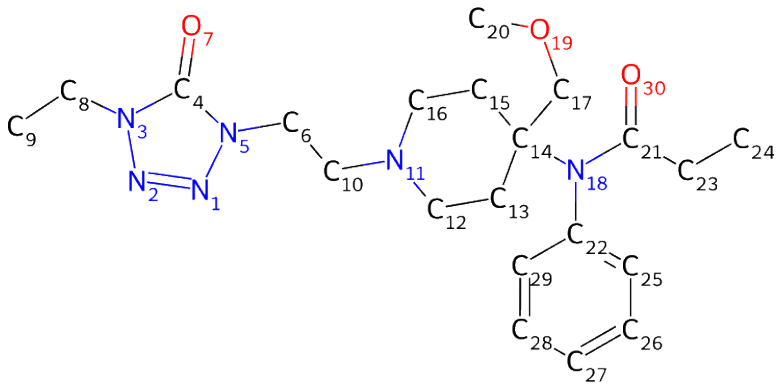
C-oxidation BDE Energy Report for: 043_alfentanil-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 043_alfentanil-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



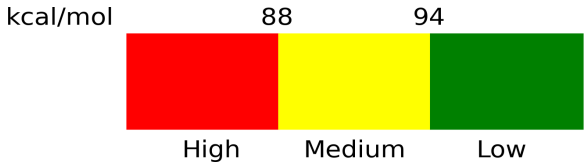
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C6	93.03	Moderate	1.67
C8	91.2	Moderate	2.25
C9	103.21	Low	6.33
C10	88.94	Moderate	0.49
C12	89.37	Moderate	0.43
C13	98.82	Low	0.20
C15	97.46	Low	0.21
C16	86.97	High	0.43
C17	93.2	Moderate	0.00
C20	96.36	Low	8.61
C23	91.1	Moderate	0.47
C24	101.5	Low	6.18
C26	112.08	Low	10.59
C27	112.67	Low	14.64
C28	112.26	Low	10.85

C29	112.61	Low	0.81

Missing Sites:

C25.

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.*