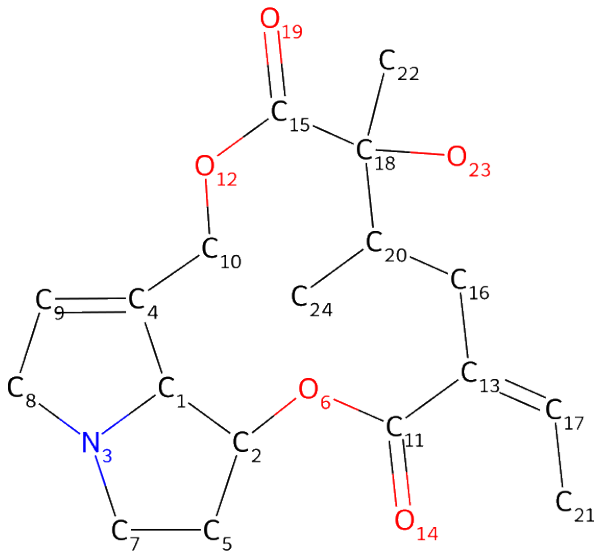
C-oxidation BDE Energy Report for: 033_SENECIONINE-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 033_SENECIONINE-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

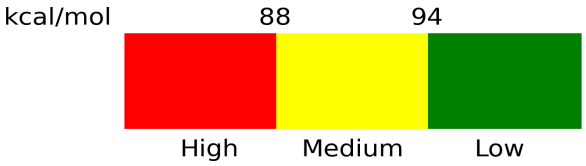


Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	76.45	High	0.00
C2	95.64	Low	0.00
C5	97.54	Low	0.00
C7	90.19	Moderate	3.10
C8	75.89	High	0.92
C9	113.77	Low	3.08
C10	82.92	High	0.78
C17	105.17	Low	22.68
C20	91.14	Moderate	25.60
C22	102.18	Low	75.10

Missing Sites:

C16, C21, C24.

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.*