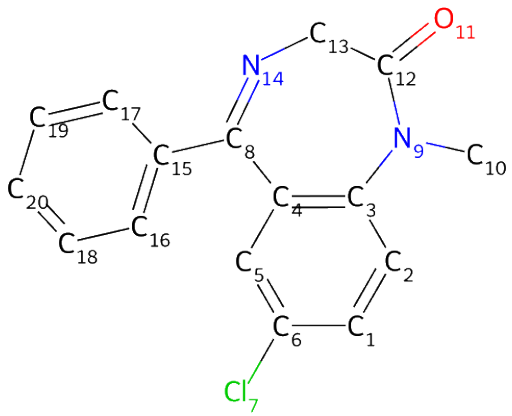
C-oxidation BDE Energy Report for: 112_diazepam-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 112_diazepam-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

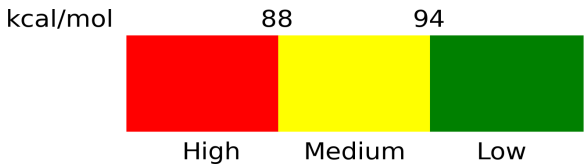


Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	113.75	Low	29.73
C2	111.87	Low	17.54
C5	112.83	Low	10.78
C10	93.82	Moderate	26.55
C13	79.07	High	26.99
C16	113.58	Low	14.13
C17	111.0	Low	24.86
C18	112.24	Low	35.79
C19	112.39	Low	35.83
C20	112.49	Low	35.94

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.*