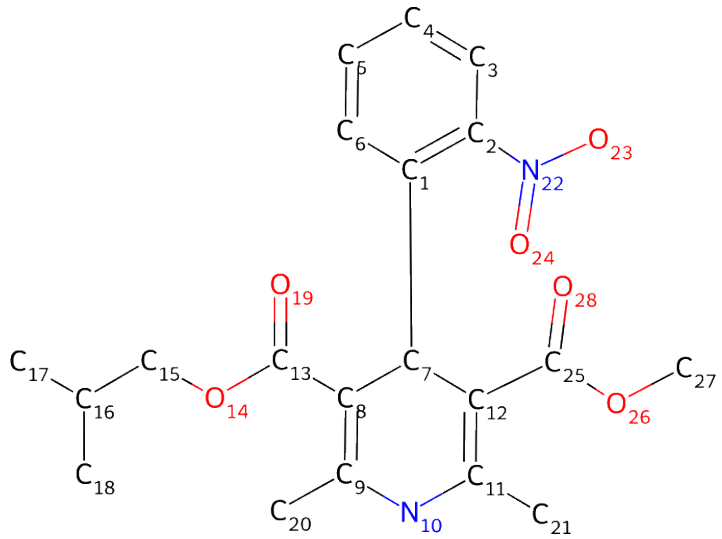
C-oxidation BDE Energy Report for: nisoldipine

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

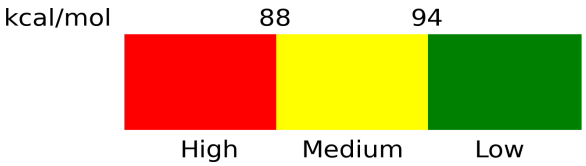


Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C3	113.77	Low	7.32
C4	112.98	Low	10.99
C5	112.45	Low	5.26
C6	112.73	Low	0.41
C7	72.77	High	0.00
C15	96.49	Low	0.82
C16	93.6	Moderate	0.00
C17	102.55	Low	4.75
C18	102.24	Low	4.71
C20	88.91	Moderate	7.44
C21	88.43	Moderate	7.52
C27	98.04	Low	8.13

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.*