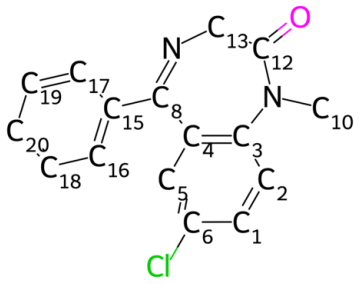
C-oxidation BDE Energy Report for: 112_diazepam-out

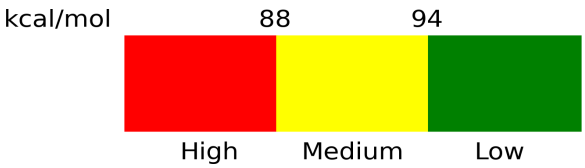
This report covers the results for BDE calculations performed for: 112_diazepam-out. Oxidation propensity is established using C-H Bond Dissociation Enthalpies (BDE). The lower the C-H BDE values the higher the propensity for C-oxidation. Details for the DFT calculations and overall workflow are explained at the end of this document

Bond Dissociation Energies (kcal/mol)



Atom	BDE (kcal/mol)	Propensity
C1	113.75	Low
C2	111.87	Low
C5	112.83	Low
C10	93.82	Moderate
C13	79.07	High
C16	113.58	Low
C17	111.0	Low
C18	112.24	Low
C19	112.39	Low
C20	112.49	Low

Risk Scale:



Calculation details and output files

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.*