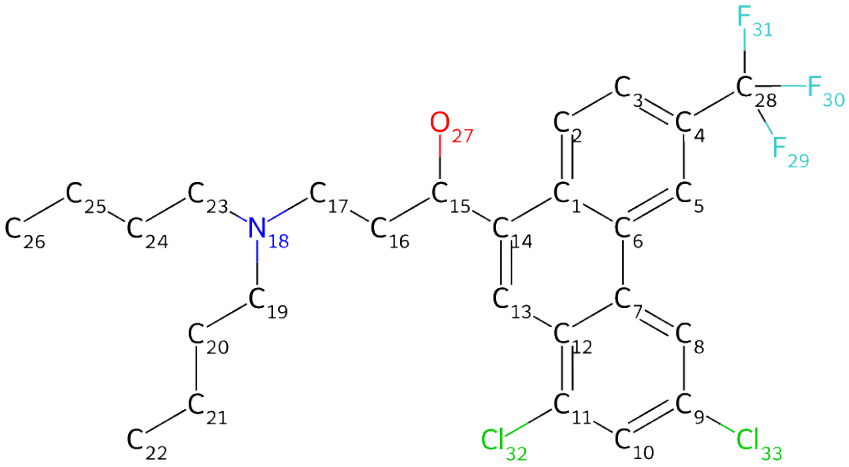
C-oxidation BDE Energy Report for: 158_halofantrine-out

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



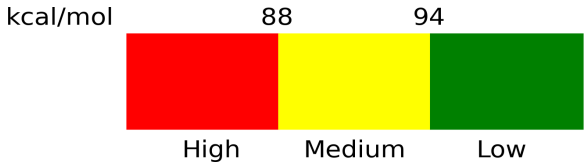
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C2	110.22	Low	5.93
C3	113.52	Low	10.27
C5	111.3	Low	6.67
C8	112.22	Low	11.29
C10	115.21	Low	12.70
C13	113.29	Low	5.15
C15	79.68	High	0.01
C16	98.48	Low	0.08
C17	92.37	Moderate	0.24
C19	92.98	Moderate	0.24
C20	96.49	Low	0.26
C21	96.65	Low	0.62
C22	101.5	Low	6.10
C23	92.74	Moderate	0.27

C24	96.68	Low	0.27
C25	97.08	Low	0.62
C26	101.47	Low	6.01

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.*