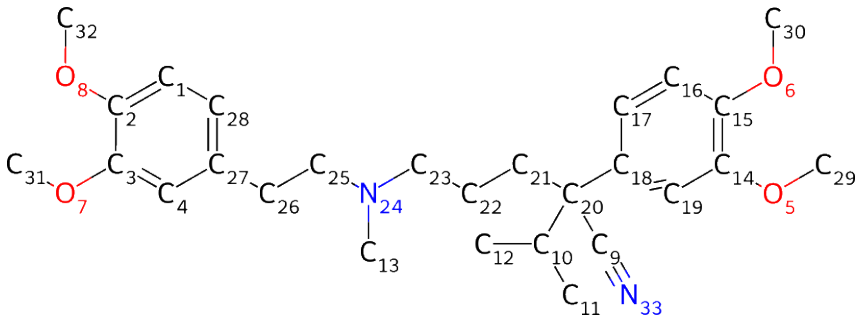
C-oxidation BDE Energy Report for: verapamil

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

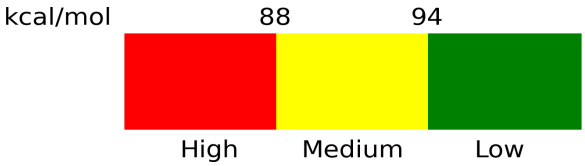


Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	112.03	Low	8.70
C4	111.51	Low	4.47
C10	94.22	Low	0.00
C11	102.16	Low	5.05
C12	100.81	Low	4.99
C13	91.13	Moderate	6.39
C16	111.84	Low	5.98
C17	111.26	Low	2.02
C19	111.78	Low	0.42
C21	96.59	Low	0.03
C22	94.82	Low	0.10
C23	89.72	Moderate	0.29
C25	88.89	Moderate	0.31
C26	85.45	High	0.97
C28	111.98	Low	8.49
C29	97.3	Low	9.04
C30	96.79	Low	9.25
C31	96.3	Low	8.43
C32	95.87	Low	9.40

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.*