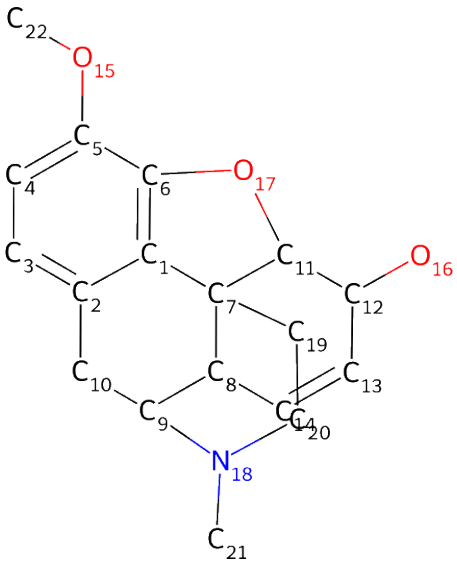
C-oxidation BDE Energy Report for: 091_codeine-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 091_codeine-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

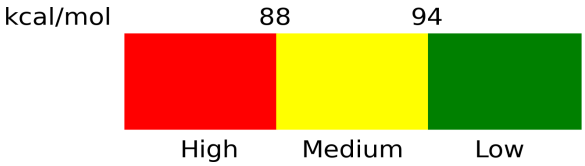


Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C3	112.38	Low	29.30
C4	111.7	Low	16.52
C8	83.17	High	6.67
C9	96.42	Low	13.62
C10	83.39	High	20.04
C11	98.23	Low	17.79
C12	72.95	High	22.42
C13	110.82	Low	30.61
C14	108.59	Low	22.03
C19	98.9	Low	17.35
C20	89.56	Moderate	19.30
C21	91.13	Moderate	25.30
C22	96.7	Low	32.58

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.*