Practical Session 7: Quantum-Chemical Calculations Using WebMO

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- *Complete the table from page 69 with your calculated values for the charges on the terminal reactive carbon atoms and the LUMO energies. Please note that these values will vary slightly depending on your exact input geometry.*

Compound	Substituent	GSH $t_{1/2}$ (min)	Charge	E_{LUMO} (eV)
20	4-amino	816	*-0.183*	*-0.02777*
24	-	299	*-0.173*	*-0.04033*
31	4-cyano	32.9	*-0.161*	*-0.06257*

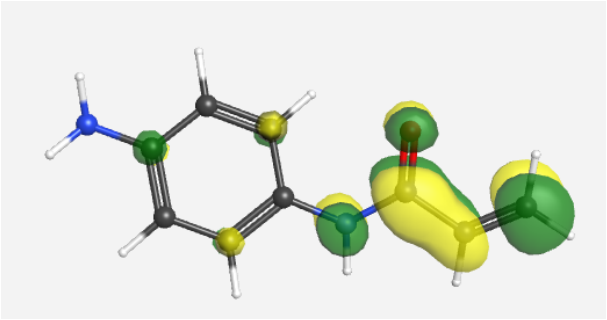
- *Describe how the calculated charges and orbital energies relate to the experimentally measured reactivities ($t_{1/2}$ values). Are they correlated or anti-correlated? Can you try to explain why?*

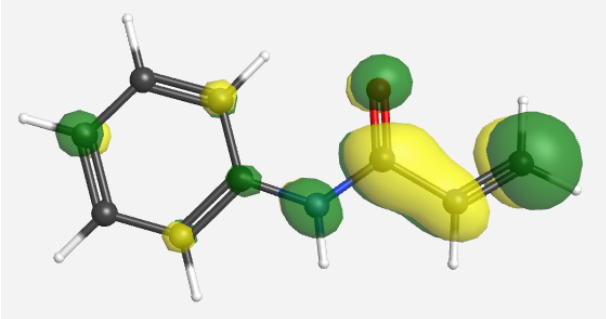
Experimentally, compound **31** reacts the fastest with glutathione and is therefore the most reactive, while compound **24** has a medium reactivity, and compound **20** is the least reactive. During the reaction, the negatively charged sulfur atom of GSH attacks the terminal electrophilic carbon atom.

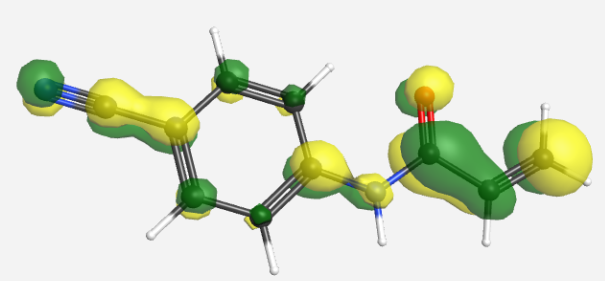
The experimentally observed activities correlate with the charges on the terminal carbon atom. The less negative the charge, the more reactive the atom/compound. In compound **31** this charge is less negative, because electron density is partially delocalized to the electron-withdrawing cyano substituent.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

The energy of the LUMO is anti-correlated with the charges on the terminal carbon atom and the reaction speed. The lower its energy, the faster the reaction. Compound **31** has the lowest LUMO energy and therefore gains most from a nucleophilic attack, which compound **20** has the highest LUMO energy and therefore gains least from a nucleophilic attack.

- *Here are the pictures of the three LUMOs.*







Please note that the LUMO is the orbital with the lowest energy that is not occupied by electrons. It has a different number depending on the atoms/electrons in the molecule. (The inversion of the color does not have a physical meaning.)

- *In the three compounds, are the LUMOs partially localized on the reactive terminal carbon atom? And on the phenyl substituents 4-amino, 4-hydrogen, and 4-cyano?*

All LUMOs have important contributions on the Michael acceptor group, especially on the terminal reactive carbon atom.

The LUMOs of compound **20** and compound **24** look quite similar. However, in compound **31**, the LUMO is more delocalized on the cyano substituent. As stated above, this lowers the LUMO energy and makes the compound more reactive.