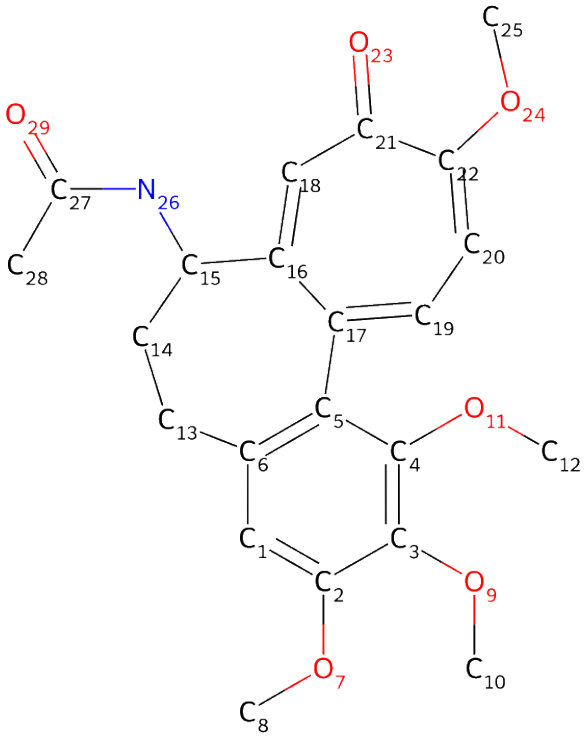
C-oxidation BDE Energy Report for: 092_colchicine-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 092_colchicine-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



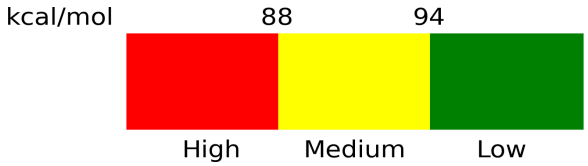
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	111.63	Low	0.00
C8	97.2	Low	0.00
C10	97.98	Low	0.50
C12	97.24	Low	0.00
C13	88.99	Moderate	7.50
C14	97.34	Low	6.76
C15	84.64	High	14.69
C18	107.68	Low	4.54

C19	105.68	Low	0.45
C20	104.85	Low	1.88
C25	96.71	Low	6.67
C28	97.37	Low	18.69

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.*