SYNTHESIS OF QUINOXALINE CONTAINING ORGANOFULLERENES – THE POTENTIAL BIOLOGICALLY ACTIVE COMPOUNDS

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Introduction

It is well known that the fullerenes and their derivatives – organofullerenes are powerful building blocks for the creation of new materials and drugs [1]. The fullerenes cause are interest due to their the unusual donor and acceptor properties, as well as photophysical and photochemical properties. At that the research, concerning the addition of biological active addends to carbon fullerene sphere, is intensively developed [2]. These addends greatly expand the properties of the fullerenes It is shown that the organofullerenes had the inhibition activity of HIV protease, photodrivan DNA cleavage, antibacterial and antioxidant activities [3]. This contribution is devoted to the synthesis of organofullerenes with quinoxaline fragments, which are the basis of a series of drugs.

Results and discussion

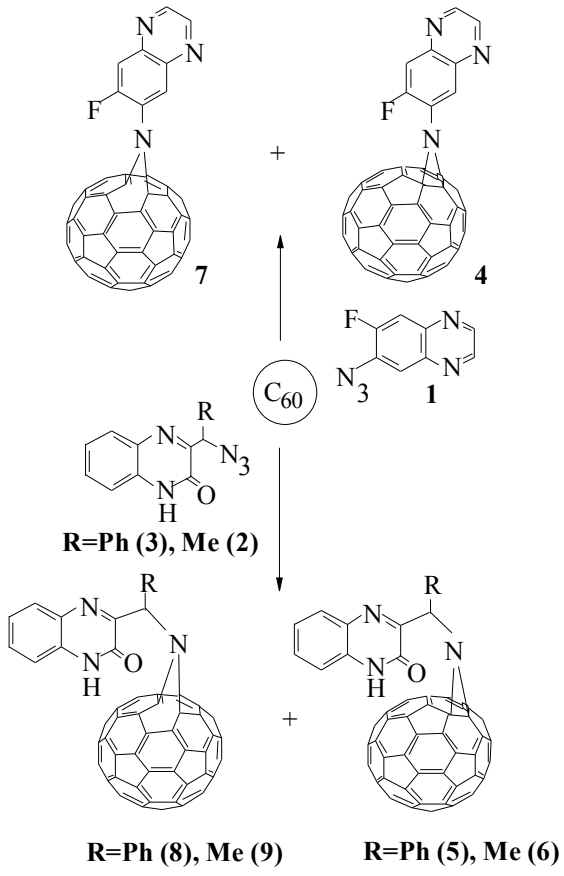
The reaction of fullerene C_{60} with organic azides was selected from a large number of the methods for fullerene functionalization, since this reaction offers synthesis of organofullerenes with varied structure. This reaction leads to the formation of following monoorganofullerenes: [60]fullereno-[1,2-*c*]triazolines, [60]fullereno[1,2-*b*]aziridines, [60]fullereno[1,6-*b*]aziridines and azahomo[60]-fullerenes. Both quinoxaline-containing azide (**1**) and quinoxalines containing azides (**2** and **3**) were used in this research.

The reactions of C_{60} with the azides (**1-3**) were carried out in *o*-dichlorobenzene. The temperature varied from 60 to 180ºC. All the reactions not proceeded at temperature below 100ºC. The rise in temperature resulted in the increase of the fullerene C_{60} conversion. The reaction mixtures were studied by the TLC and MALDI methods.

It has been found that two types of monoorganofullerenes and the mixture of polyorganofullerenes were obtained in each reaction at 100 to 180ºC.

The unreacted fullerene and the reaction products were separated by the column chromatography.

The monoorganofullerenes were separated as individual compounds. After the chromatography the yields of the products **4**, **5**,**7** and **8** were about 15-20% of the amount of fullerene involved in the reactions. At the same time the yields of the products **6** and **9** not exceed 5-7 %, what stipulated by their very poor solubility of these products in common solvent.



The IR, UV-VIS, ^{1}H and ^{13}C NMR spectroscopy, as well as elemental analysis were used for the determination of the monoorganofullerenes structure.

It was shown that [60]fullereno[1,2-b]aziridines **4-6** (the 6,6-closed mono-organofullerenes) and azahomo[60]fullerenes **7-9** (the 5,6-opened monoorganofullerenes) had been obtained in these reactions. Others monoorganofullerenes were not detected.

The same absorption bands, characteristic for the organic fragments, as were fixed the IR spectra of the pristine azides **1-3**, were observed in the IR spectra of corresponding separated monoorganofullerenes. Moreover the band at 527 cm^{-1}, which was characteristic for the 6,6-closed monoorgano-fullerenes, presented in all the spectra.

The narrow band at 420 nm was observed in the UV spectra of the 6,6-closed mono-organofullerenes **4-6**, which was absent in the same spectra of products **7-9**.

NMR spectra were recorded in $CDCl_3$ for the compounds **4** and **7**, and in CS_2 for the compounds **5** and **8**. Due to poor solubility of monoorganofullerenes **6** and **9**, satisfactory NMR spectra for these compounds were not recorded.

The signals were fixed in the ^{1}H NMR spectra of obtained products, which were observed in the same spectrum of pristine azides. At that the signals from the hydrogen atoms, which were in direct proximity to the exoedral nitrogen atom of the monoorganofullerene molecules, were shifted to low field compared to the same signals in the spectra of pristine azides. The shift value was 0.3 ppm for the [60]fullerene[1,2-*c*]aziridines **4** and **5**, while this value for the azahomofullerenes **7** and **8** was about 1 ppm.

The signals at δ 101.14 ppm and 84.56 ppm were observed in the ^{13}C NMR spectra of compounds **4** and **5,** correspondingly. These signals are characteristic for the sp^3 hybridized carbon atoms of the fullerene sphere. The fullerene spheres of these compounds were characterized by 14 signals at δ 140 –145 ppm, what indicated C_{2v} symmetry of molecules. It is necessary to note that such high symmetry is not characteristic for all known in literature [60]fullereno[1,2-*c*]azides. As a rule the C_s symmetry is realized. We consider that the realization of this higher C_{2v} symmetry for the compounds **4** and **5** is stipulated by the fast inversion of exoedral nitrogen atom of the aziridine fragments.

It is well known that the biological properties of organofullerenes are conditioned by their ability to take part in electron exchange process. In this connection we studied the electrochemical properties of obtained mono-organofullerenes by cyclic voltammetry.

It was shown that the quinoxaline containing organofullerenes accepted the several electrons step-by-step, as the pristine fullerene C_{60}. The first reduction peak in all cases corresponded to the reversible reduction of the fullerene sphere, and this process proceeded in more cathodic field compared to the reduction field of nonmodified fullerene C_{60}.

Conclusion

Several quinoxaline-containing organofullerenes with highly active functional groups have been obtained. These groups allow to synthesize new biologically active compounds with more complex structure.

References

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