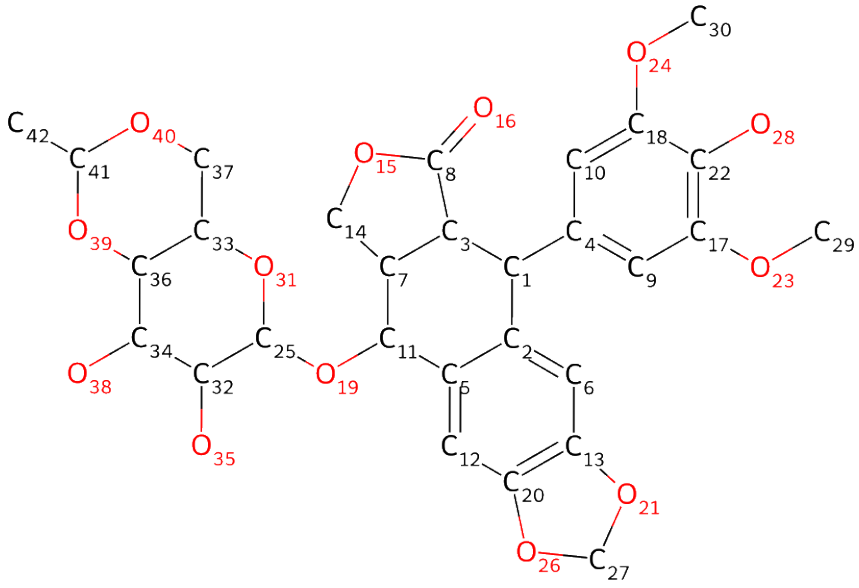
C-oxidation BDE Energy Report for: 137_etoposide-out

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



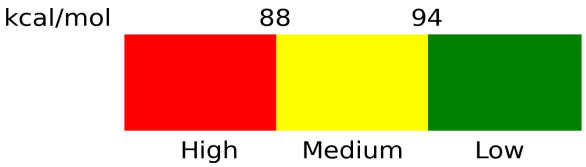
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	82.72	High	0.00
C3	85.63	High	0.00
C6	115.14	Low	7.36
C7	90.82	Moderate	0.00
C9	112.13	Low	1.23
C10	112.39	Low	1.23
C11	84.3	High	0.00
C12	114.44	Low	7.28
C14	96.81	Low	2.41
C25	91.09	Moderate	0.00
C27	90.96	Moderate	5.28

C29	96.98	Low	8.58
C30	96.51	Low	8.62
C32	92.36	Moderate	0.00
C33	91.65	Moderate	0.00
C34	93.91	Moderate	0.00
C36	92.93	Moderate	0.00
C37	95.02	Low	1.99
C41	91.61	Moderate	0.15
C42	104.27	Low	6.39

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.*