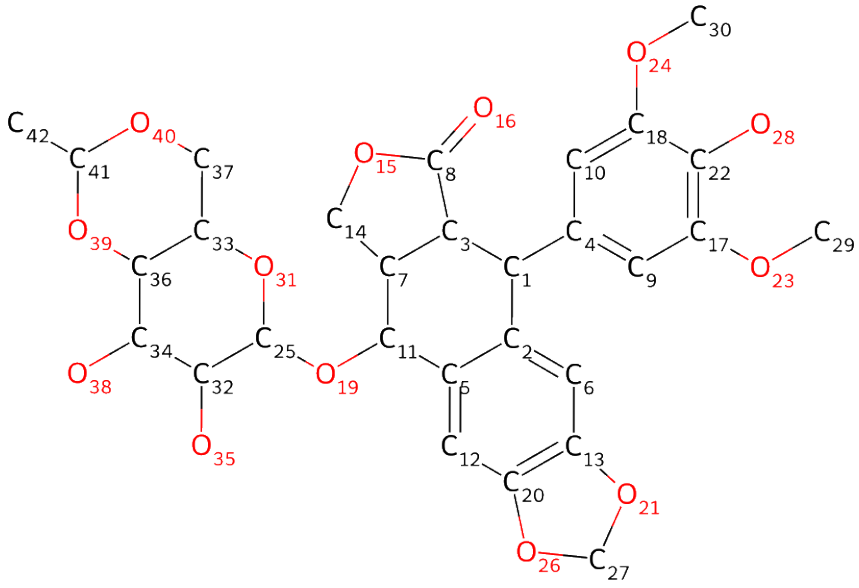
C-oxidation BDE Energy Report for: 137_etoposide-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 137_etoposide-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



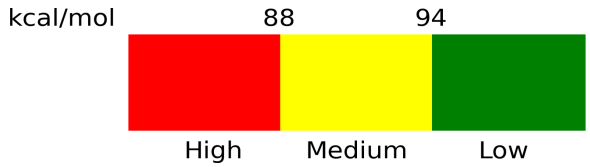
Atom	BDE (kcal/mol)	Propensity
C1	82.72	High
C3	85.63	High
C6	115.14	Low
C7	90.82	Moderate
C9	112.13	Low
C10	112.39	Low
C11	84.3	High
C12	114.44	Low
C14	96.81	Low
C25	91.09	Moderate
C27	90.96	Moderate

C29	96.98	Low
C30	96.51	Low
C32	92.36	Moderate
C33	91.65	Moderate
C34	93.91	Moderate
C36	92.93	Moderate
C37	95.02	Low
C41	91.61	Moderate
C42	104.27	Low

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.*