Endohedral gadolinium-containing metallofullerenes in the trifluoromethylation reaction

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An efficient method for the synthesis of trifluoromethyl derivatives of endohedral gadolinium-containing metallofullerenes was proposed. High-purity (98—99%) trifluoromethyl derivatives $Gd@C_{82}(CF_3)_5$ (two isomers) and $Gd_2@C_{80}(CF_3)$ have been synthesized for the first time. They were isolated and characterized by HPLC, MALDI-TOF mass spectrometry, and UV—Vis spectroscopy.

Key words: endohedral metallofullerenes, dimethylformamide, gadolinium, high performance liquid chromatography, trifluoromethylation, mass spectrometry, UV—Vis spectroscopy.

Endohedral metallofullerenes (EMFs) are unique nanocarbon compounds containing one or several metal atoms inside the fullerene molecule. A wide list of elements from the D. I. Mendeleev Table, whose atoms are incorporated into a fullerene molecule, is presently known.[1,2] The EMFs containing atoms from the second (Ca, Sr, Ba) and third (Sc, Y, La) Groups, as well as lanthanides, are most actively studied. The most part of the EMFs have such an electronic structure that all or some valence electrons of the metal atom, which is situated inside the fullerene cage, transfer to the fullerene molecule. As a result, the EMF molecule gains properties that differ from those of "empty" fullerenes. The presence of additional weakly bound electrons at the external shell of the EMF molecules imparts properties of a strong reducing agent to these compounds and causes their high reactivity and a possibility to participate in various chemical reactions leading to the addition of diverse atoms, molecules, or radicals to the EMFs. Successful functionalization of "empty" fullerenes and the synthesis of new materials[3] from these fullerenes suggest that one should search for routes of practical use of the EMFs in the synthesis of their derivatives with higher solubility and unique electric, magnetic, optical, chemical, and biological properties.

At present, the chemistry of the EMFs, unlike the properties of the well-known exohedral modifications of "empty" fullerenes, is poorly studied. Such an important question as an effect of different metal atoms incapsulated into the fullerene shell on the reactivity of the EMFs remains unanswered. This situation is related to the restricted accessibility of the EMFs caused by difficulties of isolation of pure EMFs, which requires the labor-consuming and expensive multistage separation using HPLC.[1,2,4] As a result, the chromatographically pure EMFs are available only in milligram amounts, which impedes the development of the EMF chemistry. Presently, the state of investigation in this area can be compared with that of the studies of fullerenes before the discovery of the efficient electric arc method for synthesis of fullerenes C_{60},[5] which was proposed in 1990. Due to this method, fullerenes became accessible to a wide range of synthetic chemists, and this was the start of the vigorous development of the C_{60} chemistry. Unlike fullerenes, the problems of synthesis of the EMFs in preparative amounts has not been solved yet, explaining a small number of studies on EMF functionalization.

The evolution of investigations in the field of the EMFs can be seen from several studies. The first EMF derivatives were synthesized in 1995 using milligram amounts of the chromatographically pure EMFs. It was found[6] that the cycloaddition of disilacyclopropane to $Gd@C_{82}$ occurred with a higher rate than the cycloaddition to analogous "empty" fullerene. Then other EMF cycloadducts were synthesized.[7,8] In addition, the [2+2] cycloadduct of $Gd@C_{82}(C_6H_4)$ (two isomers) was synthesized, isolated, and characterized by HPLC, mass spectrometry, and UV—Vis spectroscopy.[9] Perfluoroalkylation at the interface was successfully used for the synthesis of $La@C_{82}(C_8F_{17})_2$.[10] However, the structure of the synthesized compounds was not developed by NMR spectroscopy because of their paramagnetic nature. In the recent time, the water-soluble EMF derivatives were synthesized in order to use them as contrast agents in NMR tomography.[11—13] The water-soluble polyhydroxy derivatives of EMFs $Gd@C_{82}(OH)_n$ were synthesized,

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and their higher efficiency as contrast agents for NMR tomography compared to the presently accessible commercial compounds was shown.[11] Chromatographically pure (<99%) Gd@C_{82} was used as the starting EMF. The structure of the synthesized compound was not determined, because the product represented a mixture of the polyhydroxy derivatives Gd@$C_{82}(OH)_n$ ($n \approx 40$). An original method for the synthesis of water-soluble EMF derivatives Gd@$C_{60}(C(COOH)_2)_{10}$ was proposed[12] using the sample enriched in Gd@C_{60}. Thus, an analysis of published data showed that the development of investigation on the chemistry of EMFs based on chromatographically pure EMFs is a rather difficult task.

In this work, to synthesize the trifluoromethyl derivatives of EMFs Gd@$C_{82}(CF_3)_x$, we propose to use stable anionic complexes of EMFs as DMF extracts enriched in Gd@C_{82} instead of the chromatographically pure neutral EMFs. The problem of the synthesis of the anionic EMF complexes in the form of DMF extracts in gram amounts has successfully been solved earlier.[14—16]

Experimental

The soot containing the Gd@C_{2n} EMFs was prepared by the evaporation of the composite graphite electrodes compounded by gadolinium in the electric arc reactor designed and produced by us.[14,17,18] The endohedral metallofullerene Gd@C_{82} in the anionic form was isolated by two-stage extraction from the soot consequently with *o*-dichlorobenzene (DCB) and DMF. A weighed sample of the soot (10—15 g) was loaded into a cellulose extraction thimbler (Whatman Int. Ltd.), and the thimbler was placed in a glass flask containing 1 L of the solvent. At the first stage, the soot was multiply extracted with DCB, which well purified the soot from fullerenes C_{60}, C_{70} and higher fullerenes (C_{76}, C_{78}, C_{82}, C_{84}, and others) and also isolated an insignificant amount of the EMFs. The extraction with DCB (≥99%, Aldrich) was carried out under argon for 3—4 h at the boiling temperature of the solvent (180.5 °C). Then a solution of the fullerenes and EMFs was thoroughly filtered (0.5 μ PTFE, Phenomenex Filter Membranes), the solvent was distilled off on a rotary evaporator, and the residue was dried for ~1 h. The extraction was carried out until the fresh portion of the solvent almost stopped coloring (usually 7—9 cycles). The DCB extract (5% yield from the soot weight), according to the MALDI-TOF mass spectrometric (Fig. 1, *a*) and HPLC data, mainly contained fullerenes C_{60} and C_{70}, higher fullerenes (C_{76}, C_{78}, C_{82}, and C_{84}), and an insignificant amount of the Gd@C_{82} EMF. After the "empty" fullerenes were removed from the soot, at the second stage the soot residue was multiply treated with the polar solvent DMF (≥99% (GC), Sigma-Aldrich) to obtain the EMFs in the anionic form. The EMFs were extracted from the soot for 3—4 h under argon at the boiling temperature of the solvent (0.5 μ PTFE, Phenomenex Filter Membranes), the solvent was distilled off on a rotary evaporator, and the residue was dried for 1 h *in vacuo* at 90 °C. The extraction was continued until the fresh portion of the solvent nearly stopped coloring (usually 6—7 cycles). After the solvent was removed, the DMF extract (5—8% yield of the soot weight) contained at most 11—13 wt.% DMF; according to the data of MALDI-TOF mass spectrometry (see Fig. 1, *b*) and UV—Vis spectroscopy, the extract contained almost no "empty" fullerenes and represented a mixture of the EMFs, whose main component was Gd@C_{82} (~80 mol.%) combined with small amounts of Gd@C_{80} and Gd_2@C_{80}.

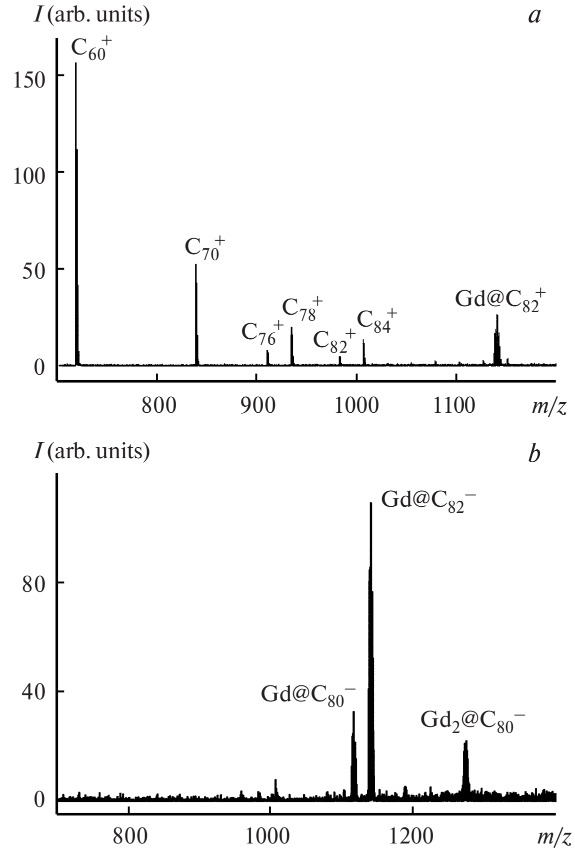

Fig. 1. The MALDI-TOF mass spectra of positive ions from the DCB extract of the soot (*a*) and negative ions from the DMF extract of the soot (*b*).

To carry out the high-temperature solid-phase reaction of the DMF extract of Gd@C_{2n} with silver trifluoroacetate, 100 mg of the DMF extract of Gd@C_{2n} was mixed with 500 mg of CF_3COOAg (≥98.0%, Aldrich). The mixture was loaded into a quartz reactor, rapidly heated (heating rate 40 °C min^{-1}) to 300—400 °C in dynamic vacuum (10^{-6} Torr), and kept for 6—10 h. The depth of the reaction was monitored by IR spectroscopy. The reaction was carried out until the bands at 724, 805, and 840 cm^{-1}, which are characteristic of CF_3COOAg, disappeared from the IR spectra of the reaction product.

The pure (~98%) trifluoromethyl EMF derivatives were isolated by multistage preparative HPLC (HP-1050, Hewlett Packard Co.) using consecutively columns with two types of sorbents: Cosmosil Buckyprep (20 mm × 250 mm) and Riges Buckyclutcher (21 mm × 250 mm) with toluene or a toluene—hexane mixture as eluent.

Mass spectrometry was carried out on a time-of-flight mass spectrometer with laser desorption/ionization (MALDI-TOF, Voyager-DE™ PRO Biospectrometry™ Workstation, Applied Biosystems, USA). The pulse nitrogen laser with a wavelength of 337 nm, a frequency of 3 Hz, and a pulse duration of 0.5 ns was used. Positive and negative ions were detected in the reflectron mode. A sulfur (S_8) solution in toluene was applied as a matrix. The sample under study and the matrix were mixed in the ~1 : 1000 ratio, the mixture was deposited as a microdroplet on a metallic target, and the solvent was evaporated at room temperature to obtain the film of the studied substance.

UV—Vis spectra of the trifluoromethyl EMF derivatives were recorded in toluene in the wavelength range from 300 to 1100 nm on a Varian Cary 500 Scan UV-Vis-NIR spectrophotometer in 10-mm standard quartz cells.

Results and Discussion

The MALDI-TOF mass spectrum of the product of the high-temperature reaction of silver trifluoroacetate and the DMF extract of the EMFs enriched in $Gd@C_{82}$ is shown in Fig. 2, *a*. In addition to the major component of the reaction product $Gd@C_{82}(CF_3)_5$, the mass spectrum exhibits ions of the trifluoromethyl EMF derivative $Gd_2@C_{80}$ with one or three CF_3 groups. We have earlier**[19]** shown that a similar composition of the products is obtained due to the reaction of silver trifluoroacetate and the DMF extract of the EMFs enriched in $Y@C_{82}$. It is interesting that the EMFs containing yttrium and gadolinium form derivatives containing less than five CF_3 groups, whereas the usual high-temperature reactions between CF_3COOAg and "empty" fullerenes afford mixtures of the $C_{60/70}(CF_3)_n$ products with a very wide distribution of the functional groups (n = 2—22).**[20—22]**

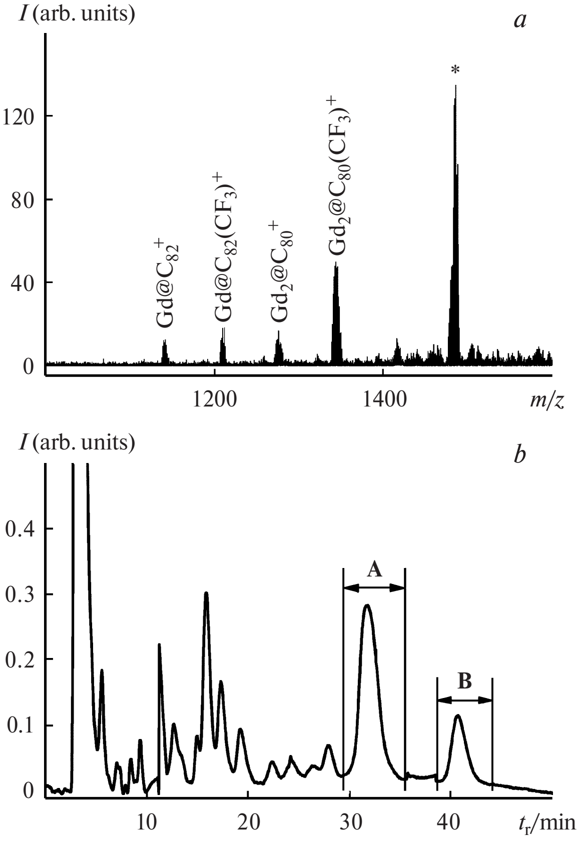

Fig. 2. The MALDI-TOF mass spectrum of positive ions (*a*) and the HPLC chromatogram (Cosmosil Buckyprep column, toluene as eluent, eluting rate 18 mL min^{-1}) (*b*) of the trifluoromethylation products $Gd@C_{82}(CF_3)_x$. The peak marked by * belongs to the $Gd@C_{82}(CF_3)_5{}^+$ ions. Here and in Figs 3 and 6, t_r is the retention time.

The HPLC chromatogram (Cosmosil Buckyprep column) of the products of the reaction between the DMF extract of the gadolinium-containing EMFs and CF_3COOAg is presented in Fig. 2, *b*. At the first stage of the separation of the $Gd@C_{82}(CF_3)_x$ sample (see Fig. 2, *b*), fractions **A** and **B** with retention times of 31 and 40.5 min, respectively, were collected. They mainly contained different isomers of $Gd@C_{82}(CF_3)_5$ (according to the MALDI-TOF mass spectrometric data). At the second stage (Fig. 3), the individual compound $Gd@C_{82}(CF_3)_5$ (retention time 9 min) was isolated from fraction **B** (see Fig. 3, *b*), and fraction **A** was divided into four parts (**A-1—A-4**) (see Fig. 3, *a*). The mass spectrometric analysis of these fractions showed that fractions **A-2** and **A-4** contained $Gd@C_{82}(CF_3)_3$ and $Gd@C_{82}(CF_3)$, respectively, and fraction **A-3** is the trifluoromethyl dimetallofullerene derivative $Gd_2@C_{80}(CF_3)$. The mass spectrum of fraction **A-3** (Fig. 4, *a*) contains two peaks: the main peak (*m/z* 1343) corresponds to the $Gd_2@C_{80}(CF_3)^+$ molecular ion and the peak with *m/z* 1274 corresponds to the $Gd_2@C_{80}$ fragmentation ion. The isotope distribution observed for the peak with *m/z* 1343 (see Fig. 4, *b*) agrees well with that theoretically calculated for the $Gd_2@C_{80}(CF_3)$ molecule (see Fig. 4, *c*), which confirms the molecular formula $Gd_2@C_{80}(CF_3)$ of the isolated compound.

According to the mass spectrometric data, fraction **A-1**, which was isolated as a sole peak on the Regis Buckyclutcher column (toluene as eluent), contained two components (Fig. 5, *a*): $Gd@C_{82}(CF_3)_5$ (*m/z* 1486) and $Gd_2@C_{80}(CF_3)_3$ (*m/z* 1481). These compounds have close molecular weights, but the isotope distribution con-

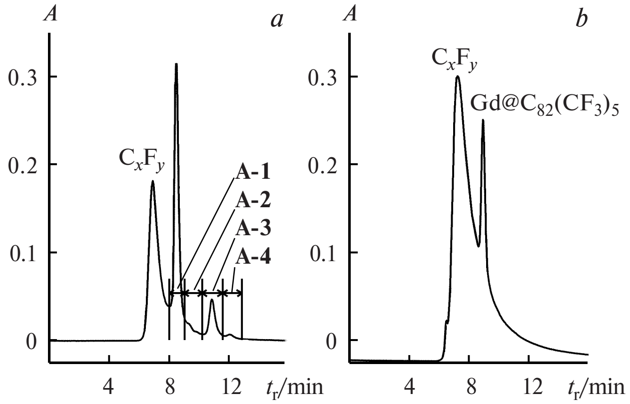

Fig. 3. The HPLC chromatograms (Regis Buckyclutcher column, toluene as eluent, eluting rate 12 mL min^{-1}) of fractions **A** (*a*) and **B** (*b*).

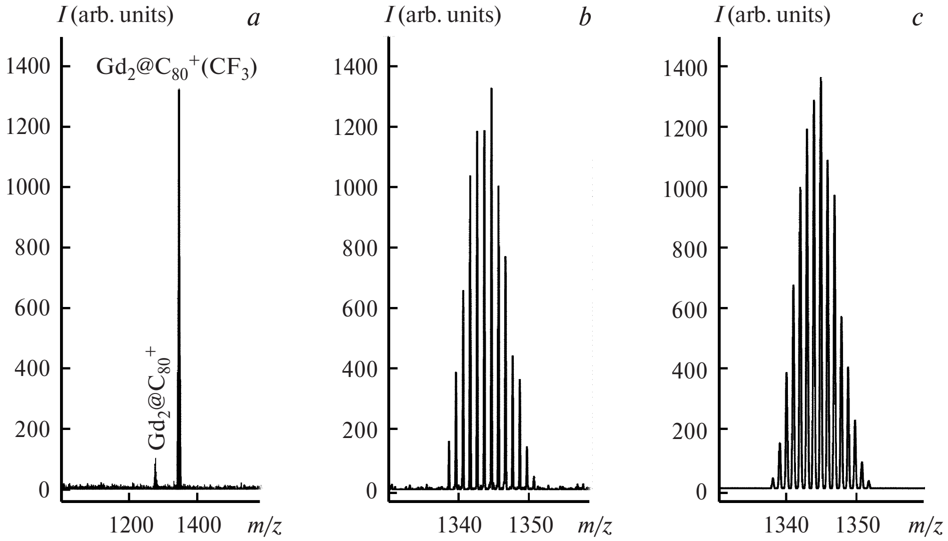

Fig. 4. The MALDI-TOF mass spectrum of positive ions of the pure trifluoromethyl derivative $Gd_2@C_{80}(CF_3)$ (*a*), the observed isotope distribution of the peak with *m/z* 1344 (*b*), and the theoretical isotope distribution for the $Gd_2@C_{80}(CF_3)$ molecule (*c*).

firms the presence of two components in the sample (see Fig. 5, *b*). The subsequent separation of fraction **A-1** (Fig. 6) on the Regis Buckyclutcher column (toluene—hexane (40 : 60) mixture as eluent) made it possible to isolate the individual trifluoromethyl derivative $Gd@C_{82}(CF_3)_5$ (retention time 20.4 min) (fraction **A-1-1**) and a mixture of two isomers of the trifluoromethyl derivatives of the $Gd_2@C_{80}(CF_3)_3$ dimetallofullerene (fraction **A-1-2**).

The mass spectrum of fraction **A-1-1** (see Fig. 5, *c*) exhibits only the peak with *m/z* 1486, which corresponds to the molecular ion of $Gd@C_{82}(CF_3)_5$. The observed isotope distribution of the peak with *m/z* 1486 (see Fig. 5, *c*) is well consistent with the spectrum theoretically cal-

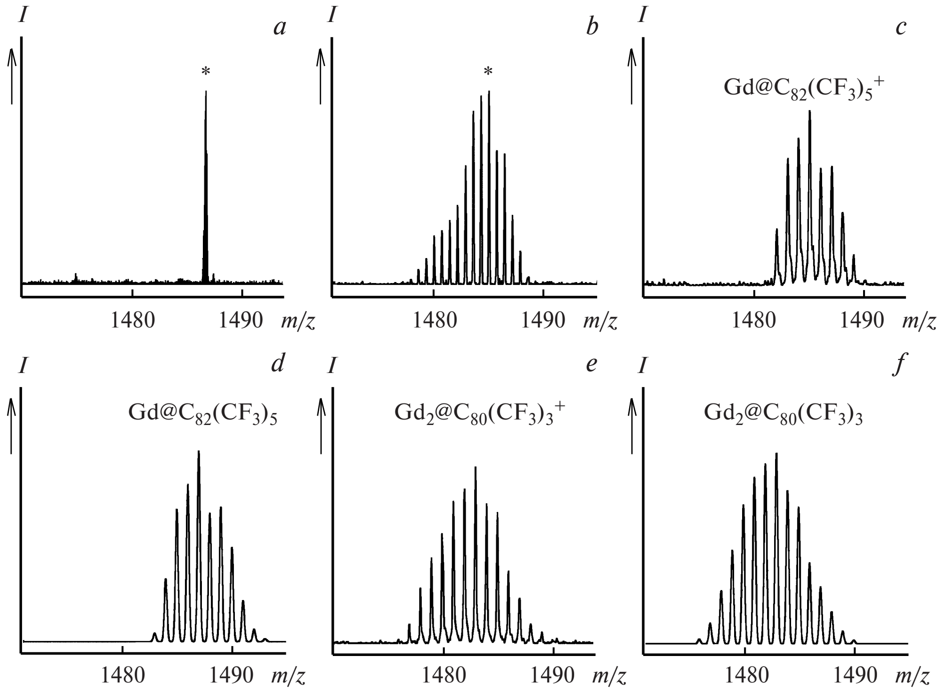

Fig. 5. The MALDI-TOF mass spectra of positive ions: fraction **A-1** isolated on the Regis Buckyclutcher column (toluene as eluent, eluting rate 12 mL min^{-1}) (*a*); mass spectral region of fraction **A-1** with *m/z* 1470—1500 (*b*); fraction **A-1-1** (*c*); theoretical isotope distribution for the $Gd@C_{82}(CF_3)_5$ molecule (*d*); fraction **A-1-2** (*e*) and the theoretical isotope distribution for the $Gd_2@C_{80}(CF_3)_3$ molecule (*f*). The peak marked by * belongs to $Gd@C_{82}(CF_3)_5^+$ and $Gd_2@C_{80}(CF_3)_3^+$.

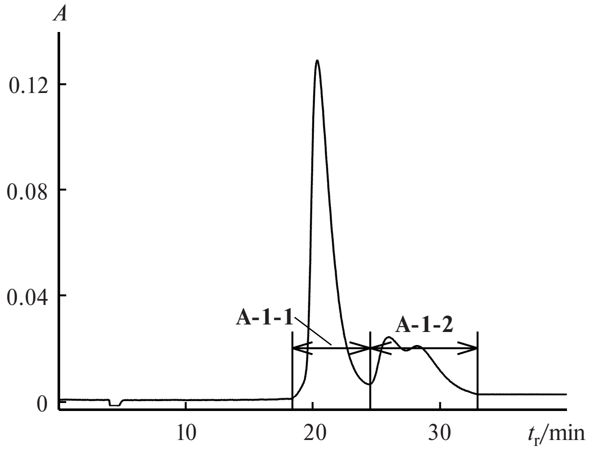

Fig. 6. The HPLC chromatogram of fraction **A-1** on the Regis Buckyclutcher column (toluene—hexane (40 : 60) mixture as eluent, eluting rate 12 mL min^{-1}).

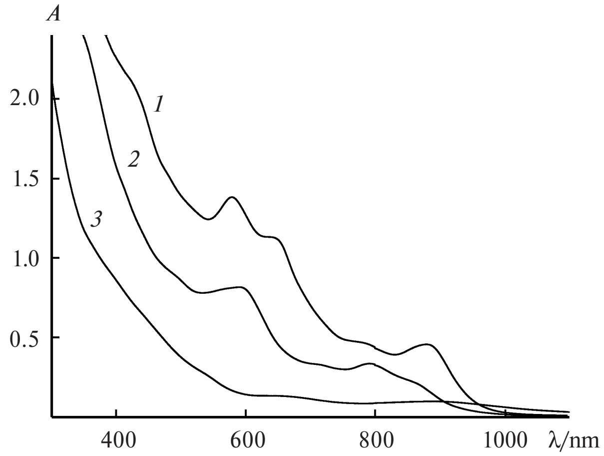

Fig. 7. The UV—Vis spectra of the trifluoromethyl EMF derivatives in toluene: $Gd@C_{82}(CF_3)_5$, isomer 1 (*1*); $Gd@C_{82}(CF_3)_5$, and isomer 2 (*2*); $Gd_2@C_{80}(CF_3)$ (*3*).

culated for the $Gd@C_{82}(CF_3)_5$ molecule (see Fig. 5, *d*), which confirms this molecular formula of the isolated compound. The mass spectrum of fraction **A-1-2** (see Fig. 5, *e*) contains only the peak with *m/z* 1481 corresponding to the molecular ion $Gd_2@C_{80}(CF_3)_3$, and the isotope distribution observed for this ion (see Fig. 5, *e*) agrees well with that theoretically calculated for the $Gd_2@C_{80}(CF_3)_3$ molecule (see Fig. 5, *f*), confirming the molecular formula $Gd_2@C_{80}(CF_3)_3$ for the isolated compounds.

According to the HPLC and MALDI-TOF mass spectrometric data, the purity of the isolated compounds $Gd@C_{82}(CF_3)_5$ (isomers 1 and 2) and $Gd_2@C_{80}(CF_3)$ was ~98—99%.

The absorption spectra of the trifluoromethyl EMF derivatives $Gd@C_{82}(CF_3)_5$ (isomers 1 and 2) and $Gd_2@C_{80}(CF_3)$ in toluene measured in the visible and near-IR interval are presented in Fig. 7. The absorption spectrum of $Gd_2@C_{80}(CF_3)$ has weak bands at 650 and 890 nm and the absorption edge at 1100 nm. The spectra of isomers 1 and 2 of $Gd@C_{82}(CF_3)_5$ (see Fig. 7) differ substantially from the UV—Vis absorption spectrum of the starting $Gd@C_{82}$ EMF containing the characteristic bands at 631, 966, and 1409 nm. The spectra of the isomers of the trifluoromethyl derivative $Gd@C_{82}(CF_3)_5$ have no common features and are presented by intrinsic sets of the bands: at 435, 578, 645, 780, and 880 nm with the absorption edge at 1000 nm and at 490, 590, 714, 792, and 865 nm with the absorption edge at 1000 nm for isomers 1 and 2, respectively. At the same time, the spectra of the EMFs $Y@C_{82}(CF_3)_5$ (isomer 1)^{23} and $Gd@C_{82}(CF_3)_5$ (isomer 1) contain common features. A similar pattern is also observed for $Y@C_{82}(CF_3)_5$ (isomer 2)^{23} and $Gd@C_{82}(CF_3)_5$ (isomer 2). Probably, this is related to the fact that the carbon cages with the grafted functional groups have the same structure and mutual position of the functional groups. Therefore, the major distinctive features of the UV—Vis spectra of molecules of the trifluoromethyl EMF derivatives are determined by the structure of the fullerene shell and the motif of addition of the CF_3 groups rather than by the nature of the inserted metal atom.

Thus, the efficient method was proposed for the synthesis of the trifluoromethyl gadolinium-containing EMF derivatives from the DMF extracts enriched in $Gd@C_{82}$. The $Gd@C_{82}(CF_3)_5$ (isomers 1 and 2) and $Gd_2@C_{80}(CF_3)$ trifluoromethyl derivatives of high purity (98—99%) have been synthesized for the first time and isolated by preparative HPLC. It was found that the high-temperature solid-phase reaction of silver trifluoroacetate with the DMF extract of the $Gd@C_{2n}$ EMFs, unlike the reaction with fullerene C_{60}, is selective and its major product is the diamagnetic compound $Gd@C_{82}(CF_3)_5$.

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