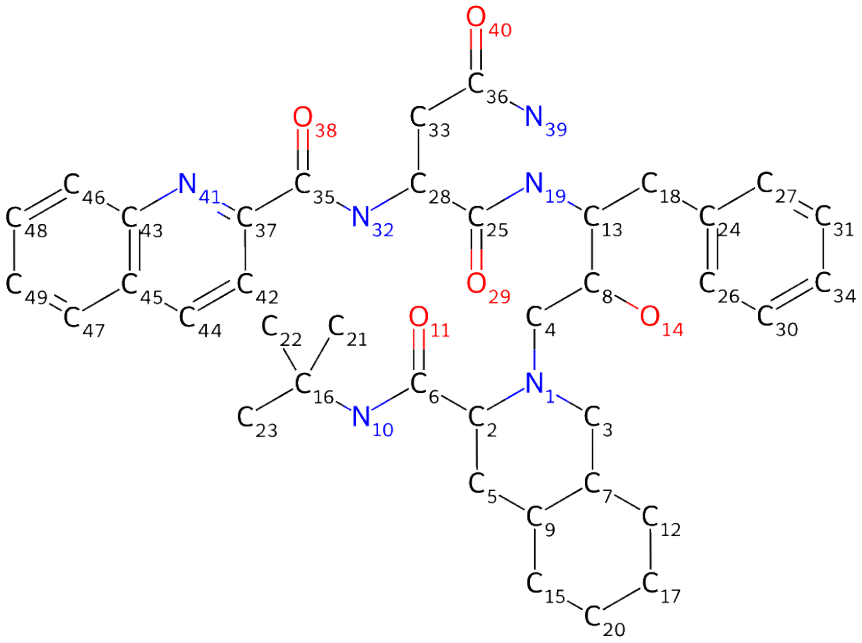
C-oxidation BDE Energy Report for: 268_saquinavir-out

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



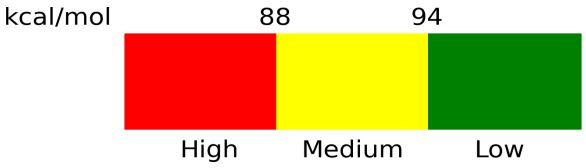
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C2	85.57	High	7.16
C3	91.45	Moderate	7.92
C4	94.31	Low	4.25
C5	97.85	Low	10.65
C7	95.24	Low	14.88
C8	89.72	Moderate	4.28
C9	95.29	Low	16.28
C12	96.43	Low	13.38
C13	89.8	Moderate	3.81
C15	97.53	Low	19.07

C17	97.84	Low	24.53
C18	87.03	High	11.33
C20	97.38	Low	25.25
C21	102.96	Low	20.02
C22	102.54	Low	15.28
C23	101.56	Low	17.84
C26	113.09	Low	11.37
C27	111.08	Low	14.39
C28	86.62	High	5.26
C30	111.98	Low	24.65
C31	111.83	Low	27.31
C33	94.46	Low	13.75
C34	112.26	Low	26.67
C42	114.54	Low	13.97
C44	111.46	Low	26.43
C46	114.65	Low	25.08
C47	112.14	Low	27.32
C48	112.2	Low	35.48
C49	112.41	Low	35.82

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.*