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New Gelators Based on 2-Amino-2-phenylethanol: Close Gelator-Chiral Structure Relationship

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Abstract: New gelators for organic fluids based on 2-amino-2-phenylethanol are developed and their gelation ability is examined. It is expected that a chiral compound having plural hydrogen bonding sites results in formation of large chiral aggregates, which then grow long and become entangled; consequently, physical gelation occurs.

During the last decade, particular attention has been paid to the development of low molecular weight gelators for organic fluids.[1] Although some dozens of structurally different classes of gelators were reported so far, there are several unanswered questions. For example 1) why do gelators in fluids form metastable gels instead of thermally-stable crystals? and 2) what, if any, are the necessary and sufficient requirements for designing gelators? As yet, we can give no answer to these questions; however, it is interesting to note that most of the reported gelators possess chiral carbon in their chemical structure,[2] although 2,3-bis-n-alkoxy anthracene,[3] tetraalkylammonium halide,[4] bis-urea compounds,[5] and tris(stearoylamino)triphenylamine,[6] are notable exceptions. Actually, we have synthesized several types of gelators from chiral compounds[7] and found that racemates tend to crystallize and not to form gels.[8] Considering that the most difficult point involved in the development of gelators is how to prevent the transformation from the metastable gel to a crystalline state, we assume the chirality in gelators probably promotes the formation of chiral aggregates which develop into the network structure for gels. The chiral structure in compounds, although it is neither a necessary nor sufficient requirement, will play a vital role in developing gelators. In this communication, we report a new type of gelators from 2-amino-2-phenylethanol, which we focus on as a chiral starting material.

(R)-2-Amino-2-phenylethanol derivatives **1-5** were prepared from (R)-(-)-2-amino-2-phenylethanol and examined as gelators.[9] The results of gelation tests[10] (Table 1) showed (i) (R)-2-acylamino-2-phenylethanols **1-4** can gelate aromatic molecules, mineral oils, silicone oil, and edible oils; (ii) the gelation ability of **1** is inferior to that of **2-4**, suggesting the optimal carbon numbers of the acyl substituent exist in enhancing the gelation

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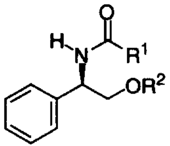
process; (iii) both the acyl substituents at the N atom and a hydroxy group are essential for effective gelation, from the fact that neither (R)-(-)-2-amino-2-phenylethanol nor **5** can gelate any fluids. It should be mentioned that the compounds **1-4** are too soluble in high-polar solvents such as alcohols, ketones, chloroform, DMF, and DMSO to act as gelators, while the compound **5** crystallizes from most of the organic fluids. As we would predict, the racemate consisting of **2** and (S)-2-undecylamino-2-phenylethanol gave crystals, though (S)-2-undecylamino-2-phenylethanol itself exhibited the same gelation behavior as **2**.



1-5

1; R^1 = Pr, R^2 = H
2; R^1 = *n*-undecyl, R^2 = H
3; R^1 = *n*-heptadecyl, R^2 = H
4; R^1 = 2-ethylhexyl, R^2 = H
5; R^1 = *n*-heptadecyl,
R^2 = *n*-octadecylaminocarbony

Table 1. Gelation test of **1-5** at 25 °C.[a]

Solvent	**1**	**2**	**3**	**4**	**5**
cyclohexane	cryst.	10	cryst.	3	cryst.
benzene	26	25	22	>50	cryst.
toluene	>50	29	18	20	cryst.
chlorobenzene	29	35	10	soln.	cryst.
nitrobenzene	soln.	soln.	12	soln.	cryst.
tetrachloromethane	cryst.	soln.	cryst.	17	cryst.
kerosene	cryst.	22	10	6	cryst.
light oil	cryst.	16	10	3	cryst.
silicone oil	15	3	5	vf.	cryst.
salad oil	soln.	vf.	vf.	vf.	cryst.
soybean oil	soln.	vf.	vf.	2	cryst.

[a] Values mean the minimum gel concentration, whose unit is g L^{-1} (gelator/fluid). cryst. = crystallization, soln. = solution, vf. = viscous fluid.

The necessity of the acyl substituents at the N atom and the hydroxy group suggests the participation of hydrogen bonding in gelation. The formation of hydrogen bondings was easily confirmed by FT-IR spectroscopy. The FT-IR spectrum of the decane gel of **2** was characterized by 3379, 3310, and 1639 cm^{-1} which are assigned to O-H, N-H, and C=O hydrogen bonding stretching vibrations; on the contrary, the FT-IR spectrum of the isotropic solution of **2** in chloroform showed N-H and C=O stretching vibrations at 3440 and 1663 cm^{-1} for non-hydrogen bonding. The X-ray crystallographic analysis of (R)-(-)-2-acetylamino-2-phenylethanol indicates that two kinds of intermolecular hydrogen bondings are formed between the O atom of amide and H atom of hydroxy and between the O atom of hydroxy and H atom of amide. This is probably the reason why the acyl substituents at the N atom and the hydroxy group are indispensable for gelation.

To study the chiral structure of aggregates formed by the gelator, CD spectra were measured at different temperatures. The CD spectra of decane gel of **2** and its S-enantiomer (1.5 mM) are shown in Figure 1. The gelator **2** at 20 °C reveals a strong negative peak due to the carbonyl and/or phenyl unit; $[\theta]_{207} = -2.74 \times 10^4$.

This strong CD peak almost disappeared at 50 °C, when the gel was transformed to an isotropic solution. As such a much-enhanced CD is derived from exciton coupling among the organized chromophores,[11] the observed CD data indicate that the component molecules in the aggregate are cooperatively organized to be CD-active in the decane gel. The original chirality of **2** seems to be essential for the formation of the chiral aggregates responsible for gelation.

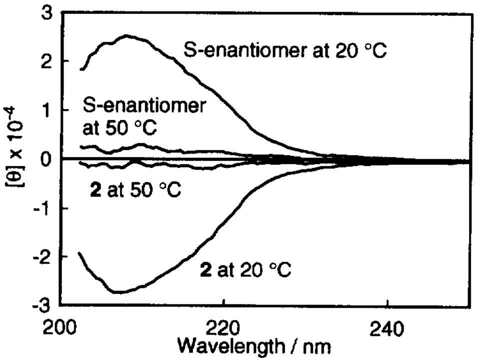


Fig. 1. CD spectra of **2** and its S-enantiomer in decane; [**2**] = [S-enantiomer] = 1.5 mM. The molar ellipticity [θ] is given in deg cm^2 dmol^{-1}.

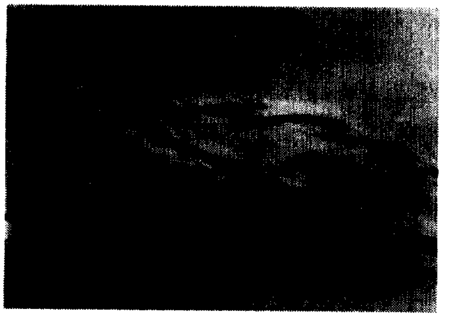


Fig. 2. TEM image of ethyl acetate gel of S-enantiomer of **3** stained by osmic acid. Magnification: x 6000.

It occurred to us that chiral aggregates could be visually detected by transmission electron microscopy. The TEM of an ethyl acetate gel of the S-enantiomer of **3**, (S)-2-heptadecylamino-2-phenylethanol, negatively stained by osmic acid is shown in Figure 2. The chiral aggregates were found to be large helical ribbons, 500 nm wide and up to 10 µm in length, whose helicity was exclusively right-handed. It is very important to note that TEM images for the ethyl acetate gel of **3**, were left-handed helical ribbons. The helical aggregates account for the formation of metastable gels instead of thermally-stable crystals. When the helical ribbons are sufficiently long and entangled, the fluids are entrapped in the three-dimensional network; consequently, physical gelation occurs.

We may therefore conclude that a chiral compound having plural hydrogen bonding sites which especially forms helical aggregates in solvents is a candidate for gelators, though chirality and hydrogen bonding are not sufficient requirements for gelation.

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9. **2**: mp 83-84 °C (ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 5H), 6.41 (brs, 1H), 5.02 (q, 1H), 3.83 (d, 2H), 3.27 (brs, 1H), 2.20 (t, 2H), 1.60 (m, 2H), 1.26 (s, 16H), 0.90 (t, 3H); Anal. Calcd for $C_{20}H_{33}NO_2$: C, 75.19; H, 10.41; N, 4.38. Found C, 75.08; H, 10.67; N, 4.90.
10. A typical procedure for gelation test: a weighed sample was mixed with an organic fluid (2 mL) in a test tube with screw cap (inside diameter; 14 mm) and the mixture was heated until the solid was dissolved. The resulting solution was cooled at 25 °C for 2 h and then the gelation was checked visually. When upon inversion there was no fluid running down the walls of the tube, we judged it "gel". When a highly viscous solution was formed, it was distinguished as "viscous fluid" from the gel. When the samples caused gelation, we quantitatively evaluated the gelation ability by minimum gel concentrations which are the minimum concentrations of gelators necessary for gelation at 25 °C.
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