Trifluoromethyl derivatives of cerium endohedral metallofullerenes

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A method was developed for the synthesis of trifluoromethyl derivatives of endohedral metallofullerenes (EMF) encapsulating cerium based on the high-temperature solid-state reaction of silver trifluoroacetate with a DMF extract of EMF enriched with $Ce@C_{82}$. The trifluoromethyl derivatives $Ce@C_{82}(CF_3)_5$ (isomers I—III) with high purity (98—99%) were synthesized and isolated for the first time. These compounds were characterized by HPLC, S_8-MALDI-TOF mass spectrometry, and optical spectroscopy.

Key words: endohedral metallofullerenes, *N*,*N*-dimethylformamide, cerium, high performance liquid chromatography, trifluoromethylation, mass spectrometry, optical spectroscopy.

Endohedral metallofullerenes (EMF) are unique compounds, which are promising construction elements for the design of new-generation nanosized materials.[1] The synthesis of new EMF derivatives exhibiting unique electrical, magnetic, optical, and chemical properties is a topical problem. Unlike the well-developed chemistry of fullerenes C_{60} and C_{70}, the reactivity of EMF is currently poorly known. This is associated with the fact that EMF are difficult to synthesize. The available methods for the synthesis of EMF (laser and electric-arc vaporization of composite graphite electrodes) and conventional methods of the isolation of these compounds from soot make it possible to obtain extracts with a very low EMF content. Endohedral metallofullerenes are isolated from extracts by preparative high performance liquid chromatography (HPLC). However, due to a low EMF content in extracts, the chromatographic isolation is a laborious process.[1—3] Pure EMF (96—99%) were prepared only in milligram amounts. As opposed to fullerenes,[4,5] the problem of the synthesis of EMF in preparative amounts remains to be solved, and this is why there are a few publications on the functionalization of EMF. The development of the research on the chemistry of EMF can be seen from the following studies. First EMF derivatives were synthesized in 1995 with the use of milligram amounts of chromatographically pure EMF. It was found[6] that the cycloaddition reaction of disilacyclopropane with $Gd@C_{82}$ occurs at a higher rate than the cycloaddition to the related empty fullerene. More recently, other cycloadducts of EMF were synthesized.[7,8] In the study,[9] the [2+2] cycloadducts of EMF $Gd@C_{82}(C_6H_4)$ (two isomers) were synthesized, isolated, and characterized (HPLC, mass spectrometry, and optical spectroscopy). Shinohara and coworkers[10] successfully used the perfluoroalkylation at the interface for the synthesis of $La@C_{82}(C_8F_{17})_2$. However, the structures of the reaction products could not be determined by NMR spectroscopy because of their paramagnetic nature. In recent years, attempts have been made to synthesize water-soluble EMF derivatives with the aim of using them as contrast agents in NMR tomography.[11—13] For example, water-soluble polyhydroxylated EMF $Gd@C_{82}(OH)_n$ were synthesized, and it was shown that these compounds are more efficient contrast agents in NMR tomography compared with commercially available agents.[11] Chromatographically pure (~99%) $Gd@C_{82}$ was used as the starting EMF. The structure of the resulting compound was not determined, because the product was a mixture of polyhydroxylated EMF $Gd@C_{82}(OH)_n$ ($n \approx 40$). An original method was developed for the synthesis of the water-soluble EMF derivatives $Gd@C_{60}(C(COOH)_2)_{10}$ with the use of samples enriched with $Gd@C_{60}$.[12] Therefore, the analysis of the data published in the literature showed that the development of the chemistry of EMF based on chromatographically pure EMF is a rather difficult task.

In the present study, we used for the first time not chromatographically pure neutral EMF but their stable anionic complexes in the form of DMF extracts enriched with EMF $Ce@C_{82}$ for the synthesis of trifluoromethyl derivatives of EMF encapsulating cerium. The problem of the synthesis of the latter complexes in gram amounts has been solved in our earlier studies.[14—16]

Experimental

Soot containing EMF $Ce@C_{2n}$ was obtained by the electric-arc vaporization of composite graphite electrodes compounded

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with cerium in a helium atmosphere under reduced pressure in an electric-arc reactor, which we have designed and constructed earlier.[14—19]

Endohedral metallofullerene $Ce@C_{82}$ was isolated in the anionic form by the two-step extraction of fullerene-containing soot with *o*-dichlorobenzene (*o*-DCB) and *N*,*N*-dimethylformamide (DMF). A weighed sample of the soot (10—15 g) was put in a cellulose extraction thimble (Whatman Int., Ltd.), and the thimble was placed in a glass flask containing ~1 L of the solvent. In the first step, the soot was repeatedly extracted with *o*-DCB (≥99%, Aldrich), which well purifies the soot from C_{60}, C_{70}, and higher fullerenes (C_{76}, C_{78}, C_{82}, C_{84}, *etc.*) and also extracts a small amount of neutral EMF. The extraction with *o*-DCB was performed under an argon atmosphere at the boiling point of the solvent (180.5 °C) for 3—4 h. Then the solution of fullerenes and EMF was filtered (0.5 μ PTFE, Phenomenex Filter Membranes), the solvent was rotary evaporated, and the extract was dried for ~1 h. The extraction was performed until (generally six—eight cycles) no coloration of a fresh portion of the solvent was observed. According to the S_8-MALDI-TOF mass spectrometry and HPLC data, the extract in *o*-DCB (the yield was 4—5% based on the weight of the soot) contained primarily C_{60}, C_{70}, and higher fullerenes (C_{76}, C_{78}, C_{82}, C_{84}), as well as a small amount of EMF $Ce@C_{82}$. After the removal of empty fullerenes from the soot, the residue of the soot was repeatedly extracted with the polar solvent DMF (≥99%, Sigma-Aldrich) with the aim of obtaining EMF in the anionic form. The extraction of EMF from the soot was performed under an argon atmosphere at the boiling point of DMF (153 °C) for 3—4 h. Then the solution of EMF was filtered (0.5 μ PTFE, Phenomenex Filter Membranes), the solvent was rotary evaporated, and the product was dried *in vacuo* at 90 °C for 1 h. The extraction was performed until (generally six—seven cycles) no coloration of a fresh portion of the solvent was observed. According to the S_8-MALDI-TOF mass spectrometry data (Fig. 1) and the results of optical spectroscopy, the DMF extract (the yield was 5—7% based on the weight of the soot) contained almost no empty fullerenes and was a mixture of EMF anions, with $Ce@C_{82}$ as the major component (~80 mol.%); in addition, the extracts contained small amounts of mono-EMF $Ce@C_{80}$ and di-EMF $Ce_2@C_{80}$.

The high-temperature solid-state reaction of the DMF extract of EMF $Ce@C_{2n}$ with silver trifluoroacetate was carried out according to the following scheme: the DMF extract of EMF $Ce@C_{2n}$ (100 mg) was mixed with CF_3COOAg (≥98.0%, Aldrich) (500 mg), the mixture was placed in a quartz reactor, and the reactor was rapidly heated (the heating rate was 40 °C min^{-1}) to 300—400 °C in dynamic vacuum of 10^{-6} Torr and then kept for 6—10 h. The course of the reaction was monitored by IR spectroscopy. The reaction was performed until the bands characteristic of CF_3COOAg at 724, 805, and 840 cm^{-1} disappeared in the IR spectra of the reaction product. The reaction products, unlike the starting DMF extracts of EMF, are readily soluble in toluene and can easily be extracted from the reaction mixture for the further separation into individual components.

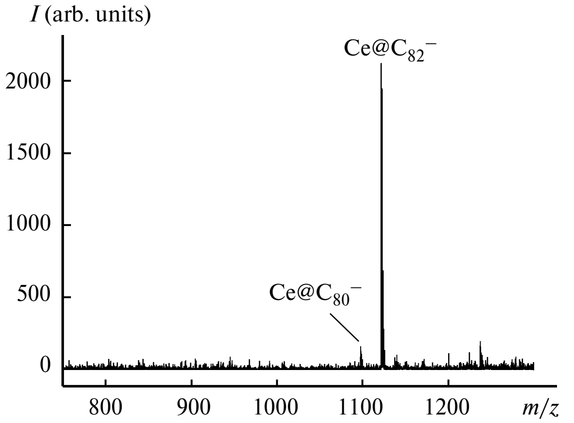

Fig. 1. Negative-ion S_8-MALDI-TOF mass spectrum of a DMF extract of Ce-EMF-containing soot.

The isolation of pure (~98%) trifluoromethyl derivatives of EMF doped with cerium was performed by multi-step preparative HPLC (HP-1050, Hewlett Packard Co.) with the successive use of columns packed with two types of sorbents, *viz.*, Cosmosil Buckyprep (20 mm × 250 mm) and Riges Buckyclutcher (21 mm × 250 mm). Toluene was used as the eluent.

The mass spectrometric studies were carried out on a matrix-assisted laser-desorption/ionization time-of-flight mass spectrometer (S_8-MALDI-TOF, Voyager-DE PRO Biospectrometry Workstation, Applied Biosystems, USA). A pulsed nitrogen laser with a wavelength of 337 nm, a frequency of 3 Hz, and a pulse duration of 0.5 ns was employed. The positive and negative ions were detected in the reflector mode. A solution of sulfur (S_8) in toluene was used as the matrix. The analyte and the matrix were mixed (in a molar ratio of ~1 : 1000) and deposited as a microdrop on a metallic target. The solvent was evaporated at room temperature to prepare a film of the analyte.

Samples of chromatographically pure trifluoromethyl derivatives of EMF encapsulating cerium were studied by IR spectroscopy using the ATR—FTIR technique, which allows the use of microgram amounts of compounds as dilute solutions.

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

Results and Discussion

Figure 2 shows the S_8-MALDI-TOF mass spectrum for the products of the high-temperature reaction of silver trifluoroacetate with the DMF extract of EMF enriched with $Ce@C_{82}$. In addition to the main component of the reaction product $Ce@C_{82}(CF_3)_5$, the mass spectrum shows peaks corresponding to ions of the trifluoromethyl derivative of EMF $Ce@C_{80}$ containing three and five CF_3 groups and $Ce_2@C_{80}$, which was not involved in trifluoromethylation. It is interesting that EMF encapsulating yttrium,[20,21] gadolinium,[22] and cerium form derivatives containing at most five CF_3 groups, whereas the usual high-temperature reactions of CF_3COOAg with empty fullerenes give mixtures of products with a very wide distribution of functional groups $C_{60/70}(CF_3)_n$ (where n = 2—22).[23—25]

The HPLC chromatogram of the products prepared by the reaction of the DMF extract of Ce-EMF with CF_3COOAg is shown in Fig. 3. According to the S_8-MALDI-

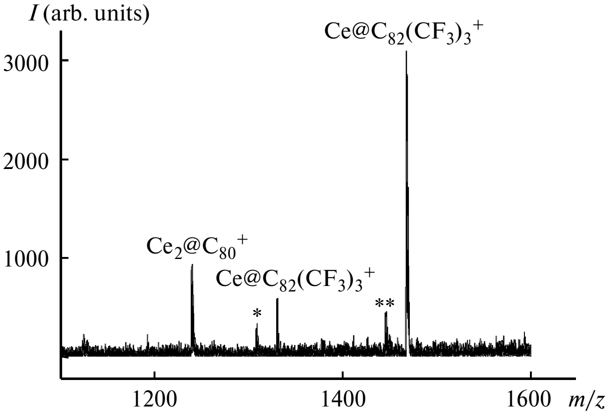

Fig. 2. Positive-ion S_8-MALDI-TOF mass spectrum of the compounds $Ce@C_{82}(CF_3)_x$. The peaks marked with an asterisk and a double asterisk belong to $Ce@C_{80}(CF_3)_3^+$ and $Ce@C_{80}(CF_3)_5^+$, respectively.

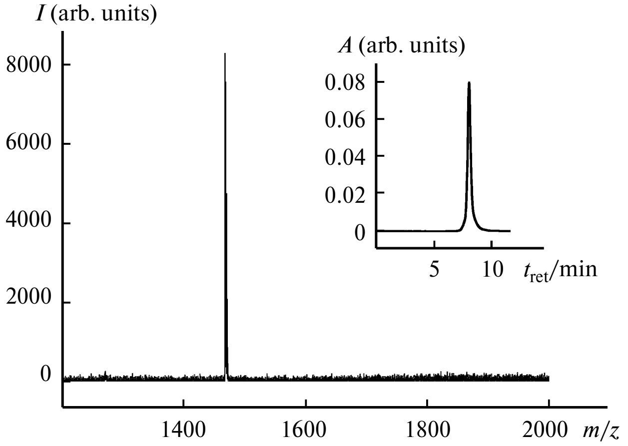

Fig. 4. Positive-ion S_8-MALDI-TOF mass spectrum and the HPLC chromatogram (in the inset) of pure isomer III of the compound $Ce@C_{82}(CF_3)_5$.

TOF mass spectrometry data, the fractions *A*, *B*, and *C* contain primarily the trifluoromethyl derivatives $Ce@C_{82}(CF_3)_5$ (three isomers), whereas the fraction *D* contains unconsumed di-EMF $Ce_2@C_{80}$. Unlike the reactions of Y-EMF (see Ref. 20) or Gd-EMF (see Ref. 22) with silver trifluoroacetate, which afforded two isomers of $Y@C_{82}(CF_3)_5$ and derivatives $M_2@C_{80}(CF_3)_{1,3}$ (M = Y, Gd), the reaction of Ce-EMF with CF_3COOAg gave three isomers of $Ce@C_{82}(CF_3)_5$, whereas $Ce_2@C_{80}$ remained unconsumed and was isolated in the pure form.

The S_8-MALDI-TOF mass spectrum and the HPLC chromatogram of the isolated $Ce@C_{82}(CF_3)_5$ (isomer III) are presented in Fig. 4. The mass spectrum shows only a peak at m/z 1469 corresponding to the $Ce@C_{82}(CF_3)_5^+$ ion. The fragmentation of this ion leads to the loss of CF_3 groups up to the formation of the $Ce@C_{82}^+$ ion. According to the HPLC and S_8-MALDI-TOF mass spectrometry data, the purity of the isolated compounds $Ce@C_{82}(CF_3)_5$ (isomers I—III) was ~98—99%.

Samples of chromatographically pure trifluoromethyl derivatives of EMF $Ce@C_{82}(CF_3)_5$ (isomers I—III) were studied by IR spectroscopy. Table 1 gives the normal vibrational frequencies of C—F bonds of the compounds $Ce@C_{82}(CF_3)_5$ (isomers I—III). The IR spectra are characteristic of CF_3 derivatives. Thus, the most intense stretching bands of C—F bonds are observed at 1100—1260 cm^{-1}. It should be noted that each isomer under consideration is characterized by its own set of vibrational bands, and these bands are shifted to higher wavenumbers compared, for example, with silver trifluoroacetate (C—F vibrations at 1135 and 1213 cm^{-1}). It should also be noted that the spectra are more complex in the region of C—F vibrations, which is indicative of the differences in the structures of these compounds and nonequivalent positions of CF_3 groups on the carbon cage.

The absorption spectra of the trifluoromethyl derivatives of EMF $Ce@C_{82}(CF_3)_5$ (isomers I—III) in toluene recorded in the visible and near-IR spectral regions are shown in Fig. 5. The spectra of $Ce@C_{82}(CF_3)_5$ (isomers I—III) substantially differ from the optical absorption

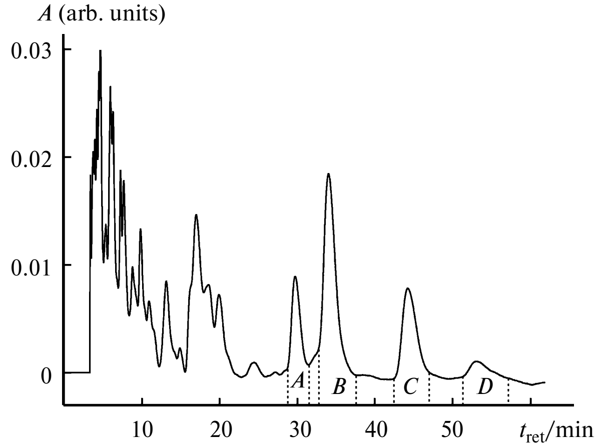

Fig. 3. HPLC chromatogram of the reaction products of EMF $Ce@C_{2n}$ with CF_3COOAg (Cosmosil Buckyprep column, toluene as the eluent, the rate of elution was 18 mL min^{-1}). The peaks in the regions *A*, *B*, and *C* belong to isomers I, II, and III of EMF $Ce@C_{82}(CF_3)_5$, respectively, the peak in the region *D* belongs to EMF $Ce_2@C_{80}$. Here and in Fig. 4, *b*, t_{ret} is the retention time.

Table 1. Normal vibrational frequencies of C—F bonds in the spectra of isomers of EMF $Ce@C_{82}(CF_3)_5$

Isomer	ν/cm^{-1}
I	1180, 1252
II	1178, 1248
III	1177, 1252

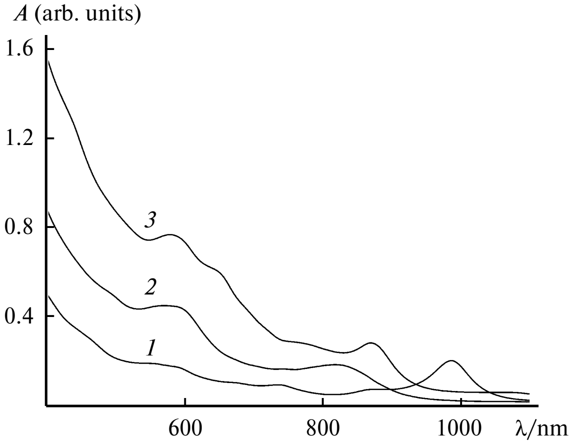

Fig. 5. Optical absorption spectra of isomers I (*1*), II (*2*), and III (*3*) of the trifluoromethyl derivative of EMF $Ce@C_{82}(CF_3)_5$ in toluene.

spectrum of the starting EMF $Ce@C_{82}$, which shows three characteristic bands at 638, 980, and 1412 nm. The spectrum of isomer I of the compound $Ce@C_{82}(CF_3)_5$ shows three characteristic bands at 593, 738, and 987 nm and an adsorption edge at 950 nm, the spectrum of isomer II has four bands at 436, 582, 650, and 872 nm and an adsorption edge at 950 nm, and the spectrum of isomer III shows two bands at 593 and 826 nm and an adsorption edge at 1100 nm. It was found that the absorption spectra of EMF derivatives encapsulating metals, for example, $Y@C_{82}(CF_3)_5$ (isomer I),[20] $Gd@C_{82}(CF_3)_5$ (isomer I),[22] and $Ce@C_{82}(CF_3)_5$ (isomer II), have common characteristic features. A similar situation was observed for the derivatives $Y@C_{82}(CF_3)_5$ (isomer II),[20] $Gd@C_{82}(CF_3)_5$ (isomer II),[22] and $Ce@C_{82}(CF_3)_5$ (isomer III). This character of the IR spectra is apparently associated with the fact that the carbon cages with grafted functional groups have identical structures and the identical mutual arrangement of the functional groups. Consequently, the main characteristic features of the optical absorption spectra of trifluoromethyl derivatives of EMF are determined mainly by the structure of the fullerene shell and the addition pattern of CF_3 groups rather than by the nature of the encapsulated metal atom.

In conclusion, we developed an efficient method for the synthesis of trifluoromethyl derivatives of EMF based on DMF extracts of cerium-encapsulating EMF. Trifluoromethyl derivatives $Ce@C_{82}(CF_3)_5$ (isomers I—III) with a high degree of purity (98—99%) were synthesized and isolated (by preparative HPLC) for the first time. It was found that the high-temperature solid-state reaction of silver trifluoroacetate with a DMF extract of EMF $Ce@C_{2n}$, unlike the reaction with fullerene C_{60}, proceeds selectively to give the diamagnetic compound containing five CF_3 groups, $Ce@C_{82}(CF_3)_5$, as the major product.

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