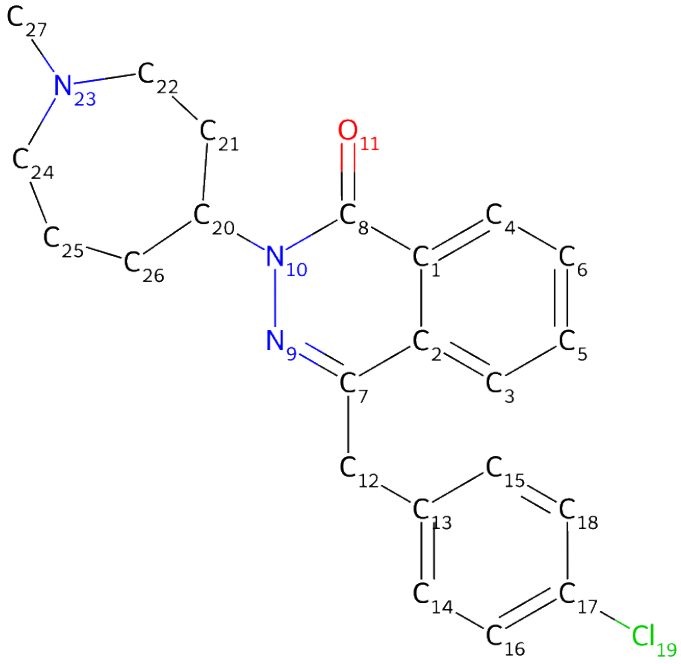
C-oxidation BDE Energy Report for: 061_azelastine-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 061_azelastine-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



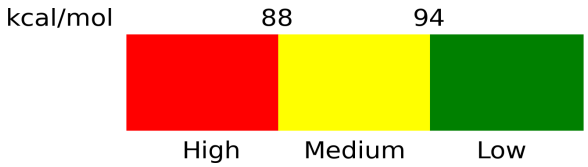
Atom	BDE (kcal/mol)	Propensity	SASA (Å²)
C3	111.68	Low	8.27
C4	114.85	Low	23.64
C5	112.35	Low	35.56
C6	112.67	Low	35.83
C12	78.23	High	17.65
C14	112.24	Low	16.89
C15	112.23	Low	14.40
C16	113.68	Low	28.51
C18	113.68	Low	28.61
C20	90.16	Moderate	8.35

C21	96.27	Low	16.22
C22	91.14	Moderate	15.29
C24	90.15	Moderate	17.32
C25	97.48	Low	22.16
C26	96.2	Low	16.34
C27	92.32	Moderate	26.85

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.*