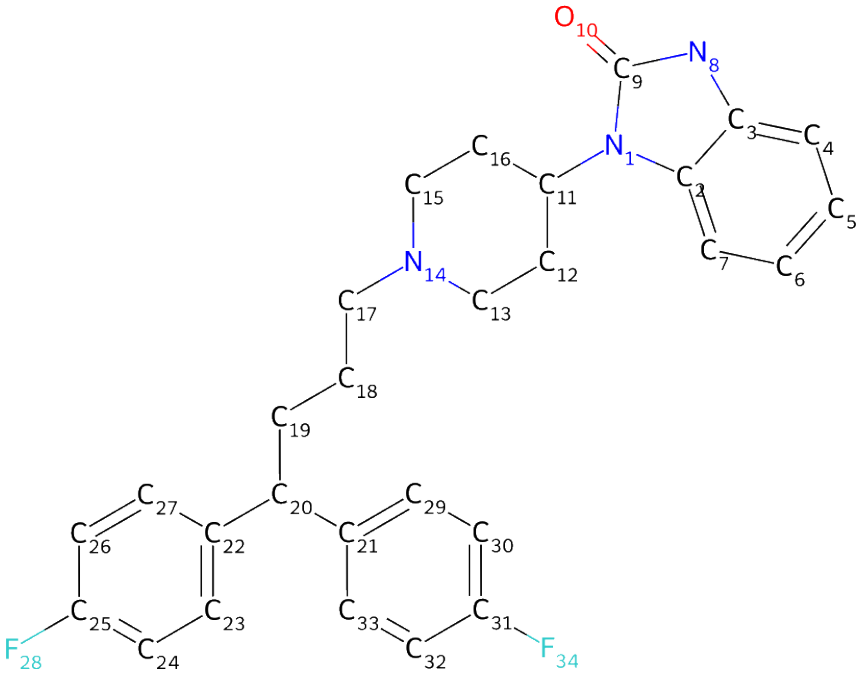
C-oxidation BDE Energy Report for: 235_pimozide-out

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



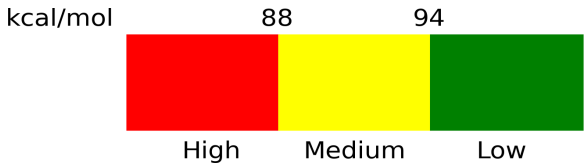
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C4	113.89	Low	32.19
C5	113.07	Low	35.73
C6	112.89	Low	34.68
C7	113.26	Low	13.42
C11	93.5	Moderate	7.32
C12	100.34	Low	18.37
C13	91.01	Moderate	13.50
C15	90.78	Moderate	13.44
C16	100.55	Low	18.43

C17	91.2	Moderate	13.40
C19	96.24	Low	12.03
C23	111.06	Low	15.49
C24	114.59	Low	32.12
C26	114.61	Low	32.18
C27	111.9	Low	13.36
C29	112.05	Low	17.62
C30	114.55	Low	32.25
C32	114.61	Low	31.95
C33	111.11	Low	11.21

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.*