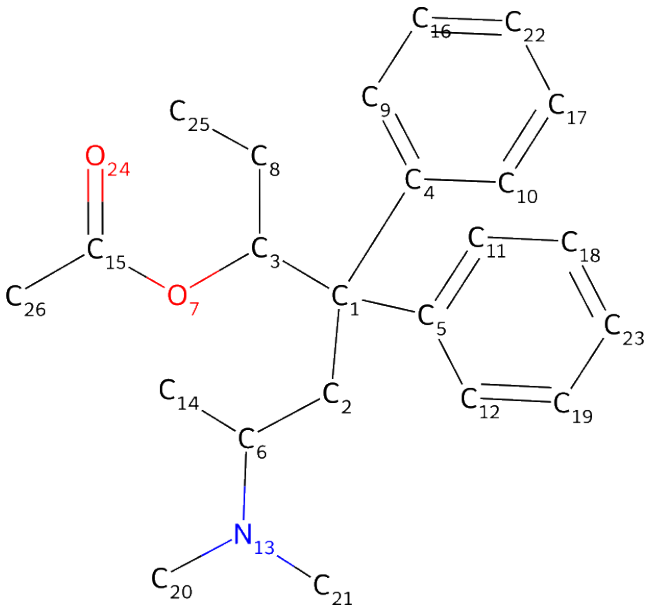
C-oxidation BDE Energy Report for: 178_laam-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 178_laam-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



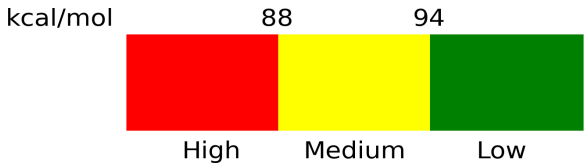
Atom	BDE (kcal/mol)	Propensity
C2	94.53	Low
C3	94.84	Low
C6	88.11	Moderate
C8	96.63	Low
C9	109.08	Low
C10	110.81	Low
C11	110.09	Low
C12	109.64	Low
C14	99.86	Low
C16	112.09	Low
C17	111.98	Low
C18	111.89	Low
C19	111.88	Low

C20	90.29	Moderate
C21	90.15	Moderate
C22	112.67	Low
C23	112.52	Low
C25	100.89	Low
C26	97.27	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.*