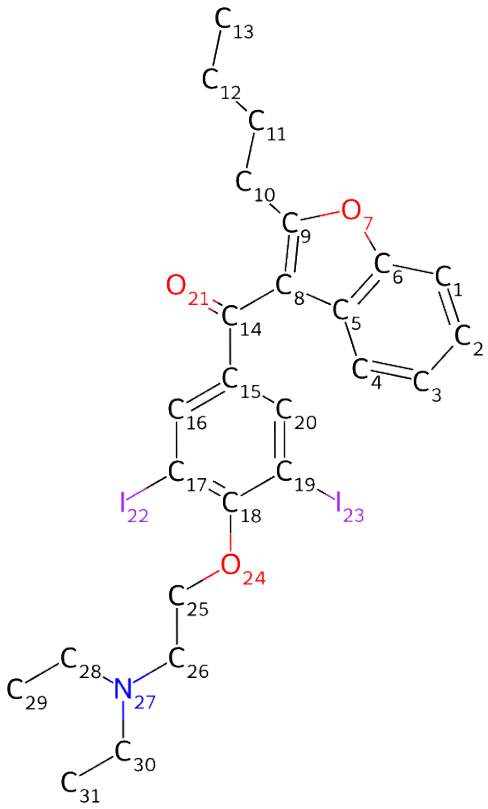
C-oxidation BDE Energy Report for: amiodarone

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



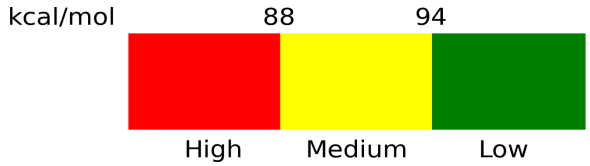
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	114.76	Low	33.86
C2	112.6	Low	35.99
C3	112.62	Low	31.82
C4	114.28	Low	12.31
C10	78.52	High	15.85
C11	96.49	Low	16.75
C12	95.68	Low	18.97
C13	99.39	Low	28.21

C20	111.05	Low	5.15
C25	94.94	Low	7.53
C26	77.16	High	9.18
C28	86.41	High	15.87
C29	99.17	Low	25.49
C30	86.44	High	15.98
C31	99.65	Low	25.64

Missing Sites:

C16.

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.*