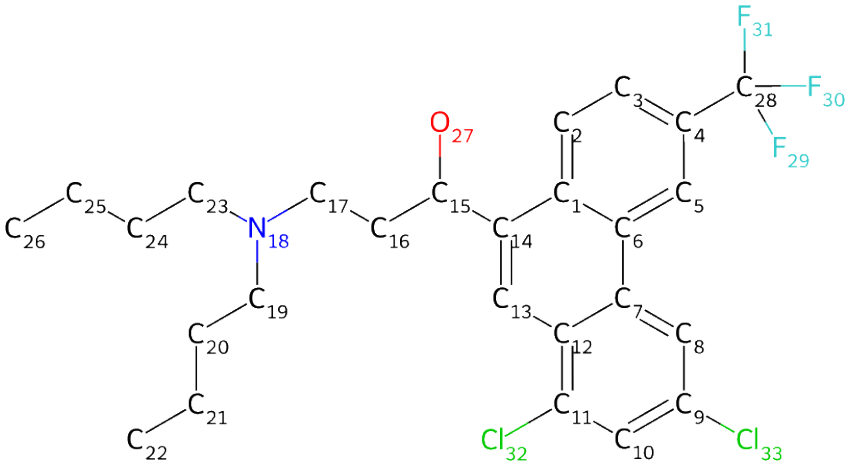
C-oxidation BDE Energy Report for: 158_halofantrine-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 158_halofantrine-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



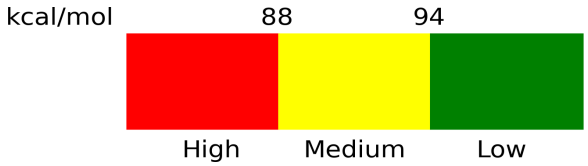
Atom	BDE (kcal/mol)	Propensity
C2	110.22	Low
C3	113.52	Low
C5	111.3	Low
C8	112.22	Low
C10	115.21	Low
C13	113.29	Low
C15	79.68	High
C16	98.48	Low
C17	92.37	Moderate
C19	92.98	Moderate
C20	96.49	Low
C21	96.65	Low
C22	101.5	Low
C23	92.74	Moderate

C24	96.68	Low
C25	97.08	Low
C26	101.47	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.*