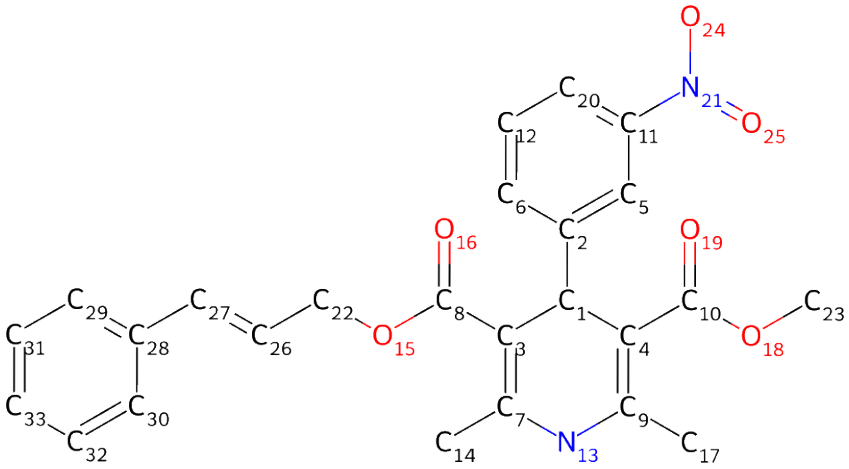
C-oxidation BDE Energy Report for: 447_pranidipine-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 447_pranidipine-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



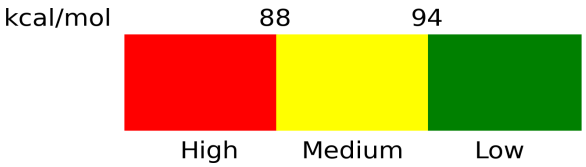
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	82.02	High	8.32
C5	114.03	Low	1.43
C6	112.06	Low	0.32
C12	112.49	Low	0.68
C14	88.33	Moderate	19.16
C17	87.97	High	75.81
C20	114.91	Low	7.73
C22	73.83	High	0.68
C23	98.03	Low	6.32
C26	107.76	Low	19.44
C27	101.36	Low	8.77
C29	112.39	Low	37.84
C30	111.17	Low	35.29
C31	112.09	Low	20.80

C32	112.0	Low	27.56
C33	112.58	Low	27.56

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.*