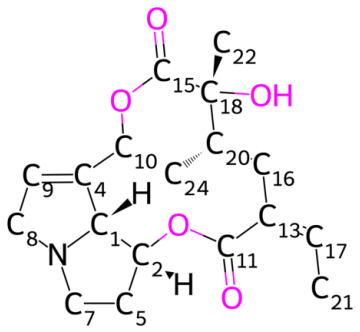
C-oxidation BDE Energy Report for: 033_SENECIONINE-out

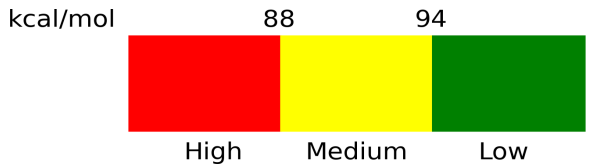
This report covers the results for BDE calculations performed for: 033_SENECIONINE-out. Oxidation propensity is established using C-H Bond Dissociation Enthalpies (BDE). The lower the C-H BDE values the higher the propensity for C-oxidation. Details for the DFT calculations and overall workflow are explained at the end of this document

Bond Dissociation Energies (kcal/mol)



Atom	BDE (kcal/mol)	Propensity
C1	76.45	High
C2	95.64	Low
C5	97.54	Low
C7	90.19	Moderate
C8	75.89	High
C9	113.77	Low
C10	82.92	High
C17	105.17	Low
C20	91.14	Moderate
C22	102.18	Low

Risk Scale:



Calculation details and output files

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.*