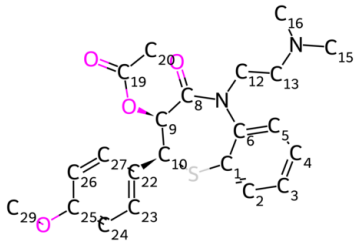
C-oxidation BDE Energy Report for: 116_diltiazem-out

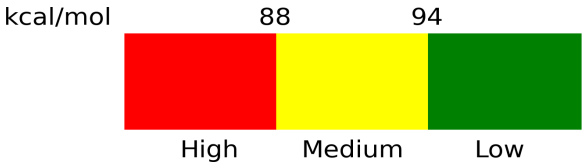
This report covers the results for BDE calculations performed for: 116_diltiazem-out. Oxidation propensity is established using C-H Bond Dissociation Enthalpies (BDE). The lower the C-H BDE values the higher the propensity for C-oxidation. Details for the DFT calculations and overall workflow are explained at the end of this document

Bond Dissociation Energies (kcal/mol)



Atom	BDE (kcal/mol)	Propensity
C2	112.34	Low
C3	112.75	Low
C4	112.41	Low
C5	111.53	Low
C9	92.21	Moderate
C10	82.52	High
C12	94.75	Low
C13	89.92	Moderate
C15	92.45	Moderate
C16	92.66	Moderate
C20	97.37	Low
C23	111.95	Low
C24	111.75	Low
C26	114.38	Low
C27	111.99	Low
C29	96.91	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.*