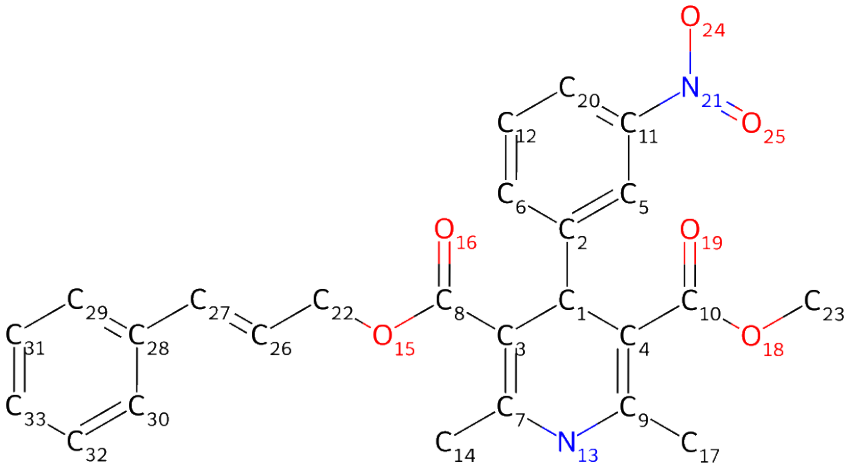
C-oxidation BDE Energy Report for: 447_pranidipine-out

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



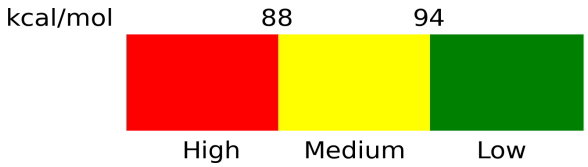
Atom	BDE (kcal/mol)	Propensity
C1	82.02	High
C5	114.03	Low
C6	112.06	Low
C12	112.49	Low
C14	88.33	Moderate
C17	87.97	High
C20	114.91	Low
C22	73.83	High
C23	98.03	Low
C26	107.76	Low
C27	101.36	Low
C29	112.39	Low
C30	111.17	Low
C31	112.09	Low

C32	112.0	Low
C33	112.58	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.*