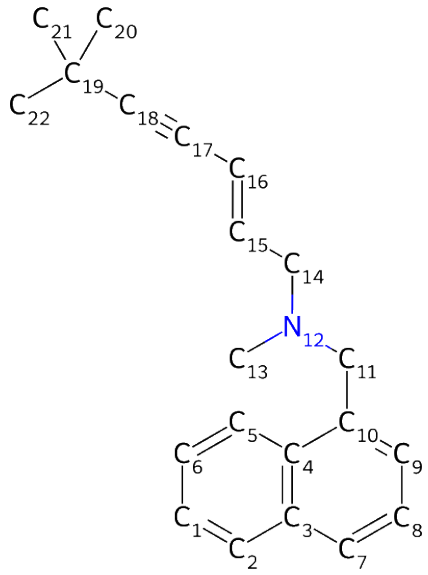
C-oxidation BDE Energy Report for: terbinafine

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

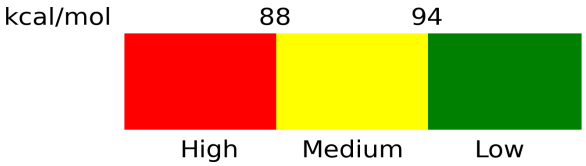


Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	112.35	Low	15.91
C2	112.25	Low	13.95
C5	112.38	Low	7.61
C6	112.09	Low	15.18
C7	112.58	Low	13.70
C9	112.38	Low	7.88
C11	83.98	High	0.84
C13	93.14	Moderate	6.49
C14	70.33	High	0.87
C15	111.88	Low	5.28
C20	103.02	Low	4.75
C21	102.46	Low	4.83
C22	102.46	Low	4.75

Missing Sites:

C8, C16.

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.*