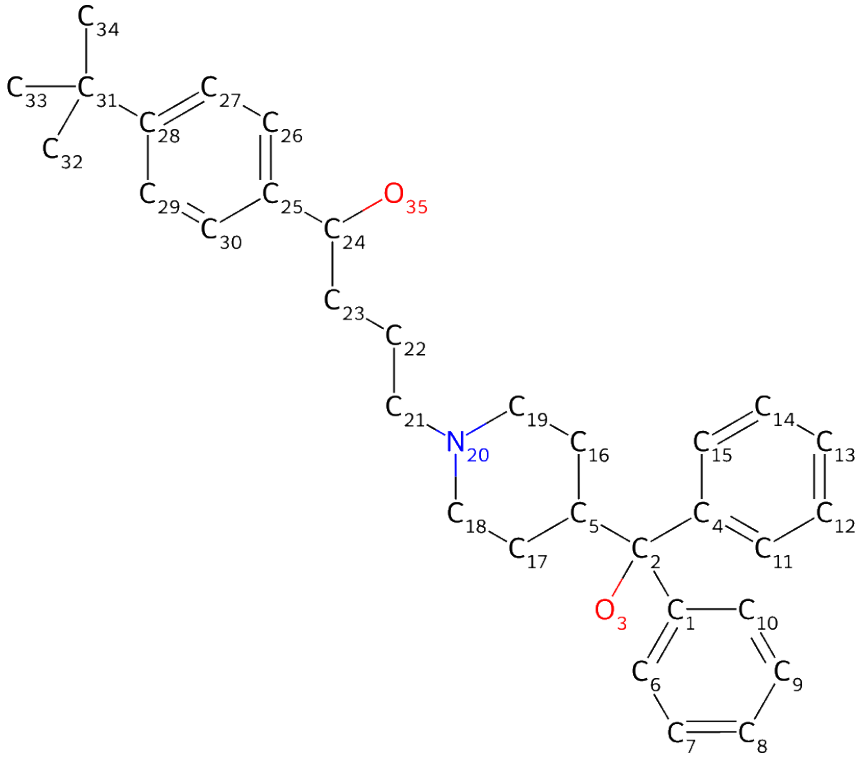
C-oxidation BDE Energy Report for: 290_terfenadine-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 290_terfenadine-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



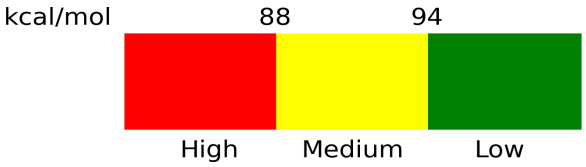
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C5	95.11	Low	3.56
C6	111.82	Low	15.31
C7	111.96	Low	35.30
C8	112.62	Low	35.73
C9	112.02	Low	34.74
C10	109.57	Low	9.47
C11	112.66	Low	13.56
C12	111.89	Low	35.31

C13	112.51	Low	35.74
C14	112.06	Low	34.82
C15	110.17	Low	11.22
C16	99.52	Low	9.97
C17	97.42	Low	10.06
C18	92.95	Moderate	15.54
C19	93.12	Moderate	15.33
C21	93.2	Moderate	15.21
C22	95.95	Low	11.00
C23	97.36	Low	15.29
C24	77.43	High	14.96
C26	112.76	Low	19.02
C27	109.79	Low	13.57
C29	110.12	Low	13.15
C30	110.98	Low	19.18
C32	101.46	Low	22.75
C33	101.45	Low	22.01
C34	101.92	Low	22.75

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.*