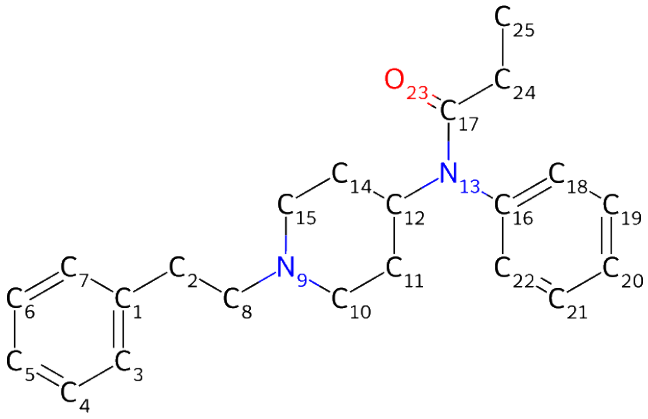
C-oxidation BDE Energy Report for: 142_fentanyl-out

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



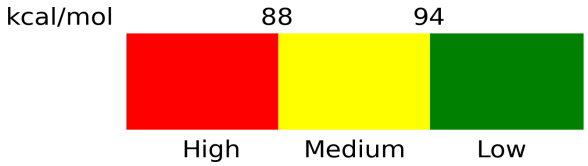
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C2	85.59	High	18.90
C3	111.76	Low	20.09
C4	111.95	Low	34.62
C5	112.31	Low	35.93
C6	111.8	Low	35.19
C7	111.25	Low	20.85
C8	90.8	Moderate	15.71
C10	90.76	Moderate	15.57
C11	99.19	Low	12.02
C12	92.81	Moderate	4.98
C14	99.32	Low	12.16
C15	90.95	Moderate	15.58
C18	112.6	Low	15.97
C19	112.17	Low	35.59
C20	112.74	Low	35.91
C21	112.18	Low	35.58

C22	112.63	Low	15.44
C24	91.07	Moderate	16.63
C25	101.49	Low	30.03

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.*