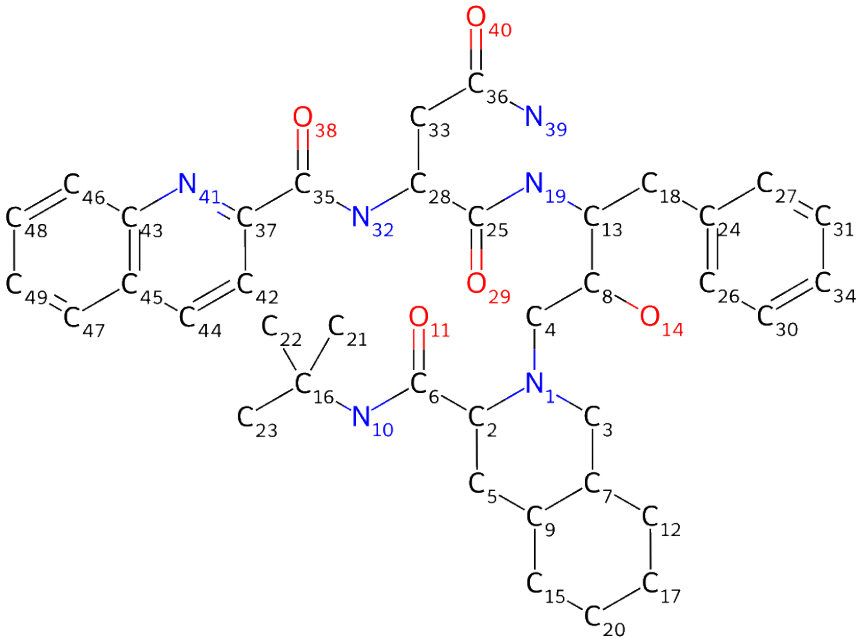
C-oxidation BDE Energy Report for: 268_saquinavir-out

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



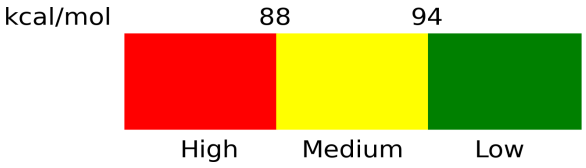
Atom	BDE (kcal/mol)	Propensity
C2	85.57	High
C3	91.45	Moderate
C4	94.31	Low
C5	97.85	Low
C7	95.24	Low
C8	89.72	Moderate
C9	95.29	Low
C12	96.43	Low
C13	89.8	Moderate
C15	97.53	Low

C17	97.84	Low
C18	87.03	High
C20	97.38	Low
C21	102.96	Low
C22	102.54	Low
C23	101.56	Low
C26	113.09	Low
C27	111.08	Low
C28	86.62	High
C30	111.98	Low
C31	111.83	Low
C33	94.46	Low
C34	112.26	Low
C42	114.54	Low
C44	111.46	Low
C46	114.65	Low
C47	112.14	Low
C48	112.2	Low
C49	112.41	Low

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.*