Small Molecular Gelling Agents to Harden Organic Liquids: Trialkyl *cis*-1,3,5-Cyclohexanetricarboxamides

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Trialkyl *cis*-1,3,5-cyclohexanetricarboxamides were able to cause physical gelation in organic liquids to afford completely transparent organogel. The main driving force for gelation was intermolecular hydrogen bonding between amides and van der Waals interaction among hydrophobic alkyl chains.

Some dilute binary solutions of low-molecular weight compounds can form thermally-reversible physical gel in appropriate organic liquids. In general, such organogel-forming compounds self-associate spontaneously to harden organic liquids on cooling of appropriate isotropic solution. The gelation by low-molecular weight compounds is also interesting in the field of supramolecular chemistry[1,2] due to the fact that the main driving forces for the physical gelation are hydrogen bonding, hydrophobic interaction, π–π interaction, and electrostatic interaction. However, only twenty families of compounds[3-9] are known as molecules capable of causing physical gelation. Although we have discovered the strong gelation abilities of derivatives of trans-(*1R,2R*)-1,2-diaminocyclohexane,[3,4] in this paper we wish to report trialkylamides (**1**-**4**)[10] of *cis*-1,3,5-cyclohexanetricarboxylic acid as new organogel-forming molecule, designed in the hope that it might aggregate spontaneously as a result of two cooperating noncovalent forces: intermolecular hydrogen bonding among the amides located at equatorial positions of cyclohexane ring and hydrophobic association among the long hydrocarbon tails. It should be mentioned that three carboxylic groups of *cis*-1,3,5-cyclohexanetricarboxylic acid and two amino groups of trans-(*1R,2R*)-1,2-diaminocyclohexane are located at the equatorial positions of the cyclohexane ring.

A typical procedure for gelation test is described below: a weighed compound was mixed with organic liquid (1 cm^3) in a septum-capped test tube and the mixture was heated until the solid was dissolved. The resulting solution was cooled at 25 ℃ for 1 h and then the gelation was checked out visually. A test tube filled with gelled sample could be turned upside down without significant flow. When highly viscoelastic fluid was formed in the tube, we judged it to be "gel-like".

The results of gelation test are summarized in Table 1. Trihexyl *cis*-1,3,5-cyclohexanetricarboxamide (**1**) has almost no gelation ability in organic fluids except for pyridine, while tridodecyl and trioctadecyl *cis*-1,3,5-cyclohexanetricarboxamides (**2**, **3**) are excellent gel-forming molecules for nonpolar organic fluids, including THF, cyclohexane, benzene, toluene, chlorobenzene, kerosene, and salad oil. The fact that gel fails to form when the chain is shortened from 12 carbons (**2**) to 6 carbons (**1**) implies the significance of intermolecular hydrophobic interaction among the alkyl chains. The formed gels, which were colorless and completely transparent in appearance, were so stable that they were not converted to crystals or viscoelastic fluids even after a half year. The value in parenthesis means minimum gel concentration which is the mass (g) of **1**-**4** necessary to solidify 1 dm^3 of liquid. For example, the amounts of **3** necessary to solidify 1 dm^3 of tetrachloromethane, THF, hexane, cyclohexane, benzene, and pyridine are 5 g, 9 g, 1 g, 2 g, 3 g, and 1 g, respectively. These mean that 1 molecule of **3** immobilizes *ca.* 2000 molecules of tetrachloromethane, *ca.* 1300 molecules of THF, *ca.* 7400 molecules of hexane, *ca.* 4400 molecules of cyclohexane, *ca.* 3600 molecules of benzene, and *ca.* 12000 molecules of pyridine. The gelation abilities of **2**-**4** were almost comparable to those of alkylamides[3] and alkylureas[4] derived from trans-(*1R,2R*)-1,2-diaminocyclohexane.

1; R = $CH_2(CH_2)_4CH_3$
2; R = $CH_2(CH_2)_{10}CH_3$
3; R = $CH_2(CH_2)_{16}CH_3$
4; R = $CH_2CH_2CH(CH_3)CH_2CH_2CH_2CH(CH_3)_2$

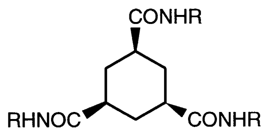


Table 1. Gelation test of trialkyl *cis*-1,3,5-cyclohexanetricarboxamides (**1**-**4**) toward organic solvents at 25 ℃[a]

solvent	1	2	3	4
ethanol	insol.	cryst.	cryst.	cryst.
ethyl acetate	insol.	cryst.	cryst.	insol.
2-butanone	insol.	cryst.	cryst.	cryst.
DMF	cryst.	cryst.	cryst.	cryst.
Me_2SO	cryst.	cryst.	cryst.	cryst.
chloroform	insol.	cryst.	cryst.	cryst.
tetrachloromethane	insol.	gel-like	gel(5)	gel-like
THF	insol.	gel(25)	gel(9)	soln.
hexane	insol.	insol.	gel(1)	gel(60)
cyclohexane	insol.	gel(1)	gel(2)	gel-like
benzene	insol.	gel(5)	gel(3)	gel-like
toluene	insol.	gel(2)	gel(5)	gel(60)
chlorobenzene	insol.	gel(6)	gel(3)	gel(60)
pyridine	gel(3)	gel(15)	gel(1)	gel-like
kerosene	insol.	gel(3)	gel(1)	gel(17)
salad oil	insol.	gel(13)	gel(2)	insol.

[a] insol. = almost insoluble; cryst. = crystallization; gel-like = highly viscoelastic fluid; soln. = isotropic solution at a glance.

It is noteworthy that the marked rise of viscosity was observed by adding **2** or **4** to some organic liquids at very low concentration. The indication of "gel-like" in Table 1 shows the formation of such transparent highly viscoelastic fluids. Viscosity was calculated by corrected density and kinematic viscosity determined by using Ubbelohde viscometer. The viscosity of **2**-containing tetrachloromethane of the concentration of 5 mg cm^{-3} (**2**/tetrachloromethane) increases to be 2500 cP at 25 ℃, though the viscosity of tetrachloromethane is 0.908 cP at 25 ℃.[11] The remarkable rise of viscosity suggests that these compounds are effective as not only gelling agent but also viscoelastic material-forming one.

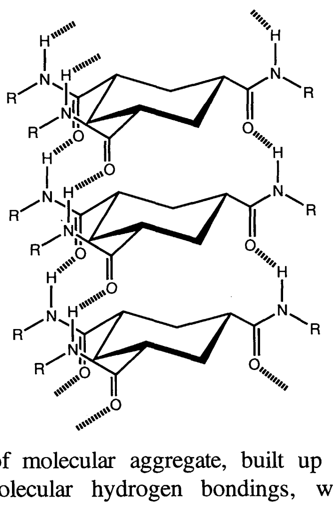
The participation of intermolecular hydrogen bonding in gelation was studied by FT-IR spectroscopy. The observed frequencies (cm^{-1}) for amide of **2** and **4** in different states are summarized in Table 2. The N-H and C=O stretching vibrations of intermolecular hydrogen bonding were recognized in gel and gel-like state as well as solid-state of both compounds, whereas THF solution containing **4** showed 3573, 3505, and 1652 cm^{-1} indicative of non-hydrogen bonding stretching vibration in addition to the hydrogen bonding stretching vibration (3294, 1642 cm^{-1}). These spectral data strongly indicate that the hydrogen bondings formed in gel and gel-like state are essentially similar to those in solid-state. Neither gel nor gel-like state is formed by **4** in THF, as described in Table 1. This can be explained by taking into account the incomplete hydrogen bonding of **4** in THF, that is to say, huge aggregate necessary for gelation fails to form due to the incomplete hydrogen bonding.

Table 2. Observed FT-IR spectroscopic frequencies (cm^{-1}) for amide of **2** and **4**

	state	νN-H	νC=O
2	solid-state[a]	3296	1642
2	gel in cyclohexane[b]	3291	1644
4	solid-state[a]	3302	1640
4	gel-like in CCl_4[c]	3293	1640
4	solution in THF[c]	3573, 3505, 3294	1652, 1642

[a] KBr-pellet method.
[b] Liquid cell method; concentration is 2mg cm^{-3} (**2**/cyclohexane).
[c] Liquid cell method; concentration is 5mg cm^{-3} (**4**/solvent).

Throughout FT-IR spectroscopic results and molecular modeling studies, it is reasonable to assume that the three equatorial amide-CO and amide-NH of **1**-**4** can direct themselves parallel to each other and perpendicular to the cyclohexane ring. Therefore, an extended molecular aggregate as described below, stabilized by three intermolecular hydrogen bondings between each molecule, is formed.



The image of molecular aggregate, built up by association through intermolecular hydrogen bondings, was caught by transmission electron micrograph (TEM). The TEM of a gel formed by **2** in benzene (Figure 1) shows the gathering of numerous slender fibers, the thinnest diameter of which is *ca.* 20 nm. Considering that the diameter of **2** estimated from space-filling molecular model is *ca.* 4 nm, it is unknown whether the thinnest fiber that we have been able to detect in TEM is the "unit fiber" described above.

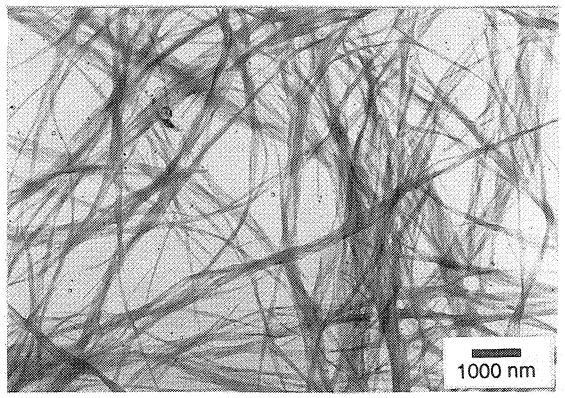


Figure 1. TEM of loose gel from **2** in benzene, negatively stained by osmic acid.

It is thought that the transformation of isotropic solution to crystal, gel, or viscoelastic fluid on cooling process depends on the structure of R group and the type of solvent. When favorable hydrophilic-hydrophobic balance of trialkyl *cis*-1,3,5-cyclohexanetricarboxamides against solvent is performed, gel or highly viscoelastic gel-like fluid is formed. The formation of macromolecular-like aggregate through intermolecular hydrogen bondings described as **5** will bring about the remarkable rise of viscosity. Furthermore, the juxtaposing and/or interlocking of the macromolecular-like aggregates by van der Waals interaction among hydrophobic alkyl chains immobilizes solvent molecules in the network, consequently, gelation occurs.

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References and Notes

1 F. Vögtle, "Supramolecular Chemistry," Wiley, England, (1991).
2 J.-M. Lehn, "Supramolecular Chemistry: Concepts and Perspectives," VCH, Weinheim, (1995).
3 K. Hanabusa, M. Yamada, M. Kimura, and H. Shirai, *Angew. Chem., Int. Ed. Engl.*, **35**, 1949 (1996), and references therein.
4 K. Hanabusa, K. Shimura, K. Hirose, M. Kimura, and H. Shirai, *Chem. Lett.*, **1996**, 885.
5 S. W. Jeong, K. Murata, and S. Shinkai, *Supramol. Sci.*, **3**, 83 (1996).
6 S. Yamamoto, *J. Chem. Soc. Japan, Ind. Chem. Soc.*, **46**, 779 (1943) (C.A. **46**, 7047i).
7 T. Tachibana, T. Mori, and K. Hori, *Bull. Chem. Soc. Jpn.*, **53**, 1714 (1980).
8 Y. Lin, B. Kachar, and R. G. Weiss, *J. Am. Chem. Soc.*, **111**, 5542 (1989).
9 T. Brotin, R. Utermölen, F. Fages, H. Bouas-Laurent, and J. Desvergne, *J. Chem. Soc., Chem. Commun.*, **1991**, 416.
10 Trialkyl *cis*-1,3,5-cyclohexanetricarboxamides (**1**-**4**) were synthesized in two efficient steps by refluxing *cis*-1,3,5-cyclohexanetricarboxylic acid (Aldrich Chem. Co.) in thionyl chloride, followed by reaction of the resulting *cis*-1,3,5-cyclohexanetricarbonyl trichloride with corresponding alkylamines. Elemental analysis data for **1**: Found: C, 69.57; H, 10.81; N, 8.80%. Calcd for $C_{27}H_{51}N_3O_3$: C, 69.63; H, 11.04; N, 9.02%. Data for **2**: Found: C,75.21; H, 12.08; N, 5.69%. Calcd for $C_{45}H_{87}N_3O_3$: C,75.26; H, 12.21; N, 5.85%. Data for **3**: Found: C, 77.37; H, 12.57; N, 4.45%. Calcd for $C_{63}H_{123}N_3O_3$: C, 77.95; H, 12.77; N, 4.33%. Data for **4**: Found: C, 73.50; H, 11.73; N, 6.92%. Calcd for $C_{39}H_{75}N_3O_3$: C, 73.88; H, 11.92; N, 6.63%.
11 "Handbook of Chemistry and Physics, 76th Edition" ed by D. R. Lide, CRC, (1995-1996), Chap. 6, p. 245.