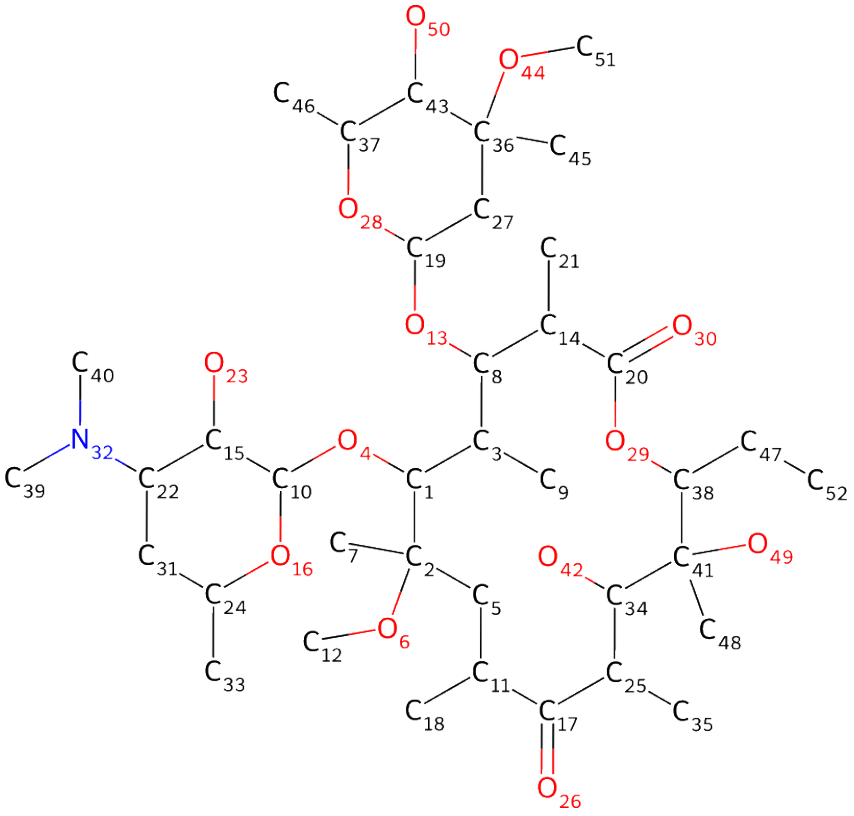
C-oxidation BDE Energy Report for: CLARITHROMYCIN

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



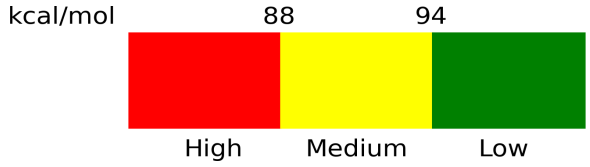
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	91.16	Moderate	0.00
C3	90.5	Moderate	0.00
C5	94.77	Low	0.02
C7	101.71	Low	0.54
C8	95.28	Low	0.00
C9	100.3	Low	4.15

C10	94.14	Low	0.00
C11	83.87	High	0.00
C12	94.85	Low	6.55
C14	83.76	High	0.00
C15	89.61	Moderate	0.00
C18	100.64	Low	0.13
C19	92.1	Moderate	0.00
C21	101.55	Low	3.27
C22	92.29	Moderate	0.00
C24	92.38	Moderate	0.00
C25	98.4	Low	0.00
C27	99.42	Low	0.04
C31	99.16	Low	0.00
C33	102.69	Low	5.17
C34	87.79	High	0.00
C35	101.07	Low	4.54
C37	93.41	Moderate	0.00
C38	94.34	Low	0.00
C39	92.86	Moderate	6.78
C40	92.84	Moderate	6.79
C43	95.89	Low	0.00
C45	101.51	Low	4.77
C46	102.45	Low	5.16
C47	96.83	Low	0.28
C48	103.0	Low	0.76
C51	95.65	Low	6.87
C52	100.97	Low	6.09

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.*