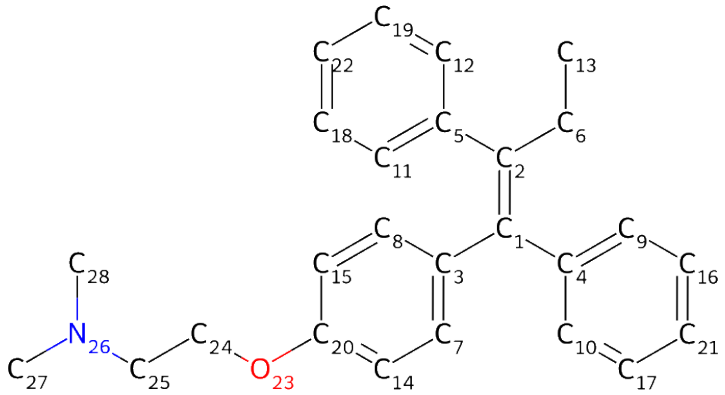
C-oxidation BDE Energy Report for: 280_tamoxifen-out

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



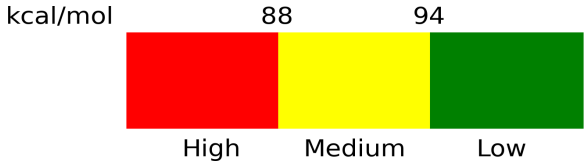
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C6	78.31	High	14.89
C7	110.62	Low	10.95
C8	111.97	Low	13.91
C9	112.36	Low	15.07
C10	111.13	Low	14.25
C11	111.83	Low	14.27
C12	110.96	Low	15.48
C13	101.19	Low	23.67
C14	111.6	Low	20.62
C15	113.93	Low	20.85
C16	111.92	Low	35.86
C17	111.92	Low	35.85
C18	111.9	Low	33.92
C19	111.84	Low	35.73
C21	112.43	Low	35.93

C22	112.44	Low	35.45
C24	93.65	Moderate	17.23
C25	89.46	Moderate	16.82
C27	93.2	Moderate	25.31
C28	92.42	Moderate	25.09

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.*