J Incl Phenom Macrocycl Chem (2007) 58:389–398
DOI 10.1007/s10847-006-9287-7

ORIGINAL ARTICLE

Solution structure and equilibrium of new calix[4]resorcinarene complexes—prototype of molecular machines. NMR data

S. V. Kharlamov · A. Y. Ziganshina · A. V. Aganov · A. I. Konovalov · Sh. K. Latypov

Received: 21 September 2006 / Accepted: 14 December 2006 / Published online: 23 January 2007

Abstract Association properties and molecular machine application of water soluble calix[4]resorcinarene (**1**) with two aromatic guests (2-naphthol (**2**) and 1,5-naphthalenediamine (**3**)) have been investigated by various NMR methods (chemical shift, nOe and diffusion measurements) in aqueous solution at different concentrations and pH range. In neutral solution **1** strongly associates with **2**, while only moderately associating with **3**. Increase in concentration causes an increase in the stability of **1** + **3** and **1** + **2** + **3** complexes and produces high order complexes. The decrease of pH does not have an influence on **1** + **2** association, but disrupts **1** + **3** assembly. **1** can be used for the separation of **2** + **3** mixture in aqueous solution at moderate concentrations. The pH dependency of the association properties of the **1** + **3** system makes these compounds prime candidates for pH-responsive molecular machines applications.

Keywords NMR · DOSY · Molecular machine · Host–guest complex

S. V. Kharlamov · A. Y. Ziganshina · A. I. Konovalov · Sh.K. Latypov (✉)
Institute of Organic and Physical Chemistry, Kazan Scientific Centre, Russian Academy of Sciences, Arbuzov St., 8, Kazan 420088, Russia
e-mail: lsk@iopc.knc.ru

A. V. Aganov
Kazan State University, Kremlevskaya St., 18, Kazan 420008, Russia

Abbreviations

NMR	Nuclear magnetic resonance
UV	Ultraviolet
NOe	Nuclear Overhauser enhancement (effect)
NOESY	Nuclear Overhauser enhancement spectroscopy
DOSY	Diffusion ordered spectroscopy
BPP-STE-LED	Bipolar pulse pair–Stimulated echo–Longitudinal eddy current delay
CS	Chemical shift
CSPs	Chemical shift perturbations

Introduction

Design of molecular complexes that are able to carry out the mechanical motions described by the classical theory (molecular machines) is a very important problem. Recently there has been an explosion of interest in such kinds of systems [1]. The extension of the concept of a machine to a molecular level is of interest not only for the advancement of basic theory, but also for the growth of nanotechnology. The miniaturization of components used for the construction of modern devices, is a main requirement for electronic and technology development and thus new models and systems are highly needed [2].

Molecular-level machine is an assembly of molecular components that is intended for performing machine-like movements upon external stimulus [2]. The assembly consists of, at least, two parts: stationary and mobile. The external action (input) stimulates a

displacement (output) of the mobile part toward the stationary one [3]. Most molecular machines are built on the base of rotaxanes, pseudorotaxanes, catenanes, which consist of molecules with rigid cyclic and well-organized structures composing the stationary part: cucurbit[n]uriles, cyclodextrines, bisviologencyclophanes [4, 5]. Movements of the component parts within a molecular-level machine of supramolecular nature are usually the result of the making and breaking of intercomponent noncovalent bonds [2].

In principle, the best energy inputs to make a molecular machine work are photons (photochemical stimulus) and electrons (electrochemical one). In the case of electrochemical stimulation an acid/base control can be effectively used [1, 2, 5].

According to our preliminary results the water-soluble derivative of calix[4]resorcinarene (**1**) with flexible viologen units on the upper rim can be used as a stationary part in the construction of electrochemically controlled molecular machines (Fig. 1). It has positive charged fragments and therefore it can selectively bind only uncharged or negatively charged guest-molecules (see Scheme 1). It cannot bind the positively charged guests due to electrostatic repulsion. Consequently, it is expected that the changing of charge of the guest can stimulate a displacement of a guest-molecule (mobile part) toward the host (stationary one). So the reversible dethreading/rethreading cycles of the complex can be performed [2] by varying of the guest charge (e.g. by acid/base stimulation).

Here we report some results of our NMR investigation on an association properties of new water soluble calix[4]resorcinarene (**1**) with two aromatic guests (2-naphthol (**2**) and 1,5-naphthalenediamine (**3**)) in

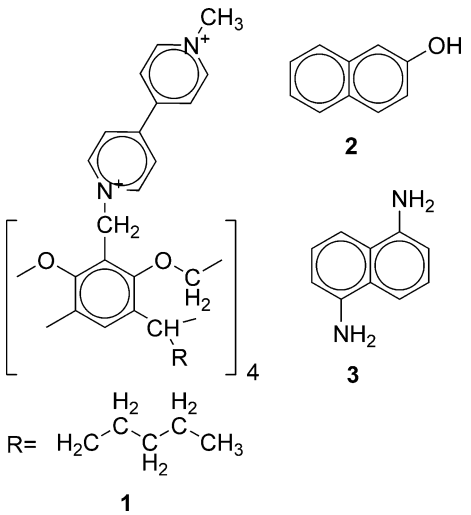
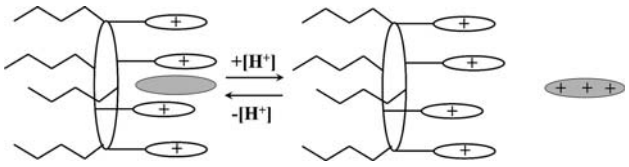


Fig. 1 Structural parts of the molecular machine model



Scheme 1 pH control of host binding properties (gray filled oval represents a guest-molecule)

regards to their use as model pH-controllable molecular machine.

Experimental

2-Naphthol and 1,5-naphthalenediamine were obtained from ''Sigma''. Tetramethylviologen-Calix[4]resorcinarene **1** has been synthesized using literature procedure [6].

All of the samples were prepared in D_2O at pH = 5 or in D_2O + HCl (10 mM) at pH = 2 solutions.

All of the NMR experiments were performed with a Bruker AVANCE-600 spectrometer with a 5 mm diameter inverse probe head with Z-active shielded gradients working at 600.013 MHz in ^1H.

The 2D DOSY experiments were performed by BPP-STE-LED sequence [7]. Data was acquired with a 50 ms diffusion delay in all experiments, bipolar gradient pulses duration from 1.8 to 4.2 ms (depending on a system under investigation), 1.1 ms spoil gradient pulse (30%) and a 5 ms eddy current delay. The bipolar pulse gradient strength was varied incrementally from 0.01 to 0.32 T/m. The experimentally observed diffusion coefficients were then determined from 2D DOSY plots obtained by Bruker XWinNmr software package. Several measures of D were obtained at more than one place in the spectrum and all experiments were carried out in duplicate or triplicate. The reported results are the mean value of multiple data points (see Table 1) and the standard deviations are less than 0.01×10^{-9} m^2/s in all cases.

The temperature was set and controlled at 298 K with a 535 l/h airflow rate in order to avoid any temperature fluctuations owing to sample heating during the magnetic field pulse gradients.

Results and discussion

Preliminary NMR and UV data indicates that **1** is able to bind **2** and/or **3** (Fig. 1) and the stability of these host-guest complexes depends on the nature of the

guests and the media. Therefore **1** can be used as an effective stationary part and **2** and **3** as mobile parts in molecular machine.

CS and nOe data

Before starting the investigation of the pH dependence of **1**–**3** systems' association properties, we have analyzed the influence of the concentration and pH on individual components of the systems. It was found that ^{1}H CSs (Table 1) of **1** and **2** depend only slightly on acidity of the media (CSPs less than 0.01 ppm). CSs of **3** strongly depend on pH (proton signals low-field shifted by 0.32–0.61 ppm when pH varies from 5 to 2) due to the protonation of aminogroups of **3** (pK_a^2 = 4.65, pK_a^1 = 2.60 [8]). The observed chemical shifts for the charged forms of **3** are in qualitative agreement with the calculated ones: according to GIAO DFT estimations low-field shifts up to 1.0–1.8 ppm can be expected under full protonation of amino groups of **3**.

It was also found that the concentration variations in neutral media (C = 1 mM and 5 mM) do not affect the ^{1}H CS of **2** and slightly influence on **1** ones. There are 0.07–0.16 ppm upfield CSPs for protons of down-rim of **1** and less than 0.05 ppm lowfield CSPs for other protons. At neutral media upfield shifts (0.06–0.12 ppm) are observed for protons of **3** when the concentration is increased. Increasing of the concentration at pH = 2 leads to insignificant (less than 0.03 ppm) upfield shifts of proton CSs of **3**. Therefore, it seems, that at neutral media **3** self-associates in stack-like structures (shielding effect), while in acidic medium these assemblies became less stable.

Table 1 Self-diffusion coefficients D ($\times 10^{-9}$ m^2/s) for the **1**, **2**, **3** and their combinations in different medium, T = 298 K

System	pH of system; concentration, mM	D_1	D_2	D_3
1	5; 1	0.21	–	–
1	5; 5	0.16	–	–
1	2; 1	0.21	–	–
2	5; 1	–	0.77	–
2	2; 1	–	0.77	–
2	2; 5	–	0.76	–
3	5; 1	–	–	0.72
3	5; 5	–	–	0.71
3	2; 1	–	–	0.59
3	2; 5	–	–	0.58
2 + **3**	5; 1	–	0.79	0.75
1 + **2**	5; 1	0.18	0.21	–
1 + **2**	2; 1	0.18	0.20	–
1 + **3**	5; 1	0.20	–	0.43
1 + **3**	2; 1	0.21	–	0.58
1 + **3**	5; 5	0.14	–	0.15
1 + **3**	2; 5	0.14	–	0.51
1 + **2** + **3**	5; 2	0.15	0.17	0.29
1 + **2** + **3**	5; 5	0.12	0.13	0.16
1 + **2** + **3**	2; 2	0.16	0.15	0.59
1 + **2** + **3**	2; 5	0.13	0.13	0.57

The changes of CS for the **2** + **3** combination in comparison with individual solutions at the concentration C = 1 mM are small (no effect on protons of **2** and upfield shifts less than 0.06 ppm for protons of **3**). Moreover, there are no noticeable CSPs for all protons of **2** and **3** when increasing the concentration. So, it looks like these molecules do not associate.

Thus, according to the CS data, **2** does not self-associate in neutral nor in acid media. For **3** the increasing of media acidity leads only to the protonation of **3**. Any self-associations of **3** have not been found out. In neutral media the CS data allows to stipulate that **1** and **3** are inclined to self association**.**

Then ^{1}H CSPs in different equimolar combinations of **1**, **2** and **3** were analyzed.

Characteristic upfield shifts (up to 1.16 ppm for **1** + **2** system and 0.57 ppm for **1** + **3** one) of the guests proton signals were observed (concentration of compounds **1**–**3** C = 1 mM). The latter means that there are strong host-guest complexes in these systems (and it seems that protons of **2** are much shielded by **1** in the **1** + **2** system, then the protons of **3** in the **1** + **3** system). It was found that the acidity of the medium does not have an influence on the stability of the **1** + **2** complex (CSPs are below 0.06 ppm with pH variation). At the same time, decreasing the media pH (from 5 until 2) results in dramatic changes of CS of **3** in the **1** + **3** system (lowfield shift 0.76–1.11 ppm). So, increasing the medium acidity causes the protonation of the guest molecule **3** and the complex disruption due to the electrostatic repulsion between host and guest.

All of these results are strongly supported by NOESY data. For **1** + **2** system strong nOes between protons of upper rim of **1** and the protons of **2**. There were no nOes observed in case of the **1** + **3** system in neutral nor in acid media. The lack of nOes in the **1** + **3** system in neutral media is possibly a consequence of weak association between molecules and fast exchange (relative to NMR time scale) between the bound and the free state of **3** in this system.

In addition, the guest protons are shifted upfield by 0.98 ppm in the **1** + **3** system in neutral media when concentration of **1** and **3** increases up to 5 mM. The reason for this phenomenon is that, the **1** + **3** bound state becomes more favourable at higher concentrations. Moreover, at high concentration there were strong nOes observed between protons of upper rim of **1** and **3**.

It is interesting to note that at high concentration decreasing the media pH does not fully destroy the

association of **1** + **3**. This phenomenon is strongly supported by CS and nOe data (CSs of **3** in the **1** + **3** system at pH = 2 are upfield shifted in comparison with those for free **3** at the same pH and solution concentrations. There are weak nOes between the protons of upper rim of **1** and **3** seen for this combination (pH = 2, C = 5 mM)).

Finally, the **1** + **2** + **3** combination was examined. When 1 mM of **1** aqueous solution was mixed with 1 mM of **2** and 1 mM of **3** solutions in neutral media the CSs upfield shifts (0.34–0.88 ppm for **2** and 0.04–0.08 ppm for **3**) were observed. At the concentration of compounds C = 5 mM 0.55–1.39 and 0.92–0.99 ppm upfield shift of proton signals of guests **2** and **3** were monitored, respectively. In addition, nOes between guests and hosts signals are weak in the case of C = 1 mM and strong for C = 5 mM. Thus, the increasing of the concentration results in a shift in equilibrium towards the bound state in this case as well (see above).

There is a very specific influence of the media acidity on the association stability of the **1** + **2** + **3** system. The association is partly destroyed when pH varies from 5 to 2 at C = 5 mM: CSPs of **2** are below 0.18 ppm and up to 1.62 ppm for **3**. At the same time, there were nOes only between the signals of **1** and **2** for pH = 2. Thus, the acidation of the system opens a way for selective adjustment of the composition and the structure of the association.

2D DOSY data

Despite the above reported considerations, the stoichiometry, sizes and stability of the complexes are still not completely understood. Moreover, there are some difficulties related with used solvent (D_2O) in NMR experiments—an improper dynamic range, overlapping of some signals of studied molecules, and residual H_2O. Therefore, in order to get direct proof of the formation of the complexes and their sizes, we have measured NMR diffusion coefficients (see Table 1). The coefficients are interconnected with the sizes of the complexes and therefore one can obtain reliable information on sizes and stochiometry of the complexes [9, 10].

As it can be seen from Table 1, D values of host and guests are significantly different and correlate with the size of the molecules.

In addition, we have found the value of $D_{\mathbf{1}}$ decreases (0.21×10^{-9} m^2/s vs. 0.16×10^{-9} m^2/s) upon increasing the concentration of **1**. This may be due to self-association of **1** and the change of D which corresponds to increasing volume by ca. 2 times, i.e. **1** at 5 mM exists as dimer. It is strongly supported by nOe data—there are cross-peaks in 2D NOESY spectra between protons of upper and lower rim.

At the same time there are no indications of the self-association of **2** and **3** and the association of **2** with **3**.

1 associates with **2** producing a strong assembly which can be characterized by identical D value for hosts and guests proton signals (of which the ca. value corresponds to the whole, indivisible **1** + **2** system). The D value of the complex (0.18×10^{-9} m^2/s) is only slightly less than that of the free host (0.21×10^{-9} m^2/s). However, for a useful analysis of these data it is necessary to clear up the relation between molecular weight (M) and D of a particular assembly. It should be realized that the shape of a given molecular species can significantly affect the relation between M and the diffusion coefficient, which can complicate a direct analysis of the data. Since **1** has flexible viologen units on its upper rim, which can self-adjust under the form of the guest molecule, it is expected that the shape of the complex is rod-like in this case (see Scheme 1). It has been claimed that the ratio of diffusion coefficients for two different species (D_i/D_j) is inversely proportional to the square-root of the ratio of their M for such kinds of molecules or to the cubic-root for spherical ones [11]. Thus, in order to estimate molecular weight changes from DOSY data, we suppose that $(M_j/M_i)^{-3} \leq (D_i/D_j) \leq (M_j/M_i)^{-2}$.

Hence, since the molecular weight of **1** is about 1500 a.m.u., weight augmentation by ca. 500–900 is observed in the case of **1** + **2** system at C = 1 mM. So it seems that there are more than one guest per host ($M_{\mathbf{2}}$~150) in this system. Therefore, the stoichiometry order is much higher than 1:1.

In addition, it should be noted that the medium acidity does not have an influence on the complex stability.

At the same time, for the **1** + **3** system the D of **3** is higher than that of **1** for all pH. However, at neutral aqueous media $D_{\mathbf{3}}$ is still less than it is for free **3** and this value increases with decreasing pH. These data can be explained in terms of fast exchange between two states (free and bound) and short lifetime of **3** in bound state (relative to diffusion and NMR timescale), i.e. weak association constant. Thus a weighted average D is observed [12].

To verify this assumption the experiment for **1** + **3** system at higher concentration (5 mM) was performed. It was found (see Table 1) that $D_{\mathbf{3}}$ is ca. equal to $D_{\mathbf{1}}$ in neutral aqueous media and becomes much higher in acid media pH = 2. However at pH = 2 the $D_{\mathbf{3}}$ (0.51×10^{-9} m^2/s) is still less than the value for the free protonated form of **3** at the same concentration. This is probably due to a partial disruption of the **1** + **3**

complex when the pH is decreased. Indeed, when we added some more acid to the solution D_3 increased up to 0.56×10^{-9} m^2/s while the D_1 value did not change.

Thus, the host–guest complex of **1** + **3** is strong in neutral media and disrupts at low pH value.

There are some more conclusions, which can be derived on the stoichiometry of the **1** + **3** complex from D data:

(1) **1** + **3** complexed state is more favourable at high concentration.
(2) When complex **1** + **3** is formed, D_1 decreases from 0.16×10^{-9} up to 0.14×10^{-9} m^2/s (see Table 1, C = 5 mM, pH = 5). At this concentration **1** exists as a dimer, this decrease of D for **1** + **2** complex corresponds to a system weight augmentation of ca. 900–1500. So it seems (M_3~160) that the stoichiometry order is even higher than 2:2 in this case.

Finally, we decided to study the ability of the host to bind more than one guest simultaneously. 2D DOSY experiments for the **1** + **2** + **3** combination were performed (see Table 1). There is a host–guest complex in this system and its stability depends dramatically on the initial concentration of the components: only at 5 mM D_3 becomes ca. equal D_1 (see Table 1). It was also found that the host is capable to capsulate both guests into its cavity. 2D DOSY experiments show that at C = 5 mM self-diffusion coefficients of all components in this system are similar. Hence, a whole **1** + **2** + **3** complex takes place.

It was also found that the acidity of the medium has an influence on the complex stability: the decrease of pH causes **3** to leave the complex, while **2** remains in bound state at any pH.

Conclusion

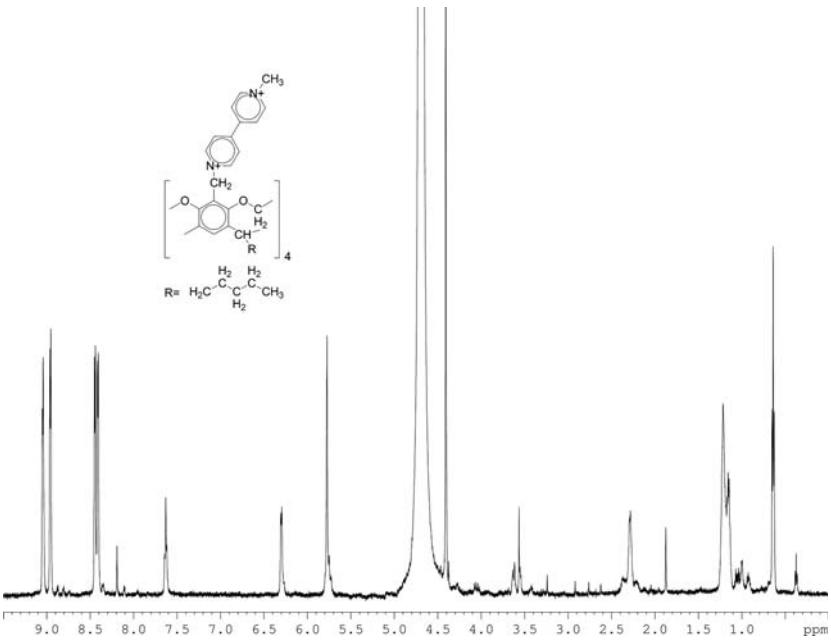
The investigation of binding abilities of water-soluble derivatives of calix[4]resorcinarenes with charged substituents was undertaken. Model of pH-controllable machine was considered. It was found that **1** can form strong complexes with **2** and **3** separately and concurrently that the stability of complexes depends on the acidity of the solution.

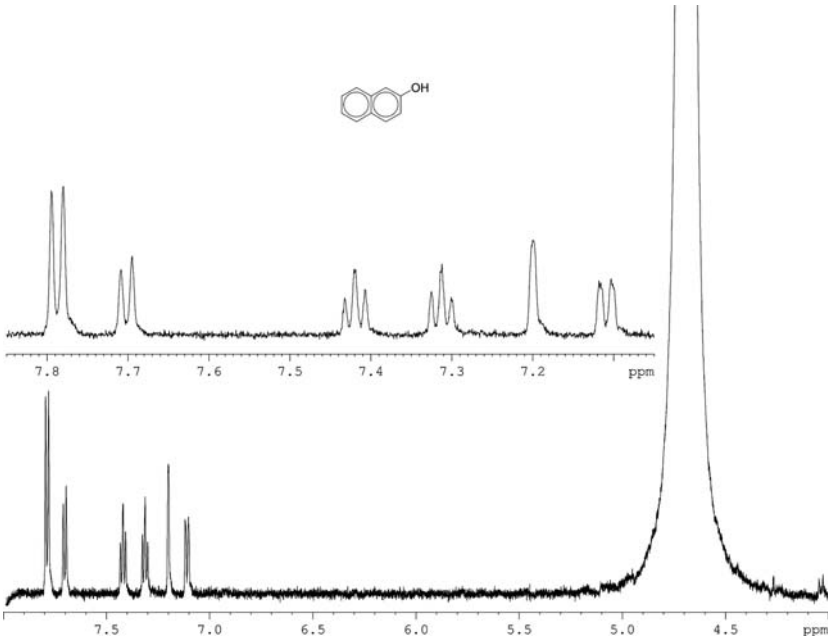
According to 2D DOSY data the **1** + **2** and **1** + **3** systems (at C = 5 mM) produce complexes with a high order of stoichiometry.

Acknowledgements We gratefully acknowledge the Russian Foundation for Basic Research (Grants ## 05-03-32558-a, 06-03-32199-a) and Federal Collective Use Center (contracts ## 02.451.11.7036 and 02.451.11.7019) for the financial support of this work.

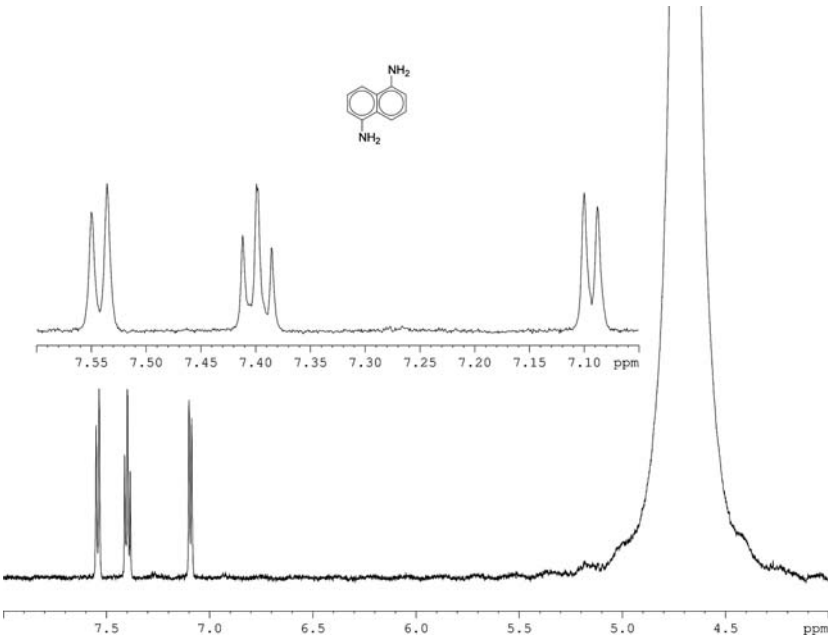
Appendix

1D ^{1}H spectrum (600 MHz, 303 K) of calix[4]resorcinarene in D_2O, 1 mM

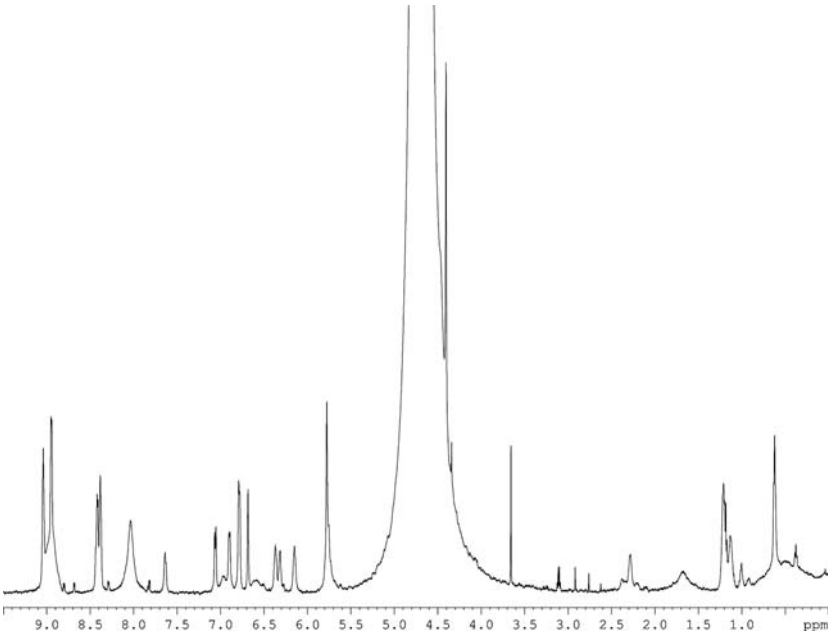




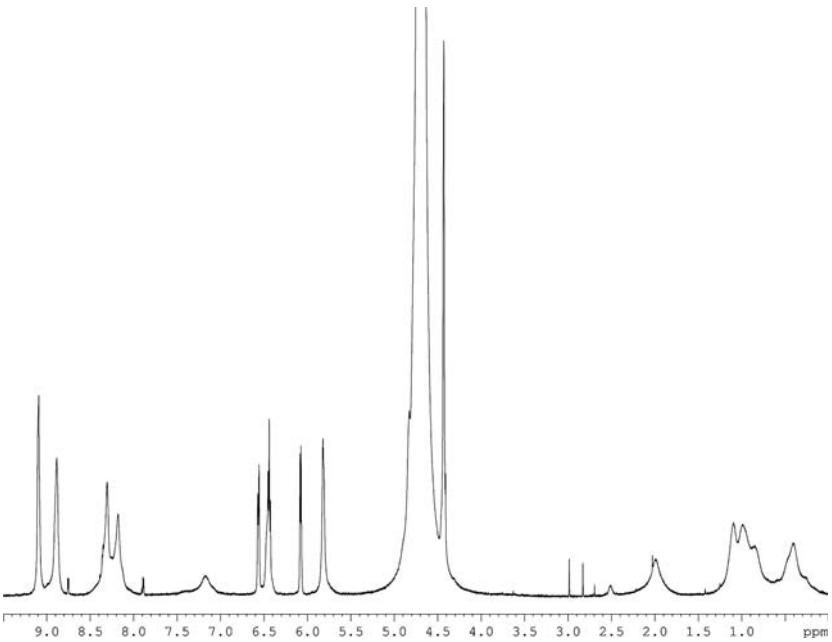
1D ^{1}H spectrum (600 MHz, 303 K) of 2-naphthol in D_2O, 1 mM



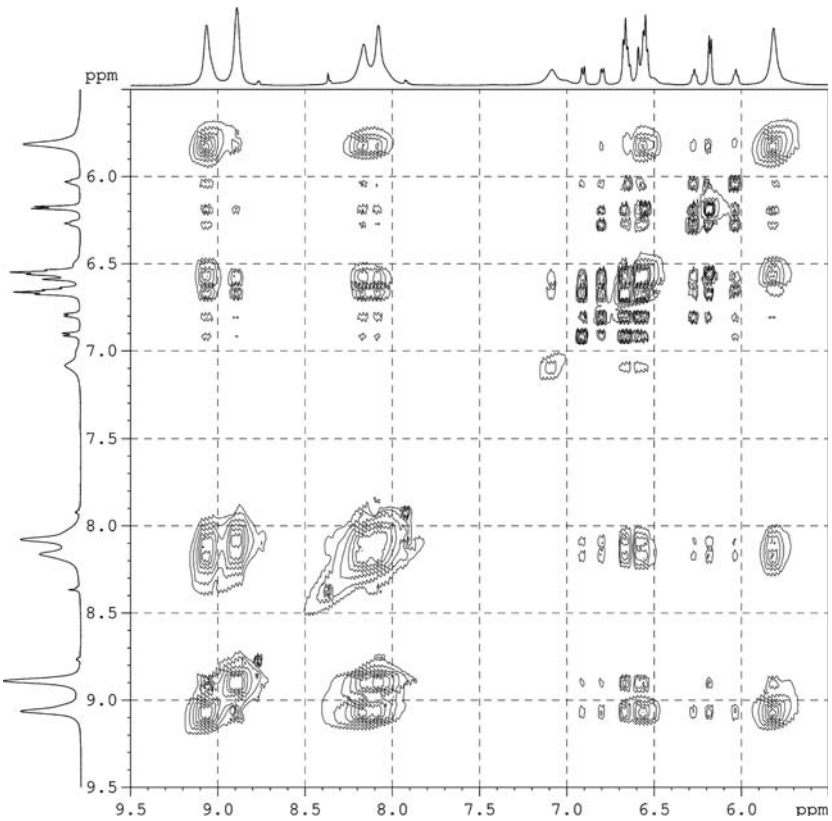
1D ^{1}H spectrum (600 MHz, 303 K) of 1,5-naphthalenediamine in D_2O, 1 mM



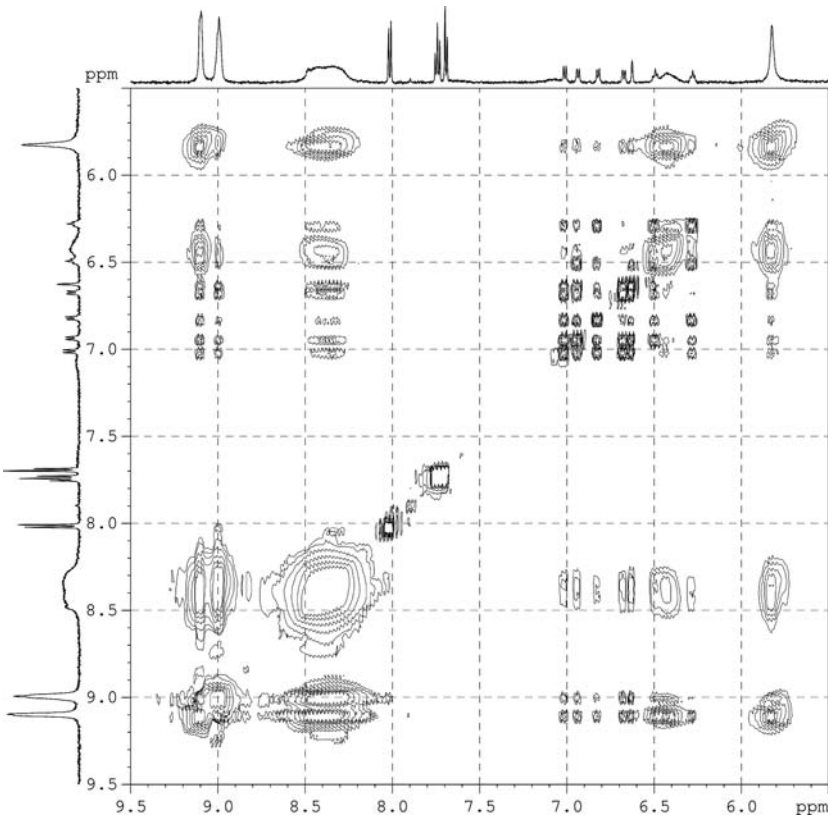
1D ^{1}H spectrum (600 MHz, 303 K) of equimolar mixture of calix[4]resorcinarene and 2-naphthol in D_2O, 1 mM



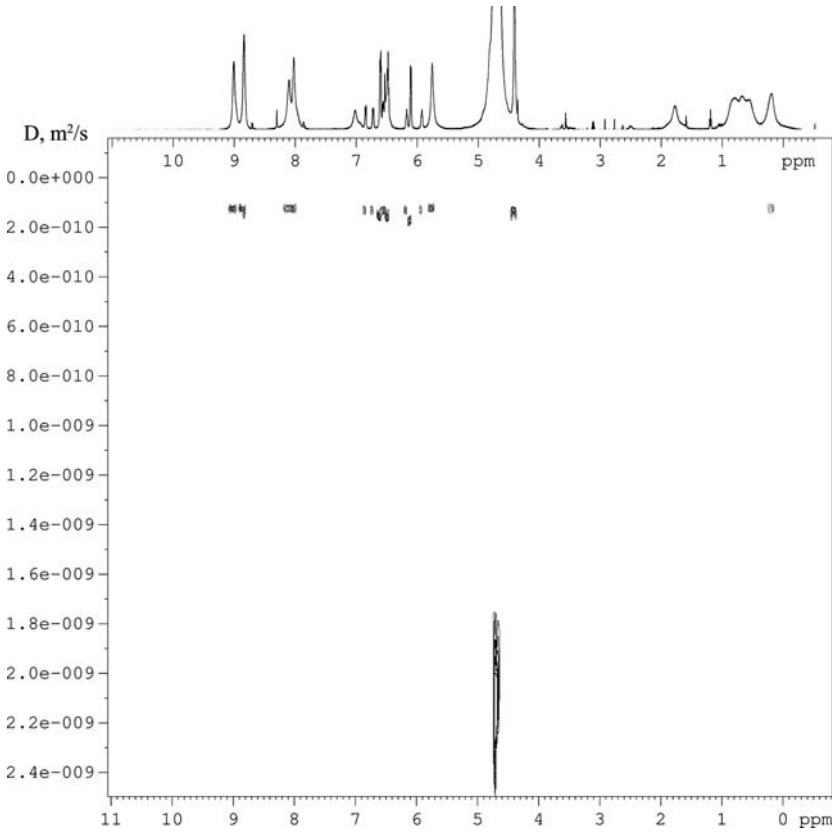
1D ^{1}H spectrum (600 MHz, 303 K) of equimolar mixture of calix[4]resorcinarene and 1,5-naphthalenediamine in D_2O, 5 mM



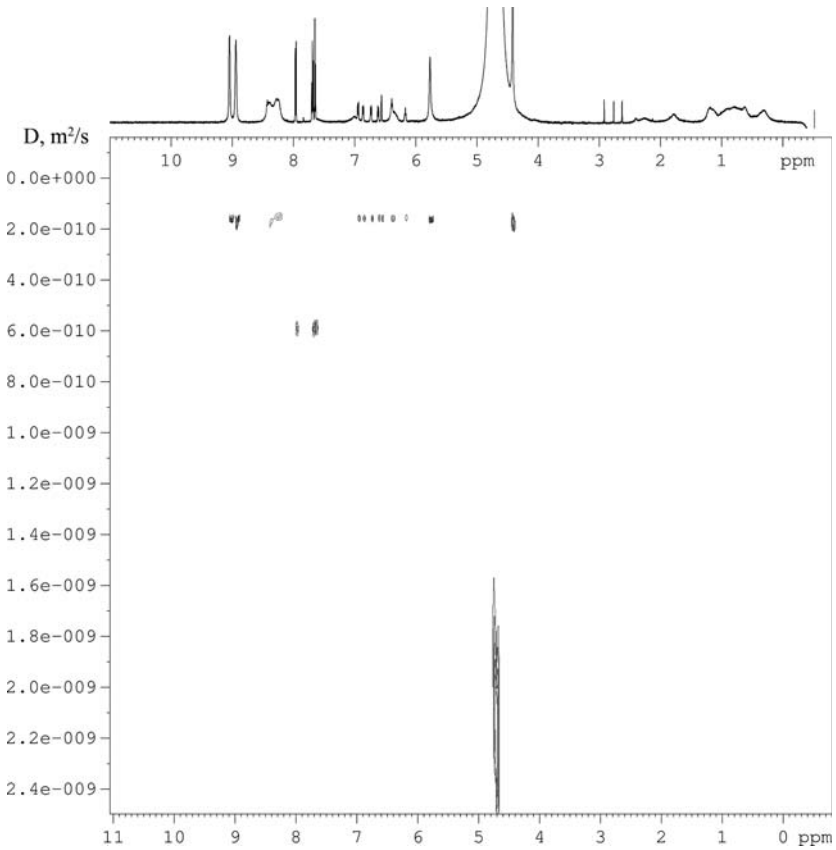
Fragment of 2D NOESY spectrum (600 MHz, 303 K) of equimolar mixture of calix[4]resorcinarene, 2-naphthol and 1,5-naphthalenediamine in D_2O, 5 mM



Fragment of 2D NOESY spectrum (600 MHz, 303 K) of equimolar mixture of calix[4]resorcinarene, 2-naphthol and 1,5-naphthalenediamine in D_2O + HCl (10 mM), 2 mM



2D DOSY spectrum (600 MHz, 298 K) of equimolar mixture of calix[4]resorcinarene, 2-naphthol and 1,5-naphthalenediamine in D_2O, 5 mM



2D DOSY spectrum (600 MHz, 298K) of equimolar mixture of calix[4]resorcinarene, 2-naphthol and 1,5-naphthalenediamine in D_2O + HCl (10 mM), 2 mM

References

1. Balzani, V., Credi, A., Venturi, M.: Molecular Devices and Machines – A Journey into the Nano World. Wiley-VCH, Weinheim (2003)
2. Balzani, V., Credi, A., Raymo, F.M., Stoddart, J.F.: Machines at the molecular level. Angew. Chem. Int. Ed. **39**, 3348–3391 (2000)
3. Lehn, J.-M.: Supramolecular Chemistry, Concepts and Perspectives. Wiley-VCH, Weinheim (1995)
4. (a) Asfari, Z., Vicens, J.: Molecular machines. J. Incl. Phenom. **36**, 101–115 (2000); (b) Kelly, T.R., Silva, R.A., De Silva, H., Jasmine, S., Zhao, Y.: A rationally designed prototype of a molecular motor. J. Am. Chem. Soc. **122**, 6935–6949 (2000); (c) Ballardini, R., Balzani, V., Clemente-Leon, M., Credi, A., Gandolfi, M.T., Ishow, E., Perkins, J., Stoddart, J.F., Tseng, H.-R., Wenger, S.: Photoinduced electron transfer in a triad that can be assembled/disassembled by two different external inputs. Toward molecular-level electrical extension cables. J. Am. Chem. Soc. **124**, 12786–12795 (2002)
5. (a) Mattews, O.A., Raymo, F.M., Stoddart, J.F., White, A.J.P., Williams, D.J.: Acid/Base-controlled supramolecular switch. New J. Chem. **22**, 1131–1134 (1998); (b) Balzani, V., Credi, A., Matersteig, G., Matthews, O.A., Raymo, F.M., Stoddart, J.F., Venturi, M., White, A.J.P., Williams, D.J.: Switching of pseudorotaxanes and catenanes incorporating a tetrathiafulvalene unit by redox and chemical inputs. J. Org. Chem. **65**, 1924–1936 (2000); (c) Asakawa, M., Ashton, P.R., Balzani, V., Credi, A., Matersteig, G., Matthews, O.A., Montalti, M., Spencer, N., Stoddart, F., Venturi, M.: Electrochemically induced molecular motions in pseudorotaxanes: A case of dual-mode (oxidative and reductive) dethreading. Chem. Eur. J. **3**, 1992–1996 (1997)
6. (a) Peinador, C., Román, E., Kaifer, A.E., Abboud, Kh.: Novel cavitands containing electrochemically active 4,4′-bipyridinium subunits Chem. Commun. 1887–1888 (1999); (b) Toba, R., Quintela, J.M., Peinador, C., Román, E., Kaifer, A.E.: Dendritic cavitands: preparation and electrochemical properties. Chem. Commun. 1768–1769 (2002)
7. Wu, D., Chen, A., Johnson, C.S. Jr.: An improved diffusion-ordered spectroscopy experiment incorporating bipolar-gradient pulses. J. Magn. Reson. A. **115**, 260–264 (1995)
8. Takehira, K., Sugawara, Y., Kowase, S., Tobita, S.: A picosecond time-resolved study on prototropic reactions of electronically excited 1,5- and 1,8-diaminonaphthalenes in aqueous solution. Photochem. Photobiol. Sci. **4**, 287–293 (2005)
9. (a) Johnson, C.S. Jr.: Diffusion ordered nuclear magnetic resonance spectroscopy: principles and applications. Prog. NMR Spectrosc. **34**, 203–256 (1999); (b) Antalek, B.: Using pulsed gradient spin echo NMR for chemical mixture analysis: How to obtain optimum results. Concepts Magn. Reson. **14**(4), 225–258 (2002); (c) Cohen, Y., Avram, L., Frish, L.: Diffusion NMR spectroscopy in supramolecular and combinatorial chemistry: An old parameter – new insights. Angew. Chem. Int. Ed. **44**, 520–554 (2005)
10. (a) Viel, S., Mannina, L., Segre, A.: Detection of a π–π complex by diffusion-ordered spectroscopy (DOSY). Tetrahedron Lett. **43**(14), 2515–2519 (2002); (b) Avram, L., Cohen, Y.: Complexation in pseudorotaxanes based onα-cyclodextrin and different, α,ω-diaminoalkanes by NMR diffusion measurements. J. Org. Chem. **67**(8), 2639–2644 (2002); (c) Kapur, G.S., Cabrita, E.J., St. Berger: The qualitative probing of hydrogen bond strength by diffusion-ordered NMR spectroscopy. Tetrahedron Lett. **41**, 7181–7185 (2000); (d) Cameron, K.S., Fielding, L.: NMR diffusion coefficient study of steroid–cyclodextrin inclusion complexes. Magn. Reson. Chem. **40**, S106–S109 (2002)
11. (a) Holtz, M., Mao, X., Seiferling, D., Sacco, A.: Experimental study of dynamic isotope effects in molecular liquids: Detection of translation-rotation coupling. J. Chem. Phys. **104**, 669–679 (1996); (b) Waldeck, A.R., Kuchel, P.W., Lennon, A.J., Capman, B.E.: NMR diffusion measurements to characterise membrane transport and solute binding. Prog. Nucl. Magn. Reson. Spectrosc. **30**, 39–68 (1997); (c) Timmerman, P., Weidmann, J.-L., Jolliffe, K.A., Prins, L.J., Reinhoudt, D.N., Shinkai, S., Frish, L., Cohen, Y.: NMR diffusion spectroscopy for the characterization of multi-component hydrogen-bonded assemblies in solution. J. Chem. Soc., Perkin Trans. 2, 2077–2089 (2000); (d) Brand, T., Cabrita, E.J., St. Berger: Intermolecular interaction as investigated by NOE and diffusion studies. Prog. NMR Spectrosc. **46**, 159–196 (2005)
12. (a) Moonen, C.T.H., Van Gelderen, P., Vuister, G.W., Van Zijl, P.C.M.: Gradient-enhanced exchange spectroscopy. J. Magn. Reson. **97**, 419 (1992); (b) Cabrita, E.J., St. Berger: HR-DOSY as a new tool for the study of chemical exchange phenomena. Magn. Reson. Chem. **40**, S122–S127 (2002)