

Practical Session 7: Quantum-Chemical Calculations Using WebMO

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- Complete the table from page 7 with your calculated values and explain how the calculated charges and orbital energies relate to the experimentally measured reactivities.

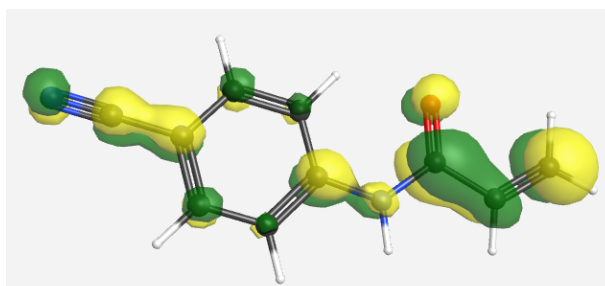
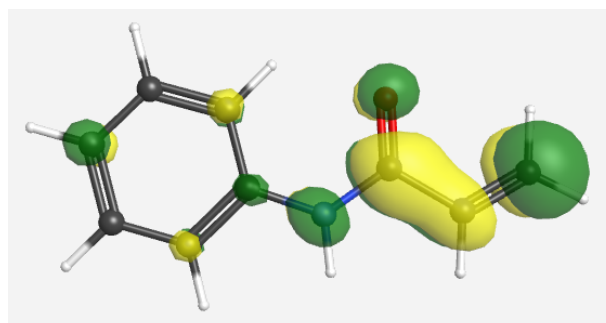
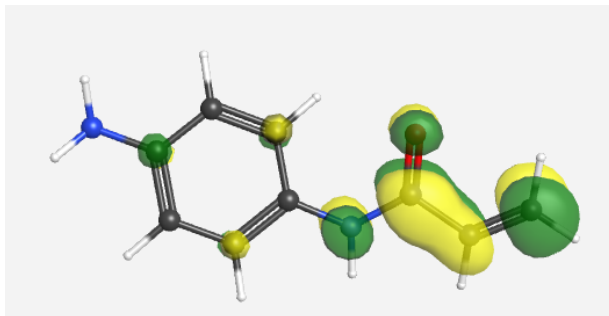
Compound	Substituent	GSH $t_{1/2}$ (min)	Log k_{GSH} ($\text{M}^{-1}\text{s}^{-1}$)	Charge	E_{LUMO} (eV)
20	4-amino	816	-2.51	-0.183	-0.02777
24	-	299	-2.08	-0.173	-0.04033
31	4-cyano	32.9	-1.12	-0.161	-0.06257

Experimentally, compound 31 reacts the fastest with glutathione and is therefore the most reactive, while compound 24 has a medium reactivity, and compound 20 is the least reactive. During the reaction, the negatively charged sulfur atom of GSH attacks the terminal electrophilic carbon atom.

The experimentally observed activities correlate with the charges on the terminal carbon atom. The less negative the charge, the more reactive the atom/compound. In compound 31 this charge is less negative, because electron density is partially delocalized to the electron withdrawing cyano substituent. In compound 20, the charge is more negative because the amino substituent is an electron donating group.

The same trends can be observed in the energy of the LUMO. Compound 31 has the lowest LUMO energy and therefore gains most from a nucleophilic attack, while compound 20 has the highest LUMO energy and therefore gains least from a nucleophilic attack.

- Compare the LUMOs of the three compounds. What are the differences? On which atoms does it have important contributions in each of the molecules?
- Can you relate the differences in the LUMOs of the three compounds to their different reactivities?



All LUMOs have important contributions on the Michael acceptor group, especially on the terminal carbon atom. (The inversion of the color does not have a physical meaning.)

The LUMOs of ward20 and ward24 look quite similar. However, in ward31, the LUMO is more delocalized on the cyano substituent. As stated above, this lowers the LUMO energy and makes the compound more reactive.