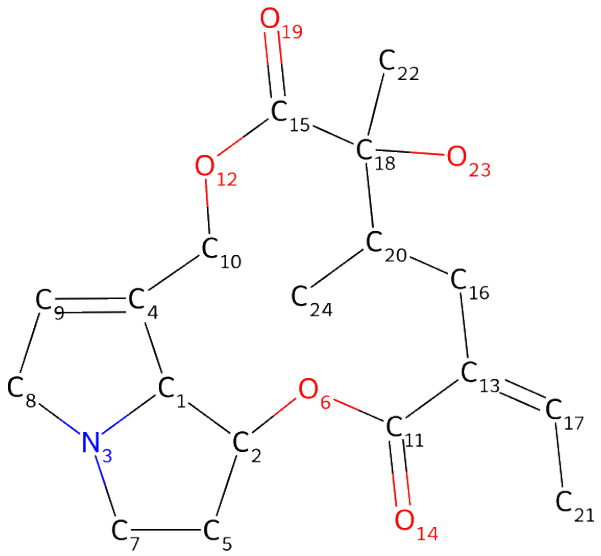
C-oxidation BDE Energy Report for: 033_SENECIONINE-out

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

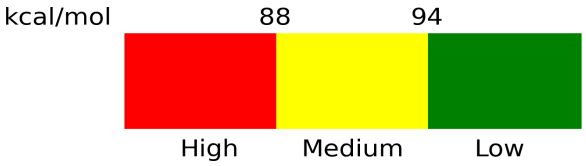


Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	76.45	High	19.96
C2	95.64	Low	11.01
C5	97.54	Low	20.66
C7	90.19	Moderate	25.61
C8	75.89	High	26.28
C9	113.77	Low	25.86
C10	82.92	High	20.35
C17	105.17	Low	15.98
C20	91.14	Moderate	9.56
C22	102.18	Low	21.08

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.*