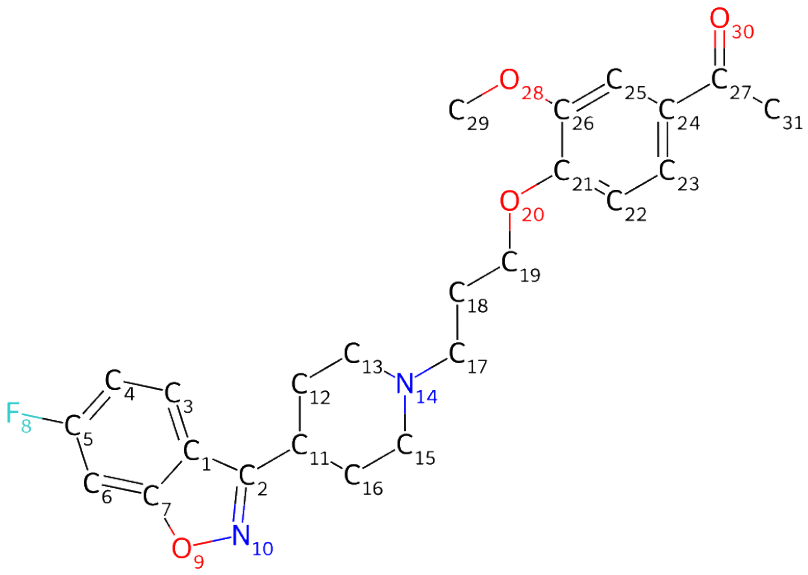
C-oxidation BDE Energy Report for: iloperidone

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for iloperidone. 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



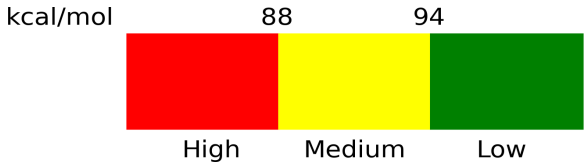
Atom	BDE (kcal/mol)	Propensity
C3	112.99	Low
C4	115.68	Low
C6	117.79	Low
C11	85.15	High
C12	100.0	Low
C13	90.81	Moderate
C15	91.34	Moderate
C16	99.66	Low
C17	91.02	Moderate
C18	98.3	Low
C19	94.49	Low
C22	111.93	Low
C23	111.41	Low

C25	113.89	Low
C29	97.24	Low
C31	95.21	Low

Missing Sites:

None

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.*