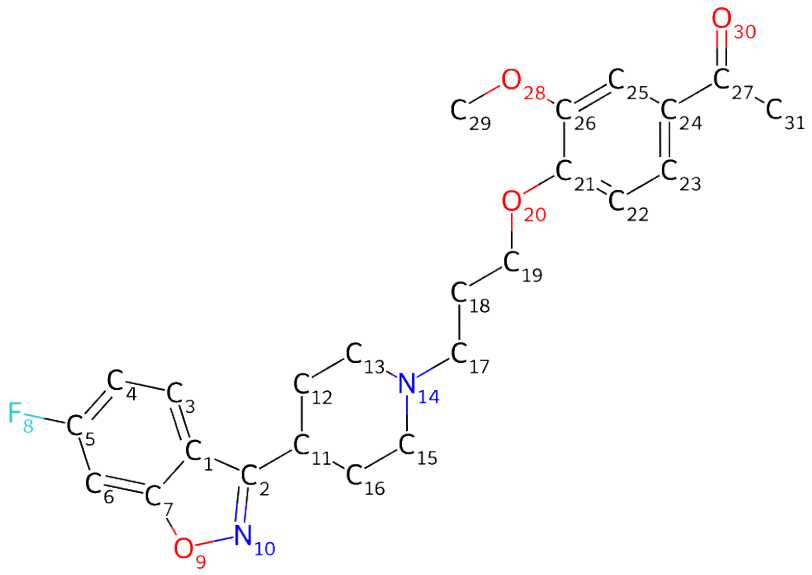
C-oxidation BDE Energy Report for: iloperidone

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



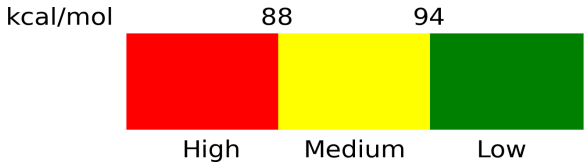
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C3	112.99	Low	0.00
C4	115.68	Low	0.33
C6	117.79	Low	1.37
C11	85.15	High	14.33
C12	100.0	Low	5.52
C13	90.81	Moderate	14.60
C15	91.34	Moderate	89.97
C16	99.66	Low	0.29
C17	91.02	Moderate	0.84
C18	98.3	Low	4.62
C19	94.49	Low	3.74
C22	111.93	Low	8.72
C23	111.41	Low	15.81

C25	113.89	Low	60.85
C29	97.24	Low	14.85
C31	95.21	Low	14.99

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.*