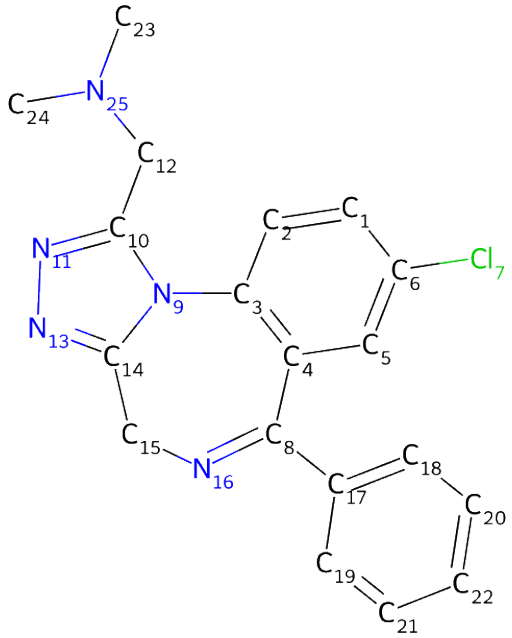
C-oxidation BDE Energy Report for: 039_adinazolam-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 039_adinazolam-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



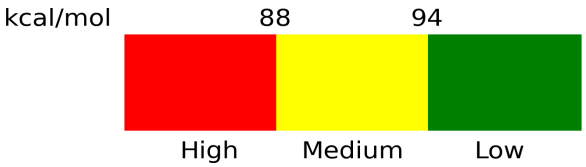
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	113.83	Low	28.82
C2	111.49	Low	11.91
C5	113.02	Low	10.04
C12	80.06	High	11.29
C15	76.08	High	27.87
C18	110.9	Low	7.79
C19	113.6	Low	25.06
C20	112.43	Low	35.20
C21	112.3	Low	35.83
C22	112.54	Low	35.90

C23	94.55	Low	23.41
C24	93.66	Moderate	23.32

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.*