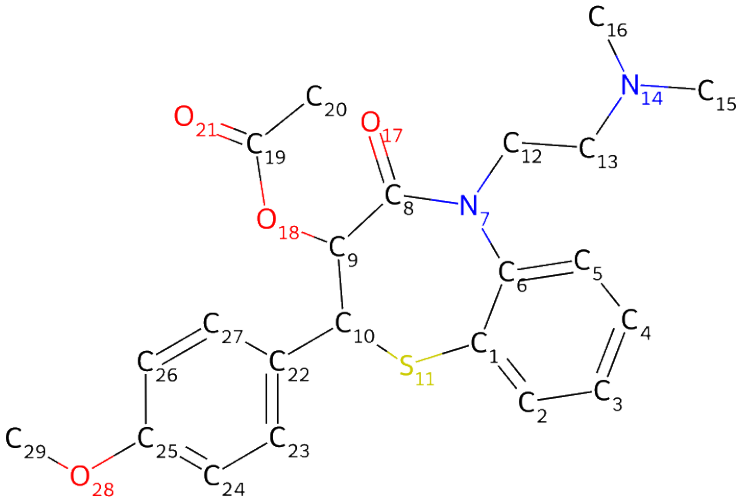
C-oxidation BDE Energy Report for: 116_diltiazem-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 116_diltiazem-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



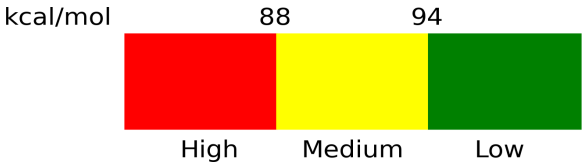
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C2	112.34	Low	25.64
C3	112.75	Low	35.91
C4	112.41	Low	35.17
C5	111.53	Low	13.17
C9	92.21	Moderate	5.84
C10	82.52	High	10.89
C12	94.75	Low	12.02
C13	89.92	Moderate	8.71
C15	92.45	Moderate	24.26
C16	92.66	Moderate	24.19
C20	97.37	Low	26.90
C23	111.95	Low	11.79
C24	111.75	Low	29.85

C26	114.38	Low	14.60
C27	111.99	Low	11.23
C29	96.91	Low	32.55

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.*