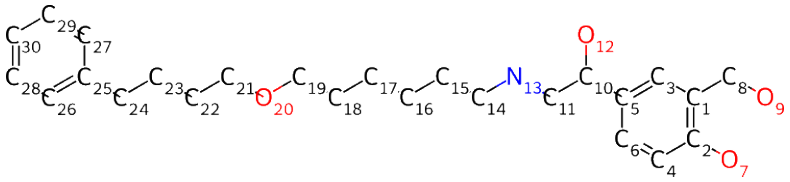
C-oxidation BDE Energy Report for: 267_salmeterol-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 267_salmeterol-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



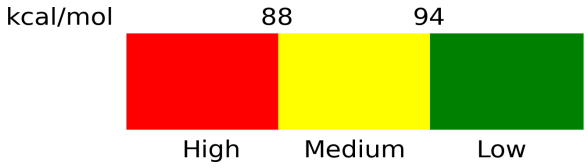
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C3	112.47	Low	4.57
C4	113.99	Low	13.82
C6	110.72	Low	7.59
C8	82.23	High	2.19
C10	78.93	High	0.01
C11	90.61	Moderate	0.23
C14	92.65	Moderate	0.42
C15	97.75	Low	0.27
C16	96.74	Low	0.19
C17	97.64	Low	0.19
C18	97.75	Low	0.37
C19	92.92	Moderate	0.64
C21	93.93	Moderate	0.62
C22	97.9	Low	0.35
C23	97.5	Low	0.30
C24	85.36	High	1.25
C26	111.76	Low	8.74
C27	111.93	Low	8.75
C28	111.91	Low	15.13
C29	111.96	Low	15.18

C30	112.37	Low	15.72

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.*