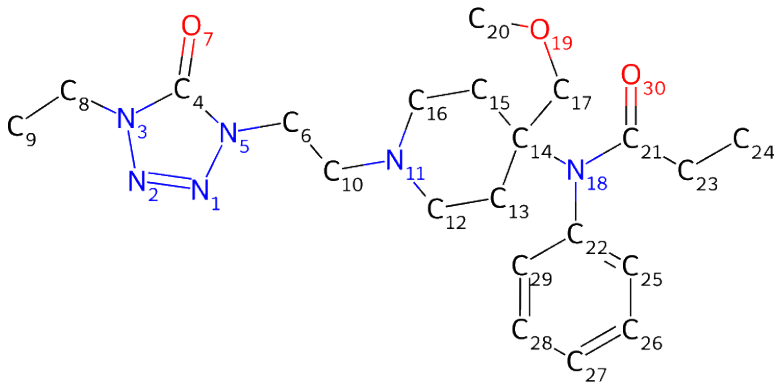
C-oxidation BDE Energy Report for: 043_alfentanil-out

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



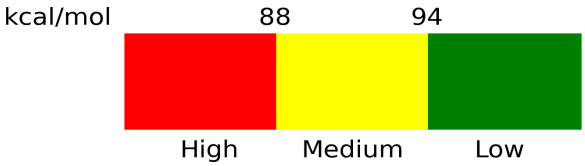
Atom	BDE (kcal/mol)	Propensity
C6	93.03	Moderate
C8	91.2	Moderate
C9	103.21	Low
C10	88.94	Moderate
C12	89.37	Moderate
C13	98.82	Low
C15	97.46	Low
C16	86.97	High
C17	93.2	Moderate
C20	96.36	Low
C23	91.1	Moderate
C24	101.5	Low
C26	112.08	Low
C27	112.67	Low
C28	112.26	Low

C29	112.61	Low

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.*