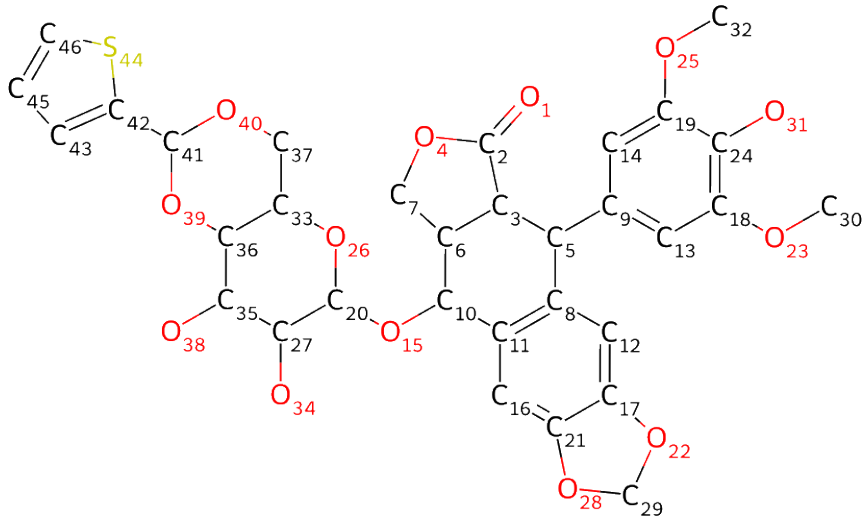
C-oxidation BDE Energy Report for: 285_teniposide-out

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



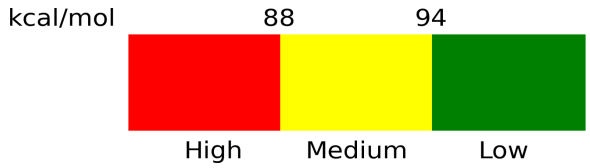
Atom	BDE (kcal/mol)	Propensity
C3	85.55	High
C5	81.31	High
C6	96.1	Low
C7	97.72	Low
C10	83.16	High
C12	115.03	Low
C13	112.27	Low
C14	111.74	Low
C16	113.71	Low
C20	93.62	Moderate
C27	93.2	Moderate
C29	91.11	Moderate

C30	96.56	Low
C32	96.72	Low
C33	94.85	Low
C35	93.57	Moderate
C36	95.03	Low
C37	96.69	Low
C41	81.03	High
C43	115.34	Low
C45	115.47	Low
C46	117.7	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.*