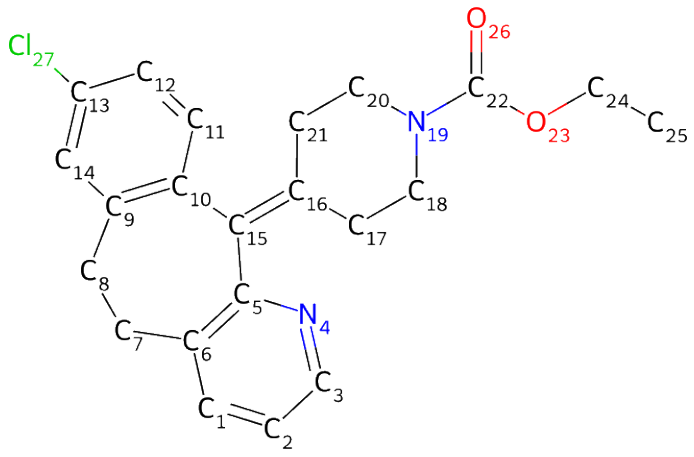
C-oxidation BDE Energy Report for: 187_loratadine-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 187_loratadine-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

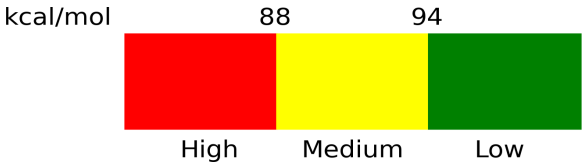


Atom	BDE (kcal/mol)	Propensity
C1	110.86	Low
C2	112.72	Low
C3	106.42	Low
C7	84.24	High
C8	85.1	High
C11	112.14	Low
C12	113.73	Low
C14	113.2	Low
C17	82.32	High
C18	92.66	Moderate
C20	92.37	Moderate
C21	81.17	High
C24	95.84	Low
C25	102.67	Low

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.*