Abstract

Retrosynthetic analysis involves planning the synthesis of a structurally complicated compound by systematically disconnecting it into smaller fragments until commercially available or simple to synthesize compounds are obtained. The resulting systems are called synthons and are usually not stable in their isolated form. The choice of stable synthetic equivalents is not a simple procedure and, in consequence, prolongs the process of designing the synthesis. The possibility of direct usage of stable synthons would allow for elimination of searching for stable equivalents and significantly simplify the entire synthesis. The main objective of my PhD project was to verify the stability of selected isolated synthons, namely, anionic borata-alkene synthons (H₂C=BR₂)⁻ (where R=H, CH₃, C₆H₅, C₆F₅, Mes) and (H₂C=B=CH₂)⁻, anionic phosphaalkene synthons (P=CR₂)⁻ (R=H, CH₃, C₆H₅, C₆F₅, Mes), cationic and anionic α -cyanovinyl synthons (H₂CCCN)^{+/-}, and evaluating the possibility of their direct application in laboratory practice. My research was performed using computational quantum chemistry methods.

I verified electronic and thermodynamic stability of the anionic synthons $(H_2C=BR_2)^-$ (R= H, CH₃, C₆H₅, C₆F₅, Mes) on the basis of their determined equilibrium structures. I have analysed the fragmentation reactions that the synthon $(H_2C=BH_2)^-$ could undergo, showing that all the energies of these reactions are positive, which means that this system does not spontaneously break into smaller fragments and is thermodynamically stable. In order to verify the electronic stability of all the borata-alkene anions studied, I determined their values of vertical electron detachment energies, which are in the range of 1.70-3.29 eV (which confirms the electronic stability of the systems). In addition, I have proved that the presence of the sodium cation, playing the counter ion role, does not significantly affect the geometries or the electron density distribution of these systems.

The research on borata-alkene synthons was extended to examine how an extra electron affects isomer stability. I have demonstrated that the attachment of an electron to high-energy structure can stabilize it by shifting down its energy, and thus making it competitive with the other isomeric anions. Particularly interesting is the $(H_3B-C=CH)^-$ isomer, which is the most stable anion, alongside the isoenergetic isomer $(H_2C=B=CH_2)^-$, while the corresponding neutral structure has the highest energy of the considered neutral systems.

Analysing phosphaalkene synthons, with the general formula $(PCR_2)^-$ (R = H, CH₃, C₆H₅, C₆F₅, Mes), I determined the structures of their most stable isomers. As it turned out, they correspond to the $(P=CR_2)^-$ formula, with the exception of R=C₆F₅, whose preferred isomer is

 $(P=CF-R-R)^-$. In order to verify the thermodynamic stability of these isomers, I examined 29 fragmentation pathways for the R=H substituted system, and 301 fragmentation reactions for the R=CH₃ substituted systems. None of them led to products with lower energy than the analysed anions. On the basis of the obtained results, I selected a potentially probable fragmentation pathway for the systems with the other substituents, which led to the following products: $(P=C)^-$ and R-R. The values of the obtained energies of these fragmentations were positive for all synthons considered, indicating their thermodynamic stability. I also determined the values of the vertical electron detachment energy. The positive VDE values were in the range 0.924-3.118 eV, indicating the electronic stability of the investigated anions.

The properties of the isolated ionic forms of the C_3H_2N radical and their potential use as cyanovinyl synthons were verified in the final paper included in my dissertation. The most stable isomers of the neutral C_3H_2N radical are the α - and β -cyanovinyl species, containing vinyl groups. The relative energies of the β -cyanovinyl radicals (with respect to the global minimum of α -CVR) are about 6 kcal/mol, and conversion of the α -CVR isomer to the trans- β -CVR isomer requires overcoming a large kinetic barrier (54.7 kcal/mol). The neutral α -CVR is thermodynamically stable and does not undergo any fragmentation processes, as demonstrated by calculated energies of these reactions.

Upon removal of an electron from the α -cyanovinyl radical, the $(C_3H_2N)^+$ cation is obtained. My calculations show that the most stable isomer corresponds to the linear HCCCNH⁺, which does not contain a vinyl moiety in its structure. The isomer that structurally corresponds to the neutral CVR system has rather high relative energy (38.6 kcal/mol) and is the third structure in the energetic order of stable cationic isomers. The other $(C_3H_2N)^+$ isomers that I have identified, despite their local geometrical stability, cannot be considered as potential stable cationic cyanovinyl synthons due to their high relative energies.

The most stable anionic isomer $(C_3H_2N)^-$ corresponds to a structure analogous to that of α -CVR and has a vinyl fragment. The low-energy anionic isomers trans- β -CVA and cis- β -CVA, which can be considered as trans- β -CVR and cis- β -CVR, respectively, with an excess electron attached, are systems having relative energies of 9.3 and 10.1 kcal/mol, respectively (with respect to the global minimum of α -CVA). In order to verify the electronic stability of α -CVA, trans- β -CVA and cis- β -CVA, I determined the vertical electron detachment energies characterizing these anions. The positive VDE values (2.38-2.47 eV), indicate that the mentioned anions are not susceptible to autodetachment of an excess electron. To investigate the thermodynamic stability of the α -CVA system, I analyzed various fragmentation reactions. All values of the energies of fragmentation processes turned out to be positive (18-214 kcal/mol), which means that the α -CVA anion does not undergo any isomerization or fragmentation reactions. Therefore, the cyanovinyl anion (α -CVA) can be considered as a stable synthon.

The results of the presented investigations clearly show that among the systems I have studied, there are synthons that exhibit geometrical, electronic, and thermodynamic stability in their isolated form. This is important because, for stable synthons, the step of searching for synthetic equivalents can be omitted, which significantly simplifies synthesis and reduces the time required for planning laboratory procedures.