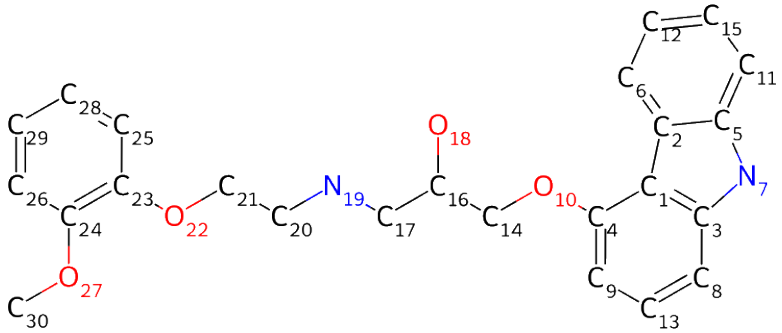
C-oxidation BDE Energy Report for: carvedilol

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

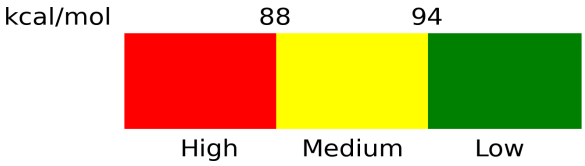


Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C6	113.0	Low	5.55
C8	114.37	Low	30.80
C9	112.36	Low	13.52
C11	113.19	Low	30.82
C12	112.75	Low	28.83
C13	112.13	Low	33.70
C14	95.37	Low	15.37
C15	112.39	Low	34.57
C16	88.98	Moderate	14.76
C17	92.9	Moderate	13.40
C20	97.15	Low	18.76
C21	95.12	Low	19.44
C25	112.79	Low	14.02
C26	111.61	Low	15.71
C28	113.0	Low	33.32
C29	112.42	Low	33.73
C30	97.71	Low	28.13

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.*