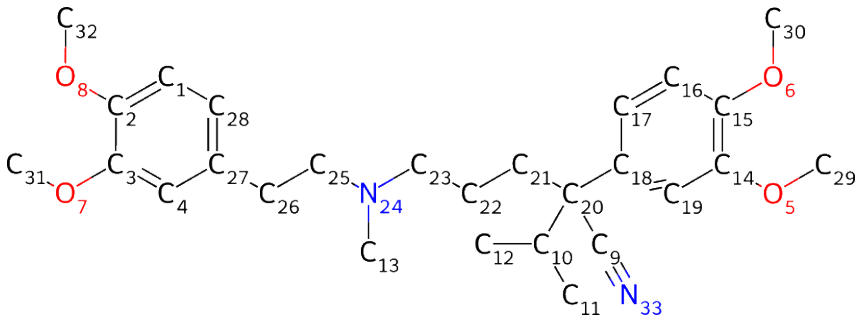
C-oxidation BDE Energy Report for: verapamil

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

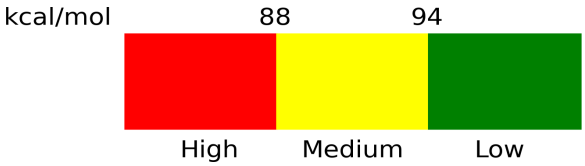


Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	112.03	Low	13.79
C4	111.51	Low	2.95
C10	94.22	Low	9.45
C11	102.16	Low	20.09
C12	100.81	Low	20.43
C13	91.13	Moderate	22.40
C16	111.84	Low	14.07
C17	111.26	Low	10.59
C19	111.78	Low	0.08
C21	96.59	Low	6.67
C22	94.82	Low	4.91
C23	89.72	Moderate	12.45
C25	88.89	Moderate	11.05
C26	85.45	High	14.93
C28	111.98	Low	18.41
C29	97.3	Low	25.25
C30	96.79	Low	29.00
C31	96.3	Low	26.38
C32	95.87	Low	29.57

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.*