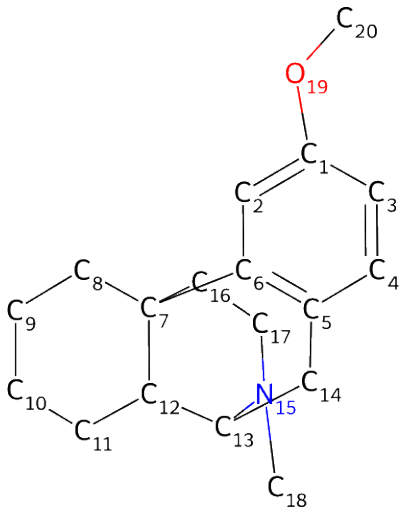
C-oxidation BDE Energy Report for: 109_dextromethorphan-out

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



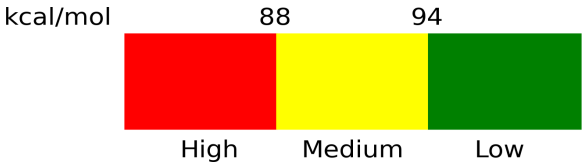
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C2	111.94	Low	4.99
C3	111.98	Low	24.24
C4	111.25	Low	26.54
C8	97.17	Low	15.50
C9	98.09	Low	21.58
C10	98.02	Low	27.98
C11	97.25	Low	16.66
C12	97.31	Low	3.67
C13	96.04	Low	11.97
C14	83.08	High	19.02
C16	98.46	Low	16.05
C17	89.35	Moderate	18.77
C18	90.78	Moderate	25.28

C20	96.62	Low	31.25

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.*