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Organogels of azacrown-appended cholesterol derivatives can be stabilized by host–guest interactions

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Abstract

The gelation ability of crown-ether-containing cholesterol derivatives was investigated in the presence of mono- and diamines. The organogels were remarkably stabilized in the presence of certain diamines. This is the first example for the stabilization of organogels by host–guest-type interactions. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: gelators; azacrown-containing cholesterol; intermolecular hydrogen-bond; chirality.

Recently, exploitation of new organic gelators which can gelate various organic solvents has become an active research area of endeavor.[1–12] These organogels are of particular interest in that being different from polymer gels, fibrous aggregates of low molecular-weight compounds formed by non-covalent interactions are responsible for such gelation phenomena. This is why the xerogels can exhibit various superstructures, reflecting the monomeric structure of each gelator.

Since the organogel stability should be closely related to the superstructures thus formed, we considered that it would be sensitively affected by modification of the superstructures by additives which can interact with the gelators (e.g., by the host–guest interaction). It particular, when the additives can enhance the sol-gel phase-transition temperature (T_{gel}), it follows that the fragility, a common drawback of organogels, may be rectified to some extent. Very recently, the validity of this idea was demonstrated in a few systems.[13,14]

We considered that the host–guest-type interaction by which two (or more) gelators are bridged would be useful to enhance the gelation ability. It is known that certain (aza)crown-appended cholesterol derivatives can act as good gelators of organic solvents.[7,11] In these systems, the major driving-force for the gel formation is considered to be molecular stacking between cholesterol moieties and between azobenzene moieties.[7,12] Hence, these gelators can be readily bridged by diamines (or oligoamines) using an amine-(aza)crown hydrogen-bonding interaction. We thus attempted the reinforcement of organogels

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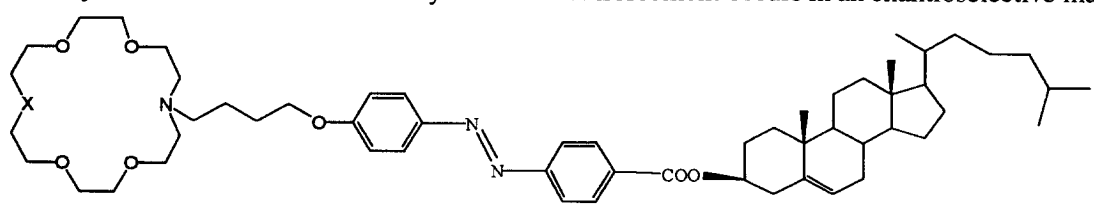
Table 1
Influence of added diamines on the gelation ability[a]

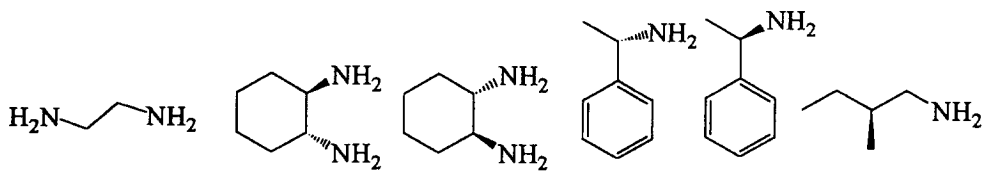
solvent	1	1/3	1/(S)-4	1/(R)-4	2	2/3	2/(S)-4	2/(R)-4
1-butanol	G	G	G	G	G	G	G	G
1-hexanol	G	G	G	G	G	G	G	G
1-octanol	G	G	G	G	G	G	G	G
DMSO	G	G	G	G	G	G	G	G
n-hexane	I	I(G)[b]	I(G)[b]	I(G)[b]	I	I(G)[b]	I(G)[b]	I(G)[b]
cyclohexane	PG	G	G	G	PG	PG	G	G
methylcyclohexane	PG	G	G	G	G	G	G	G
dichloromethane	S	S	S	S	S	S	S	S
THF	S	S	S	S	S	S	S	S
benzene	S	S	S	S	S	S	S	S
toluene	S	S	S	S	S	S	S	S

[a][Gelator]=5.0 wt%, [amine]/[gelator]=1:2 mol/mol); [b][amine]/[gelator]=10:1 (mol/mol); G = stable gel formed at room temperature; S = solution; I = insoluble; PG=partially gelatinzed.

supported by azacrown-appended cholesterol derivatives **1** and **2** using diamines **3** and **4**. Monoamines **5** and **6** were used as reference compounds. Surprisingly, we found that the gelation ability was significantly intensified by the diamines and in certain systems the reinforcement occurs in an enantioselective manner.



1: X=NH, **2**: X=O



3 (R)-4 (S)-4 (R)-5 (S)-5 (S)-6

Compounds **1** and **2** were synthesized by treating mono- and diaza-18-crown-6 with a monobromobutyloxyazobenzene derivative of cholesterol in refluxing butyronitrile for 48 h. Compounds **1** and **2** were obtained in 35 and 45% yields, respectively, after workup with chromatography and identified by IR, ^{1}H NMR, ^{13}C NMR and MS (SIMS) spectral evidence and elemental analyses.

The gelation test was carried out in the absence and the presence of the amines in 11 organic solvents. The results are summarized in Table 1. It is seen from Table 1 that **1** and **2** can gelate most alcoholic solvents. The specific effect of the diamines appeared in cyclohexane and *n*-hexane. '**PG** and **I**' for **1** and **2** in cyclohexane and *n*-hexane became '**G**' in the presence of **3**, (*R*)-**4** and (*S*)-**4** (for the notation see (a) in Table 1). This phase change is attributed to the intermolecular hydrogen-bonding interaction between one diamine and two azacrown rings. This bridging effect should result in the stabilization of the organogel state.

We further observed the details of gelation properties in 1-hexanol. Very surprisingly, the stoichiometric ratio for the host–guest interaction was easily established by measuring the T_{gel} as a function of the

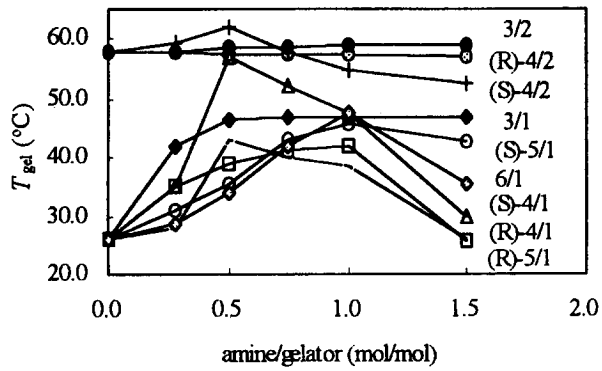


Figure 1. Influence of guest addition on T_{gel} of **1** and **2** according to a molar ratio plot: [**1**] or [**2**]=5.0×10^{-2} mol dm^{-3} in 1-hexanol

molar ratio of amines keeping the gelator concentration constant. It is clearly seen from Fig. 1 that the T_{gel} values of **1** in the presence of **4** increase at [**4**]/[**1**]<0.5 while they decrease at [**4**]/[**1**]>0.5, giving rise to a maximum at [**4**]/[**1**]=0.5. A similar result was also obtained from **3**: the T_{gel} gradually increases at [**3**]/[**1**]<0.5 and then maintains nearly the constant value above [**3**]/[**1**]=0.5.[15] In contrast, plots for the monoamines give rise to a maximum or a saturation at [**5**] or [**6**]/[**1**]=1.0. The results clearly support the hydrogen-bonding modes that one diamine interacts with two **1** gelators whereas monoamine and **1** form a 1:1 stoichiometric complex. It is also seen from Fig. 1 that the T_{gel} values of **1** with diamines are higher than those of monoamines at their optimum molar ratio. These results suggest that the bridging effect expected for the diamines only is the primary driving-force for stabilization of these mixed organogel systems. The increase in the T_{gel} of **2** with amines was not as striking as that of **1**. Presumably, this difference is rationalized as such that the hydrogen-bond acceptability of the NO_5 crown in **2** is not as strong as the N_2O_4 crown in **1**.

Careful examination of Fig. 1 reveals another interesting feature of the present host–guest-type organogel system. The T_{gel} values for **1** are different between (*R*)-**4** and (*S*)-**4** and between (*R*)-**5** and (*S*)-**5**: the T_{gel} for (*S*)-**4** is higher than that for (*R*)-**4** at all concentration region. These results indicate that the present organogel system, which is comprised of 'chiral' cholesterol derivatives, is 'enantioselectively' reinforced by chiral amine additives.

To obtain an insight into the influence of added amines on the gel stability, we prepared xerogel in the absence and the presence of **3** and **4** from cyclohexane and observed their morphology by SEM (Fig. 2). The purpose was to visually detect the influence of added amines, particularly, of the enantiomeric amines on the superstructures. It is seen from these SEM pictures that **1** constructs a cylindrical structure with 45–75 nm wall thickness and 170–390 nm inside tube diameter. However, no significant difference was found in their visual morphology between **1** in the absence and those in the presence of diamines. Hence, the influence of added amines is not so large as to change the superstructure.

The change in complementarity in the hydrogen-bonding interaction between host and guest in the organogel system was conveniently and sensitively monitored by FT-IR spectroscopy.[9] Hence, we measured the IR spectra to obtain evidence for the difference in the hydrogen-bonding network. Compound **1** in the cyclohexane solution gave ν_{NH} at 3340 cm^{-1} whereas the cyclohexane gel of **1** gave a new peak at 3320 cm^{-1} in addition to that at 3340 cm^{-1}. These results imply that the 3320 cm^{-1} peak arises from aggregated **1** in the organogel. When diamines were added, this new peak was markedly intensified indicating that diamines are trapped in the gel phase by the hydrogen-bonding interaction. This peak is ascribed to the hydrogen-bonded NH peak between **1** and added amines. These results imply

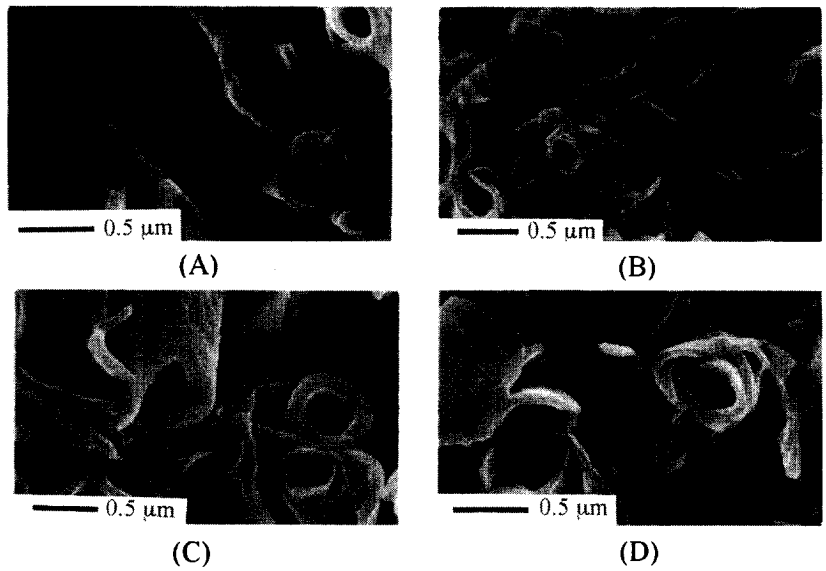


Figure 2. SEM pictures of organogel **1** from cyclohexane in the: (A) absence and the presence of (B) **3**, (C) (*R*)-**4** and (D) (*S*)-**4**

that the major driving force for the gel reinforcement is the intermolecular hydrogen-bonding interaction between the gelator and added amines. However, no significant spectral difference was formed between (*R*)-**4** and (*S*)-**4**.

It is known that a subtle change in the superstructures of cholesterol-based gelators can be detected by CD (circular dichroism) spectra.[7,11] In the present system the organogels were obtained only at the high gelator concentration, so that the CD spectra could not be measured even with the thinnest 0.05 mm cell. Hence, we sandwiched the sample with two glass plates to make the light path as thin as possible. The 1-hexanol gels of **1** (5.0×10^{-2} mol dm^{-3})+(*R*)-**4** and (*S*)-**4** (2.5×10^{-2} mol dm^{-3}) gave excitation–coupling-type CD spectra with $\lambda_{\theta=0}$362 nm which was in accord with the absorption maximum 362 nm (the spectra are not shown here). The first positive Cotton effect was observed at 398 nm for the (*R*)-**4**-containing gel and at 393 nm for the (*S*)-**4** containing gel. The difference implies that the chiral orientation of **1** is affected by these chiral amines.

In conclusion, we have demonstrated for the first time that the organogels comprised of crown-containing gelators can be more stabilized by the hydrogen-bond-based bridging effect. Furthermore, some gelator can discriminate the 'chirality' of amines in the gelation process. We believe that these gel systems will lead to molecular design of new gelators stabilized by host–guest interactions and chiral discrimination of amines in the gel state will become possible.

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