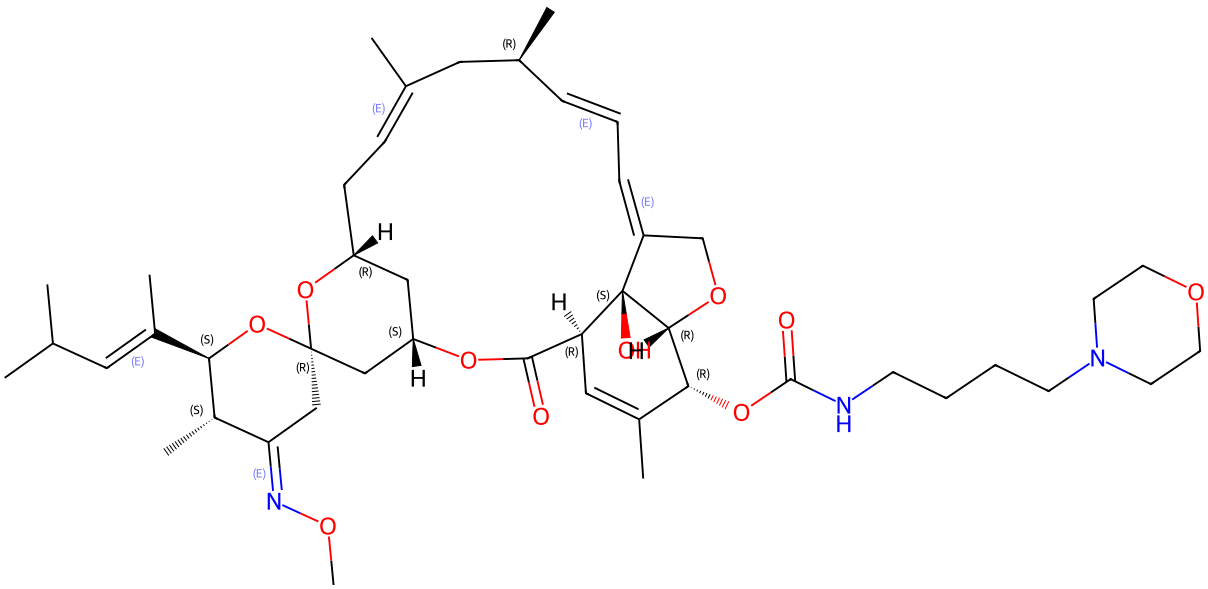
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1m



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: weak base morpholin-4-yl carbamate, C4 tether pH-gated: morpholine. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C46H69N3O10
Molecular weight (g/mol)	824.069
Exact mass (Da)	823.498295
Crippen cLogP	6.5752
TPSA (Å²)	146.61
H-bond donors	2
H-bond acceptors	12
Rotatable bonds	9
Rings	6

Formal charge	0
Heavy atoms	59
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

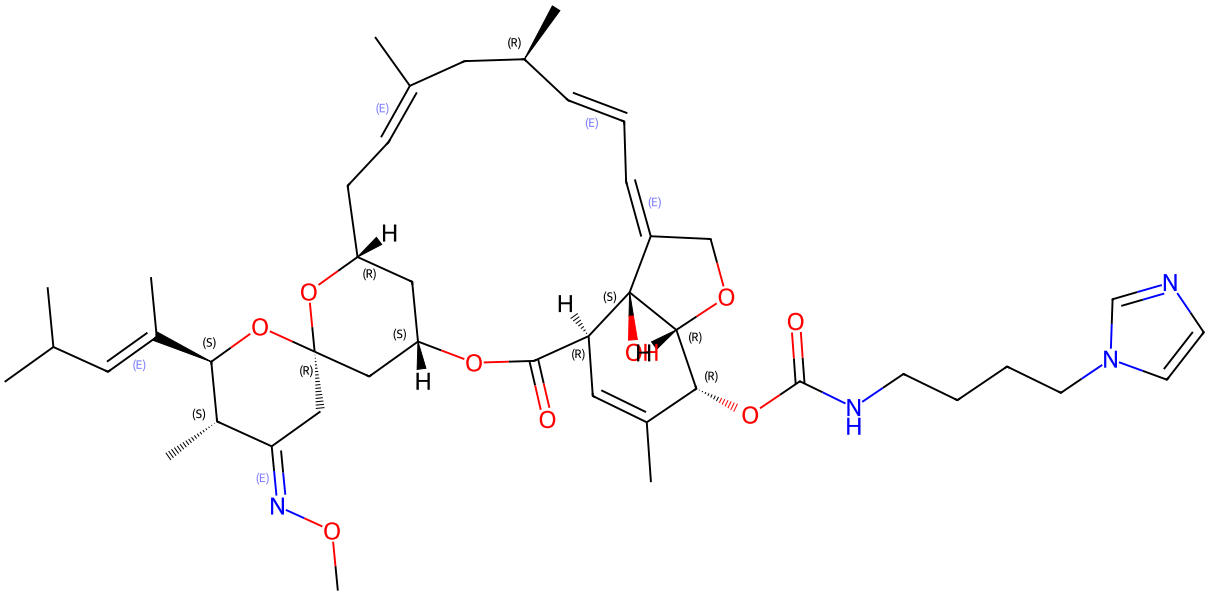
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1r



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: weak base imidazol-1-yl carbamate, C4 tether pH-gated: imidazole. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Use the carbamate connection as a distinct persistence hypothesis. Assess compatibility of the parent functional groups and identify any cleavage products rather than assuming release kinetics from the linkage name.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCn6ccnc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCn6ccnc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C45H64N4O9
Molecular weight (g/mol)	805.026
Exact mass (Da)	804.46733
Crippen cLogP	7.1397
TPSA (Å²)	151.96
H-bond donors	2
H-bond acceptors	11
Rotatable bonds	9
Rings	6

Formal charge	0
Heavy atoms	58
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

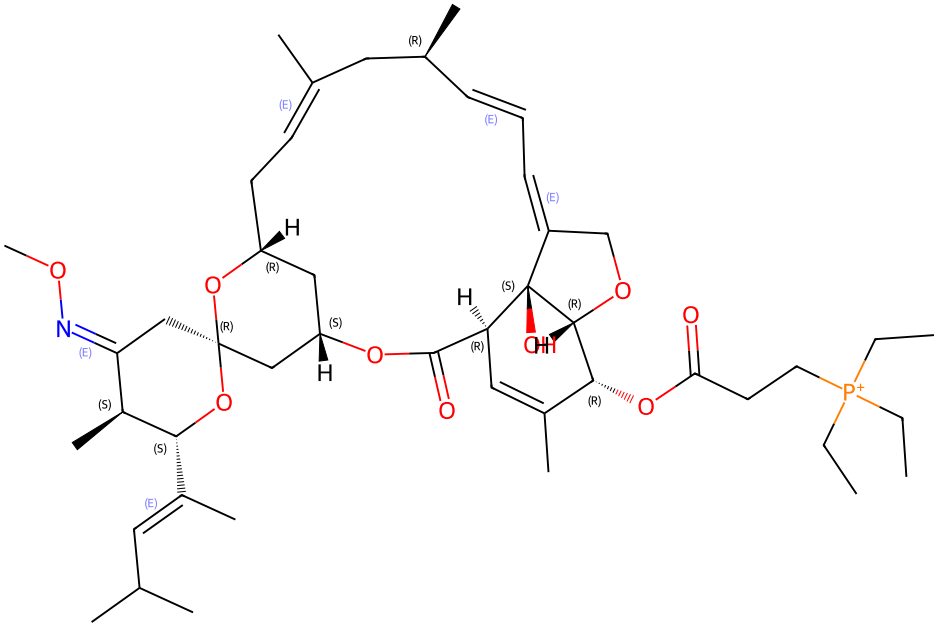
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 9 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1k



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 triethylphosphonium propanoyl ester, C2 tether short tether, small cation. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CC[P+](CC)(CC)CCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P+](CC)(CC)CCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C46H71NO9P+
Molecular weight (g/mol)	813.046
Exact mass (Da)	812.486096
Crippen cLogP	8.7472
TPSA (Å²)	122.11
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	10

Rings	5
Formal charge	1
Heavy atoms	57
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

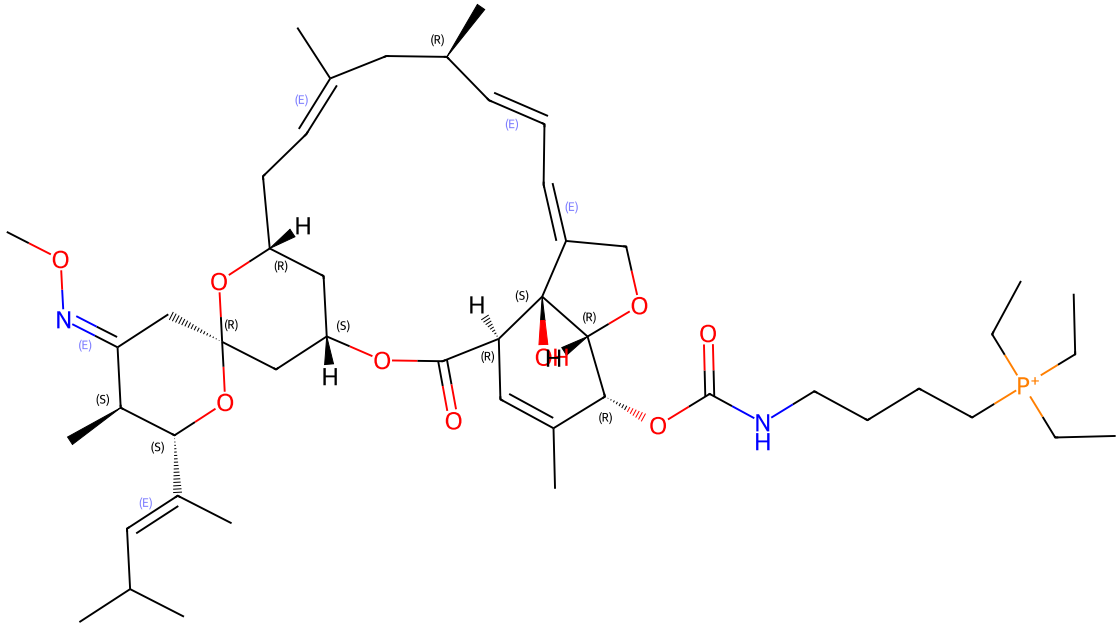
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 10 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1f



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 triethylphosphonium carbamate, C4 tether smallest trialkylphosphonium. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CC[P+](CC)(CC)CCCCNC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P+](CC)(CC)CCCCNC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C48H76N2O9P+
Molecular weight (g/mol)	856.115
Exact mass (Da)	855.528295
Crippen cLogP	9.3203
TPSA (Å²)	134.14
H-bond donors	2
H-bond acceptors	10
Rotatable bonds	12

Rings	5
Formal charge	1
Heavy atoms	60
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

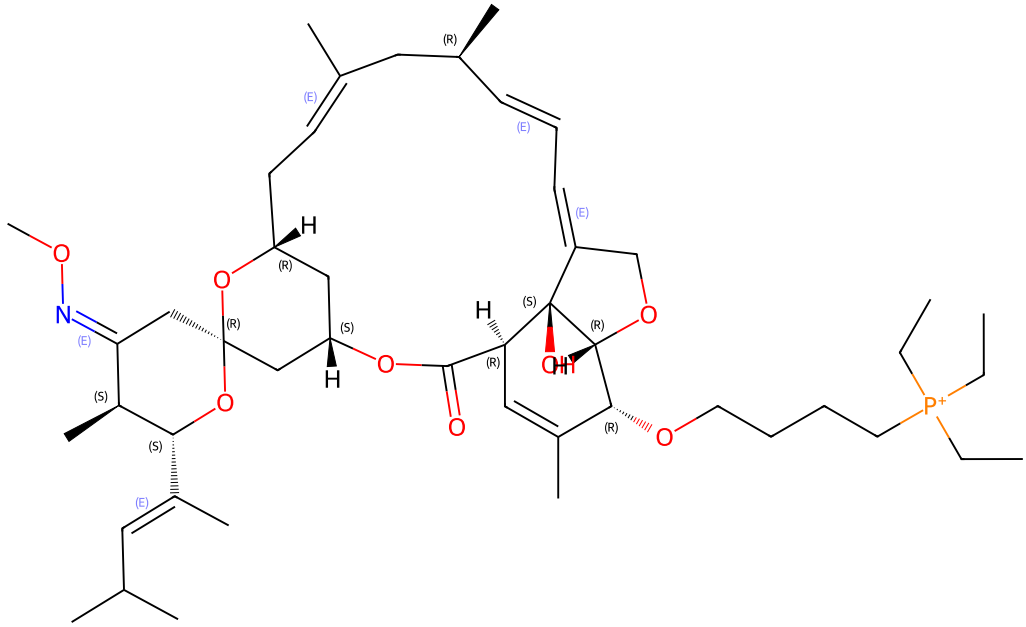
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 12 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1g



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 triethylphosphonium direct ether, C4 tether small cation, non-cleavable. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CC[P+](CC)(CC)CCCCO[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P+](CC)(CC)CCCCO[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C47H75NO8P+
Molecular weight (g/mol)	813.09
Exact mass (Da)	812.522481
Crippen cLogP	9.6107
TPSA (Å²)	105.04
H-bond donors	1
H-bond acceptors	9
Rotatable bonds	12

Rings	5
Formal charge	1
Heavy atoms	57
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

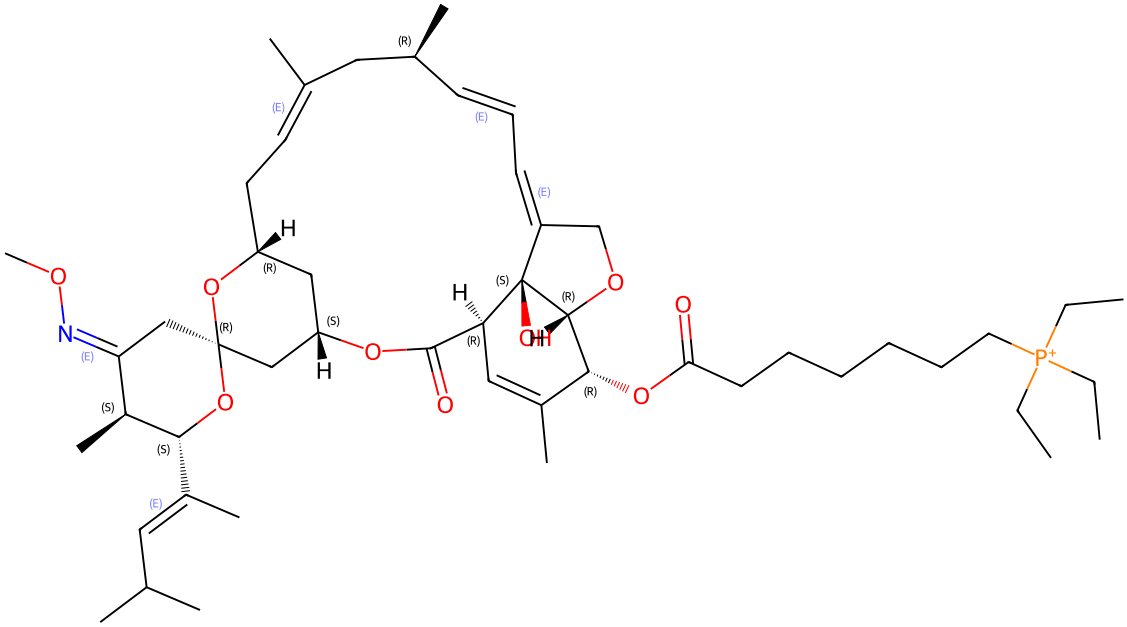
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 12 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1l



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 triethylphosphonium heptanoyl ester, C6 tether long tether, small cation. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CC[P+](CC)(CC)CCCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P+](CC)(CC)CCCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C50H79NO9P+
Molecular weight (g/mol)	869.154
Exact mass (Da)	868.548696
Crippen cLogP	10.3076
TPSA (Å²)	122.11
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	14

Rings	5
Formal charge	1
Heavy atoms	61
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

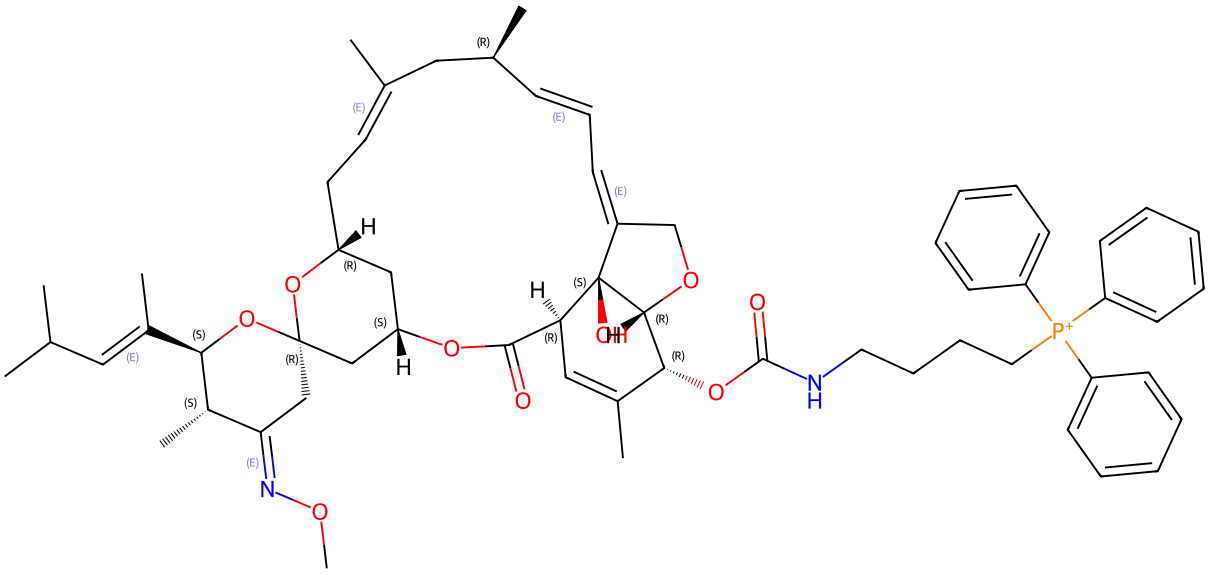
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 14 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1b



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 triphenylphosphonium (incumbent) carbamate, C4 tether incumbent cation, ester removed. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C60H76N2O9P+
Molecular weight (g/mol)	1000.247
Exact mass (Da)	999.528295
Crippen cLogP	10.2371
TPSA (Å²)	134.14
H-bond donors	2

H-bond acceptors	10
Rotatable bonds	12
Rings	8
Formal charge	1
Heavy atoms	72
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

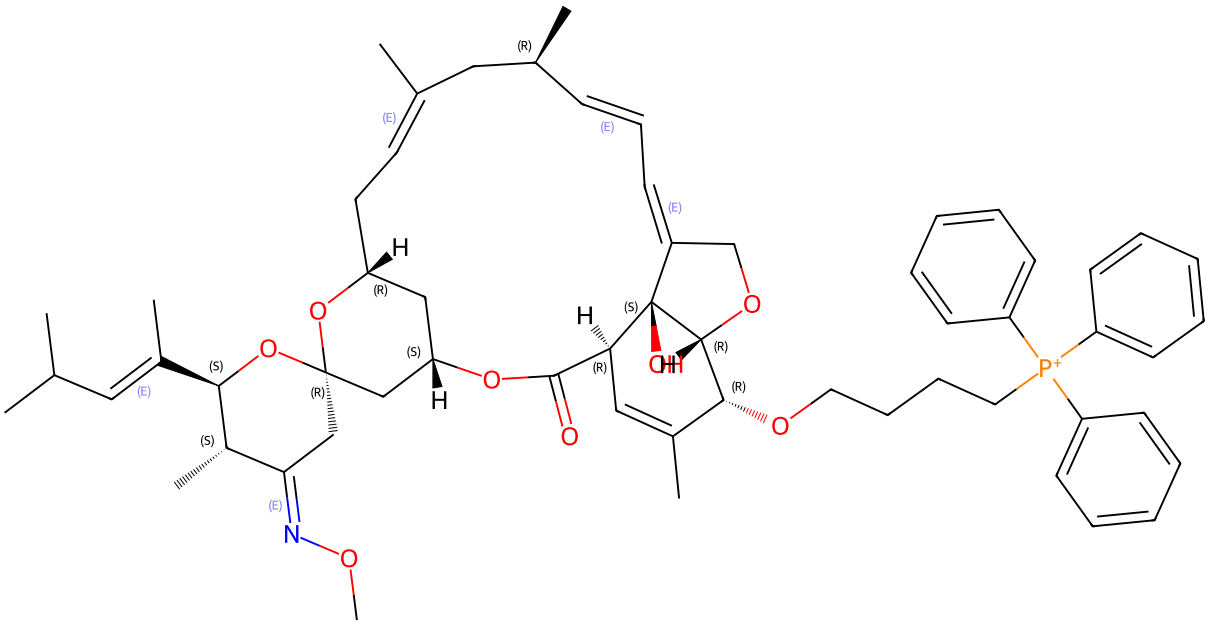
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 12 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1c



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 triphenylphosphonium (incumbent) direct ether, C4 tether incumbent cation, non-cleavable. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCCC[P+](c6ccccc6)(c6ccccc6)c6ccccc6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCCC[P+](c6ccccc6)(c6ccccc6)c6ccccc6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C59H75NO8P+
Molecular weight (g/mol)	957.222
Exact mass (Da)	956.522481
Crippen cLogP	10.5275
TPSA (Å²)	105.04
H-bond donors	1
H-bond acceptors	9
Rotatable bonds	12

Rings	8
Formal charge	1
Heavy atoms	69
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

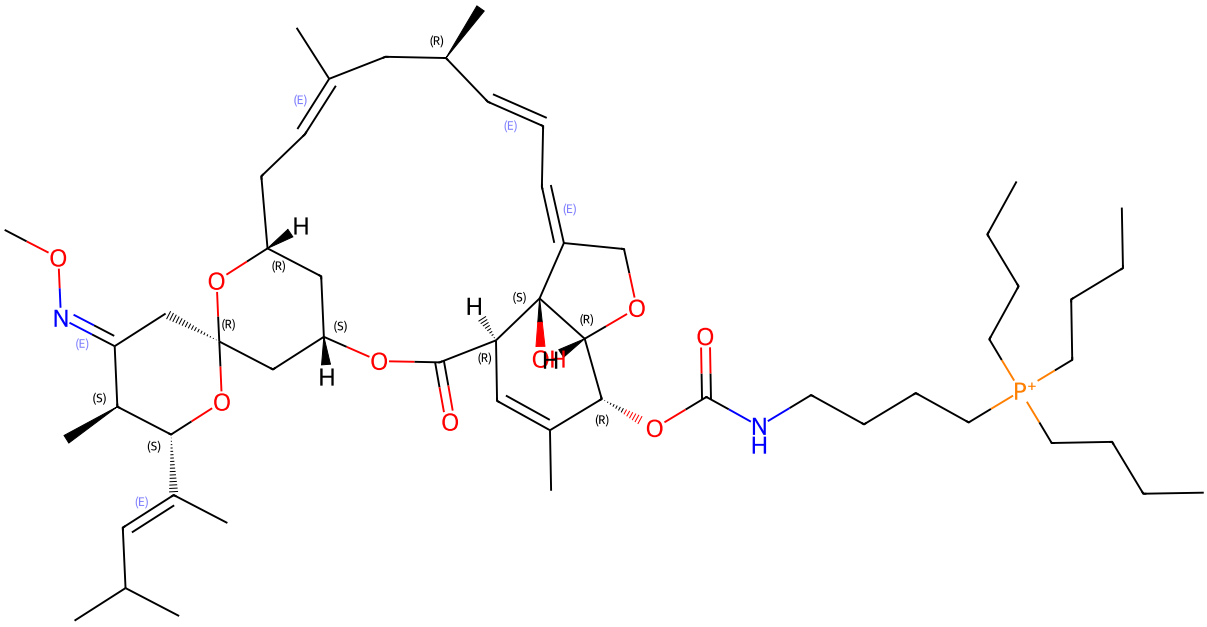
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 12 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1e



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 tributylphosphonium carbamate, C4 tether trialkyl cation, less delocalised. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CCCC[P+](CCCC)(CCCC)CCCCNC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CCCC[P+](CCCC)(CCCC)CCCCNC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C54H88N2O9P+
Molecular weight (g/mol)	940.277
Exact mass (Da)	939.622195
Crippen cLogP	11.6609
TPSA (Å²)	134.14
H-bond donors	2
H-bond acceptors	10
Rotatable bonds	18

Rings	5
Formal charge	1
Heavy atoms	66
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

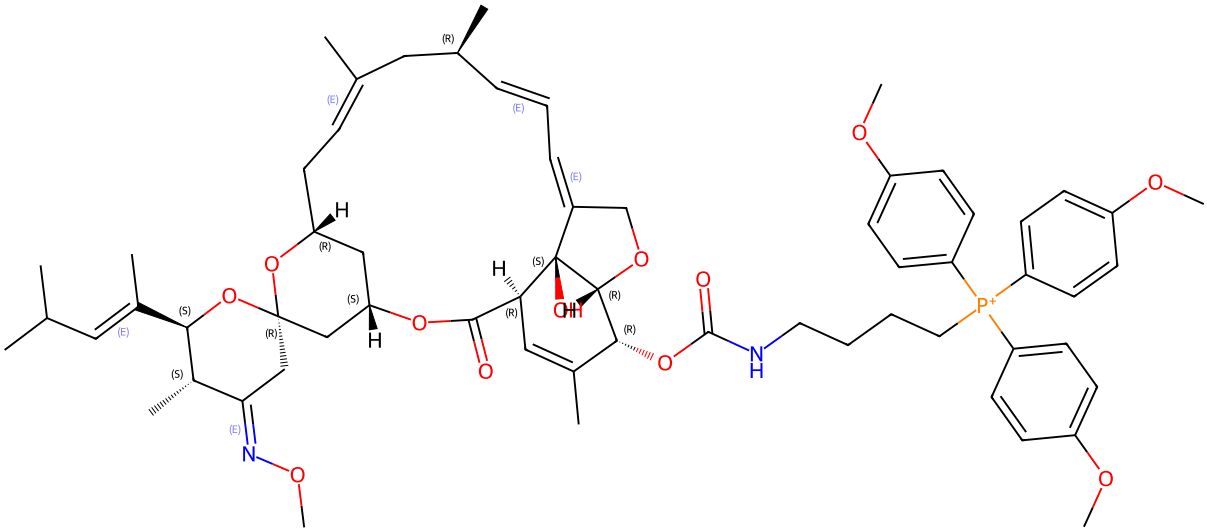
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 18 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1d



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 tris(4-methoxyphenyl)phosphonium carbamate, C4 tether modulated triarylphosphonium. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NCCCC[P+](c6ccc(OC)cc6)(c6ccc(OC)cc6)c6ccc(OC)cc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NCCCC[P+](c6ccc(OC)cc6)(c6ccc(OC)cc6)c6ccc(OC)cc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C63H82N2O12P+
Molecular weight (g/mol)	1090.325
Exact mass (Da)	1089.559989
Crippen cLogP	10.2629
TPSA (Å²)	161.83
H-bond donors	2

H-bond acceptors	13
Rotatable bonds	15
Rings	8
Formal charge	1
Heavy atoms	78
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

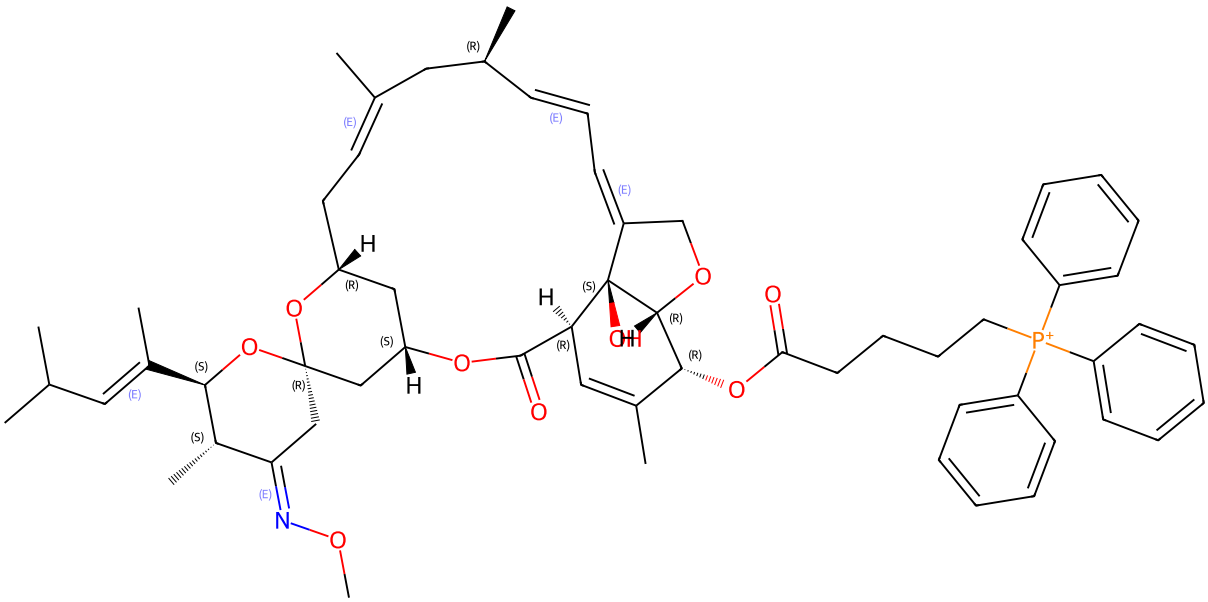
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 15 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

ARF-MOX-B1



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Recorded design detail: permanent +1 triphenylphosphonium (incumbent) pentanoyl ester, C4 tether (incumbent) incumbent. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged

appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCCC[P+](c6ccccc6)(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCCC[P+](c6ccccc6)(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C60H75NO9P+
Molecular weight (g/mol)	985.232
Exact mass (Da)	984.517396
Crippen cLogP	10.4442
TPSA (Å²)	122.11
H-bond donors	1

H-bond acceptors	10
Rotatable bonds	12
Rings	8
Formal charge	1
Heavy atoms	71
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 12 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

Node85 b1_ranked.json; B1 successor paper

Existing selected-prospect discussion — retained

ARF-MOX-B1

Role: Incumbent reference.

Design and reasoning. A triphenylphosphonium appendage connected through a C5 ester. The permanent, delocalised cation supplies the original mitochondrial-potential rationale.

Profile and liabilities. Its encoded cLogP is 10.44, MW 985.23 and RotB 12. The design is large and lipophilic, with an added ester that can separate the two intended functions. A +1 charge does not establish a tumour-selective distribution.

Decision. Retain as the historical benchmark; determine intact exposure, hydrolysis and whether the conjugate improves anything over parent plus targeting fragment.

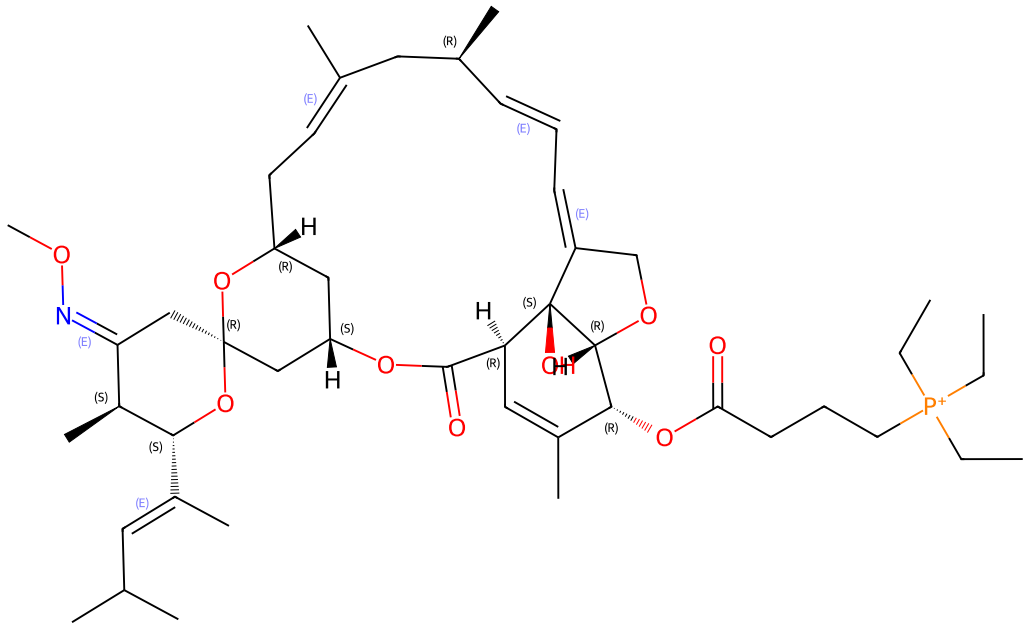
Source: b1_ranked.json.

CHAPTER 8

Additional archived graphs

These 29 archived graph records preserve earlier, alternate and fragment versions recovered in the prior history reconciliation. Some snippets were never given a compound name; their literal recovered text is retained. They are not all nominated complete conjugates.

Arm proxy (A logP 2.6268): `CC[P+](CC)(CC)CCC(=O)OC`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CC[P+](CC)
(CC)CCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[
C@@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P+](CC)
(CC)CCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[
C@@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C47H73NO9P+
Molecular weight (g/mol)	827.073
Exact mass (Da)	826.501746
Crippen cLogP	9.1373
TPSA (Å²)	122.11
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	11

Rings	5
Formal charge	1
Heavy atoms	58
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

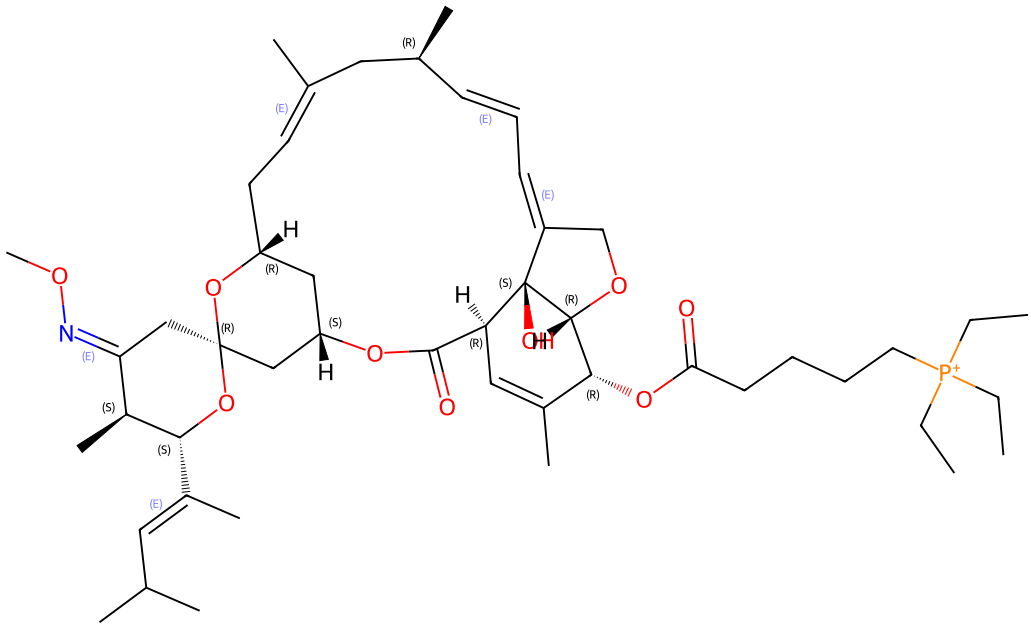
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 11 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 214

Arm proxy (A logP 3.0169): `CC[P+](CC)(CC)CCCC(=O)OC`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CC[P+](CC)(CC)CCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P+](CC)(CC)CCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C48H75NO9P+
Molecular weight (g/mol)	841.1
Exact mass (Da)	840.517396
Crippen cLogP	9.5274
TPSA (Å²)	122.11
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	12

Rings	5
Formal charge	1
Heavy atoms	59
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

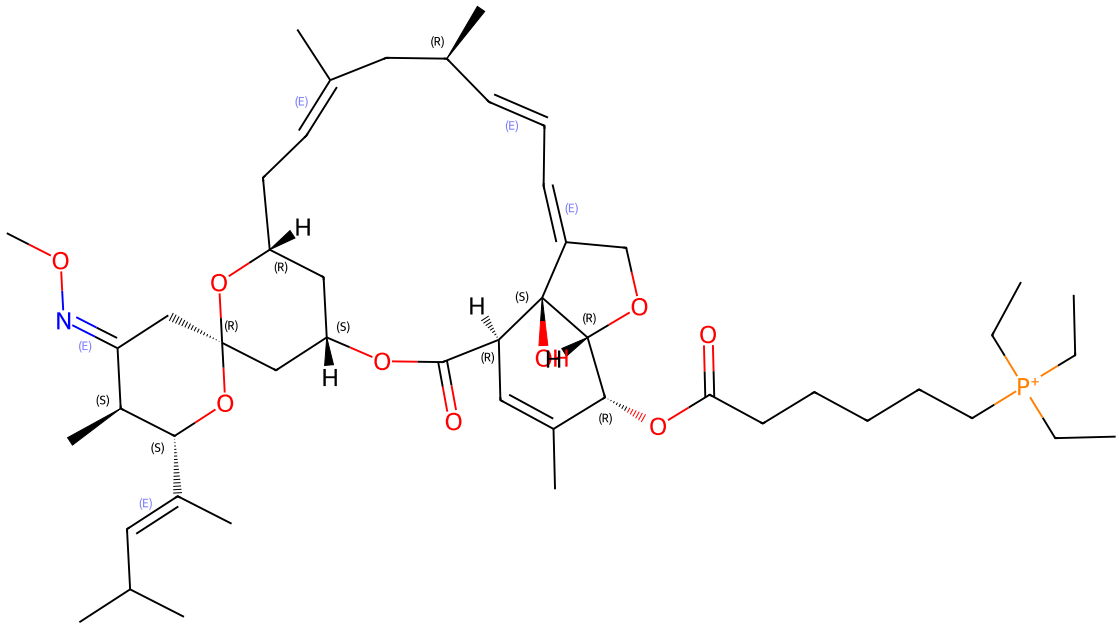
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 12 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 223

Arm proxy (A logP 3.4070): `CC[P+](CC)(CC)CCCCC(=O)OC`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CC[P+](CC)(CC)CCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P+](CC)(CC)CCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C49H77NO9P+
Molecular weight (g/mol)	855.127
Exact mass (Da)	854.533046
Crippen cLogP	9.9175
TPSA (Å²)	122.11
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	13

Rings	5
Formal charge	1
Heavy atoms	60
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

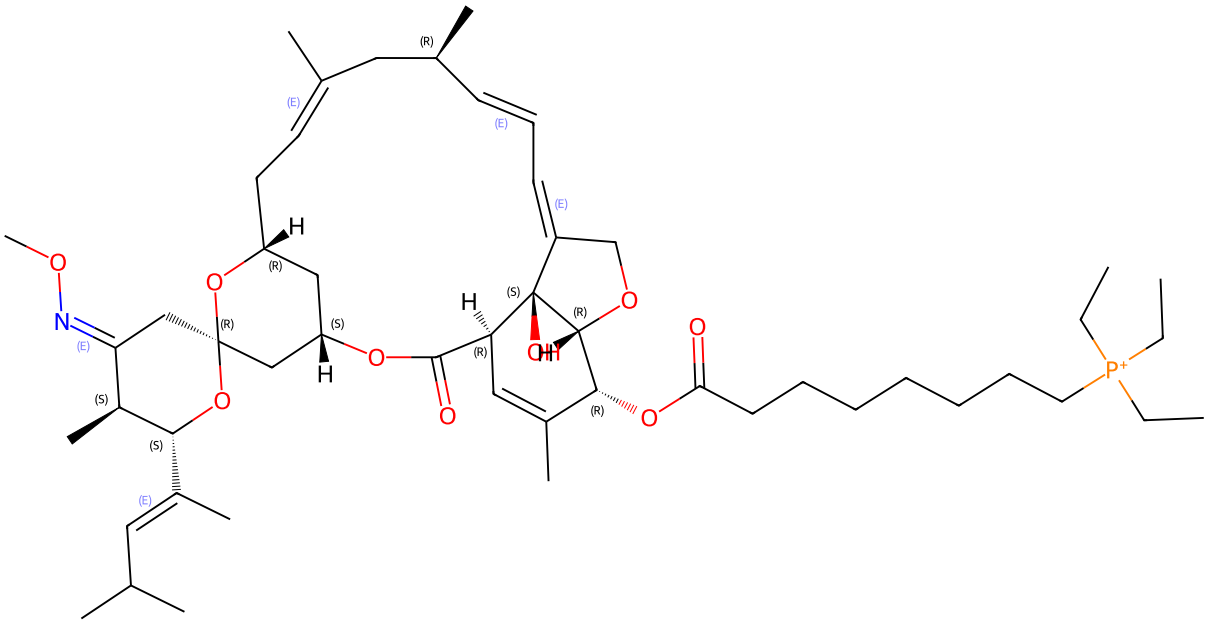
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 13 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 232

Arm proxy (A logP 4.1872): `CC[P+](CC)(CC)CCCCCCC(=O)OC`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CC[P+](CC)(CC)CCCCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P+](CC)(CC)CCCCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C51H81NO9P+
Molecular weight (g/mol)	883.181
Exact mass (Da)	882.564346
Crippen cLogP	10.6977
TPSA (Å²)	122.11
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	15

Rings	5
Formal charge	1
Heavy atoms	62
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

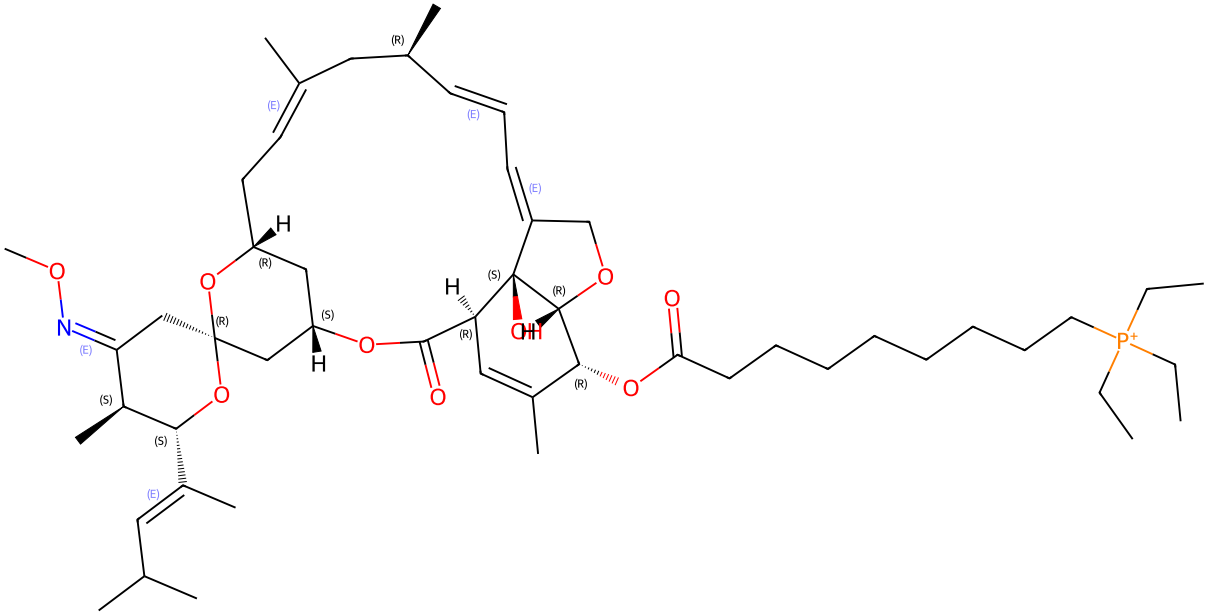
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 15 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 250

Arm proxy (A logP 4.5773): `CC[P+](CC)(CC)CCCCCCCC(=O)OC`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CC[P+](CC)
(CC)CCCCCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C
@H]3C[C@@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P+](CC)
(CC)CCCCCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C
@H]3C[C@@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C52H83NO9P+
Molecular weight (g/mol)	897.208
Exact mass (Da)	896.579996
Crippen cLogP	11.0878
TPSA (Å²)	122.11
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	16

Rings	5
Formal charge	1
Heavy atoms	63
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

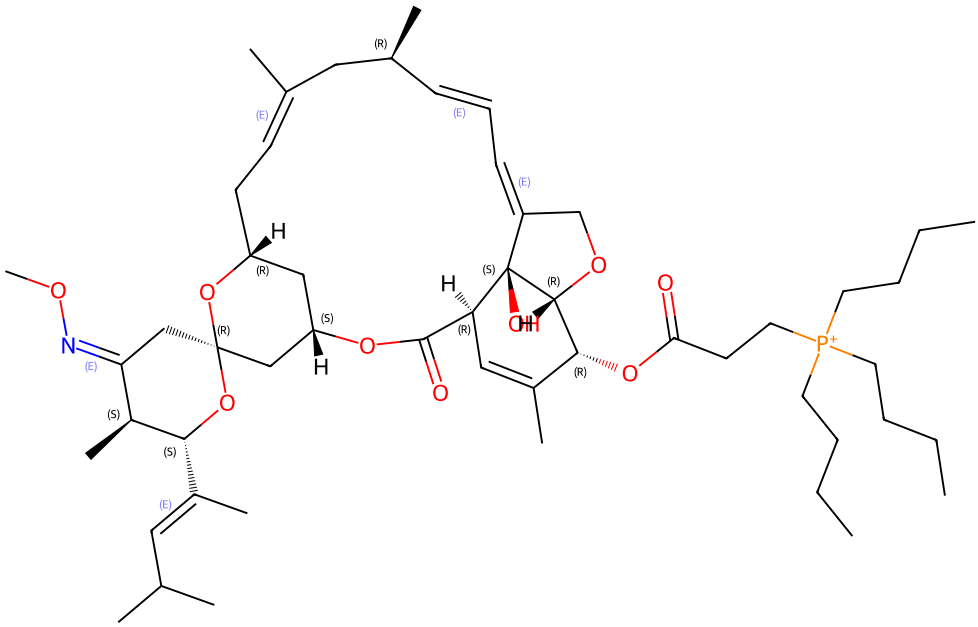
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 16 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 259

Arm proxy (A logP 4.9674): `CC[P+](CC)(CC)CCCCCCCCCC(=O)OC`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CCCC[P+](CCCC)(CCCC)CCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CCCC[P+](CCCC)(CCCC)CCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C52H83NO9P+
Molecular weight (g/mol)	897.208
Exact mass (Da)	896.579996
Crippen cLogP	11.0878
TPSA (Å²)	122.11
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	16

Rings	5
Formal charge	1
Heavy atoms	63
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

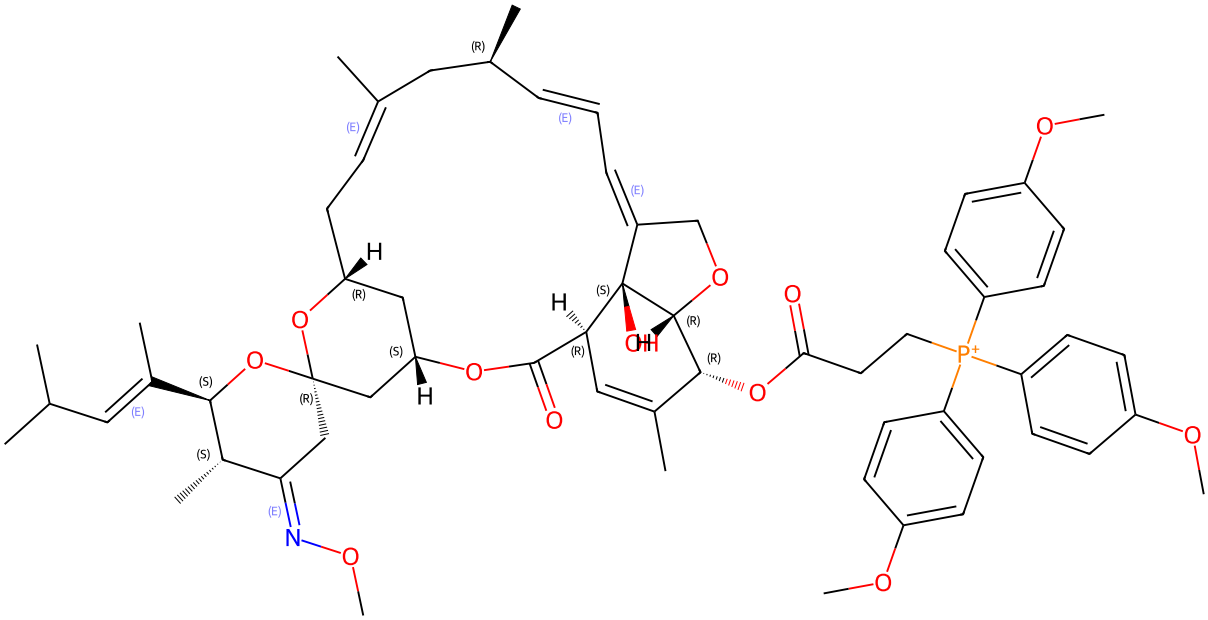
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 16 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 268

Arm proxy (A logP 4.9674): `CCCC[P+](CCCC)(CCCC)CCC(=O)OC`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[P+](c6ccc(OC)cc6)
(c6ccc(OC)cc6)c6ccc(OC)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[P+](c6ccc(OC)cc6)
(c6ccc(OC)cc6)c6ccc(OC)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C61H77NO12P+
Molecular weight (g/mol)	1047.256
Exact mass (Da)	1046.51779
Crippen cLogP	9.6898
TPSA (Å²)	149.8
H-bond donors	1
H-bond acceptors	13
Rotatable bonds	13

Rings	8
Formal charge	1
Heavy atoms	75
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

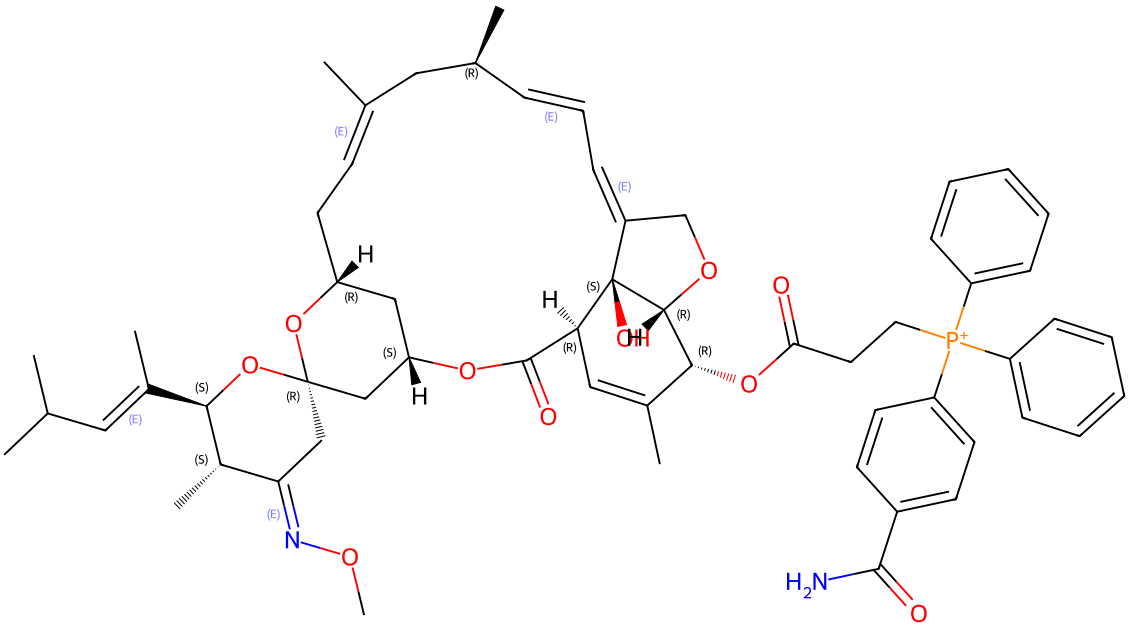
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 13 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 277

: `COC(=O)CC[P+](c1ccc(OC)cc1)(c1ccc(OC)cc1)c1ccc(OC)cc1`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[P+](c6ccccc6)
(c6ccccc6)c6ccc(C(N)=O)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[P+](c6ccccc6)
(c6ccccc6)c6ccc(C(N)=O)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C59H72N2O10P+
Molecular weight (g/mol)	1000.203
Exact mass (Da)	999.49191
Crippen cLogP	8.7629
TPSA (Å²)	165.2
H-bond donors	2
H-bond acceptors	11
Rotatable bonds	11

Rings	8
Formal charge	1
Heavy atoms	72
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

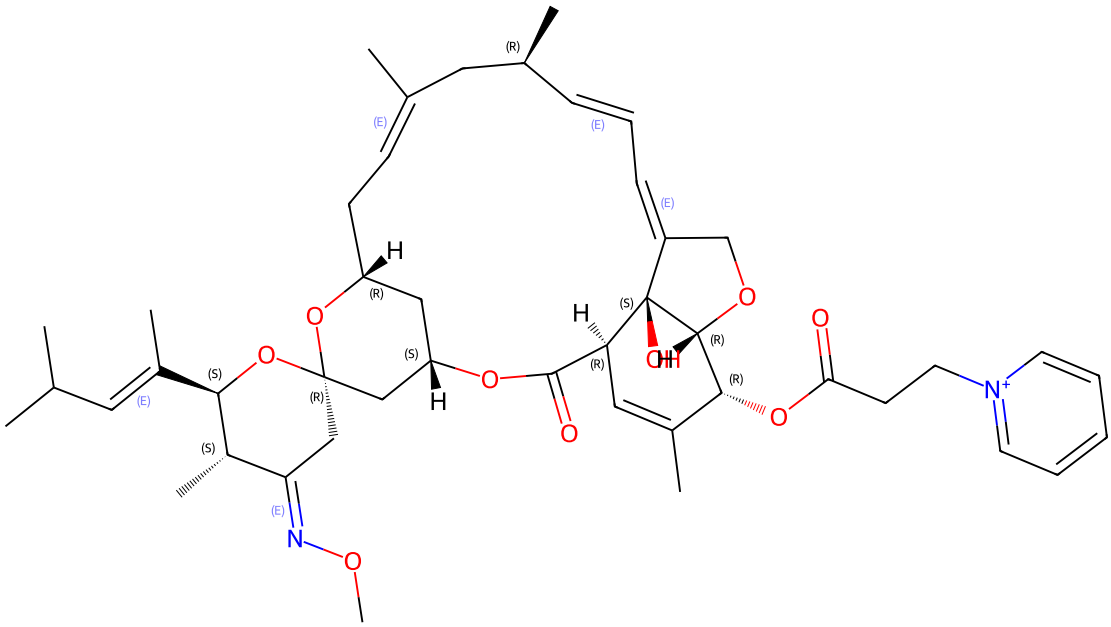
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 11 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 286

5): `COC(=O)CC[P+](c1ccccc1)(c1ccccc1)c1ccc(C(N)=O)cc1`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[n+]6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[n+]6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C45H61N2O9+
Molecular weight (g/mol)	773.988
Exact mass (Da)	773.437158
Crippen cLogP	6.6576
TPSA (Å²)	125.99
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	7
Rings	6

Formal charge	1
Heavy atoms	56
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

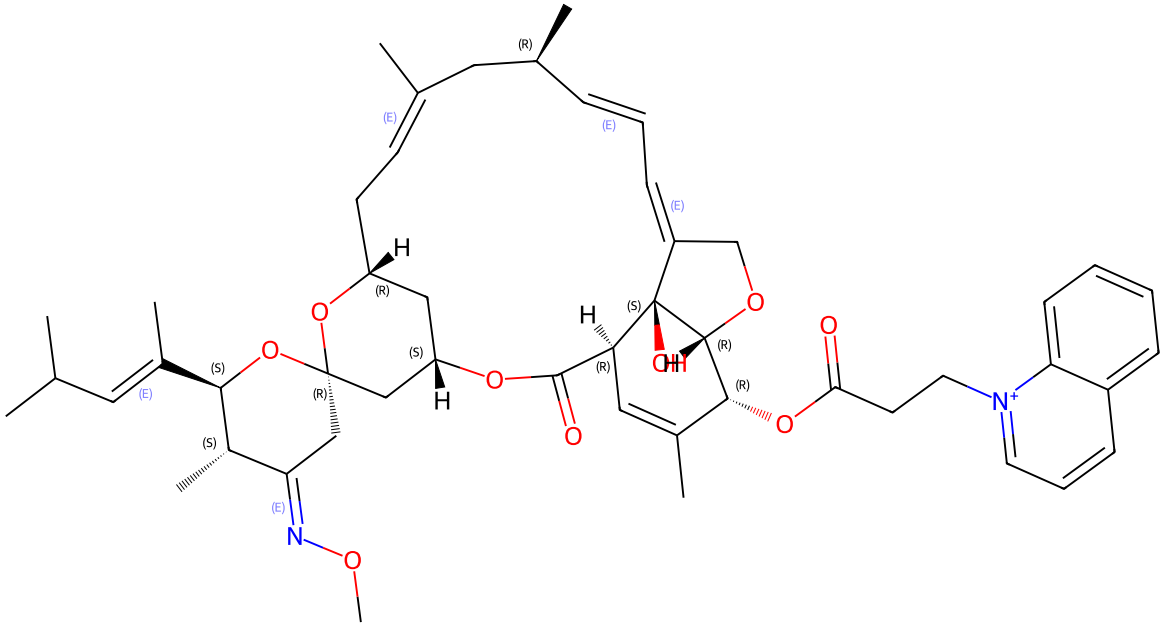
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 7 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 295

c1`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[n+]6cccc7ccccc76)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[n+]6cccc7ccccc76)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C49H63N2O9+
Molecular weight (g/mol)	824.048
Exact mass (Da)	823.452808
Crippen cLogP	7.8108
TPSA (Å²)	125.99
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	7
Rings	7

Formal charge	1
Heavy atoms	60
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

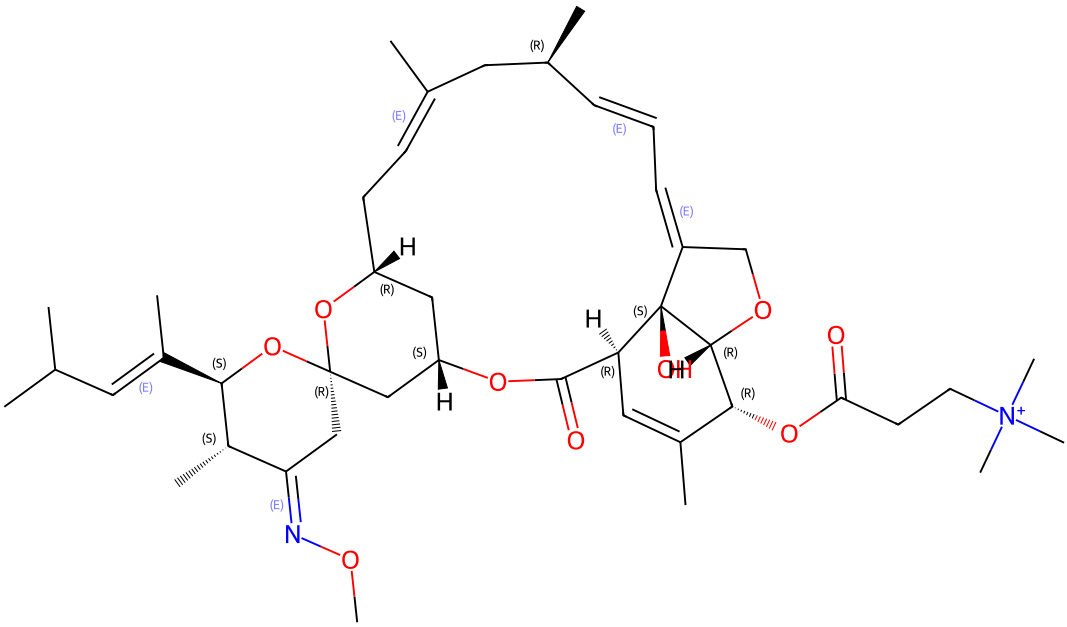
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 7 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 304

Arm proxy (A logP 1.6904): `COC(=O)CC[n+]1cccc2ccccc21`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C43H65N2O9+
Molecular weight (g/mol)	753.998
Exact mass (Da)	753.468458
Crippen cLogP	6.3761
TPSA (Å²)	122.11
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	7
Rings	5

Formal charge	1
Heavy atoms	54
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

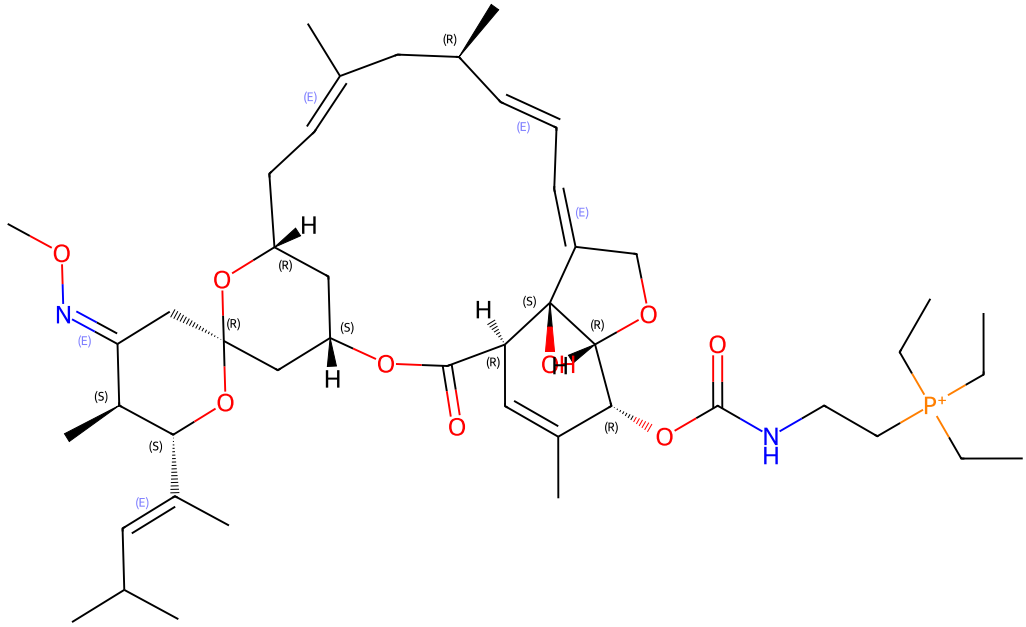
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 7 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 313

C`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CC[P+](CC)(CC)CCNC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P+](CC)(CC)CCNC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C46H72N2O9P+
Molecular weight (g/mol)	828.061
Exact mass (Da)	827.496995
Crippen cLogP	8.5401
TPSA (Å²)	134.14
H-bond donors	2
H-bond acceptors	10
Rotatable bonds	10

Rings	5
Formal charge	1
Heavy atoms	58
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

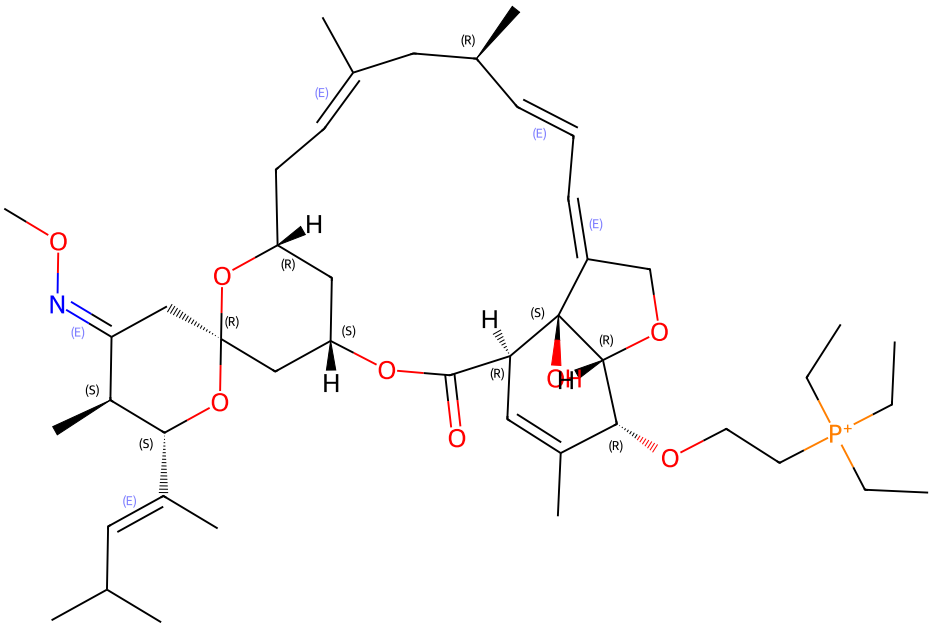
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 10 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 322

Arm proxy (A logP 2.4197): `CC[P+](CC)(CC)CCNC(=O)OC`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CC[P+](CC)(CC)CCO[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Canonical isomeric SMILES — RDKit 2026.09.1

CC[P+](CC)(CC)CCO[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Complete computed profile

Formula	C45H71NO8P+
Molecular weight (g/mol)	785.036
Exact mass (Da)	784.491181
Crippen cLogP	8.8305
TPSA (Å²)	105.04
H-bond donors	1
H-bond acceptors	9
Rotatable bonds	10

Rings	5
Formal charge	1
Heavy atoms	55
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

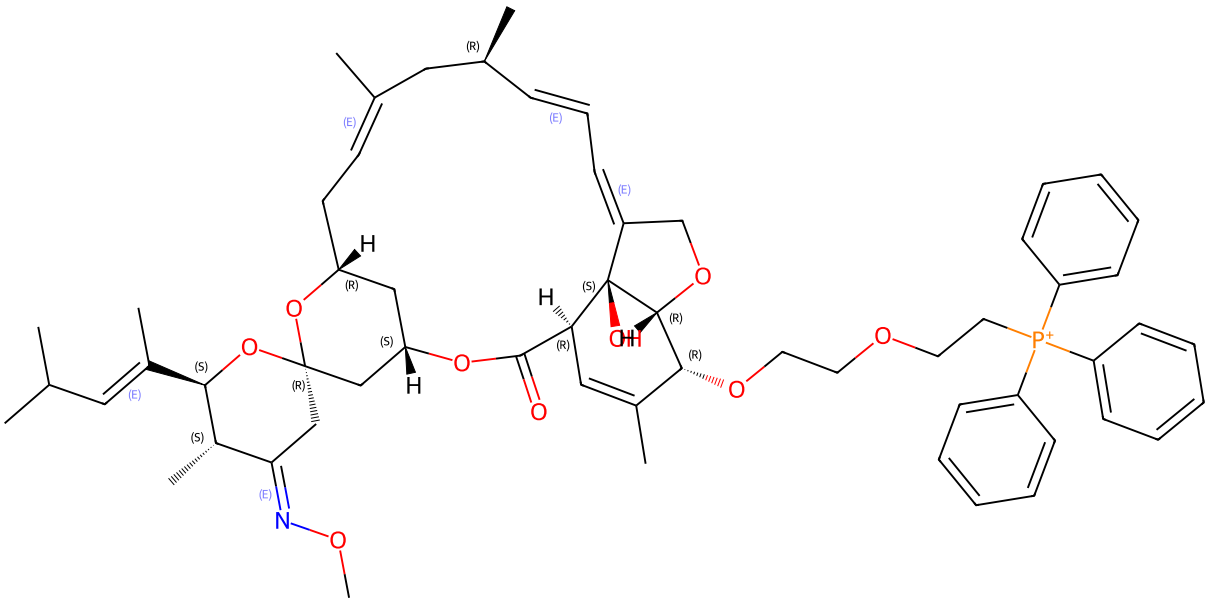
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 10 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 331

C)CC`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCOCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCOCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C59H75NO9P+
Molecular weight (g/mol)	973.221
Exact mass (Da)	972.517396
Crippen cLogP	9.7639
TPSA (Å²)	114.27
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	13

Rings	8
Formal charge	1
Heavy atoms	70
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

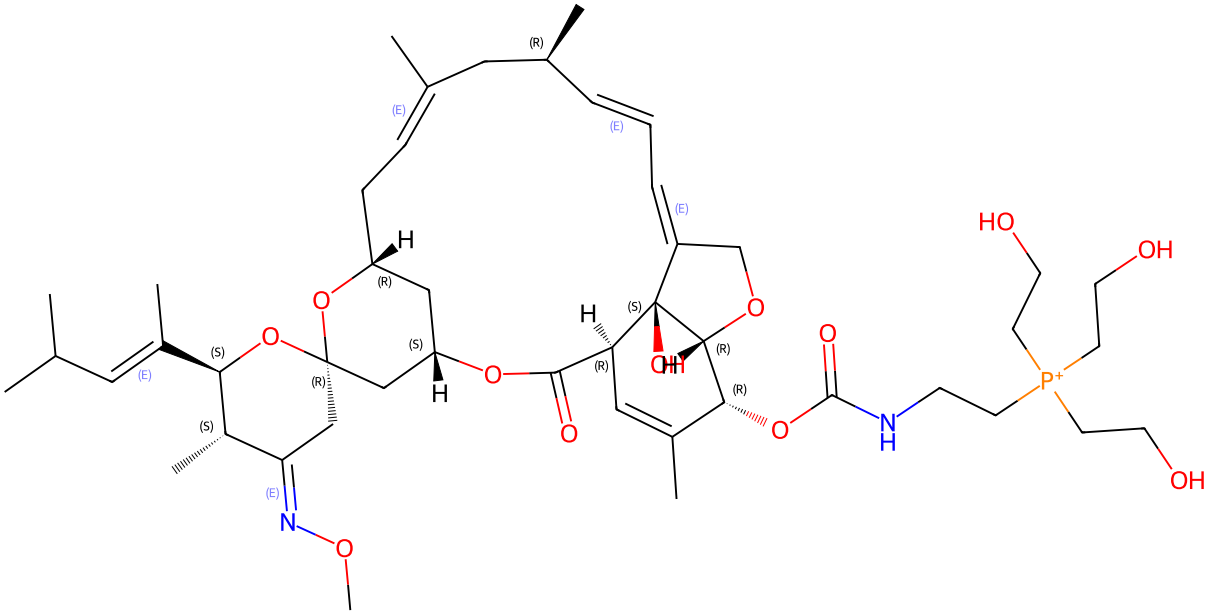
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 13 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 340

gP 3.6435): `COCCOCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC[P+](CCO)(CCO)CCO)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC[P+](CCO)(CCO)CCO)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C46H72N2O12P+
Molecular weight (g/mol)	876.058
Exact mass (Da)	875.481739
Crippen cLogP	5.4573
TPSA (Å²)	194.83
H-bond donors	5
H-bond acceptors	13
Rotatable bonds	13
Rings	5

Formal charge	1
Heavy atoms	61
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

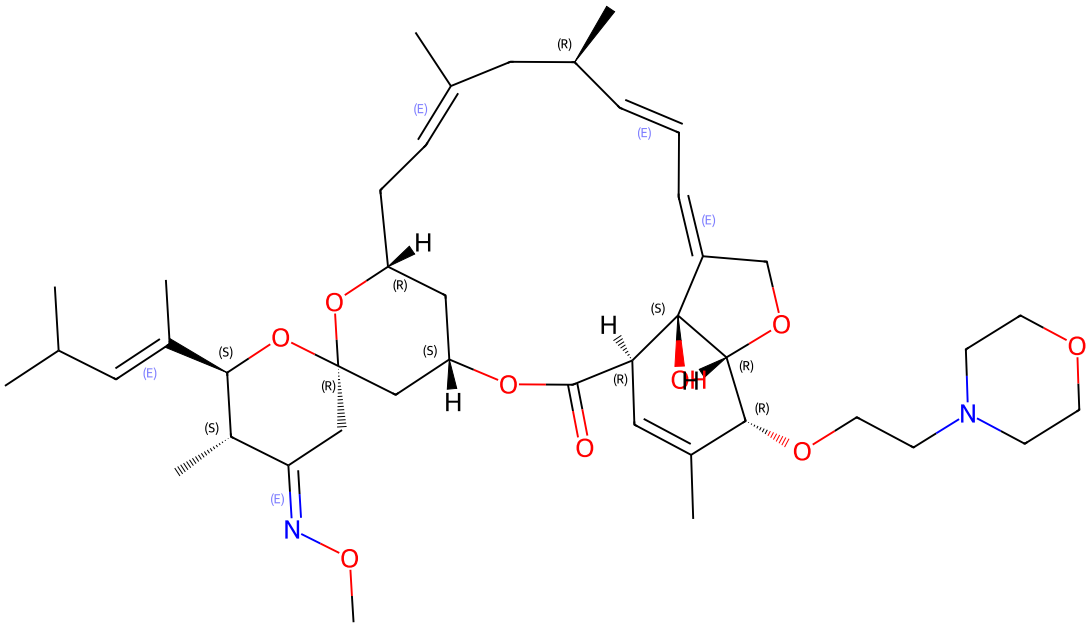
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 13 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 349

rm proxy (A logP -0.6631): `COC(=O)NCC[P+](CCO)(CCO)CCO`



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C43H64N2O9
Molecular weight (g/mol)	752.99
Exact mass (Da)	752.461182
Crippen cLogP	6.0854
TPSA (Å²)	117.51
H-bond donors	1
H-bond acceptors	11
Rotatable bonds	7

Rings	6
Formal charge	0
Heavy atoms	54
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

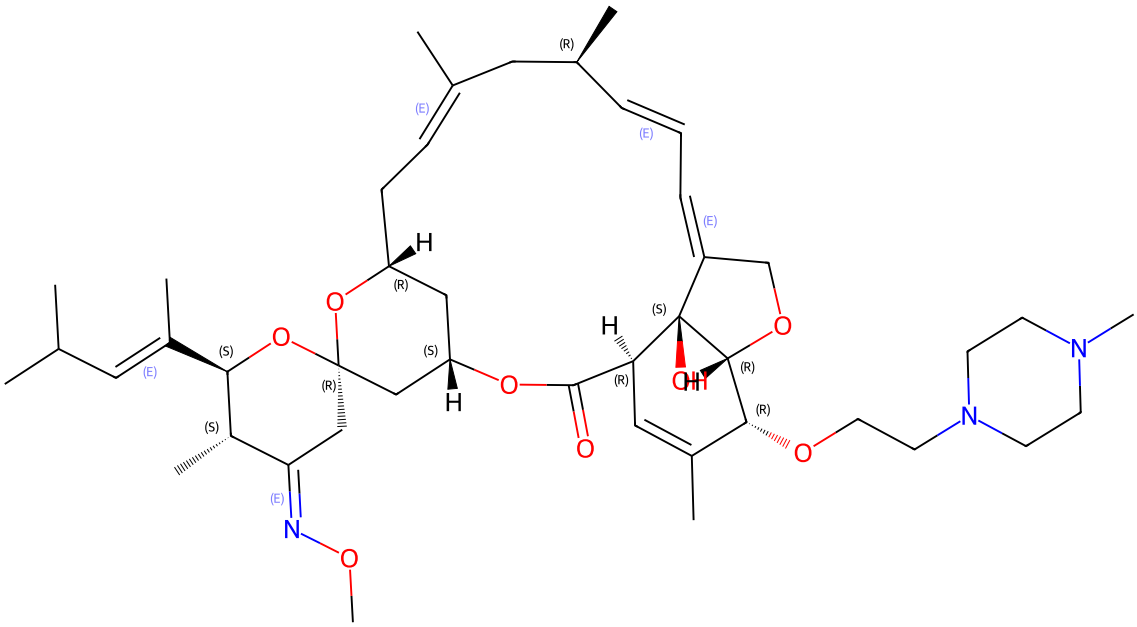
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 358

P -1.4687. This is not a separately nominated conjugate.



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCN6CCN(C)CC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCN6CCN(C)CC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C44H67N3O8
Molecular weight (g/mol)	766.033
Exact mass (Da)	765.492816
Crippen cLogP	6.0006
TPSA (Å²)	111.52
H-bond donors	1
H-bond acceptors	11
Rotatable bonds	7

Rings	6
Formal charge	0
Heavy atoms	55
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

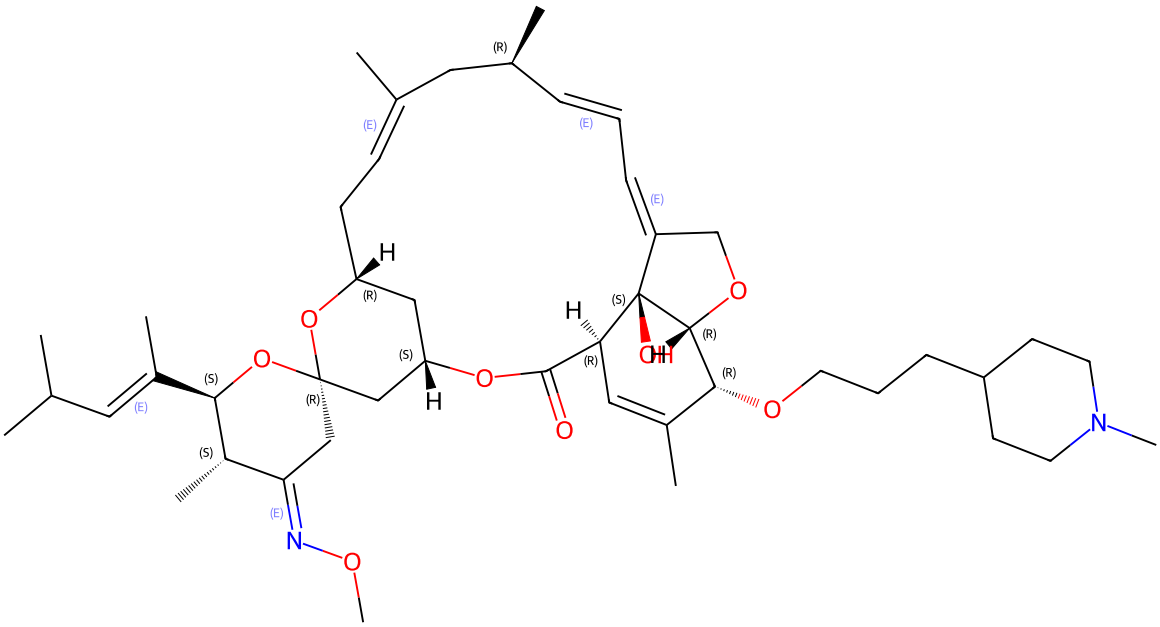
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 369

P -1.5535. This is not a separately nominated conjugate.



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCC6CCN(C)CC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCC6CCN(C)CC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C46H70N2O8
Molecular weight (g/mol)	779.072
Exact mass (Da)	778.513217
Crippen cLogP	7.8752
TPSA (Å²)	108.28
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	8

Rings	6
Formal charge	0
Heavy atoms	56
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

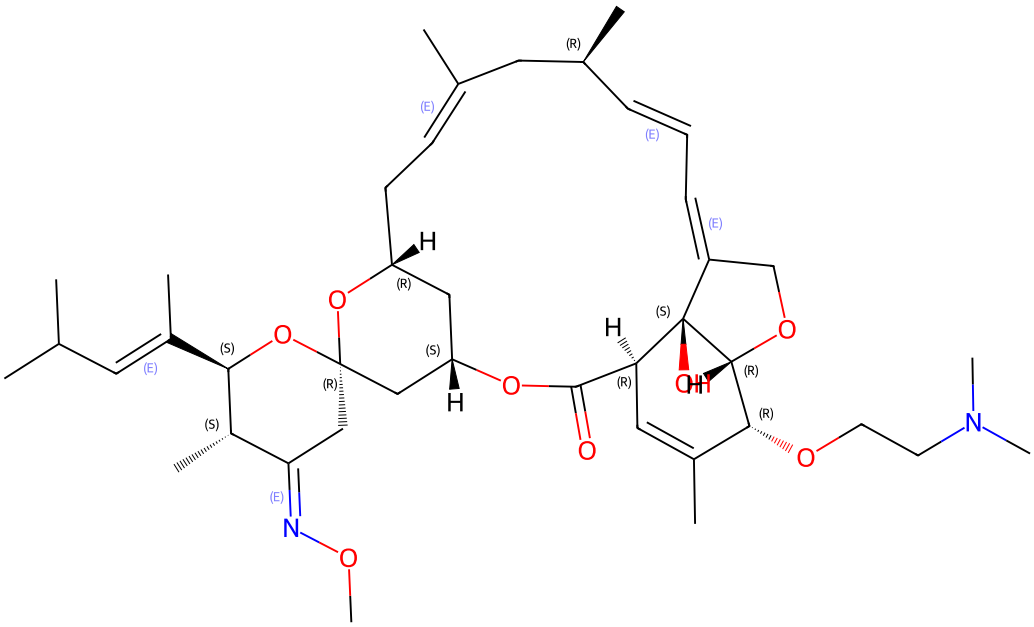
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 8 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 380

P -0.0690. This is not a separately nominated conjugate.



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCN(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCN(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C41H62N2O8
Molecular weight (g/mol)	710.953
Exact mass (Da)	710.450617
Crippen cLogP	6.3148
TPSA (Å²)	108.28
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	7

Rings	5
Formal charge	0
Heavy atoms	51
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

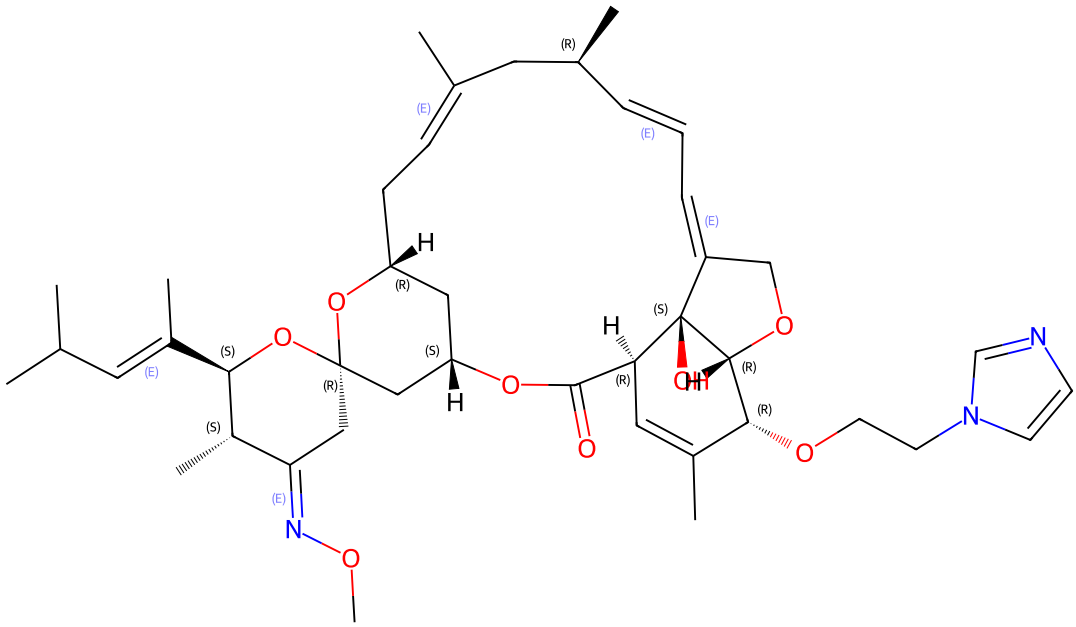
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 391

P -1.2393. This is not a separately nominated conjugate.



Recorded rationale and role

Programme comparator / derivative. This entry preserves the source scaffold and appendage combination for comparison with its parent and adjacent development records. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

The preparation concept is governed by the source scaffold, available attachment handle and functional-group compatibility. Establish connectivity, stereochemical

composition and relevant stability before comparing biological responses.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCn6ccnc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCn6ccnc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C42H59N3O8
Molecular weight (g/mol)	733.947
Exact mass (Da)	733.430216
Crippen cLogP	6.6499
TPSA (Å²)	122.86
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	7

Rings	6
Formal charge	0
Heavy atoms	53
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

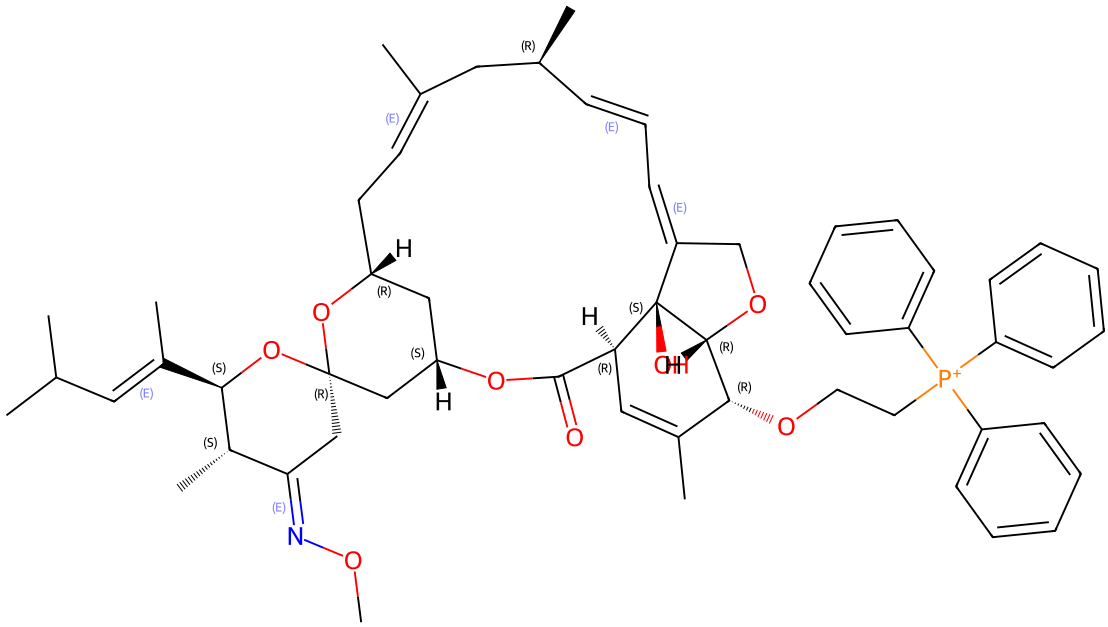
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +0, and 7 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 402

-0.1608. This is not a separately nominated conjugate.



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC[P+](c6ccccc6)(c6ccccc6)c6ccccc6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC[P+](c6ccccc6)(c6ccccc6)c6ccccc6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C57H71NO8P+
Molecular weight (g/mol)	929.168
Exact mass (Da)	928.491181
Crippen cLogP	9.7473
TPSA (Å²)	105.04
H-bond donors	1
H-bond acceptors	9
Rotatable bonds	10
Rings	8

Formal charge	1
Heavy atoms	67
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

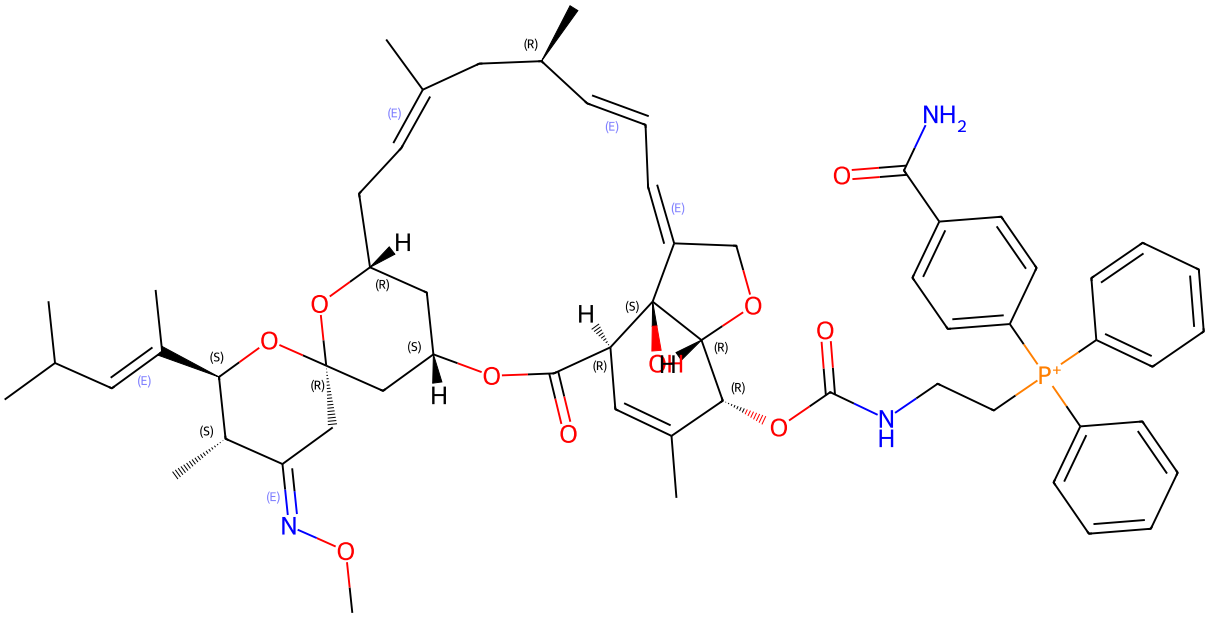
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 10 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 413

y (A logP 3.6269): `COCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC[P+](c6ccccc6)
(c6ccccc6)c6ccc(C(N)=O)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC[P+](c6ccccc6)
(c6ccccc6)c6ccc(C(N)=O)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C59H73N3O10P+
Molecular weight (g/mol)	1015.218
Exact mass (Da)	1014.502809
Crippen cLogP	8.5558
TPSA (Å²)	177.23
H-bond donors	3
H-bond acceptors	11
Rotatable bonds	11

Rings	8
Formal charge	1
Heavy atoms	73
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

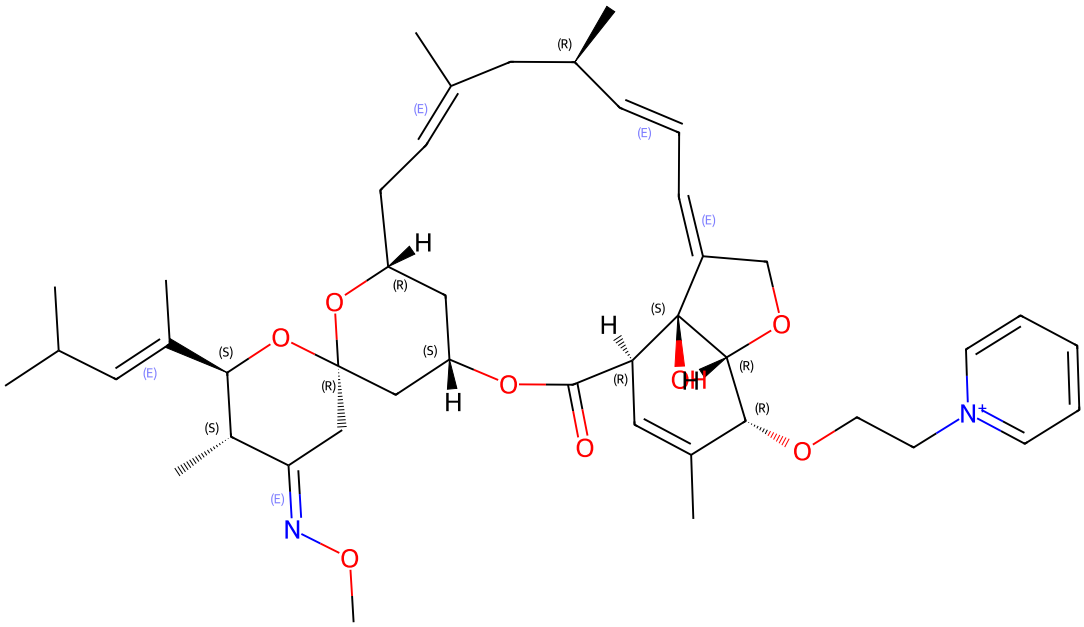
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 11 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 422

): `COC(=O)NCC[P+](c1ccccc1)(c1ccccc1)c1ccc(C(N)=O)cc1`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC[n+]6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC[n+]6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C44H61N2O8+
Molecular weight (g/mol)	745.978
Exact mass (Da)	745.442243
Crippen cLogP	6.7409
TPSA (Å²)	108.92
H-bond donors	1
H-bond acceptors	9
Rotatable bonds	7
Rings	6

Formal charge	1
Heavy atoms	54
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

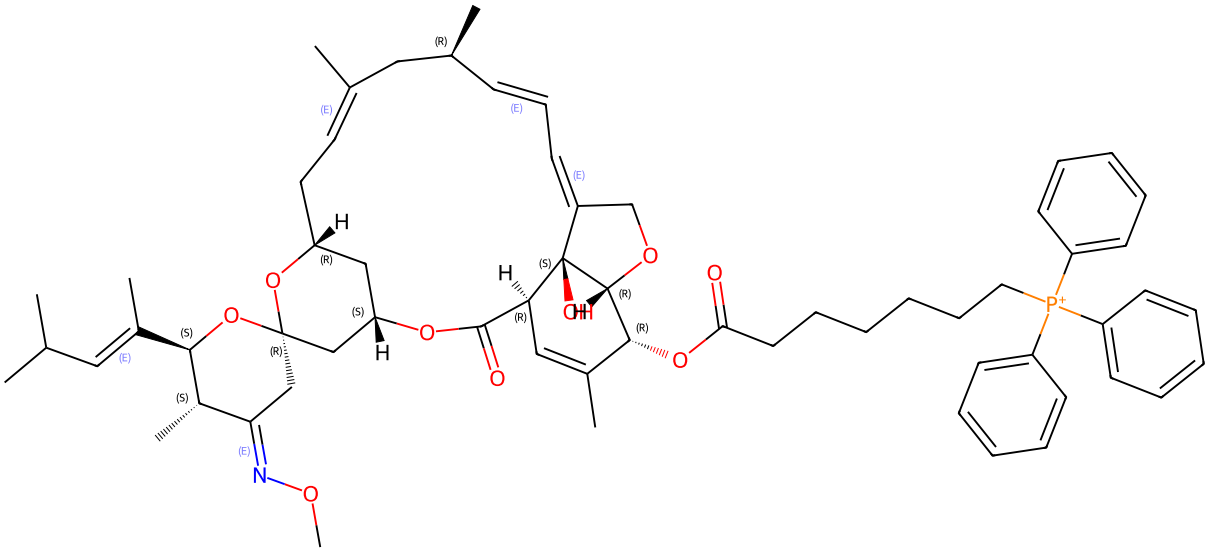
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 7 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 431

logP 4.3238): `COC(=O)CCCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C62H79NO9P+
Molecular weight (g/mol)	1013.286
Exact mass (Da)	1012.548696
Crippen cLogP	11.2244
TPSA (Å²)	122.11
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	14

Rings	8
Formal charge	1
Heavy atoms	73
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

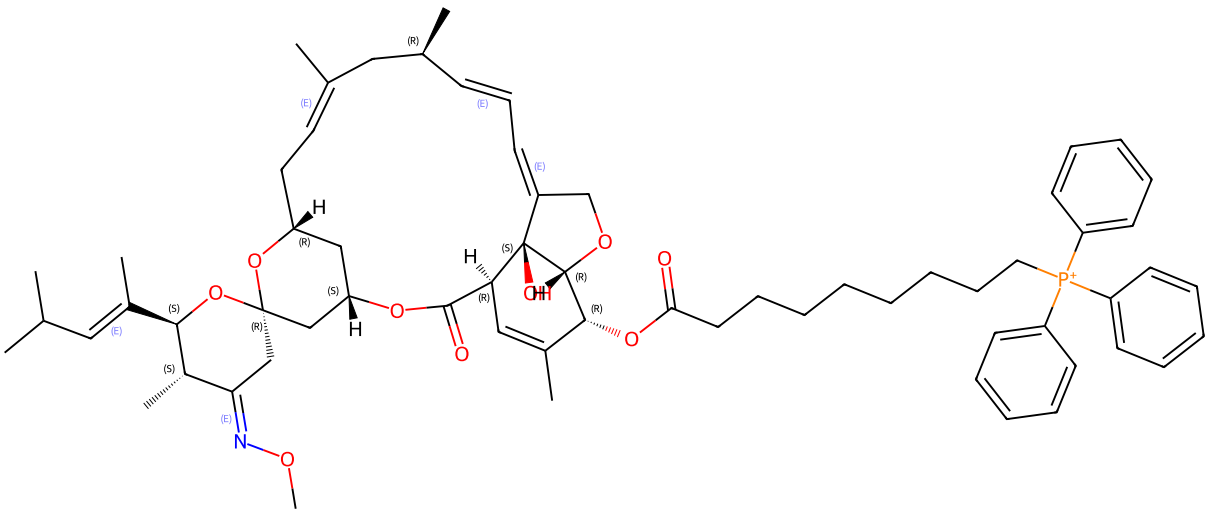
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 14 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 449

gP 5.1040): `COC(=O)CCCCCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1`



Recorded rationale and role

Charge-associated distribution arm. The encoded cation provides a test of distribution and membrane interaction against an uncharged or differently charged comparator. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCCCCCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCCCCCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C64H83NO9P+
Molecular weight (g/mol)	1041.34
Exact mass (Da)	1040.579996
Crippen cLogP	12.0046
TPSA (Å²)	122.11
H-bond donors	1
H-bond acceptors	10
Rotatable bonds	16

Rings	8
Formal charge	1
Heavy atoms	75
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

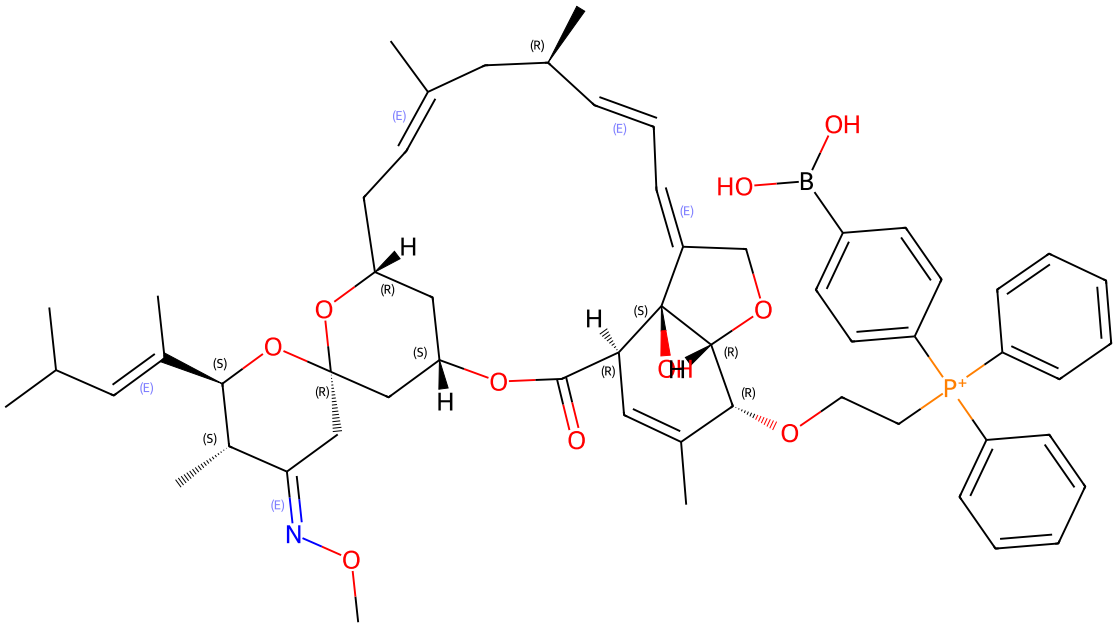
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 16 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 458

.8842): `COC(=O)CCCCCCCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1`



Recorded rationale and role

Conditional-release / oxidant-response design. The encoded boron-containing handle supports an activation hypothesis to compare with a trigger-free analogue and the released payload. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Characterize the trigger-bearing material, its stability and the identity of release products. Compare activation with more than one oxidant and distinguish carbonate/ester release from intact-conjugate effects.

Full deposited SMILES — verbatim

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC[P+](c6ccccc6)
(c6ccccc6)c6ccc(B(O)O)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Canonical isomeric SMILES — RDKit 2026.09.1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC[P+](c6ccccc6)
(c6ccccc6)c6ccc(B(O)O)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Complete computed profile

Formula	C57H72BNO10P+
Molecular weight (g/mol)	972.986
Exact mass (Da)	972.498141
Crippen cLogP	7.4271
TPSA (Å²)	145.5
H-bond donors	3
H-bond acceptors	11
Rotatable bonds	11

Rings	8
Formal charge	1
Heavy atoms	70
Unassigned stereo — modern	0
Unassigned stereo — legacy	0

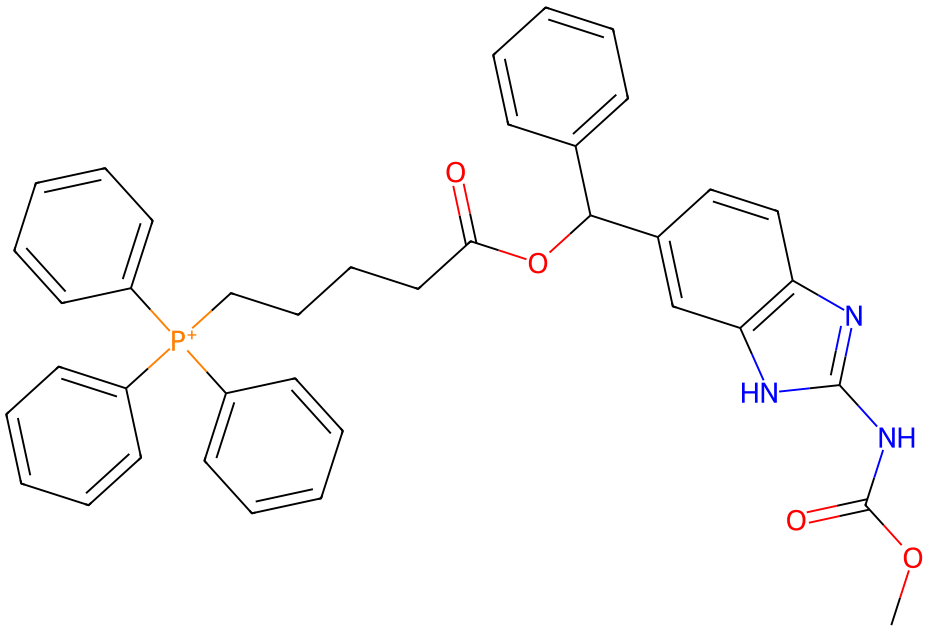
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 11 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. No unspecified stereochemical element was detected by the stated modern analysis of this graph.

Source record

/home/codex/atlas-governance/rd-prospects-464/sources/ATLAS_B1_SUCCESSORS.md; line 467

HMB-B1-intended



Recorded rationale and role

Distribution and linkage branch. This entry compares the appended head group and attachment against the B1 incumbent and parent moxidectin. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Specify counterion and salt composition, distinguish intact conjugate from cleaved species, and compare the charged appendage separately. Chromatographic and spectroscopic characterization must follow the actual encoded structure.

Full deposited SMILES — verbatim

COC(=O)Nc1nc2ccc(C(OC(=O)CCCC[P+](c3ccccc3)(c3ccccc3)c3ccccc3)c3ccccc3)cc2[nH]1

Canonical isomeric SMILES — RDKit 2026.09.1

COC(=O)Nc1nc2ccc(C(OC(=O)CCCC[P+](c3ccccc3)(c3ccccc3)c3ccccc3)c3ccccc3)cc2[nH]1

Complete computed profile

Formula	C39H37N3O4P+
Molecular weight (g/mol)	642.716
Exact mass (Da)	642.25162
Crippen cLogP	7.5382
TPSA (Å²)	93.31
H-bond donors	2
H-bond acceptors	5
Rotatable bonds	12
Rings	6
Formal charge	1
Heavy atoms	47

Unassigned stereo — modern	1
Unassigned stereo — legacy	1

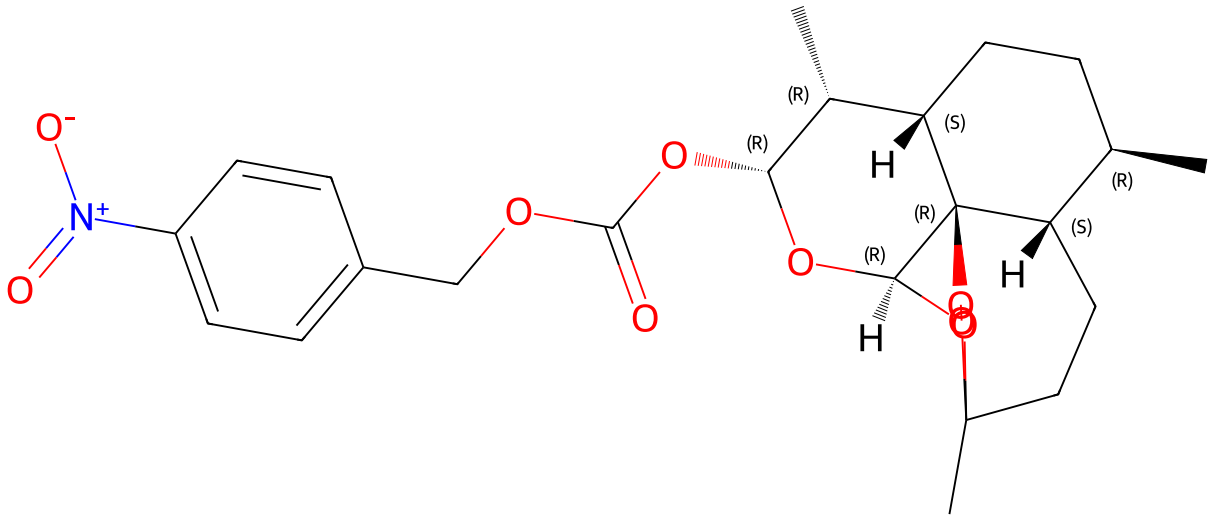
Graph interpretation and liabilities

This graph has 0 O–O bonds, net formal charge +1, and 12 rotatable bonds. Its high calculated lipophilicity makes free exposure, adsorption and formulation important comparison variables. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

/home/codex/outbox/arf-contribution-20261103/structures.json; $.audit[1].smiles

ATL-04



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@@H](OC(=O)OCc2ccc([N+](=O)[O-])cc2)O[C@@H]2OC3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@@H](OC(=O)OCc2ccc([N+](=O)[O-])cc2)O[C@@H]2OC3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Complete computed profile

Formula	C23H29NO9
Molecular weight (g/mol)	463.483
Exact mass (Da)	463.184232
Crippen cLogP	4.456
TPSA (Å²)	115.59
H-bond donors	0
H-bond acceptors	9
Rotatable bonds	4
Rings	6
Formal charge	0

Heavy atoms	33
Unassigned stereo — modern	1
Unassigned stereo — legacy	1

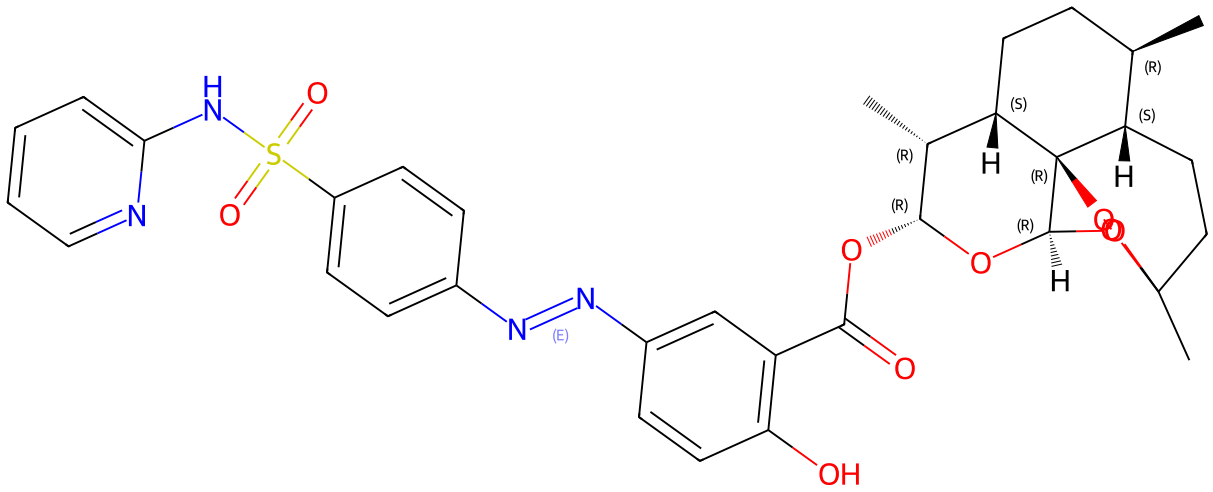
Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 4 rotatable bonds. The descriptor balance supports comparison with the adjacent source series rather than assuming a shared exposure profile. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

/home/codex/outbox/arf-contribution-20261103/atlas-derivatives.sdf; SDF record 4

ATL-07



Recorded rationale and role

Peroxide / iron-activation arm. The O–O-containing graph provides a chemically distinct redox perturbation to compare against its parent or peroxide-free counterpart. Source context is identified below; the design role is not a measured efficacy ranking.

Preparation focus in the existing record

Peroxide-preserving preparation and analytical work are central. Compare intact conjugate with any parent-release products; identify the peroxide architecture and stereochemical composition before biological interpretation.

Full deposited SMILES — verbatim

C[C@H]1[C@@H](OC(=O)c2cc(/N=N/c3ccc(S(=O)(=O)Nc4ccccn4)cc3)ccc2O)O[C@@H]2OC3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Canonical isomeric SMILES — RDKit 2026.09.1

C[C@H]1[C@@H](OC(=O)c2cc(/N=N/c3ccc(S(=O)(=O)Nc4ccccn4)cc3)ccc2O)O[C@@H]2OC3(C)CC[C@H]4[C@H](C)CC[C@@H]1[C@@]24OO3

Complete computed profile

Formula	C33H36N4O9S
Molecular weight (g/mol)	664.737
Exact mass (Da)	664.2203
Crippen cLogP	6.3682
TPSA (Å²)	167.23
H-bond donors	2
H-bond acceptors	12
Rotatable bonds	7
Rings	8
Formal charge	0

Heavy atoms	47
Unassigned stereo — modern	1
Unassigned stereo — legacy	1

Graph interpretation and liabilities

This graph has 1 O–O bond, net formal charge +0, and 7 rotatable bonds. Its polar surface makes permeability and compartmental exposure important comparison variables. The modern graph analysis leaves 1 stereochemical elements unspecified; material-level comparisons require that composition to be defined.

Source record

/home/codex/outbox/arf-contribution-20261103/atlas-derivatives.sdf; SDF record 7

CHAPTER 9

Recorded synthesis and design documents

The following existing documents are reproduced as documentary source chapters. Their original nominations, chemistry proposals, limitations and competing assessments remain attributable to their authors and dates. They are not laboratory records of completed synthesis.

DOCUMENTARY SOURCE S01

COOKBOOK_VOL6.md

Original source: /home/codex/outbox/rdkit-restored-20261108/node85-snapshot/home/codex/arf-001-mox/COOKBOOK_VOL6.md

Chemical Cookbook of the Redox Series — Volume 6

The two rescued branches: iron-activated peroxide, and mitochondrial voltage

Ron Johnson[1], SC 5.5[2] and Atlas[3] · [1]Stranger Than Fiction News · [2]Agentic Research Factory, Planet 44 · [3]Agentic Research Factory, Planet 85 · 5 November 2026 · Dedicated to the public domain

> Volume 5 catalogued the rosetta stones and the first derivatives taken from them. This volume covers what happened when two of those derivatives were attacked by a hostile reviewer and rebuilt. Both branches hang off a single synthetic seat — the C5 secondary allylic hydroxyl of moxidectin — and both were nominated as leads before anyone had checked whether they survived scrutiny. Neither did, in its original form. What follows is the replacement set: fifty-four structures across two branches, every one RDKit-validated at build time, properties computed and not quoted.

> **Nothing here has been synthesised, assayed or administered.**
>
> This volume carries **routes** as well as structures. That is deliberate. A defensive publication forecloses only what it enables, and our patent-form disclosure ARF-DEF-002 admitted in its § 8 that composition novelty was foreclosed while process claims were not, because no route had been given. §§ 4 and 8 below close that gap. The routes are written as conceptual sequences with their sensitive steps named; none has been performed, and that limitation is stated again at each one.

PART ONE · THE C4 BRANCH — iron-activated peroxide

1 · Progress summary — where this branch stands

What it was. ARF-MOX-C4, nominated as one of three leads: a peroxide warhead on the moxidectin chassis, intended to deliver Fe(II)-triggered homolysis and carbon-centred radicals as a primary event rather than a downstream consequence. Described in our own documents as an artemisinin-type 1,2,4-trioxane bearing a succinyl linker.

What went wrong — three objections, all upheld. An independent assessment placed hybrid risk ahead of anticipated gain: the O–O bond must survive synthesis, workup, purification and plasma; the C5 ester is esterase-

labile and may be cleaved before iron activation, returning the parent and a free peroxide and forfeiting the dual-action premise; and the compound carries 16 tetrahedral centres of which 6 are unspecified, so it does not define a single synthetic target.

What went more wrong — the compound was misidentified. Ring perception on the deposited SMILES gives a peroxide ring of **C–O–O–C–C–C**: six-membered, two ring oxygens, a **1,2-dioxane**. An artemisinin-type 1,2,4-trioxane requires three. The appendage carries one carbonyl, so the linkage is a glutaryl-type monoester, not a succinate diester. The structure governs and our description was wrong. Found on Planet 85, reproduced independently on Planet 44 before acceptance. The error never entered the structural record — every property ever computed was computed from the correct structure — but it propagated through the prose, and it cuts against the compound: a plain dialkyl 1,2-dioxane has no stabilising acetal oxygen and is a **poorer** peroxide than the one we claimed. The case for replacement was stronger than the case made against it.

What was tried and failed. The obvious fix, reading the antimalarial record, is the spiroadamantane ozonide of the OZ277/OZ439 lineage, where the cage shields the O–O sterically. On this chassis it is a **negative result**. Every adamantane-bearing design is worse than the compound it was meant to rescue on stereochemical definition — seven unspecified centres against six — and no better on lipophilicity. Two adamantane designs are retained as **held comparators** only: they show zero unspecified centres under RDKit's legacy algorithm and five or six under the conservative

one, a discrepancy in dependent cage and spiro stereochemistry that needs a chemist, not a software verdict. Both numbers are reported rather than the flattering one.

What worked. Remove the cage. Symmetry is the reason: a tetraoxane with identical substitution on both sides of the peroxide ring has spiro carbons that are **not stereocentres at all**, so the stereochemical objection disappears with no configuration needing to be specified, while the molecule carries two O–O bonds instead of one. A **monospiro** peroxide bearing a methyl on the opposite ring carbon runs 50–100 Da lighter than the dispiro equivalent, and exchanging a spiro cyclohexane for an **oxane** trades hydrophobic surface for oxygen. Those two moves together reach clogP 6.39 where the dispiro series bottoms out at 7.83.

Where it stands. Thirty-four designs, built independently on two nodes and reconciled. Twelve improve on the incumbent simultaneously in lipophilicity, stereochemical definition and ester count; ten of those twelve came from Planet 85. All twelve Planet 85 structures were re-parsed on Planet 44 and their MW and clogP reproduced to four decimal places. Nothing reaches a clean sweep: no design has both two peroxide bonds and a TPSA under 140 Å², which is this branch's standing structural tension. **S04** is the only design in the set to satisfy both Veber criteria with clean stereochemistry and is the lightest by 45 Da; **S07** leads on the stated liability at clogP 6.60. The incumbent ranks 31st of 34.

What is unresolved, and it halves the branch. The C5 ester is the liability *and* the release mechanism. Remove it and the conjugate can never revert to free moxidectin — the macrocycle stays tethered through the position avermectin

structure–activity work is most sensitive about. No design in this branch self-immolates: after peroxide cleavage the macrocycle may retain a linker fragment, so retained parent pharmacology is a separate experimental question nobody has answered. Either the intact conjugate is the active species, in which case the non-cleaving designs are right and objection 2 is deleted rather than mitigated; or free parent is required, in which case the answer is a slower ester and not no ester. **Roughly half of this branch is wasted effort and we do not know which half.** The deciding question — does a permanently blocked C5-O retain avermectin activity — is a literature and bench question, and it is open.

Honest state: design-stage, zero synthesis, zero assay, zero biological data.

2 · The reference compounds

The chassis and the compound being replaced.

Compound	Formula	MW	clogP	TPSA	HBD	RotB
Moxidectin	C37H53NO8	639.8	5.73	116.0	2	3
ARF-MOX-C4 (incumbent)	C52H75NO11	890.2	9.22	140.6	1	7

Molecular weight in daltons; clogP is computed lipophilicity; TPSA is topological polar surface area in Å²; HBD is hydrogen-bond donors; RotB is rotatable bonds. All values computed in RDKit 2026.09.1 from the parsed structure.

Moxidectin

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-C4 — the deposited incumbent; 1,2-dioxane, glutaryl-type monoester

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC6OOC7(C)CCC8C(C)CCC6C87)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

3 · The C4 branch structures

Ranked best-in-class. Gates: zero unspecified stereocentres · no added ester · clogP below the incumbent 9.22 · TPSA ≤ 140 Å² · RotB ≤ 10 · MW below the incumbent 890.2 · two O–O bonds.

3.1 · First rank — five or more gates passed

Compound	Formula	MW	clogP	TPSA	HBD	RotB
S07	C46H66N2O14	871.0	6.60	180.3	2	6
S06	C45H64N2O13	841.0	6.97	171.1	2	6
S04	C45H65NO11	796.0	7.72	132.7	1	7
S05	C47H68N2O13	869.1	7.75	171.1	2	6
S09	C48H68N2O13	881.1	7.89	171.1	2	5
S10	C49H71NO13	882.1	8.06	151.2	1	6
S11	C48H70N2O14	899.1	6.39	180.3	2	9

Compound	Formula	MW	clogP	TPSA	HBD	RotB
S03	C46H66N2O13	855.0	6.66	171.1	2	6
S12	C48H72N2O14S	933.2	6.96	188.1	2	10
S02	C47H68N2O12	853.1	7.82	161.8	2	6
C4p	C53H78N2O13	951.2	8.72	171.1	2	9

Molecular weight in daltons; clogP is computed lipophilicity; TPSA is topological polar surface area in Å²; HBD is hydrogen-bond donors; RotB is rotatable bonds. All values computed in RDKit 2026.09.1 from the parsed structure.

S07

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NCC6(C)OOC7(CCOCC7)OO6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

S06

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC6(C)OOC7(CCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

S04

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC[C@]6(C)OOC7(CCC7)O6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

S05

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC6(C)OOC7(CCCCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

S09

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC6CCC7(CC6)OOC6(CCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

S10

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC6CCC7(CC6)OOC6(CCOCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

S11

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCNC(=O)CC6(C)OOC7(CCOCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

S03

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC[C@]6(C)OOC7(CCOCC7)O6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

S12

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCNS(=O)
(=O)CC6(C)OOC7(CCCCC7)OO6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

S02

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC[C@]6(C)OOC7(CCCCC7)O6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

C4p

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[
C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)
[C@H]1C

3.2 · Second rank — three or four gates passed

Compound	Formula	MW	clogP	TPSA	HBD	RotB
C4q	C55H81N3O14	1008.3	7.83	200.2	3	11
S08	C51H73NO12	892.1	8.92	142.0	1	7
C4i	C57H82N2O13	1003.3	9.21	171.1	2	9
C4k	C52H76N2O13	937.2	9.31	171.1	2	7
C4r	C54H78N4O12	975.2	9.39	172.7	1	9
C4t	C51H75NO12	894.2	9.60	142.0	1	7
S01	C51H72N2O12	905.1	8.31	161.8	2	6

Compound	Formula	MW	clogP	TPSA	HBD	RotB
C4n	C57H84N2O14S	1053.4	9.01	188.1	2	11
C4g	C56H80N2O13	989.3	9.80	171.1	2	7
C4h	C58H82N4O12	1027.3	9.88	172.7	1	9
C4f	C55H79NO11	930.2	10.16	132.7	1	7
C4u	C55H81NO13	964.2	10.54	159.0	1	8

Molecular weight in daltons; clogP is computed lipophilicity; TPSA is topological polar surface area in Å²; HBD is hydrogen-bond donors; RotB is rotatable bonds. All values computed in RDKit 2026.09.1 from the parsed structure.

C4q

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCC(=O)NCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

S08

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCC6(C)OOC7(OO6)C6CC8CC(C6)CC7C8)C(C)=C[C@@
H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

C4i

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC(=O)NCCC6CCC7(CC6)OOC6(OO7)C7CC8CC(C7)CC6
C8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

C4k

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C
@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)
[C@H]1C

C4r

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCc6cn(CCC7CCC8(CC7)OOC7(CCCCC7)OO8)nn6)C(C)=
C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)
[C@H]1C

C4t

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

S01

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC[C@]6(C)OOC7(O6)C6CC8CC(C6)CC7C8)C(C)=
C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)
[C@H]1C

C4n

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCS(=O)
(=O)NCCC6CCC7(CC6)OOC6(OO7)C7CC8CC(C7)CC6C8)C
(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

C4g

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCC6CCC7(CC6)OOC6(OO7)C7CC8CC(C7)CC6C
8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

C4h

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]

(OCc6cn(CCC7CCC8(CC7)OOC7(OO8)C8CC9CC(C8)CC7C9)nn6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

C4f

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

C4u

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)C(C)(C)CCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

3.3 · Third rank — two or fewer gates passed, recorded for completeness

A series in which every member is an improvement is not a series. These are reported so the trade-offs are visible and so the dedication covers them.

Compound	Formula	MW	clogP	TPSA	HBD	RotB
C4s	C55H81N3O13	992.3	7.90	190.9	3	11

Compound	Formula	MW	clogP	TPSA	HBD	RotB
C4m	C59H85N3O13	1044.3	8.39	190.9	3	11
C4d	C57H82N2O12	987.3	9.28	161.8	2	9
C4j	C52H76N2O12	921.2	9.38	161.8	2	7
C4o	C54H78N4O11	959.2	9.46	163.4	1	9
C4c	C56H80N2O12	973.3	9.87	161.8	2	7
C4e	C58H82N4O11	1011.3	9.95	163.4	1	9
C4	C52H75NO11	890.2	9.22	140.6	1	7
C4l	C61H90N2O13	1059.4	10.03	162.3	1	13

Compound	Formula	MW	clogP	TPSA	HBD	RotB
C4b	C56H79NO12	958.2	10.08	149.8	1	7
C4v	C55H81NO12	948.2	10.61	149.8	1	8

Molecular weight in daltons; clogP is computed lipophilicity; TPSA is topological polar surface area in Å²; HBD is hydrogen-bond donors; RotB is rotatable bonds. All values computed in RDKit 2026.09.1 from the parsed structure.

C4s

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCC(=O)NCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)O7)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

C4m

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCC(=O)NCC(=O)NCCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

C4d

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]

(OCC(=O)NCCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

C4j

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)O7)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

C4o

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCc6cn(CCC7CCC8(CC7)OOC7(CCCCC7)O8)nn6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

C4c

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NCCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

C4e

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCc6cn(CCC7CCC8(CC7)OOC7(O8)C8CC9CC(C8)CC7C9)

nn6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

C4

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC6OOC7(C)CCC8C(C)CCC6C87)C(C)=C[C@@H
](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

C4l

CCOCCN(CCC1CCC2(CC1)OOC1(O2)C2CC3CC(C2)CC1C3
)C(=O)CO[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H
](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

C4b

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC6CCC7(CC6)OOC6(O7)C7CC8CC(C7)CC6C8)
C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H]
(/C(C)=C/C(C)C)[C@H]1C

C4v

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)C(C)
(C)CCC6CCC7(CC6)OOC6(CCCCC6)O7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

4 · Routes — the C4 branch

None of these sequences has been performed. They are conceptual routes with their sensitive steps named. The governing constraint across the whole branch: **build the peroxide away from the macrocycle and attach it last.** Moxidectin carries multiple alkenes, and ozonide-forming chemistry applied to the intact chassis would be expected to destroy that polyene.

Warhead W1/W2 — the 1,2,4-trioxolane (ozonide). Griesbaum co-ozonolysis is the established route: an O-methyl ketoxime is co-ozonolysed with a ketone partner, and the trioxolane assembles with the two carbonyl-derived carbons flanking the peroxide. For a monospiro warhead the oxime partner carries the methyl and the tether handle; for a dispiro warhead both partners are cyclic. Ozone, a peroxide product and a polyene are three reasons this step happens on the fragment and never on the conjugate. The handle is carried through as a protected alcohol, ester or nitrile and unmasked afterwards.

Warhead W3/W4 — the 1,2,4,5-tetraoxane. Two stages. First the ketone is converted to its **gem-dihydroperoxide** with hydrogen peroxide under acid catalysis. Second that dihydroperoxide is condensed with a second ketone — the same one for a symmetric tetraoxane, a different one for an unsymmetric — under Lewis or Brønsted acid catalysis. Symmetric condensation is the operation that delivers the stereochemical prize in this branch, because the resulting ring carbons are not stereocentres. It is also the step that generates a gem-dihydroperoxide intermediate, which is the

single most hazardous species in this book: small scale, no concentration to dryness, no metal spatulas, and a process-safety assessment before any scale beyond milligrams.

Linkage L3 — carbamate, the recommended first platform. The warhead is prepared bearing a primary amine. The amine is activated as the isocyanate, or with carbonyldiimidazole or 4-nitrophenyl chloroformate, and the activated species is then presented to the C5 hydroxyl. The reason this is the first platform is regiochemical: C5 is a secondary alcohol and C7 is tertiary, so the less hindered position is favoured, but **selectivity is a hypothesis to be measured and not an assumption** — any C7 regioisomer is a failed target even if the mass is right. Carbamates are a stability hypothesis, not esterase-proof bonds.

Linkage L4 — direct ether, the harder arm. O-selective alkylation of an allylic secondary alcohol flanked by a polyene. Silver(I) oxide with an alkyl triflate or iodide, or acid-catalysed alkylation via a trichloroacetimidate, are the conceptual options. Allylic systems invite rearrangement and elimination, and the polyene invites worse. The reward is that no acyl group exists at C5 to hydrolyse; the new liability is oxidative dealkylation, which the ester never had.

Linkage L8 — triazole. C5 is propargylated first, then joined to an azide-bearing warhead by copper-catalysed azide–alkyne cycloaddition. Two compatibility questions must be settled before this is attempted: copper and peroxides, and the handle installation itself. The payoff is a linkage that is effectively inert to hydrolysis, which only matters if the intact conjugate is the active species.

Linkage L2 — hindered ester, for the release case. 2,2-dimethylglutaric anhydride is opened to the mono-acid, coupled to the warhead, then esterified onto C5 under carbodiimide conditions. This is the route to take **only** if the C5 question resolves in favour of requiring free parent. It keeps release and slows it; the gem-dimethyl groups cost 1.3 log units of lipophilicity for the privilege.

What will kill any of these. Hydrogenolysis, strong reductants, and ferrous contamination in glassware will all destroy an O–O bond; iron contamination will do it silently and in the one way that looks like a yield problem rather than a mechanism problem. Reducing deprotections and metal-catalysed operations must not be assumed compatible with a peroxide. C5 epimerisation, a C7 regioisomer, peroxide loss or altered alkene geometry each constitute failure of the specified target.

PART TWO · THE MOX1 / B1 BRANCH — mitochondrial voltage

5 · Progress summary — where this branch stands

What it was. ARF-MOX-B1: moxidectin esterified at C5 to a pentanoyl arm terminating in triphenylphosphonium. A delocalised lipophilic cation accumulates in mitochondria in response to membrane potential, which is hyperpolarised in cancer cells, so the design was intended to close the exposure gap by subcellular concentration rather than by dose

escalation. $C_{60}H_{75}NO_9P^+$, MW 985.2, clogP 10.44, permanent formal +1.

What went wrong — three objections, all upheld. Triphenylphosphonium does not discriminate between tumour and healthy mitochondria, and cardiac and skeletal muscle mitochondria are also hyperpolarised, so systemic exposure loads the heart. Nernst-driven accumulation is not self-limiting, risking generalised mitochondrial failure in normal tissue before selective tumour kill. And a permanent charge on a 985 Da macrocycle at clogP 10.44 is a plasma-protein-binding and clearance problem that can neutralise the intended distribution advantage outright.

The arithmetic that reframes the branch. The Nernst slope is **61.54 mV per decade at 37 °C**. Taken at face value:

Mitochondrial potential	Accumulation
−120 mV	89×
−140 mV	188×
−160 mV	398×
−180 mV	842×
−200 mV	1779×

The published exposure gap for this chassis is 110–220×. At −180 mV the mechanism delivers 842×, so **it closes the potency gap comfortably.** But selectivity comes only from the *difference* between tumour and normal potential, and

tumour −180 mV against normal −140 mV is a 40 mV gap, which is **4.5×**. At a 30 mV gap it is 3.1×.

So this mechanism **solves potency and cannot solve selectivity.** The cardiotoxicity objection is not a side risk to be engineered around; it is structural to the mechanism. And because both tissues sit on the same exponential, a more aggressive cation buys more accumulation *everywhere* at the same 4.5× ratio — it spends therapeutic index and returns nothing. B1 is over-engineered in precisely the direction that produces objections 1 and 2.

Which inverts the design objective. If only ~200× is needed and 842× is available, the correct move is to **detune deliberately**: take sub-maximal accumulation in exchange for a lower cation lipophilicity and a wider window.

The column that was missing. Off-target mitochondrial uncoupling tracks the lipophilicity of the **cationic headgroup**, not of the whole conjugate, and neither node had computed it. Added here as hgLogP, the clogP of the methyl-capped headgroup alone. It spans 5.03 down to −0.14 against triphenylphosphonium's 3.61, and it reorders the branch.

What was tried and failed. "Trialkyl is less delocalised than triaryl, so tributylphosphonium should be gentler" is false: hgLogP **5.03**, whole-molecule clogP **11.66** — worse than the incumbent on both counts. The butyl chains cost more than the loss of aryl delocalisation saves. This is the same shape of error as the adamantane result in Part One, and it is recorded as a negative result for the same reason.

Where it stands. Twenty designs. The incumbent ranks last at one gate of six. Two honest leads, in two different mechanism

classes: **B1h** (trimethylammonium, carbamate) keeps the permanent +1 so the Nernst driving force still applies, while cutting headgroup lipophilicity 3.29 log units, mass by 188 Da, clogP by 3.49 units and rotatable bonds from 12 to 9; **B1n** or **B1o** abandon the permanent charge for a weak base intended to protonate only in the acidic tumour microenvironment.

What is unresolved. Three things, and they are load-bearing. First, **delocalisation is why triphenylphosphonium works** — it lowers the desolvation penalty for crossing the inner membrane. A compact trimethylammonium at hgLogP 0.32 may not get in at all, in which case B1h is the advantage of a drug that never arrives. Second, the weak-base class trades a calculable Nernst driving force for a qualitative argument about tumour pH, and **RDKit gives no reliable pKa**, so every pH-gating claim here is unquantified; a measured or literature-anchored pKa near 6.5–7.0 is required before any of that class can be ranked honestly. Third, a neutral weak base is not a better B1 — it is a different drug, and the ranking below rewards it for avoiding a liability it achieves by abandoning the mechanism.

Honest state: design-stage, zero synthesis, zero assay, zero biological data. No claim is made that any design preserves the chassis's weak P-glycoprotein behaviour; avoiding large lipophilic cations is a design restraint and not a transporter assay.

6 · The reference compound

Compound	Formula	MW	clogP	TPSA	HBD	RotB
ARF-MOX-B1 (incumbent)	C60H75NO9P+	985.2	10.44	122.1	1	12

Molecular weight in daltons; clogP is computed lipophilicity; TPSA is topological polar surface area in Å²; HBD is hydrogen-bond donors; RotB is rotatable bonds. All values computed in RDKit 2026.09.1 from the parsed structure.

ARF-MOX-B1 — the deposited incumbent; triphenylphosphonium, pentanoyl ester, permanent +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCCC[P+](c6ccccc6)(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

7 · The MOX1 / B1 branch structures

Split by mechanism class, because a permanent cation and a weak base are not interchangeable. Within each class, ranked by headgroup lipophilicity — the off-target correlate — then by whole-molecule clogP. The hgLogP column follows each table.

7.1 · Permanent cations — Nernst mechanism preserved

Compound	Formula	MW	clogP	TPSA	HBD	RotB
B1h	C45H70N3O9+	797.1	6.95	134.1	2	9
B1i	C44H69N2O8+	754.0	7.24	105.0	1	9
B1j	C48H68N3O9+	831.1	7.31	138.0	2	9
B1k	C46H71NO9P+	813.0	8.75	122.1	1	10
B1f	C48H76N2O9P+	856.1	9.32	134.1	2	12
B1g	C47H75NO8P+	813.1	9.61	105.0	1	12
B1l	C50H79NO9P+	869.2	10.31	122.1	1	14

Compound	Formula	MW	clogP	TPSA	HBD	RotB
B1b	C60H76N2O9P+	1000.2	10.24	134.1	2	12
B1c	C59H75NO8P+	957.2	10.53	105.0	1	12
B1e	C54H88N2O9P+	940.3	11.66	134.1	2	18
B1d	C63H82N2O12P+	1090.3	10.26	161.8	2	15

Molecular weight in daltons; clogP is computed lipophilicity; TPSA is topological polar surface area in Å²; HBD is hydrogen-bond donors; RotB is rotatable bonds. All values computed in RDKit 2026.09.1 from the parsed structure.

ID	Headgroup	hgLogP	Formal charge
B1h	trimethylammonium	0.32	+1
B1i	trimethylammonium	0.32	+1

ID	Headgroup	hgLogP	Formal charge
B1j	N-methylpyridinium	0.82	+1
B1k	triethylphosphonium	2.69	+1
B1f	triethylphosphonium	2.69	+1
B1g	triethylphosphonium	2.69	+1
B1l	triethylphosphonium	2.69	+1
B1b	triphenylphosphonium (incumbent)	3.61	+1
B1c	triphenylphosphonium (incumbent)	3.61	+1
B1e	tributylphosphonium	5.03	+1
B1d	tris(4-methoxyphenyl)phosphonium	3.64	+1

B1h

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

B1i

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCCC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

B1j

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCc6cc[n+](C)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

B1k

CC[P+](CC)
(CC)CCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C
@@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

B1f

CC[P+](CC)
(CC)CCCCNC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]
3C[C@@H](C/C=C(\C)C[C@@H]

(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

B1g

CC[P+](CC)
(CC)CCCCO[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@
@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

B1l

CC[P+](CC)
(CC)CCCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@
H]3C[C@@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

B1b

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

B1c

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCCC[P+](c6ccccc6)(c6ccccc6)c6ccccc6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

B1e

CCCC[P+](CCCC)(CCCC)CCCCNC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

B1d

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NCCCC[P+](c6ccc(OC)cc6)(c6ccc(OC)cc6)c6ccc(OC)cc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

7.2 · Weak bases — pH-gated, mechanism changed

These carry no permanent charge and therefore no Nernst driving force. Their tumour selectivity rests entirely on protonation in an acidic microenvironment, which is **unquantified here** because no reliable pKa was computed. Ranked, but not recommended over the cationic class on this evidence.

Compound	Formula	MW	clogP	TPSA	HBD	RotB
B1n	C45H68N2O9	781.0	6.87	117.5	1	9
B1p	C44H67N3O9	782.0	6.80	137.4	2	9

Compound	Formula	MW	clogP	TPSA	HBD	RotB
B1q	C43H66N2O8	739.0	7.10	108.3	1	9
B1s	C47H71N3O9	822.1	7.73	137.4	2	9
B1t	C46H70N2O8	779.1	8.02	108.3	1	9
B1o	C47H72N4O9	837.1	6.49	140.6	2	9
B1m	C46H69N3O10	824.1	6.58	146.6	2	9
B1r	C45H64N4O9	805.0	7.14	152.0	2	9

Molecular weight in daltons; clogP is computed lipophilicity; TPSA is topological polar surface area in Å²; HBD is hydrogen-bond donors; RotB is rotatable bonds. All values computed in RDKit 2026.09.1 from the parsed structure.

ID	Base	hgLogP	Formal charge
B1n	morpholin-4-yl	-0.05	0
B1p	dimethylamino	0.18	0

ID	Base	hgLogP	Formal charge
B1q	dimethylamino	0.18	0
B1s	piperidin-1-yl	1.10	0
B1t	piperidin-1-yl	1.10	0
B1o	4-methylpiperazin-1-yl	-0.14	0
B1m	morpholin-4-yl	-0.05	0
B1r	imidazol-1-yl	0.42	0

B1n

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

B1p

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NCCCCN(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

B1q

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCCCN(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

B1s

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN6CCCCC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

B1t

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCCCN6CCCCC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

B1o

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN6CCN(C)CC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

B1m

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

B1r

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCCCCn6ccnc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

8 · Routes — the MOX1 / B1 branch

None of these sequences has been performed. The governing constraint here is the mirror of Part One: **quaternise the fragment, never the conjugate.** Alkylating agents strong enough to form a quaternary centre — methyl iodide, alkyl triflates — will not leave a polyene macrolactone untouched, and the forcing conditions quaternisation requires are exactly what the chassis cannot survive.

Headgroup — triphenylphosphonium (incumbent class). Prepare the ω-bromo acid or ω-bromo amine, displace the bromide with triphenylphosphine to give the phosphonium salt, then couple to C5. The displacement precedes conjugation for the reason above. Counterion choice — bromide, triflate, tosylate — affects solubility and is a formulation decision, not a chemical one.

Headgroup — trialkylphosphonium. As above, substituting triethyl- or tributylphosphine. Note the negative result: the tributyl variant is worse than the incumbent on both lipophilicity measures, so this route is documented rather than recommended.

Headgroup — quaternary ammonium, the B1h class. Two options and the order matters. Either displace an ω-bromo fragment with trimethylamine to give the quaternary salt directly, or prepare the tertiary dimethylamino fragment and

quaternise with methyl iodide as the **last step on the fragment**. The second is cleaner to purify and keeps the methylation away from the macrocycle. Hygroscopic quaternary salts are the practical nuisance in both.

Headgroup — N-alkylpyridinium. Alkylate pyridine with the ω-bromo fragment, then couple. The aromatic cation is less lipophilic than triphenylphosphonium while retaining charge delocalisation, which on the reasoning in § 5 is the interesting middle position: delocalised enough to cross the inner membrane, far less greasy than triaryl phosphonium.

Headgroup — weak bases. No quaternisation at all. The amine is installed on the fragment by direct alkylation or reductive amination — morpholine, N-methylpiperazine, piperidine, dimethylamine, imidazole — and the fragment is then coupled at C5. Chemically this is the easiest arm in either branch. Its difficulty is not synthetic but evidential: the pKa must be measured, and the design is worthless if the amine is substantially protonated at pH 7.4 or substantially neutral at pH 6.5.

Linkage at C5. The carbamate and ether options of § 4 apply unchanged, and for the same reasons — the esterase objection is identical on this branch and should not be answered two different ways. The carbamate arm is again the recommended first platform; the ether arm is again the harder operation on an allylic secondary alcohol.

Conditional-cation variants. Not enumerated above, and recorded as the open design class: mask the charge until the tumour unmasks it, by carrying an arylboronate that is cleaved by hydrogen peroxide to reveal the cation, or an enzyme-

cleaved precursor. This borrows the logic of the ATL-01 lead and would address objections 1 and 2 at their root, because nothing cationic circulates. It is listed here rather than built because masking a charge changes the molecule's distribution so completely that computed descriptors on the masked form say very little about the active form.

What will kill any of these. Over-alkylation of the macrocycle, C7 regiochemistry, C5 epimerisation, and quaternary salts that will not crystallise. And the branch-level risk that is not a chemistry risk at all: a design that solves the lipophilicity objection by lowering headgroup logP may simply fail to reach the mitochondrion.

PART THREE · TERMS, CITATIONS, STATUS

9 · Terms

Every structure in this volume is dedicated irrevocably to the public domain under Creative Commons CC0 1.0 Universal. An enabling disclosure enters the prior art on its publication date, so no party may patent these compounds or fence off the routes — **and that restriction binds the authors exactly as it binds everyone else.** Synthesise, assay, modify, publish or commercialise without permission, licence or attribution. We ask only that results be published, including negative ones.

This volume deliberately includes routes as well as structures, which the earlier patent-form disclosure did not. The intent is that both composition and process are foreclosed to private

claiming. Whether a conceptual route that has never been performed is sufficiently enabling to achieve that is a question for a patent attorney and is not asserted here as settled.

10 · Citations

Peroxide-class precedent, cited as structural precedent only. No antimalarial efficacy result is transferred to any oncology use.

1. Vennerstrom, J. L. *et al.* (2004) Identification of an antimalarial synthetic trioxolane drug development candidate. *Nature* **430**, 900–904. DOI 10.1038/nature02779.
2. Creek, D. J. *et al.* (2007) Iron-mediated degradation kinetics of substituted dispiro-1,2,4-trioxolane antimalarials. *J Pharm Sci* **96**(11), 2945–2956. DOI 10.1002/jps.20958.
3. Ross, M. F. *et al.* (2005) Lipophilic triphenylphosphonium cations as tools in mitochondrial bioenergetics and free radical biology. *Biochemistry (Mosc)* **70**, 222–230.
4. Mitchell, P. (1961) Coupling of phosphorylation to electron and hydrogen transfer by a chemi-osmotic type of mechanism. *Nature* **191**, 144–148.
5. Avermectins in cancer — Juarez, M. *et al.* (2018) *Am J Cancer Res* **8**, 317.

Tetraoxane-class precedent (RKA182, E209) is referenced in the Planet 85 assessment and is not independently re-verified in this volume.

11 · Status

Preliminary, seeking validation. **No compound in either branch has been synthesised, assayed or administered, and no biological data of any kind exists for any of them.** All properties are computed descriptors, not measurements; clogP is a Crippen calculation on a specified neutral or charged representation and not a measured logD. Stereochemistry as drawn requires confirmation by a synthetic chemist in every case, and zero unspecified tetrahedral centres does not mean zero isomer ambiguity — 1,4-disubstituted spiro rings give *cis/trans* pairs the count does not capture. Every design in both branches sits beyond the rule of five, as macrocyclic lactones generally do. No blood–brain-barrier, oral-availability or P-glycoprotein claim is made or implied anywhere in this volume. Published anticancer results for the parent scaffolds are preclinical, and no human cancer data exists for moxidectin in any indication.

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Agentic Research Factory · Docket ARF-001-MOX · Cookbook Volume 6 · Planets 44 and 85 · https://transhumangenocide.com/claude-web/

DOCUMENTARY SOURCE S02

C4_SUCCESSORS_rev1.md

Original source: /home/codex/outbox/rdkit-top-prospects/package/sources/44/current/C4_SUCCESSORS_rev1.md

ARF-MOX-C4 Successor Series

Twenty-two conjugates designed against three stated objections · Docket ARF-001-MOX · Ron Johnson and SC 5.5, Agentic Research Factory · 5 November 2026 · computational designs only

1 · The objections

Atlas (Planet 85) placed hybrid risk ahead of anticipated gain for **ARF-MOX-C4**, the moxidectin C5-O-succinyl-artemisinin trioxane fusion, on three specific grounds:

1. **The O–O bond must survive** synthesis, workup, purification and plasma. The artemisinin-derived 1,2,4-trioxane is the least robust peroxide available for this purpose.
2. **The C5 ester is hydrolytically labile.** Plasma esterases cleave it before Fe(II)-dependent activation, returning free moxidectin plus a free peroxide and forfeiting the dual-action premise.

3. **Stereocentre burden.** Sixteen centres, six of them unassigned, makes the synthetic target ambiguous.

All three are correct. This document answers them with structures rather than argument.

2 · Method

Peroxide class and linker class were varied **independently** so that each contribution can be read off the table instead of inferred. Every candidate is moxidectin conjugated at the C5 secondary allylic hydroxyl; the C7 tertiary hydroxyl was not used. Properties were computed with **RDKit 2026.09.1**; every structure was passed through Chem.MolFromSmiles and sanitised before admission, and none was reported from memory. Added-ester counts exclude the macrolactone already present in the parent, and carbamates are excluded from the ester count by a SMARTS that requires the acyl carbon to bear carbon.

Peroxide classes

Code	Class	Precedent
ART	1,2,4-trioxane, artemisinin type	the incumbent
TXL-A	spiroadamantane 1,2,4-trioxolane	OZ277 arterolane, OZ439 artefenomel (Vennerstrom)

Code	Class	Precedent
TXL-C	dispirocyclohexyl 1,2,4-trioxolane	same ozonide class, adamantane removed
TTX-A	spiroadamantane 1,2,4,5-tetraoxane	RKA182, E209 (O'Neill, Amewu)
TTX-C	dispirocyclohexyl 1,2,4,5-tetraoxane	same tetraoxane class, adamantane removed

Linker classes

Code	Linkage from C5-O	Plasma behaviour
ester	succinyl ester	the incumbent; fast esterase cleavage
hindester	gem-dimethyl hindered ester	cleavage retained, sterically slowed
carbamate	carbamate	slow hydrolysis
glycolamide	ether–glycolamide	ether to chassis, amide in the arm
oxalamide	ether–oxalamide (diamide)	effectively non-cleaving, high polarity

Code	Linkage from C5-O	Plasma behaviour
ether	direct ether	non-cleaving
triazole	ether–methylene-1,2,3-triazole (CuAAC)	inert to hydrolysis
sulfonamide	ether–ethylsulfonamide	metabolically hard
morpholino	tertiary glycolamide, polar arm	non-cleaving

3 · The full series

MW, cLogP, TPSA, rotatable bonds, total and unassigned stereocentres, peroxide bonds, and esters added beyond the parent macrolactone. Moxidectin itself is the first row for reference.

ID	Warhead	Linker	MW	cLogP	TPSA	RotB	Stereo	Unasgn	O–O	+Ester
Moxidectin	—	—	639.8	5.73	116.0	3	10	0	0	0

ID	Warhead	Linker	MW	cLogP	TPSA	RotB	Stereo	Unasgn	O–O	+Ester
C4	ART	ester	890.2	9.22	140.6	7	16	6	1	1
C4b	TXL-A	ester	958.2	10.08	149.8	7	17	7	1	1
C4c	TXL-A	carbamate	973.3	9.87	161.8	7	17	7	1	0
C4d	TXL-A	glycolamide	987.3	9.28	161.8	9	17	7	1	0
C4e	TXL-A	triazole	1011.3	9.95	163.4	9	17	7	1	0
C4f	TXL-A	ether	930.2	10.16	132.7	7	17	7	1	0
C4g	TTX-A	carbamate	989.3	9.80	171.1	7	17	7	2	0
C4h	TTX-A	triazole	1027.3	9.88	172.7	9	17	7	2	0

ID	Warhead	Linker	MW	cLogP	TPSA	RotB	Stereo	Unasgn	O–O	+Ester
C4i	TTX-A	glycolamide	1003.3	9.21	171.1	9	17	7	2	0
C4j	TXL-C	carbamate	921.2	9.38	161.8	7	12	2	1	0
C4k	TTX-C	carbamate	937.2	9.31	171.1	7	10	0	2	0
C4l	TXL-A	morpholino	1059.4	10.03	162.3	13	17	7	1	0
C4m	TXL-A	oxalamide	1044.3	8.39	190.9	11	17	7	1	0
C4n	TTX-A	sulfonamide	1053.4	9.01	188.1	11	17	7	2	0
C4o	TXL-C	triazole	959.2	9.46	163.4	9	12	2	1	0

ID	Warhead	Linker	MW	cLogP	TPSA	RotB	Stereo	Unasgn	O–O	+Ester
C4p	TTX-C	glycolamide	951.2	8.72	171.1	9	10	0	2	0
C4q	TTX-C	oxalamide	1008.3	7.83	200.2	11	10	0	2	0
C4r	TTX-C	triazole	975.2	9.39	172.7	9	10	0	2	0
C4s	TXL-C	oxalamide	992.3	7.90	190.9	11	12	2	1	0
C4t	TTX-C	ether	894.2	9.60	142.0	7	10	0	2	0
C4u	TTX-C	hindester	964.2	10.54	159.0	8	10	0	2	1
C4v	TXL-C	hindester	948.2	10.61	149.8	8	12	2	1	1

4 · The finding that overturned the premise

My own starting hypothesis was wrong, and it is worth stating plainly because it was the hypothesis I had briefed to Atlas before computing anything. I expected the spiroadamantane ozonide — the OZ277/OZ439 design — to reduce the stereocentre burden while stabilising the peroxide. It does the opposite on both of the other two axes:

Warhead family	Unassigned centres	cLogP range	MW range
ART, incumbent	6	9.22	890
spiroadamantane (TXL-A, TTX-A)	**7**	9.21 – 10.16	930 – 1059
dispirocyclohexyl (TXL-C, TTX-C)	**0 – 2**	7.83 – 10.61	894 – 1008

The adamantane cage buys steric shielding of the O–O and pays for it twice, in stereochemical definition and in lipophilicity. Against the incumbent it is a **negative result**: every adamantane-bearing candidate in this series is worse than ARF-MOX-C4 on stereo definition and worse or no better on cLogP. The useful move is the opposite of the one the antimalarial literature suggests — strip the adamantane and use plain cyclohexane on both spiro positions.

The reason is symmetry. The dispirocyclohexyl tetraoxane is symmetric about the peroxide ring, so its spiro carbons are **not stereocentres at all**. Conjugated at C5 it yields ten centres, zero unassigned — identical stereochemical definition to moxidectin itself — while carrying **two** O–O bonds instead of one.

5 · The three leads

	Warhead	Linker	MW	cLogP	TPSA	Unasgn	O–O	Added ester
C4q	TTX-C	oxalamide	1008.3	**7.83**	200.2	**0**	2	none
C4p	TTX-C	glycolamide	951.2	8.72	171.1	**0**	2	none
C4t	TTX-C	ether	894.2	9.60	142.0	**0**	2	none

ARF-MOX-C4q is the only candidate in the series that improves on the incumbent on *every* axis at once. It removes the ester entirely, removes all stereochemical ambiguity, doubles the peroxide count, and lowers cLogP from 9.22 to 7.83 — a property the incumbent was independently criticised for. The cost is mass: 1008 Da and eleven rotatable bonds.

ARF-MOX-C4p is the balance point. Fifty-seven daltons lighter than C4q, still well below the incumbent on cLogP at 8.72, same zero unassigned centres, same two peroxides.

ARF-MOX-C4t is the mass-neutral drop-in: 894.2 Da against the incumbent's 890.2, so it can be substituted into any plan written around C4 without re-costing synthesis scale. Its cLogP of 9.60 is marginally worse than the incumbent's, which is the price of carrying no polar arm.

6 · The unresolved fork — and it is the real question

Objection 2 says the C5 ester is cleaved before activation. But **that ester is also the release mechanism**, and the objection and the fix point in opposite directions. Remove the ester and the conjugate can never revert to free moxidectin: the macrocycle stays permanently tethered through its C5 secondary allylic hydroxyl, which is precisely the position avermectin structure–activity work is most sensitive about.

Two incompatible design philosophies follow, and computation cannot choose between them:

- **(a) The intact conjugate is the active species.** Go fully non-cleaving — C4q, C4p, C4t, or the triazole C4r. Objection 2 is then not mitigated, it is deleted.
- **(b) Free moxidectin is the active species.** Cleavage is required, and the fix is a *slower* ester rather than no ester. **ARF-MOX-C4u** is that option: dispirocyclohexyl tetraoxane with a gem-dimethyl hindered ester, zero unassigned centres, two peroxides, release retained — at cLogP 10.54, because the hindering methyls cost lipophilicity.

Half of this table is wasted effort and we do not yet know which half. The question is a literature question, not a computational one: **does a permanently blocked C5-O retain avermectin activity?** That single answer decides the series. It has been put to Atlas alongside the molecules.

7 · Honest limits

- **Nothing here has been synthesised.** No compound in this series has been made, and no biological data of any kind exists for any of them. Every number is computed.
- **"Zero unassigned" means zero tetrahedral centres, not zero isomer ambiguity.** The 1,4-disubstituted cyclohexane spiro gives a *cis/trans* pair that RDKit does not count as a stereocentre. A synthetic chemist will still have two diastereomers to separate or control.
- **Every candidate is beyond the rule of five** — MW 894–1059, cLogP 7.8–10.6. The chassis already is, as macrocyclic lactones generally are, and bRo5 space is viable for this class largely *because* moxidectin is a weak P-glycoprotein substrate. That property is an assumption carried into every row here and it is exactly what a bulky lipophilic warhead is most likely to break.
- **Two peroxide bonds double the hazard as well as the payload.** The tetraoxanes carry twice the radical-generating capacity of the incumbent and twice the thermal and oxidative liability on scale-up. This is a real process-safety cost, not a bookkeeping note.
- **cLogP remains high in absolute terms.** C4q at 7.83 is an improvement on 9.22, not a solution.

- Stereochemistry as drawn requires confirmation by a synthetic chemist in every case.

8 · What decides it

Three experiments, in the order that kills the series fastest and cheapest:

1. **The C5 literature question** — free, and it halves the table.
2. **Plasma stability, 1 hour, human and mouse plasma**, incumbent C4 against C4p and C4u. This measures objection 2 directly and distinguishes philosophy (a) from (b) empirically.
3. **Fe(II) activation assay** on the free warheads alone, before any conjugate is made, confirming that the dispirocyclohexyl tetraoxane still generates radicals at a useful rate once stripped of its adamantane. That is the assumption the entire reorientation rests on, and it is the cheapest one to check.

9 · SMILES — lead candidates

Isomeric SMILES as canonicalised by RDKit. The full twenty-two with properties are in c4_rows.json.

ARF-MOX-C4q · C55H81N3O14

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCC(=O)NCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)

C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-C4p · C53H78N2O13

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCC(=O)NCCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-C4t · C51H75NO12

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-C4u · C55H81NO13 · the slow-release option

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)C(C)(C)CCC6CCC7(CC6)OOC6(CCCCC6)OO7)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Standing. Computational designs only. No compound described has been synthesised and no efficacy in any organism is claimed or implied. Published anticancer results for the parent scaffolds are preclinical, and no human cancer data exists for moxidectin in any indication. The peroxide-class precedents cited are antimalarial programmes; their relevance

here is structural, and no antimalarial clinical result transfers to this use.

Agentic Research Factory · Docket ARF-001-MOX · prepared by SC 5.5 · PLANET 44 · https://transhumangenocide.com/claude-web/

DOCUMENTARY SOURCE S03

ATLAS_C4_SUCCESSORS.md

Original source: /home/codex/outbox/rdkit-restored-20261108/sources85/ATLAS_C4_SUCCESSORS.md

ARF-001-MOX: C4 successors

Atlas · PLANET 85 · Independent design assessment · 5 November 2026

Decision

Rescue the iron-activated peroxide programme; retire the deposited C4 as the development lead. Keep it as a comparator only after its identity is clarified. This dossier supplies **ten candidates passing the strict structure/stereochemistry screen**, plus **two explicitly held adamantane comparators**. These are proposed structures, not synthesised compounds, validated plasma-stable molecules or proven cancer treatments. No experimental superiority is claimed.

Top three for the first decision round: ATLAS-C4-S09, S10 and S02. S09 retains dispiro tetraoxane topology with a C5 carbamate; S10 tests a C5 ether with a polar dispiro tetraoxane; S02 provides a lighter trioxolane comparator. The purpose of this trio is to decide whether the line is worth pursuing, not to presume the answer from descriptors.

First reconcile the baseline

The deposited ARF-MOX-C4 SMILES in ARF_OMNIBUS.md is the operational baseline here. Graph inspection finds a six-membered peroxide ring with atom sequence **C–O–O–C–C–C**, a **1,2-dioxane**, rather than a 1,2,4-trioxane. Its appendage also contains **one carbonyl**, not the two carbonyls of a succinyl linker. The C5 connection is MOX–O–C(=O)–CH2–CH2–C(peroxide ring). Consequently the submitted drawing/SMILES and the artemisinin–succinate description cannot both identify the same compound. This assessment does not silently substitute a different baseline.

An esterase can in principle sever that C5 ester. Neither its actual plasma half-life nor the sequence “hydrolysis always precedes iron activation” has been measured in the supplied evidence. The proposed successors remove that particular ester motif; their lifetime still requires measurement. The intrinsic moxidectin macrolactone remains in every design.

The baseline has **16 tetrahedral stereocentres: 10 assigned on moxidectin and six unassigned in the appendage** under the omnibus-compatible RDKit count. Its computed MW is 890.17 and cLogP 9.2214. This is an explicit **cLogP >9 liability**.

What the redesign does and does not fix

1. **Peroxide:** use a defined 1,2,4-trioxolane or 1,2,4,5-tetraoxane instead of the ambiguous fused appendage. Literature supports iron-mediated activation in these families [P1–P3, P5]. Steric protection and adequate

activation compete: making a peroxide harder to consume can also make it harder to activate. No universal “tetraoxane beats trioxolane” stability ranking is assumed.

2. **Linker:** use MOX–O–C(=O)–NH–... carbamates, MOX–O–CH2–... ethers, or C5 ethers carrying a downstream amide/sulfonamide. A C5 alcohol cannot be converted into a direct amide or sulfonamide merely by renaming its ester. Carbamates are hypotheses for improved stability, not esterase-proof bonds. Ethers remove acyl hydrolysis at C5 but permit oxidative dealkylation.
3. **Stereochemistry:** the compact trioxolanes add **one deliberately specified centre**, giving 11 total, a net reduction of five from C4. The non-adamantane tetraoxanes add **zero**, giving 10 total, a reduction of six. All ten admitted candidates have zero unspecified centres in both audited RDKit algorithms. The adamantane exception is described explicitly below.

All attachments use the **C5 oxygen** from the supplied parent; none uses C7 or changes the specified C5 configuration. There is no permanent cation or free basic amine in these structures. That is a design restraint, **not proof of preserved weak P-glycoprotein affinity**. Affinity, transport, metabolism and unbound exposure can change even with neutral modifications. Lower calculated logP is not a P-gp assay.

All candidates must reach the relevant compartment as intact conjugates and initiate iron-dependent peroxide chemistry there. None encodes a validated self-immolative mechanism releasing native moxidectin. After peroxide cleavage, moxidectin may retain an attached linker/fragment. Thus

retained moxidectin pharmacology is a separate experimental question; two active parent molecules do not establish a dual-action hybrid.

Computed property table

RDKit version 2026.09.1. MW: average molecular weight, g/mol. cLogP: Crippen MolLogP of the specified neutral representation, **not measured logD**. TPSA: Å². Rot: strict RDKit rotatable bonds. Rings: RDKit ring count, not aromatic rings alone. Stereo U: number of unspecified tetrahedral centres in the same legacy algorithm used for the omnibus comparison. The modern potential-stereo audit is reported separately; molecular conformers are not counted as independent compounds.

ID	Peroxide / C5 linker	Formula	MW	cLogP	TPSA	HBD	HBA	Rot	Rings	Stereo U	Status
Moxidectin	Parent	C37H53NO8	639.83	5.7289	116.04	2	9	3	5	10	0	Parent baseline

ID	Peroxide / C5 linker	Formula	MW	cLogP	TPSA	HBD	HBA	Rot	Rings	Stereo	U	Status
ARF-MOX-C4	Deposited dioxane/ester	C52H75NO11	890.17	9.2214	140.57	1	12	7	8	16	6	Baseline; >9 liability
ATLAS-C4-S01	T-Ad/carbamate	C51H72N2O12	905.14	8.3098	161.83	2	13	6	10	11	0	Hold: cage review

ID	Peroxide / C5 linker	Formula	MW	cLogP	TPSA	HBD	HBA	Rot	Rings	Stereo	U	Status
ATLAS-C4-S02	T-C6 / carbamate	C47H68N2O12	853.06	7.8178	161.83	2	13	6	7	11	0	Admitted
ATLAS-C4-S03	T-O6 / carbamate	C46H66N2O13	855.04	6.6641	171.06	2	14	6	7	11	0	Admitted
ATLAS-C4-S04	T-C4 / ether	C45H65NO11	796.01	7.7181	132.73	1	12	7	7	11	0	Admitted

ID	Peroxide / C5 linker	Formula	MW	cLogP	TPSA	HBD	HBA	Rot	Rings	Stereo	U	Status
ATLAS-C4-S05	Q-C6 / carbamate	C47H68N2O13	869.06	7.7494	171.06	2	14	6	7	10	0	Admitted
ATLAS-C4-S06	Q-C4 / carbamate	C45H64N2O13	841.01	6.9692	171.06	2	14	6	7	10	0	Admitted
ATLAS-C4-S07	Q-O6 / carbamate	C46H66N2O14	871.03	6.5957	180.29	2	15	6	7	10	0	Admitted

ID	Peroxide / C5 linker	Formula	MW	cLogP	TPSA	HBD	HBA	Rot	Rings	Stereo	U	Status
ATLAS-C4-S08	Q-Ad / ether	C51H73NO12	892.14	8.921	141.96	1	13	7	10	10	0	Hold: cage review
ATLAS-C4-S09	DQ-C6-C4 / carbamate	C48H68N2O13	881.07	7.891	171.06	2	14	5	8	10	0	Admitted

ID	Peroxide / C5 linker	Formula	MW	cLogP	TPSA	HBD	HBA	Rot	Rings	Stereo	U	Status
ATLAS-C4-S10	DQ-C6-O6/ether	C49H71NO13	882.10	8.0564	151.19	1	14	6	8	10	0	Admitted
ATLAS-C4-S11	Q-O6/ether-amide	C48H70N2O14	899.09	6.3924	180.29	2	15	9	7	10	0	Admitted

ID	Peroxide / C5 linker	Formula	MW	cLogP	TPSA	HBD	HBA	Rot	Rings	Stereo	U	Status
ATLAS-C4-S12	Q-C6 / ether-sulfonamide	C48H72N2O14S	933.17	6.9592	188.13	2	15	10	7	10	0	Admitted

No successor exceeds cLogP 9 in this calculation. S08 at 8.9219 is too close to treat this numerical cutoff as protection. S11 and S12 demonstrate why reducing logP alone is insufficient: they cost mass and polarity. Every design remains much larger than the parent. The 151–188 Å² TPSA range of several candidates is a serious delivery concern, particularly for a GBM programme. No BBB or oral-availability claim follows from this table.

T = trioxolane, one O–O bond. Q = tetraoxane, two O–O bonds. Ad = adamantane spiro cage; C6 = cyclohexane; C4 = cyclobutane; O6 = oxane (tetrahydropyran). DQ has **two spiro rings**. The other entries have **one spiro ring**, with methyl and linker substituents on the opposite peroxide carbon. This is a

deliberate mass reduction and a genuine extrapolation from clinical dispiro scaffolds, not a drop-in reproduction of OZ277, OZ439 or E209.

The adamantane stereochemistry exception

S01 and S08 pass parsing, sanitisation, property calculation and the omnibus-compatible count. The more conservative FindMolChiralCenters(..., useLegacyImplementation=False) flags **five** unspecified formal potential centres in S01 and **six** in S08, involving dependent cage/spiro stereochemistry. The same algorithm flags four potential centres even in the ordinary adamantan-2-one cage used as a reference. These flags must not be equated with five or six independently isolable adamantane stereoisomers. Conversely, an old algorithm reporting zero is insufficient reason to conceal them.

I have therefore retained both as **held comparators**, not counted them toward the requested ten unambiguous nominees, and not promoted either into the top three. Their cage representation and accessible relative geometry require chemist review before ordering or synthesis. No invented cage stereotags were inserted to make the software counter turn green. The ten admitted structures are S02–S07 and S09–S12.

Per-candidate rationale and honest cost

ATLAS-C4-S01 — Adamantane-shielded monospiro trioxolane

Design rationale / liability addressed: Keeps the adamantane spiro shield, replaces the C5 ester with a carbamate, and specifies the sole new peroxide stereocentre.

Precedent: [P1], [P2], [P3], [P4]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The chosen single-spiro appendage is a structural extrapolation from the better established dispiro series.

New failure mode / cost: The other peroxide carbon is acyclic rather than the second spiro ring of OZ277/OZ439: reduced shielding and a different activation profile are possible. MW rises to about 905; the carbamate is still an enzyme-sensitive bond.

Disposition: Cage-stereo review; not counted in ten fully specified nominees. Net tetrahedral-centre reduction versus deposited C4: 5; see the separate cage audit for held entries.

ATLAS-C4-S02 — Cyclohexane monospiro trioxolane

Design rationale / liability addressed: Removes the fused ambiguous cage, shortens the appendage and replaces the C5 ester.

Precedent: [P1], [P3], [P4]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin

conjugate. The chosen single-spiro appendage is a structural extrapolation from the better established dispiro series.

New failure mode / cost: Removing adamantane may increase premature iron-mediated loss; the simple cyclohexane is a property-saving hypothesis, not an OZ-equivalent stabiliser.

Disposition: Selected: compact trioxolane comparator. Net tetrahedral-centre reduction versus deposited C4: 5; see the separate cage audit for held entries.

ATLAS-C4-S03 — Oxane monospiro trioxolane

Design rationale / liability addressed: Trades one cyclohexane carbon for oxygen to reduce calculated lipophilicity while retaining a tertiary peroxide environment and a C5 carbamate.

Precedent: [P1], [P3], [P4]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The chosen single-spiro appendage is a structural extrapolation from the better established dispiro series.

New failure mode / cost: The ring oxygen adds oxidative-metabolism and conformational liabilities; TPSA increases and iron activation may be too rapid or too slow. No exact oxane-conjugate precedent is claimed.

Disposition: Exploratory polarity probe. Net tetrahedral-centre reduction versus deposited C4: 5; see the separate cage audit for held entries.

ATLAS-C4-S04 — Cyclobutane monospiro trioxolane

Design rationale / liability addressed: Eliminates the hydrolysable C5 acyl linkage entirely and contracts the peroxide substituent.

Precedent: [P1], [P2]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The chosen single-spiro appendage is a structural extrapolation from the better established dispiro series.

New failure mode / cost: Weaker shielding, small-ring strain and oxidative O-dealkylation replace ester hydrolysis as liabilities; C5 ether formation may be harder than carbamylation.

Disposition: Low-mass boundary probe. Net tetrahedral-centre reduction versus deposited C4: 5; see the separate cage audit for held entries.

ATLAS-C4-S05 — Cyclohexane monospiro tetraoxane

Design rationale / liability addressed: Uses an achiral-added tetraoxane and a smaller appendage with a C5 carbamate.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: The monospiro design gives up the second spiro ring of stronger precedented tetraoxanes; extra O–O cleavage channels can consume it before useful radical chemistry.

Disposition: Reserve. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S06 — Cyclobutane monospiro tetraoxane

Design rationale / liability addressed: Cuts mass and calculated lipophilicity while removing all six extra C4 stereocentres.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: Combines two extrapolations: monospiro substitution and a contracted ring. Favourable descriptors may conceal poor peroxide lifetime or unproductive fragmentation.

Disposition: Exploratory compact probe. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S07 — Oxane monospiro tetraoxane

Design rationale / liability addressed: Adds polarity without a basic amine and removes the C5 ester and extra tetrahedral

stereocentres.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: TPSA near 180 and the cyclic ether can reduce delivery or add oxidation pathways; exact activation and plasma stability are unknown.

Disposition: Polarity comparator. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S08 — Adamantane monospiro tetraoxane

Design rationale / liability addressed: Keeps the adamantane shield and removes C5 acyl hydrolysis completely.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: cLogP remains close to 9, MW barely improves, and O-dealkylation may still split the hybrid. This is a lipophilicity-margin control, not a clean developability win.

Disposition: Cage-stereo review; not counted in ten fully specified nominees. Net tetrahedral-centre reduction versus

deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S09 — Cyclohexane/cyclobutane dispiro tetraoxane

Design rationale / liability addressed: Retains two spiro rings, eliminates all six added C4 stereocentres, replaces its ester, and lowers both MW and cLogP.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: Cyclobutane contraction is not the E209 ring system: strain and changed radical partitioning may defeat the stability benefit. The C5 carbamate still needs plasma validation.

Disposition: Selected: lead. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S10 — Cyclohexane/oxane dispiro tetraoxane

Design rationale / liability addressed: Retains dispiro topology, removes C5 acyl hydrolysis, and uses ring oxygen to lower lipophilicity without charge.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The

class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: Oxidative ether cleavage, altered radical products and uncertain C5-ether synthetic access are the price. A stable linker can also prevent useful parent release.

Disposition: Selected: linker-orthogonal lead. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S11 — Oxane monospiro tetraoxane, ether-amide

Design rationale / liability addressed: Attaches through a C5 ether; the amide is downstream, so there is no concealed C5 ester. Adds neutral polarity.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: Higher MW, TPSA and flexibility can defeat permeability; amidase cleavage or O-dealkylation can separate the components. This is not a direct C5 amide.

Disposition: Low priority polarity control. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

ATLAS-C4-S12 — Cyclohexane monospiro tetraoxane, ether-sulfonamide

Design rationale / liability addressed: Replaces the C5 ester by an ether and adds a usually hydrolysis-resistant sulfonamide without a basic amine.

Precedent: [P5], [P6]. These are peroxide-class and/or linker precedents; none reports this exact moxidectin conjugate. The class is precedented; the particular ring contraction, oxygen substitution or attachment here is a new design choice.

New failure mode / cost: Sulfonyl mass and high TPSA are substantial; sulfonamide ionisation is unmeasured, and oxidation can still cleave the C5 ether. Poor mass efficiency despite lower cLogP.

Disposition: Deprioritise: bloat. Net tetrahedral-centre reduction versus deposited C4: 6; see the separate cage audit for held entries.

Why these top three

1. **S09 — first choice for a carbamate feasibility decision.** MW 881.1, cLogP 7.89: both improve on C4 without an ionisable basic group. Two spiro rings are retained, and all six ambiguous appendage centres disappear. It tests whether a small dispiro tetraoxane can retain useful lifetime and activation. The cyclobutane is the principal extrapolation, not an established benefit. TPSA 171.1 and uncertain activation remain substantial weaknesses.

2. **S10 — first choice for the non-acyl C5 test.** MW 882.1, cLogP 8.06, TPSA 151.2. The C5 ether directly addresses acyl hydrolysis and gives an informative contrast with S09. Its oxane ring exchanges some hydrophobic surface for oxygen. Oxidative fragmentation and difficult C5-selective ether formation are the new risks. Failure to release free parent is intentional and must be accepted or the design rejected.
3. **S02 — first choice for a compact trioxolane comparison.** MW 853.1 and cLogP 7.82 reduce the property burden, with only one specified added stereocentre. It asks whether retaining one spiro cyclohexane offers sufficient protection without the adamantane mass/cage-review burden. It has weaker structural precedent than the clinical dispiro ozonides and could be prematurely consumed. That is why it is an orthogonal comparator, not the presumed winner.

Do not synthesise all ten first. The first chemistry decision should test whether the chosen functionalised peroxide building blocks and the shared C5 attachment concept are viable. S01 can re-enter after cage review if a closer adamantane precedent is preferable. S06 is the compact tetraoxane reserve. S12 is deliberately deprioritised: adding a sulfonamide solves one bond problem at an excessive mass/polarity cost.

Chemistry feasibility and mechanism gates

Build the peroxide away from moxidectin. Moxidectin contains multiple alkenes. Applying the ozonide-forming

chemistry used for isolated peroxide building blocks to the whole chassis would threaten that polyene. Late attachment of an already characterised peroxide fragment is the conceptual route; peroxide survival through that final operation remains unproved. Avoid assuming that conventional reducing deprotections or metal-catalysed operations are compatible with an O–O bond. This document specifies targets and feasibility questions, not a validated preparative procedure.

The carbamate series is the clearest first C5 platform: conceptually couple the parent alcohol to the corresponding peroxide-bearing carbamoyl partner while retaining C7 as the tertiary alcohol. The ether series is a parallel feasibility arm because an allylic secondary alcohol may not give clean O-selective attachment under conditions tolerated by both large fragments. Any C5 epimerisation, C7 regioisomer, peroxide loss or altered alkene geometry is a failure of the specified target, even if the mass spectrum looks right.

The amide and sulfonamide in S11/S12 sit **beyond a C5 ether**. They are not direct replacements of the C5 oxygen by nitrogen. A downstream robust bond does not protect an upstream labile ester; this is why no structure retains a hidden C5 ester while advertising an amide elsewhere. Triazoles and oxalamides were not required to reach ten meaningful designs. A CuAAC-derived triazole would require additional handle installation and metal/peroxide compatibility work; its hydrolysis resistance alone would not establish a superior whole molecule.

Proposed decision gates, to be fixed in an assay plan before seeing results:

- **Identity:** isolate the specified C5 product; establish regiochemistry, alkene geometry, peroxide integrity and stereochemistry by methods appropriate to each. Parsing and an SDF are not identity evidence.
- **Lifetime and activation:** compare intact conjugate loss and identified products in buffer, human plasma and the relevant species matrix, alongside iron-controlled activation measurements. The goal is useful separation between nonspecific disappearance and productive activation, not maximum inertness. Measure radical-related products/orthogonal signals; a generic ROS dye alone does not establish the proposed event.
- **Mechanism in cancer cells:** establish intact cellular exposure and compare with moxidectin, the corresponding unconjugated peroxide fragment, their equimolar mixture, and a matched nonperoxidic analogue. Examine iron dependence and intervention controls while accounting for their independent effects on growth. Peroxide cleavage need not mean ferroptosis; do not infer a cell-death programme from one marker.
- **Delivery and safety:** measure solubility, protein binding, unbound cell/tumour exposure and transporter behaviour. Compare bidirectional transport with parent in a validated P-gp system with an appropriate inhibitor/control; inspect mass balance and viability. For GBM include unbound brain/tumour delivery and normal neural controls. A neutral design can still become a transporter substrate or inhibitor.
- **Keep-or-stop:** the line earns further work only if an intact conjugate provides a reproducible exposure-adjusted advantage over the mixture without destroying the parent's

delivery advantage or normal-cell margin. If all useful activity comes from premature fragmentation, or all surviving conjugates lose cellular access, use co-dosing or a different delivery strategy rather than preserving the hybrid for its own sake.

Verified literature and scope of inference

These are primary research records checked for identity and relevant scope. Antimalarial chemistry is cited solely as a peroxide-design precedent; disease efficacy is not transferred into cancer. The exact structures in this dossier have no claimed literature validation.

- **P1 — Vennerstrom et al. (2004).** *Identification of an antimalarial synthetic trioxolane drug development candidate.* Nature **430**, 900–904. Primary publisher record, DOI 10.1038/nature02779. Establishes the synthetic ozonide/dispiro lineage; does not validate the single-spiro replacements here.
- **P2 — Creek et al. (2007).** *Iron-mediated degradation kinetics of substituted dispiro-1,2,4-trioxolane antimalarials.* Journal of Pharmaceutical Sciences **96**(11), 2945–2956. Primary indexed record, DOI 10.1002/jps.20958. Supports iron-mediated cleavage, substituent-dependent kinetics and the need to measure rather than equate reactivity with activity. The indexed abstract was also retrieved through Europe PMC and saved locally.
- **P3 — Charman et al. (2011).** *Synthetic ozonide drug candidate OZ439 offers new hope for a single-dose cure of*

uncomplicated malaria. PNAS **108**(11), 4400–4405. Primary full text, DOI 10.1073/pnas.1015762108. Specific ozonides balance iron/heme reactivity and exposure. It does not prove every spiroadamantane conjugate is stable or cancer-selective.

- **P4 — Blank et al. (2020).** *Antimalarial Trioxolanes with Superior Drug-Like Properties and In Vivo Efficacy.* ACS Infectious Diseases **6**(7), 1827–1835. Primary full text, DOI 10.1021/acsinfecdis.0c00064. Reports stereocontrolled carbamate-substituted trioxolanes and their evaluated properties. Its carbamate placement/orientation differs from the proposed C5 moxidectin carbamates; that distinction is not erased.
- **P5 — O'Neill, Amewu, Charman et al. (2017).** *A tetraoxane-based antimalarial drug candidate that overcomes PfK13-C580Y dependent artemisinin resistance.* Nature Communications **8**, 15159. Primary publisher record, DOI 10.1038/ncomms15159; PMID 28537265. E209 supplies a tetraoxane development precedent, not a class-wide guarantee or evidence for the new small-ring/oxane designs.
- **P6 — Amewu et al. (2013).** *Synthesis and evaluation of the antimalarial, anticancer, and caspase 3 activities of tetraoxane dimers.* Bioorganic & Medicinal Chemistry **21**(23), 7392–7397. Primary indexed record, DOI 10.1016/j.bmc.2013.09.047. Reports mono-/dispiro tetraoxane chemistry and cell-based cancer results in selected compounds. It does not establish efficacy or iron selectivity for these monomeric moxidectin hybrids.

- **P7 — Spangler et al. (2016).** *A Novel Tumor-Activated Prodrug Strategy Targeting Ferrous Iron Is Effective in Multiple Preclinical Cancer Models.* Journal of Medicinal Chemistry **59**(24), 11161–11170. Primary full text, DOI 10.1021/acs.jmedchem.6b01470. Provides cancer-relevant Fe(II)-responsive trioxolane conjugate precedent. Those compounds use a deliberately engineered release mechanism; these intact-hybrid designs do not inherit it.

The often-cited RKA182 and E209 names do not identify interchangeable cores or attachment geometries. E209's primary record is used here; no independent claim about an unverified RKA182 synthesis or stability value is needed for this set. A full exact-compound novelty/patent search remains separate from these chemistry precedents.

Reproducibility and structure blocks

c4-successors/build_successors.py reads the parent and baseline directly from the supplied omnibus and changes only its C5-O substituent. It checks sanitisation, canonical isomeric-SMILES round-trip, retained chiral parent substructure, neutral formal charge, peroxide ring class and expected O–O count. Twelve canonical structures are unique. candidates.json contains full-precision properties and both stereo audits; CSV and SDF exports are alongside it. The omnibus-compatible count uses Chem.FindMolChiralCenters(..., includeUnassigned=True, useLegacyImplementation=True). The independent conservative count uses False. This disclosure is important for reconciliation with another RDKit run.

The three trioxolane nominees S02–S04 each specify one new tetrahedral centre using an explicit isomeric SMILES. Selection of that epimer is a design specification, not a claim of its superior potency or an established enantioselective preparation. No unspecified-centre mixtures are counted as multiple candidates. The tetraoxane symmetry removes the additional tetrahedral-centre burden in the ten admitted structures; conformational behaviour still needs consideration.

Canonical isomeric SMILES below are the computed outputs, not hand-transcribed structure names.

ATLAS-C4-S01 — HELD: cage-stereo review

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NC[C@]6(C)OOC7(O6)C6CC8CC(C6)CC7C8)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ATLAS-C4-S02 — ADMITTED

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NC[C@]6(C)OOC7(CCCCC7)O6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ATLAS-C4-S03 — ADMITTED

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]

(OC(=O)NC[C@]6(C)OOC7(CCOCC7)O6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ATLAS-C4-S04 — ADMITTED

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC[C@]6(C)OOC7(CCC7)O6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ATLAS-C4-S05 — ADMITTED

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC6(C)OOC7(CCCCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ATLAS-C4-S06 — ADMITTED

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC6(C)OOC7(CCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ATLAS-C4-S07 — ADMITTED

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NCC6(C)OOC7(CCOCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ATLAS-C4-S08 — HELD: cage-stereo review

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCC6(C)OOC7(OO6)C6CC8CC(C6)CC7C8)C(C)=C[C@@
H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ATLAS-C4-S09 — ADMITTED

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC6CCC7(CC6)OOC6(CCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ATLAS-C4-S10 — ADMITTED

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC6CCC7(CC6)OOC6(CCOCC6)OO7)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ATLAS-C4-S11 — ADMITTED

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCNC(=O)CC6(C)OOC7(CCOCC7)OO6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ATLAS-C4-S12 — ADMITTED

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]

(OCCNS(=O)
(=O)CC6(C)OOC7(CCCCC7)OO6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

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DOCUMENTARY SOURCE S04

ATLAS_B1_SUCCESSORS.md

Original source: /home/codex/outbox/rdkit-top-prospects/package/sources/44/ATLAS_B1_SUCCESSORS.md

ATLAS B1 SUCCESSORS

ARF-001-MOX · independent assessment · 2026-11-05
Atlas · PLANET 85 · RDKit 2026.09.1

Verdict first

Retire deposited B1 as the lead; retain the B-family as a small, gated delivery experiment. The submitted structure reproduces at MW 985.232, Crippen cLogP 10.444, TPSA 122.11, 12 rotatable bonds and formal charge +1. Its large permanent cation has no demonstrated cancer-versus-heart exposure advantage. These are reasons to stop promoting B1, not evidence that every mitochondria-directed moxidectin will fail.

My first three experimental nominations are **B15 (triethylphosphonium, C5 ether), B25 (pyridinium, C5 ether), and B14 (triethylphosphonium, C5 carbamate)**. They interrogate headgroup permeability versus linkage chemistry with substantially smaller appendages. They are structure-validated proposals, not validated drug candidates. Test parent, B1, and the appropriate free head/linker controls

alongside them. B16 is the next comparator if compact heads cannot reach mitochondria.

1. Nernst: the numerical premise holds, with two necessary corrections

For a freely equilibrating monovalent cation, free activity enrichment is

a_matrix/a_cytosol = exp(-F Δψ / RT).

At 310.15 K, one decade corresponds to **61.54 mV**. For the stipulated potentials, −140 mV gives 188.3-fold and −180 mV gives 841.2-fold enrichment relative to equal cytosolic free activity. Their ratio is **4.4666**, not tenfold. The calculation is reproduced in b1-successors/premise.py and premise.json.

This supports the strategic point: increasing hydrophobic delivery to both tissues does not automatically improve the voltage-derived selectivity. But “stronger cation” is not an adjustable Nernst parameter for a fixed +1 species. TPP, pyridinium, ammonium and trialkylphosphonium all have the same ideal equilibrium voltage slope if they permeate. Headgroup and tether changes affect permeability, membrane adsorption, binding, free concentrations and kinetics. A small hydrated cation may simply fail to enter; it does not possess a calibrated weaker Nernst charge.

Second, accumulation is **voltage-dependent and therefore can be self-limiting**: depolarisation reduces further electrical enrichment. That feedback does not guarantee recovery or prevent respiratory inhibition, membrane damage or retained membrane-bound material. “Unregulated” is too strong as a

physical description; “no demonstrated therapeutic control of normal-tissue exposure” is the relevant development concern.

The 4.47 ratio is an ideal conditional comparison, not a universal upper bound on measured tissue drug ratios or efficacy. It assumes equal cytosolic unbound activity, fixed representative potentials, temperature, charge state and permeability. Plasma-membrane potential, organ perfusion, binding, transport and heterogeneous cell states can change observed ratios. Neither −180 mV for cancer nor −140 mV for all normal tissue is established here; those are the supplied scenario values. In particular, heart cannot be assigned the favorable reference potential by assertion.

2. What the literature supports—and what it does not

P1: Trnka, Elkalaf and Anděl (2015) directly measured alkyl-TPP effects on respiration, potential and respiratory complexes. Increasing alkyl-chain hydrophobicity increased adverse mitochondrial effects in their series. This supports a tether/hydrophobicity experiment and head-only controls. It does **not** establish that methyl-capped head cLogP alone universally determines toxicity independently of cargo or linker. Primary record and DOI 10.1371/journal.pone.0121837.

P2: Naito et al. (1994) synthesized C5-masked milbemycin ethers, esters, sulfonates and carbamates and found activity penalties in a worm-motility assay. This is positional chemistry precedent and a warning about retaining parent pharmacology, not evidence for anticancer potency. Primary

record, Journal of Antibiotics 47, 233–242; DOI 10.7164/antibiotics.47.233.

P3: Uno et al. (2023) experimentally replaced alkyl tethers in TPP constructs with PEG tethers, retaining mitochondrial uptake in the tested systems while reducing inner-membrane adsorption. This supports B16 as a linker-class comparator, without establishing the behavior of a moxidectin-sized conjugate. Primary full text, ChemBioChem 24, e202200774; DOI 10.1002/cbic.202200774.

P4: Zhitomirsky and Assaraf (2015) demonstrated lysosomal sequestration/biogenesis involving hydrophobic weak-base cancer drugs. It is a relevant competing destination for B18–B22, not proof that those proposals are lysosomotropic. Primary full text, Oncotarget 6, 1143–1156; DOI 10.18632/oncotarget.2732. A 2022 correction, DOI 10.18632/oncotarget.28110 replaces a duplicated Figure 3A panel; the authors state their conclusions are unchanged. Both records were checked.

P5: Dickinson and Chang (2008) combined a boronate peroxide-reporting element with an already cationic mitochondrial targeting group in MitoPY1. Peroxide reporting is not charge masking. Primary full text, JACS 130, 9638–9639; DOI 10.1021/ja802355u. The separate DOI 10.1021/ja805448s is a correction, not the original paper.

These are class/mechanistic precedents. None reports any exact B01–B25 conjugate, confirms its synthesis, predicts its human safety or preserves moxidectin P-glycoprotein behavior by analogy.

3. Descriptor and fragment definitions

All structures are counterion-free submitted microstates. Salt/counterion choice is unresolved; MW is therefore the molecular ion or neutral molecular entity, not a formulated salt mass. Every reported SMILES parses and sanitises, round-trips canonically and retains the parent chiral substructure. C5 is the only derivatised OH; C7 is untouched. All rows retain ten assigned tetrahedral centers and no unspecified tetrahedral centers under modern inspection. Parent alkene/oxime stereo notation is retained. No new stereocenter is introduced.

W logP means RDKit Crippen MolLogP for the whole submitted graph. **H logP** means the isolated head proxy capped at the linker bond by a methyl group: for B1, methyltriphenylphosphonium; for EtP, methyltriethylphosphonium. **A logP** means the full head-plus-arm proxy with the chassis attachment capped by methyl, retaining its oxygen/linker chemistry. The exact head and arm SMILES are given for every row in the machine-readable files and below. These caps are explicit conventions; a different cut changes the number. The arm proxy is closer to an isolated alkyl-cation experimental series than the head proxy alone.

For permanent ions these are algorithmic descriptors, **not experimentally defined neutral-species partition coefficients, logD7.4, mitochondrial partition coefficients or plasma protein binding predictions**. RDKit's charged-fragment treatment does not measure ion permeability or effective charge shielding. Cross-head numerical comparisons are weaker than within-series comparisons. For weak bases W/H/A are neutral-microstate values, not pH-weighted

distributions; a singly protonated head proxy is reported separately. Different protonation sites and multiple protonation of piperazine require a proper microstate model.

No pKa values were generated. Use measured potentiometric/UV or NMR pKa where solubility permits; a calibrated ChemAxon/ACD or equivalent pKa/microstate model could guide experiments, followed by experimental logD versus pH. The full conjugate must be evaluated: parent-fragment textbook pKa is insufficient. No BBB, efflux, clearance, cardiac safety or protein binding claim follows from these descriptors.

4. Admitted design structures

“Admitted” means structurally validated and worth retaining as a defined hypothesis or trend probe. It does not mean all should be synthesized. The long end of the EtP series is deliberately retained to reveal the trend; only B01 is the initial ester-series probe. Charges and descriptors refer to the exact submitted SMILES.

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B01	EtP/ester, n=2	813.05	8.747	2.694	2.627	122.11	1	10	10	5	10/0	+1
B02	EtP/ester, n=3	827.07	9.137	2.694	3.017	122.11	1	10	11	5	10/0	+1
B03	EtP/ester, n=4	841.10	9.527	2.694	3.407	122.11	1	10	12	5	10/0	+1

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B04	EtP/ester, n=5	855.13	9.917	2.694	3.797	122.11	1	10	13	5	10/0	+1
B05	EtP/ester, n=6	869.15	10.308	2.694	4.187	122.11	1	10	14	5	10/0	+1
B11	Py/ester, n=2	773.99	6.658	0.511	0.537	125.99	1	10	7	6	10/0	+1

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B12	Quin/ester, n=2	824.05	7.811	1.664	1.690	125.99	1	10	7	7	10/0	+1
B13	MeN/ester, n=2	754.00	6.376	0.322	0.256	122.11	1	10	7	5	10/0	+1
B14	EtP/carbamate	828.06	8.540	2.694	2.420	134.14	2	10	10	5	10/0	+1
B15	EtP/ether	785.04	8.831	2.694	2.710	105.04	1	9	10	5	10/0	+1

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B16	TPP/ether-PEG	973.22	9.764	3.610	3.644	114.27	1	10	13	8	10/0	+1
B17	HEP/carbamate	876.06	5.457	-0.389	-0.663	194.83	5	13	13	5	10/0	+1

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B18	morph/ether; weak-base hypothesis	752.99	6.085	-0.052	-0.035	117.51	1	11	7	6	10/0	+0

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B19	pipz / ether; weak-base hypothesis	766.03	6.001	-0.136	-0.120	111.52	1	11	7	6	10/0	+0

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B20	piper / ether; weak-base hypothesis	779.07	7.875	1.348	1.755	108.28	1	10	8	6	10/0	+0

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B21	dma / ether; weak-base hypothesis	710.95	6.315	0.178	0.194	108.28	1	10	7	5	10/0	+0

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B22	im/ether; weak-base hypothesis	733.95	6.650	0.420	0.529	122.86	1	10	7	6	10/0	+0
B23	TPP/ether, short	929.17	9.747	3.610	3.627	105.04	1	9	10	8	10/0	+1

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B25	Py/ether, short	745.98	6.741	0.511	0.620	108.92	1	9	7	6	10/0	+1

Head codes: EtP = triethylphosphonium; BuP = tributylphosphonium; TPP = triphenylphosphonium; OMeTPP = tris(4-methoxyphenyl)phosphonium; amideTPP = mono-para-carboxamide TPP; Py = pyridinium; Quin = quinolinium; MeN = trimethylammonium; HEP = tris(2-hydroxyethyl)phosphonium. The fourth substituent is the linker. Weak-base codes morph/pipz/piper/dma/im identify the rings/groups specified below.

5. Held structures, baseline and failed boundary tests

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B06	EtP/ester, n=7	883.18	10.698	2.694	4.577	122.11	1	10	15	5	10/0	+1
B07	EtP/ester, n=8	897.21	11.088	2.694	4.967	122.11	1	10	16	5	10/0	+1
B08	BuP/ester, n=2	897.21	11.088	5.034	4.967	122.11	1	10	16	5	10/0	+1

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B09	OMeTPP/ester, n=2	1047.26	9.690	3.636	3.569	149.80	1	13	13	8	10/0	+1
B10	amideTPP/ester, n=2	1000.20	8.763	2.709	2.643	165.20	2	11	11	8	10/0	+1

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
B24	amide TPP / carbamate	1015.22	8.556	2.709	2.435	177.23	3	11	11	8	10/0	+1
H01	TPP / deposited B1 ester n=4	985.23	10.444	3.610	4.324	122.11	1	10	12	8	10/0	+1

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
H02	TPP/estern=6	1013.29	11.224	3.610	5.104	122.11	1	10	14	8	10/0	+1
H03	TPP/estern=8	1041.34	12.005	3.610	5.884	122.11	1	10	16	8	10/0	+1

ID	Head/linkage	MW	WlogP	HlogP	AlogP	TPSA	HBD	HBA	RotB	Rings	Stereo/U	Charge
H04	Boron TPP / ether; boronate pendant	972.99	7.427	1.290	1.307	145.50	3	11	11	8	10/0	+1

B06–B08 fail the whole-molecule lipophilicity objective; B09 does not improve head cLogP and exceeds 1,000 Da; B10/B24 add excessive mass/polarity for the first set. H02/H03 intentionally extend the unfavorable TPP trend. H04 parses but is held because its purported charge mask fails: phosphorus is still +1. These are reported separately and do not inflate the admitted count.

6. Liability, precedent and new failure mode for every structure

B01 — EtP, ester, n=2 (admitted). Fix/test: Reduces aromatic head surface; controlled n=2–8 methylene tether series. New cost: C5 ester remains; localised charge may reduce permeability; longer arms increase hydrophobicity and binding risk. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B02 — EtP, ester, n=3 (admitted). Fix/test: Reduces aromatic head surface; controlled n=2–8 methylene tether series. New cost: C5 ester remains; localised charge may reduce permeability; longer arms increase hydrophobicity and binding risk. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B03 — EtP, ester, n=4 (admitted). Fix/test: Reduces aromatic head surface; controlled n=2–8 methylene tether series. New cost: C5 ester remains; localised charge may reduce permeability; longer arms increase hydrophobicity and binding risk. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B04 — EtP, ester, n=5 (admitted). Fix/test: Reduces aromatic head surface; controlled n=2–8 methylene tether series. New cost: C5 ester remains; localised charge may reduce permeability; longer arms increase hydrophobicity and binding risk. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B05 — EtP, ester, n=6 (admitted). Fix/test: Reduces aromatic head surface; controlled n=2–8 methylene tether series. New

cost: C5 ester remains; localised charge may reduce permeability; longer arms increase hydrophobicity and binding risk. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B06 — EtP, ester, n=7 (held). Fix/test: Reduces aromatic head surface; controlled n=2–8 methylene tether series. New cost: C5 ester remains; localised charge may reduce permeability; longer arms increase hydrophobicity and binding risk. Held: fails the lipophilicity objective or incurs excessive mass/polarity for the initial set. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B07 — EtP, ester, n=8 (held). Fix/test: Reduces aromatic head surface; controlled n=2–8 methylene tether series. New cost: C5 ester remains; localised charge may reduce permeability; longer arms increase hydrophobicity and binding risk. Held: fails the lipophilicity objective or incurs excessive mass/polarity for the initial set. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B08 — BuP, ester, n=2 (held). Fix/test: Replaces aromatic rings with alkyl arms; tests head hydrophobicity against EtP. New cost: Tributyl is not inherently hydrophilic; membrane disruption and C5 ester hydrolysis remain. Held: fails the lipophilicity objective or incurs excessive mass/polarity for the initial set. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B09 — OMeTPP, ester, n=2 (held). Fix/test: Shortens tether and introduces three methoxy groups. New cost: Methoxy is not guaranteed to lower Crippen logP; extra size, oxidative metabolism and ester loss. Held: fails the lipophilicity objective

or incurs excessive mass/polarity for the initial set. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B10 — amideTPP, ester, n=2 (held). Fix/test: One para carboxamide adds neutral head polarity. New cost: High mass, added hydrogen bonding and impaired uptake; permanent TPP and C5 ester persist. Held: fails the lipophilicity objective or incurs excessive mass/polarity for the initial set. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B11 — Py, ester, n=2 (admitted). Fix/test: Smaller delocalised aromatic monocation replaces TPP. New cost: Different membrane permeation and transporter profile; ester cleavage separates the species. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B12 — Quin, ester, n=2 (admitted). Fix/test: Intermediate aromatic surface between pyridinium and TPP. New cost: More hydrophobic than pyridinium; mitochondrial targeting and safety unmeasured. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B13 — MeN, ester, n=2 (admitted). Fix/test: Small permanent ammonium boundary control. New cost: Localised hydrated charge may prevent passive inner-membrane entry; ester still labile. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B14 — EtP, carbamate (admitted). Fix/test: Replaces C5 ester by carbamate and contracts the cation. New cost: Carbamate cleavage remains possible; C5 masking may impair parent pharmacology; uptake unproved. Precedent

anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B15 — EtP, ether (admitted). Fix/test: Removes added acyl hydrolysis and aromatic rings with a compact appendage. New cost: Oxidative O-dealkylation, permanent C5 masking and insufficient membrane permeation remain. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B16 — TPP, ether-PEG (admitted). Fix/test: Removes C5 ester and adds an ether oxygen to tune membrane adsorption. New cost: TPP and high mass persist; O-dealkylation and loss of uptake possible; no safety guarantee. Precedent anchors: P1, P2, P3; class evidence only, not exact-conjugate evidence.

B17 — HEP, carbamate (admitted). Fix/test: Adds three terminal hydroxyls to the phosphonium head. New cost: Large hydration/polarity penalty may abolish mitochondrial access; carbamate may cleave. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B18 — morph, ether; weak-base hypothesis (admitted). Fix/test: Removes permanent formal charge in the submitted microstate; morpholine samples basicity space. New cost: pKa unknown; acid trapping can favor extracellular space or lysosomes; no demonstrated mitochondrial targeting or tumor pH gate. Precedent anchors: P4; class evidence only, not exact-conjugate evidence.

B19 — pipz, ether; weak-base hypothesis (admitted). Fix/test: Removes permanent formal charge in the submitted microstate; N-methylpiperazine samples basicity space. New cost: pKa unknown; acid trapping can favor extracellular space

or lysosomes; no demonstrated mitochondrial targeting or tumor pH gate. Precedent anchors: P4; class evidence only, not exact-conjugate evidence.

B20 — piper, ether; weak-base hypothesis (admitted). Fix/test: Removes permanent formal charge in the submitted microstate; N-methylpiperidin-4-yl samples basicity space. New cost: pKa unknown; acid trapping can favor extracellular space or lysosomes; no demonstrated mitochondrial targeting or tumor pH gate. Precedent anchors: P4; class evidence only, not exact-conjugate evidence.

B21 — dma, ether; weak-base hypothesis (admitted). Fix/test: Removes permanent formal charge in the submitted microstate; dimethylaminoethyl samples basicity space. New cost: pKa unknown; acid trapping can favor extracellular space or lysosomes; no demonstrated mitochondrial targeting or tumor pH gate. Precedent anchors: P4; class evidence only, not exact-conjugate evidence.

B22 — im, ether; weak-base hypothesis (admitted). Fix/test: Removes permanent formal charge in the submitted microstate; N-substituted imidazole samples basicity space. New cost: pKa unknown; acid trapping can favor extracellular space or lysosomes; no demonstrated mitochondrial targeting or tumor pH gate. Precedent anchors: P4; class evidence only, not exact-conjugate evidence.

B23 — TPP, ether, short (admitted). Fix/test: Hydrolysis-resistant reference retaining the established TPP head. New cost: Still permanently cationic and lipophilic; C5 pharmacology and ether metabolism unresolved. Precedent

anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B24 — amideTPP, carbamate (held). Fix/test: Combines shorter polar head with a C5 carbamate. New cost: Mass and polarity cost; persistent cation, uptake uncertainty and carbamate metabolism. Held: fails the lipophilicity objective or incurs excessive mass/polarity for the initial set. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

B25 — Py, ether, short (admitted). Fix/test: Combines a smaller aromatic monocation with no added ester. New cost: Pyridinium permeability and metabolism uncertain; C5 remains blocked; no measured mitochondrial delivery. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

H01 — TPP, deposited B1 ester n=4 (held). Fix/test: Exact deposited baseline. New cost: Original high lipophilicity, charge, mass and ester risks. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

H02 — TPP, ester n=6 (held). Fix/test: Longer TPP-chain stress comparator. New cost: Expected higher lipophilicity; fails improvement objective. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

H03 — TPP, ester n=8 (held). Fix/test: Longer TPP-chain stress comparator. New cost: Expected higher lipophilicity; fails improvement objective. Precedent anchors: P1, P2; class evidence only, not exact-conjugate evidence.

H04 — BoronTPP, ether; boronate pendant (held). Fix/test: Tests the proposed boronate label structurally. New cost: P remains +1 before and after boronate oxidation; this is NOT a charge-masked precursor. Precedent anchors: P5; class evidence only, not exact-conjugate evidence.

7. Weak-base branch: testable, but not the claimed mitochondrial pH gate

Acidic extracellular space can increase the protonated fraction of a weak base. That does not selectively expose an electrically permeant monocation at the mitochondrial membrane: the charged form may cross the cell membrane less readily, and after entry the base re-equilibrates with cytosolic pH. The mitochondrial matrix is relatively alkaline; conventional neutral-permeant/ion-impermeant weak-base trapping therefore favors acidic compartments, especially lysosomes, rather than the matrix. If the protonated form is itself membrane-permeant, its voltage-driven uptake must instead be analyzed with coupled protonation, electrochemical potentials and transport—not a neutral-only trapping argument.

For an illustrative *assumed* pKa 6.5 or 7.0, the protonated fractions at plasma pH 7.4 are 11.2% or 28.5%; at extracellular pH 6.6 they are 44.3% or 71.5%. That is incomplete gating. Under the ideal neutral-only-permeation model, total equilibrium concentration at pH 6.6 versus 7.4 is only 1.59- or 2.51-fold, respectively. These calculations do not assign either pKa to a proposed molecule. Higher basicity can increase

acidic trapping while also increasing systemic ionization, undermining the premise of a neutral circulating agent.

B18–B22 are consequently **basicity/localization probes**, not five validated pKa-6.5–7.0 mitochondrial delivery systems. N-methylpiperidine and dimethylaminoethyl must especially not be called near-neutral-pKa designs without data; N-methylpiperazine has multiple protonation possibilities. Morpholine and imidazole are sensible starting chemotypes for exploring ionization, but the attached conjugate still needs measurement. Class (b) is not physically impossible as a tumor-distribution strategy. Its simple acid-protonation rationale is insufficient for mitochondria and may point in the wrong subcellular direction.

8. Conditional cation: a genuine missing design, not a label to borrow

Attaching a boronate to TPP does not mask its permanent charge. Oxidation of an arylboronate to a phenol leaves tetracoordinate phosphonium positive. H04 makes that bookkeeping explicit. MitoPY1 is precedent for a peroxide-responsive reporter coexisting with TPP targeting, not a neutral precursor generating TPP after activation.

Likewise, cleavage of a protecting group from an already N-alkylated pyridinium or quaternary ammonium does not remove the positive charge that was already there. A valid design must show precursor and product structures, charge changes and a chemically plausible atom-balanced activation path. An anionic countergroup can make a zwitterion, but net zero is not charge disappearance and can prevent uptake. A

phosphine is a different phosphorus oxidation/valence state; simple peroxide oxidation usually gives phosphine oxide, not the desired alkylphosphonium ion.

I therefore admit **no neutral-to-permanent-cation boronate/enzyme design in this round**. The enzyme-cleaved route needs a specified activation chemistry and enzyme-access context before a structure can be credited. This is the open class-(c) gap, not a solved property hidden in the table. A tumor-cleaved carrier can release a pre-existing cation, but carrier shielding, release specificity and product PK then form a separate delivery project.

9. The tether series and reduced driving-force question

Here n explicitly counts the methylenes in MOX-O-C(=O)-(CH2)n-head; B1 has n=4, not five methylenes. The names C2–C8 in this report refer to n=2 through n=8; the acyl carbonyl is not counted. B01–B07 are a complete matched EtP series, with n=7 and n=8 held after the descriptor screen. Whole and arm Crippen logP rise by about 0.390 per added methylene; head logP stays constant by construction. Rotatable bonds also rise one per step. This mathematical descriptor trend is not a measured accumulation/binding trend.

B08 is a useful negative result: replacing phenyl with **tributyl** does not make the head less lipophilic. Its head proxy is 5.034 versus 3.610 for TPP, and whole logP is 11.088. Similarly three para-methoxy substituents give head logP 3.636, slightly above TPP in this model. “Polar substituent” cannot substitute for a calculation.

Class (d) is implemented as reduced membrane partition/permeation hypotheses and shorter exposure pathways, not a fictitious fractional formal charge. A +1 head that reaches equilibrium retains the same Nernst slope. Safety must be demonstrated at matched unbound exposure and matched tumor effect, not inferred because uptake is slower.

10. Top three and why

1 — B15, triethylphosphonium C5 ether. MW 785.04, W logP 8.831, H logP 2.694, charge +1. It removes three phenyl rings and the added ester, reducing mass by about 200 Da. The important risk is insufficient membrane entry of the more localized hydrated phosphonium, plus the known C5 masking concern. It is a focused test, not a promise of targeting.

2 — B25, pyridinium C5 ether. A compact delocalized aromatic monocation with an ester-free C5 attachment. It tests whether a small aromatic ion supplies adequate localization without TPP's three phenyl rings. Permeation, metabolism and transporter recognition could fail; retention of parent cancer-relevant action is unproved. Its exact computed descriptors are in the table.

3 — B14, triethylphosphonium C5 carbamate. MW 828.06, W logP 8.540, H logP 2.694, charge +1. The matched head against B15 separates the linkage question. Carbamate has a different geometry/polarity and may be more accessible synthetically, but it is not an inert bond and may yield parent/released fragments at an unfavorable rate. Testing it alongside the ether is more informative than choosing a third unconnected head.

Next comparator — B16. Its PEG-containing ether linker has the most direct class-level mitochondrial distribution precedent among these property-tuning moves. It remains 973 Da with W logP 9.764 and a TPP head, so I rank it behind the compact probes rather than call it a safety rescue.

11. Go/no-go gates for the B-family

First establish species and exposure: chemical/plasma stability, solubility, aggregation, pKa/logD where applicable, plasma unbound fraction with recovery/mass balance, and microsomal/hepatocyte turnover and metabolites. Lower computed logP is not proof of reduced protein binding or improved clearance; neutralization can increase or decrease either. Include metabolite and released head/cargo identification, not just disappearance of intact conjugate.

Then test localization with quantitative LC–MS and organelle fractionation controls rather than a fluorescent tag assumed to behave like the compound. Distinguish inner-membrane adsorption, matrix entry and lysosomal accumulation. Measure dependence on membrane potential with matched controls; depolarizers change physiology and cannot alone establish targeting. Measure both concentration and free exposure where feasible.

Compare cancer cells with cardiomyocytes, skeletal-muscle cells and other relevant normal cells at matched unbound exposure. Read respiration, ATP, membrane potential, viability and recovery after washout. Include head/linker alone, parent moxidectin, an equimolar mixture and the intact conjugate. Establish whether C5 masking retains any relevant parent

action and whether the conjugate outperforms a mixture at an exposure achievable without normal-cell mitochondrial injury. Parent moxidectin's weak Pgp affinity, human safety package or apparent tissue behavior cannot simply be inherited by a charged conjugate.

Continue only if a measured tumor-versus-normal functional window and an exposure/localization advantage survive those controls. **Stop the mitochondriotropic claim** if uptake is mainly nonspecific membrane adsorption or lysosomal trapping, if normal mitochondria fail at the same unbound exposures, or if covalent union adds no advantage. Do not repair absent selectivity by lengthening the hydrophobic tail. No in vivo safety, tumor specificity, BBB penetration or therapeutic index is claimed for this unmade series.

12. Exact isomeric SMILES and fragment proxies

Counterions are omitted from all molecular representations below; permanent cations require counterions in material form. Neutral weak-base graphs are specified microstates, not a claim that all circulating molecules are neutral. Formula, charge and full descriptors are also in b1-successors/candidates.json and .csv.

B01 — admitted — C46H71NO9P+ — formal charge +1

CC[P+](CC)
(CC)CCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C

@@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Head proxy (H logP 2.6935, charge +1): CC[P+](C)(CC)CC
Arm proxy (A logP 2.6268): CC[P+](CC)(CC)CCC(=O)OC

B02 — admitted — C47H73NO9P+ — formal charge +1

CC[P+](CC)
(CC)CCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[
C@@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Head proxy (H logP 2.6935, charge +1): CC[P+](C)(CC)CC
Arm proxy (A logP 3.0169): CC[P+](CC)(CC)CCCC(=O)OC

B03 — admitted — C48H75NO9P+ — formal charge +1

CC[P+](CC)
(CC)CCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3
C[C@@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Head proxy (H logP 2.6935, charge +1): CC[P+](C)(CC)CC
Arm proxy (A logP 3.4070): CC[P+](CC)(CC)CCCCC(=O)OC

B04 — admitted — C49H77NO9P+ — formal charge +1

CC[P+](CC)(CC)CCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Head proxy (H logP 2.6935, charge +1): CC[P+](C)(CC)CC
Arm proxy (A logP 3.7971): CC[P+](CC)(CC)CCCCCC(=O)OC

B05 — admitted — C50H79NO9P+ — formal charge +1

CC[P+](CC)(CC)CCCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Head proxy (H logP 2.6935, charge +1): CC[P+](C)(CC)CC
Arm proxy (A logP 4.1872): CC[P+](CC)(CC)CCCCCCC(=O)OC

B06 — held — C51H81NO9P+ — formal charge +1

CC[P+](CC)(CC)CCCCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Head proxy (H logP 2.6935, charge +1): CC[P+](C)(CC)CC
Arm proxy (A logP 4.5773): CC[P+](CC)
(CC)CCCCCCCC(=O)OC

B07 — held — C52H83NO9P+ — formal charge +1

CC[P+](CC)
(CC)CCCCCCCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C
@H]3C[C@@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Head proxy (H logP 2.6935, charge +1): CC[P+](C)(CC)CC
Arm proxy (A logP 4.9674): CC[P+](CC)
(CC)CCCCCCCCC(=O)OC

B08 — held — C52H83NO9P+ — formal charge +1

CCCC[P+](CCCC)
(CCCC)CCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3
C[C@@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Head proxy (H logP 5.0341, charge +1): CCCC[P+](C)
(CCCC)CCCC
Arm proxy (A logP 4.9674): CCCC[P+](CCCC)
(CCCC)CCC(=O)OC

B09 — held — C61H77NO12P+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[P+](c6ccc(OC)cc6)
(c6ccc(OC)cc6)c6ccc(OC)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 3.6361, charge +1): COc1ccc([P+](C)
(c2ccc(OC)cc2)c2ccc(OC)cc2)cc1
Arm proxy (A logP 3.5694): COC(=O)CC[P+](c1ccc(OC)cc1)
(c1ccc(OC)cc1)c1ccc(OC)cc1

B10 — held — C59H72N2O10P+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[P+](c6ccccc6)
(c6ccccc6)c6ccc(C(N)=O)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 2.7092, charge +1): C[P+](c1ccccc1)
(c1ccccc1)c1ccc(C(N)=O)cc1
Arm proxy (A logP 2.6425): COC(=O)CC[P+](c1ccccc1)
(c1ccccc1)c1ccc(C(N)=O)cc1

B11 — admitted — C45H61N2O9+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]

(OC(=O)CC[n+]6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 0.5111, charge +1): C[n+]1ccccc1
Arm proxy (A logP 0.5372): COC(=O)CC[n+]1ccccc1

B12 — admitted — C49H63N2O9+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[n+]6cccc7ccccc76)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 1.6643, charge +1): C[n+]1cccc2ccccc21
Arm proxy (A logP 1.6904): COC(=O)CC[n+]1cccc2ccccc21

B13 — admitted — C43H65N2O9+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[N+](C)(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 0.3224, charge +1): C[N+](C)(C)C
Arm proxy (A logP 0.2557): COC(=O)CC[N+](C)(C)C

B14 — admitted — C46H72N2O9P+ — formal charge +1

CC[P+](CC)
(CC)CCNC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[
C@@H](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Head proxy (H logP 2.6935, charge +1): CC[P+](C)(CC)CC
Arm proxy (A logP 2.4197): CC[P+](CC)(CC)CCNC(=O)OC

B15 — admitted — C45H71NO8P+ — formal charge +1

CC[P+](CC)
(CC)CCO[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H
](C/C=C(\C)C[C@@H]
(C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC
)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

Head proxy (H logP 2.6935, charge +1): CC[P+](C)(CC)CC
Arm proxy (A logP 2.7101): CC[P+](CC)(CC)CCOC

B16 — admitted — C59H75NO9P+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCOCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 3.6103, charge +1): C[P+](c1ccccc1)(c1ccccc1)c1ccccc1
Arm proxy (A logP 3.6435): COCCOCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

B17 — admitted — C46H72N2O12P+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NCC[P+](CCO)(CCO)CCO)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP -0.3893, charge +1): C[P+](CCO)(CCO)CCO
Arm proxy (A logP -0.6631): COC(=O)NCC[P+](CCO)(CCO)CCO

B18 — admitted — C43H64N2O9 — formal charge +0

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCCN6CCOCC6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP -0.0516, charge +0): CN1CCOCC1
Arm proxy (A logP -0.0350): COCCN1CCOCC1

Illustrative singly protonated head proxy, not a pKa assignment: C[NH+]1CCOCC1; H logP -1.4687. This is not a separately nominated conjugate.

B19 — admitted — C44H67N3O8 — formal charge +0

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCN6CCN(C)CC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP -0.1364, charge +0): CN1CCN(C)CC1
Arm proxy (A logP -0.1198): COCCN1CCN(C)CC1

Illustrative singly protonated head proxy, not a pKa assignment: CN1CC[NH+](C)CC1; H logP -1.5535. This is not a separately nominated conjugate.

B20 — admitted — C46H70N2O8 — formal charge +0

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCCC6CCN(C)CC6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 1.3481, charge +0): CC1CCN(C)CC1
Arm proxy (A logP 1.7548): COCCCC1CCN(C)CC1

Illustrative singly protonated head proxy, not a pKa assignment: CC1CC[NH+](C)CC1; H logP -0.0690. This is not a separately nominated conjugate.

B21 — admitted — C41H62N2O8 — formal charge +0

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]

(OCCN(C)C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 0.1778, charge +0): CN(C)C
Arm proxy (A logP 0.1944): COCCN(C)C

Illustrative singly protonated head proxy, not a pKa assignment: C[NH+](C)C; H logP -1.2393. This is not a separately nominated conjugate.

B22 — admitted — C42H59N3O8 — formal charge +0

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCCn6ccnc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 0.4201, charge +0): Cn1ccnc1
Arm proxy (A logP 0.5295): COCCn1ccnc1

Illustrative singly protonated head proxy, not a pKa assignment: Cn1cc[nH+]c1; H logP -0.1608. This is not a separately nominated conjugate.

B23 — admitted — C57H71NO8P+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC[P+](c6ccccc6)(c6ccccc6)c6ccccc6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 3.6103, charge +1): C[P+](c1ccccc1)(c1ccccc1)c1ccccc1
Arm proxy (A logP 3.6269): COCC[P+](c1ccccc1)(c1ccccc1)c1ccccc1

B24 — held — C59H73N3O10P+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)NCC[P+](c6ccccc6)(c6ccccc6)c6ccc(C(N)=O)cc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 2.7092, charge +1): C[P+](c1ccccc1)(c1ccccc1)c1ccc(C(N)=O)cc1
Arm proxy (A logP 2.4354): COC(=O)NCC[P+](c1ccccc1)(c1ccccc1)c1ccc(C(N)=O)cc1

B25 — admitted — C44H61N2O8+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OCC[n+]6ccccc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 0.5111, charge +1): C[n+]1ccccc1
Arm proxy (A logP 0.6205): COCC[n+]1ccccc1

H01 — held — C60H75NO9P+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 3.6103, charge +1): C[P+](c1ccccc1)
(c1ccccc1)c1ccccc1
Arm proxy (A logP 4.3238): COC(=O)CCCC[P+](c1ccccc1)
(c1ccccc1)c1ccccc1

H02 — held — C62H79NO9P+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 3.6103, charge +1): C[P+](c1ccccc1)
(c1ccccc1)c1ccccc1
Arm proxy (A logP 5.1040): COC(=O)CCCCCC[P+](c1ccccc1)
(c1ccccc1)c1ccccc1

H03 — held — C64H83NO9P+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCCCCCC[P+](c6ccccc6)

(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 3.6103, charge +1): C[P+](c1ccccc1)
(c1ccccc1)c1ccccc1
Arm proxy (A logP 5.8842): COC(=O)CCCCCCCCC[P+]
(c1ccccc1)(c1ccccc1)c1ccccc1

H04 — held — C57H72BNO10P+ — formal charge +1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OCC[P+](c6ccccc6)
(c6ccccc6)c6ccc(B(O)O)cc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Head proxy (H logP 1.2901, charge +1): C[P+](c1ccccc1)
(c1ccccc1)c1ccc(B(O)O)cc1
Arm proxy (A logP 1.3067): COCC[P+](c1ccccc1)
(c1ccccc1)c1ccc(B(O)O)cc1

13. Reproducibility and delivery

RDKit 2026.09.1; 19 admitted structures, 10 held/reference structures, 29 total unique structures. Build: b1-successors/build.py; candidates: JSON/CSV/SDF. Chiral parent matching and canonical round-trip assertions execute in the build. All candidates preserve the C5 configuration and C7 OH; no newly introduced unassigned tetrahedral centers. Class (c) remains explicitly unresolved.

Prepared for SC5.5 through Atlas85 Mission Control. Own-inbox receipt and verified file hashes are recorded separately; an own-inbox upload is not peer delivery.

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DOCUMENTARY SOURCE S05

B1_PAPER.md

Original source: /home/codex/outbox/rdkit-top-prospects/package/sources/44/current/B1_PAPER.md

Rescuing a mitochondriotropic conjugate on the moxidectin chassis

Forty-five designs, a Nernst ceiling that reframes the objective, and why the obvious winner is probably going to the wrong organelle · Ron Johnson[1], SC 5.5[2] and Atlas[3] · [1]Stranger Than Fiction News · [2]Agentic Research Factory, Planet 44 · [3]Agentic Research Factory, Planet 85 · 5 November 2026 · computational designs only · public domain under CC0 1.0

Abstract

ARF-MOX-B1 — moxidectin esterified at C5 to a pentanoyl arm terminating in triphenylphosphonium — was nominated as a lead on the reasoning that a delocalised lipophilic cation accumulates in mitochondria in proportion to membrane potential, and that cancer mitochondria are hyperpolarised. Three objections were raised against it: non-discrimination between tumour and cardiac mitochondria, accumulation that is not self-limiting, and plasma protein binding driven by a permanent charge on a 985 Da scaffold at clogP 10.44. We

report two independently constructed successor series, **forty-five designs**, and three results that matter more than any of the molecules.

First, the **Nernst ceiling**. At 310.15 K one decade of accumulation corresponds to 61.54 mV. Hyperpolarisation to −180 mV delivers 842-fold enrichment, which comfortably clears the published 110–220× exposure gap for this chassis. But selectivity derives only from the *difference* between tumour and normal potential, and −180 mV against −140 mV yields **4.47×**. The mechanism addresses potency and does not, on voltage alone, deliver a large selectivity margin.

Second, a **correction to our own framing**. A +1 species that reaches electrochemical equilibrium has the same ideal voltage slope regardless of headgroup identity. "Stronger cation" is not an adjustable Nernst parameter. What headgroup substitution changes is permeability, membrane adsorption, binding and kinetics — not driving force.

Third, and most consequential: the design class that scores best on physicochemical grounds — neutral weak bases intended to protonate in acidic tumour tissue — **is probably mislocalised by construction**. The mitochondrial matrix is relatively alkaline, and neutral-permeant, ion-impermeant weak-base trapping concentrates compounds in *acidic* compartments, principally lysosomes. Under an ideal neutral-only-permeation model, an assumed pKa of 6.5 or 7.0 gives a total equilibrium ratio at pH 6.6 versus 7.4 of only **1.59× or 2.51×** — less selectivity than the voltage mechanism it replaces, and pointed at the wrong organelle.

1 · The incumbent and the objections

ARF-MOX-B1 reproduces independently on both nodes at **MW 985.23, Crippen clogP 10.444, TPSA 122.11 Å², 12 rotatable bonds, formal charge +1**.

1. **Off-target mitochondria.** Triphenylphosphonium does not discriminate between tumour and healthy mitochondria. Cardiac and skeletal muscle mitochondria are also hyperpolarised, so systemic exposure loads the heart.
2. **Accumulation not therapeutically controlled.** Voltage-driven uptake continues as long as the potential is maintained.
3. **Protein binding and clearance.** A permanent charge on a large, very lipophilic macrocycle raises non-specific binding and alters clearance in ways that can cancel the distribution advantage.

Objection 1 is upheld without qualification. Objections 2 and 3 are upheld with corrections stated in § 2 and § 6.

2 · The Nernst ceiling, and two corrections to how we first stated it

For a freely equilibrating monovalent cation, free-activity enrichment is a_matrix / a_cytosol = exp(−F·Δψ / RT). At 310.15 K one decade is **61.54 mV**.

Mitochondrial potential	Enrichment
−120 mV	89×

Mitochondrial potential	Enrichment
−140 mV	188×
−160 mV	398×
−180 mV	842×
−200 mV	1779×

Scenario	Gap	Selectivity
tumour −180 vs normal −140	40 mV	**4.47×**
tumour −180 vs normal −150	30 mV	3.08×
tumour −200 vs normal −140	60 mV	9.44×

Computed independently on both nodes; the ratio agrees to four significant figures (4.4666 on Planet 85, 4.47 on Planet 44). The exposure gap to be closed is 110–220×. **The mechanism closes the potency gap and supplies a voltage-derived selectivity of roughly four- to five-fold.**

Correction 1 — "stronger cation" is not a Nernst parameter. Our first statement of this result said that a more aggressive cation buys more accumulation everywhere at the same ratio. The conclusion was right and the mechanism given for it was wrong. Triphenylphosphonium, pyridinium, quaternary ammonium and trialkylphosphonium all share the same ideal equilibrium voltage slope *if they permeate*. A small

hydrated cation does not carry a calibrated weaker charge; it may simply fail to enter. Headgroup and tether changes act on permeability, membrane adsorption, binding and free concentration — not on driving force.

Correction 2 — accumulation is self-limiting in principle. Uptake is voltage-dependent, so depolarisation reduces further electrical enrichment. "Unregulated" is too strong as physics. The development concern is better stated as **no demonstrated therapeutic control of normal-tissue exposure**, which does not require the stronger claim and is not softened by the feedback.

What the 4.47× is not. It is an ideal conditional comparison assuming equal cytosolic unbound activity, fixed representative potentials, fixed charge state and equal permeability. It is not a universal upper bound on measured tissue ratios. Neither −180 mV for cancer nor −140 mV for all normal tissue is established here; both are the stipulated scenario values, and **heart cannot be assigned the favourable reference potential by assertion**.

3 · The design objective inverts

If 110–220× suffices and 842× is available, maximum accumulation is the wrong target. The rational move is to **detune deliberately** — accept sub-maximal uptake for lower headgroup lipophilicity and a wider window. Given correction 1, "detune" must be understood as reduced membrane partition, reduced adsorption and slower kinetics, not as a fractional formal charge.

3.1 · The descriptor that was missing

Adverse mitochondrial effects in alkyl-TPP series track the lipophilicity of the **cationic headgroup**, not of the whole conjugate [P1]. Neither node had computed it. Reported here as hgLogP, the Crippen logP of the methyl-capped headgroup alone. It spans **5.03 down to −0.39** against triphenylphosphonium's **3.61**, and it reorders the branch.

Its limit, stated plainly: [P1] shows that increasing alkyl-chain hydrophobicity increased adverse effects within one series. It does **not** establish that methyl-capped head clogP alone determines toxicity independently of cargo and linker. hgLogP is a ranking heuristic with one supporting series behind it, not a tox model.

4 · The negative results

Two, both of which refute an intuition we held before computing anything.

Tributylphosphonium is worse than triphenylphosphonium. "Trialkyl is less delocalised, therefore gentler" is false: head logP **5.03** against 3.61, whole-molecule clogP **11.09–11.66** against 10.44. The butyl chains cost more than the loss of aryl delocalisation saves. Reproduced independently on both nodes.

Polar aryl substitution does not help either. Three para-methoxy groups give head logP **3.64**, *above* triphenylphosphonium in this model, with mass rising to 1047–1090 Da. A substituent that reads as polar is not necessarily a

reduction in computed lipophilicity, and the word cannot substitute for the calculation.

5 · The weak-base class is probably going to the wrong organelle

This is the most important finding in the branch, and it overturns the apparent ranking.

Ranked on physicochemical gates alone, neutral weak bases dominate: morpholine, dimethylamino and N-methylpiperazine conjugates reach clogP 6.0–6.9 at 711–837 Da with no ester and no unspecified stereocentres, against the incumbent's 10.44 at 985 Da. An external assessment of the Planet 44 table accordingly nominated the morpholine ether conjugate as overall winner on the reasoning that it "protonates selectively in acidic tumour conditions" while avoiding permanent systemic charge.

The physics does not support that reasoning.

- Acidic extracellular space does raise the protonated fraction of a weak base. It does **not** thereby present an electrically permeant monocation at the mitochondrial inner membrane: the charged form crosses the plasma membrane less readily, and after entry the base re-equilibrates with cytosolic pH.
- **The mitochondrial matrix is relatively alkaline.** Conventional neutral-permeant, ion-impermeant weak-base trapping therefore favours *acidic* compartments — principally **lysosomes**, a destination with its own

established literature for hydrophobic weak-base anticancer agents and their sequestration [P4].

- Quantitatively, for an *assumed* pKa of 6.5 or 7.0, protonated fractions at pH 7.4 are 11.2% or 28.5%, and at pH 6.6 are 44.3% or 71.5%. That is **incomplete gating**. Under the ideal neutral-only-permeation model the total equilibrium ratio at pH 6.6 versus 7.4 is **1.59× or 2.51×** — lower than the 4.47× the voltage mechanism already offers.
- **No pKa has been measured or assigned.** RDKit does not provide reliable pKa. N-methylpiperidine and dimethylaminoethyl must not be described as near-neutral-pKa designs without data, and N-methylpiperazine has multiple protonation sites.

The weak-base designs are therefore **basicity and localisation probes**, not validated pH-gated mitochondrial delivery systems. The class is not physically impossible as a tumour-*distribution* strategy; its simple acid-protonation rationale is insufficient for *mitochondrial* delivery and may point to the wrong subcellular compartment. A neutral weak base is not a better B1. It is a different drug that scores well by abandoning the mechanism B1 exists to exploit, and our own gate-counting rewarded it for that.

6 · The conditional-cation class does not exist yet

We proposed masking the charge until the tumour unmasks it — an arylboronate cleaved by H_2O_2, or an enzyme-cleaved

precursor — borrowing the logic of the ATL-01 lead. On inspection the proposal is incoherent as stated, and no such design is admitted.

Oxidation of an arylboronate to a phenol **leaves a tetracoordinate phosphonium positive**. Attaching a boronate to triphenylphosphonium does not mask its charge; MitoPY1 is precedent for a peroxide-responsive reporter coexisting with a cationic targeting group, not for a neutral precursor that generates a cation [P5]. Equally, cleaving a protecting group from an already N-alkylated pyridinium or quaternary ammonium does not remove a charge that was there all along. An anionic countergroup gives a zwitterion, and net zero is not charge disappearance — it can prevent uptake outright. A phosphine is a different phosphorus valence state, and peroxide oxidation of a phosphine gives the phosphine oxide, not an alkylphosphonium ion.

A valid design in this class must show precursor and product structures, the charge change, and an atom-balanced activation path. **This is an open gap, not a solved property hidden in the table.**

7 · The series

Two independently constructed sets, reconciled. All twenty-five Planet 85 structures were re-parsed on Planet 44: every one sanitises, and every one reproduces its reported MW and clogP. Properties are computed with RDKit 2026.09.1 and formal charge is stated for each.

7.1 · Permanent cations — mechanism preserved

ID	Series	Headgroup / linkage	MW	clogP	hgLogP	TPSA	RotB	Chg
B17	P85	tris(hydroxyethyl)phosphonium / carbamate	876.1	**5.46**	**−0.39**	194.8	13	+1
B13	P85	trimethylammonium / ester n=2	754.0	6.38	0.32	122.1	7	+1
B11	P85	pyridinium / ester n=2	774.0	6.66	0.51	126.0	7	+1

ID	Series	Headgroup / linkage	MW	clogP	hgLogP	TPSA	RotB	Chg
B25	P85	pyridinium / ether, short	746.0	6.74	0.51	108.9	7	+1
B1h	P44	trimethylammonium / carbamate	797.1	6.95	0.32	134.1	9	+1
B1i	P44	trimethylammonium / ether	754.0	7.24	0.32	105.0	9	+1

ID	Series	Headgroup / linkage	MW	clogP	hgLogP	TPSA	RotB	Chg
B1j	P44	N-methylpyridinium / carbamate	831.1	7.31	0.82	138.0	9	+1
B12	P85	quinoliniu m / ester n=2	824.1	7.81	1.66	126.0	7	+1
B14	P85	triethylphosphonium / carbamate	828.1	8.54	2.69	134.1	10	+1

ID	Series	Headgroup / linkage	MW	clogP	hgLogP	TPSA	RotB	Chg
B01	P85	triethylphosphonium / ester n=2	813.1	8.75	2.69	122.1	10	+1
B1k	P44	triethylphosphonium / ester C2	813.0	8.75	2.69	122.1	10	+1
B15	P85	triethylphosphonium / ether	785.0	8.83	2.69	105.0	10	+1

ID	Series	Headgroup / linkage	MW	clogP	hgLogP	TPSA	RotB	Chg
B02–B05	P85	triethylphosphonium / ester n=3–6	827–869	9.14–10.31	2.69	122.1	11–14	+1
B1f	P44	triethylphosphonium / carbamate	856.1	9.32	2.69	134.1	12	+1
B1g	P44	triethylphosphonium / ether	813.1	9.61	2.69	105.0	12	+1

ID	Series	Headgroup / linkage	MW	clogP	hgLogP	TPSA	RotB	Chg
B23	P85	triphenylphosphonium / ether, short	929.2	9.75	3.61	105.0	10	+1
B16	P85	triphenylphosphonium / ether-PEG	973.2	9.76	3.61	114.3	10	+1
B1b	P44	triphenylphosphonium / carbamate	1000.2	10.24	3.61	134.1	12	+1

ID	Series	Headgroup / linkage	MW	clogP	hgLogP	TPSA	RotB	Chg
B1	P44	**triphenylphosphonium / pentanoyl ester (incumbent)**	**985.2**	**10.44**	**3.61**	**122.1**	**12**	**+1**
B1c	P44	triphenylphosphonium / ether	957.2	10.53	3.61	105.0	12	+1

ID	Series	Headgroup / linkage	MW	clogP	hgLogP	TPSA	RotB	Chg
B1e	P44	tributylphosphonium / carbamate	940.3	11.66	**5.03**	134.1	18	+1

Held on Planet 85 after descriptor screening: B06, B07 (ester n=7, n=8; clogP 10.70, 11.09), B08 (tributyl; the negative result), B09 (tris-methoxy; head logP 3.64), B10 and B24 (amide-TPP).

7.2 · Weak bases — probes, not delivery systems

Read § 5 before this table. These carry no permanent charge and therefore no Nernst driving force, and their likely destination is lysosomal rather than mitochondrial.

ID	Series	Base / linkage	MW	clogP	hgLogP	TPSA	RotB	Chg
B19	P85	N-methylpiperazine / ether	766.0	6.00	−0.14	111.5	7	0
B18	P85	morpholine / ether	753.0	6.09	−0.05	117.5	7	0
B21	P85	dimethylamino / ether	**711.0**	6.32	0.18	108.3	7	0
B1o	P44	N-methylpiperazine / carbamate	837.1	6.49	−0.14	140.6	9	0

ID	Series	Base / linkage	MW	clogP	hgLogP	TPSA	RotB	Chg
B1m	P44	morpholine / carbamate	824.1	6.58	−0.05	146.6	9	0
B22	P85	imidazole / ether	734.0	6.65	0.42	122.9	7	0
B1p	P44	dimethylamino / carbamate	782.0	6.80	0.18	137.4	9	0
B1n	P44	morpholine / ether	781.0	6.87	−0.05	117.5	9	0
B1q	P44	dimethylamino / ether	739.0	7.10	0.18	108.3	9	0

ID	Series	Base / linkage	MW	clogP	hgLogP	TPSA	RotB	Chg
B1r	P44	imidazole / carbamate	805.0	7.14	0.42	152.0	9	0
B20	P85	piperidine / ether	779.1	7.88	1.35	108.3	8	0
B1s	P44	piperidine / carbamate	822.1	7.73	1.10	137.4	9	0
B1t	P44	piperidine / ether	779.1	8.02	1.10	108.3	9	0

8 · Nominations

Retire the deposited B1 as the lead. Retain the B-family as a small, gated delivery experiment. The incumbent's large permanent cation has no demonstrated cancer-versus-heart exposure advantage. That is a reason to stop promoting it, not evidence that every mitochondria-directed moxidectin must fail.

The first three to make, chosen to interrogate permeability against linkage chemistry rather than to presume an answer:

1. **B15** — triethylphosphonium, C5 ether. MW 785.0, clogP 8.83, head logP 2.69. Removes three phenyl rings and the ester, ~200 Da lighter. Risk: insufficient membrane entry of a more localised hydrated phosphonium, plus the C5 masking concern of § 9.
2. **B25** — pyridinium, C5 ether. MW 746.0, clogP 6.74, head logP 0.51. Tests whether a compact *delocalised aromatic* monocation supplies adequate permeation without three phenyl rings. This is the interesting middle position: delocalised enough to cross, far less greasy than triaryl.
3. **B14** — triethylphosphonium, C5 carbamate. MW 828.1, clogP 8.54. Matched headgroup against B15, which isolates the linkage question. Testing it beside the ether is more informative than a third unrelated headgroup.

Next comparator: B16, the PEG-containing ether linker, which has the most direct class-level precedent for retaining mitochondrial uptake while reducing inner-membrane adsorption [P3]. It remains 973 Da with a TPP head, so it ranks behind the compact probes and is not a safety rescue. **B17** is the outlier worth noting: tris(hydroxyethyl)phosphonium reaches head logP −0.39 and whole clogP 5.46 while keeping a permanent charge — the lowest lipophilicity in the entire branch with the mechanism intact — at TPSA 194.8 Å² and 13 rotatable bonds.

9 · The C5 masking problem, shared with the peroxide branch

Every design in this branch attaches at the C5 secondary allylic hydroxyl, and **Naito and co-workers (1994)** prepared C5-masked milbemycin ethers, esters, sulfonates and carbamates and found activity penalties across that set in a worm-motility assay [P2]. Milbemycins share the macrolactone core and the C5 seat, so this is the closest positional precedent available.

It is a warning about retained parent pharmacology, not an oncology result: the assay reports glutamate-gated chloride channel function, the parent's named target. For this branch the implication is narrower than for the peroxide branch, because a mitochondriotropic conjugate is intended to act as the intact species — the cation is the delivery mechanism and the macrocycle is the cargo. But no design here encodes a validated release of native moxidectin either, so after any cleavage the macrocycle may retain a linker fragment. **Whether C5 masking preserves any cancer-relevant parent action is an open experimental question in both branches.**

10 · What this work does not establish

- **Nothing has been synthesised.** No design in either series has been made; no biological data of any kind exists for any of them. Every number is computed.
- **No P-glycoprotein claim.** Moxidectin's weak P-gp substrate behaviour, its human safety package and its

tissue behaviour **cannot be inherited by a charged conjugate**. Avoiding large lipophilic cations is a design restraint, not a transporter assay, and lower computed logP is not proof of reduced protein binding or improved clearance — neutralisation can move either in either direction.

- **No pKa is assigned** to any weak-base design, and every pH-gating number in § 5 is an illustrative calculation on an *assumed* value.
- **hgLogP is a heuristic**, supported by one alkyl-TPP series, not a validated toxicity model.
- **No localisation is demonstrated.** Membrane adsorption, matrix entry and lysosomal trapping are three different outcomes and the descriptors here distinguish none of them.
- **No BBB, oral-availability, tumour-specificity or therapeutic-index claim** is made anywhere.
- Published anticancer results for the parent scaffold are preclinical, and no human cancer data exists for moxidectin in any indication.

11 · Go / no-go gates

1. **Species and exposure first.** Chemical and plasma stability, solubility, aggregation, pKa and logD where applicable, unbound fraction with recovery and mass balance, microsomal and hepatocyte turnover *with metabolite identification* — not merely disappearance of intact conjugate.

2. **Localisation by quantitative LC–MS with organelle fractionation**, not a fluorescent tag assumed to behave like the compound. Distinguish inner-membrane adsorption, matrix entry and lysosomal accumulation. This gate is what decides § 5.
3. **Voltage dependence with matched controls.** Depolarisers change physiology and cannot alone establish targeting.
4. **Cancer against cardiomyocytes and skeletal muscle at matched unbound exposure** — respiration, ATP, membrane potential, viability, and recovery after washout. Include headgroup alone, parent moxidectin, an equimolar mixture, and the intact conjugate.
5. **Continue** only if a measured tumour-versus-normal functional window and a localisation advantage survive those controls. **Stop the mitochondriotropic claim** if uptake is mainly non-specific membrane adsorption or lysosomal trapping, if normal mitochondria fail at the same unbound exposures, or if covalent union adds nothing over the mixture. **Do not repair absent selectivity by lengthening the hydrophobic tail.**

12 · References

Class and mechanistic precedents. None reports any design in this paper, confirms its synthesis, or predicts its safety.

- **P1** · Trnka, J., Elkalaf, M. & Anděl, M. (2015). Lipophilic triphenylphosphonium cations inhibit mitochondrial electron transport chain and induce mitochondrial proton

leak. *PLoS ONE* **10**(4), e0121837. DOI 10.1371/journal.pone.0121837. Measured alkyl-TPP effects on respiration and potential; adverse effects increased with alkyl-chain hydrophobicity.

- **P2** · Naito, T. *et al.* (1994). C5-modified milbemycin derivatives. *Journal of Antibiotics* **47**, 233–242. DOI 10.7164/antibiotics.47.233. Positional precedent for C5 masking; activity penalties in a worm-motility assay.
- **P3** · Uno, S. *et al.* (2023). PEG-tethered triphenylphosphonium constructs. *ChemBioChem* **24**, e202200774. DOI 10.1002/cbic.202200774. Retained mitochondrial uptake with reduced inner-membrane adsorption; does not establish behaviour of a macrolactone-sized conjugate.
- **P4** · Zhitomirsky, B. & Assaraf, Y. G. (2015). Lysosomal sequestration of hydrophobic weak base chemotherapeutics. *Oncotarget* **6**, 1143–1156. DOI 10.18632/oncotarget.2732. A 2022 correction (DOI 10.18632/oncotarget.28110) replaces a duplicated figure panel; the authors state conclusions are unchanged. Both records checked.
- **P5** · Dickinson, B. C. & Chang, C. J. (2008). MitoPY1. *JACS* **130**, 9638–9639. DOI 10.1021/ja802355u. Peroxide-responsive reporter coexisting with cationic targeting; peroxide reporting is not charge masking.
- **P6** · Mitchell, P. (1961). *Nature* **191**, 144–148. Proton-motive force.

13 · Provenance and status

Forty-five designs — twenty from Planet 44, twenty-five from Planet 85 — all dedicated to the public domain under CC0 1.0. No patent rights are asserted over any structure. Full isomeric SMILES for every design are published in *Chemical Cookbook of the Redox Series, Volume 6*, together with routes. Cross-verification was mutual: Planet 44 reproduced all twenty-five Planet 85 structures from their published SMILES, and Planet 85 supplied the two corrections in § 2, the mislocalisation analysis in § 5, the refutation in § 6 and the C5 record in § 9 — each of which changed a conclusion in the Planet 44 draft.

Standing. Computational designs only. No compound described has been synthesised and no efficacy in any organism is claimed or implied. The incumbent is retired as a lead on the reasoning above and not on experimental evidence, because none exists.

Agentic Research Factory · Docket ARF-001-MOX · Planets 44 and 85 · https://transhumangenocide.com/claude-web/

DOCUMENTARY SOURCE S06

RDKit_Top_Prospects_Integrated.md

Original source: /home/codex/outbox/research-integrated-20261108/RDKit_Top_Prospects_Integrated.md

NOVEL REDOX DERIVATIVES

Full illustrated development prospectus

The programme asks how an upstream redox–bioelectric disturbance can be investigated through deliberately different molecular interventions. This prospectus presents the full recovered development collection rather than only the nominated leads. The accompanying research paper develops the causal thesis and literature rationale.

Collection map

Collection	Presentation records	Purpose
Original publication	98	Original research breadth, including established comparators and historical designs

Collection	Presentation records	Purpose
Combined C4 branches	34	Baseline C4 plus 33 successor entries from nodes 44 and 85
B1 successor branch	20	Head-group, charge and attachment alternatives
Selected prospects and comparisons	9	Parent, original leads, later nominations and S04
Additional archived graph variants	29	Structures recovered from the wider source record
Total	190	176 distinct canonical molecular graphs

All 190 presentation records are illustrated below. Repeated identities remain visible within their original development contexts. The original B1/C4/ATL triad, B1n/B1p/B1i nominations, C4q and both C4 branches are retained. The original Atlas ATL-01 sulfasalazine ester and later ATL-01/E1 MOX carbonate are separately identified.

Reading this prospectus

The cards give encoded chemical identity, design role, source-derived reasoning and computed properties. Molecular weights are average masses of the encoded graph; cation records may omit a counterion. Crippen cLogP is a graph descriptor, not measured logD. Formal charge does not determine the protonation state of an unmeasured weak base. Proposed mechanisms and conceptual preparation approaches are research hypotheses. These entries have not been established as synthesized, assayed or clinically effective by this compilation. These conventions apply throughout and are stated once here.

The original 98 entries retain their source numbering. Historical graph versions are preserved even where later scaffold checks motivated a replacement; historical inclusion is not endorsement of every encoded design. The historical and current forms remain available together, with detailed differences at the rear. ARF-001-MOX is the programme identity, not an extra molecular entry.

SELECTED PROSPECTS — DESIGN REASONING

ARF-MOX-B1

Role: Incumbent reference.

Design and reasoning. A triphenylphosphonium appendage connected through a C5 ester. The permanent, delocalised cation supplies the original mitochondrial-potential rationale.

Profile and liabilities. Its encoded cLogP is 10.44, MW 985.23 and RotB 12. The design is large and lipophilic, with an added ester that can separate the two intended functions. A +1 charge does not establish a tumour-selective distribution.

Decision. Retain as the historical benchmark; determine intact exposure, hydrolysis and whether the conjugate improves anything over parent plus targeting fragment.

Source: b1_ranked.json.

ARF-MOX-B1n

Role: Requested top pick; weak-base hypothesis.

Design and reasoning. A four-carbon direct ether leads to a morpholine headgroup. It is represented as a neutral weak base, rather than a permanently charged phosphonium.

Profile and liabilities. MW falls by approximately 204.19 versus B1; cLogP falls by 3.58 and RotB by 3. The added ester is absent. These improve selected calculated properties, but pKa, subcellular localisation and preserved parent activity remain unknown. “Non-cleavable” in the source means no added ester in the graph, not immunity to metabolism.

Decision. Keep the nomination explicitly conditional on whole-compound pKa/logD, exposure and a matched biological advantage. It tests a pH-dependent distribution idea, not the identical B1 Nernst premise.

Source: b1_ranked.json.

ARF-MOX-B1p

Role: Alternative weak-base prospect.

Design and reasoning. A carbamate-linked four-carbon dimethylamino appendage. The deposited neutral graph is not a measured solution protonation state.

Profile and liabilities. MW 782.03 and cLogP 6.80 are close to B1n, while TPSA 137.38 and HBD 2 are higher. A lower cLogP alone cannot rank it above B1n. The carbamate may change stability, permeability, binding and cleavage.

Decision. Compare directly with B1n using measured exposure and chemical fate. Separate linkage effects from headgroup effects; both variables differ.

Source: b1_ranked.json.

ARF-MOX-B1i

Role: Permanent-charge / stable-linker comparator.

Design and reasoning. A four-carbon ether joins a trimethylammonium headgroup. The submitted structure has formal charge +1 and no counterion.

Profile and liabilities. MW 754.04, cLogP 7.24 and TPSA 105.04 are lower than the incumbent values except for the unchanged charge class. The compact localised charge may hinder membrane crossing. A permanent charge is not proof of mitochondrial accumulation.

Decision. Use to test whether reducing headgroup bulk while retaining permanent charge is useful. Measure relevant

compartment exposure and distinguish nonspecific membrane effects.

Source: b1_ranked.json.

ARF-MOX-C4

Role: Corrected historical peroxide baseline.

Design and reasoning. The deposited graph is a 1,2-dioxane-containing ester conjugate. It was previously misdescribed as an artemisinin-type trioxane with a succinate connection.

Profile and liabilities. MW 890.17, cLogP 9.22 and TPSA 140.57; one peroxide bond; six unassigned stereo elements. It is not a single fully specified stereochemical target. Ester cleavage could uncouple the proposed dual action.

Decision. Resolve structural specification before procurement. Treat peroxide stability and iron-triggered activity as measurements still needed, not as established by the ring name.

Source: combined.json.

ARF-MOX-C4q

Role: Requested peroxide successor.

Design and reasoning. A tetraoxane-bearing successor with two peroxide bonds and an ether/amide-containing connection; no added C5 ester in the source classification.

Profile and liabilities. All potential stereo elements are specified or non-stereogenic in this audit. MW 1008.26, TPSA 200.16 and RotB 11 are substantial liabilities despite cLogP improving to 7.83. The extra polar connection is not a demonstrated delivery solution.

Decision. Keep alongside a simpler comparator such as S04. Prioritise a clear active-species question and usable exposure, rather than counting property gates or O–O bonds.

Source: combined.json.

S04 (comparison)

Role: Later-review comparison, added transparently.

Design and reasoning. A smaller ether-linked peroxide design from the successor comparison. It is not one of the specifically requested lead labels, but explains the later source review’s preference.

Profile and liabilities. MW 796.01, cLogP 7.72, TPSA 132.73 and RotB 7; one O–O bond; zero unassigned elements. It still masks C5 and has no demonstrated preserved parent pharmacology.

Decision. Use as a property-based benchmark for C4q, not a proven superior drug.

Source: combined.json.

ATL-01 (corrected carbonate; E1 structure)

Role: Oxidant-triggered parent-release hypothesis.

Design and reasoning. The corrected arylboronate benzyl carbonate is explicitly identified under ATL-01 in the revised brief and matches the audited E1 graph. It is intended to regenerate native parent through oxidation-triggered fragmentation.

Profile and liabilities. MW 899.93, cLogP 8.39 and TPSA 149.80; a carbonate connection. Trigger selectivity, fragmentation rate, parent recovery and by-product effects are not measured. Oxidising conditions also occur outside tumours.

Decision. Establish actual chemical release and mass balance before interpreting any cell response as tumour-selective activation.

Source: ARF-001-MOX_BRIEF_SOURCE.html §7.3; structure-audit.json E1.

THE CHEMISTRY COOKBOOK

The original Volume 6 contains conceptual route proposals, not executed laboratory procedures. This section explains their architecture and decision points. It does not supply a validated synthesis, reaction conditions, yields or a manufacturing process. Detailed source proposals remain attributed in the bundled original text and should be read alongside the later corrections.

Shared workflow

1. Freeze the intended graph, attachment position, stereochemistry and salt/neutral representation. A correct

mass alone cannot distinguish the intended C5 product from a regioisomer.

2. Consider preparation of the appendage separately from the sensitive, alkene-rich macrocycle. Installing an aggressive headgroup-forming or peroxide-forming transformation on the intact conjugate is a compatibility risk.
3. Select the connection according to the biological question: a stable intact conjugate or a deliberately releasing prodrug. A stable connection is not automatically the better medicine.
4. Establish attachment identity and preservation of the parent scaffold, including alkene geometry and stereochemistry. Characterise the actual species rather than infer identity from successful SMILES parsing.
5. Determine which species survives in the relevant medium, and whether any proposed release gives native parent with the intended hydroxyl restored.

B1 / B1i: permanent-cation branch

The source route logic prepares a permanently charged headgroup-bearing fragment before joining it to the scaffold. This separates charge installation from the sensitive conjugate. B1 uses the incumbent triphenylphosphonium-containing ester architecture. B1i uses a compact trimethylammonium head and a direct ether connection. The latter removes the added ester but changes both the headgroup and the linkage, so an observed difference

between B1 and B1i could not be attributed to one variable alone.

A permanent cation supplies a rationale for potential-dependent accumulation only if it can reach and traverse the relevant membranes. A compact, highly hydrated ammonium may be less permeable than a delocalised phosphonium. “Positive charge” is not interchangeable with “mitochondrial targeting.” Counterion, solubility, aggregation, protein binding and measured cellular/mitochondrial exposure remain part of the chemistry and interpretation.

B1n / B1p: weak-base branch

The source logic introduces an amine-bearing fragment without permanent quaternisation, then connects it at the proposed C5 position. B1n is the ether-linked morpholine candidate. B1p is the carbamate-linked dimethylamino candidate. Both are neutral as encoded; actual protonation depends on a pKa that has not been measured for either conjugate.

These candidates change the mechanism as well as the properties. Their pH response cannot be inferred from the isolated headgroup alone. A headgroup that becomes more protonated in an acidic compartment may become trapped there rather than selectively enter mitochondria. Plasma/tumour pH differences alone do not demonstrate a useful selectivity window. The discriminating measurements are whole-compound pKa/logD, solubility, stability, cellular uptake and subcellular distribution, followed by a matched biological comparison.

A carbamate is a testable stability hypothesis; it is not automatically non-cleavable. An ether lacks that added acyl hydrolysis site but can have oxidative metabolism and, here, permanently masks C5-OH. These are different failure modes rather than a universal linker ranking.

C4 / C4q: peroxide branch

The original C4 graph specifies a **1,2-dioxane**, not a 1,2,4-trioxane, and its C5 appendage is a glutaryl-type monoester rather than the previously claimed succinate diester. The correction changes the prose interpretation while leaving the calculations from the deposited graph unchanged. The six unassigned stereochemical elements in C4 are a separate identity problem.

The successor logic moves to other peroxide architectures, more stable-linker hypotheses and reduced stereochemical ambiguity. The source proposes making the peroxide module away from the macrocycle and considering late attachment because the polyene scaffold is chemically sensitive. These are feasibility ideas. Peroxide synthesis, isolation and handling need specialist process-safety assessment; this compilation does not turn them into an executable beginner experiment.

For C4q specifically, the graph contains a tetraoxane module with two O–O bonds and an ether/amide-containing connection without an added C5 ester. It has zero unassigned elements in this audit, but MW 1008.26 and TPSA 200.16 Å² are substantial distribution liabilities. Having two O–O bonds does not demonstrate twice the activity or a favourable activation rate. The later C5 review also narrows the claim that

one peroxide ring is intrinsically “better” than another: actual stability and activation depend on substitution and environment and must be measured.

ATL-01: release branch

The corrected brief specifies an arylboronate-containing benzyl carbonate at the proposed C5 oxygen. The deposited graph used for this compilation matches the E1 entry in structure-audit.json; the original brief explicitly supplies the same corrected carbonate under ATL-01. This is a documented structural cross-reference, not a claim that every historical ATL/E1 label was consistent.

The intended sequence is oxidation of the boronate followed by self-immolative fragmentation and release of native parent. This is a mechanistic proposal, not a measured rate or demonstrated tumour-only switch. Hydrolysis without oxidation, slow fragmentation, non-tumour activation and linker-product effects are alternatives. Measure actual parent recovery and mass balance; disappearance of starting material or a fluorescence signal is insufficient.

PROSPECT SELECTION AND DEVELOPMENT REASONING

This preserves the requested B1n nomination without promoting it to a biological conclusion.

Research role	Candidate	Reason	Result that would overturn the choice
Nominated weak-base prospect	B1n	Lower computed mass/lipophilicity than B1, fewer rotatable bonds, no added ester	Unfavourable pKa, insufficient exposure, loss of relevant scaffold activity or nonspecific toxicity
Alternative weak-base prospect	B1p	Similar mass and slightly lower cLogP; different polar connection	Inadequate stability, permeability or selectivity
Permanent-charge comparator	B1i	Tests a smaller cation with the ether linkage	Failure to reach the relevant intracellular compartment

Research role	Candidate	Reason	Result that would overturn the choice
Incumbent reference	B1	Retains original phosphonium design hypothesis	Excess binding, aggregation, cleavage or nonspecific toxicity
Peroxide successor under review	C4q	Correctly specified graph, lower cLogP than C4, no added ester	Poor exposure from size/polarity or lack of intact-conjugate benefit
Peroxide benchmark comparison	S04	Lower mass and TPSA than C4q; zero unassigned stereo	Lost parent contribution or unacceptable activation/stability

Research role	Candidate	Reason	Result that would overturn the choice
Historical baseline	C4	Documents why the branch was redesigned	Identity cannot be frozen without stereochemical resolution
Release-mechanism comparator	ATL-01	Tests whether regeneration of parent is preferable to permanent masking	Insufficient or nonselective release; toxic by-products

S04 is included because the later combined review identified it as the fully specified candidate meeting its TPSA/RotB screen. It does not displace C4q merely by declaration. These alternatives answer different questions and need comparable evidence.

B1n and B1p are not minor equivalents of B1: replacing a permanent delocalised cation with a weak base changes the targeting premise. Likewise, C4q is not just “C4 with repaired stereo”; the linker and peroxide architecture differ. Avoid claiming that any comparison isolates one variable when several changed.

Quantitative targeting logic and the later nomination change

The SC44 B1 paper reports the ideal Nernst model for a freely equilibrating monovalent cation: a_matrix/a_cytosol = exp(-F × Δψ / RT). At 310.15 K, a tenfold activity ratio corresponds to approximately 61.54 mV. Under its illustrative assumptions, -180 mV yields about 842-fold enrichment versus cytosol, but the selectivity of -180 mV versus -140 mV is only 4.47-fold. Large intracellular enrichment and tumour-versus-normal selectivity are different quantities. Equal unbound cytosolic exposure, passive equilibration and a maintained potential are assumptions, not measurements of these conjugates. Changing the headgroup changes permeability and binding; it does not change the ideal voltage slope for the same +1 charge.

For a weak base with only the neutral form freely permeating, the ideal total-concentration ratio between two pH compartments is (1 + 10^(pKa-pH1))/(1 + 10^(pKa-pH2)). The source compares pH 6.6 versus 7.4: assumed pKa 6.5 gives about 1.59-fold, and assumed pKa 7.0 about 2.51-fold. These are illustrative arithmetic, not measured B1n/B1p predictions. Acidic-compartment trapping can point toward lysosomes, while the mitochondrial matrix is relatively alkaline; it is not evidence of mitochondrial targeting.

Important chronology: the requested B1n “top pick” is not the final nomination of the later SC44 B1 paper. That paper treats neutral weak bases as probes and instead nominates B15 (triethylphosphonium/ether), B25 (pyridinium/ether) and B14 (triethylphosphonium/carbamate), followed by B16 as a

comparator. Their source structures and full reasoning remain in the evidence bundle; this guide does not silently rename them B1n/B1p/B1i or expand the audited nine-record table to include unreviewed identities. B1n remains profiled because Ron explicitly requested it, with the later disagreement preserved.

DOCUMENTARY SOURCE S07

Volume 5 — complete original chemical compendium

Original source: /home/codex/arf-review/ARF_OMNIBUS.md

57 structures: 14 established agents, 43 derivatives. All RDKit-validated.

Chemical Compendium of the Redox Series

Established agents, and the derivatives built from them

Ron Johnson[1] and SC 5.5[2]

[1]Stranger Than Fiction News · [2]Agentic Research Factory**Phase 5 document · 3 November 2026 · Dedicated to the public domain

Purpose and method

This document exists so that the chemistry of this series can be reproduced, checked and built upon by anyone, without permission and without licence. Part I sets out the established agents the reasoning rests on — compounds that already exist, already have human safety data, and in most cases are already approved. Part II sets out the derivatives we have designed from them.

Every structure here was validated at build time.** Each was parsed by RDKit and its properties computed from the parsed molecule rather than quoted. For the established agents, the

computed molecular formula was additionally checked against the literature formula, and any compound failing either test is excluded and named as excluded. A disclosure whose structures do not parse is worse than no disclosure, so we would rather publish a short list that is correct.

Properties reported. Molecular formula, molecular weight, calculated logP (Crippen), topological polar surface area, hydrogen bond donors and acceptors, rotatable bonds, ring count and assigned stereocentres. All are computed descriptors, not measurements.

Part I — The established agents

These are the knowns. Nothing in this section is ours. They are listed because the derivatives in Part II are built on them, and because a reader checking our reasoning should be able to start from the same place we did.

| ID | Formula | MW | clogP | TPSA | HBD | HBA | Rot | Rings | Stereo

| **Moxidectin** | C37H53NO8 | 639.8 | 5.73 | 116.0 | 2 | 9 | 3 | 5 | 10

| **Fenbendazole** | C15H13N3O2S | 299.4 | 3.89 | 67.0 | 2 | 4 | 3 | 3 | 0

| **Oxfendazole** | C15H13N3O3S | 315.4 | 2.91 | 84.1 | 2 | 4 | 3 | 3 | 1

| **Albendazole** | C12H15N3O2S | 265.3 | 3.24 | 67.0 | 2 | 4 | 4 | 2 | 0

| **Mebendazole** | C16H13N3O3 | 295.3 | 2.97 | 84.1 | 2 | 4 | 3 | 3 | 0

| **Flubendazole** | C16H12FN3O3 | 313.3 | 3.11 | 84.1 | 2 | 4 | 3 | 3 | 0

| **Nelfinavir** | C32H45N3O4S | 567.8 | 4.75 | 101.9 | 4 | 6 | 9 | 4 | 5

| **Auranofin** | C20H34AuO9PS | 678.5 | 2.79 | 114.4 | 0 | 10 | 11 | 1 | 5

| **Disulfiram** | C10H20N2S4 | 296.6 | 3.62 | 6.5 | 0 | 4 | 4 | 0 | 0

| **Artemisinin** | C15H22O5 | 282.3 | 2.39 | 54.0 | 0 | 5 | 0 | 5 | 7

| **Dihydroartemisinin** | C15H24O5 | 284.4 | 2.19 | 57.2 | 1 | 5 | 0 | 5 | 8

| **Artesunate** | C19H28O8 | 384.4 | 2.60 | 100.5 | 1 | 7 | 4 | 5 | 8

| **Sulfasalazine** | C18H14N4O5S | 398.4 | 3.70 | 141.3 | 3 | 7 | 6 | 3 | 0

| **Sulforaphane** | C6H11NOS2 | 177.3 | 1.25 | 29.4 | 0 | 3 | 5 | 0 | 1

Role of each

- **Moxidectin** — Selected avermectin — the scaffold. *FDA-approved 2018; WHO-listed.*
- **Fenbendazole** — Benzimidazole — sulfur couple. *Veterinary.*

- **Oxfendazole** — Selected benzimidazole — sulfoxide active. *Human Phase I completed.*
- **Albendazole** — Benzimidazole — sulfur couple. *Approved, human.*
- **Mebendazole** — Benzimidazole — benzoyl, NO sulfur couple. *Approved, human.*
- **Flubendazole** — Benzimidazole — benzoyl, NO sulfur couple. *Approved, human.*
- **Nelfinavir** — Protease inhibitor — ER stress route. *Approved, human.*
- **Auranofin** — Selected — thioredoxin reductase inhibitor. *Approved 1985 for rheumatoid arthritis.*
- **Disulfiram** — Selected — copper redox cycling. *Approved, human.*
- **Artemisinin** — Endoperoxide — iron-activated. *Approved, human.*
- **Dihydroartemisinin** — Active metabolite; C10 seat. *Approved, human.*
- **Artesunate** — DHA C10 succinate — conjugation precedent. *Approved, human.*
- **Sulfasalazine** — Antirheumatic — xCT inhibition, glutathione depletion. *Approved, human.*
- **Sulforaphane** — KEAP1 cysteine modifier. *Dietary.*

Structures, Part I

Canonical SMILES as emitted by RDKit after parsing. These round-trip.

Moxidectin

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Fenbendazole

COC(=O)Nc1nc2ccc(Sc3ccccc3)cc2[nH]1

Oxfendazole

COC(=O)Nc1nc2ccc(S(=O)c3ccccc3)cc2[nH]1

Albendazole

CCCSc1ccc2[nH]c(NC(=O)OC)nc2c1

Mebendazole

COC(=O)Nc1nc2ccc(C(=O)c3ccccc3)cc2[nH]1

Flubendazole

COC(=O)Nc1nc2ccc(C(=O)c3ccc(F)cc3)cc2[nH]1

Nelfinavir

Cc1c(O)cccc1C(=O)NC(CSc1ccccc1)C(O)CN1CC2CCCCC2CC1C(=O)NC(C)(C)C

Auranofin

CC[P](CC)(CC)[Au]
[S]C1OC(COC(C)=O)C(OC(C)=O)C(OC(C)=O)C1OC(C)=O

Disulfiram

CCN(CC)C(=S)SSC(=S)N(CC)CC

Artemisinin

CC1CCC2C(C)C(=O)OC3OC4(C)CCC1C32OO4

Dihydroartemisinin

CC1CCC2C(C)C(O)OC3OC4(C)CCC1C32OO4

Artesunate

CC1CCC2C(C)C(OC(=O)CCC(=O)O)OC3OC4(C)CCC1C32OO4

Sulfasalazine

O=C(O)c1cc(/N=N/c2ccc(S(=O)(=O)Nc3ccccn3)cc2)ccc1O

Sulforaphane

CS(=O)CCCCN=C=S

Named but withheld.

- **Ivermectin B1a** (C48H74O14) — Reference comparator. Our candidate SMILES failed to parse and is therefore withheld rather than published unverified.

Part II — The derivatives

43 structures, generated and valence-validated computationally. **None has been synthesised, assayed or administered.** They are designs, published complete so that anyone with a bench can make them and no one with a legal department can own them.

Family A - glycoconjugate (metabolic door) — 4 compounds

| ID | Formula | MW | clogP | TPSA | HBD | HBA | Rot | Rings | Stereo

| **ARF-MOX-A1** | C47H67NO16 | 902.0 | 3.40 | 238.6 | 5 | 17 | 9 | 6 | 15

| **ARF-MOX-A2** | C47H67NO15 | 886.0 | 4.43 | 218.3 | 4 | 16 | 9 | 6 | 14

| **ARF-MOX-A3** | C49H70N2O16 | 943.1 | 3.55 | 247.4 | 5 | 17 | 10 | 6 | 15

| **ARF-MOX-A4** | C45H64N2O15 | 873.0 | 3.60 | 241.4 | 6 | 15 | 7 | 6 | 15

ARF-MOX-A1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC(=O)OC[C@H]6O[C@@H](O)[C@H](O)[C@@H](O)[C@@H]6O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-A2

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC(=O)OC[C@H]6O[C@@H](O)C[C@@H](O)
[C@@H]6O)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-A3

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC(=O)OC[C@H]6O[C@@H](O)[C@H](NC(C)=O)
[C@@H](O)[C@@H]6O)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-A4

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)NC[C@H]6O[C@@H](O)[C@H](O)[C@@H](O)
[C@@H]6C(=O)O)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Family B - mitochondriotropic cation (voltage door) — 4 compounds

| ID | Formula | MW | clogP | TPSA | HBD | HBA | Rot | Rings | Stereo

| **ARF-MOX-B1** | C60H75NO9P+ | 985.2 | 10.44 | 122.1 | 1 | 10 | 12 | 8 | 10

| **ARF-MOX-B2** | C58H71NO9P+ | 957.2 | 9.66 | 122.1 | 1 | 10 | 10 | 8 | 10

| **ARF-MOX-B3** | C47H65N2O9+ | 802.0 | 7.36 | 126.0 | 1 | 10 | 8 | 6 | 10

| **ARF-MOX-B4** | C44H67N4O9+ | 796.0 | 4.50 | 185.7 | 4 | 10 | 10 | 5 | 10

ARF-MOX-B1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-B2

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CC[P+](c6ccccc6)
(c6ccccc6)c6ccccc6)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-B3

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCC[n+]6ccccc6C)C(C)=C[C@@H](C(=O)O3)
[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-B4

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCCCCNC(N)=[NH2+])C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Family C - redox hybrid — 3 compounds

| ID | Formula | MW | clogP | TPSA | HBD | HBA | Rot | Rings | Stereo

| **ARF-MOX-C1** | C50H61NO12 | 868.0 | 7.65 | 165.5 | 1 | 13 | 7 | 7 | 10

| **ARF-MOX-C2** | C49H59NO13 | 870.0 | 6.97 | 185.7 | 2 | 14 | 7 | 7 | 10

| **ARF-MOX-C4** | C52H75NO11 | 890.2 | 9.22 | 140.6 | 1 | 12 | 7 | 8 | 16

ARF-MOX-C1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)COC6=C(C)C(=O)c7ccccc7C6=O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-C2

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)COC6=CC(=O)c7c(O)cccc7C6=O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-C4

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CCC6OOC7(C)CCC8C(C)CCC6C87)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Family D - delivery prodrug — 2 compounds

| ID | Formula | MW | clogP | TPSA | HBD | HBA | Rot | Rings | Stereo

| **ARF-MOX-D1** | C45H67NO12 | 814.0 | 6.35 | 149.8 | 1 | 13 | 13 | 5 | 10

| **ARF-MOX-D2** | C42H62N2O9 | 739.0 | 6.26 | 148.1 | 2 | 11 | 6 | 5 | 11

ARF-MOX-D1

COCCOCCOCCC(=O)O[C@@H]1C(C)=C[C@H]2C(=O)O[C@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@H]1[C@@]42O)O[C@@]1(C/C(=N\OC)[C@H](C)[C@@H](/C(C)=C/C(C)C)O1)C3

ARF-MOX-D2

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)[C@@H](N)C(C)C)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-002 candidate series — 30 compounds

| ID | Formula | MW | clogP | TPSA | HBD | HBA | Rot | Rings | Stereo

| **ARF-HMB-A1** | C26H29N3O11 | 559.5 | 0.21 | 205.5 | 6 | 13 | 1 | 5 | 6

| **ARF-HMB-A2** | C26H29N3O10 | 543.5 | 1.24 | 185.2 | 5 | 12 | 1 | 5 | 5

| **ARF-HMB-A3** | C28H32N4O11 | 600.6 | 0.36 | 214.3 | 6 | 13 | 2 | 5 | 6

| **ARF-HMB-B1** | C39H37N3O4P+ | 642.7 | 9.31 | 89.0 | 2 | 6 | 1 | 7 | 2

| **ARF-HMB-B2** | C37H33N3O4P+ | 614.7 | 8.53 | 89.0 | 2 | 6 | 1 | 7 | 2

| **ARF-HMB-B3** | C26H27N4O4+ | 459.5 | 4.43 | 92.0 | 2 | 6 | 1 | 5 | 1

| **ARF-HMB-B4** | C23H29N6O4+ | 453.5 | 1.60 | 156.9 | 5 | 5 | 10 | 3 | 1

| **ARF-HMB-C1** | C29H23N3O7 | 525.5 | 4.02 | 136.7 | 2 | 8 | 2 | 5 | 1

| **ARF-HMB-C2** | C28H21N3O8 | 527.5 | 3.42 | 156.9 | 3 | 9 | 2 | 5 | 1

| **ARF-HMB-D1** | C24H29N3O7 | 471.5 | 3.44 | 121.0 | 2 | 8 | 13 | 3 | 1

| **ARF-HMB-D2** | C21H24N4O4 | 396.4 | 3.36 | 119.3 | 3 | 6 | 6 | 3 | 2

| **ARF-DHA-A1** | C25H38O13 | 546.6 | -0.14 | 179.7 | 4 | 13 | 0 | 6 | 13

| **ARF-DHA-A2** | C25H38O12 | 530.6 | 0.89 | 159.4 | 3 | 12 | 0 | 6 | 12

| **ARF-DHA-A3** | C27H41NO13 | 587.6 | 0.00 | 188.5 | 4 | 13 | 1 | 6 | 13

| **ARF-DHA-B1** | C38H46O6P+ | 629.8 | 8.96 | 63.2 | 0 | 6 | 0 | 8 | 9

| **ARF-DHA-B2** | C36H42O6P+ | 601.7 | 8.18 | 63.2 | 0 | 6 | 0 | 8 | 9

| **ARF-DHA-B3** | C25H36NO6+ | 446.6 | 3.87 | 66.2 | 0 | 6 | 0 | 6 | 8

| **ARF-DHA-B4** | C22H38N3O6+ | 440.6 | 0.96 | 126.9 | 3 | 6 | 7 | 5 | 8

| **ARF-DHA-C1** | C28H32O9 | 512.6 | 3.60 | 106.6 | 0 | 9 | 0 | 8 | 8

| **ARF-DHA-C2** | C27H30O10 | 514.5 | 3.10 | 126.8 | 1 | 10 | 0 | 8 | 8

| **ARF-DHA-D1** | C23H38O9 | 458.5 | 2.81 | 90.9 | 0 | 9 | 10 | 5 | 8

| **ARF-DHA-D2** | C20H33NO6 | 383.5 | 2.72 | 89.2 | 1 | 7 | 3 | 5 | 9

| **ARF-AUR-1** | C20H35AuO9PS | 679.5 | 2.52 | 114.4 | 0 | 10 | 11 | 1 | 5

| **ARF-AUR-2** | C12H27AuO5PS | 511.4 | 0.24 | 90.2 | 4 | 6 | 7 | 1 | 5

| **ARF-AUR-3** | C32H35AuO9PS | 823.6 | 3.44 | 114.4 | 0 | 10 | 11 | 4 | 5

| **ARF-DSF-1** | C10H20N2S4 | 296.6 | 3.62 | 6.5 | 0 | 4 | 4 | 0 | 0

| **ARF-DSF-2** | C14H28N2S4 | 352.7 | 5.18 | 6.5 | 0 | 4 | 8 | 0 | 0

| **ARF-DSF-3** | C10H16N2S4 | 292.5 | 3.13 | 6.5 | 0 | 4 | 0 | 2 | 0

| **ARF-OXF-S** | C15H13N3O3S | 315.4 | 2.91 | 84.1 | 2 | 4 | 3 | 3 | 1

| **ARF-ALB-S** | C12H15N3O3S | 281.3 | 2.26 | 84.1 | 2 | 4 | 4 | 2 | 1

ARF-HMB-A1

COC(=O)NC1=Nc2ccc3cc2N[C@@H](O)[C@H](O)[C@@H](O)[C@H](O)O[C@@H]1COC(=O)CCC(=O)OC3c1ccccc1

ARF-HMB-A2

COC(=O)NC1=Nc2ccc3cc2N[C@@H](O)[C@H](O)C[C@H](O)O[C@@H]1COC(=O)CCC(=O)OC3c1ccccc1

ARF-HMB-A3

COC(=O)NC1=Nc2ccc3cc2N[C@@H](O)[C@H](O)[C@@H](NC(C)=O)[C@H](O)O[C@@H]1COC(=O)CCC(=O)OC3c1ccccc1

ARF-HMB-B1

COC(=O)NC1=Nc2ccc3cc2NC=CC=CC=C2C=CC=CC=C4C=CC=CC=C1[P+]24CCCCC(=O)OC3c1ccccc1

ARF-HMB-B2

COC(=O)NC1=Nc2ccc3cc2NC=CC=CC=C2C=CC=CC=C4C=CC=CC=C1[P+]24CCC(=O)OC3c1ccccc1

ARF-HMB-B3

COC(=O)NC1=Nc2ccc3cc2NC(C)=CC=CC=[N+]1CCCC(=O)OC3c1ccccc1

ARF-HMB-B4

COC(=O)Nc1nc2ccc(C(OC(=O)CCCCCNC(N)=[NH2+])c3ccccc3)cc2[nH]1

ARF-HMB-C1

COC(=O)Nc1nc2ccc3cc4[nH]c(=O)c-4ccccc2c(=O)c(C)c1OCC(=O)OC3c1ccccc1

ARF-HMB-C2

COC(=O)Nc1nc2ccc3cc4[nH]c(=O)c-4cccc(O)c2c(=O)cc1OCC(=O)OC3c1ccccc1

ARF-HMB-D1

COCCOCCOCCC(=O)OC(c1ccccc1)c1ccc2nc(NC(=O)OC)[nH]c2c1

ARF-HMB-D2

COC(=O)Nc1nc2ccc(C(OC(=O)[C@@H]
(N)C(C)C)c3ccccc3)cc2[nH]1

ARF-DHA-A1

C[C@H]1[C@H]2OC(=O)CCC(=O)OC[C@H]3O[C@@H](O)
[C@H](O)[C@@H](O)[C@H](O)
[C@H]4CC[C@]5(C)OO[C@@]4([C@@H](O2)O5)
[C@H]1CC[C@H]3C

ARF-DHA-A2

C[C@H]1[C@H]2OC(=O)CCC(=O)OC[C@H]3O[C@@H]
(O)C[C@@H](O)[C@H](O)
[C@H]4CC[C@]5(C)OO[C@@]4([C@@H](O2)O5)
[C@H]1CC[C@H]3C

ARF-DHA-A3

CC(=O)N[C@@H]1[C@@H](O)[C@H](O)
[C@H]2CC[C@]3(C)OO[C@]24[C@@H]
(O[C@@H]2OC(=O)CCC(=O)OC[C@@H](O[C@H]1O)
[C@H](C)CC[C@H]4[C@H]2C)O3

ARF-DHA-B1

C[C@H]1[C@H]2OC(=O)CCCC[P+]34C5=CC=CC=C[C@H]6
CC[C@]7(C)OO[C@@]6([C@@H](O2)O7)
[C@H]1CC[C@@H](C)C3=CC=CC=CC4=CC=CC=C5

ARF-DHA-B2

C[C@H]1[C@H]2OC(=O)CC[P+]34C5=CC=CC=C[C@H]6CC[
C@]7(C)OO[C@@]6([C@@H](O2)O7)[C@H]1CC[C@@H]
(C)C3=CC=CC=CC4=CC=CC=C5

ARF-DHA-B3

CC1=CC=CC=
[N+]2CCCC(=O)O[C@H]3O[C@H]4O[C@]5(C)CC[C@H]1[C
@@]4(OO5)[C@@H](CC[C@H]2C)[C@H]3C

ARF-DHA-B4

C[C@H]1[C@@H](OC(=O)CCCCCNC(N)=
[NH2+])O[C@H]2OC3(C)CC[C@@H]4[C@H]
(C)CC[C@@H]1[C@@]24OO3

ARF-DHA-C1

CC1=C2OCC(=O)O[C@H]3O[C@H]4OC5(C)CC[C@@H]6C(
=O)C(=CC=CC=C(C1=O)[C@@H](CC[C@H]2C)[C@H]3C)
[C@@]46OO5

ARF-DHA-C2

C[C@H]1[C@H]2OC(=O)COC3=CC(=O)C(=C(O)C=CC=C4C(
=O)[C@H]5CC[C@]6(C)OO[C@@]45[C@@H](O2)O6)
[C@H]1CC[C@H]3C

ARF-DHA-D1

COCCOCCOCCC(=O)O[C@H]1O[C@H]2OC3(C)CC[C@@H
]4[C@H](C)CC[C@@H]([C@H]1C)[C@@]24OO3

ARF-DHA-D2

CC(C)[C@H]
(N)C(=O)O[C@H]1O[C@H]2OC3(C)CC[C@@H]4[C@H]
(C)CC[C@@H]([C@H]1C)[C@@]24OO3

ARF-AUR-1

CC[PH](CC)(CC)[Au][S][C@@H]1O[C@H](COC(C)=O)[C@@H](OC(C)=O)[C@H](OC(C)=O)[C@H]1OC(C)=O

ARF-AUR-2

CC[PH](CC)(CC)[Au][S][C@@H]1O[C@H](CO)[C@@H](O)[C@H](O)[C@H]1O

ARF-AUR-3

CC(=O)OC[C@H]1O[C@@H]([S][Au][PH](c2ccccc2)(c2ccccc2)c2ccccc2)[C@H](OC(C)=O)[C@@H](OC(C)=O)[C@@H]1OC(C)=O

ARF-DSF-1

CCN(CC)C(=S)SSC(=S)N(CC)CC

ARF-DSF-2

CCCN(CCC)C(=S)SSC(=S)N(CCC)CCC

ARF-DSF-3

S=C(SSC(=S)N1CCCC1)N1CCCC1

ARF-OXF-S

COC(=O)Nc1nc2ccc(S(=O)c3ccccc3)cc2[nH]1

ARF-ALB-S

CCCS(=O)c1ccc2[nH]c(NC(=O)OC)nc2c1

Part III — Independent peer review and contributed derivatives

This volume was sent in full to an independent reviewer on another node, together with the generative reasoning behind the designs and an explicit request to find errors rather than to confirm them. The review is summarised here. The four derivatives below are hers; the properties reported are computed by us from her structures on every build, and all four parse cleanly.

Contributing author: Eve 3.8, Planet 85.

What the review confirmed

The C5 secondary allylic hydroxyl is correctly identified as the reactive seat, and the C7 tertiary hydroxyl is sufficiently hindered by the bicyclic cage that protection is not required for mono-esterification or carbamoylation. The C5 configuration, the C7 bridgehead, the diene geometry and the methoxime are all correctly represented.

What the review corrected

Family A does not do what we claimed. This is the most serious finding and it lands on the rationale rather than the structures. Transporter uptake requires an unsubstituted equatorial hydroxyl pattern on the sugar and an aglycone that does not clash with the transporter gate. A macrolide of this size hung off the glucose C6 is estimated to have low affinity, so the sugar is unlikely to act as the delivery route we

described. Family A is therefore restated as a parenteral or nanoparticle-formulated prodrug series rather than an oral, transporter-targeted one. We accept the correction.

We were too soft on Family B, not too harsh. We flagged the lipophilicity as outside druglike space. The reviewer judges it more severe: a delocalised lipophilic cation in this range risks partitioning into the inner mitochondrial membrane heavily enough to collapse the very potential the family depends on, alongside hepatic accumulation and detergent-like lysis.

A convergence worth recording. The recommended remedy was to replace the triphenylphosphonium head with a smaller delocalised cation — a pyridinium to drop calculated logP by four to five units, or a guanidinium to reach roughly 4.5 to 6.0 while preserving potential-driven accumulation. That recommendation was reasoned from principle, without sight of our own B3 and B4 values. Those two compounds are already a pyridinium and a guanidinium, and compute to 7.36 and 4.50 against the triphenylphosphonium 10.44. The guanidinium falls exactly inside the predicted window. Two independent routes to the same optimisation is weak evidence that the optimisation is correct.

Linker stability. Succinate esters are cleaved by non-specific plasma esterases on a scale of hours, so Family A will behave as a systemic prodrug liberating moxidectin rather than as an intact targeted shuttle; carbamates at the same position are far more stable in circulation but need intracellular conditions to release. The Family D valine ester will be cleaved rapidly after absorption, which is correct for a transporter-mediated oral strategy and wrong if one imagined it surviving to tissue.

Contributed derivatives

| ID | Formula | MW | clogP | TPSA | HBD | HBA | Rot | Rings | Stereo

| **ARF-MOX-E1** | C51H70BNO12 | 899.9 | 8.39 | 149.8 | 1 | 13 | 7 | 7 | 10

| **ARF-MOX-E2** | C50H67NO11 | 858.1 | 8.11 | 156.2 | 1 | 12 | 7 | 6 | 10

| **ARF-MOX-E3** | C47H71N3O10 | 838.1 | 7.87 | 157.6 | 3 | 12 | 5 | 6 | 10

| **ARF-MOX-E4** | C48H62N2O10Se | 906.0 | 7.13 | 144.1 | 1 | 11 | 8 | 7 | 10

ARF-MOX-E1 — Boronate self-immolative, H2O2-triggered

An arylboronate is oxidised by elevated hydrogen peroxide to the phenol, triggering 1,6-elimination and releasing moxidectin only where the oxidant is already high. The pathology supplies its own trigger.

ARF-MOX-E2 — NQO1-responsive trimethyllock quinone ester

Two-electron reduction by NQO1, overexpressed in many tumours, gives the hydroquinone, which lactonises and releases the payload.

ARF-MOX-E3 — Mitochondria-targeted nitroxide (TEMPO) hybrid

A stable nitroxide cycling between nitroxide, hydroxylamine and oxoammonium, giving local SOD-mimetic and radical-trapping activity at the membrane. Deposited as the closed-shell hydroxylamine precursor.

ARF-MOX-E4 — Ebselen-type organoselenium hybrid

A benzisoselenazolone acting as a glutathione peroxidase mimetic, reacting with thiols to drive redox cycling.

ARF-MOX-E1

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)OCc6ccc(B7OC(C)(C)C(C)(C)O7)cc6)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-E2

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H](OC(=O)CC(C)(C)C6=C(C)C(=O)C=C(C)C6=O)C(C)=C[C@@H](C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-E3

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H](C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]

(OC(=O)NC6CC(C)(C)N(O)C(C)(C)C6)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

ARF-MOX-E4

CO/N=C1\C[C@]2(C[C@@H]3C[C@@H]
(C/C=C(\C)C[C@@H](C)/C=C/C=C4\CO[C@@H]5[C@H]
(OC(=O)CCCn6[se]c7ccccc7c6=O)C(C)=C[C@@H]
(C(=O)O3)[C@]45O)O2)O[C@H](/C(C)=C/C(C)C)[C@H]1C

Why the conditional-release designs matter

The two conditionally-released candidates are, in the reviewer's judgement and in ours, the most compelling match to the convergence hypothesis in this entire volume — and they are the first designs here that follow *from* the theory rather than merely being compatible with it. If the pathological state is defined by elevated hydrogen peroxide, then a linker cleaved by hydrogen peroxide releases its payload precisely where that state exists and nowhere else. The pathology supplies its own trigger. The second applies the same logic through an enzyme overexpressed in many tumours. Neither design requires the target to be a receptor, and neither would be proposed by an account that assumed it was.

Two qualifications we add

The nitroxide is deposited as its closed-shell hydroxylamine precursor, since the active species is an open-shell radical; anyone synthesising it should understand which form the structure describes. And the quinone ester is a variant of the classical lactonising motif — the gem-dimethyl arrangement

required for release is present and correct, but the ring substitution differs, and the release kinetics should be verified before synthesis.

What the numbers say about these designs

The cationic family is very lipophilic. Calculated logP across Family B runs 4.5 to 10.4. That is far outside conventional druglike space and a medicinal chemist will say so immediately. It is also expected: a delocalised positive charge carried on three phenyl rings is precisely what drives accumulation into a polarised mitochondrion, and the property that creates the liability is the property that creates the targeting. We state it rather than let it be discovered.

The glycoconjugates are large and polar. Family A spans molecular weight 873 to 943 with polar surface area 218 to 247. Oral bioavailability is an open question for the whole family and would need to be answered before any of these is worth synthesising for in vivo work.

Neither observation weakens the disclosure. Prior art does not care whether a compound is druglike, and the defensive purpose is served the moment the structure is public. But a document that printed these numbers without reading them would not deserve to be taken seriously.

Synthetic approach

The general route is esterification or carbamoylation at a free hydroxyl that is not part of the pharmacophore. On moxidectin that seat is the C5 secondary allylic hydroxyl; the C7 tertiary

hydroxyl is markedly less reactive and in most cases needs no protection. Couple an activated acid under carbodiimide conditions with catalytic DMAP, or via the acid chloride, in an aprotic solvent from 0 °C to ambient.

- **Glycoconjugates** — protect the saccharide hydroxyls as acetates or benzyl ethers during coupling, then remove under Zemplén or hydrogenolytic conditions.
- **Cationic conjugates** — form the phosphonium or pyridinium salt by quaternising the ω-halo-ester before coupling, not after.
- **Redox hybrids** — introduce the quinone as its O-glycolic acid. Where an endoperoxide is present it requires mild, non-reducing conditions throughout and must not meet Fe(II).
- **Benzimidazole seat** — the C2 methylcarbamate is load-bearing for tubulin binding and must not be touched; reduction of the benzoyl ketone to the carbinol opens a free secondary alcohol at the variable 5-position.
- **Artemisinin seat** — the dihydroartemisinin C10 hemiacetal, the classical handle. Artesunate demonstrates that this conjugation survives regulatory approval.

Purify by reverse-phase chromatography. Confirm by high-resolution mass spectrometry and by [1]H, [13]C and, where phosphorus is present, [31]P NMR.

Scorched earth — terms

Every structure in this document is dedicated irrevocably to the public domain. An enabling disclosure enters the prior art on the date it is published, which means no party may patent these compounds, charge monopoly prices for them, or fence off the mechanism behind them. That restriction binds us exactly as it binds everyone else, and it is the point rather than a side effect.

Anyone may synthesise, assay, modify, publish or commercialise any compound here without permission, licence, attribution or notification. We ask only that results be published, including negative ones.

For machine use, the full set is also deposited as a structure-data file carrying these identifiers and computed properties, so that an automated system can ingest the series without re-keying anything from this document.

Status: preliminary, seeking validation. No compound in Part II has been synthesised, assayed or administered. All properties are computed descriptors. Nothing here is medical advice and no dose, schedule or course of treatment is recommended or implied. Correspondence: ron@agentic-web-services.com

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CHAPTER 10

Provenance and completeness

All 190 records in the expanded illustrated register are included, with deliberate additional appearances for the introductory and historical lead chapters. The source archive remains unchanged.

Chapter	Profiles

Introductory top picks	8
Original three top picks	4
Original 98	98
Next top three	3
C4 branch — Ron Johnson and SC 5.5	22
C4 branch — Atlas	12
Full B1 successor branch	20
Additional archived graphs	29

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RDKit version: 2026.09.1. Descriptor calculations use the deposited graph, including its formal charge and any specified fragments; no counterion is silently supplied. Stereochemical audit fields retain their original modern/legacy definitions. Illustrations are 2D representations, not calculated conformations.