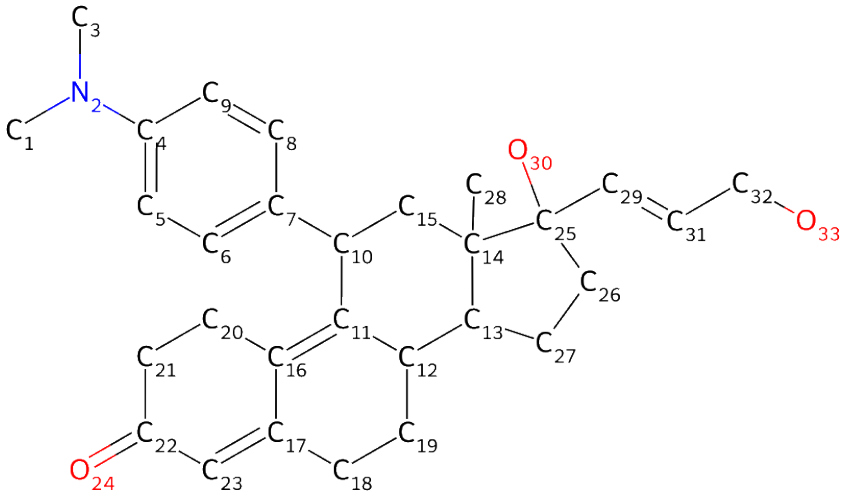
C-oxidation BDE Energy Report for: 182_lilopristone-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 182_lilopristone-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



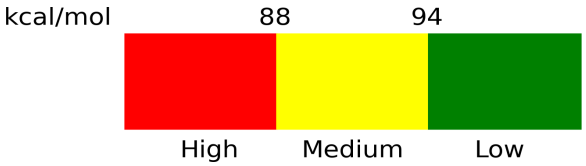
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C1	90.21	Moderate	28.10
C3	90.13	Moderate	28.10
C5	110.33	Low	15.38
C6	110.09	Low	12.06
C8	109.98	Low	12.19
C9	110.2	Low	15.38
C10	71.4	High	4.41
C12	74.51	High	3.49
C13	90.31	Moderate	0.73
C15	95.45	Low	4.99
C18	83.89	High	21.32
C19	98.16	Low	17.48
C20	82.78	High	14.56

C21	88.57	Moderate	27.44
C23	112.26	Low	23.92
C26	95.47	Low	21.35
C27	96.28	Low	16.51
C28	99.66	Low	10.77
C29	105.91	Low	7.98
C31	108.12	Low	13.81
C32	77.55	High	31.25

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.*