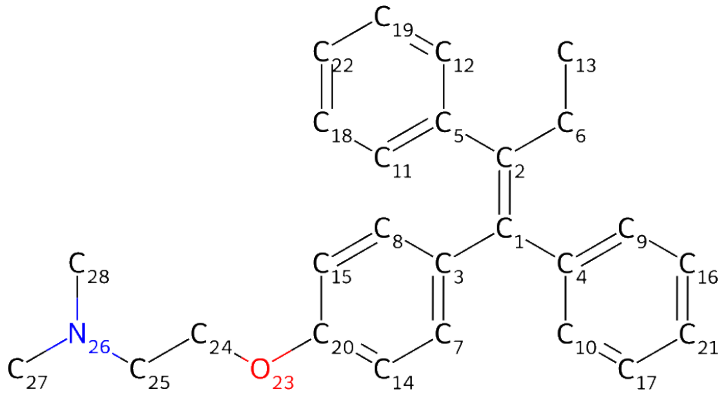
C-oxidation BDE Energy Report for: 280_tamoxifen-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 280_tamoxifen-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



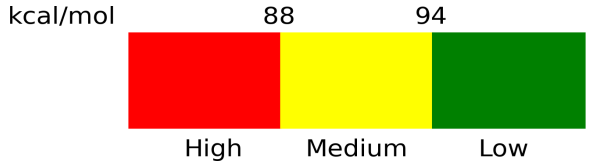
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C6	78.31	High	0.00
C7	110.62	Low	0.00
C8	111.97	Low	0.00
C9	112.36	Low	0.00
C10	111.13	Low	0.04
C11	111.83	Low	13.63
C12	110.96	Low	0.43
C13	101.19	Low	0.00
C14	111.6	Low	24.29
C15	113.93	Low	0.59
C16	111.92	Low	0.00
C17	111.92	Low	0.95
C18	111.9	Low	0.65
C19	111.84	Low	0.00
C21	112.43	Low	4.19

C22	112.44	Low	3.03
C24	93.65	Moderate	2.17
C25	89.46	Moderate	0.11
C27	93.2	Moderate	7.03
C28	92.42	Moderate	0.00

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.*