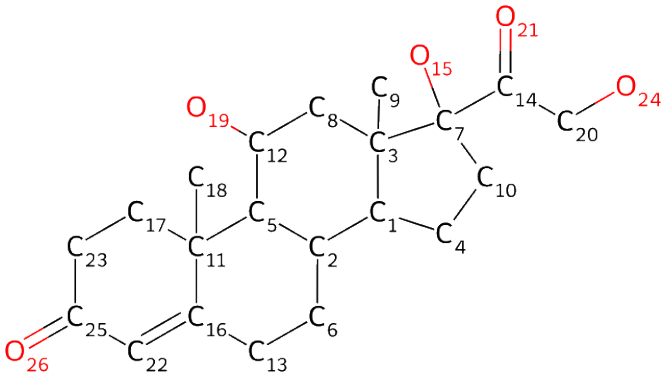
C-oxidation BDE Energy Report for: 018_CORTISOL-out

This report covers the results for bond dissociation enthalpies (BDE) and solvent accessible surface area (SASA) calculations performed for 018_CORTISOL-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

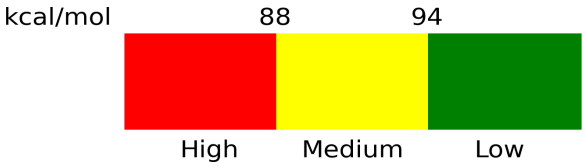


Atom	BDE (kcal/mol)	Propensity
C1	94.26	Low
C2	91.11	Moderate
C4	95.22	Low
C5	90.15	Moderate
C6	96.69	Low
C8	97.96	Low
C9	100.94	Low
C10	96.24	Low
C12	88.7	Moderate
C13	80.78	High
C17	98.22	Low
C18	100.74	Low
C20	75.06	High
C22	111.55	Low
C23	89.18	Moderate

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.*