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Self-organization of a water-soluble fullerene derivative studied by pulsed field gradient NMR spectroscopy

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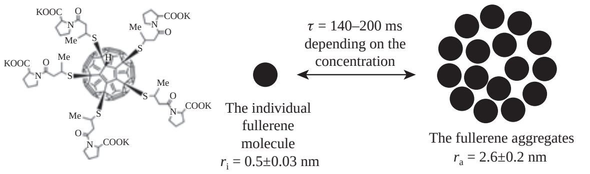
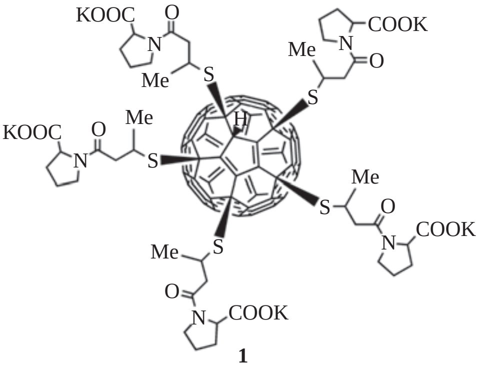
The self-organization of a water-soluble sulfur-containing fullerene adduct with captopril in deuterated water was studied by a pulsed field gradient NMR technique. Two types of fullerene particles characterized by the self-diffusion coefficients D_{s1} and D_{s2} of (4.0±0.5)×10^{-10} and (6.5±0.3)×10^{-11} $m^2 s^{-1}$, respectively, were revealed.



Water-soluble fullerene derivatives possess unique properties, and they can be used in drug delivery systems. These fullerenes are amphiphilic compounds consisting of a hydrophobic carbon framework with hydrophilic addends.[1–3] Therefore, water-soluble fullerenes are aggregated in aqueous solutions. Nanodimensional hollow spherical vesicles are formed as a result of self-organization[4,5] in aqueous and organic solutions, which was studied by dynamic light scattering,[6–8] atomic force microscopy[6,9,10] and transmission electron microscopy.[8,9,11,12] A direct way to estimate the aggregate size is molecular diffusion measurements. The efficiency of diffusion NMR spectroscopy for molecular aggregation investigations in liquids is well known.[13] Pulsed field gradient (PFG) NMR spectroscopy may be a method of choice for fullerene association testing.[11,12] Despite the PFG NMR being the obvious technique for self-diffusion coefficient measurements, this kind of experimental research of water-soluble fullerenes is fragmentary.

This work was devoted to a detailed study of the association of a water-soluble sulfur-containing fullerene adduct with captopril (compound **1**) in aqueous solutions by a pulsed field gradient NMR technique. This compound is readily soluble in water due to the presence of five hydrophilic groups.



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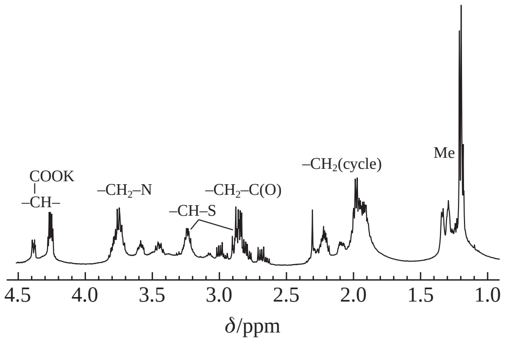

Figure 1 ^1H NMR spectrum of an aqueous solution of compound **1** (5.3 mg ml^{-1}).

A set of deuterated water solutions of compound **1** were prepared with concentrations from 2.7 to 64.4 mg ml^{-1}. The ^1H high resolution NMR spectra were recorded on a Bruker Avance-III 500 MHz spectrometer. The spectra consist of narrow multiplet lines against the background of wide lines (Figure 1). The narrow and wide components of the spectra are indicative of the existence of isolated and aggregated molecules of compound **1**.

Standard homo- and heteronuclear correlations COSY ^1H-^1H, HSQC ^{13}C-^1H were used in the spectral analysis. The ^1H and 2D spectra confirm the proposed fullerene structure.[†]

The fullerene self-diffusion coefficients were measured by a pulsed field gradient NMR technique. The ^1H NMR frequency was 400.22 MHz. The measurements were carried out on a Bruker Avance-III 400 MHz spectrometer equipped with a Bruker diff60 gradient unit. The pulsed field gradient stimulated echo sequence was used.[14–16]

Figure 2 shows the ^1H DOSY spectra for fullerene solutions of different concentrations. Two spectroscopically identical regions with different self-diffusion coefficients are observed. In order to calculate the self-diffusion coefficients more accurately,

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[†] For **1**: ^1H NMR (500 MHz, D_2O) δ: 1.18–1.34 (m, 15 H, Me), 1.86–2.33 (m, 20 H, CH_2 rings), 2.63–3.02 (m, 10 H, $CH_2C{=}O$), 2.85–2.90, 3.19–3.28 (m, 5 H, CHS), 3.42–3.82 (m, 10 H, CH_2N), 4.37–4.40, 4.24–4.28 (m, 5 H, CHCOOK).

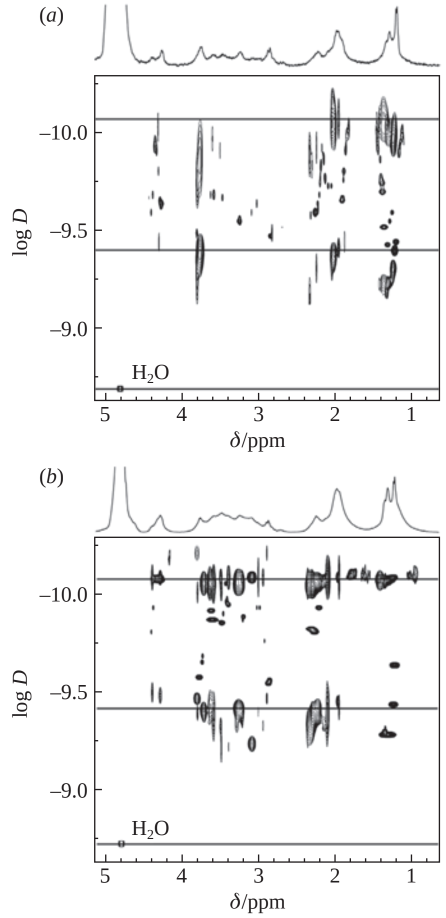

Figure 2 ^{1}H DOSY spectra of aqueous solutions of compound **1**: (*a*) 7 and (*b*) 50 mg ml^{-1}.

we analyzed the dependence of the spin echo signal integrated intensities on the square of magnetic field gradient pulses g^2 (diffusion decay).

For isotropic Brownian diffusion, the self-diffusion coefficient can be calculated from the equation

$$A(g^2) = A(0)\exp(-\gamma^2\delta^2 t_d g^2 D), \tag{1}$$

where $A(0)$ is the echo intensity at a zero magnetic field gradient, γ is the gyromagnetic ratio of the ^{1}H nucleus, g is the gradient pulse amplitude, δ is the gradient pulse duration, $t_d = \Delta - \delta/3$ is the diffusion time, where Δ is the interval between the gradient pulses, and D_s is the self-diffusion coefficient.

The diffusion decays (Figure 3) were approximated by biexponential curves.[15,16]

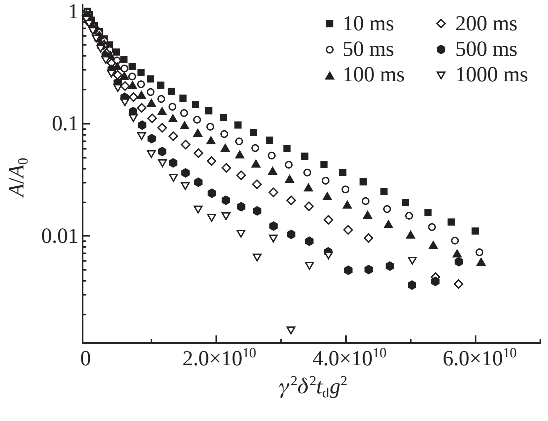

Figure 3 Diffusion decays of stimulated echo signals at different diffusion times t_d. The concentration of **1** is 64.4 mg ml^{-1}.

$$A(g) = p_1\exp(-\gamma^2 g^2\delta^2 t_d D_{s1}) + p_2\exp(-\gamma^2 g^2\delta^2 t_d D_{s2}), \tag{2}$$

where D_{s1}, D_{s2} and p_1, p_2 are the self-diffusion coefficients and the relative parts of different fullerene particles of **1**, respectively.

The diffusion decay decomposition was studied in detail previously.[16] The diffusion decay of the water proton signal is exponential, from equation (1); the self-diffusion coefficient is 1.9×10^{-9} m^2 s^{-1} regardless of concentration.

The values of D_{s1} and D_{s2} are $(4.0\pm0.5)\times10^{-10}$ and $(6.5\pm0.3)\times$ $\times10^{-11}$ m^2 s^{-1}, respectively, regardless of concentration.

It was supposed that D_{s1} and D_{s2} characterize the fullerene derivative particles of different sizes. The hydrodynamic radii of the particles r_1 and r_2 were calculated from the Stokes–Einstein equation

$$D = kT/(6\pi\eta r), \tag{3}$$

where k is the Boltzmann constant, T is the absolute temperature, η is the deuterated water viscosity, and r is the particle radius. The radius r_1 is 0.5±0.03 nm, which is close to the van der Waals radius of a fullerene frame.[17] Consequently, the particles whose radius is r_1 are isolated molecules of compound **1**. The particles with the radii r_2 = 2.6±0.2 nm are fullerene aggregations of **1**. The relative part of these aggregations p_2 increases with the concentration of compound **1**.

As mentioned above, the fullerene **1** diffusion decay is a biexponential shape and the self-diffusion coefficient D_{s2} does not depend on concentration for the whole concentration range at diffusion time t_d = 20 ms. It means that the aggregations are stable and their lifetime τ is more than 20 ms. The lifetime of fullerene **1** aggregates was estimated from the dependence $p_2(t_d)$ according to a published procedure.[18]

The example of dependences $p_2(t_d)$ is shown in Figure 4. The $p_2(t_d)$ curves are biexponential shaped and approximated by equation (4). The characteristic times of the curve tails are about 1 s that agrees well with the spin lattice relaxation times (T_1 = 0.9 s) for fullerene measured independently. The data after the subtraction of spin lattice relaxation corresponded to lines (Figure 4). From their slopes the lifetimes τ were calculated using the equation

$$p_2 = p_f\exp(-t_d/\tau) + p_s\exp(-t_d/T_1), \tag{4}$$

where τ is the lifetime, T_1 is fullerene spin lattice relaxation time, and $p_f + p_s = p_2(0)$.

The lifetimes τ are 140, 180 and 200 ms at fullerene concentrations of 64.4, 21.3 and 5.3 mg ml^{-1}, respectively.

Thus, two types of fullerene **1** particles characterized by the self-diffusion coefficients D_{s1} and D_{s2} of $(4.0\pm0.5)\times10^{-10}$ and $(6.5\pm0.3)\times10^{-11}$ m^2 s^{-1}, respectively, regardless of concentration were observed.

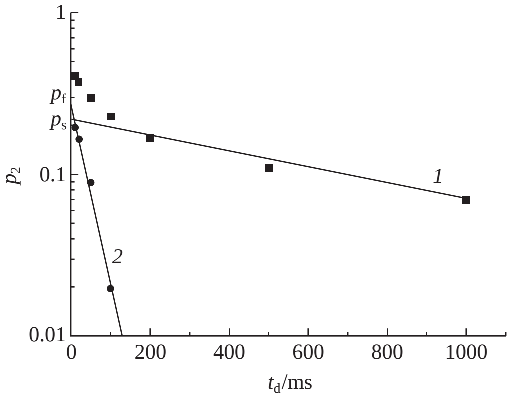

Figure 4 Dependences (*1*) $p_2(t_d)$ and (*2*) $p_2(t_d)$ after subtraction of spin lattice relaxation part.

The hydrodynamic radii were calculated from the Stokes–Einstein equation, the radius r_1 of 0.5±0.03 nm characterizes isolated fullerene **1** molecules. The particles with the radius r_2 = 2.6±0.2 nm correspond to fullerene **1** aggregations. The amount of aggregates increases with the concentration of fullerene solution. The associated lifetimes were estimated from the analysis of diffusion decay shape dependence on the diffusion time.

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References

1 A. A. Yurkova, E. A. Khakina, S. I. Troyanov, A. Chernyak, L. Shmygleva, A. S. Peregudov, V. M. Martynenko, Y. A. Dobrovolskiy and P. A. Troshin, *Chem. Commun.*, 2012, **48**, 8916.

2 N. E. Fedorova, R. R. Klimova, Yu. A. Tulenev, E. V. Chichev, A. B. Kornev, P. A. Troshin and A. A. Kushch, *Mendeleev Commun.*, 2012, **22**, 254.

3 O. L. Kobzar, V. V. Trush, V. Yu. Tanchuk, I. I. Voronov, A. S. Peregudov, P. A. Troshin and A. I. Vovk, *Mendeleev Commun.*, 2015, **25**, 199.

4 S. Zhou, C. Burger, B. Chu, M. Sawamura, N. Nagahama, M. Toganoh, U. E. Hackler, H. Isobe and E. Nakamura, *Science*, 2001, **291**, 1944.

5 T. Homma, K. Harano, H. Isobe and E. Nakamura, *J. Am. Chem. Soc.*, 2011, **133**, 6364.

6 E. Nakamura and H. Isobe, *Acc. Chem. Res.*, 2003, **36**, 807.

7 G. Zhang, Y. Liu, D. Liang, L. Gan and Y. Li., *Angew. Chem. Int. Ed.*, 2010, **49**, 5293.

8 Y. E, L. Bai, L. Fan, M. Han, X. Zhang and S. Yang, *J. Mater. Chem.*, 2011, **21**, 819.

9 W. Guanwu, Z. Guoxia and Y. Lifeng, *Chin. Sci. Bull*., 2004, **49**, 1441.

10 Q. Liao, X. Qu, L. Chen and X. Jin, *J. Phys. Chem. B*, 2006, **110**, 7153.

11 H. Kato, C. Böttcher and A. Hirsch, *Eur. J. Org. Chem.*, 2007, 2659.

12 M. Braun, U. Hartnagel, E. Ravanelli, B. Schade, C. Böttcher, O. Vostrowsky and A. Hirsch, *Eur. J. Org. Chem*., 2004, 1983.

13 V. V. Kachala, L. L. Khemchyan, A. S. Kashin, N. V. Orlov, A. A. Grachev, S. S. Zalesskiy and V. P. Ananikov, *Russ. Chem. Rev*., 2013, **82**, 648.

14 K.-J. Suh, Y.-S. Hong, V. D. Skirda, V. I. Volkov, C.-Y. J. Lee and C.-H. Lee, *Biophys. Chem*., 2003, **104**, 121.

15 A. I. Maklakov, V. D. Skirda and N. F. Fatkullin, *Samodiffuziya v rastvorakh i rasplavakh polimerov (Self-Diffusion in Polymer Solutions and Melts)*, Kazan State University Press, Kazan, 1987 (in Russian).

16 V. I. Volkov, S. A. Korotchkova, H. Ohya and Q. Guo, *J. Membr. Sci.*, 1995, **100**, 273.

17 H. Tanaka and K. Takeuchi, *Appl. Phys. A*, 2005, **80**, 759.

18 Y. S. Hong, K. C. Kim, V. I. Volkov, V. D. Skirda and C.-H. Lee, *Appl. Magn. Reson*., 2005, **29**, 351.

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