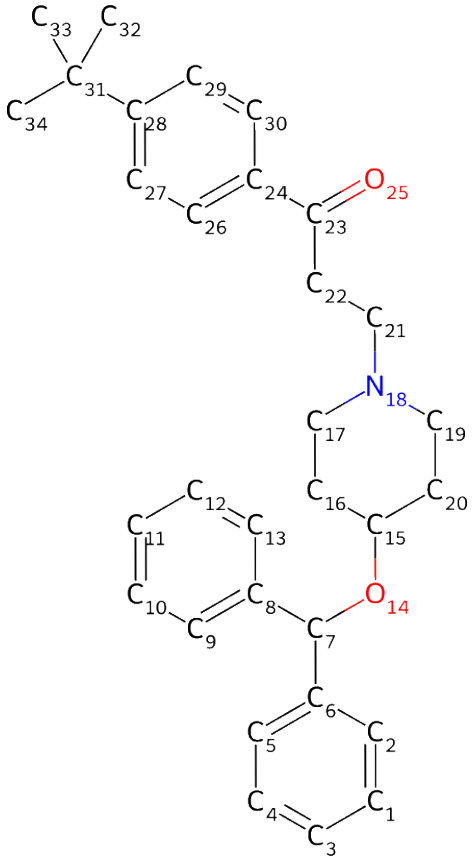
C-oxidation BDE Energy Report for: 123_ebastine-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 123_ebastine-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



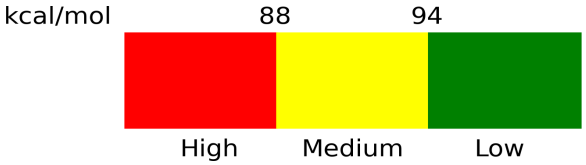
Atom	BDE (kcal/mol)	Propensity
C1	111.7	Low
C2	112.74	Low
C3	112.46	Low
C4	112.08	Low
C5	111.76	Low

C7	75.64	High
C9	111.72	Low
C10	112.09	Low
C11	112.47	Low
C12	110.01	Low
C13	112.67	Low
C15	94.14	Low
C16	99.14	Low
C17	89.19	Moderate
C19	88.93	Moderate
C20	98.27	Low
C21	90.35	Moderate
C22	88.47	Moderate
C26	113.65	Low
C27	110.17	Low
C29	109.47	Low
C30	109.55	Low
C32	101.54	Low
C33	101.37	Low
C34	101.92	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.*