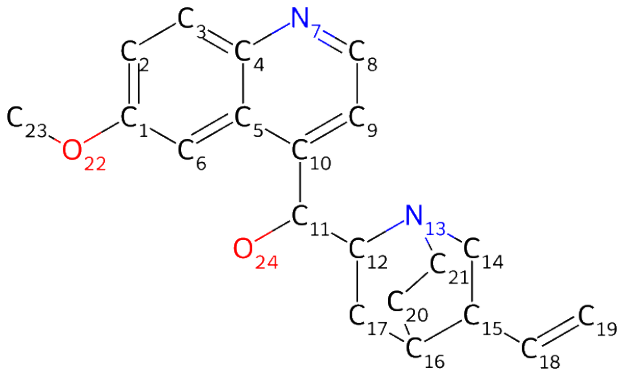
C-oxidation BDE Energy Report for: 245_quinidine-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 245_quinidine-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

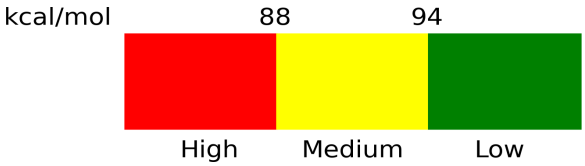


Atom	BDE (kcal/mol)	Propensity
C2	114.14	Low
C3	114.31	Low
C6	110.24	Low
C8	106.1	Low
C9	112.53	Low
C11	84.79	High
C12	93.4	Moderate
C14	95.77	Low
C15	79.44	High
C16	100.2	Low
C17	96.9	Low
C18	106.55	Low
C19	111.15	Low
C20	97.4	Low
C21	97.33	Low
C23	97.37	Low

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.*