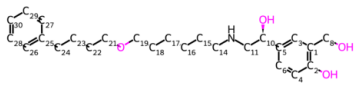
C-oxidation BDE Energy Report for: 267_salmeterol-out

This report covers the results for BDE calculations performed for: 267_salmeterol-out. Oxidation propensity is established using C-H Bond Dissociation Enthalpies (BDE). The lower the C-H BDE values the higher the propensity for C-oxidation. Details for the DFT calculations and overall workflow are explained at the end of this document

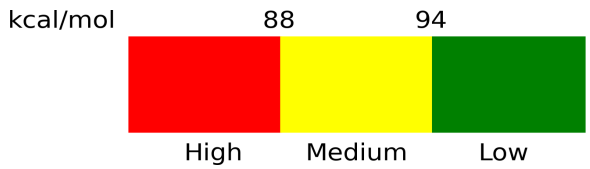
Bond Dissociation Energies (kcal/mol)



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

Risk Scale:



Calculation details and output files

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.*