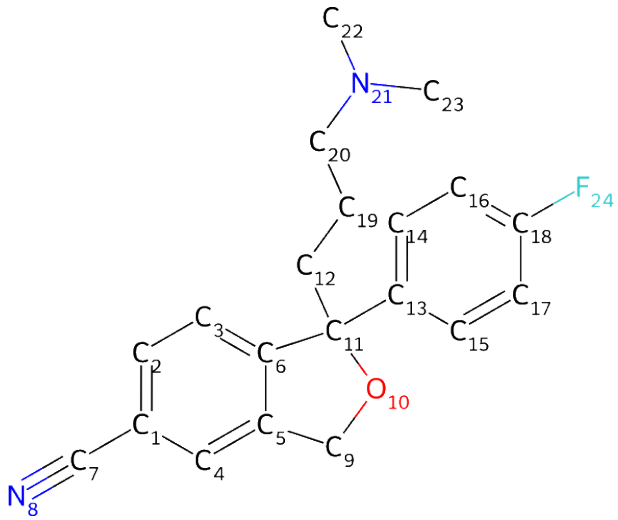
C-oxidation BDE Energy Report for: 085_citalopram-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 085_citalopram-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

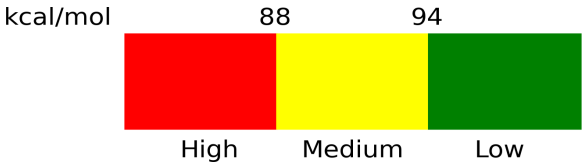


Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C2	114.14	Low	29.82
C3	111.92	Low	12.58
C4	113.87	Low	25.02
C9	80.22	High	25.45
C12	97.61	Low	11.76
C14	110.39	Low	10.12
C15	112.58	Low	12.25
C16	114.73	Low	32.56
C17	114.57	Low	32.64
C19	97.42	Low	8.61
C20	91.18	Moderate	12.77
C22	92.67	Moderate	24.92
C23	92.9	Moderate	24.80

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.*