Slide 22: NYX-059

Initial Task: BBBP

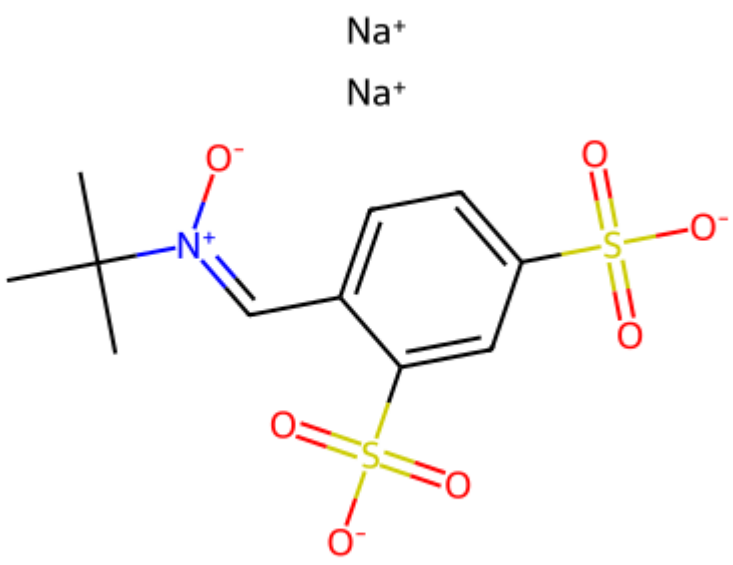
SMILES: `CC(C)(C)[N+]([O-])=Cc1ccc(cc1S(=O)(=O)[O-])S(=O)(=O)[O-].[Na+].[Na+]`

NYX-059 - Optimization Results

🔗 Optimization Path

📊 Overall Comparison - Initial → Final

Initial Molecule `CC(C)(C)[N+]([O-])=Cc1ccc(cc1S(=O)(=O)[O-])S(=O)(=O)[O-].[Na+].[Na+]`

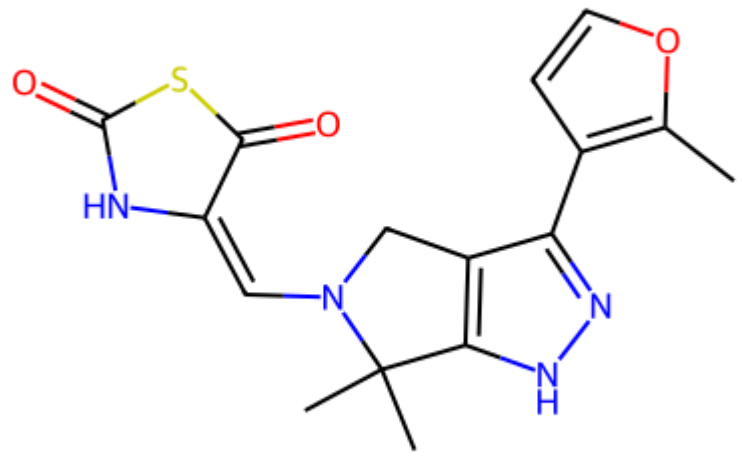


QED (Drug-likeness): 0.1268 **Number of Blocks:** 3

▶ ***Show ADMET Scores***

Task	Score
AMES	0.531967
BBBP	0.001933
CYP3A4	0.000120
DILI	0.483893
HIA	0.994940
PGP	0.765508

Final Optimized `Cc1occc1-c1n[nH]c2c1CN(C=C1NC(=O)SC1=O)C2(C)C`



QED (Drug-likeness): 0.8142 (+0.6874) ✅ **Number of Blocks:** 3 (+0) ➡️
Total Block Changes: 7

▶ ***Show ADMET Scores***

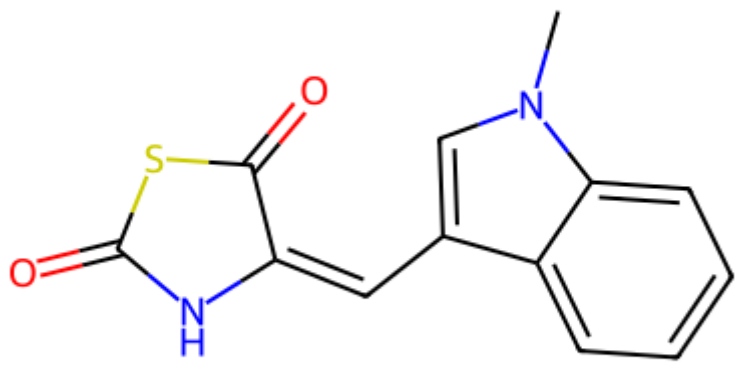
Task	Score	Change	Rel. Improvement	% Change
AMES ❌	0.609732	+0.077765	-0.1462	+14.62%
BBBP ✅	0.002764	+0.000832	+0.4304	+43.04%
CYP3A4 ❌	0.004026	+0.003907	-32.6844	+3268.44%
DILI ❌	0.741515	+0.257622	-0.5324	+53.24%
HIA ✅	0.996004	+0.001064	+0.0011	+0.11%
PGP ✅	0.583655	-0.181853	+0.2376	-23.76%

Optimization Steps:

DETAILS*PLACEHOLDER2*

After (Step 1)

`Cn1cc(C=C2NC(=O)SC2=O)c2ccccc21`



QED: 0.7995 (+0.6727) ✅

Number of Blocks: 2 (-1) ↓

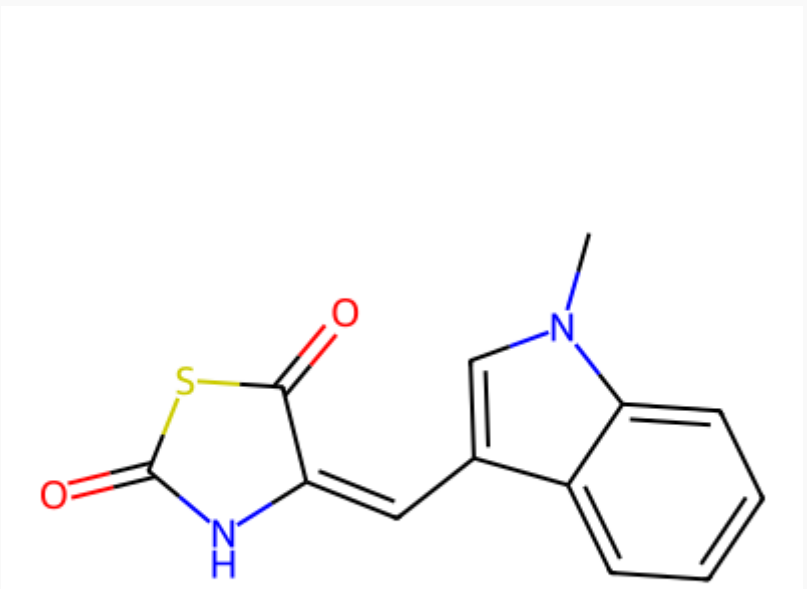
Block Changes: 4 (+2, -2)

BBBP Score: 0.001933 → 0.998710 (+0.996778)

DETAILS*PLACEHOLDER*3

▶ Step 2: AMES (-0.1157 ↓) ✅

Before (Step 1) `Cn1cc(C=C2NC(=O)SC2=O)c2ccccc21`

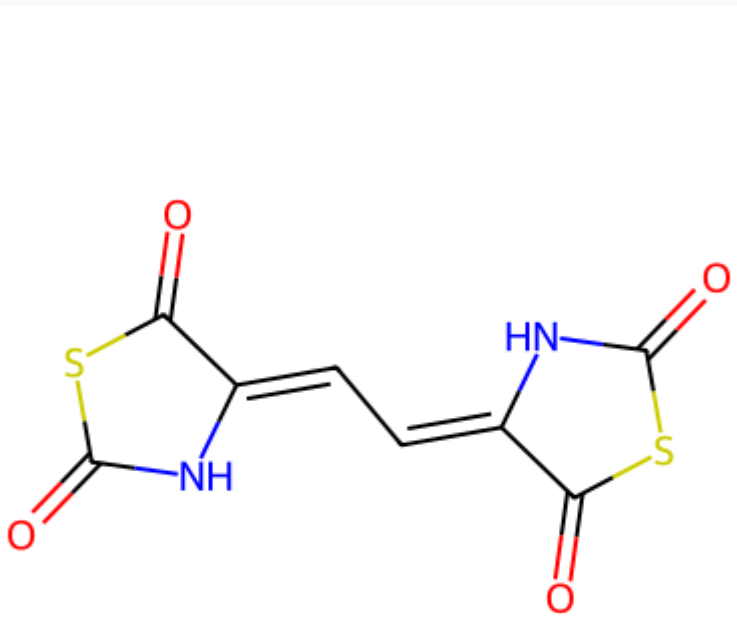


QED: 0.7995 **Number of Blocks:** 2

▶ ***All ADMET Scores***

Task	Score	Direction
AMES	0.324786	↓ lower
BBBP	0.998710	↑ higher
CYP3A4	0.007588	↓ lower
DILI	0.633693	↓ lower
HIA	0.999192	↑ higher
PGP	0.479166	↓ lower

After (Step 2) `O=C1NC(=CC=C2NC(=O)SC2=O)C(=O)S1`



QED: 0.6715 (-0.1280) ❌

Number of Blocks: 2 (+0) ➡️

Block Changes: 1 (+0, -1)

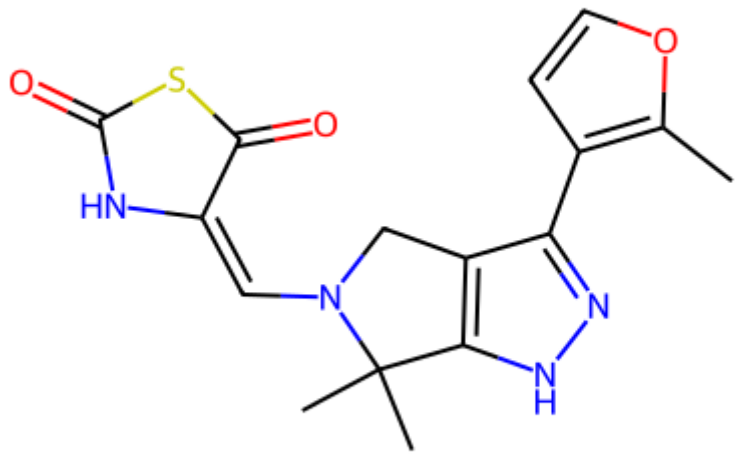
AMES Score: 0.324786 → 0.209113 (-0.115673)

DETAILS*PLACEHOLDER5*

DETAILS*PLACEHOLDER6*

After (Step 3)

`Cc1occc1-c1n[nH]c2c1CN(C=C1NC(=O)SC1=O)C2(C)C`



QED: 0.8142 (+0.1427) ✅

Number of Blocks: 3 (+1) ↑

Block Changes: 2 (+2, -0)

PGP Score: 0.676219 → 0.583655 (-0.092563)

DETAILS*PLACEHOLDER7*

📊 Step Details

Step 1: BBBP ✅

Original	New	Change
0.001933	0.998710	+0.996778 ↑

```
Cn1cc(C=C2NC(=O)SC2=O)c2ccccc21
```

Step 2: AMES ✅

Original	New	Change
0.324786	0.209113	-0.115673 ↓

```
O=C1NC(=CC=C2NC(=O)SC2=O)C(=O)S1
```

Step 3: PGP ✅

Original	New	Change
0.676219	0.583655	-0.092563 ↓

```
Cc1occc1-c1n[nH]c2c1CN(C=C1NC(=O)SC1=O)C2(C)C
```

📊 ADMET Comparison

Task	Direction	Initial	Final	Change	Rel. Improvement	% Change	Status
AMES	↓ lower	0.531967	0.609732	+0.077765	-0.1462	+14.62%	❌ Declined
BBBP	↑ higher	0.001933	0.002764	+0.000832	+0.4304	+43.04%	✅ Improved
CYP3A4	↓ lower	0.000120	0.004026	+0.003907	-32.6844	+3268.44%	❌ Declined
DILI	↓ lower	0.483893	0.741515	+0.257622	-0.5324	+53.24%	❌ Declined
HIA	↑ higher	0.994940	0.996004	+0.001064	+0.0011	+0.11%	✅ Improved
PGP	↓ lower	0.765508	0.583655	-0.181853	+0.2376	-23.76%	✅ Improved

Improved: 3/6 (50.0%) | **Molecules:** 133 | **Paths:** 300

🔍 Safety Threshold Analysis

Status: 2/6 meet thresholds

⚠️ **Below threshold:** 4

Task	Score	Threshold	Gap
BBBP	0.0028	↑ 0.5	0.4972
DILI	0.7415	↓ 0.4	0.3415
AMES	0.6097	↓ 0.3	0.3097
PGP	0.5837	↓ 0.3	0.2837

✅ **Passing:** 2

Task	Score	Threshold
CYP3A4	0.0040	↓ 0.55
HIA	0.9960	↑ 0.2