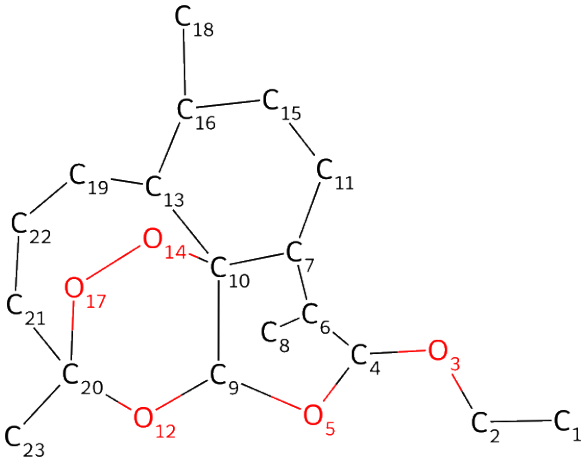
C-oxidation BDE Energy Report for: 063_beta_arteether-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 063_beta_arteether-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



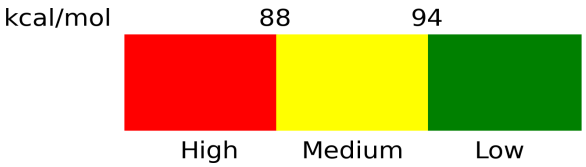
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	102.64	Low	30.85
C2	95.62	Low	21.37
C4	95.02	Low	15.42
C6	91.43	Moderate	15.98
C7	83.73	High	5.55
C8	99.58	Low	16.55
C9	77.75	High	0.00
C11	98.99	Low	17.86
C13	95.21	Low	7.58
C15	96.76	Low	21.17
C16	93.49	Moderate	10.20
C18	100.61	Low	24.06
C19	93.58	Moderate	12.39
C21	97.05	Low	22.45

C22	94.76	Low	21.99
C23	102.99	Low	23.98

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.*