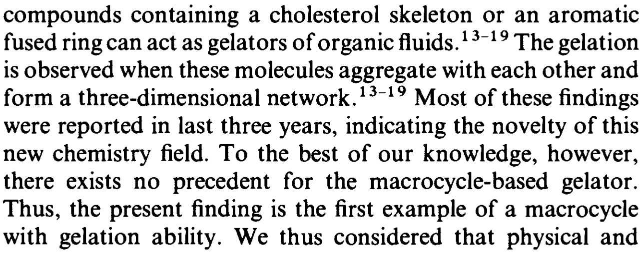
Molecular Design and Characterizations of New Calixarene-based Gelators of Organic Fluids

Masayoshi Aoki, Kazuaki Nakashima, Hirosuke Kawabata, Satoru Tsutsui and Seiji Shinkai *
Chemirecognics Project, ERATO, Research Development Corporation of Japan, 332-1, Kamikoga, Chikushino, Fukuoka 818, Japan

We have found that certain calix[*n*]arenes having long acyl groups at the *p*-positions (*e.g.*, 5,11,17,23,29,35,41,47-octadodecanoylcalix[8]arene-49,50,51,52,53,54,55,56-octol: $\mathbf{2}_8\mathrm{C}_{12}$) act as excellent and unique gelators of various organic solvents (*e.g.*, toluene, carbon tetrachloride, carbon disulfide, hexane, isopropanol, *etc.*). The sol–gel phase transition temperatures (T_{gel}) could be determined by the inverted test-tube method or by the DSC method. The change in the aggregation mode at the phase transition temperature was directly observable by an optical microscope: below T_{gel} the fibrillar network (diameter *ca.* 1 μm) appeared whereas above T_{gel} it 'melted' down. It was shown on the basis of these measurements that the sol–gel phase transition occurs reversibly. The spectroscopic studies using ^{1}H NMR and IR spectroscopy and the comparative experiments using the analogues of $\mathbf{2}_8\mathrm{C}_{12}$ (nine cyclic and six non-cyclic) established that the prerequisites for the formation of the stable organic gels are (*i*) the intermolecular C=O ··· HO hygrogen-bonding interaction to form the three-dimensional network and (*ii*) the moderate affinity of gelators with solvent molecules. The results offer important strategies useful for the molecular design of new gelators of organic fluids.

Calix[*n*]arenes having long aliphatic chains at the *p*-positions have been of increasing concern in molecular recognition and Langmuir monolayer formations.[1-7] They can be synthesized by two different methods: (*i*) one-step synthesis by condensation of *p*-alkylphenol with formaldehyde[6-9] and (*ii*) three-step synthesis going from *O*-acylation of calix[*n*]arenes ($\mathbf{1}_n$) to *p*-acylcalix[*n*]arenes (Fries rearrangement) followed by Wolff-Kishner reduction.[5,10-12] We were interested in the improvement of method (*ii*).[12] In the course of the study, we 'accidentally' experienced a surprising phenomenon that recrystallization of certain *p*-acylcalix[*n*]arenes from benzene, hexane, or cyclohexane results in stable organic gels. We learned from the survey of the past literature that low molecular-weight compounds containing a cholesterol skeleton or an aromatic fused ring can act as gelators of organic fluids.[13-19] The gelation is observed when these molecules aggregate with each other and form a three-dimensional network.[13-19] Most of these findings were reported in last three years, indicating the novelty of this new chemistry field. To the best of our knowledge, however, there exists no precedent for the macrocycle-based gelator. Thus, the present finding is the first example of a macrocycle with gelation ability. We thus considered that physical and chemical characterizations of these organic gels would be of great value to provide a basic guiding principle for the molecular design of new macrocycle-based gelators.



$\mathbf{1}_n$ $\mathbf{2}_n\mathrm{C}_m$ $\mathbf{3}_n\mathrm{C}_m$

Experimental

Materials.—Preparations of $\mathbf{2}_n\mathrm{C}_m$ and $\mathbf{3}_n\mathrm{C}_m$ (n = 4, 6 and 8; m = 6 and 12) were reported previously.[12] $\mathbf{2}_n\mathrm{C}_{18}$ (n = 4, 6 and 8) were synthesized from $\mathbf{1}_n$ and octadecanoyl chloride according to the method described previously.[12] Recorded here is the analytical data. *J* values are given in Hz.

5,11,17,23-*Tetraoctadecanoylcalix*[4]*arene*-25,26,27,28-*tetrol* ($\mathbf{2}_4\mathrm{C}_{18}$).—Yield (16.7 g, 72%), m.p. 108–109 °C (Found: C, 80.2; H, 10.2. $C_{100}H_{160}O_8$ requires C, 80.58; H, 10.83%); ν_{max}(KBr)/cm^{-1} 3193 (OH) and 1676 (C=O); δ_H(90 MHz; CDCl$_3$; Me$_4$Si; 30 °C) 0.88 [12 H, br t, $CH_2(CH_2)_{15}CH_3$], 1.26–1.63 [120 H, m, $CH_2(CH_2)_{15}CH_3$], 2.83 (8 H, t, *J* 7, COCH$_2$), 3.99 (8 H, br s, ArCH$_2$Ar), 7.75 (8 H, s, ArH) and 10.07 (4 H, s, OH).

5,11,17,23,29,35-*Hexaoctadecanoylcalix*[6]*arene*-37,38,39,40,41,42-*hexol* ($\mathbf{2}_6\mathrm{C}_{18}$).—Yield (10.4 g, 63%), m.p. > 200 °C (Found: C, 80.55; H, 10.85. $C_{150}H_{240}O_{12}$ requires C, 80.58; H, 10.83%); ν_{max}(KBr)/cm^{-1} 3250 (OH), 1682 (C=O); δ_H(90 MHz; CDCl$_3$; Me$_4$Si; 30 °C) 0.88 [18 H, br t, $CH_2(CH_2)_{15}CH_3$], 1.26–1.59 [180 H, m, $CH_2(CH_2)_{15}CH_3$], 2.90 (12 H, t, *J* 7, COCH$_2$), 3.98 (12 H, s, ArCH$_2$Ar), 7.85 (12 H, s, ArH) and 10.40 (6 H, s, OH).

5,11,17,23,29,35,41,47-*Octaoctadecanoylcalix*[8]*arene*-49,50,51,52,53,54,55,56-*octol* ($\mathbf{2}_8\mathrm{C}_{18}$).—Yield (2.80 g, 60%), m.p. > 200 °C (Found: C, 80.1; H, 10.7. $C_{200}H_{320}O_{16}$ requires C, 80.58; H, 10.83%); ν_{max}(KBr)/cm^{-1} 3339 (OH) and 1682 (C=O); δ_H(90 MHz; CDCl$_3$; Me$_4$Si; 30 °C) 0.88 [24 H, br t, $CH_2(CH_2)_{15}CH_3$], 1.26–1.67 [240 H, m, $CH_2(CH_2)_{15}CH_3$], 2.88 (16 H, t, *J* 7, COCH$_2$), 4.00 (16 H, s, ArCH$_2$Ar), 7.80 (16 H, s, ArH) and 9.54 (8 H, br s, OH).

5,11,17,23,29,35,41,47-*Octadodecanoyl*-49,50,51,52,53,54,55,56-*octamethoxycalix*[8]*arene* ($\mathbf{4}_8\mathrm{C}_{12}$).—Compound $\mathbf{2}_8\mathrm{C}_{12}$ (0.50 g, 0.22 mmol), Cs$_2$CO$_3$ (1.13 g, 3.46 mmol) and MeI (1.0 g, 7.0 mmol) were mixed in dehydrated acetone (20 cm^3) and the reaction mixture was stirred at the reflux temperature for 110 h. The solid material was removed by filtration, the filtrate being evaporated to dryness. The solid residue was subjected to purification by column chromatography (silica gel, CHCl$_3$), and finally recrystallized from chloroform–methanol, yield

(0.21 g, 40%), m.p. 93.3–94.3 °C (Found: C, 80.25; H, 10.1. $C_{160}H_{240}O_{16}$ requires C, 79.42; H, 10.00%); ν_{max}(KBr)/cm^{-1}: no ν_{OH} was observed; δ_H(90 MHz; $CDCl_3$; Me_4Si; 30 °C) 0.87 [24 H, br t, $CH_2(CH_2)_9CH_3$], 1.24–1.54 [144 H, m, $CH_2(CH_2)_9CH_3$], 2.75 (16 H, t, *J* 7, $COCH_2$), 3.48 (24 H, s, OCH_3), 4.05 (16 H, s, $ArCH_2Ar$) and 7.57 (16 H, s, ArH).

2,6-*Dimethyl*-4-*hexanoylphenol* ($\mathbf{2'}_1\mathrm{C}_6$).—This compound was synthesized from 2,6-dimethylphenol and hexanoyl chloride in a manner similar to that described for $\mathbf{2}_n\mathrm{C}_m$[12]: yield (2.20 g, 50%), m.p. 97.5–99.0 °C (Found: C, 76.0; H, 9.05. $C_{14}H_{20}O_2$ requires C, 76.31; H, 9.16%); ν_{max}(KBr)/cm^{-1} 3366 (OH) and 1657 (C=O); δ_H(90 MHz; $CDCl_3$; Me_4Si; 30 °C) 0.91 [3 H, br t, $CH_2(CH_2)_3CH_3$], 1.38–1.72 [6 H, m, $CH_2(CH_2)_3CH_3$], 2.29 (6 H, s, $ArCH_3$), 2.88 (2 H, t, *J* 7, $COCH_2$), 5.17 (1 H, s, OH) and 7.63 (2 H, s, ArH).

2,6-*Dimethyl*-4-*dodecanoylphenol* ($\mathbf{2'}_1\mathrm{C}_{12}$).—This compound was synthesized from 2,6-dimethylphenol and dodecanoyl chloride in a manner similar to that described for $\mathbf{2}_n\mathrm{C}_m$,[12] yield (2.6 g, 51%), m.p. 52.0–52.5 °C (Found: C, 79.7; H, 10.55. $C_{20}H_{32}O_2$ requires C, 78.89; H, 10.60%); ν_{max}(KBr)/cm^{-1} 3350 (OH), 1653 and 1671 (C=O); δ_H(90 MHz; $CDCl_3$; Me_4Si; 30 °C) 0.88 [3 H, br t, $CH_2(CH_2)_9CH_3$], 1.27–1.72 [18 H, m, $CH_2(CH_2)_9CH_3$], 2.29 (6 H, s, $ArCH_3$), 2.88 (2 H, t, *J* 7, $COCH_2$), 5.20 (1 H, s, OH) and 7.63 (2 H, s, ArH).

2,6-*Dimethyl*-4-*octadecanoylphenol* ($\mathbf{2'}_1\mathrm{C}_{18}$).—This compound was synthesized from 2,6-dimethylphenol and octadecanoyl chloride in a manner similar to that described for $\mathbf{2}_n\mathrm{C}_m$,[12] yield (0.40 g, 10%), m.p. 62.0–62.5 °C (Found: C, 80.15; H, 11.5. $C_{26}H_{44}O_2$ requires C, 80.34; H, 11.42%); ν_{max}(KBr)/cm^{-1} 3355 (OH), 1651 and 1662 (C=O); δ_H(90 MHz; $CDCl_3$; Me_4Si; 30 °C) 0.85 [3 H, br t, $CH_2(CH_2)_{15}CH_3$], 1.30–1.70 [30 H, m, $CH_2(CH_2)_{15}CH_3$], 2.26 (6 H, s, $ArCH_3$), 2.87 (2 H, t, *J* 7, $COCH_2$), 5.07 (1 H, br s, OH) and 7.60 (2 H, s, ArH).

Bis(2-*hydroxy*-3-*methyl*-5-tert-*butylphenyl*)*methane*.—2-Methyl-4-*tert*-butylphenol (11.5 g; 70 mmol), formaldehyde (4.5 g of 37% solution; 70 mmol) and NaOH solution (1.6 cm^3 of 10 mol dm^{-3} solution) were mixed in *p*-xylene (200 cm^3). The mixture was refluxed at 130 °C for 6 h in a vessel with a Dean-Stark trap. After cooling, the dark yellow precipitate was separated and dissolved in chloroform. The solution was washed with dilute HCl solution three times and evaporated to dryness. The solid residue was recrystallized from hexane (8.00 g, 67%), m.p. 138–139 °C (Found: C, 81.3; H, 9.45. $C_{23}H_{32}O_2$ requires C, 81.12; H, 9.48%); ν_{max}(KBr)/cm^{-1} 3305 and 3445 (OH), 1605 (C=C); δ_H(90 MHz; $CDCl_3$; Me_4Si; 30 °C) 1.26 (18 H, s, Bu^t), 2.21 (6 H, s, CH_3), 3.91 (2 H, s, CH_2), 6.03 (2 H, br s, OH), 6.99 (2 H, s, ArH) and 7.17 (2 H, s, ArH).

Bis(2-*hydroxy*-3-*methylphenyl*)*methane* ($\mathbf{1'}_2$).—De-*tert*-butylation was performed in a manner similar to that described for calix[*n*]arenes,[20] yield (3.00 g, 65%), m.p. 129–130 °C (Found: C, 79.3; H, 7.1. $C_{15}H_{16}O_2$ requires C, 78.91; H, 7.07%); ν_{max}(KBr)/cm^{-1} 3316 and 3449 (OH); δ_H(90 MHz; $CDCl_3$; Me_4Si; 30 °C) 2.24 (6 H, s, CH_3), 3.93 (2 H, s, CH_2), 5.92 (2 H, s, OH) and 7.16–6.99 (6 H, m, ArH).

The following three compounds were synthesized from $\mathbf{1'}_2$ and the corresponding acid chlorides in a manner similar to that described for $\mathbf{2}_n\mathrm{C}_m$. Recorded here is their analytical data.

Bis(2-*hydroxy*-3-*methyl*-5-*hexanoylphenyl*)*methane* ($\mathbf{2'}_2\mathrm{C}_6$).—Yield (1.1 g, 55%), m.p. 141–142 °C (Found: C, 77.7; H, 8.5. $C_{27}H_{36}O_4$ requires C, 76.73; H, 8.55%); ν_{max}(KBr)/cm^{-1} 3365 (OH), 1684 and 1654 (C=O); δ_H(90 MHz; $CDCl_3$; Me_4Si; 30 °C) 0.90 [6 H, br t, $CH_2(CH_2)_3CH_3$], 1.34–1.77 [12 H, m, $CH_2(CH_2)_3CH_3$], 2.28 (6 H, s, $ArCH_3$), 2.88 (4 H, t, *J* 7, $COCH_2$), 3.99 (2 H, s, $ArCH_2Ar$), 6.53 (2 H, br s, OH), 7.65 (2 H, s, ArH) and 7.79 (2 H, s, ArH).

Bis(2-*hydroxy*-3-*methyl*-5-*dodecanoylphenyl*)*methane* ($\mathbf{2'}_2\mathrm{C}_{12}$).—Yield (1.2 g, 46%), m.p. 95.6–96.8 °C (Found: C, 79.75; H, 10.1. $C_{39}H_{60}O_4$ requires C, 78.99; H, 10.21%; ν_{max}(nujol)/cm^{-1} 3366 (OH), 1655 and 1672 (C=O); δ_H(90 MHz; $CDCl_3$; Me_4Si; 30 °C) 0.87 [6 H, br t, $CH_2(CH_2)_9CH_3$], 1.26–1.68 [36 H, m, $CH_2(CH_2)_9CH_3$], 2.28 (6 H, s, CH_3), 2.87 (4 H, t, *J* 7, $COCH_2$), 4.00 (4 H, s, $ArCH_2Ar$), 7.65 (2 H, s, ArH) and 7.78 (2 H, s, ArH).

Bis(2-*hydroxy*-3-*methyl*-5-*octadecanoylphenyl*)*methane* ($\mathbf{2'}_2\mathrm{C}_{18}$).—Yield (2.5 g, 65%), m.p. 87.4–90.0 °C (Found: C, 80.4; H, 11.0. $C_{51}H_{84}O_4$ requires C, 80.46; 11.13%); ν_{max}(nujol)/cm^{-1} 3310 (OH), 1655 and 1673 (C=O); δ_H(90 MHz; $CDCl_3$; Me_4Si; 30 °C) 0.88 [6 H, br t, $CH_2(CH_2)_{15}CH_3$], 1.32–1.67 [60 H, m, $CH_2(CH_2)_{15}CH_3$], 2.28 (6 H, s, $ArCH_3$), 2.87 (4 H, br t, *J* 7, $COCH_2$), 3.99 (2 H, s, $ArCH_2Ar$), 6.77 (2 H, s, OH), 7.65 (2 H, br s, ArH) and 7.77 (2 H, br s, ArH).

Gelation Tests.—$\mathbf{2}_n\mathrm{C}_m$ or $\mathbf{2'}_n\mathrm{C}_m$ (17.3 µmol in the benzene unit mol: *e.g.*, 5.0 mg for $\mathbf{2}_8\mathrm{C}_{12}$) was mixed with test solvent (0.5 cm^3) in a septum-capped test tube and the mixture was heated until the solid was dissolved. The solution was cooled to room temperature and concentrated gradually at room temperature (method A). Then, the solution was adjusted to 0.10 cm^3 and cooled to −20 °C (method B). All solvents used herein were of special grade.

T_{gel} *Measurements*.—To determine the sol–gel phase transition temperature (T_{gel}), we set up an inverted test tube containing the gel in a thermocontrolled water-bath. We raised the bath temperature at 1.0 °C min^{-1} and determined the temperature where the gel melted down. The T_{gel} values could be reproduced to an accuracy of ± 1.0 °C.

Miscellaneous.—The gel formation was observed by using an optical microscope (Olympus BH-2) with or without a phase differential condenser. Thermographic measurements were carried out using a DSC apparatus (Seiko Denshi DSC-220). Spectroscopic data were obtained by means of Bruker 250 MHz FT-NMR (AC-250P) for ^1H NMR spectroscopy and Shimadzu FT-IR 8100 for IR spectroscopy.

Results and Discussion

Physical Properties of Calixarene-based Gelators.—We previously found that recrystallization of $\mathbf{2}_8\mathrm{C}_{12}$ from benzene, hexane, or cyclohexane results in gels of these organic solvents. We thus performed the extensive gelation test for a variety of organic solvents. As shown in Table 1, the gelation at room temperature (method A) was observed for carbon disulfide, hydrocarbon solvents such as hexane, decane and cyclohexane, and alcohols such as isopropanol, butanol and hexanol. When the solution was cooled to −20 °C (method B), the gelation also occurred in carbon tetrachloride and aromatic hydrocarbon solvents such as toluene and benzene. Except for a few alcohol solvents, oxygen-containing solvents (*e.g.*, acetone, THF, *etc.*) did not gelate.

Gelation temperatures (T_{gel}) were determined for the heating process by means of the inverted test-tube method.[21] As illustrated in Fig. 1, the T_{gel} value increased with increasing $\mathbf{2}_8\mathrm{C}_{12}$ concentration. It is seen from Fig. 1 that the T_{gel} values for hexane (35–43 °C) are much higher than those for cyclohexane (16–27 °C) and carbon disulfide (18–24 °C), indicating the thermostability of the hexane gel, and the slope ($= \mathrm{d}T_{gel}/\mathrm{d}C$, °C/mg g^{-1}) is in the order of cyclohexane ($\mathrm{d}T_{gel}/\mathrm{d}C =$

Table 1 Organic fluids tested for gelation by 2_8C_{12}[a]

Organic fluids	Room temperature (method A)	0 °C (method B)
Toluene	S	G
Benzene	S	G[b]
Carbon tetrachloride	S	G
Chloroform	S → P	P
Dichloromethane	S	S
Carbon disulfide	S → G	G
Hexane	S → G	G
Decane	S → G	G
Cyclohexane	S → G	G
Acetone	I	I
Ethyl acetate	S → P	P
Dioxane	S → P	P
Tetrahydrofuran	S	P
Methanol	I	I
Ethanol	I	I
Isopropanol	S → G	G
Butanol	S → G	G
Hexanol	S → G	G

[a] S, soluble; P, precipitate formed; G, gel formed; I, insoluble. [b] The gel was formed before benzene solvent was solidified.

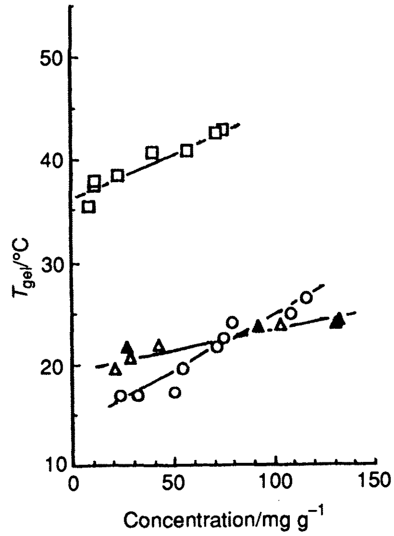


Fig. 1 Plots of T_{gel} *vs.* 2_8C_{12} concentration (2_8C_{12} mg per added solvent g): □, hexane; ○, cyclohexane; △, carbon disulfide; (T_{gel} values determined by an inverted test-tube method) and ▲, carbon disulfide (T_{gel} values determined by a DSC method)

0.107) > hexane (0.092) > carbon disulfide (0.041), indicating the thermosensitivity of the cyclohexane gel. To obtain the complementary data for these T_{gel} values, we estimated them by means of the DSC method. As shown in Fig. 2, the 2_8C_{12}–carbon disulfide gel gave a strong endothermic peak at 20–25 °C, and the peak minimum shifted to the higher temperature region with increasing 2_8C_{12} concentration. The similar curves were obtained for the cooling process, indicating that the sol–gel phase transition occurs reversibly. In spite of the shift of the peak minimum, the endothermic change always commenced at constant temperature (13.5 ± 1.4 °C: arrows in Fig. 2). The results indicate that the 'melting' of this gel starts at a constant temperature but the peak minimum is affected by the gelator concentration. The peak minimum obtained from the DSC method is plotted in Fig. 1. Clearly, these values are in good agreement with those determined by the inverted test-tube method. One can thus conclude that the T_{gel} determined herein corresponds to the sol–gel phase transition of these organic gels.

Interestingly, we found that the sol–gel phase transition is directly observable by an optical microscope. When the homogeneous carbon disulfide solution containing 2_8C_{12} was cooled below T_{gel}, the fibrillar aggregates appeared and finally grew up as a network [Fig. 3(*a*)]. The diameter of the fibrilles was about 1 μm. With the appearance of the network, the solution was transformed to the gel. The network was held permanently below 15 °C. When the gel was heated, the fibrillar aggregates melted at around T_{gel} and almost disappeared at 30 °C [Fig. 3(*b*)]. This process could be repeated reversibly many times.

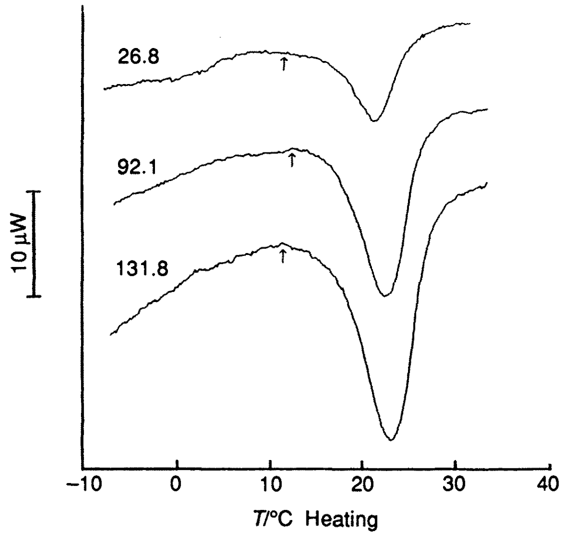
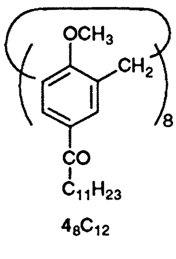


Fig. 2 DSC heating curves for the 2_8C_{12}–CS_2 gel: heating speed 2.0 °C min^{-1}. The numbers in the figure denote the concentration of 2_8C_{12} (mg g^{-1}).

We now consider why 2_8C_{12} is capable of transforming certain organic solvents into gels. In order to make the molecular network 2_8C_{12} must aggregate intermolecularly with the aid of some secondary valence forces. The possible forces expected for the intermolecular aggregation of 2_8C_{12} would be the C=O ··· HO hydrogen-bonding interaction and the C=O ··· C=O dipole–dipole interaction. To discriminate between these two interactions we synthesized 3_nC_m (n = 4, 6 and 8; m = 6 and 12)[12] which do not have the carbonyl group and 4_8C_{12} in which the OH groups are converted to the MeO groups. We confirmed that none of these compounds can transform the organic solvents (tested in Table 1) into gels. The finding establishes that the network is formed basically owing to the C=O ··· HO hydrogen-bonding interaction but not owing to the C=O ··· C=O dipole–dipole interaction. In order to find further evidence for such C=O ··· HO hydrogen-bonding interactions we measured the IR spectra of 2_8C_{12} in several solvents (hexane, cyclohexane, carbon disulfide, carbon tetrachloride, *etc.*) at several concentrations (1.81–33.1 mg g^{-1}) and several temperatures (20.0–75.0 °C). It is known that the formation of the C=O ··· HO hydrogen bond induces the shift of ν_{OH} and $\nu_{C=O}$ to lower frequency region and the broadening of the ν_{OH} band.[22] In $2'_1C_{12}$ (in carbon tetrachloride at 26.0 °C), for example, the ν_{OH} band appears at 3611 cm^{-1} at the low concentration (3.01 mg g^{-1}) whereas it appears as a broad band at 3610–3100 cm^{-1} at the high concentration (60.4 mg g^{-1}: Fig. 4). The former is assigned to a free OH stretching band whereas



4_8C_{12}

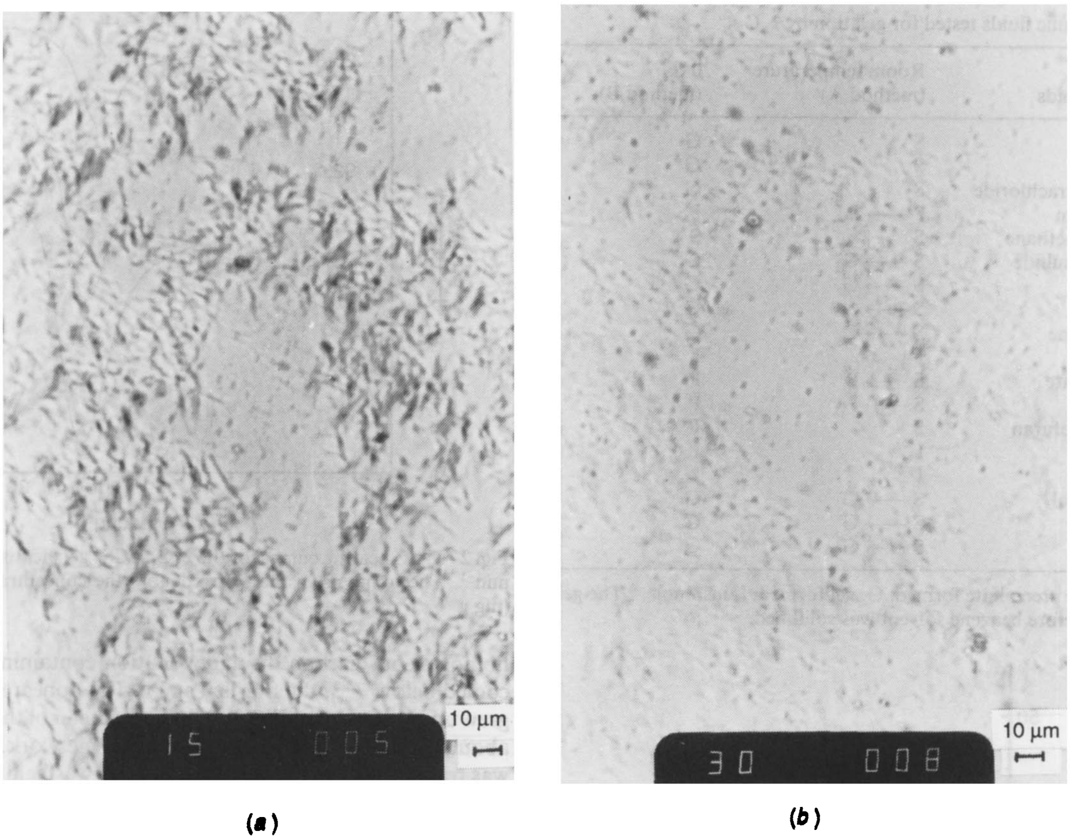


Fig. 3 Optical micrographs of 2_8C_{12} in carbon disulfide: $[2_8C_{12}] = 36.4$ mg g^{-1}: (*a*) the network which grew up at 15 °C, (*b*) the sample which was obtained when (*a*) was heated at 30 °C

the latter to a hydrogen-bonded OH stretching band. The $\nu_{C=O}$ band (1682 cm^{-1} at the low concentration) also shifts to lower frequency region (1664 cm^{-1} at the high concentration). In 2_8C_{12}, on the other hand, a broad ν_{OH} band appeared at 3250 cm^{-1} and an additional peak assignable to a free OH stretching band was not found (Fig. 4). The spectrum was scarcely affected by the temperature and the concentration. As is well-known, calix[*n*]arenes feature strong intramolecular hydrogen-bonding interactions.[1,2,23,24] The initial findings thus imply that even though a significant amount of intermolecular C=O • • • HO hydrogen bonds are formed, it is difficult to detect them separately from intramolecular C=O • • • HO hydrogen bonds. Also, the significant shift of the $\nu_{C=O}$ band was not observed for 2_8C_{12}. In conclusion, we could not obtain any concrete evidence for the formation of the intermolecular hydrogen bond from IR spectroscopy. We consider, however, that the gel network is effectively maintained if one or two OH groups in 2_8C_{12} of eight OH groups can be used for the formation of the intermolecular hydrogen bond. This problem will be discussed again later in comparison with the non-cyclic analogues.

As shown in Table 1, the gel formation is limited to hydrocarbon solvents (except a few alcohols) which do not involve an oxygen atom. This suggests that the oxygen atom in solvent molecules can compete with the C=O groups for the formation of the hydrogen bond and can destroy the gel network. We measured the DSC thermograph for the carbon disulfide gel in the presence of a small amount of acetone. As shown in Fig. 5, the peak maximum gradually shifted to lower temperature region and finally disappeared at 20.5 mg acetone in 1.0 g carbon disulfide. The result clearly indicates that the formation of the intermolecular C=O • • • HO hydrogen bond plays a crucial role for the stabilization of the gel network.

We tested the gelation ability of nine 2_nC_m homologues. Among three 2_8C_m homologues (m = 6, 12 and 18) 2_8C_{12} and 2_8C_{18} showed the gelation ability but 2_8C_6 did not. The similar

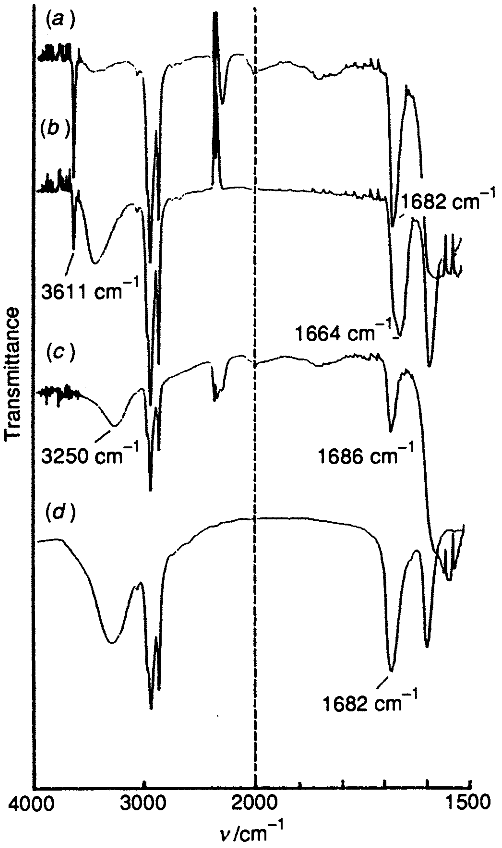


Fig. 4 IR spectra of $2'_1C_{12}$ and 2_8C_{12}: (*a*) $2'_1C_{12}$ (3.01 mg g^{-1} in CCl$_4$) at 26 °C, (*b*) $2'_1C_{12}$ (60.4 mg g^{-1} in CCl$_4$) at 26 °C, (*c*) 2_8C_{12} (1.81 mg g^{-1}) in CCl$_4$ at 20 °C and (*d*) 2_8C_{12} in the solid state

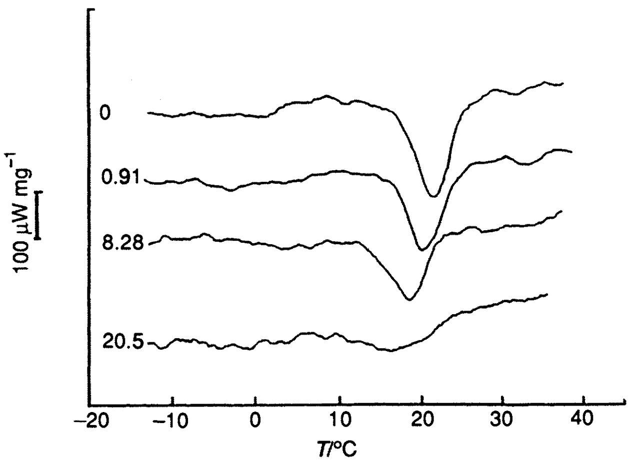


Fig. 5 DSC heating curves of the 2_8C_{12}–CS_2 gel in the presence of acetone. The numbers in the figure denote the concentration of added acetone (in mg g^{-1}). 2_8C_{12} concentration: 40.1 mg g^{-1}.

Table 2 Gelation ability of 2_nC_m and their non-cyclic analogues $2'_nC_m$[a]

	2_nC_m			$2'_nC_m$	
m	*n* = 4	6	8	*n* = 1	2
6	×	×	×	×	×
12	×	×	○(20.0 °C)[b]	×	×
18	○(31.2 °C)[b]	×	○(31.4 °C)[b]	×	○(37.5 °C)[b]

[a] ○ denotes that the compound is capable of gelatinizing hydrocarbon solvents (toluene, benzene, hexane and cyclohexane), carbon tetrachloride, and carbon disulfide at 0 °C. × denotes that the gelation is not observed in any solvents listed in Table 1. [b] T_{gel} in toluene (concentration 80.0 mg g^{-1}).

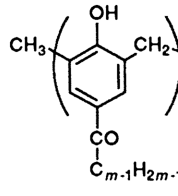
Table 3 Organic fluids tested for gelation by $2'_2C_{18}$[a]

Organic fluids	Room temperature (method A)	0 °C (method B)
Toluene	S → G	G
Benzene	S → G	G
Carbon tetrachloride	S → P	G
Carbon disulfide	S → P	G
Cyclohexane	S → G	S → G
Hexane	S → P	S → G
iso-Propanol	S → P	P
Butanol	S → P	P
Hexanol	S → P	P

[a] S, soluble; P, precipitate formed; G, gel formed.

trend was observed for 2_4C_m homologues: 2_4C_{18} showed the gelation ability but 2_4C_6 and 2_4C_{12} did not. As mentioned above, the first prerequisite for the gel formation is the moderate intermolecular interaction among gelator molecules. The data in Table 2 reveal that the second prerequisite is the moderate 'affinity' between gelator and solvent, because the formation of the stable organic gels is limited to 2_8C_{12}, 2_8C_{18} and 2_4C_{18} that have the longer aliphatic chains. The solvent effect observed for alcohols may be explained on the same basis. 2_8C_{12} is insoluble in methanol and ethanol whereas it is soluble in isopropanol, butanol and hexanol (Table 1). Thus, provided that the moderate intermolecular interaction exists in the latter solvents and the network is formed, 2_8C_{12} can act as a gelator of these solvents. Basically, the OH group in alcoholic solvents can act as both a proton donor and a proton acceptor and therefore may destroy the gel network of 2_8C_{12}. The gel formation observed for 2_8C_{12} implies that the $(2_8C_{12})C{=}O \cdots HO(2_8C_{12})$ interaction is stronger than the $(2_8C_{12})C{=}O \cdots HO$(alcohol) interaction and the $(2_8C_{12})OH \cdots OH$(alcohol) interaction. It is clear that the C=O oxygen is more electronegative than the alcoholic OH oxygen[25] and the phenolic OH proton in 2_8C_{12} is more acidic than the alcoholic OH proton.[26-29] Thus, the aggregation of 2_8C_{12} is achieved by the combination of the more electronegative proton acceptor and the more acidic proton donor. This is why the gelation can take place even in some alcoholic solvents. However, 2_8C_{12} is a rare example which shows the gelation ability for alcohols. Strangely, none of 2_6C_m homologues showed the significant gelation ability. This reason is not well understood at present. We only know that the solubility of 2_6C_m homologues is much inferior to that of 2_4C_m and 2_8C_m homologues. Presumably, 2_6C_m homologues cannot satisfy the second prerequisite.

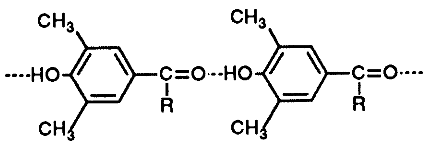
Molecular Design of Non-cyclic Gelators.—As discussed above, 2_4C_{18}, 2_8C_{12} and 2_8C_{18} act as excellent gelators of many organic solvents. It is undoubted that the driving force for the gelation is the intermolecular interaction through the C=O ··· HO hydrogen bonds, but we could not estimate how many OH groups are included in the formation of such intermolecular hydrogen bonds. It occurred to us that the minimum number of hydrogen bonds required for the gelation may be estimated through the examination of the non-cyclic analogues. With this object in mind we synthesized $2'_nC_m$ homologues (*n* = 1 and 2; *m* = 6, 12 and 18). The gelation ability of these homologues (if any) may also provide an answer to the question of the macrocyclic structure being indispensable to the gelation.



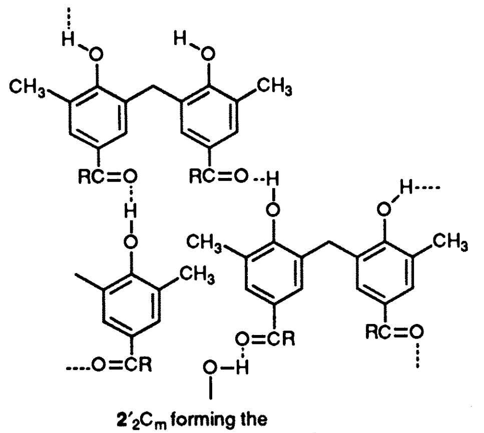
$2'_nC_m$

The results of the gelation test are summarized in Tables 2 and 3. We found that among six non-cyclic analogues, $2'_2C_{18}$ with the longer aliphatic chains shows the gelation ability comparable with 2_nC_m (although they could not transform alcohols into gels). Here again, the results support that the second prerequisite (*i.e.*, the moderate affinity between gelator and solvent) is indispensable. Interesting is the comparison of $2'_1C_{18}$ and $2'_2C_{18}$: it is expected that these two compounds have the similar solvent affinity, but $2'_2C_{18}$ can act as a gelator whereas $2'_1C_{18}$ cannot. The difference should be attributed to the first prerequisite (*i.e.*, the intermolecular interaction). $2'_1C_{18}$ has one C=O and one OH, so that the intermolecular interaction through the C=O ··· HO hydrogen bonds results in a linear 'polymer.' The linear 'polymer' cannot form the three-dimensional network. In contrast, $2'_2C_{18}$ has two C=O and two OH, so that the three-dimensional network can be constructed through the C=O ··· HO hydrogen bonds. We believe that this network formation is the origin of the gelation.

The results tell us that in the gelation by 2_8C_{12}, two of eight OH groups (at least) should be used for the formation of the intermolecular hydrogen bonds. Calix[8]arenes have the largest number of OH groups. Also, it is considered that the intramolecular hydrogen bonds in calix[8]arenes are relatively weaker than those in calix[4]arenes and calix[6]arenes.[26-29] These two advantages in the intermolecular aggregation are related to the superiority of calix[8]arenes over calix[4]arenes and calix[6]arenes as a gelator.



$\mathbf{2'_1C_m}$ forming
the linear 'polymer'



$\mathbf{2'_2C_m}$ forming the
three-dimensional network

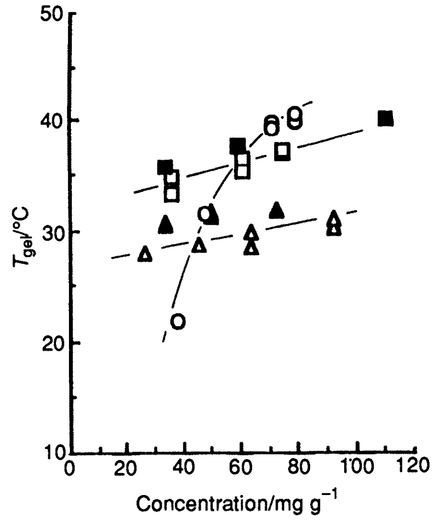


Fig. 6 Plots of T_{gel} *vs.* $\mathbf{2'_2C_{18}}$ concentration ($\mathbf{2'_8C_{18}}$ mg per added solvent g): ○, carbon tetrachloride; □, toluene; △, carbon disulfide by the inverted test-tube method; ■, toluene; ▲, carbon disulfide by the DSC method

We further characterized the gelation process in $\mathbf{2'_2C_{18}}$. Fig. 6 shows plots of T_{gel} (determined by the inverted test-tube method) *vs.* $\mathbf{2'_2C_{18}}$ concentration. The T_{gel} values for $\mathbf{2'_2C_{18}}$ appeared at around 30 °C and the slopes ($\mathrm{d}T_{gel}/\mathrm{d}C$, 0.083 °C/mg g^{-1} for toluene and 0.039 °C/mg g^{-1} for carbon disulfide) were comparable with those for $\mathbf{2_8C_{12}}$. The results show that the thermal stability of non-cyclic $\mathbf{2'_2C_{18}}$ is comparable with that of $\mathbf{2_8C_{12}}$ and the macrocyclic structure is not necessarily required for the gelation. The sol–gel phase transition could be also monitored by the DSC method. The peak minima are plotted in Fig. 6. Clearly, the T_{gel} values determined by the DSC method are in good agreement with those determined by the inverted test-tube method. It is also seen from Fig. 6 that carbon tetrachloride shows the exceptionally steep concentration dependence: T_{gel} = 24.3 °C at [$\mathbf{2'_2C_{18}}$] = 40.0 mg g^{-1} and T_{gel} = 37.5 °C at [$\mathbf{2'_2C_{18}}$] = 60.0 mg g^{-1}.

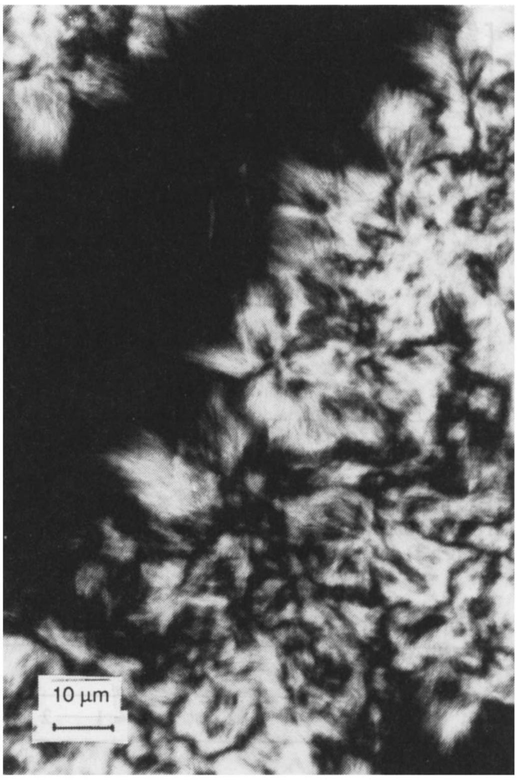


Fig. 7 Optical micrograph of $\mathbf{2'_2C_{18}}$ (150.7 mg g^{-1}) in carbon disulfide under crossed Nicol prisms at room temperature. Under these conditions the sample is in the gel phase.

The network formed from $\mathbf{2'_2C_{18}}$ could not be observed directly by an optical microscope. Instead, we found that when the sample is observed under crossed Nicol prisms, the bright network pattern appears below T_{gel} (Fig. 7). When the sample was heated, the pattern disappeared at around T_{gel} to give a dark background. Since this process can be reproduced many times, the sol–gel phase transition of $\mathbf{2'_2C_{18}}$ is also reversible.

The ^{1}H NMR spectra gave several lines of interesting information about the molecular motion of the $\mathbf{2'_2C_{18}}$–toluene gel (Figs. 8 and 9). At 55 °C (sol phase: T_{gel} is 37 °C under the conditions recorded in the caption to Fig. 8) we can assign all peaks to $\mathbf{2'_2C_{18}}$ and toluene (impurity in [$^2H_8$]toluene) and the vicinal coupling can be distinctly observed. At around T_{gel} the peaks for $\mathbf{2'_2C_{18}}$ are significantly broadened whereas those for toluene are not (Fig. 9). Below T_{gel} the peaks for $\mathbf{2'_2C_{18}}$ are no longer detectable because of the line-broadening and those for toluene are broadened gradually with decreasing temperature. The foregoing temperature-dependent spectral change implies that the molecular motion of $\mathbf{2'_2C_{18}}$ is allowed to some extent at around T_{gel} whereas it is completely quenched below T_{gel}. On the other hand, toluene molecules in the gel are bound less tightly even below T_{gel}.

The concentration change also gives the interesting information on the aggregation property. In the IR spectra in carbon tetrachloride at 26 °C, three different ν_{OH} bands (at 3483, 3382 and 3600 cm^{-1}) appear at low concentration region (Fig. 10). These are assigned to the ν_{OH} for C=O ••• HO, HO ••• HO (both inter- and intra-molecular) and free OH, respectively.[22] With the increase in the concentration the intensity in the free OH band decreases and the residual two bands coalesce to shift to a lower frequency region. Complementarily to this change, the $\nu_{C=O}$ band (1680 cm^{-1} at the low concentration) shifts to lower frequency region and finally is split into two peaks (1659 and 1673 cm^{-1}). It is clear that the new band at 1659 cm^{-1} is assigned to the hydrogen-bonded C=O group.[22]

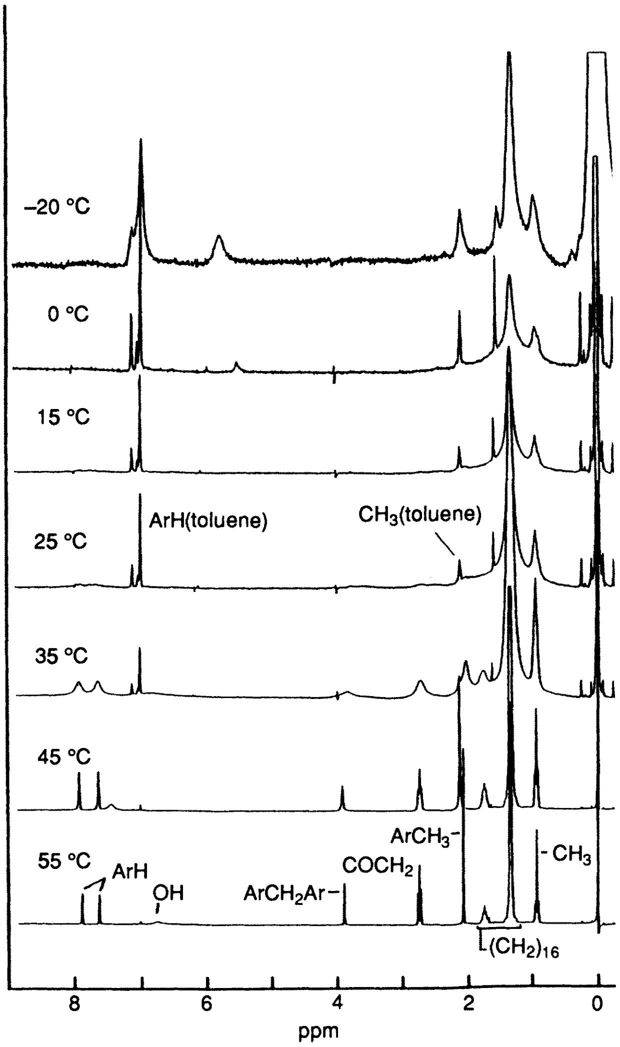


Fig. 8 ^{1}H NMR spectra of $2'_2C_{18}$ (78.3 mg g^{-1}) in [$^2H_8$]toluene on heating process (gel to solution)

Conclusions

The motive of the present study is the 'accidental' finding that certain *p*-acylated calix[*n*]arenes are capable of transforming various organic solvents into gels. Through the mechanistic studies it was shown that the macrocyclic calix[*n*]arene structure is not necessarily required for the gelation. The basic requirements are (i) the intermolecular hydrogen-bonds to construct the three-dimensional network and (ii) the moderate affinity between gelator and solvent. Combination of the phenolic OH (as a hydrogen-bond donor) and the C=O group (as a hydrogen-bond acceptor) is excellent because the OH group is moderately acidic and the carbonyl oxygen is relatively electronegative. This is why 2_8C_{12} can make the stable gels even in alcohol solvents. Although the macrocyclic calix[*n*]arene structure is not necessarily required, 2_nC_m homologues are still superior to non-cyclic $2'_nC_m$ homologues, for example, in the gelation of alcohols. Presumably, this is due to the stronger acidity of OH group in 2_nC_m, which arises from the ring structure.[26–29]

We believe that the findings systematically reviewed in this paper would provide basic strategies for the design of new gelators of organic fluids. This system will become useful, from a practical viewpoint, for use in the condensation of alcohols, recovery of organic solvents, molecular recognition in gels, *etc.*

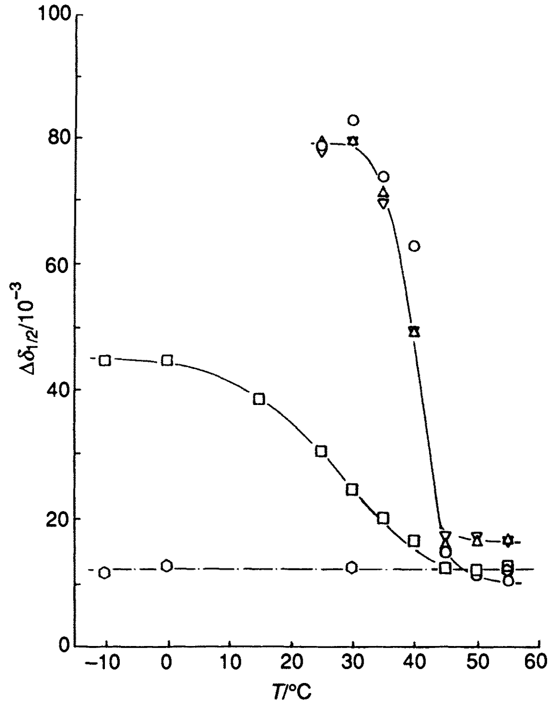


Fig. 9 Plots of the half-height peak-width ($\Delta\delta_{\frac{1}{2}}$, *vs.* temperature. The figure is made from the spectral change in Fig. 8: △ and ▽, ArH of $2'_2C_{18}$ (lower and higher field, respectively); ○, $ArCH_2Ar$; □ and ◯, ArH due to the solvent in the presence and absence of $2'_2C_{18}$, respectively.

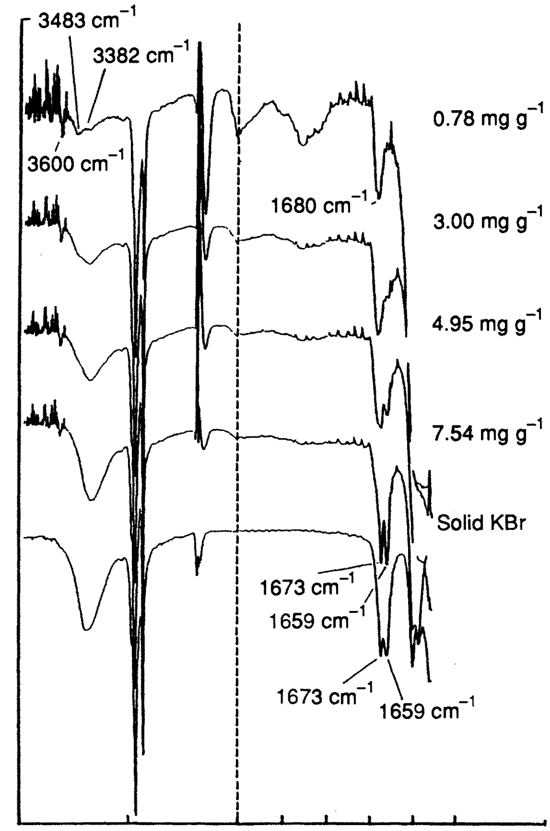


Fig. 10 IR spectra of $2'_2C_{18}$ in carbon tetrachloride at 26 °C

Acknowledgements

We thank Dr. T. D. James for helpful discussions and Mrs. S. Uchida for technical assistance.

References

1 C. D. Gutsche, *Calixarenes*, Royal Society of Chemistry, Cambridge, 1989.

2 C. D. Gutsche, *J. Inclusion Phenom. Mol. Recog.*, 1989, 7, 61.

3 M. A. Markowitz, R. Bielski and S. L. Regen, *Langmuir*, 1989, **5**, 276.

4 M. A. Markowitz, V. Janout, D. G. Castner and S. L. Regen, *J. Am. Chem. Soc.*, 1989, **111**, 8192.

5 Y. Nakamoto, G. Kallinowski, V. Böhmer and W. Vogt, *Langmuir*, 1989, **5**, 1116.

6 S. Shinkai, H. Kawabata, T. Arimura, T. Matsuda, H. Satoh and O. Manabe, *J. Chem. Soc., Perkin Trans. 1*, 1989, 1073.

7 S. Shinkai, T. Arimura, K. Araki, H. Kawabata, H. Satoh, T. Tsubaki, O. Manabe and J. Sunamoto, *J. Chem. Soc., Perkin Trans. 1*, 1989, 2039.

8 Y. Nakamoto, T. Ozu, S. Ohya and S. Ishida, *Netsu Kohkasei Jushi*, 1985, **6**, 51.

9 Z. Asfai and J. Vicens, *Tetrahedron Lett.*, 1988, **29**, 2659.

10 K. No, Y. Noh and Y. Kim, *Bull. Korean Chem. Soc.*, 1986, **7**, 422.

11 T. Arimura, S. Shinkai, T. Matsuda, Y. Hirata, H. Satoh and O. Manabe, *Bull. Chem. Soc. Jpn.*, 1988, **61**, 3733.

12 S. Shinkai, T. Nagasaki, K. Iwamoto, A. Ikeda, G.-X. He, T. Matsuda and M. Iwamoto, *Bull. Chem. Soc. Jpn.*, 1991, **64**, 381.

13 Y.-C. Lin, B. Kachar and R. G. Weiss, *J. Am. Chem. Soc.*, 1989, **111**, 5542.

14 T. Brotin, R. Utermohlen, F. Fages, H. Bouas-Laurent and J.-P. Desvergne, *J. Chem. Soc., Chem. Commun.*, 1991, 416.

15 R. J. Twieg, T. P. Russell, R. Siemeus and J. F. Rabolt, *Macromolecules*, 1985, **18**, 1361.

16 R. H. Wade, P. Terech, E. A. Hewat, R. Ramasseul and F. Volino, *J. Colloid Interface Sci.*, 1986, **114**, 422.

17 K. Murata, M. Aoki, T. Nishi, A. Ikeda and S. Shinkai, *J. Chem. Soc., Chem. Commun.*, 1991, 1715.

18 K. Murata, M. Aoki and S. Shinkai, *Chem. Lett.*, 1992, 739.

19 M. Aoki, K. Murata and S. Shinkai, *Chem. Lett.*, 1991, 1715 (preliminary communication).

20 C. D. Gutsche and L.-G. Lin, *Tetrahedron*, 1986, **42**, 1633.

21 M. Irie and R. Iga, *Makromol. Chem., Rapid Commun.*, 1985, **6**, 403.

22 B. George and P. McIntyre, in *Infrared Spectroscopy*, John Wiley & Sons, London, 1987.

23 C. D. Gutsche, *Acc. Chem. Res.*, 1983, **16**, 161.

24 C. D. Gutsche and L. J. Bauer, *J. Am. Chem. Soc.*, 1985, **107**, 6052.

25 T. Sakaki, I. Aoki, T. Harada, G. Deng, Y. Kawahara and S. Shinkai, to be submitted.

26 K. Araki, K. Iwamoto, S. Shinkai and T. Matsuda, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 3480.

27 S. Shinkai, K. Araki, P. D. J. Grootenhuis and D. N. Reinhoudt, *J. Chem. Soc., Perkin Trans. 2*, 1991, 1833.

28 I. Yoshida, N. Yamamoto, F. Sagara, D. Ishii, K. Ueno and S. Shinkai, *Bull. Chem. Soc. Jpn.*, 1992, **65**, 1012.

29 J.-P. Scharff and M. Mahjoubi, *New. J. Chem.*, 1991, **15**, 883.

Paper 2/05281D
Received 1*st October* 1992
Accepted 30*th November* 1992