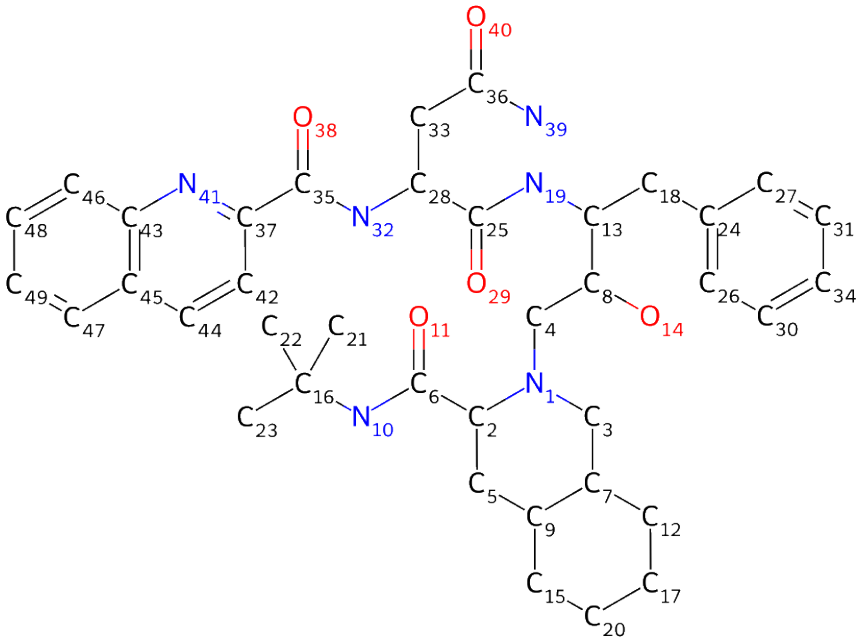
C-oxidation BDE Energy Report for: 268_saquinavir-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 268_saquinavir-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



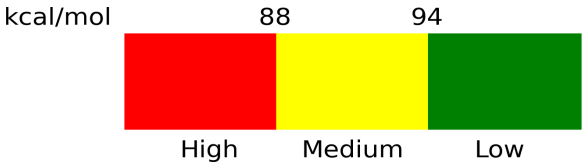
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C2	85.57	High	0.00
C3	91.45	Moderate	0.17
C4	94.31	Low	0.05
C5	97.85	Low	0.17
C7	95.24	Low	0.00
C8	89.72	Moderate	0.00
C9	95.29	Low	0.00
C12	96.43	Low	0.43
C13	89.8	Moderate	0.00
C15	97.53	Low	0.59

C17	97.84	Low	0.95
C18	87.03	High	0.65
C20	97.38	Low	1.03
C21	102.96	Low	4.19
C22	102.54	Low	3.03
C23	101.56	Low	3.89
C26	113.09	Low	6.57
C27	111.08	Low	7.03
C28	86.62	High	0.00
C30	111.98	Low	9.30
C31	111.83	Low	10.75
C33	94.46	Low	0.79
C34	112.26	Low	10.74
C42	114.54	Low	9.03
C44	111.46	Low	12.42
C46	114.65	Low	12.97
C47	112.14	Low	14.21
C48	112.2	Low	16.04
C49	112.41	Low	16.40

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.*