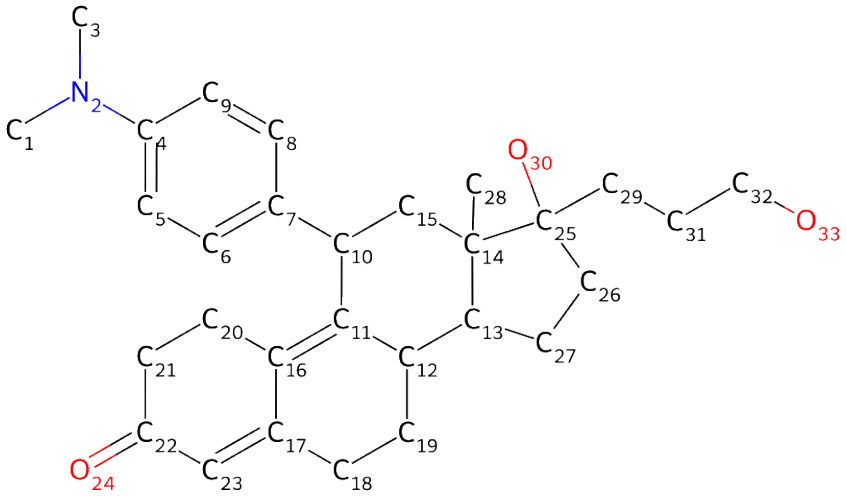
C-oxidation BDE Energy Report for: 219_onapristone-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 219_onapristone-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



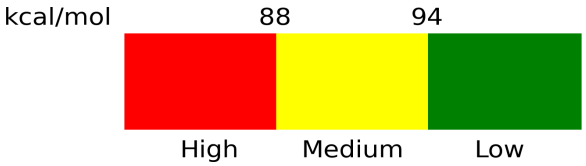
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	90.11	Moderate	27.50
C3	90.11	Moderate	27.48
C5	110.28	Low	13.15
C6	111.27	Low	7.81
C8	110.07	Low	8.43
C9	110.24	Low	13.33
C10	72.03	High	5.42
C12	66.56	High	6.35
C13	82.51	High	1.33
C15	94.81	Low	7.14
C18	83.34	High	24.03
C19	98.37	Low	13.06
C20	81.89	High	13.30

C21	88.04	Moderate	26.94
C23	111.45	Low	23.81
C26	94.76	Low	18.04
C27	95.55	Low	17.98
C28	100.35	Low	12.60
C29	96.37	Low	6.64
C31	96.4	Low	15.26
C32	94.44	Low	23.32

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.*