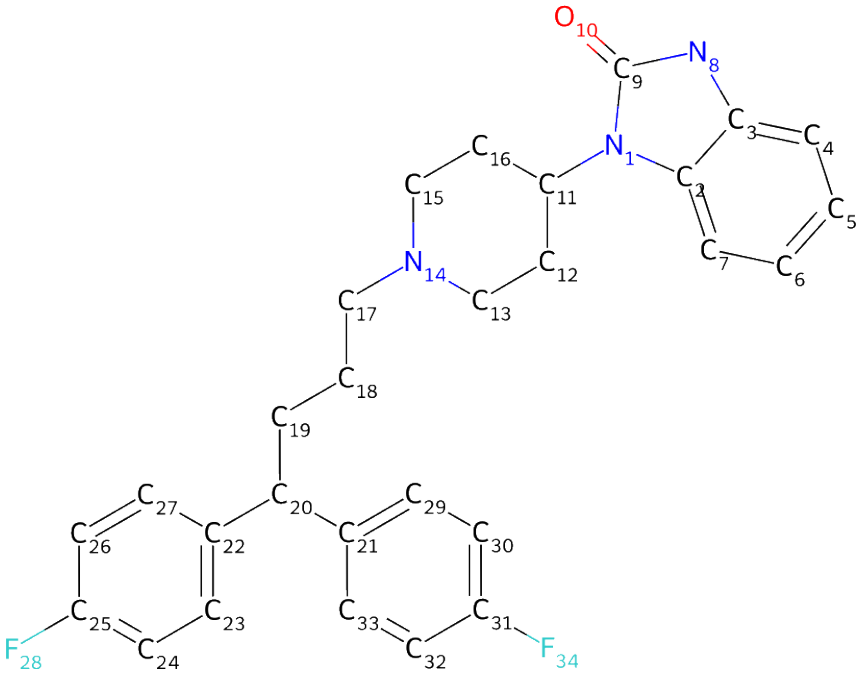
C-oxidation BDE Energy Report for: 235_pimozide-out

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



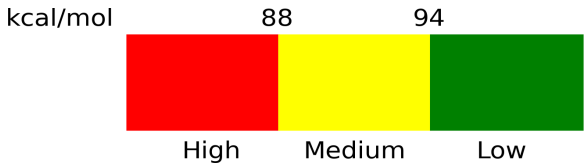
Atom	BDE (kcal/mol)	Propensity
C4	113.89	Low
C5	113.07	Low
C6	112.89	Low
C7	113.26	Low
C11	93.5	Moderate
C12	100.34	Low
C13	91.01	Moderate
C15	90.78	Moderate
C16	100.55	Low

C17	91.2	Moderate
C19	96.24	Low
C23	111.06	Low
C24	114.59	Low
C26	114.61	Low
C27	111.9	Low
C29	112.05	Low
C30	114.55	Low
C32	114.61	Low
C33	111.11	Low

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.*