Angewandte Chemie International Edition

NMR Spectroscopy

International Edition: DOI: 10.1002/anie.201506683
German Edition: DOI: 10.1002/ange.201506683

Hexameric Capsules Studied by Magic Angle Spinning Solid-State NMR Spectroscopy: Identifying Solvent Molecules in Pyrogallol[4]arene Capsules

Liat Avram, Amir Goldbourt,* and Yoram Cohen**

Abstract: *Powders of pyrogallol[4]arene hexamers were produced by evaporation from organic solvents and were studied, for the first time, by magic angle spinning solid-state NMR (MAS ssNMR). Evaporation selectively removed non-encapsulated solvent molecules leaving stable hexameric capsules encapsulating solvent molecules. After exposure of the powder to solvent vapors, $^{1}H/^{13}C$ heteronuclear correlation MAS ssNMR experiments were used to assign the signals of the external and encapsulated solvent molecules. The formed capsules were stable for months and the process of solvent encapsulation was reversible. According to the ssNMR experiments, the encapsulated solvent molecules occupy different sites and those sites differ in their mobility. The presented approach paves the way for studying guest exchange, guest affinity, and gas storage in hexamers of this type in the solid state.*

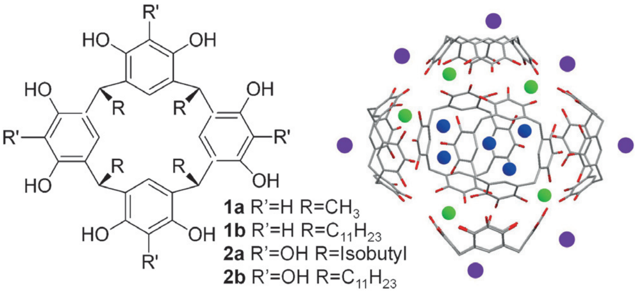

Figure 1. Chemical structures of resorcin[4]arenes (**1**) and pyrogallol[4]arenes (**2**) and a schematic representation of the hexamer of **2b** showing the potential sites occupied by solvent molecules (blue, green, and purple spheres; stick model: C = gray, O = red).

Self-assembled molecular capsules have attracted much interest over the past two decades.[1,2] Their importance stems, inter alia, from their ability to serve as nanoreactors where new chemistry and catalysis may emerge. One intriguing family of self-assembled molecular capsules is resorcin[4]arenes and pyrogallol[4]arenes hexamers (**1** and **2**, Figure 1),[3–7] which have been found to be more abundant than previously thought.[8a,b] Resorcin[4]arene hexamers accommodate a much larger range of guests than pyrogallol[4]arene hexamers do[8] and several examples of catalysis within the resorcin[4]arene hexamers have been reported.[9] To partially overcome the limited range of guests that can be encapsulated in organic solutions of pyrogallol[4]arene hexamers, Purse and co-workers employed the melting approach; however, this approach is applicable only in certain cases.[10] The information gathered to date on the hexameric capsules of systems **1** and **2** was obtained in the solid-state by X-ray crystallography[11] or in solution by NMR, diffusion NMR,[12] and small-angle neutron scattering.[13] Schalley and co-workers also studied these hexameric capsules in the gas phase.[14] However, these spectroscopic methods afford only limited information on the encapsulated molecules. Solid-state NMR has been used to study macromolecules and supramolecular systems,[15] but magic angle spinning solid-state NMR (MAS ssNMR) has been used only once to study dimeric capsules[15c] and never to study hexameric capsules. MAS ssNMR experiments yield detailed information on the structure and the dynamics of systems that are not amenable to crystallization. In X-ray studies of pyrogallol[4]arene hexamers[4,11] limited information, if any, was obtained on the encapsulated guest molecules. Therefore in the present study we used MAS ssNMR to study the systems formed by slow evaporation of organic solutions of **2b**, focusing on solvents which showed peculiar ^{1}H NMR resonance signals in solution for the encapsulated solvent molecules.[16]

Figures 2A and 2B show the ^{1}H and extracts of the ^{13}C cross-polarization MAS (CPMAS) ssNMR spectra of the system obtained by evaporation of the CHCl$_3$ solution of **2b**. The signals assigned to the encapsulated CHCl$_3$ molecules resonate at about $\delta = 5.0$ ppm and just below 80 ppm in the proton and carbon NMR spectra, respectively. Figures 2C and 2D show data on this sample after a short exposure to CHCl$_3$ vapors. The shifts of the additional signals detected in the ^{1}H and ^{13}C NMR spectra are similar to shifts detected in solution[16] and therefore these additional signals were attributed to solvent molecules that reside outside the capsules. To further corroborate the assignments of the solvent signals, we performed ^{1}H/^{13}C heteronuclear correlation (HETCOR) NMR experiments (Figure 2G,H). Based on the proton chemical shifts of the solvent molecules, which were similar to those observed in solution,[16] we assigned also the ^{13}C NMR signals of the encapsulated and non-encapsulated solvent molecules.

Glutaric acid **3**, known to have high affinity for the cavity of **1b**,[8a] replaced in solution the encapsulated chloroform

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[*] Dr. L. Avram, Dr. A. Goldbourt, Prof. Dr. Y. Cohen
School of Chemistry
The Raymond and Beverly Sackler Faculty of Exact Sciences
Tel Aviv University, Ramat Aviv, Tel Aviv, 69978 (Israel)
E-mail: avramli@gmail.com
amirgo@post.tau.ac.il
ycohen@post.tau.ac.il

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201506683.

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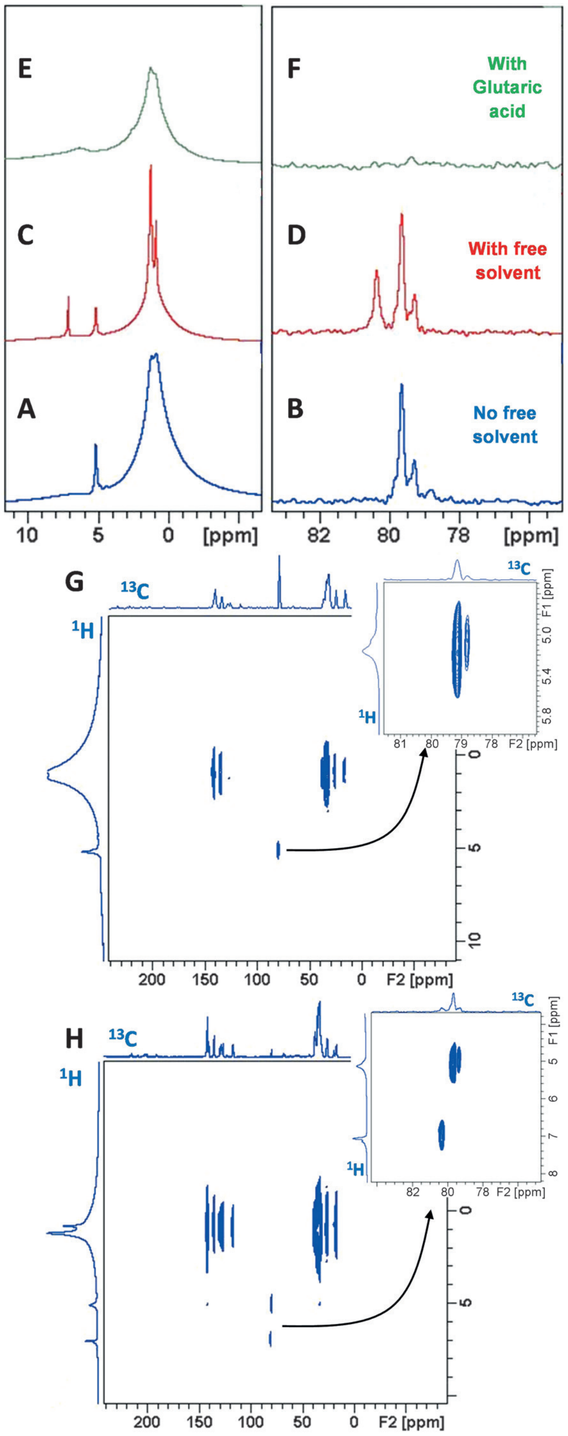

Figure 2. MAS ssNMR spectra of the powder of **2b** obtained by evaporation of the $CHCl_3$ solution (A–D, G, H) or after evaporation of a $CHCl_3$ solution of **2b** containing glutaric acid (E, F). A, C, E) ^{1}H NMR spectra. B, D, F) Regions of ^{13}C CPMAS spectra. G, H) The ^{1}H/^{13}C HETCOR spectra of the powders of **2b** before (G) and after (H) exposure to $CHCl_3$ vapors.

molecules in the hexamers of **2b** (see the Supporting Information, Figure S1). Figures 2E and 2F show spectra of the pyrogallol[4]arene powder obtained when the $CHCl_3$ solution of **2b** containing an excess of glutaric acid (and shown in Figure S1D) was evaporated. No signals attributable to encapsulated chloroform solvent molecules were found. The CPMAS spectral features remained similar to those of the hexamers with other guests and an additional small carbonyl signal could be detected shifted to a higher field. All of these results suggest that the glutaric acid molecules replaced all of the molecules of $CHCl_3$ within the capsules, as found in solution. The lack of signals in the INEPT NMR spectrum seems to suggest that the encapsulated glutaric acid molecules are relatively rigid, effectively filling the capsule cavity. Similar spectra of hexamers containing only $CHCl_3$ molecules showed intense INEPT signals, suggesting high mobility for the encapsulated chloroform molecules (Figure S2).

Very recently we found that the hexamer of **2b** is also formed in a CH_3I solution.[16b] Therefore, we performed MAS ssNMR of powders obtained by slow evaporation of the CH_3I solution of **2b**, before and after a short exposure to CH_3I vapors, in order to verify that powders of **2b** preserve the hexameric capsular structure in the presence of this solvent (Figure 3; Figure S3). The spectra before exposure to CH_3I vapors show the typical encapsulated ^{1}H-CH_3I signal at $\delta \approx 0$ ppm and several ^{13}C NMR signals around -20 ppm, characteristic of carbons attached to iodine atoms and reflecting several different environments for the encapsulated solvent molecules. After exposure to CH_3I vapor, an additional signal was detected (Figure 3B, D), and there were some changes in the linewidth of signals within the ^{1}H NMR spectrum. The ^{1}H NMR signals were clearly narrower (compare Figure 3A and 3B), as was also found for other solvents.

To further study the various methyl iodide signals and to assign and verify the distinction between encapsulated and non-encapsulated species, we performed a series of ^{1}H/^{13}C HETCOR experiments (Figure 3G; Figure S4). The data indicate that the CH_3I molecules occupy several different sites within the cavity of the capsule and that exposure to CH_3I vapors restored the population of external CH_3I molecules (resonating at $\delta_{1H} = 2.0$ ppm and $\delta_{13C} = -21.5$ ppm). Figures 3E and 3F present part of the ^{13}C CPMAS, one-pulse, and INEPT MAS ssNMR spectra of this system before and after a short exposure to CH_3I vapors (see also Figure S3). The relative signal intensities obtained from the different ^{13}C MAS ssNMR experiments provide an indication of the degree of mobility of the encapsulated solvent molecules since CPMAS experiments detect protonated, rigid ^{13}C species, one-pulse experiments are quantitative, and INEPT experiments more effectively detect mobile species than do CPMAS experiments. For example, by comparing the CPMAS and the INEPT spectra (Figure 3E), it is clear that the INEPT intensities of the resonance signals at low field decreased more than other signals, indicating that these signals correspond to more rigid encapsulated CH_3I molecules. A more detailed and quantitative description of the motion will require a different experimental approach for example, ^{2}H line-shape analysis of static ssNMR experiments.[17] We also compared the signal intensities in experiments performed on the sample after exposure to CH_3I solvent vapor (Figure 3F). The intensities of the signals attributed to free solvent molecules were relatively higher in the INEPT spectrum than in the one-pulse and CPMAS

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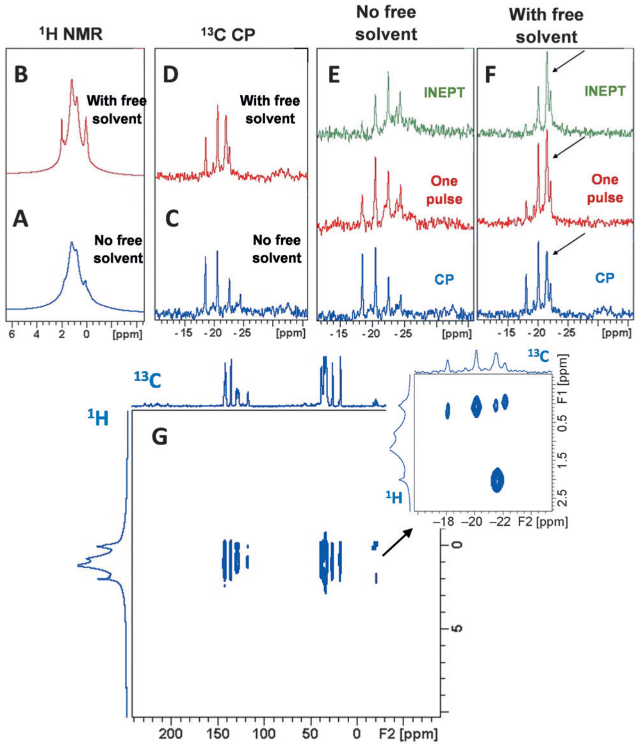

Figure 3. MAS ssNMR spectra of the **2b** powder obtained by evaporation of the CH_3I solution. A, B) ^1H NMR spectra and C, D) regions of ^{13}C CPMAS spectra are shown before (A, C) and after (B, D) exposure to CH_3I vapors. E, F) Regions of the ^{13}C CPMAS, one-pulse, and INEPT spectra before (E) and after (F) exposure of the powder to CH_3I vapors. G) The $^1H/^{13}C$ HETCOR spectrum of the powder of **2b** after exposure to CH_3I vapors. Arrows indicate the non-encapsulated solvent signal, which is well resolved in the ^1H NMR spectrum and appears at about $\delta = 2.0$ ppm in the 2D spectrum.

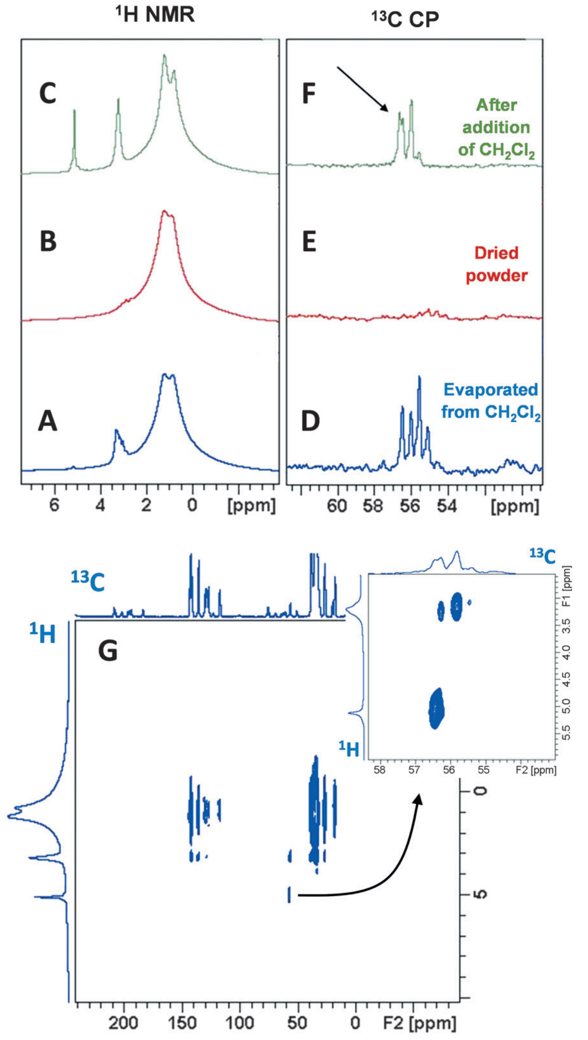

Figure 4. MAS ssNMR spectra of the **2b** powder obtained by evaporation of the CH_2Cl_2 solution. A–C) ^1H spectra. D–F) Regions of the ^{13}C CPMAS spectra. The spectra were recorded A, D) following gentle evaporation, B, E) after evaporation under higher vacuum, and C, F) after exposure of the samples shown in (B) and (E) to CH_2Cl_2 vapors. In (F), the arrow indicates the signal for non-encapsulated solvent. G) The $^1H/^{13}C$ HETCOR MAS ssNMR spectrum of the powder of **2b** after exposure to CH_2Cl_2 vapors.

spectra indicating that this signal represents, as expected, the least rigid molecules in the self-assembled systems. We also tested the stability of the hexamers formed from CH_3I solution by analysis of the powder after fifteen months at room temperature. Only minor changes in the spectra were detected, demonstrating the high stability of such powdered hexameric capsules (Figure S5).

The ^1H and ^{13}C ssNMR spectra of the powder of **2b** obtained from slow and gentle evaporation of a CH_2Cl_2 solution, a highly volatile solvent, are shown in Figure 4A and 4D, respectively. The proton and carbon signals at about $\delta = 3.0–3.5$ ppm and 55–57 ppm, respectively, are attributed to encapsulated CH_2Cl_2 molecules occupying different sites. Interestingly, when the sample was evaporated to dryness, these peaks disappeared nearly completely (Figure 4B, E). We assumed that this indicated collapse of the capsules, since such large empty capsules would presumably be unstable.[18] However, comparisons of the ^{13}C ssNMR spectra presented in Figure S6 and Figure S8 do not corroborate this conclusion. The ^{13}C NMR spectra of the system obtained after extended evaporation of the CH_2Cl_2 differed from the spectrum of the system obtained by evaporation of the acetone solution of **2b** in which **2b** is known to be monomeric.[2c] Therefore, it is more likely that after extended drying the capsules undergo a structural rearrangement rather than complete disaggregation. After exposure of the dried powder to CH_2Cl_2 vapors, signals attributable to both free and encapsulated solvent molecules were detected in the ^1H and ^{13}C spectra (Figure 4C, 4F; Figures S6). This indicated that the encapsulation process is reversible; however, what form the capsules take after severe dehydration is not clear.

The assignment of the solvent signals was again corroborated by employing $^1H/^{13}C$ HETCOR experiments. The 2D HETCOR spectra shown in Figure 4G and Figure S9 unequivocally allow identification of the CH_2Cl_2 molecules that reside outside the capsules ($\delta_{1H} \approx 5$ ppm, $\delta_{13C} \approx 56.5$ ppm) and those that are encapsulated ($\delta_{1H} \approx 3.2$ ppm, $\delta_{13C} \approx 56$ ppm). Multiple sites are detected for the encapsulated CH_2Cl_2 molecules, as was in the case when CH_3I was the solvent and in contrast to the findings in the case of $CHCl_3$, where one major signal is detected for the encapsulated

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molecules. These results are in accordance with what was recently reported for the same capsules in solution.[16b] As in the case of CH_3I, here also the sites show different relative mobilities (Figure S7). However, current experiments are not sufficient to compare the mobilities between different guests or to relate them to particular sites within the hexamer.

In summary, we have demonstrated that evaporation of different organic solutions of the lipophilic pyrogallol[4]arene **2b** provided powders of the hexameric capsules that encapsulate solvent molecules. The encapsulated solvent molecules clearly occupied multiple sites when **2b** was evaporated from CH_3I and CH_2Cl_2, an observation that has also been reported from solution NMR studies. It is highly likely that these sites are located within a single hexamer since according to prior solution NMR studies, the effect of different hexamer packing on chemical shifts is very small, smaller than the ssNMR linewidths,[16] and therefore indistinguishable in the solid state. With the aid of $^1H/^{13}C$ heteronuclear correlation MAS ssNMR experiments, we unequivocally assigned the ^1H and ^{13}C resonance signals for the external and encapsulated solvent molecules. The formed capsules were stable for months, and the process of solvent encapsulation was reversible by exposure of the powder to the solvent vapor. Even when apparently extended evaporation of the solvent took place (in the case of CH_2Cl_2), the ssNMR spectroscopic results did not support the complete collapse of the hexameric structure and re-exposure of the powder to solvent vapor reformed the solvated hexameric capsules. Using different ^{13}C ssNMR experiments, we also showed that for each type of solvent the different encapsulation sites have a range of mobilities on the NMR timescale and future experiments will allow us to quantify and describe these motions. The methods presented here pave the way for future studies of such capsules evaluating guest exchange, guest affinity, and gas storage in the solid state. Such studies are currently underway in our laboratory.

Acknowledgements

Y.C. wishes to thank the Israel Science Foundation (ISF; Grant Number 804/13) for financial support.

Keywords: hexameric capsules · host–guest systems · magic angle spinning · NMR spectroscopy · self-assembly

How to cite: *Angew. Chem. Int. Ed.* **2016**, *55*, 904–907
Angew. Chem. **2016**, *128*, 916–919

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Received: July 20, 2015
Revised: October 6, 2015
Published online: December 7, 2015