Slide 15: Paclitaxel / other taxanes

Initial Task: BBBP

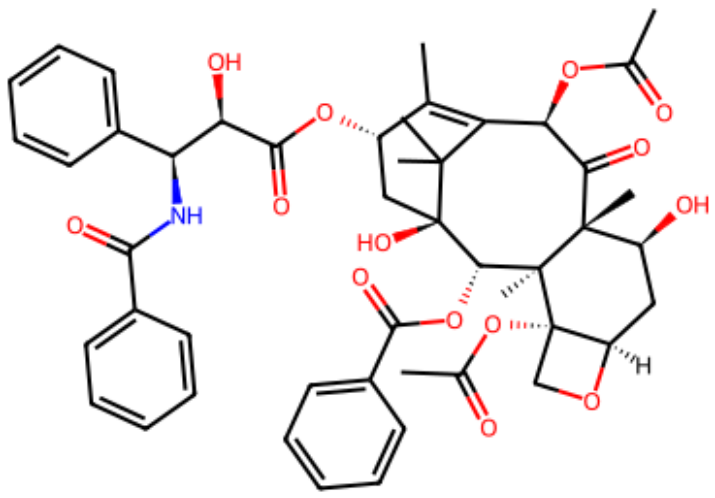
SMILES: `CC1=C2[C@H](C(=O)[C@]3(C)[C@H](C[C@@H]4[C@@](CO4)([C@@]3(C)[C@@H]([C@](C[C@@H]1OC(=O)[C@@H]([C@H](C5=CC=CC=C5)NC(=O)C6=CC=CC=C6)O)(C2(C)C)O)OC(=O)C7=CC=CC=C7)OC(=O)C)O)OC(=O)C`

Paclitaxel / other taxanes - Optimization Results

🔗 Optimization Path

📊 **Overall Comparison - Initial → Final**

Initial Molecule `CC1=C2[C@H](C(=O)[C@]3(C)[C@H](C[C@@H]4[C@@](CO4)([C@@]3(C)[C@@H]([C@](C[C@@H]1OC(=O)[C@@H]([C@H](C5=CC=CC=C5)NC(=O)C6=CC=CC=C6)O)(C2(C)C)O)OC(=O)C7=CC=CC=C7)OC(=O)C)O)OC(=O)C`

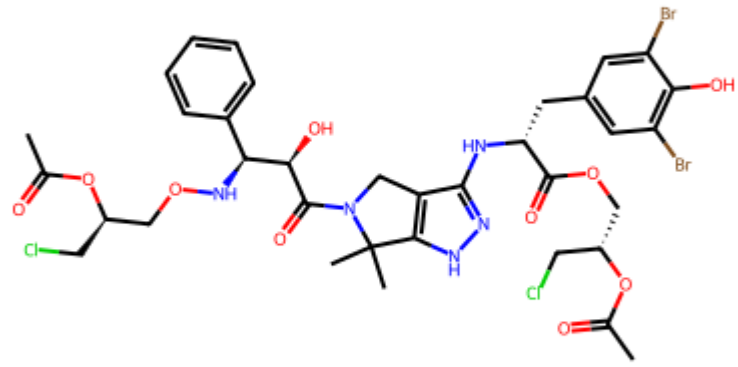


QED (Drug-likeness): 0.1280 **Number of Blocks:** 4

▶ ***Show ADMET Scores***

Task	Score
AMES	0.766300
BBBP	0.000153
CYP3A4	0.009794
DILI	0.767576
HIA	0.750817
PGP	0.573305

Final Optimized `CC(=O)O[C@H](CCl)CON[C@@H](c1ccccc1)[C@@H](O)C(=O)N1Cc2c(N[C@H](Cc3cc(Br)c(O)c(Br)c3)C(=O)OC[C@@H](CCl)OC(C)=O)n[nH]c2C1(C)C`



QED (Drug-likeness): 0.0507 (-0.0773) ❌ **Number of Blocks:** 5 (+1) ↑ **Total Block Changes:** 18

▶ ***Show ADMET Scores***

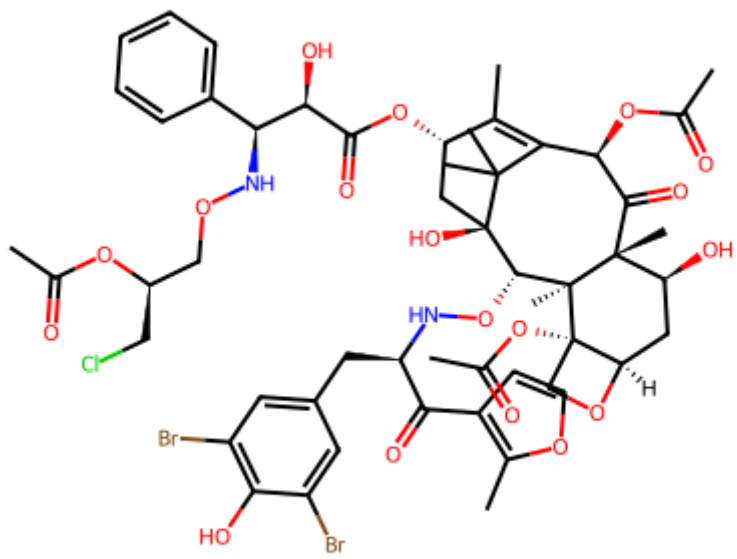
Task	Score	Change	Rel. Improvement	% Change
AMES ✅	0.233688	-0.532611	+0.6950	-69.50%
BBBP ✅	1.000000	+0.999847	+6552.6969	+655269.69%
CYP3A4 ✅	0.001079	-0.008715	+0.8899	-88.99%
DILI ✅	0.459665	-0.307911	+0.4011	-40.11%
HIA ✅	0.999811	+0.248993	+0.3316	+33.16%
PGP ❌	0.862906	+0.289601	-0.5051	+50.51%

Optimization Steps:

DETAILS*PLACEHOLDER2*

After (Step 1)

`CC(=O)O[C@H](CCl)CON[C@@H](c1ccccc1)[C@@H](O)C(=O)O[C@H]1C[C@@]2(O)[C@@H](ON[C@H](Cc3cc(Br)c(O)c(Br)c3)C(=O)c3ccoc3C)[C@]3(C)[C@]4(OC(C)=O)CO[C@@H]4C[C@H](O)[C@@]3(C)C(=O)[C@H](OC(C)=O)C(=C1C)C2(C)C`



QED: 0.0210 (-0.1070) ❌

Number of Blocks: 4 (+0) ➡️

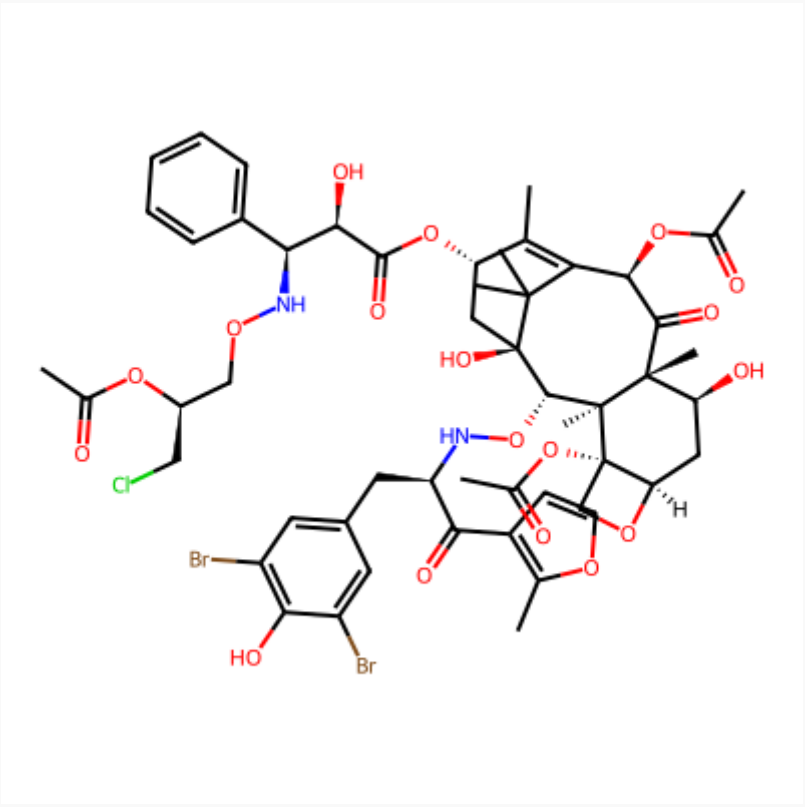
Block Changes: 7 (+4, -3)

BBBP Score: 0.000153 → 0.000113 (-0.000040)

DETAILS*PLACEHOLDER*3

▶ Step 2: AMES (-0.1010 ↓) ✅

Before (Step 1) `CC(=O)O[C@H](CCl)CON[C@@H](c1ccccc1)[C@@H](O)C(=O)O[C@H]1C[C@@]2(O)[C@@H](ON[C@H](Cc3cc(Br)c(O)c(Br)c3)C(=O)c3ccoc3C)[C@]3(C)[C@]4(OC(C)=O)CO[C@@H]4C[C@H](O)[C@@]3(C)C(=O)[C@H](OC(C)=O)C(=C1C)C2(C)C`

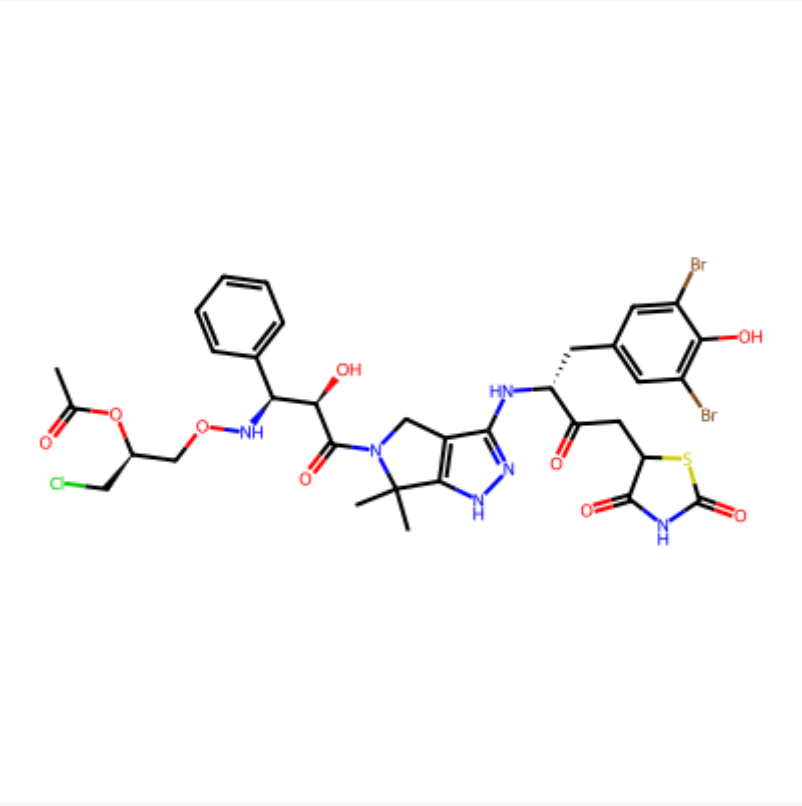


QED: 0.0210 **Number of Blocks:** 4

▶ ***All ADMET Scores***

Task	Score	Direction
AMES	0.677737	↓ lower
BBBP	0.000113	↑ higher
CYP3A4	0.004253	↓ lower
DILI	0.616722	↓ lower
HIA	0.943954	↑ higher
PGP	0.731751	↓ lower

After (Step 2) `CC(=O)O[C@H](CCl)CON[C@@H](c1ccccc1)[C@@H](O)C(=O)N1Cc2c(N[C@H](Cc3cc(Br)c(O)c(Br)c3)C(=O)CC3SC(=O)NC3=O)n[nH]c2C1(C)C`



QED: 0.0672 (+0.0462) ✅

Number of Blocks: 5 (+1) ↑

Block Changes: 3 (+2, -1)

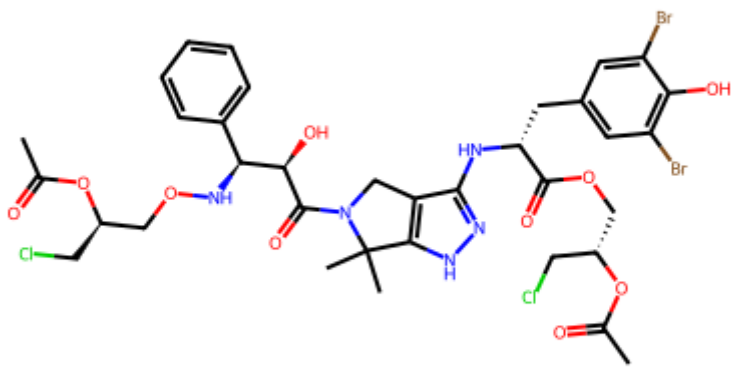
AMES Score: 0.677737 → 0.576776 (-0.100962)

DETAILS*PLACEHOLDER*5

DETAILS*PLACEHOLDER*6

After (Step 3)

`CC(=O)O[C@H](CCl)CON[C@@H](c1ccccc1)[C@@H](O)C(=O)N1Cc2c(N[C@H](Cc3cc(Br)c(O)c(Br)c3)C(=O)OC[C@@H](CCl)OC(C)=O)n[nH]c2C1(C)C`



QED: 0.0507 (-0.0165) ❌

Number of Blocks: 5 (+0) ➡️

Block Changes: 8 (+4, -4)

AMES Score: 0.576776 → 0.233688 (-0.343087)

DETAILS*PLACEHOLDER7*

📊 Step Details

Step 1: BBBP ⚠️

Original	New	Change
0.000153	0.000113	-0.000040 ↑

```
CC(=O)O[C@H](CCl)CON[C@@H](c1ccccc1)[C@@H](O)C(=O)O[C@H]1C[C@@]2(O)[C@@H](ON[C@H](Cc3cc(Br)c(O)c(Br)c3)C(=O)c3ccoc3C)[C@]3(C)[C@]4(O
```

Step 2: AMES ✅

Original	New	Change
0.677737	0.576776	-0.100962 ↓

```
CC(=O)O[C@H](CCl)CON[C@@H](c1ccccc1)[C@@H](O)C(=O)N1Cc2c(N[C@H](Cc3cc(Br)c(O)c(Br)c3)C(=O)CC3SC(=O)NC3=O)n[nH]c2C1(C)C
```

Step 3: AMES ✅

Original	New	Change
0.576776	0.233688	-0.343087 ↓

```
CC(=O)O[C@H](CCl)CON[C@@H](c1ccccc1)[C@@H](O)C(=O)N1Cc2c(N[C@H](Cc3cc(Br)c(O)c(Br)c3)C(=O)OC[C@@H](CCl)OC(C)=O)n[nH]c2C1(C)C
```

📊 ADMET Comparison

Task	Direction	Initial	Final	Change	Rel. Improvement	% Change	Status
AMES	↓ lower	0.766300	0.233688	-0.532611	+0.6950	-69.50%	✅ Improved
BBBP	↑ higher	0.000153	1.000000	+0.999847	+6552.6969	+655269.69%	✅ Improved
CYP3A4	↓ lower	0.009794	0.001079	-0.008715	+0.8899	-88.99%	✅ Improved
DILI	↓ lower	0.767576	0.459665	-0.307911	+0.4011	-40.11%	✅ Improved
HIA	↑ higher	0.750817	0.999811	+0.248993	+0.3316	+33.16%	✅ Improved
PGP	↓ lower	0.573305	0.862906	+0.289601	-0.5051	+50.51%	❌ Declined

Improved: 5/6 (83.3%) | **Molecules:** 187 | **Paths:** 2468

🔍 Safety Threshold Analysis

Status: 4/6 meet thresholds

⚠️ **Below threshold:** 2

Task	Score	Threshold	Gap
PGP	0.8629	↓ 0.3	0.5629
DILI	0.4597	↓ 0.4	0.0597

✅ **Passing:** 4

Task	Score	Threshold
AMES	0.2337	↓ 0.3
BBBP	1.0000	↑ 0.5
CYP3A4	0.0011	↓ 0.55
HIA	0.9998	↑ 0.2