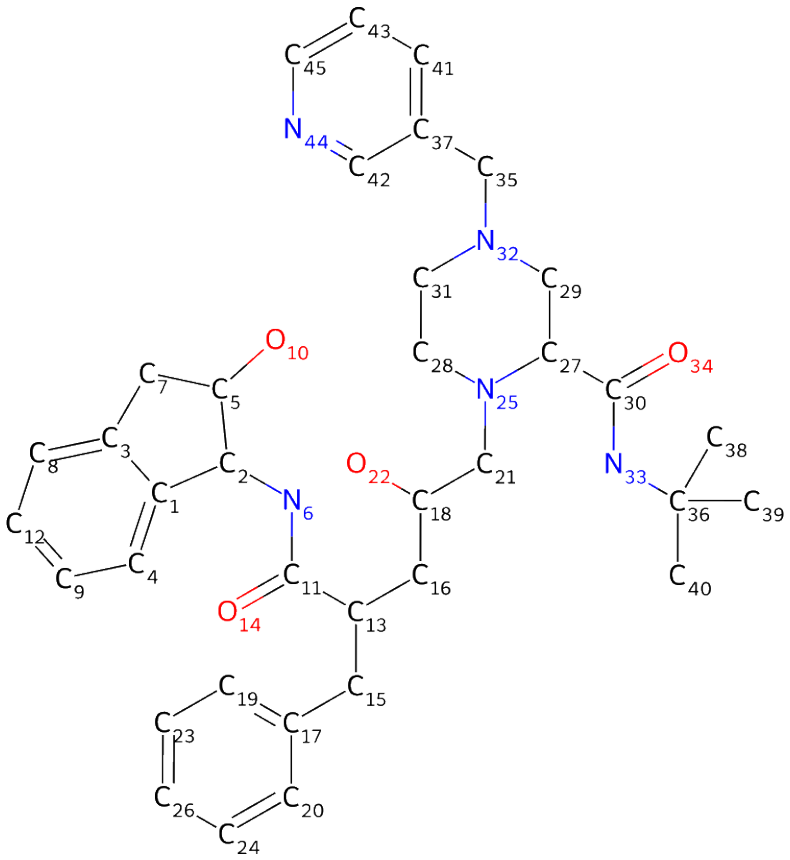
C-oxidation BDE Energy Report for: 167_indinavir-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 167_indinavir-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



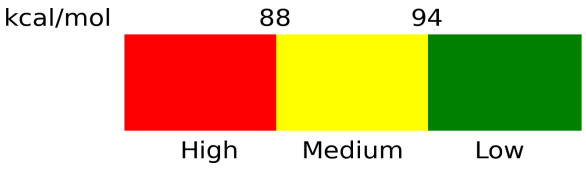
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C2	78.25	High	0.81
C4	113.23	Low	15.68
C5	90.92	Moderate	9.04
C7	85.0	High	8.01
C8	112.29	Low	61.11

C9	112.21	Low	34.83
C12	112.19	Low	0.57
C13	89.57	Moderate	0.51
C15	86.61	High	0.50
C16	98.43	Low	0.57
C18	88.62	Moderate	0.35
C19	111.67	Low	1.15
C20	112.82	Low	5.71
C21	90.12	Moderate	4.98
C23	111.87	Low	12.18
C24	111.86	Low	5.09
C26	112.27	Low	5.68
C27	87.38	High	7.76
C28	89.62	Moderate	10.06
C29	91.76	Moderate	9.62
C31	90.97	Moderate	8.60
C35	80.75	High	11.52
C38	102.9	Low	16.76
C39	102.95	Low	13.56
C40	102.79	Low	16.42
C41	112.5	Low	13.35
C42	106.04	Low	15.95
C43	112.43	Low	23.32
C45	107.06	Low	14.29

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.*