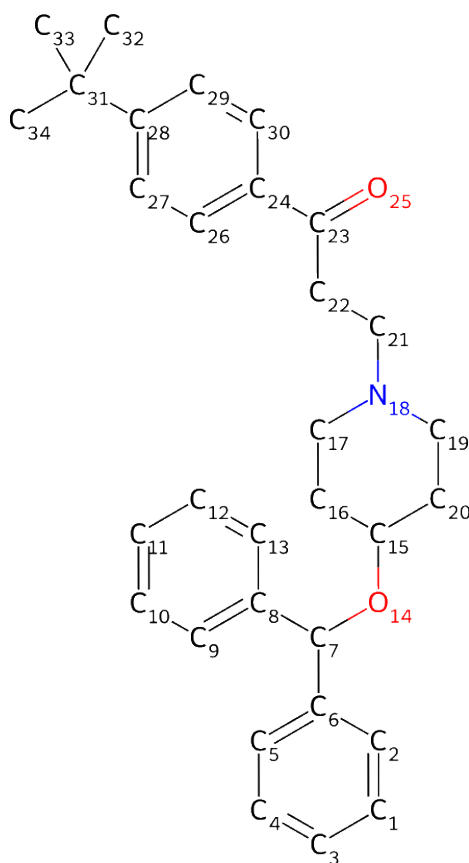


C-oxidation BDE Energy Report for: 123_ebastine-out

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



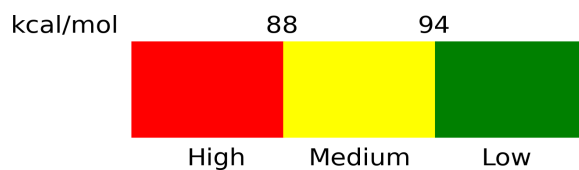
Atom	BDE (kcal/mol)	Propensity	SASA (Å ²)
C1	111.7	Low	35.12
C2	112.74	Low	16.32
C3	112.46	Low	35.48
C4	112.08	Low	35.38
C5	111.76	Low	13.18

C7	75.64	High	3.02
C9	111.72	Low	17.22
C10	112.09	Low	35.10
C11	112.47	Low	35.32
C12	110.01	Low	35.11
C13	112.67	Low	11.98
C15	94.14	Low	8.08
C16	99.14	Low	15.33
C17	89.19	Moderate	15.20
C19	88.93	Moderate	15.22
C20	98.27	Low	15.75
C21	90.35	Moderate	16.13
C22	88.47	Moderate	15.76
C26	113.65	Low	16.28
C27	110.17	Low	13.61
C29	109.47	Low	13.38
C30	109.55	Low	16.65
C32	101.54	Low	22.97
C33	101.37	Low	22.21
C34	101.92	Low	22.65

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.*