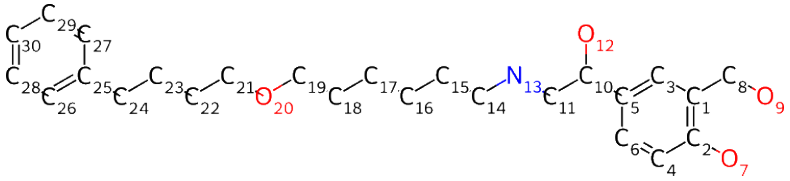
C-oxidation BDE Energy Report for: 267_salmeterol-out

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



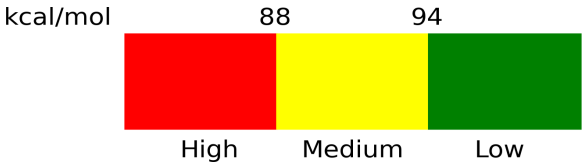
Atom	BDE (kcal/mol)	Propensity
C3	112.47	Low
C4	113.99	Low
C6	110.72	Low
C8	82.23	High
C10	78.93	High
C11	90.61	Moderate
C14	92.65	Moderate
C15	97.75	Low
C16	96.74	Low
C17	97.64	Low
C18	97.75	Low
C19	92.92	Moderate
C21	93.93	Moderate
C22	97.9	Low
C23	97.5	Low
C24	85.36	High
C26	111.76	Low
C27	111.93	Low
C28	111.91	Low
C29	111.96	Low

C30	112.37	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.*