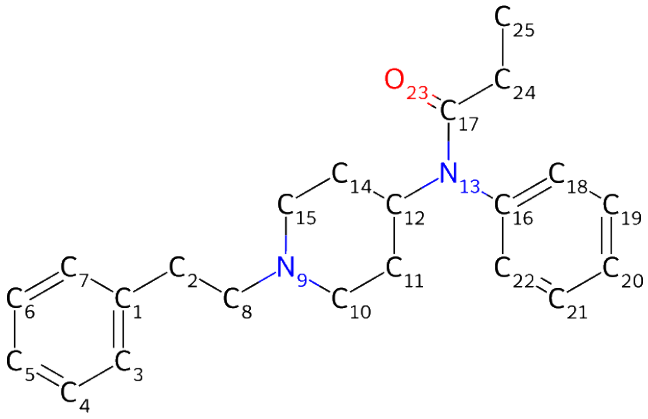
C-oxidation BDE Energy Report for: 142_fentanyl-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 142_fentanyl-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



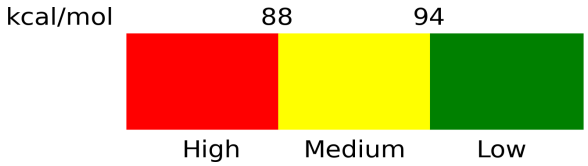
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C2	85.59	High	0.77
C3	111.76	Low	0.00
C4	111.95	Low	0.24
C5	112.31	Low	0.86
C6	111.8	Low	7.36
C7	111.25	Low	0.00
C8	90.8	Moderate	4.77
C10	90.76	Moderate	1.23
C11	99.19	Low	0.00
C12	92.81	Moderate	7.28
C14	99.32	Low	2.41
C15	90.95	Moderate	26.20
C18	112.6	Low	5.30
C19	112.17	Low	2.03
C20	112.74	Low	4.94
C21	112.18	Low	26.17

C22	112.63	Low	7.18
C24	91.07	Moderate	13.27
C25	101.49	Low	0.00

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.*