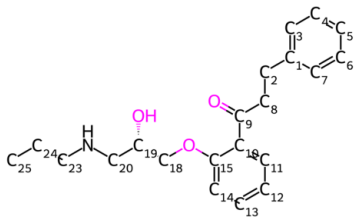
C-oxidation BDE Energy Report for: 240_propafenone-out

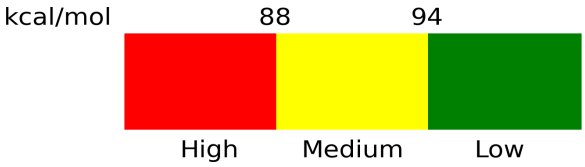
This report covers the results for BDE calculations performed for: 240_propafenone-out. Oxidation propensity is established using C-H Bond Dissociation Enthalpies (BDE). The lower the C-H BDE values the higher the propensity for C-oxidation. Details for the DFT calculations and overall workflow are explained at the end of this document

Bond Dissociation Energies (kcal/mol)



Atom	BDE (kcal/mol)	Propensity
C2	85.65	High
C3	112.69	Low
C4	111.87	Low
C6	111.71	Low
C7	111.43	Low
C8	88.52	Moderate
C11	113.47	Low
C12	113.27	Low
C13	111.99	Low
C14	111.24	Low
C18	94.65	Low
C19	88.64	Moderate
C20	90.42	Moderate
C23	91.3	Moderate
C24	97.68	Low
C25	100.64	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.*