^{1}H NMR Investigations of Host–Guest Complexation between a Macrocyclic Host of the Cyclophane Type and Aromatic Guests in Aqueous Solution

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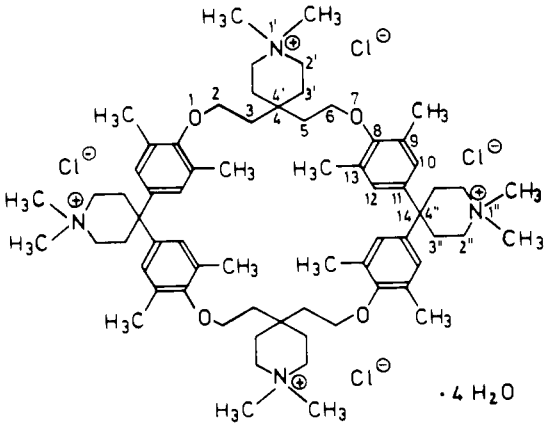
Abstract: The ^{1}H NMR spectra of D_2O solutions of host–guest complexes of the macrocyclic host **1** with various aromatic guests have been recorded below the critical micelle concentration (cmc) of **1**. Ample evidence for exclusive 1:1 host–guest complexation in aqueous solution was obtained. At 303 K signals at the average of the chemical shifts of free and complexed host and free and complexed guest appear in all except one solution. Strong changes of the chemical shifts of specific protons of host and guest upon complexation were observed, indicating the formation of highly structured complexes. For many host–guest complexes one specially favored geometry could be clearly assigned on the basis of the ^{1}H NMR data. The exclusivity of water in providing strong host–guest binding between **1** and neutral arenes could be demonstrated. The ^{1}H NMR spectra reflect a strong influence of neutral polar substituents attached to the aromatic guests on the structure of host–guest complexes of **1** in aqueous solution. The most highly structured complexes are formed with aromatic guests bearing anionic (sulfonate) residues. Complexes of the latter type make use of attractive forces of both apolar and electrostatic nature.

In the preceding papers[1,2] we described the synthesis and properties of **1**, a new water-soluble macrocyclic host of the cyclophane type. **1** was found to be a powerful host in aqueous solution for neutral arenes as well as for arenes bearing anionic (sulfonate) residues. In order to come to a better understanding of the complexation behavior of **1**, extended ^{1}H NMR studies of host–guest complexation with aromatic guests were undertaken in aqueous solution below the critical micelle concentration (cmc) of **1** (7.5×10^{-3} mol·L^{-1}). Host **1** is especially suitable for these investigations since its aromatic protons appear as a singlet. Accordingly there is a large open "window" in the aromatic region of the ^{1}H NMR spectra for the monitoring of the signals of aromatic guests.



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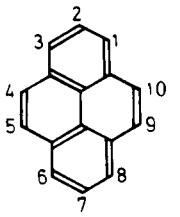
Detailed information about the geometrical relationship between host and guest in the complexes could be expected from the changes of the chemical shifts of the protons of host and guest upon complexation. The chemical shifts of the 10 different groups of protons of host **1** should be influenced at various degree by the diatropy of aromatic guests incorporated into the cavity of **1**. A change of the chemical shift upon complexation should be observed for those protons of the guest which in the complex are oriented close to the diphenylmethane units of **1**.

Experimental Section

The preparation of host **1** and the purification of most of the guests have been previously reported.[1,2] 1- and 2-naphthol (Ega) were recrystallized from water. Solutions of host–guest complexes with arenes which have a low solubility in water were prepared by solid-liquid extraction as previously described.[2] The concentration of the host in most of these experiments was 5.5×10^{-3} mol·L^{-1}. All ^{1}H NMR spectra were recorded on a Bruker HX-360 MHz spectrometer at 303 K if not stated otherwise. All δ values of spectra recorded in D_2O refer to sodium 2,2,3,3-tetradeuterio-3-(trimethylsilyl)propionate (TSP) as external standard in D_2O which is in a capillary tube placed inside the NMR tube. In temperature-dependent NMR experiments, the temperature is measured with ethylene glycol above 310 K and with methanol below 310 K using published equations.[3]

Results and Discussion

A. ^{1}H NMR Studies of Aqueous Solutions of Host–Guest Complexes of 1 with Unsubstituted or Methyl-Substituted Arenes. The ^{1}H NMR studies of host–guest complexation of **1** with pyrene (**2**) will be presented first since this complexation has been the most thoroughly investigated. With a 5.5×10^{-3} M solution of **1** in D_2O by solid-liquid extraction a solution of host–guest complex with a concentration of pyrene of 2.8×10^{-3} mol·L^{-1} was prepared.[4] As the maximum solubility of pyrene in water is only 8×10^{-7} mol·L^{-1}, virtually all pyrene and about 50% of the host in the solution are complexed.[2] Figure 1 shows the spectra of pure host in D_2O and of pure pyrene in methanol-d_4 as compared to the spectrum of the D_2O solution of the host–guest complex.



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At 303 K significant changes of the chemical shifts can be observed for the protons of both host and guest in the solution

(1) Diederich, F.; Dick, K. *Angew. Chem.* **1983**, *95*, 730; *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 715; *Angew. Chem. Suppl.* **1983**, 957–972.

(2) Diederich, F.; Dick, K. *J. Am. Chem. Soc.*, preceding paper in this issue.

(3) Gordon, A. J.; Ford, R. A. "The Chemists Companion"; Wiley: New York, 1972; p 303.

(4) The concentrations of pyrene determined from the integration of the ^{1}H NMR spectra or by electronic absorption spectroscopy[2] varied between 2.7×10^{-3} and 2.9×10^{-3} mol·L^{-1} from extraction to extraction when the concentration of host in the aqueous solution was 5.5×10^{-3} mol·L^{-1}. The small differences in the measured concentrations of extracted pyrene are apparently due to the errors of the two analytical methods applied for their determination rather than to differences in the efficiency of the solid-liquid extraction: the chemical shifts of the host and guest were found identical within 0.01 ppm in the spectra of solutions of complexes resulting from six independent extraction experiments.

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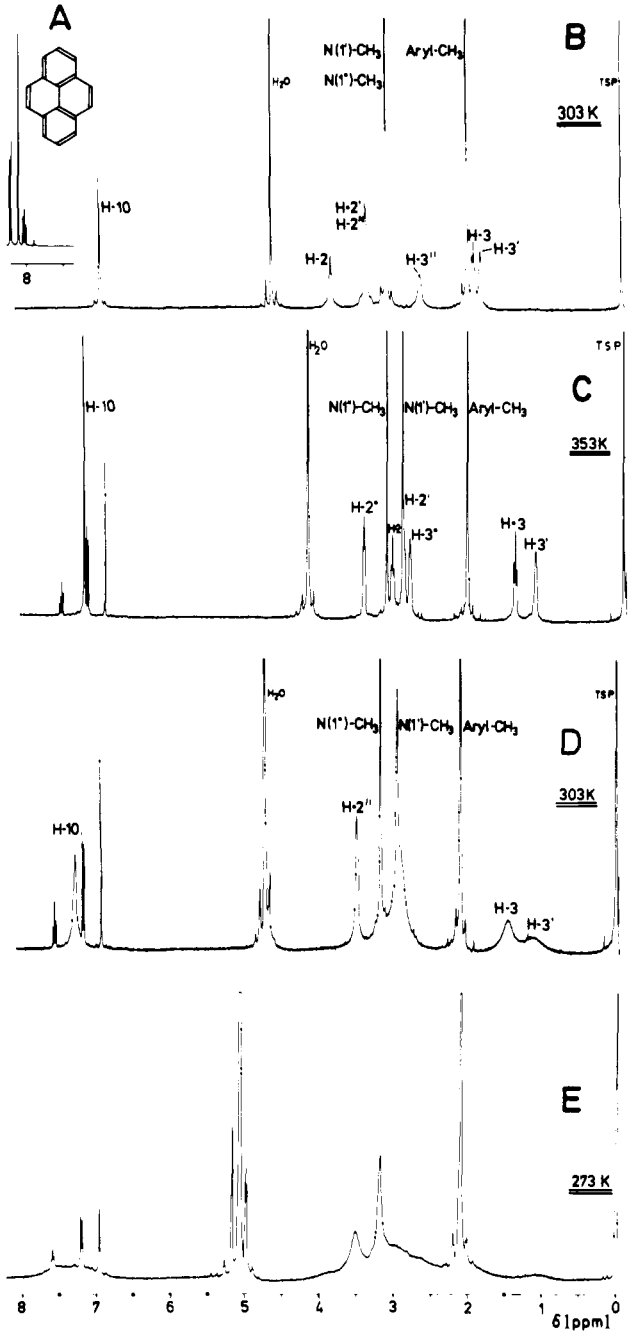
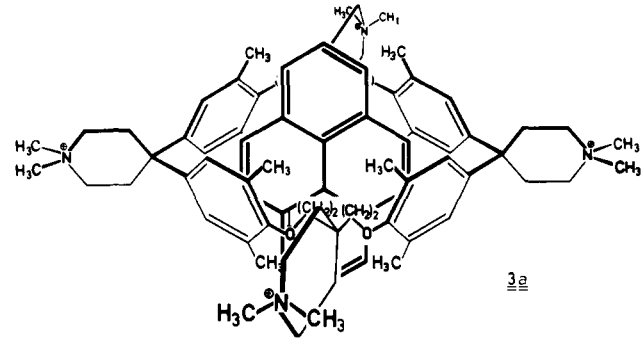
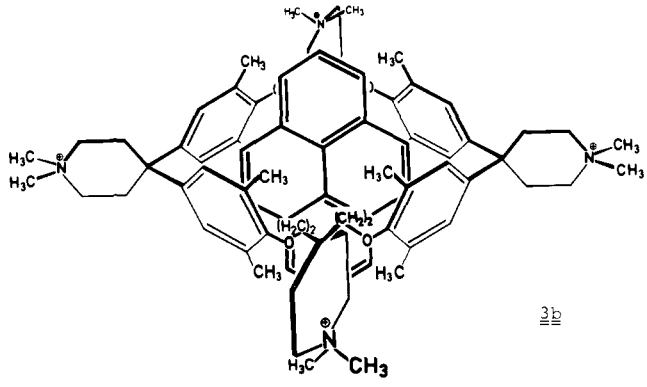


Figure 1. 360-MHz ^{1}H NMR spectra of a 2.8×10^{-3} M solution of pyrene in methanol-d_4 at 303 K (A), δ against TSP_{ext} in methanol-d_4;[1] of a 5.5×10^{-3} M solution of **1** in D_2O at 303 K (B), δ against TSP_{ext} in D_2O and of a solution of the **1**–pyrene complex in D_2O (TSP_{ext}; $H_{tot} = 5.5 \times 10^{-3}$ mol·L^{-1}, $G_{tot} = 2.8 \times 10^{-3}$ mol·L^{-1}) at 353 K (C), 303 K (D), and 273 K (E).

of the complex as compared to the solutions of the pure components. They can be best explained by the following highly structured and highly favored geometry of complex. The benzene rings of **1** are oriented perpendicular to the mean molecular plane of the host. Pyrene is included axially in the cavity of **1**. The long C_2-axis of pyrene through C(2),C(7) is in the direction of the C_2-axis of **1** through the cavity perpendicular to the mean molecular plane of the host. As can be observed at CPK molecular models, a pyrene molecule fits completely into the cavity of **1** only if its molecular plane is located within the plane through the spiro carbon atoms of the two diphenylmethane units perpendicular to the mean molecular plane of the host. Pyrene can only rotate to a limited extend in this plane since its extension between H-2 and H-7 is larger than the extension of the cavity between the spiro atoms of the two diphenylmethane units. The narrowness of the cavity between the aliphatic bridges allows only a limited rotation of pyrene located as described in the cavity around its C_2-axis through C(2),(C7). The discussed position of pyrene in the cavity of **1** is shown by **3**.



3a



3b

In accord with the proposed geometry of the complex, H-2,7 of pyrene are oriented out of the cavity and therefore their triplet exhibits the weakest change of chemical shift upon complexation. The two other groups of protons of pyrene H-1,3,6,8 and H-4,5,9,10 are directed toward the diphenylmethane units and are strongly shifted upfield by $\Delta\delta = +1.02$ and $+1.25$, respectively[5] (Table I).

The changes of the chemical shifts of the host protons also support the proposed geometry of the complex. At 303 K the signals of the host appear at the average of the chemical shifts of free (≈50%) and complexed (≈50%) host. The protons of the host which are located in the plane defined by the molecular plane of complexed pyrene, e.g., the aromatic protons H-10, are shifted downfield. All protons in the direction perpendicular to the plane of pyrene like H-2, H-3, and H-3′ are shifted upfield (Table I).

Unexpected was the significant upfield shift of the protons of **1** which are located close to the quaternary nitrogens of the piperidinium rings fixed in the aliphatic bridges. Upon complexation N(1′)-CH_3 is shifted upfield by $\Delta\delta = +0.20$ and H-2′ by $\Delta\delta \approx +0.49$. If the two piperidinium rings fixed in the aliphatic bridges are located within the mean molecular plane of the host **3a**, H-2′ and N(1′)–CH_3 cannot be so significantly influenced by the diatropy of the enclosed pyrene. The distance between these protons of **1** and the guest would be too large. These upfield shifts can be best explained by considering the conformational flexibility of the aliphatic C_5 bridges of **1** in the complex. It allows the two piperidinium rings attached to these bridges to turn out of the mean plane of the host and to approach the enclosed pyrene. The piperidinium rings can approach pyrene on one or on both sides (**3b**) of the cavity. Examinations of CPK molecular models indicate that the two piperidinium rings can take a position in which their least planes are about perpendicular to the mean molecular plane of **1**. According to the model examinations, the cavity is then significantly deepened between the aliphatic bridges. Pyrene is held more rigidly inside the cavity of **1** and is more efficiently

(5) The + signal refers to a shift to higher magnetic field. $\Delta\delta = -$ (δ of host or guest in the solution of the host–guest complex – δ of pure host or pure guest in solution).

Table I. 360-MHz ^1H NMR Spectra of a 5.5×10^{-3} M Solution of Host **1**, of a 2.8×10^{-3} M Solution of Pyrene, and of a Solution of the **1**-Pyrene Complex ($H_{tot} = 5.5 \times 10^{-3}$ mol·L^{-1}; $G_{tot} = 2.8 \times 10^{-3}$ mol·L^{-1})[a]

		δ								
host **1**[b]	temp, K	H-3′	H-3	aryl-CH_3	H-3″	N(1′)–CH_3	N(1″)–CH_3	H-2′	H-2″	H-2	H-10
1 in D_2O	303	1.90 (m)	1.99 (t, J = 7 Hz)	2.08 (s)	2.70 (m)	3.16 (s)			3.43 (m)	3.91 (t, J = 7 Hz)	6.99 (s)
	353	1.87	1.96	2.08	2.68	3.15			3.41	3.88	6.95
1–pyrene in D_2O	303	1.13 (m, br)	1.47 (m, br)	2.10 (s)	*c*	2.96 (s)	3.18 (s)	*c*	3.50 (m)	*c*	7.30 (s)
	353[d]	1.17 (m)	1.45 (t, J = 7.5 Hz)	2.09 (s)	2.86 (m)	2.96 (s)	3.17 (s)	2.94 (m)	3.48 (m)	3.10 (t, J = 7.5 Hz)	7.23 (s)
1 in methanol-d_4	303	2.01	2.15	2.17	2.69	3.21	3.18	3.49	3.41	3.89	6.91
1–pyrene in methanol-d_4	303	1.90	1.92	2.16	2.77	3.17	3.20	3.41	3.43	3.57	7.02
1 in Me_2SO-d_6	303	1.91	2.09	2.19	2.70	3.22	3.18	3.36		3.81	7.03
1–pyrene in Me_2SO-d_6	303	1.90	2.08	2.19	2.69	3.22	3.18	3.36		3.80	7.03

		δ		
pyrene	temp, K	H-1	H-2	H-4
pyrene in methanol-d_4	303	8.21 (d, J = 7.6 Hz)	8.02 (t, J = 7.6 Hz)	8.10 (s)
1–pyrene in D_2O	303	7.19 (d, J = 7.5 Hz)	7.58 (t, J = 7.5 Hz)	6.95 (s)
	353	7.19 (d, J = 7.5 Hz)	7.54 (t, J = 7.5 Hz)	6.95 (s)
1–pyrene in methanol-d_4	303	7.91	7.85	7.79
pyrene in Me_2SO-d_6	303	8.38	8.16	8.27
1–pyrene in Me_2SO-d_6	303	8.36	8.14	8.25

[a] In D_2O (TSP_{ext} in D_2O), in methanol-d_4 (TSP_{ext} in methanol-d_4), and in Me_2SO-d_6 (TSP_{ext} in Me_2SO-d_6). [b] The centers of the always symmetrical multiplets of **1** are given for better comparison. [c] These signals are very broad and collapse with other signals between 2.6 and 3.1 ppm. [d] All assignments in D_2O at 353 K are supported by double-resonance experiments.

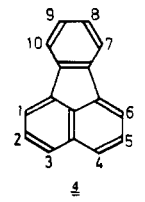
shielded from the water molecules. The observed upfield shifts upon complexation of H-2′ and N(1′)–CH_3 suggest that the conformations of **1** like **3b** with the piperidinium rings enveloping the enclosed guest represent a significant contribution to the actual geometry of host **1** in the aqueous solution of the **1**–pyrene complex.

In contrast to the highly resolved signals of the complexed pyrene over the whole concentration range measured (353–273 K), the signals of the host are broadened below 333 K (Figure 1). The reason for this broadening at lower temperatures is that the exchange of pyrene with host molecules which are present in excess slows on the 360-MHz NMR time scale. The coalescence temperature of the aromatic protons H-10 of the host is 273 K (Figure 1). As expected from the high association constant of the **1**–pyrene complex ($K_a = 1.1 \times 10^6$ L·mol^{-1})[2] the positions of the signals of host and guest in the solution of the complex are almost identical over the whole temperature range.

A ^1H NMR spectrum was recorded at 303 K of a solution of the **1**–pyrene complex with concentrations that were $^1/_{40}$ the size of those given in Table I ($H_{tot} = 1.4 \times 10^{-4}$ mol·L^{-1}, $G_{tot} = 7.0 \times 10^{-5}$ mol·L^{-1}, and $HG = 6.9 \times 10^{-5}$ mol·L^{-1}). The chemical shifts of the protons of both host and guest in the dilute solution were identical with those in the more concentrated solution. In addition to the optical spectra[2] this was further evidence that the same **1**–pyrene complex is forming at all concentrations below the cmc of **1**. The line broadening at 303 K of the signals of the host was more important in the spectrum at lower concentrations than in the spectrum at higher ones.

As expected for hydrophobic interactions being the major driving force for complexation, we found that strong host–guest complexation between **1** and pyrene occurs only in aqueous solution. In the ^1H NMR spectrum of a methanol-d_4 solution with concentrations of **1** and pyrene as in D_2O all signals of host and guest are shifted in the same up- or donwfield direction as in D_2O (Table I). This supports the formation of a complex of similar structure in both solvents. The considerably smaller extend of the up- and downfield shifts, however, indicates a significantly weaker complexation. H-4 of pyrene for example is shifted upfield by $\Delta\delta = +0.31$ in methanol-d_4 as compared to an upfield shift of $\Delta\delta = +1.25$ in D_2O. The association constant in methanol-d_4 can be estimated under the assumption that the upfield shift of H-4 in D_2O, where all pyrene is complexed, is also the upfield shift for saturation binding in methanol-d_4. The estimated association constant of $K_a \approx 70$ L·mol^{-1} for the **1**–pyrene complex in methanol indicates that complexation in water is about 15 000 times stronger. In Me_2SO-d_6 with the same concentration of **1** and pyrene, no changes of the chemical shifts at all were observed for the protons of both host and guest. No or only very weak complexation occurs in this solvent.

The ^1H NMR data of D_2O solutions of complexes of **1** with other aromatic hydrocarbons, prepared by solid-liquid extraction,[2] are shown in Table II. For all these complexes at 303 K, signals at the average of the chemical shifts of free and complexed host and free and complexed guest were obtained. The spectrum at 303 K of the D_2O solution of the **1**–fluoranthene complex ($H_{tot} = 5.5 \times 10^{-3}$ mol·L^{-1}, $G_{tot} = HG = 3.5 \times 10^{-3}$ mol·L^{-1}) shows up- and downfield shifts of the protons of host and guest comparable to those of the solution of the **1**–pyrene complex. Again, a highly structured geometry of complex has to be admitted. The molecular plane of fluoranthene (**4**) is located in the cavity of **1** in the same plane like pyrene (**5a** and **5b**). All protons of **1** in this plane are shifted downfield; all protons of **1** in the direction perpendicular to this plane show large upfield shifts. The considerable upfield shifts upon complexation of H-2′ and N(1′)–CH_3 of **1** demonstrates again that the piperidinium rings fixed in the aliphatic bridges are approaching and enveloping the enclosed guest. The signals of H-1,2,3,4,5,6 of **4** in the solution of the complex are easily assigned by their coupling pattern. The assignment of the signals to H-7,10 and H-8,9 is a tentative one based on CPK molecular model examinations (Table **II**). The upfield shifts upon complexation of H-1,6 and H-7,10 can be easily explained by an axial inclusion as indicated by **5a** (only the



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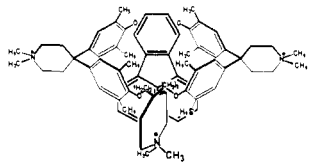
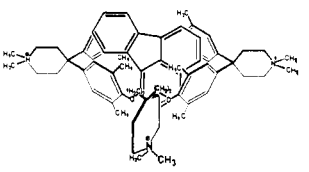


5a



5b

conformation of **1** is outlined where the two piperidinium rings approach the guest on one side of the cavity). The significant upfield shifts of H-3,4, however, suggest that conformations like **5b** contribute to a large extent to the actual geometry of the complex. The extensions of **4** between C(3) and C(8) or C(4) and C(9) do not allow a complete rotation of **4** in the plane in which it is located in the cavity of **1**. Below 330 K, line broadening of the signals of the host appears, which is very similar to the broadening of the signals of **1** in the solution of the **1**–pyrene complex.

For naphthalene, a smaller sized guest than pyrene or fluoranthene, significantly more freedom of motion could be expected in the complex with **1**. CPK molecular models indicate that naphthalene, if located in the same plane in the cavity as pyrene and fluoranthene, can take all orientations in this plane either by rotation within this plane or by decomplexation–complexation. Furthermore, the models indicate that axially included naphthalene (Figure 3) could possibly rotate around its C_2-axis which intersects the C(2)–C(3) and the C(6)–C(7) bonds.

The ^{1}H NMR data of the D_2O solution with $H_{1o1} = 5.5 \times 10^{-3}$ mol·L^{-1}, $G_{1o1} = 4.1 \times 10^{-3}$ mol·L^{-1}, and $HG = 3.9 \times 10^{-3}$ mol·L^{-1} exhibited again the distinct pattern of up- and downfield shifts of the signals of the host encountered for the complexes of **1** with the larger guests **2** and **4**. Naphthalene too seems to be located exclusively in the plane through the spiro carbon atoms of the diphenyl methane units perpendicular to the mean molecular plane of **1**. We shall name from now on this plane the aromatic guest plane of **1** since in all complexes of **1** with aromatic guests that we have studied, the aromatic guest is located in this plane. The significant upfield shifts upon complexation of both H-1[6] and H-2 indicate that all positions of naphthalene in this plane are possible. The larger upfield shift of H-1 of the guest suggests a higher contribution of axial-type than of equatorial-type inclusion (Figure 3) to the actual geometry of the complex in solution. H-2′ and N(1′)–CH_3 of the host are again shifted upfield upon complexation although to a smaller extend than in the solutions of complexed **2** and **4**.

All signals of **1** and naphthalene in the solution of the complex are highly resolved at 303 K with the exception of a very broad signal for H-3″ of **1**. This specific broadening of the signal of H-3″ was observed at 303 K in all solutions of complexes in which a high percentage of host is complexed. In the solutions of the **1**–pyrene and **1**–fluoranthene complexes, this specific broadening is superposed by the broadening of all signals of the host due to the slowing of the exchange of guest with host. The broadening of the signal of H-3″ indicates that the chair–chair inversion of the spiro piperidinium rings of the diphenylmethane units of **1** slows on the NMR time scale. Such a broadening of the signal of H-3″ appears only at 273 K in an aqueous solution of pure **1**.[7]

The appearance of the line broadening at higher temperatures in the solutions of complexes could result from a larger difference $\Delta\nu$ (Hz) of the signals of H-3″$_{ax}$ and H-3″$_{eq}$ in these solutions. It cannot be excluded, however, that the broadening at higher temperature indicates a higher activation barrier for the chair inversion in the solutions of complexes than in the solution of pure **1**.

Examinations of CPK molecular models suggested that 1,5-dimethylnaphthalene enclosed in the cavity of **1** should be able to take all orientations in the aromatic guest plane. For 2,6-dimethylnaphthalene, however, with its large extension between the two methyl groups a free rotation in the aromatic guest plane should not be possible. This difference between the two isomeric dimethylnaphthalenes is reflected in the ^{1}H NMR spectra. Table II shows that the upfield shifts of the three groups of aromatic protons of the 1,5-isomer in the solution of the complex ($H_{1o1} = 5.5 \times 10^{-3}$ mol·L^{-1}, $G_{1o1} \approx HG = 1.9 \times 10^{-3}$ mol·L^{-1}) are very similar. The comparable upfield shifts upon complexation of the aromatic protons together with a considerable upfield shift of $\Delta\delta = +0.76$ of the methyl protons of 1,5-dimethylnaphthalene support the formation of a less structured complex. According to the ^{1}H NMR data, a considerably more structured complex is formed by 2,6-dimethylnaphthalene. In the D_2O solution ($H_{1o1} = 5.5 \times 10^{-3}$ mol·L^{-1}, $G_{1o1} \approx HG = 9.8 \times 10^{-4}$ mol·L^{-1}) the methyl protons of the guest show a relatively weak upfield shift. H-1 ($\Delta\delta = +1.39$) and especially H-4 ($\Delta\delta = +1.55$) are shifted upfield to a considerably larger extend than H-3 ($\Delta\delta = +0.98$). This pattern of changes of the chemical shifts upon complexation is typical for a favored pseudoaxial position of a naphthalene derivative in the aromatic guest plane in the cavity of **1** (Figure 3). In a pseudoaxial position, H-4,8 of the naphthalene guest have the closest orientation toward the shielding region of the diphenylmethane units of **1**.

Durene resembles naphthalene with regard to space filling size and shape. According to examinations of CPK molecular models, durene should take all orientations within the aromatic guest plane of **1**. The ^{1}H NMR spectrum of the D_2O solution ($H_{1o1} = 5.5 \times 10^{-3}$ mol·L^{-1}, $G_{1o1} = 3.9 \times 10^{-4}$ mol·L^{-1}, and $HG = 3.4 \times 10^{-4}$ mol·L^{-1}) is in agreement with the model examination. Considerable upfield shifts are obtained for both methyl and aromatic protons. Highly favored axial inclusion would lead to a specific upfield shift of the aromatic protons; highly favored equatorial inclusion would lead to a large upfield shift of specifically the methyl protons. The larger upfield shift of the aromatic protons indicates some preference for an axial orientation of durene in the aromatic guest plane.

The studies of host–guest complexation between **1** and neutral arenes of various size have shown that there exists a specific plane in the cavity of **1** in which are located the molecular planes of suitably sized aromatic guests. As we shall see, not only the neutral arenes but also all aromatic hydrocarbons with polar or ionic substituents which we have studied as guests are located in this specific plane. We have called this plane the aromatic guest plane of **1**. The ^{1}H NMR chemical shifts clearly reflect the location of the aromatic guests in this plane through the spiro carbon atoms of the diphenylmethane units perpendicular to the mean molecular plane of **1**. For the protons of the host in proximity to the enclosed guest a specific pattern of up- and downfield shifts upon complexation is observed. All protons of **1** in the aromatic guest plane are shifted downfield; all protons of the host perpendicular to this plane are shifted upfield. Such a specific orientation of aromatic guests cannot be expected in the host–guest complexes formed by hosts with a cylindrical cavity like the cyclodextrins. The cavity of **1** represents a good model for the hydrophobic pocket located at the substrate binding site of α-chymotrypsin.[8] In this hydrophobic pocket the aromatic side chain of a tyrosine, phenylalanine, or tryptophane residue of the substrate is also located in a specific plane defined by the narrowness of the pocket. The specific location of aromatic guests in the cavity of **1** results

(6) The assignment of the moiety at higher field of the AA′BB′ pattern of naphthalene in the solution of complex to H-1 (Table II) is supported by a series of ^{1}H NMR spectra with various host:guest ratios.

(7) Diederich, F.; Dick, K. *Chem. Ber.*, submitted for publication.
(8) Blow, D. M. *Acc. Chem. Res.* **1976**, *9*, 145.

Table II. 360-MHz ^1H NMR Spectra of Host **1** in D_2O (TSP_{ext} in D_2O), of the Guests in Methanol-d_4 (TSP_{ext} in Methanol-d_4) and of Host and Guest in D_2O Solutions of Host–Guest Complexes Formed by Solid-Liquid Extractions

host **1**[a]	temp, K	δ H-3′	H-3	aryl–CH_3	H-3″	N(1′)–CH_3		N(1″)–CH_3	H-2′		H-2″	H′2	H-10
1 in D_2O	303	1.90	1.99	2.08	2.70		3.16			3.43		3.91	6.99
	353	1.87	1.96	2.08	2.68		3.15			3.41		3.88	6.95
1–fluoranthene(H_{tot} = 5.5 × 10^{-3} mol·L^{-1}; G_{tot} = HG = 3.5 × 10^{-3} mol·L^{-1})[c]	303	1.23	1.41	2.07	*b*	2.99		3.17	*b*		3.50	*b*	7.34
	353[d]	1.30	1.42	2.06	2.89	2.99		3.16	2.97		3.48	3.05	7.26
1–naphthalene (H_{tot} = 5.5 × 10^{-3} mol·L^{-1}; G_{tot} = 4.1 × 10^{-3} mol·L^{-1}; HG = 3.9 × 10^{-3} mol·L^{-1})	303	1.32	1.49	2.12	2.87[e]	3.05		3.16	3.16		3.47	3.11	7.30
1–1,5-dimethylnaphthalene (H_{tot} = 5.5 × 10^{-3} mol·L^{-1}; G_{tot} = HG = 1.9 × 10^{-3} mol·L^{-1})	303	1.57	1.73	2.11	2.81	3.10		3.16	3.27		3.46	3.51	7.15
1–2,6-dimethylnaphthalene (H_{tot} = 5.5 × 10^{-3} mol·L^{-1}; G_{tot} = HG = 9.8 × 10^{-4} mol·L^{-1})	303	1.81	1.89	2.08	2.75	3.15		3.16	3.39		3.45	3.72	7.06
1–durene (H_{tot} = 5.5 × 10^{-3} mol·L^{-1}; G_{tot} = 3.9 × 10^{-4} mol·L^{-1}; HG = 3.4 × 10^{-4} mol·L^{-1})	303	1.86	1.95	2.09	2.72		3.16		3.42		3.43	3.85	7.02

guests	temp, K	δ H-1	H-2	H-3	H-7	H-8
fluoranthene						
in methanol-d_4[f]	303	7.94 (d, J = 6.9 Hz)	7.60 (t, J = 7.5 Hz)	7.81 (d, J = 8.2 Hz)	7.90 (m)	7.34 (m)
in the solution of complex	303	6.57 (d, J = 6.9 Hz)	7.11 (t, J = 7.5 Hz)	6.46 (d, J = 8.1 Hz)	6.91 (m)[g]	7.25 (m)[g]
	353	6.58	7.14	6.61	6.80	7.18
naphthalene						
in methanol-d_4[f]	303	7.72 (m)	7.34 (m)			
in the solution of complex	303	6.56 (m)	6.59 (m)			
1,5-dimethylnaphthalene		CH_3			H-4	
in methanol-d_4[f]	303	2.66 (s)	7.30 (d, J = 6.9 Hz)	7.37 ("t", J = 7.6 Hz)	7.86 (d, J = 8.4 Hz)	
in the solution of complex	303	1.90 (s)	6.21 (d, J = 7.0 Hz)	6.26 ("t", J = 6.7 Hz)	6.14 (d, J = 8 Hz)	
2,6-dimethylnaphthalene		CH_3	H-1		H-4	
in methanol-d_4[f]	303	2.47 (s)	7.55 (s, br)	7.27 (d, J = 8.4 Hz)	7.63 (d, J = 8.4 Hz)	
in the solution of complex	303	2.06 (s)	6.16 (s, br)	6.29 (d, J = 8.2 Hz)	6.08 (d, J = 8.2 Hz)	
durene		CH_3	H_{arom}			
in methanol-d_4[f]	303	2.13 (s)	6.81 (s)			
in the solution of complex	303	1.35 (s)	5.53 (s)			

[a] The centers of the always symmetrical multiplets of **1** are given for better comparison. [b] These signals are very broad and collapse with other signals between 2.6 and 3.1 ppm. [c] H_{tot} and G_{tot} are the total concentrations of host and guest in the solution of complex; HG is the concentration of the complex in solution. [d] All assignments at 353 K are supported by double-resonance experiments. [e] This signal is strongly broadened. [f] The concentration of the guests in methanol-d_4 was always about 3 × 10^{-3} mol·L^{-1}. [g] Tentative assignments on the basis of CPK molecular models.

certainly in large parts from the specific geometry of the two diphenylmethane units as aromatic spacers in **1**. The location of aromatic guests in a similar specific plane has also been found by Koga et al. for 1:1 host–guest complexes of a protonated 1,6,20,25-tetraaza[6.1.6.1]paracyclophane as host with 2,7-dihydroxynaphthalene in acidic aqueous solution (^1H NMR)[9] and with durene in the solid state (X-ray analysis).[10] This host also has two diphenylmethane units as aromatic cavity walls. Another reason for the specific location of aromatic guests in the cavity of **1** could be the possibility of a close enveloping of the guest located in the aromatic guest plane by the piperidinium rings attached to the aliphatic bridges of **1**.

B. ^1H NMR Studies of Aqueous Solutions of Host–Guest Complexes of 1 with Naphthols and Dihydroxynaphthalenes. The next step in our ^1H NMR studies was the investigation of complexes formed between **1** and naphthalenes bearing neutral polar substituents. 1- and 2-Naphthol as well as several isomeric dihydroxynaphthalenes were chosen as guests for these studies. With these guests the formation of highly structured complexes should result not only from the space-filling capacity of the substituents as observed for the complex with 2,6-dimethylnaphthalene as guest but also from the polarity of the substituents. Polar groups should be preferably oriented outside of the cavity. An equimolar solution of host and guest (H_{tot} = G_{tot} = 4 × 10^{-3} mol·L^{-1}) in D_2O was used in all experiments. From the known association constants of complexes with dihydroxynaphthalenes ($K_a \approx 10^4$ mol·L^{-1}; 292.5 K)[2] it can be estimated that in all seven considered solutions about 85% of host and guest are present in complexed form. From the

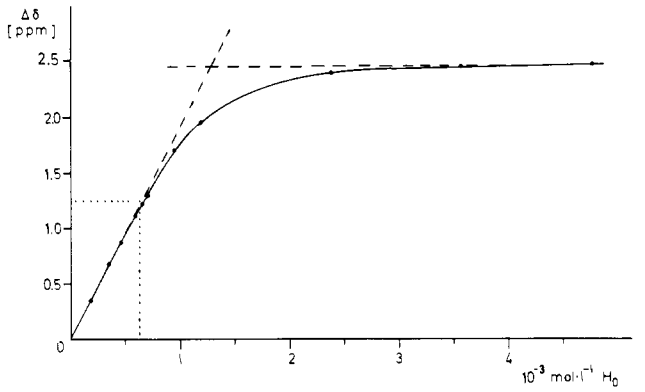


Figure 2. ^1H NMR titration curve showing the change of the chemical shift of H-4 of 2,6-dihydroxynaphthalene as a function of the total concentration of host **1** in D_2O; T = 303 K, G_{tot} = 1.15 × 10^{-3} mol·L^{-1}.

^1H NMR data of Table III, several structural features common to the seven host–guest complexes are apparent. The guest is always located in the aromatic guest plane of **1**. For all complexes a certain approach of the piperidinium rings fixed in the aliphatic bridges of **1** toward the enclosed guest has to be admitted from the upfield shifts of H-2′ and N(1′)–CH_3 of **1** upon complexation. Signals at the average of the chemical shifts of free and complexed host and free and complexed guest are obtained in all spectra. With the exception of the signal of H-3″ of **1** all signals of host and guest are highly resolved at 303 K.

A 1:1 host–guest complexation of **1** with dihydroxynaphthalenes was exemplarily demonstrated by ^1H NMR titration curves for the complexes of 1,5- and 2,6-dihydroxynaphthalenes. For a given amount of guest, the change of the chemical shift of a proton of

(9) Odashima, K.; Itai, A.; Iitaka, Y.; Arata, Y.; Koga, K. *Tetrahedron Lett.* **1980**, *21*, 4347.
(10) Odashima, K.; Itai, A.; Iitaka, Y.; Koga, K. *J. Am. Chem. Soc.* **1980**, *102*, 2504.

Table III. 360-MHz ^{1}H NMR Spectra (303 K) of D_2O Solutions (TSP_{ext}) of Pure Host **1** ($c = 4 \times 10^{-3}$ mol·L^{-1}), of Pure Guest ($c = 4 \times 10^{-3}$ mol·L^{-1}), and of Host–Guest Complexes ($H_{tot} = G_{tot} = 4 \times 10^{-3}$ mol·L^{-1})[a]

		δ											
host **1**[b]		H-3′	H-3	aryl–CH_3	H-3″	N(1′)–CH_3		N(1″)–CH_3	H-2′		H-2″	H-2	H-10
1 in D_2O		1.90	1.99	2.08	2.70		3.16			3.43		3.91	6.99
1–1,3-dihydroxynaphthalene		1.33	1.49	2.12	2.89[c]	3.07		3.16	3.15		3.48	3.04	7.30
1–1,5-dihydroxynaphthalene		1.34	1.48	2.12	2.88[c]	3.05		3.16	3.17		3.48	3.08	7.27
1–2,3-dihydroxynaphthalene		1.39	1.51	2.10	2.91[c]	3.07		3.16	3.18		3.48	3.01	7.31
1-2,6-dihydroxynaphthalene		1.66	1.57	2.05	2.90[c]	3.09		3.16	3.29		3.49	2.86	7.31
1–2,7-dihydroxynaphthalene		1.41	1.50	2.10	2.90[c]	3.07		3.16	3.22		3.48	3.06	7.32
1–1-naphthol		1.21	1.42	2.14	2.98[c]	3.04		3.16	3.14		3.48	3.10	7.34
1–2-naphthol		1.43	1.54	2.11	2.88[c]	3.08		3.16	3.22		3.47	3.12	7.28

		δ							
guests alone (A)[d] and in the solutions of complexes (B)[e]		H-1	H-2	H-3	H-4	H-5	H-6	H-7	H-8
1,3-dihydroxynaphthalene	A		6.66 (d, J = 2.1 Hz)		6.90 (d, J = 2.1 Hz)	7.75 (d, J = 8.1 Hz)	7.53 ("t", J = 6.8 Hz)	7.40 ("t", J = 6.9 Hz)	8.09 (d, J = 8.1 Hz)
	B		6.26 (d, J = 2.1 Hz)		5.72 (d, J = 2.1 Hz)	5.83 (d, J = 8 Hz)	6.41 (t, J = 7.5 Hz)	6.00 (t, J = 7.7 Hz)	6.73 (d, J = 8.7 Hz)
1,5-dihydroxynaphthalene	A		7.03 (d, J = 6.8 Hz)	7.43 (t, J = 7.8 Hz)	7.76 (d, J = 8.3 Hz)				
	B		6.28 (d, J = 7.3 Hz)	6.20 (t, J = 7.7 Hz)	6.64 (d, J = 8.1 Hz)				
2,3-dihydroxynaphthalene	A	7.33 (s)				7.74 (m)	7.38 (m)		
	B	6.29 (s)				5.96 (m)	6.21 (m)		
2,6-dihydroxynaphthalene	A	7.25 (d, J = 2.5 Hz)		7.17 (dd, J = 8.8 + 2.5 Hz)	7.72 (d, J = 8.8 Hz)				
	B	6.11 (d, J = 2.4 Hz)		6.27 (dd, J = 8.8 + 2.4 Hz)	5.70 (d, J = 8.5 Hz)				
2,7-dihydroxynaphthalene	A	7.14 (d, J = 2.3 Hz)		7.03 (dd, J = 8.9 + 2.3 Hz)	7.79 (d, J = 8.9 Hz)				
	B	5.95 (s, br)		6.01 (dd, J = 9 + 1.7 Hz)	5.96 (d, J = 9 Hz)				
1-naphthol	A		7.01 (d, J = 7.5 Hz)	7.44 (t, J = 7.9 Hz)	7.55 (d, J = 8.5 Hz)	7.94 (m)	7.59 (m)		8.20 (m)
	B		6.25 (d, J = 7.3 Hz)	6.18 (t, J = 7.9 Hz)	5.78 (d, J = 8.4 Hz)	5.94 (d, J = 8.6 Hz)	6.45 ("t", J = 7.7 Hz)	6.64 ("t", J = 7.6 Hz)	7.35 (d, J = 8 Hz)
2-naphthol	A	7.31 (d, J = 2.4 Hz)		7.22 (dd, J = 8.7 + 2.4 Hz)	7.90 (d, J = 8.7 Hz)	7.90 (d, J = 8.7 Hz)	7.42 (m)	7.53 (m)	7.81 (d, J = 8.1 Hz)
	B	6.32 (d, J = 2.4 Hz)		6.38 (dd, J = 8.4 + 2.4 Hz)	6.01 (d, J = 8.4 Hz)	6.31 (m)		6.11 ("t", J = 7.3 Hz)	6.20 (d, J = 8.4 Hz)

[a] About 85% of all host and guest in the solutions of complexes are present in complexed form. [b] The centers of the always symmetrical multiplets of **1** are given for better comparison. [c] H-3″ is strongly broadened in all seven solutions of complexes. [d] All assignments are supported if needed by double-resonance experiments. They agree with the assignments for other naphthalene derivatives of comparable substitution patterns in other solvents: see, Brügel, W. "Handbook of NMR Spectral Parameters"; Heyden: London, 1979; Vol. 2. [e] Most assignments are supported by double-resonance experiments. A ^{1}H NMR titration ($G_{tot} = 2 \times 10^{-3}$ mol·L^{-1}, $H_{tot} = 4 \times 10^{-4}$–$4 \times 10^{-3}$ mol·L^{-1}) supports the assignments of the guest protons in the solution of the complex between **1** and 1,5-dihydroxynaphthalene. Tentative assignments on the basis of CPK molecular models are explicitly mentioned in the text.

the guest was plotted as a function of increasing concentration of the host. With both guests the titration curves exhibit a knee at a 1:1 molar ratio of host and guest. The plot for H-4 of 2,6-dihydroxynaphthalene is shown in Figure 2. Saturation binding of this guest occured below the cmc of **1**. Evaluation of the titration curve at half-saturation binding of the guest[2] gave for the complex between **1** and 2,6-dihydroxynaphthalene an association constant of $K_a(303\ K) = 1.0 \times 10^4\ L \cdot mol^{-1}$. This value is in the range of the association constants determined at 292.5 K for the complexes of 1,3-dihydroxynaphthalene ($K_a = 9.8 \times 10^3\ L \cdot mol^{-1}$) and 2,7-dihydroxynaphthalene ($K_a = 1.9 \times 10^4\ L \cdot mol^{-1}$).[2]

The protons of 2,6-dihydroxynaphthalene show the same pattern of upfield shifts upon complexation as the protons of 2,6-dimethylnaphthalene. Characteristic of a pseudoaxial inclusion (Figure 3), H-4 is shifted more strongly upfield ($\Delta\delta = +2.48$ at saturation binding) than H-1 ($\Delta\delta = +1.39$) and H-3 ($\Delta\delta = 1.10$). Pseudoaxial inclusion of the 2,6-dihydroxy derivative has to be considered as significantly more favored than pseudoaxial inclusion of the 2,6-dimethyl derivative. The upfield shift upon complexation of H-4 of the 2,6-dihydroxy derivative is almost 1 ppm larger at saturation binding of both guests whereas H-1 and H-3 of both guests exhibit similar upfield shifts. A partial rotation of 2,6-dimethylnaphthalene in the aromatic guest plane of **1** around the pseudoaxial position leads to favorable contacts between the methyl groups of the guest and the apolar walls of the cavity. Such a partial rotation of the dihydroxy derivative is unfavorable since it brings the hydrated phenolic hydroxy groups in proximity to the apolar cavity walls and therefore 2,6-dihydroxynaphthalene takes a more rigid pseudoaxial position. A polar substituent of an aromatic guest has therefore a strong influence on the structure of host–guest complexes formed with hosts like **1** having a cavity of pronounced apolar character. Aside from their space-filling capacity, the structuring influence of polar groups is resulting especially from the higher affinity of these groups to the aqueous solution than to the apolar cavity walls of **1**.

On the basis of the significantly higher upfield shift upon complexation of H-4 as compared to the upfield shifts of H-1 and H-3 (Table III) a highly favored pseudoaxial inclusion has also to be admitted for 2,7-dihydroxynaphthalene.[11]

For 2,3-dihydroxynaphthalene as guest a preferred axial inclusion is suggested by the ^1H NMR data. From the larger upfield shift of H-5 ($\Delta\delta = +1.78$) as compared to the upfield shift of H-1 ($\Delta\delta = 1.04$), it can be concluded that the unsubstituted ring is located deeper within the cavity between the diphenylmethane units than the ring bearing the two hydroxy groups. As the hydroxy groups are thus located remote from the apolar walls of the cavity, a considerable rotation of the guest in the aromatic guest plane around the axial position seems possible. This explains the considerable upfield shift of H-6 ($\Delta\delta = +1.17$) not expected for a more rigid axial inclusion.

An axial-type inclusion can be admitted as preferred position of 1,3-dihydroxynaphthalene in the cavity of **1**. The ring bearing the two hydroxy groups is reaching out of the cavity and only a weak upfield shift upon complexation of H-2 ($\Delta\delta = +0.40$) is resulting. The deeper position in the cavity of the unsubstituted ring is clearly indicated by the considerable upfield shifts upon complexation of all the protons of this ring. The assignments of H-5 and H-8 of the guest in the solution of the complex (Table III) are based on observations at CPK molecular models. The doublet at δ 5.83 cannot be assigned to H-8 since the orientation of the guest in the cavity, which could lead to an upfield shift of $\Delta\delta = +2.26$ of H-8, would locate the hydroxy group at C(1) closely to the apolar walls of the cavity. The assignments of H-6 and H-7 of the guest in the solution of the complex are connected to the assignments of H-5 and H-8 by double-resonance spectroscopy.

(11) Pseudoaxial inclusion of 2,7-dihydroxynaphthalene in the cavity of a 1,6,20,25-tetraaza[6.1.6.1]paracyclophane in acidic solution has been suggested on the basis of the changes of the ^1H NMR chemical shifts by Koga et al.[9] In this type of host–guest complex the upfield shifts upon complexation of both H-4 and H-1 of the guest are comparable and significantly stronger than the upfield shift upon complexation of H-3.

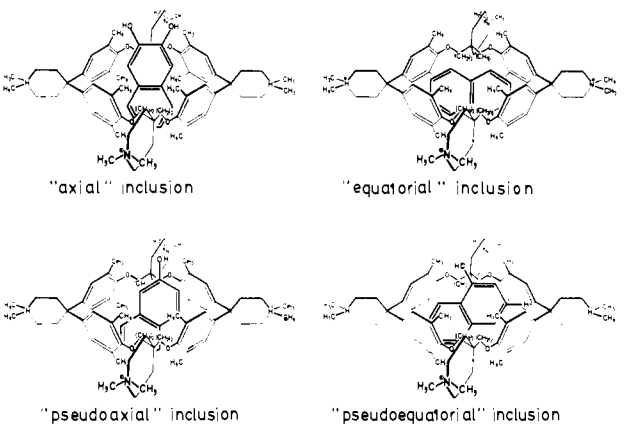


Figure 3. Different possible positions of naphthalene and of substituted naphthalenes in the cavity of **1**. The nomenclature proposed in ref 9 is used. The position of the spiro piperidinium rings fixed in the aliphatic chains of **1** within the mean molecular plane of **1** is arbitrarily chosen.

1,5-Dihydroxynaphthalene enclosed in the cavity of **1** shows the largest upfield shift for H-3 ($\Delta\delta = +1.23$). This is typical for a favored pseudoequatorial orientation of a naphthalene derivative in the aromatic guest plane (Figure 3). A pseudoequatorial position directs H-3 more than H-2 and H-4 toward the shielding region of the diphenylmethane units of **1**. The pseudoequatorial inclusion of 1,5-dihydroxynaphthalene is, however, not very highly favored since the difference between the upfield shifts upon complexation of H-3 and H-2,H-4 is not very large.

The protons of 1-naphthol in the solution of the complex could all be assigned under the assumption that H-8, like H-2 adjacent to the phenolic hydroxy group, exhibits the smallest upfield shift upon complexation. A favored orientation of 1-naphthol in the aromatic guest plane cannot be so easily derived from the ^1H NMR data despite large upfield shifts upon complexation of specifically H-4 ($\Delta\delta = +1.77$) and H-5 ($\Delta\delta = +2.00$). 2-Naphthol seems to have some preference for a pseudoaxial inclusion since the largest upfield shift upon complexation is obtained for H-4. On the basis of this assumption the doublet at δ 6.20 is assigned to H-8 rather than to H-5. The assignments of H-6 and H-7 in the solution of the complex are coupled to the assignments of H-5 and H-8 by double-resonance experiments. A highly favored geometry being easier established on the basis of ^1H NMR data for the complexes of the dihydroxynaphthalenes than of the naphthols reflects the higher structuring influence of two polar substituents of the arene.

There is a remarkable similarity between the chemical shifts of the protons of the host in the solutions of all seven complexes. The dominant influence on the chemical shifts of the protons of the host clearly results from the location of all seven guests within the same plane in the cavity of **1**. Only a minor influence arises from a favored axial, equatorial, or another position of the naphthalene derivative in this plane.

C. ^1H NMR Studies of Aqueous Solutions of Host–Guest Complexes of 1 with Aromatic Guests Bearing Sulfonic Residues. During the ^1H NMR investigations of the host–guest complexation between **1** and neutral-substituted or unsubstituted aromatic guests, we always observed a more or less considerable upfield shift upon complexation of H-2′ and N(1′)–CH_3 of the host. We explained these shifts by the conformational mobility of the aliphatic chains bridging the two diphenylmethane units of **1**. This mobility allows the spiro piperidinium rings attached to these chains to approach and to envelope the aromatic guest enclosed in the aromatic guest plane in the cavity of **1**. Hence **1** could also be expected to be a good host for aromatic guests bearing anionic residues. If the aromatic core of the guest is included in the cavity and the anionic residue is oriented toward the quaternary nitrogens of the piperidinium rings which approach the enclosed guest, both hydrophobic and electrostatic interactions should lead to very strong complexation and to the formation of highly structured complexes. This should be reflected in the ^1H NMR spectra, and

we therefore studied the complexation of **1** with naphthalenemonosulfonates and -disulfonates as well as *p*-toluenesulfonate. A first important evidence for the additional stabilization of these complexes by ion pairing was provided by the determination of the association constants.[2] The association contants of the complexes of arenesulfonates were found to be considerably higher than those of the complexes of naphthalene derivatives bearing neutral substituents. The ^1H NMR data of the D_2O solutions of the complexes of arenesulfonates are summarized in Table IV. The concentrations of host and guest were always 4×10^{-3} mol·L^{-1}. A concentration of complex of $\approx 3.9 \times 10^{-3}$ mol·L^{-1} is calculated for the solutions of the naphthalene derivatives and of $\approx 3.3 \times 10^{-3}$ mol·L^{-1} for the solution of *p*-toluenesulfonate. The sodium salts of the guests were used in each case.

Highly favored pseudoaxial inclusion of 2,6-naphthalenedisulfonate is supported by the very large upfield shift upon complexation of H-4 ($\Delta\delta = +3.09$) as compared to the relatively weaker upfield shifts of H-1 ($\Delta\delta = +1.36$) and H-3 ($\Delta\delta = +0.94$). Examinations of CPK molecular models indicate that the extension of the disulfonate in the pseudoaxial position is large enough to locate on each side of the cavity a sulfonate residue in closest proximity to the quaternary nitrogen of a piperidinium ring whose least plane is approximately perpendicular to the mean molecular plane of **1**. Ion pairing at each side of the cavity holds the guest in a rigid pseudoaxial position. This is reflected by the upfield shifts upon complexation of the protons of the guest in the series of complexes of 2,6-disubstituted naphthalenes. H-4 of the 2,6-disulfonate is shifted to higher field by $\Delta\delta = +3.09$, H-4 of the 2,6-diol by $\Delta\delta = +2.48$, and H-4 of the 2,6-dimethyl derivative by $\Delta\delta = +1.55$ whereas the upfield shifts of H-1 and H-3 upon complexation are comparable for all three guests.

^1H NMR spectra of a solution with a concentration of 2,6-naphthalenedisulfonate about twice as large as the concentration of **1** ($G_{tot} = 4.1 \times 10^{-3}$ mol·L^{-1}, $H_{tot} = 2.0 \times 10^{-3}$ mol·L^{-1}, Figure 4) were recorded as a function of temperature. At 273 K the exchange of host with guest was slow on the 360-MHz NMR time scale. Beside the signals of complexed host, both the signals of complexed and free guest appear in the spectrum at about equal intensity as expected for 1:1 host–guest complexation. Coalescence of the signals of H-1 and H-3 of the guest occurs between 310 and 320 K. Above this temperature, averaged signals appear for H-1 and H-3 whereas the averaged signal of H-4 cannot be detected even at 353 K since it is broadened over a range of $\Delta\nu \approx 1100$ Hz. In the spectrum at 273 K (Figure 4) the slowing on the NMR time scale of the chair inversion of the spiro piperidinium rings of the diphenylmethane units of **1** is apparent from the very strong broadening of the signals of H-3″ and also of H-2″ and N(1″)–CH_3.

Similarly in the spectrum at 273 K of a solution with a concentration of host twice as large as the concentration of guest ($H_{tot} = 4.0 \times 10^{-3}$ mol·L^{-1}, $G_{tot} = 2.0 \times 10^{-3}$ mol·L^{-1}), the signals of both free and complexed host appear at equal intensity beside the signals of complexed guest. At 302 K the two singlets of the aromatic protons H-10 of free and complexed host coalesce and from $\Delta\nu = 124$ Hz (360 MHz) a lifetime of the exchanging system at coalescence temperature of $\tau_{302K} = 1.8 \times 10^{-3}$ s is calculated.

Evidence for a specially favored pseudoequatorial position of 1,5-naphthalenedisulfonate in the aromatic guest plane of **1** was obtained from the very large upfield shift upon complexation of H-3 ($\Delta\delta = +3.09$) of the guest as compared to a relatively weaker upfield shift of H-2 ($\Delta\delta = +1.67$) and H-4 ($\Delta\delta = +0.96$). In an equatorial position the naphthalene moiety of the guest is deeply located in the cavity and this is reflected by the large upfield shifts upon complexation of H-2 ($\Delta\delta = +1.52$) and H-3 ($\Delta\delta = +0.76$) of the host. Again the additional rigidity of the pseudoequatorial position of the guest in the complex as a consequence of ion pairing on both sides of the cavity becomes apparent from the comparison of the upfield shifts upon complexation of the protons of various 1,5-disubstituted naphthalenes. At saturation binding of the guests, H-3 of the 1,5-disulfonate is shifted by $\Delta\delta = +3.09$, H-3 of the 1,5-diol only by $\Delta\delta = +1.23$, and H-3 of the 1,5-dimethyl derivative only by $\Delta\delta = +1.11$ whereas the difference of the upfield

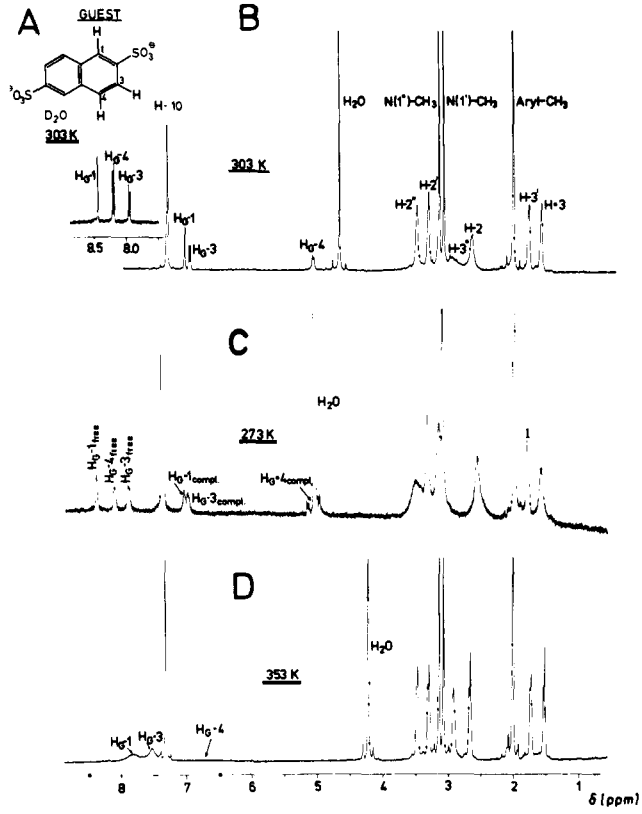


Figure 4. 360-MHz ^1H NMR spectra (A) of a 4×10^{-3} M solution of 2,6-naphthalenedisulfonate in D_2O (303 K), (B) of a solution of the complex of **1** with 2,6-naphthalenedisulfonate in D_2O (303 K, $H_{tot} = G_{tot} = 4.0 \times 10^{-3}$ mol·L^{-1}), and of a solution of **1** and 2,6-naphthalenedisulfonate ($H_{tot} = 2.0 \times 10^{-3}$ mol·L^{-1}, $G_{tot} = 4.1 \times 10^{-3}$ mol·L^{-1}) at 273 K (C) and 353 K (D) in D_2O (TSP_{ext}).

shifts of H-2 and H-4 of the three guests is not as striking. A ^1H NMR titration (303 K, $G_{tot} = 4.0 \times 10^{-3}$ mol·L^{-1}, $H_{tot} = 4.0 \times 10^{-4}$–$6.4 \times 10^{-3}$ mol·L^{-1}) showed that the exchange of host with guest is fast on the 360-MHz time scale. Averaged signals of the protons of host and guest were obtained at all considered host:guest ratios. If one component was present in excess in the solution of complex, the signals for its protons were, however, significantly broadened. The titration curve exhibits a very sharp knee at the molar host:guest ratio of 1:1.

The complexes of **1** with guests bearing only one sulfonate residue are as expected less highly structured. The ^1H NMR data (Table IV) suggest some preference for a pseudoaxial position of 2-naphthalenesulfonate in the complex. The unsubstituted ring of the guest is located more deeply in the cavity than the ring bearing the sulfonate residue. Also in the complex of **1** with 1-naphthalenesulfonate, the moiety of the guest bearing the substituent is located more outside of the cavity. Accordingly, H-3,4,5,6 of this guest are positioned deeply in the cavity and they exhibit large upfield shifts. For the two complexes it is reasonable to assume that the piperidinium rings of the aliphatic bridges of **1** are both turned preferably to the same side of the cavity. Thus both quaternary nitrogens can interact with the sulfonate residue of the complexed guest.

In the complex of **1** with *p*-toluenesulfonate, the guest takes an axial position in the aromatic guest plane. Close proximity of the ionic centers of host and guest is evidenced by the ^1H NMR data. The part of the guest bearing the sulfonate residue is significantly drawn out of the cavity. The aromatic proton H-2 of the guest is shifted upfield upon complexation by $\Delta\delta = +0.95$ whereas the aromatic proton H-3, located more deeply in the cavity, is shifted to higher field by $\Delta\delta = +1.76$ (Table IV).

In conclusion, the ^1H NMR data reflect the additional stabilization through ion pairing of complexes formed between **1** and aromatic guests bearing sulfonate residues. The changes of the chemical shifts upon complexation reveal that in the complexes

Table IV. 360-MHz ^{1}H NMR Spectra (At 303 K If Not Otherwise Stated) of a 4×10^{-3} M Solution of **1**, of 4×10^{-3} M Solutions of Pure Aromatic Sulfonates, and of Solutions of Host–Guest Complexes ($H_{tot} = G_{tot} = 4 \times 10^{-3}$ mol·L^{-1}) in D_2O (TSP_{ext})[a]

		δ										
host **1**		H-3′	H-3	aryl–CH_3	H-3″	N(1′)–CH_3		N(1″)–CH_3	H-2′		H-2″	H-2	H-10
1 in D_2O		1.90	1.99	2.08	2.70		3.16			3.43		3.91	6.99
1–1,5-naphthalenedisulfonate		1.63	1.23	2.10	≈3.0[b]	3.06		3.16	3.28		3.51	2.39	7.37
1–2,6-naphthalenedisulfonate	303 K	1.77	1.57	2.01	2.99[b]	3.09		3.16	3.32		3.50	2.63	7.37
	353 K	1.74	1.56	2.01	2.90	3.08		3.15	3.31		3.48	2.78	7.29
1–1-naphthalenesulfonate		1.14	1.37	2.14	[c]	3.02		3.16	3.11		3.49	2.91	7.39
1–2-naphthalenesulfonate		1.27	1.39	2.09	2.93[b]	3.04		3.15	3.15		3.49	2.72	7.39
1–*p*-toluenesulfonate		1.81	1.87	2.11	2.80		3.14		3.39		3.44	3.53	7.15

		δ							
guests alone (A) and in the solutions of complexes (B)		H-1	H-2	H-3	H-4	H-5	H-6	H-7	H-8
1,5-naphthalenedisulfonate	A		8.26 (d, J = 7.4 Hz)	7.78 (t, J = 8 Hz)	8.89 (d, J = 8.6 Hz)				
	B[d]		6.59 (d, J = 7.5 Hz)	4.69 ("t", J = 7.8 Hz)	7.93 (d, J = 8.2 Hz)				
2,6-naphthalenedisulfonate	A	8.45 (d, J = 1.1 Hz)		7.96 (dd, J = 8.7 + 1.1 Hz)	8.21 (d, J = 8.7 Hz)				
353 K	A	8.43		7.96	8.19				
	B	7.09 (s)		7.02 (d, J = 7.7 Hz)	5.12 (d, J = 7.7 Hz)				
353 K	B	7.18		7.06	5.34				
1-naphthalenesulfonate[e,f]	A		8.15 (d, J = 7.4 Hz)	7.62 (t, J = 7.6 Hz)	8.15 (d, J = 7.4 Hz)	8.09 (d, J = 7.7 Hz)	7.69 (m)	7.75 (m)	8.65 (d, J = 9.1 Hz)
	B		7.28 (d, J = 6.9 Hz)	6.10 (t, J = 7.7 Hz)	5.98 (d, J = 8.9 Hz)	5.84 (d, J = 8.3 Hz)	6.38 (t, J = 7.6 Hz)	6.72 (t, J = 7.9 Hz)	8.11 (d, J = 8.9 Hz)
2-naphthalenesulfonate[e]	A	8.40 (s, br)		7.87 (d, J = 8.9 Hz)	8.09 (d, J = 8.9 Hz)	8.06 (d, J = 9.1 Hz)	≈7.69 (m)		8.09 (d, J = 8.9 Hz)
	B	7.61 (s, br)		7.33 (d, J = 8.9 Hz)	6.40 (d, J = 8.9 Hz)	≈6.45 (m)	≈6.55 (m)		≈6.45 (m)
p-toluenesulfonate	A	7.71 (d, J = 8.3 Hz, H-2)		7.39 (d, J = 8.3 Hz, H-3)		2.41 (s, CH_3)			
	B	6.76 (d, J = 7.9 Hz, H-2)		5.63 (d, J = 7.9 Hz, H-3)		1.55 (s, CH_3)			

[a] The concentrations of complexes are HG ≈ 3.9×10^{-3} mol·L^{-1} for all complexes of naphthalene derivatives and HG ≈ 3.3×10^{-3} mol·L^{-1} for the complex of *p*-toluenesulfonate. The sodium salts of the guests have been used in each case. [b] Very broad. [c] This signal is very broad and overlapped by other signals. [d] These assignments are supported by a ^{1}H NMR titration ($G_{tot} = 4 \times 10^{-3}$ mol·L^{-1}, $H_{tot} = 4 \times 10^{-4}$–$6.4 \times 10^{-3}$ mol·L^{-1}). [e] All assignments are supported if possible by double-resonance experiments. The assignments of the protons of free guest are in agreement with the assignments for other naphthalene derivatives with comparable substitution patterns in other solvents see: Brügel, W. "Handbook of NMR Spectral Parameters"; Heyden: London, 1979; Vol. 2. [f] This guest contains about 10% of 2-naphthalenesulfonate as impurity.

with **1** the guests bearing anionic residues take a more highly favored position in the aromatic guest plane than the guests of comparable substitution pattern bearing nonionic residues.

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Registry No. 1, 86765-98-2; **1·2**, 93254-45-6; **1·4**, 93254-44-5; **1**-naphthalene, 93254-50-3; **1**-1,5-dimethylnaphthalene, 93254-46-7; **1**-2,6-dimethylnaphthalene, 93254-47-8; **1**-durene, 93254-52-5; **1**-1,5-naphthalenedisulfonate, 93254-57-0; **1**-2,6-naphthalenedisulfonate, 93254-56-9; **1**-1-naphthalenesulfonate, 93254-59-2; **1**-2-naphthalenesulfonate, 93254-58-1; **1**-*p*-toluenesulfonate, 93254-61-6; **2**, 129-00-0; **4**, 206-44-0; naphthalene, 91-20-3; 1,5-dimethylnaphthalene, 571-61-9; 2,6-dimethylnaphthalene, 581-42-0; durene, 95-93-2; disodium 1,5-naphthalenedisulfonate, 1655-29-4; disodium 2,6-naphthalenedisulfonate, 1655-45-4; sodium 1-naphthalenesulfonate, 130-14-3; sodium 2-naphthalenesulfonate, 532-02-5; sodium *p*-toluenesulfonate, 657-84-1.

Structure and Reactivity of $C_7H_7^+$ Ions from the Decay of Tritiated Toluenes. 1. Reactions of Free Tolyl Ions with Methanol in the Gas and Liquid Phases

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Abstract: Labeled tolyl cations from the decay of ring-multitritiated toluene have been allowed to react with methanol in the liquid and the gas phases, at pressures ranging from 6 to 100 torr, yielding methyl tolyl ethers as the major products, without appreciable formation of benzyl methyl ether. The isomeric composition of the products from the gaseous systems depends on the pressure, the percentage of *o*-tolyl ether increasing at the expense of the para isomer as the methanol pressure is reduced. The results show that the three tolyl ions exist as distinct species in the dilute gas state. When formed in a sufficiently excited state, as from the β decay of a ^3H atom in toluene, they undergo appreciable interconversion, without detectable isomerization to the benzyl cation, at least within the pressure range accessible to the decay technique.

Interest in gaseous $C_7H_7^+$ ions has not declined since 1957, when the suggestion was first advanced that tropylium ions are formed from toluene and cycloheptatriene under electron impact.[1] Indeed, problems related to the structure and the reactivity of $C_7H_7^+$ isomers have been actively investigated by mass spectrometry and have represented a classic test for all major diagnostic techniques developed in the last quarter of a century, including the study of the fragmentation pattern of selectively labeled precursors,[2-9] ICR spectrometry,[10-14] collision activation spectrometry,[15-18] equilibrium measurements in high-pressure ion sources,[19,20] chemical ionization mass spectrometry,[21,22] and the analysis of the charged products of relevant ion–molecule reactions.[23,24] As a result of such a vigorous and sustained effort, a large body of experimental data is currently available, almost exclusively derived from mass spectrometric studies.[25] Unavoidably, the picture obtained by the application of a single, if powerful, technique is incomplete, owing especially to the recognized[26] difficulties encountered when applying purely mass spectrometric procedures to positive structural identification of isomeric ions and their mixtures. Among other consequences, this state of affairs has largely deprived the theoretical approach to the structure and the stability of gaseous $C_7H_7^+$ isomers[26,27] of the usual correlation with pertinent experimental data, particularly useful for the calibration of semiempirical methods.

In the attempt to widen the experimental approach to the problem, it was decided to undertake a study of the $C_7H_7^+$ isomers by using the method based on the β^- decay of ^3H atoms in suitably labeled toluenes. The decay technique, whose principles and applications have been reviewed,[28] is experimentally laborious, since it requires the preparation of precursors containing two or more ^3H atoms *in the same molecule*. However, it allows the introduction of free cations of specified structure into any system of interest, irrespective of its aggregation state, and to follow their reactions, owing to the presence of the residual radioactive atom(s). The unique features of the decay technique have been exploited

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