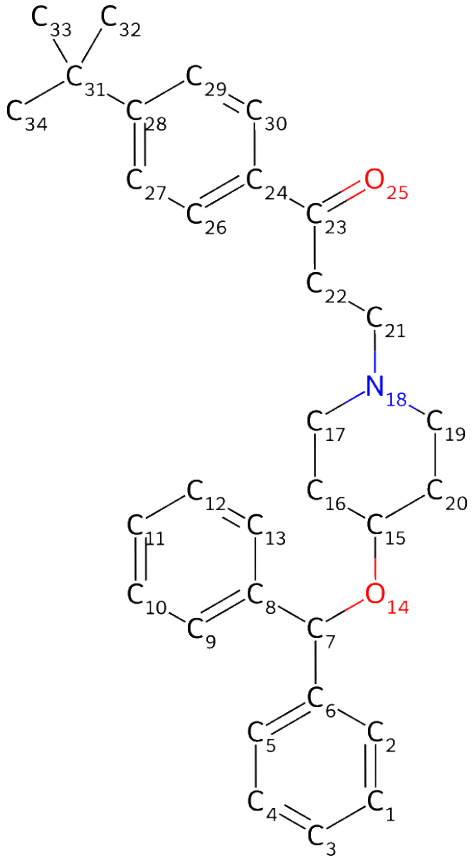
C-oxidation BDE Energy Report for: 123_ebastine-out

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



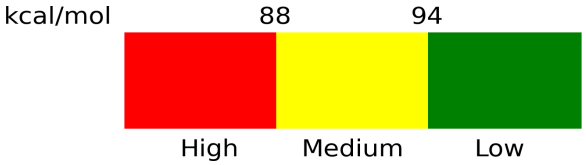
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	111.7	Low	15.48
C2	112.74	Low	5.83
C3	112.46	Low	16.12
C4	112.08	Low	15.10
C5	111.76	Low	4.79

C7	75.64	High	0.00
C9	111.72	Low	5.86
C10	112.09	Low	15.44
C11	112.47	Low	15.98
C12	110.01	Low	14.61
C13	112.67	Low	4.14
C15	94.14	Low	0.00
C16	99.14	Low	0.40
C17	89.19	Moderate	0.53
C19	88.93	Moderate	0.53
C20	98.27	Low	0.40
C21	90.35	Moderate	0.53
C22	88.47	Moderate	0.76
C26	113.65	Low	9.82
C27	110.17	Low	6.79
C29	109.47	Low	5.86
C30	109.55	Low	9.87
C32	101.54	Low	4.55
C33	101.37	Low	4.66
C34	101.92	Low	4.58

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.*