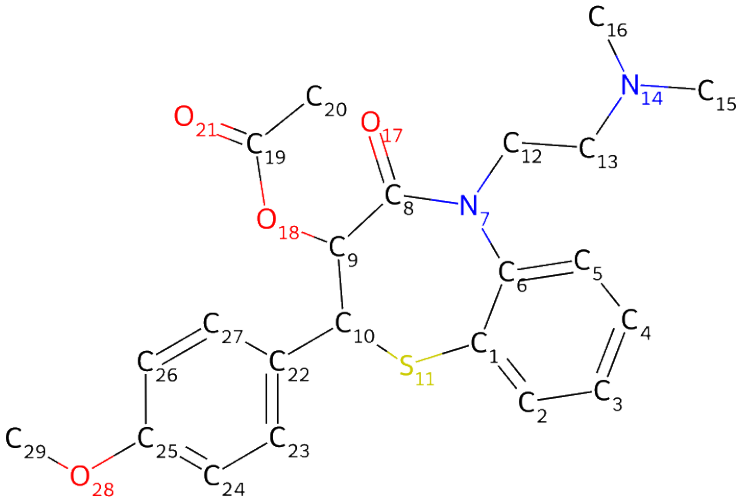
C-oxidation BDE Energy Report for: 116_diltiazem-out

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



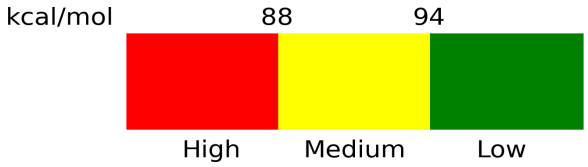
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C2	112.34	Low	9.35
C3	112.75	Low	14.33
C4	112.41	Low	12.59
C5	111.53	Low	2.77
C9	92.21	Moderate	0.00
C10	82.52	High	0.00
C12	94.75	Low	0.34
C13	89.92	Moderate	0.41
C15	92.45	Moderate	6.59
C16	92.66	Moderate	6.58
C20	97.37	Low	8.12
C23	111.95	Low	5.46
C24	111.75	Low	12.38

C26	114.38	Low	7.68
C27	111.99	Low	5.27
C29	96.91	Low	10.31

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.*