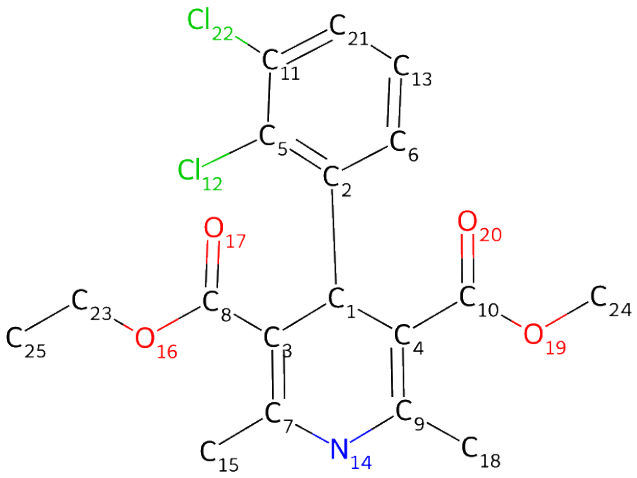
C-oxidation BDE Energy Report for: 020_FELODIPINE-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 020_FELODIPINE-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

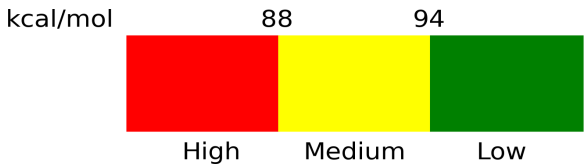


Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	79.73	High	7.67
C6	111.74	Low	9.44
C13	112.57	Low	32.46
C15	88.26	Moderate	26.22
C18	88.23	Moderate	26.47
C21	113.46	Low	29.52
C23	98.61	Low	24.33
C24	97.85	Low	28.63
C25	102.83	Low	23.96

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.*