Slide 8: Valeresol

Initial Task: HIA

SMILES: `C(CCOC1=C(C=O)C(=CC=C1)O)CC(=O)O`

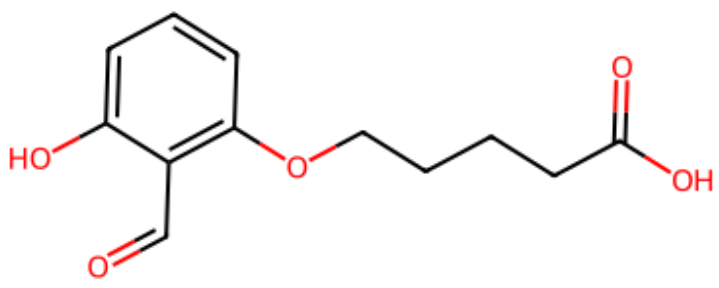
Valeresol - Optimization Results

🔗 Optimization Path

📊 Overall Comparison - Initial → Final

Initial Molecule

`C(CCOC1=C(C=O)C(=CC=C1)O)CC(=O)O`



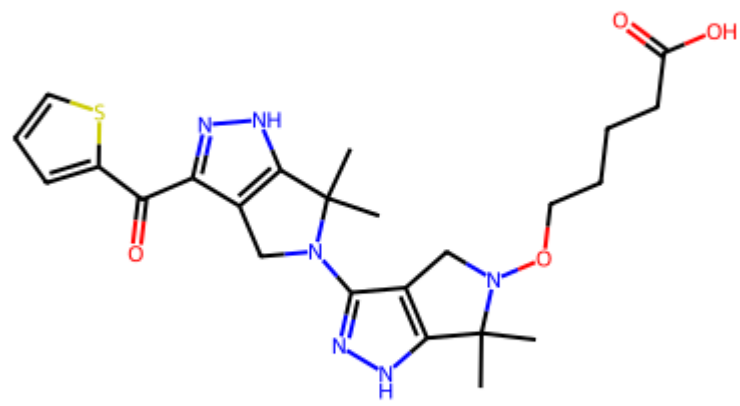
QED (Drug-likeness): 0.5590 **Number of Blocks:** 2

▶ ***Show ADMET Scores***

Task	Score
AMES	0.687406
BBBP	0.001264
CYP3A4	0.022560
DILI	0.623776
HIA	0.984511
PGP	0.615759

Final Optimized

`CC1(C)c2[nH]nc(N3Cc4c(C(=O)c5cccs5)n[nH]c4C3(C)C)c2CN1OCCCCC(=O)O`



QED (Drug-likeness): 0.2992 (-0.2597) ❌ **Number of Blocks:** 2 (+0) ➡️
Total Block Changes: 8

▶ ***Show ADMET Scores***

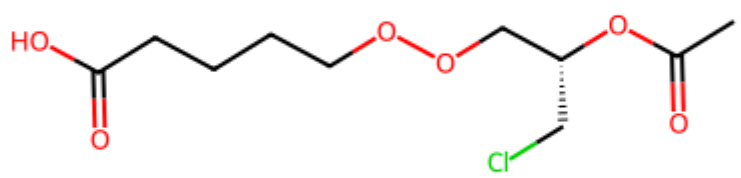
Task	Score	Change	Rel. Improvement	% Change
AMES ✅	0.368299	-0.319107	+0.4642	-46.42%
BBBP ✅	0.898326	+0.897062	+709.5506	+70955.06%
CYP3A4 ✅	0.005592	-0.016969	+0.7521	-75.21%
DILI ❌	0.676924	+0.053148	-0.0852	+8.52%
HIA ❌	0.980476	-0.004035	-0.0041	-0.41%
PGP ✅	0.498713	-0.117046	+0.1901	-19.01%

Optimization Steps:

DETAILS*PLACEHOLDER2*

After (Step 1)

`CC(=O)O[C@H](CCl)COOCCCCC(=O)O`



QED: 0.2118 (-0.3472) ❌

Number of Blocks: 1 (-1) ↓

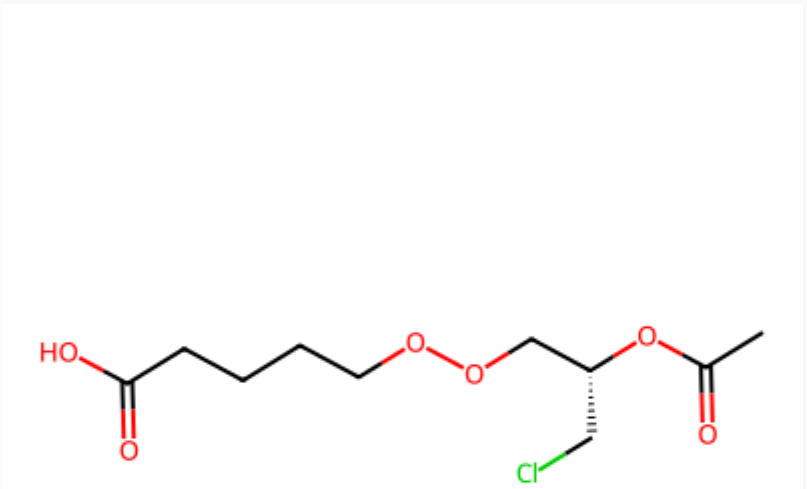
Block Changes: 3 (+1, -2)

HIA Score: 0.984511 → 0.999700 (+0.015189)

DETAILS*PLACEHOLDER3*

▶ Step 2: AMES (+0.3483 ↓) ➡️

Before (Step 1) `CC(=O)O[C@H](CCl)COOCCCCC(=O)O`

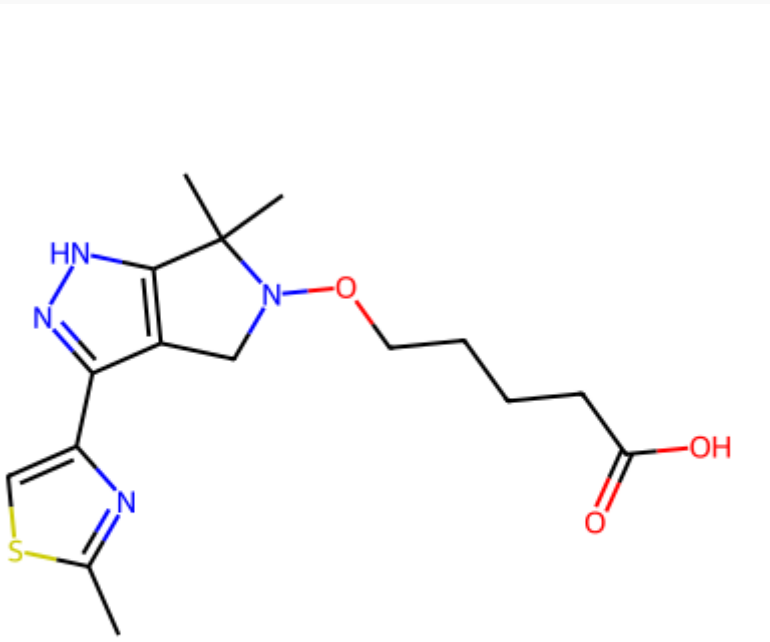


QED: 0.2118 **Number of Blocks:** 1

▶ ***All ADMET Scores***

Task	Score	Direction
AMES	0.428290	↓ lower
BBBP	1.000000	↑ higher
CYP3A4	0.063673	↓ lower
DILI	0.424375	↓ lower
HIA	0.999700	↑ higher
PGP	0.791106	↓ lower

After (Step 2) `Cc1nc(-c2n[nH]c3c2CN(OCCCCC(=O)O)C3(C)C)cs1`



QED: 0.7458 (+0.5340) ✅

Number of Blocks: 2 (+1) ↑

Block Changes: 3 (+2, -1)

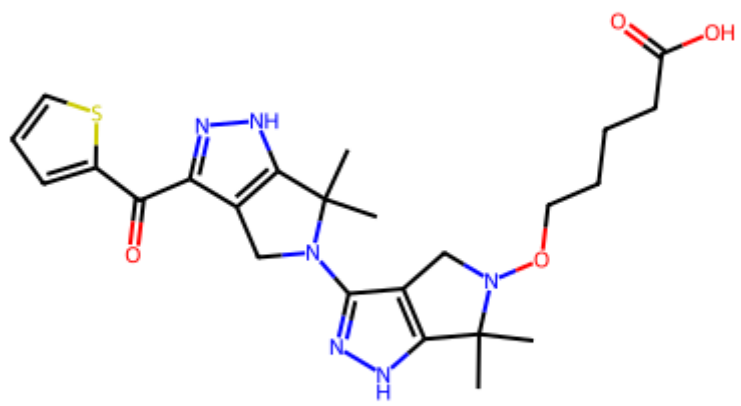
AMES Score: 0.428290 → 0.776573 (+0.348283)

DETAILS*PLACEHOLDER5*

DETAILS*PLACEHOLDER6*

After (Step 3)

`CC1(C)c2[nH]nc(N3Cc4c(C(=O)c5cccs5)n[nH]c4C3(C)C)c2CN1OCCCCC(=O)O`



QED: 0.2992 (-0.4465) ❌

Number of Blocks: 2 (+0) ➡️

Block Changes: 2 (+1, -1)

PGP Score: 0.609776 → 0.498713 (-0.111063)

DETAILS*PLACEHOLDER7*

📊 Step Details

Step 1: HIA ✅

Original	New	Change
0.984511	0.999700	+0.015189 ↑

```
CC(=O)O[C@H](CCl)COOCCCCC(=O)O
```

Step 2: AMES ⚠️

Original	New	Change
0.428290	0.776573	+0.348283 ↓

```
Cc1nc(-c2n[nH]c3c2CN(OCCCCC(=O)O)C3(C)C)cs1
```

Step 3: PGP ✅

Original	New	Change
0.609776	0.498713	-0.111063 ↓

```
CC1(C)c2[nH]nc(N3Cc4c(C(=O)c5cccs5)n[nH]c4C3(C)C)c2CN1OCCCCC(=O)O
```

📊 ADMET Comparison

Task	Direction	Initial	Final	Change	Rel. Improvement	% Change	Status
AMES	↓ lower	0.687406	0.368299	-0.319107	+0.4642	-46.42%	✅ Improved
BBBP	↑ higher	0.001264	0.898326	+0.897062	+709.5506	+70955.06%	✅ Improved
CYP3A4	↓ lower	0.022560	0.005592	-0.016969	+0.7521	-75.21%	✅ Improved
DILI	↓ lower	0.623776	0.676924	+0.053148	-0.0852	+8.52%	❌ Declined
HIA	↑ higher	0.984511	0.980476	-0.004035	-0.0041	-0.41%	❌ Declined
PGP	↓ lower	0.615759	0.498713	-0.117046	+0.1901	-19.01%	✅ Improved

Improved: 4/6 (66.7%) | **Molecules:** 85 | **Paths:** 1719

🔍 Safety Threshold Analysis

Status: 3/6 meet thresholds

⚠️ **Below threshold:** 3

Task	Score	Threshold	Gap
DILI	0.6769	↓ 0.4	0.2769
PGP	0.4987	↓ 0.3	0.1987
AMES	0.3683	↓ 0.3	0.0683

✅ **Passing:** 3

Task	Score	Threshold
BBBP	0.8983	↑ 0.5
CYP3A4	0.0056	↓ 0.55
HIA	0.9805	↑ 0.2