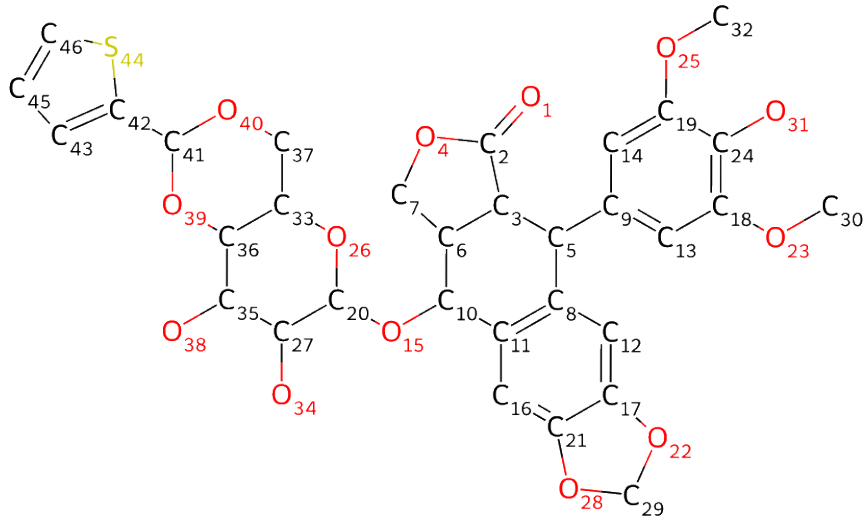
C-oxidation BDE Energy Report for: 285_teniposide-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 285_teniposide-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



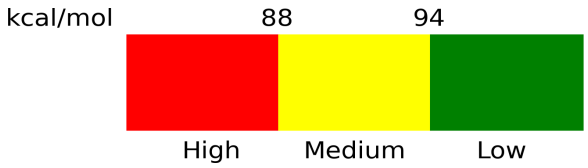
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C3	85.55	High	9.71
C5	81.31	High	11.86
C6	96.1	Low	0.24
C7	97.72	Low	18.07
C10	83.16	High	6.54
C12	115.03	Low	17.87
C13	112.27	Low	1.75
C14	111.74	Low	1.82
C16	113.71	Low	7.42
C20	93.62	Moderate	6.72
C27	93.2	Moderate	10.29
C29	91.11	Moderate	37.98

C30	96.56	Low	28.08
C32	96.72	Low	28.15
C33	94.85	Low	9.91
C35	93.57	Moderate	15.94
C36	95.03	Low	9.24
C37	96.69	Low	21.56
C41	81.03	High	13.84
C43	115.34	Low	28.32
C45	115.47	Low	38.30
C46	117.7	Low	39.01

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.*