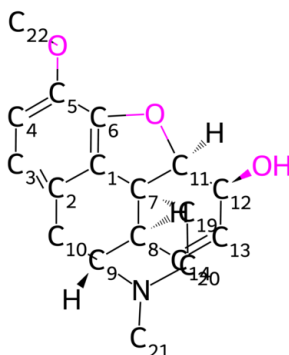


C-oxidation BDE Energy Report for: 091_codeine-out

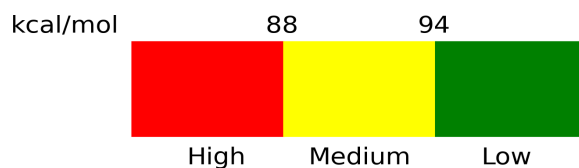
This report covers the results for BDE calculations performed for: 091_codeine-out. Oxidation propensity is established using C-H Bond Dissociation Enthalpies (BDE). The lower the C-H BDE values the higher the propensity for C-oxidation. Details for the DFT calculations and overall workflow are explained at the end of this document

Bond Dissociation Energies (kcal/mol)



Atom	BDE (kcal/mol)	Propensity
C3	112.38	Low
C4	111.7	Low
C8	83.17	High
C9	96.42	Low
C10	83.39	High
C11	98.23	Low
C12	72.95	High
C13	110.82	Low
C14	108.59	Low
C19	98.9	Low
C20	89.56	Moderate
C21	91.13	Moderate
C22	96.7	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.*