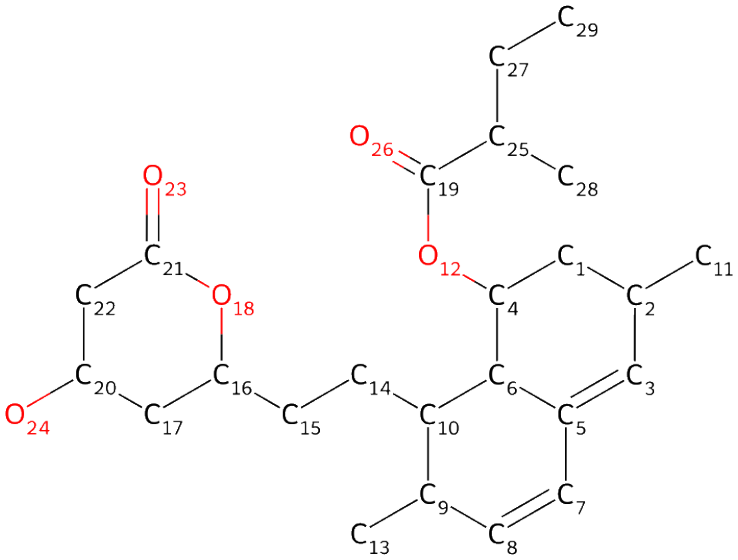
C-oxidation BDE Energy Report for: 189_lovastatin-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 189_lovastatin-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



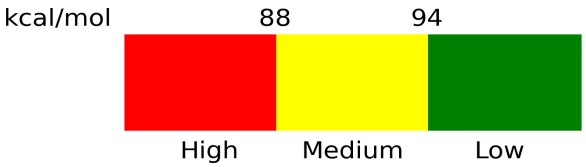
Atom	BDE (kcal/mol)	Propensity
C1	97.15	Low
C2	70.82	High
C3	109.16	Low
C4	97.4	Low
C6	81.17	High
C7	109.92	Low
C8	109.41	Low
C9	77.94	High
C10	94.92	Low
C11	101.68	Low
C13	100.63	Low
C14	97.31	Low

C15	97.87	Low
C16	91.0	Moderate
C17	97.52	Low
C20	91.22	Moderate
C22	91.66	Moderate
C25	85.89	High
C27	96.25	Low
C28	101.69	Low
C29	100.34	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.*