Russian Chemical Bulletin, International Edition, Vol. 59, No. 3, pp. 665—667, March, 2010

Optical circular dichroism of the fullerene amino acid derivatives

V. S. Romanova, K. K. Babievsky,* and I. A. Yamskov

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,
28 ul. Vavilova, 119991 Moscow, Russian Federation.
Fax: +7 (499) 135 5085. E-mail: babievsk@mail.ru

The dependence of the circular dichroism spectra of the amino acid derivatives of fullerene C_{60} on the structure of the initial α-amino acid was studied.

Key words: fullerenes, α-amino acids, circular dichroism, optical induction of electronic transitions.

Among the wide range of organofullerenes, the amino acid derivatives of buckminsterfullerene C_{60} (ADF) evoke special interest because of the unique structure of the carbon spheroid and its ability to transform oxygen into the singlet state.[1] These compounds exhibit noticeable membranotropic properties, can quench radicals,[2] and possess a wide spectrum of biological activity.[3—5]

The reactions of addition of amines to fullerene C_{60} were among the first processes discovered in the fullerene chemistry.[6] The ESR study of this process showed that the first step of the reaction considered is the single-electron transfer from the amino group to fullerene to form the radical anion. The subsequent transformations include the recombination of radicals resulting in a zwitterionic intermediate stabilized by the proton transfer from the protonated amino group to the fullerene core.[7] It has been found somewhat later[8] that the reaction involves photochemically generated singlet oxygen. It is most likely that the reaction of amino acids with fullerene proceeds similarly. A wide range of the fullerene derivatives of amino acids and peptides was thus obtained,[9] and some of them turned out to be highly water-soluble.

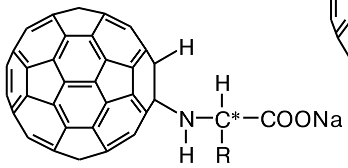
Numerous studies of the structure and properties of these interesting compounds have been carried out recently. In all synthesized products, the carboxyl group remains free, which is proved by the synthesis of various derivatives. The electrophoresis of water-soluble ADF in buffer solutions exhibited only one spot that moved toward the positively charged electrode. The IR spectra of the ADF were studied in detail.[10] All the data indicate[11] that the reactions of primary and secondary amino acids with fullerene afford individual substances rather than their mixture.

One more approach to the study of the reaction products of C_{60} with α-amino acids by the optical circular dichroism (CD) method was proposed in the present report.

Stereochemistry of the chiral fullerene derivatives still remains a poorly studied area of the chemistry of carbon clusters. The CD method has been used[12] for the first time to study optically active C_{60} bis(osmates) and later to study the fullerenylglycoside enantiomers.[13]

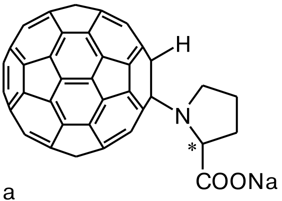
If we assume that the reaction between fullerene and optically active α-amino acids results in the direct addition of the amino acid fragments to one of the double bonds of the cycle without involving the asymmetric carbon atom, then the products should retain stereochemistry of the initial amino acid and the corresponding Cotton effects (CE) appear in the CD spectrum.

The earlier synthesized[9] water-soluble sodium salts of the reaction products of fullerene C_{60} with optically active enantiomers of L- and D-alanine (**1a** and **1b**, respectively) and L- and D-valine (**2a** and **2b**) were chosen as model objects of the study. The reaction products of fullerene with sodium salts of the same but racemic α-amino acids (**1c** and **2c**) were studied for comparison. The reaction product of fullerene C_{60} with L-proline (**3**) was studied in addition to this series of ADF.



1, **2**

R = Me (**1**), $CHMe_2$ (**2**)



3

Experimental

The CD spectra of aqueous solutions of sodium salts of ADF were recorded in a wavelength range of 450—750 nm on an SKD-2 dichrograph (designed at the Institute of Molecular

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 3, pp. 650—652, March, 2010.

Biology and the Institute of Spectroscopy, Russian Academy of Sciences) at 23 °C in a 1-cm quartz cell. The instrument was calibrated by an aqueous solution of CSA.[14] All measurements were carried out with a spectral resolution of 3 nm, an accumulation of 2.4 s, and a scan rate of 35 nm $\min^{-1}$. In all figures the dichroism values are given in ΔA (the value that expresses the difference in light absorption corresponding to the right and left circular polarization).

Results and Discussion

It should be mentioned that the short-wavelength regions of the CD spectra of solutions of ADF are closed by the characteristic unorganized noise. This specific feature is not related to the characteristics of the dichrograph, since the noise is completely absent in the spectrum of the standard compound (CSA).

As can be seen from the spectra of ADF **1a,b** (Fig. 1), the both compounds demonstrate extremes at 530 nm characteristic of the π—π*-transitions of the fullerene derivatives.[14] In this case, the CE turned out to be positive for ADF **1a** and negative for D-enantiomer **1b**. The long-wavelength part of the spectra of ADF **1a,b** exhibited also other absorption bands (at 650 and 680 nm). The substantially lower absolute CD values in this spectral region make it possible to assign them to the n—π*-transitions in the amino acid fragment including the transition to the antibonding orbitals of lone electron pairs of the oxygen and nitrogen atoms.

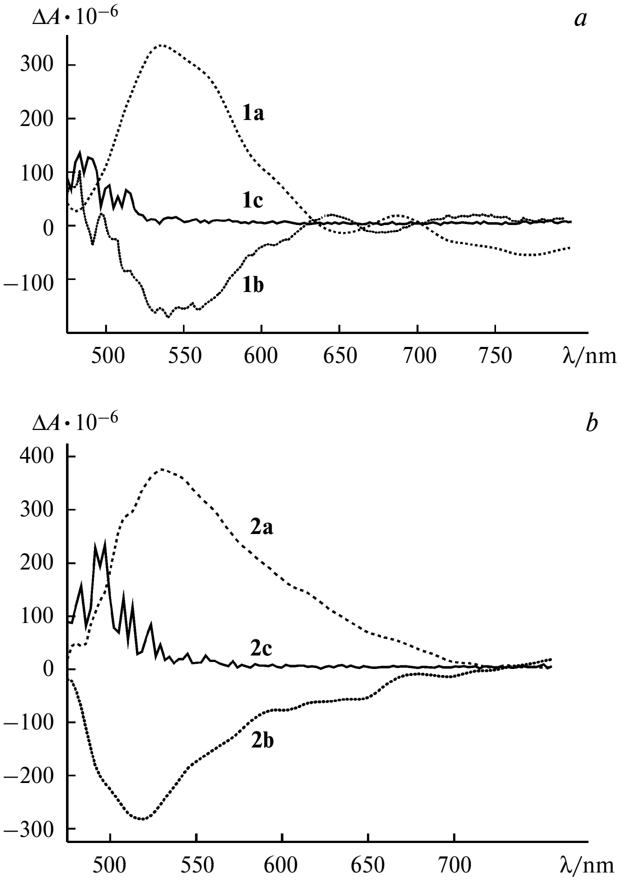


Fig. 1. The CD spectra of Na salts of ADF **1** (*a*) and **2** (*b*) in an aqueous solution: (*a*) **1a** (c = 1.5 g L^{-1}), **1b** (c = 2.0 g L^{-1}), and **1c** (c = 7.7 g L^{-1}); (*b*) **2a** (c = 5.7 g L^{-1}), **2b** (c = 6.2 g L^{-1}), and **2c** (c = 4.5 g L^{-1}).

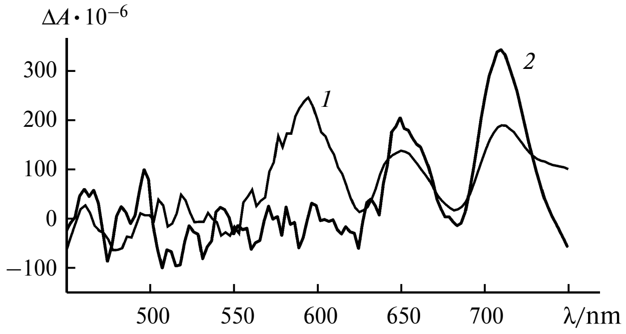


Fig. 2. The CD spectra of the fullerene derivative of L-proline **3** (c = 9.5 g L^{-1}) (*1*) and the same derivative after partial evaporation in air (*2*).

An analogous pattern is observed for the spectra of ADF **2a,b** (see Fig. 1, *b*), indicating that the electronic transitions are similar and the structures of the enantiomers studied are identical.

The CD spectrum of the fullerene derivative of L-proline **3** (Fig. 2) is somewhat different in shape, although it contains bands at 594, 650, and 710 nm corresponding to the electronic π—π*- and n—π*-transitions. However, it should be mentioned that the transition band at 594 nm disappears almost completely after the partial evaporation of a solution of compound **3** in air for 1 day. Evidently, this effect is due to the oxidation processes in the fullerene derivative core, which change the character of the occurring electronic transitions.

All above considered data concern the derivatives of optically active α-amino acids. Quite different situation is observed for the spectra of the fullerene derivatives of racemic amino acids **1c** and **2c** (see Fig. 1). No CE corresponding to the electronic transitions of the fullerene fragment are observed for these racemic compounds, which is seen from their CD spectra.

Thus, the character of the CD spectra indicates the induction of optical activity of the amino acid fragments covalently linked to the sphere of the fullerene core C_{60} upon its interaction with optically active α-amino acids.

The present study is an interesting example of investigation of the poorly studied reaction of optically active nucleophiles with achiral electron-deficient fullerene C_{60}.

The authors are sincerely grateful to Academician Yu. N. Bubnov for attention to this work.

References

1. H. Tokuyama, S. Yamago, E. Nakamura, *J. Am. Chem. Soc.*, 1993, **115**, 7918.
2. R. A. Kotelnikova, A. I. Kotelnikov, G. N. Bogdanov, V. S. Romanova, E. F. Kuleshova, Z. N. Parnes, M. E. Vol´pin, *FEBS Lett.*, 1996, **389**, 111.
3. N. E. Fedorova, C. M. Adueva, A. A. Medzhidova, B. C. Romanova, Z. N. Parnes, G. A. Galegov, A. A. Kush, *Voprosy virusologii* [*Problems of Virology*], 2002, 30 (in Russian).
4. G. G. Miller, V. S. Romanova, L. N. Pokidysheva, I. V. Titova, E. N. Kaliberda, L. D. Rumsh, O. I. Andreeva, N. P. Rybalkin, *Antibiotiki i khimioterapiya* [*Antibiotics and Chemotherapy*], 2004, **49**, 3 (in Russian).
5. S. M. Andreev, A. O. Petrukhin, A. A. Babakhin, A. V. Garmanova, V. S. Romanova, L. M. DuBuske, *Immunologiya* [*Immunology*], 2006, **27**, 343 (in Russian).
6. A. Hirsch, Q. Li, F. Wudl, *Angew. Chem.*, *Int. Ed.*, 1991, **30**, 1309.
7. F. Wudl, A. Hirsh, K. C. Khemani, T. Suzuki, P. M. Allemand, A. Koch, H. Eckert, H. G. Sradnov, H. Webb, in *Fullerenes: Synthesis, Properties, and Chemistry of Large Carbon Clusters*, Eds G. S. Hammond, V. J. Knek, *ACS. Symposium Series*, 1992, **481**, 161.
8. G. P. Miller, J. M. Millar, B. Liang, S. Uldrich, J. E. Johnson, *J. Chem. Soc., Chem. Commun.*, 1993, 897.
9. V. S. Romanova, V. A. Tsyryapkin, Yu. I. Lyakhovetskii, Z. N. Parnes, M. E. Vol´pin, *Izv. Akad. Nauk*, *Ser. Khim.*, 1994, 1154 [*Russ. Chem. Bull.* (*Engl. Transl.*), 1994, **43**, 1090].
10. Z. S. Klemenkova, V. S. Romanova, E. F. Kuleshova, Z. N. Parnes, B. V. Lokshin, *Vesti Akad. Nauk Beloruss.* [*Bull. Acad. Sci. Belorussia*], 1997, No. 2, 48 (in Russian).
11. M. E. Vol´pin, V. S. Romanova, Z. N. Parnes, *Mol. Mat.*, 1995, **7**, 53.
12. J. M. Hawkins, A. Meyer, M. Nambu, *J. Am. Chem. Soc.*, 1993, **115**, 9844.
13. A. Vasella, P. Uhlmann, C. A. Waldraff, F. Diederich, C. Thilgen, *Angew. Chem., Int. Ed.*, 1992, **31**, 1388.
14. M. F. Gillen, R. E. Williams, *Canad. J. Chem.*, 1975, **53**, 2351.

Received June 29, 2009;
in revised form October 13, 2009