Supporting Information: Efficient Multi-Objective Molecular Optimization in a Continuous Latent Space

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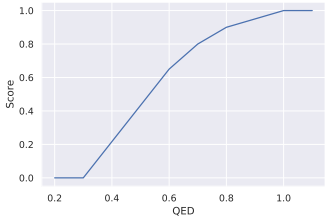
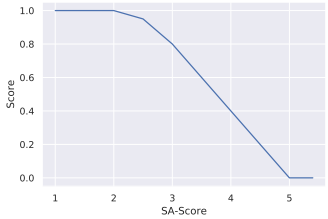
1 Desirability Scaling

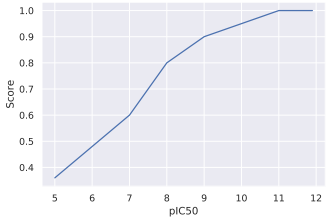
We followed the approach proposed by Cummins and Bell [1] and scale each molecular property function prediction between 0 and 1, reflecting values of low to high desirability. For each property we defined a range of values with a respective desirability score. Between these points we interpolated linearly. The resulting scaling functions are depicted in Figure 1.



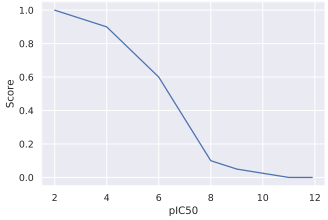
(a) QED



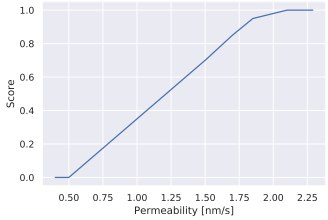
(b) Synthetic accessibility score



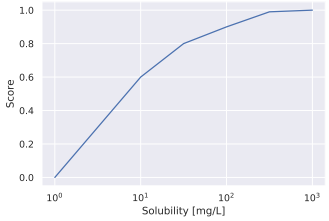
(c) Maximizing potency



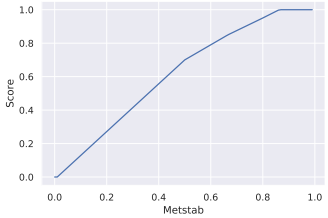
(d) Minimizing potency



(e) Permeability



(f) Solubility



(g) Metabolic stability

Figure 1: Scaling functions for different molecular properties.

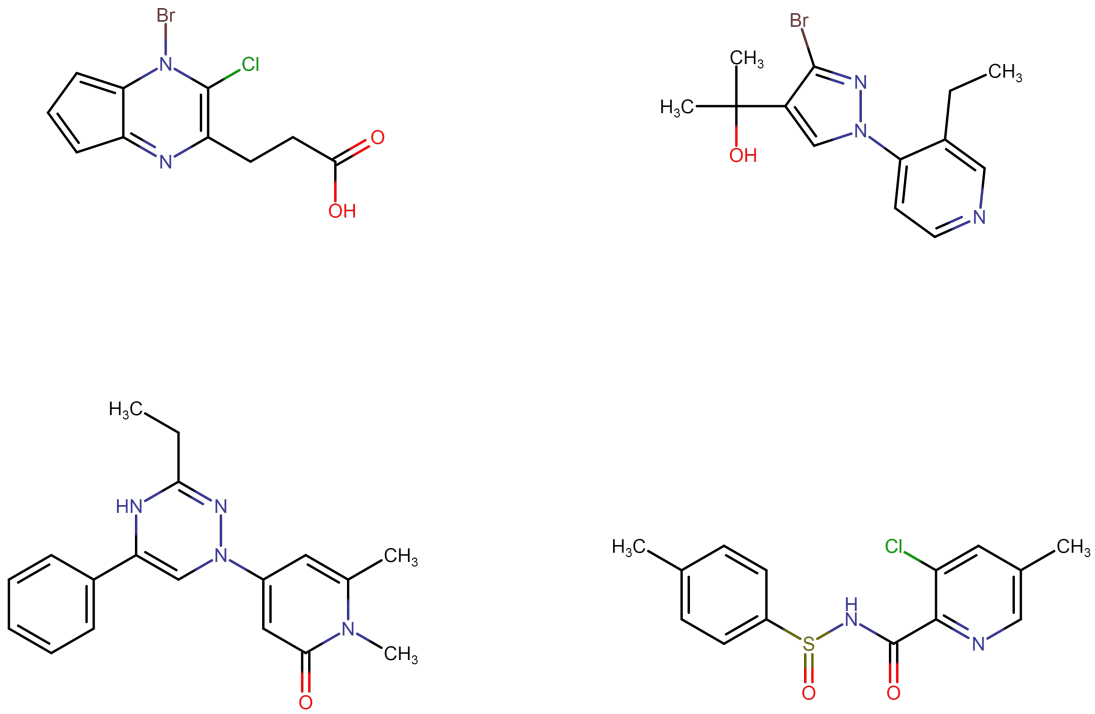


Figure 2: High resolution version of Figure 2(a).

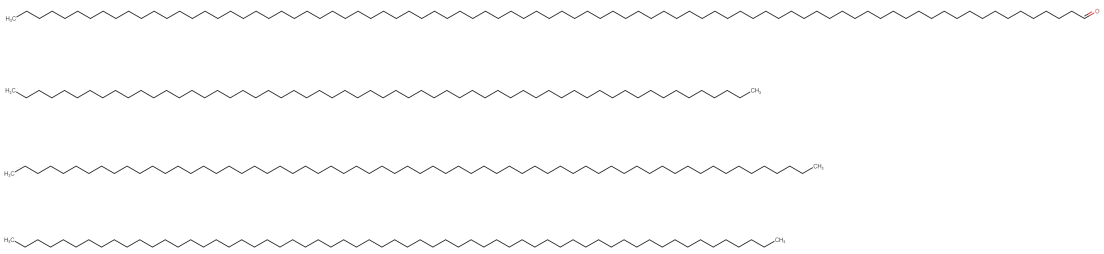


Figure 3: High resolution version of Figure 2(b).

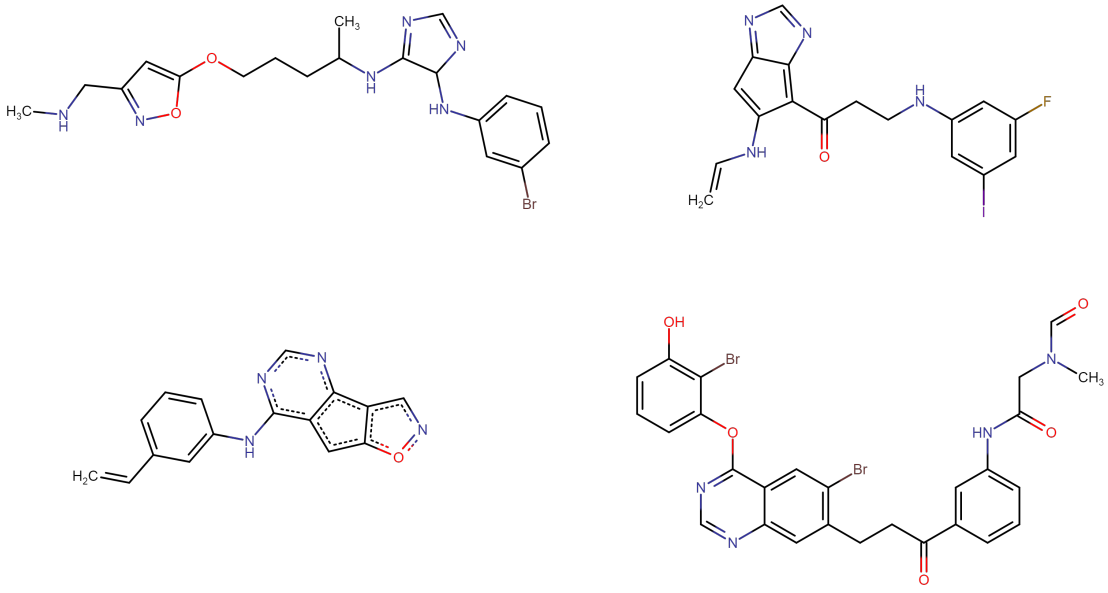


Figure 4: High resolution version of Figure 2(c).

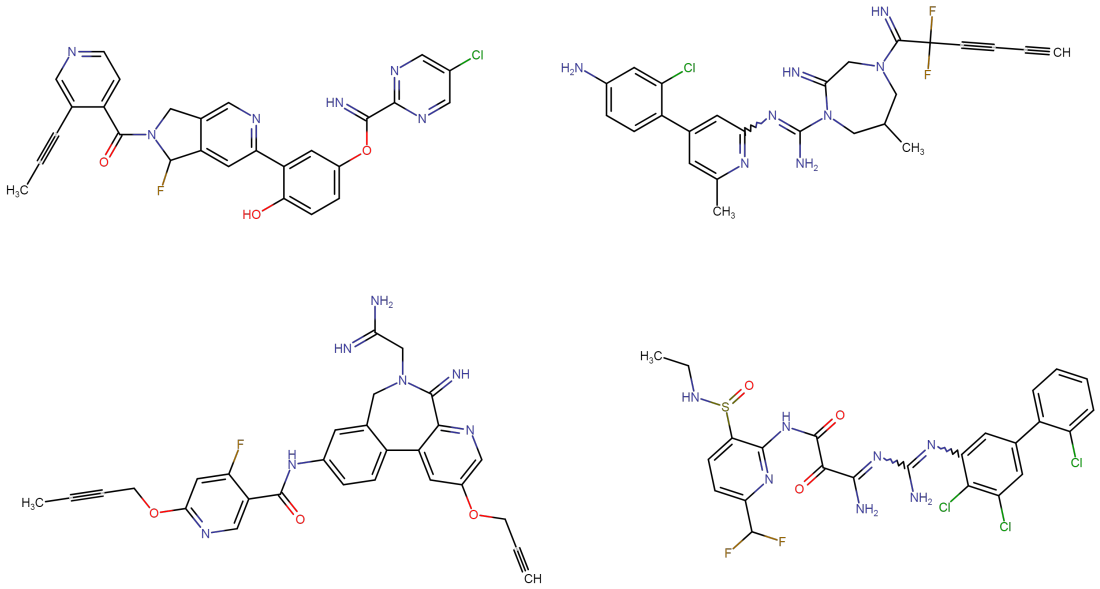


Figure 5: High resolution version of Figure 2(d).

Table 1: Results of the GuacaMol benchmark for baseline methods and our proposed method

Benchmark	Best of Data Set	SMILES GA	Graph MCTS	Graph GA	SMILES LSTM	**MSO (ours)**
Celecoxib rediscovery	0.505	0.732	0.355	**1.000**	**1.000**	**1.000**
Troglitazone rediscovery	0.419	0.515	0.311	**1.000**	**1.000**	**1.000**
Thiothixene rediscovery	0.456	0.598	0.311	**1.000**	**1.000**	**1.000**
Aripiprazole similarity	0.595	0.834	0.380	**1.000**	**1.000**	**1.000**
Albuterol similarity	0.719	0.907	0.749	**1.000**	**1.000**	**1.000**
Mestranol similarity	0.629	0.790	0.402	**1.000**	**1.000**	**1.000**
C11H24	0.684	0.829	0.410	0.971	0.993	**0.997**
C9H10N2O2PF2Cl	0.747	0.889	0.631	0.982	0.879	**1.000**
Median molecules 1	0.334	0.334	0.225	0.406	**0.438**	0.437
Median molecules 2	0.351	0.380	0.170	**0.432**	0.422	0.395
Osimertinib MPO	0.839	0.886	0.784	0.953	0.907	**0.966**
Fexofenadine MPO	0.817	0.931	0.695	0.998	0.959	**1.000**
Ranolazine MPO	0.792	0.881	0.616	0.920	0.855	**0.931**
Perindopril MPO	0.575	0.661	0.385	0.792	0.808	**0.834**
Amlodipine MPO	0.696	0.722	0.533	0.894	0.894	**0.900**
Sitagliptin MPO	0.509	0.689	0.458	**0.891**	0.545	0.868
Zaleplon MPO	0.547	0.413	0.488	0.754	0.669	**0.764**
Valsartan SMARTS	0.259	0.552	0.040	0.990	0.978	**0.994**
Scaffold Hop	0.933	0.970	0.590	**1.000**	0.996	**1.000**
Deco Hop	0.738	0.885	0.478	**1.000**	0.998	**1.000**
Total	12.144	14.396	9.009	17.983	17.340	**18.086**

References

[1] D. J. Cummins and M. A. Bell, *Journal of medicinal chemistry*, 2016, **59**, 6999–7010.