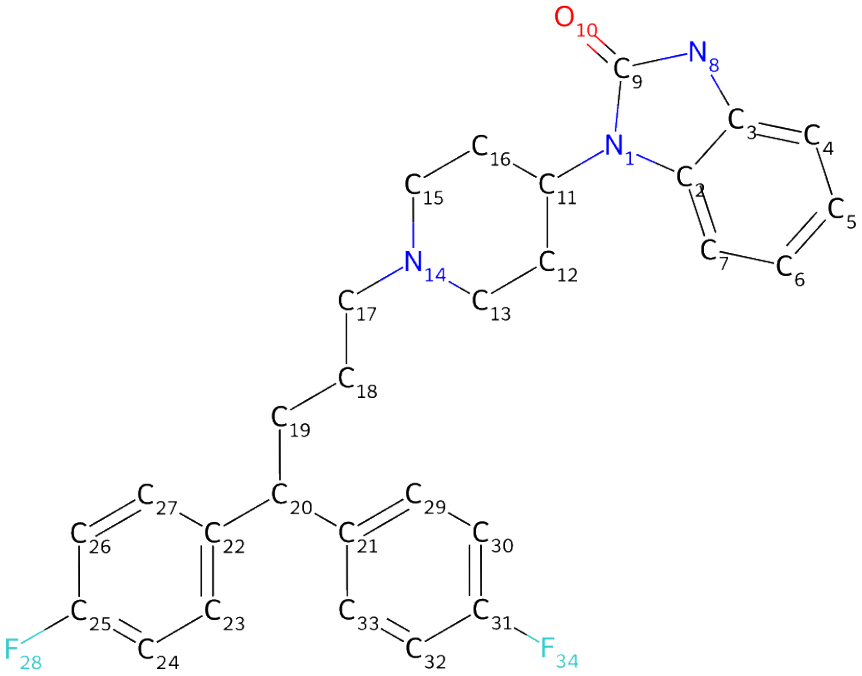
C-oxidation BDE Energy Report for: 235_pimozide-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 235_pimozide-out. Oxidation propensity is established using C-H BDE. The lower the C-H BDE values the higher the propensity for C-oxidation. Details for the density functional theory (DFT) calculations and overall workflow are explained at the end of this document.

BDE and SASA



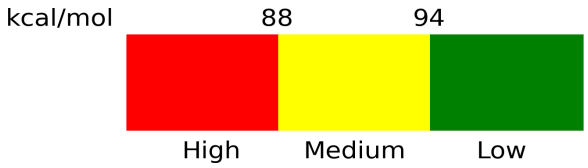
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C4	113.89	Low	16.74
C5	113.07	Low	16.62
C6	112.89	Low	16.35
C7	113.26	Low	8.37
C11	93.5	Moderate	0.00
C12	100.34	Low	0.46
C13	91.01	Moderate	0.45
C15	90.78	Moderate	0.46
C16	100.55	Low	0.46

C17	91.2	Moderate	0.43
C19	96.24	Low	0.18
C23	111.06	Low	5.34
C24	114.59	Low	14.32
C26	114.61	Low	14.44
C27	111.9	Low	4.77
C29	112.05	Low	6.14
C30	114.55	Low	14.41
C32	114.61	Low	14.29
C33	111.11	Low	3.95

Missing Sites:

C18, C20.

Risk Scale:



Calculation Details

Conformational search calculations were performed only for the base ground state molecule. The lowest energy conformer was selected to generate radicals and run optimization DFT calculations. DFT calculations were performed using Gaussian with B3LYP level of theory and 6-31G(d,p) basis set. The BDE protocol was adapted from: *Lienard, P., Gavartin, J., Boccardi, G., & Meunier, M. (2015). Predicting drug substances autoxidation. Pharmaceutical research, 32, 300-310.*