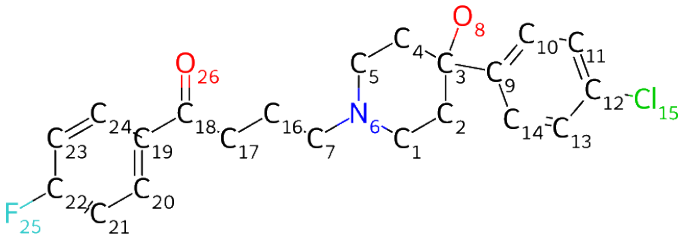
C-oxidation BDE Energy Report for: 159_haloperidol-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 159_haloperidol-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

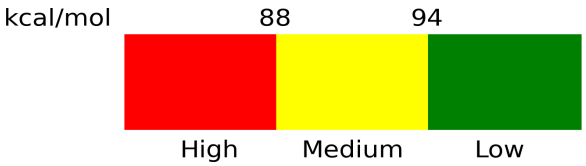


Atom	BDE (kcal/mol)	Propensity
C1	91.47	Moderate
C2	100.57	Low
C4	98.37	Low
C5	90.54	Moderate
C7	91.05	Moderate
C10	110.86	Low
C11	113.44	Low
C13	113.33	Low
C14	112.08	Low
C16	99.04	Low
C17	88.84	Moderate
C20	110.22	Low
C21	114.94	Low
C23	114.59	Low
C24	114.06	Low

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.*