Organogel Formation of Optically Active 1,6-di-*O*-TIPDS-*myo*-inositol

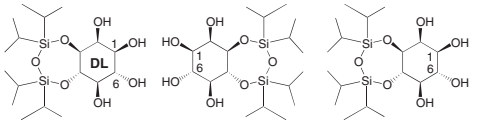
Asao Hosoda,* Yasuhito Miyake, Eisaku Nomura, and Hisaji Taniguchi
Industrial Technology Center of Wakayama Prefecture, 60 Ogura, Wakayama 649-6261

(Received August 13, 2003; CL-030752)

Two novel optically active *myo*-inositol derivatives having a bulky alkyl–silyl group as a hydrophobic part were synthesized. These compounds acted as a gelator toward nonpolar hydrophobic solvents such as *n*-hexane, cyclohexane, and toluene via the formation of an intermolecular OH···O hydrogen bonding network.

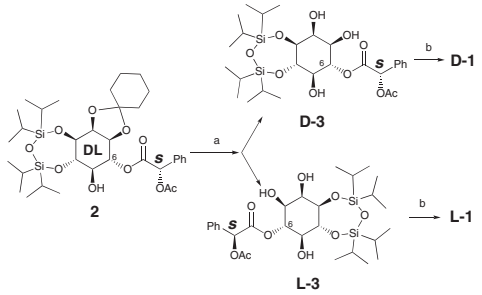
Low molecular weight organogelators, which are capable of immobilizing various organic fluids, have recently received much attention. A number of gelators have been reported in the literature.[1–6] These gelators can be classified into some categories according to the "base-compound" such as aliphatic amide derivatives,[2] amino acid derivatives,[3] saccharide derivatives,[4] steroid derivatives,[5] anthryl derivatives,[6] and etc. Most of these derivatives have long aliphatic chains or aromatic groups in order to acquire the moderate solvent affinity.

In a previous paper, we reported an efficient method for the introduction of ferulic acid to the 1,6-vicinal hydroxy groups of (±)-3,4-*O*-(1,1,3,3-tetraisopropyldisiloxanedi-1,3-yl)-*myo*-inositol [(±)-3,4-*O*-TIPDS-*myo*-inositol, DL-**1**] and the effect of intermolecular hydrogen bonding of DL-**1** on the esterification reaction.[7] Recently we have found that the optically active *myo*-inositol derivatives, L and D-3,4-*O*-TIPDS-*myo*-inositols (L-**1** and D-**1**) in which they do not have any long aliphatic chains and aromatic groups, can act as organogelators. Although a number of *myo*-inositol derivatives are reported,[8] the organogel formation of these derivatives have not yet been reported so far. We report here the gelation behavior of L-**1** and D-**1** as the first example of *myo*-inositol-based organogelators.



The chiral compounds L-**1** and D-**1** were prepared from a diastereoisomer **2** (Scheme 1). We referred to the literature for the preparation of **2**.[8b,9] The reaction of **2** with ethylene glycol in the presence of *p*-toluenesulfonic acid in chloroform afforded 6-*O*-mandelate derivatives L-**3** and D-**3**.[8b] These two diastereoisomers were cleanly separated by column chromatography on silica gel. The deacylation of L-**3** and D-**3** gave optically active L-**1**[10] $\{[\alpha]^{20}_{D} + 8.4$ (c 1.03, MeOH)$\}$ and D-**1**[11] $\{[\alpha]^{20}_{D} - 9.79$ (c 1.468, MeOH)$\}$ in high yields. The racemic compound DL-**1** was prepared according to the literature.[7]

The gelation test was carried out as follows: the sample (DL-**1**, L-**1**, and D-**1**: 5.0 mg) was mixed with a solvent (1.0 cm^3) in a septum-capped test tube and the mixture was heated until the solid dissolved. The solution was cooled to room temperature and left for over night. As the results, it became clear that L-**1** and D-**1** act as organogelators toward nonpolar hydrophobic solvents (Table 1). In contrast, the racemic compound DL-**1** did not form a gel at all. When the solution of L-**1** was added to the solution of D-**1** at the molar ratio of 1:1, the gelation was not observed.



Scheme 1. Reagents and conditions: (a) $HOCH_2CH_2OH$, p-TsOH, $CHCl_3$, rt, 5 h; (b) $NH_2NH_2{\cdot}H_2O$, $CHCl_3$, rt, 1 h.

The ^{1}H NMR studies were carried out for 10 mM solution of L-**1** in toluene-d_8 at different temperatures between 60 and −20 °C. As shown in Figure 1, the chemical shifts of the proton signals and OH signals of the inositol skeleton shifted downfield with a decrease of temperature, and these signals broadened on a NMR time scale at −20 °C. Among them, the signals of OH groups bonded to carbons 1 and 6 shifted drastically downfield from 2.5 to 6.0–6.5 ppm.[12] These results suggest that the compound L-**1** forms an aggregate through an OH···O intermolecular hydrogen bonding network. In particular, the OH groups bonded to carbons 1 and 6 play an important role toward the formation of this network. The temperature-dependent ^{1}H NMR spectra of DL-**1** in toluene-d_8 revealed that the DL-**1** also forms the intermolecular hydrogen bonding in a manner similar to that of L-**1**. But it became clear that the OH proton signals bonded to carbons 1 and 6 of DL-**1** appeared at a downfield compared with

Table 1. Geletion test of L-**1**, D-**1** and DL-**1** (5.0 mg/cm^3)[a]

Solvent	L-**1**	D-**1**	DL-**1**
n-Hexane	G	G	S
n-Heptane	G	G	S
Cyclohexane	G	G	S
Benzene	G	G	S
Toluene	G	G	S
o-Xylene	G	G	S
m-Xylene	G	G	S
CCl_4	S	S	S
$CHCl_3$	S	S	S
Acetone	S	S	S
EtOAc	S	S	S
MeCN	I	I	S
MeOH	S	S	S

[a]G = gel; S = solution; I = insoluble

Copyright © 2003 The Chemical Society of Japan

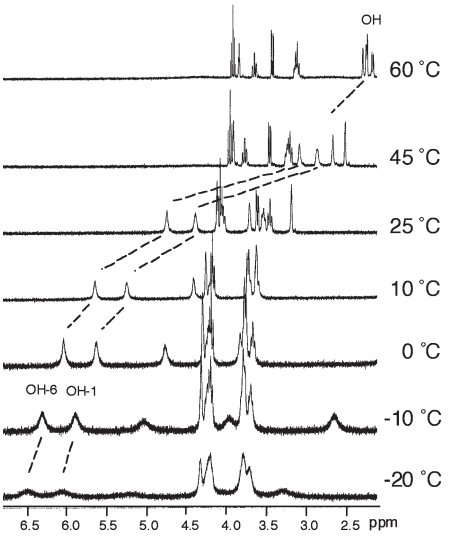


Figure 1. Temperature-dependent ^{1}H NMR spectra of L-**1** (400 MHz, toluene-d_8).

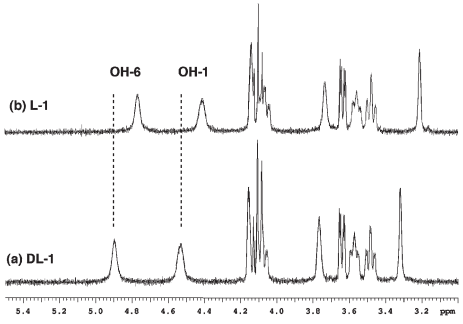


Figure 2. ^{1}H NMR in toluene-d_8 (10 mM) at 25 °C (a) L-**1**, (b) DL-**1**.

that of L-**1** at the same concentration and tempetarure (Figure 2). This phenomenon was observed at every temperature below 45 °C. This fact suggests that, (i) the compound DL-**1** forms stronger intermolecular hydrogen bonding than that of the compound L-**1**, and (ii) the aggregation mode of DL-**1** is different from L-**1**, i.e., most of the molecules in the solution of DL-**1** exist as a D-L dimer.

To obtain a visual insight into molecular aggregate, we prepared a dry sample for scanning electron microscopy (SEM). Figure 3 shows a typical picture obtained from the xerogels (a) L-**1** and (b) D-**1** (toluene gel). It is clear that the gelator forms a 3-D network with 100–500-nm frizzled fibrils.

In conclusion, the present study has demonstrated the first example that the *myo*-inositol derivatives are building-blocks for the gelators. *myo*-Inositol is a useful material obtained from rice bran as a renewable resource. Currently, we are investigating in detail the macroscopic and microscopic features of this family of organogelating *myo*-inositol derivatives.

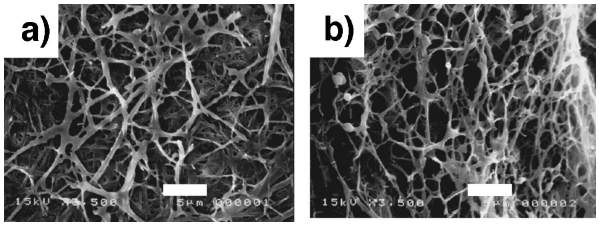


Figure 3. SEM images of the xerogel. (a) the L-**1**/toluene system. (b) the D-**1**/toluene system; bar is 5 μm.

References and Notes

1 a) J. H. van Esch and B. L. Feringa, *Angew. Chem., Int. Ed.*, **39**, 2263 (2000). b) P. Terech and R. G. Weiss, *Chem. Rev.*, **97**, 3133 (1997).
2 a) K. Hanabusa, M. Yamada, M. Kimura, and H. Shirai, *Angew. Chem., Int. Ed.*, **35**, 1949 (1996). b) K. Tomioka, T. Sumiyoshi, S. Narui, Y. Nagaoka, A. Iida, Y. Miwa, T. Taga, M. Nakano, and T. Handa, *J. Am. Chem. Soc.*, **123**, 11817 (2001).
3 a) K. Hanabusa, K. Okuni, K. Karaki, T. Koyama, and H. Shirai, *J. Chem. Soc., Chem. Commun.*, **1992**, 1371. b) J. Becerril, M. I. Burguete, B. Escuder, S. V. Luis, J. F. Miravet, and M. Querol, *Chem. Commun.*, **2002**, 738.
4 a) K. Yoza, Y. Ono, K. Yoshimara, T. Akao, H. Shinmori, M. Takeuchi, S. Shinkai, and D. N. Reinhodt, *Chem. Commun.*, **1998**, 907. b) N. Amanokura, Y. Kanekiyo, S. Shinkai, and D. N. Reinhodt, *J. Chem. Soc., Perkin Trans. 2*, **1999**, 1995. c) R. J. H. Hafkamp, M. C. Feiters, and R. J. M. Nolte, *J. Org. Chem.*, **64**, 412 (1999).
5 a) K. Murata, M. Aoki, T. Suzuki, T. Harada, H. Kawabata, T. Komori, F. Ohseto, K. Ueda, and S. Shinkai, *J. Am. Chem. Soc.*, **116**, 6664 (1994). b) J. H. Jung, Y. Ono, K. Sakurai, M. Sano, and S. Shinkai, *J. Am. Chem. Soc.*, **122**, 8648 (2000).
6 a) F. Placin, M. Colomes, and J.-P. Devergne, *Tetrahedron Lett.*, **38**, 2665 (1997). b) T. Brotin, R. Utermöhlen, F. Fages, H. Bouas–Laurent, and J.-P. Desvergne, *J. Chem. Soc., Chem. Commun.*, **1991**, 416.
7 A. Hosoda, E. Nomura, K. Mizuno, and H. Taniguchi, *J. Org. Chem.*, **66**, 7199 (2001).
8 a) Y. Watanabe, "Studies in Natural Products Chemistry," ed. by Atta-ur-Rahman, Elsevier Science B. V. (1996), Vol. 18, pp 391–456. b) Y. Watanabe, *J. Synth. Org. Chem. Jpn.*, **58**, 1057 (2000), and references therein.
9 a) N. Chida, E. Yamada, and S. Ogawa, *J. Carbohydr. Chem.*, **7**, 555 (1988). b) Y. Watanabe and M. Nakatomi, *Tetrahedron Lett.*, **39**, 1583 (1998).
10 L-**1**: mp 130–133 °C; $[\alpha]^{20}_{D} + 8.4$ (*c* 1.03, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.45–4.65 (m, 4H, OH), 3.70–3.75 (m, 2H, H-2 & H-4), 3.52 (dd, 1H, $J = 2.8$, 9.2 Hz, H-3), 3.41 (m, 1H, H-6), 3.20 (m, 1H, H-1), 3.02 (m, 1H, H-5), 0.86–1.10 (m, 28H, CH_3 & CH); ^{13}C NMR (DMSO-d_6) δ 77.00, 75.60, 75.06, 72.96, 72.38, 71.48, 17.56, 17.48, 17.38, 17.21, 12.51, 11.67, 11.84 ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 77.00, 75.61, 75.08, 72.97, 72.38, 71.51, 17.61, 17.57, 17.50, 17.39, 17.22, 12.54, 12.00, 11.87 ppm. Anal. Calcd for $C_{18}H_{38}O_7Si_2$: C, 51.15; H, 9.06%. Found: C, 51.12; H, 9.22%.
11 D-**1**: mp 129–132 °C; $[\alpha]^{20}_{D} - 9.79$ (*c* 1.468, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.45–4.65 (m, 4H, OH), 3.70–3.75 (m, 2H, H-2 & H-4), 3.52 (dd, 1H, $J = 2.4$, 8.8 Hz, H-3), 3.41 (m, 1H, H-6), 3.20 (m, 1H, H-1), 3.02 (m, 1H, H-5), 0.86–1.10 (m, 28H, CH_3 & CH) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ 77.00, 75.60, 75.06, 72.96, 72.38, 71.48, 17.56, 17.48, 17.38, 17.21, 12.51, 11.67, 11.84 ppm. Anal. Calcd for $C_{18}H_{38}O_7Si_2$: C, 51.15; H, 9.06%. Found: C, 51.02; H, 9.24%.
12 The position of the hydroxy groups in these derivatives was established by ^{1}H–^{1}H Correlation Spectroscopy (COSY).

Published on the web (Advance View) October 13, 2003; DOI 10.1246/cl.2003.1042