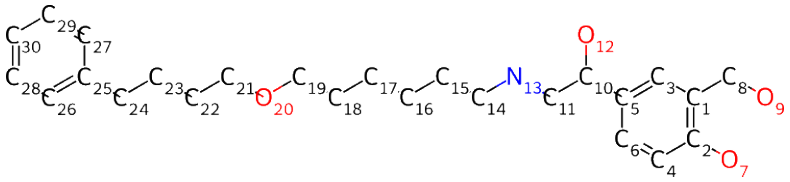
C-oxidation BDE Energy Report for: 267_salmeterol-out

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



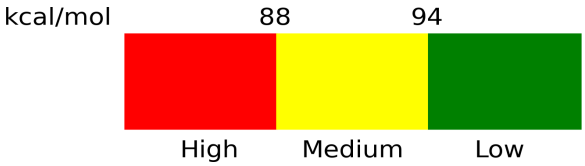
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C3	112.47	Low	9.32
C4	113.99	Low	29.60
C6	110.72	Low	20.01
C8	82.23	High	24.31
C10	78.93	High	15.69
C11	90.61	Moderate	15.91
C14	92.65	Moderate	17.88
C15	97.75	Low	17.67
C16	96.74	Low	15.20
C17	97.64	Low	14.81
C18	97.75	Low	19.87
C19	92.92	Moderate	19.35
C21	93.93	Moderate	19.27
C22	97.9	Low	16.88
C23	97.5	Low	14.73
C24	85.36	High	20.36
C26	111.76	Low	21.07
C27	111.93	Low	21.05
C28	111.91	Low	34.05
C29	111.96	Low	34.02

C30	112.37	Low	34.25

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.*