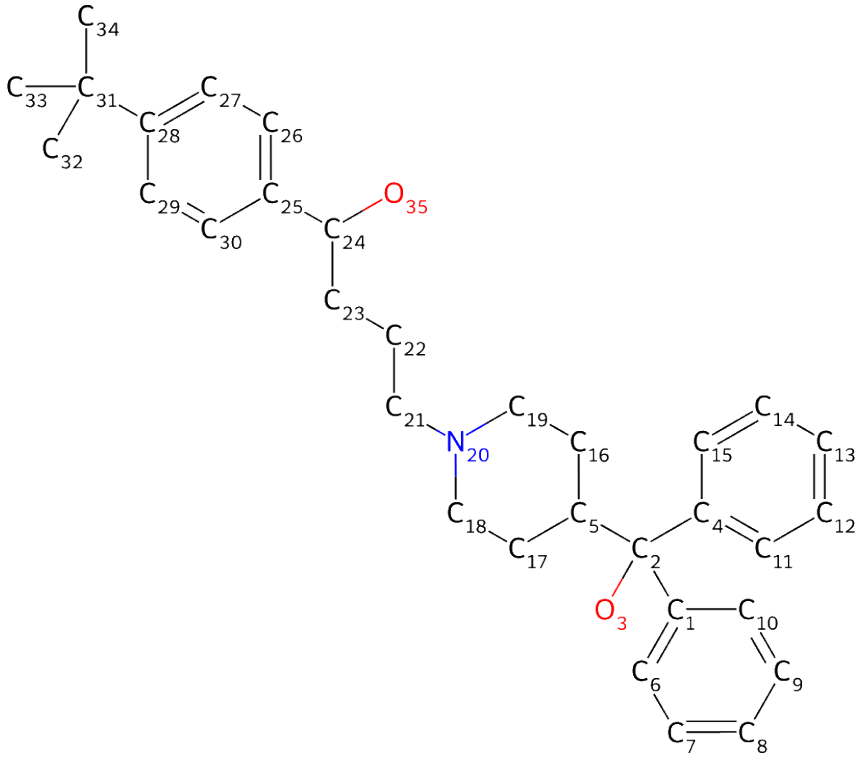
C-oxidation BDE Energy Report for: 290_terfenadine-out

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



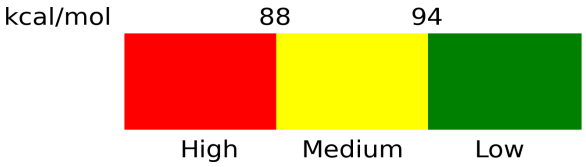
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C5	95.11	Low	0.00
C6	111.82	Low	0.00
C7	111.96	Low	2.58
C8	112.62	Low	0.89
C9	112.02	Low	0.00
C10	109.57	Low	0.00
C11	112.66	Low	0.13
C12	111.89	Low	7.12

C13	112.51	Low	0.10
C14	112.06	Low	0.10
C15	110.17	Low	1.07
C16	99.52	Low	3.89
C17	97.42	Low	3.85
C18	92.95	Moderate	5.32
C19	93.12	Moderate	5.30
C21	93.2	Moderate	3.26
C22	95.95	Low	27.83
C23	97.36	Low	14.22
C24	77.43	High	7.84
C26	112.76	Low	1.22
C27	109.79	Low	0.00
C29	110.12	Low	5.28
C30	110.98	Low	10.25
C32	101.46	Low	10.25
C33	101.45	Low	0.00
C34	101.92	Low	30.03

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.*