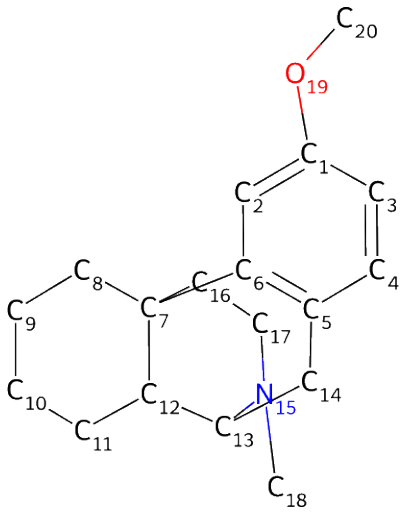
C-oxidation BDE Energy Report for: 109_dextromethorphan-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 109_dextromethorphan-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



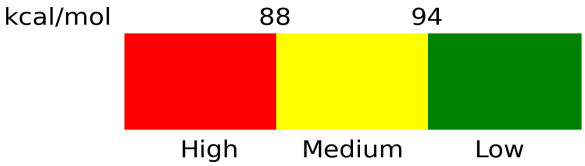
Atom	BDE (kcal/mol)	Propensity
C2	111.94	Low
C3	111.98	Low
C4	111.25	Low
C8	97.17	Low
C9	98.09	Low
C10	98.02	Low
C11	97.25	Low
C12	97.31	Low
C13	96.04	Low
C14	83.08	High
C16	98.46	Low
C17	89.35	Moderate
C18	90.78	Moderate

C20	96.62	Low

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.*