Pyridine-containing Cholesterols as Versatile Gelators of Organic Solvents and the Subtle Influence of Ag(I) on the Gel Stability

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New cholesterol-based gelators bearing a 4-, 3-, or 2-pyridyl group (**1**, **2**, or **3**, respectively) have been designed. Compound **1** gelled 16 of the 19 solvents tested, indicating that **1** acts as a very versatile gelator. The gelation ability of compound **2** was significantly improved by added AgOTf, owing to an Ag(I)-pyridine interaction. The findings indicate that the pyridyl group is very useful to impart new functions to organogel systems.

Recently, the development of new low molecular-weight gelators has been of much concern.[1–5] The gelation ability of such organogelators is evaluated by three different factors: that is, (1) the critical gelation concentration (CGC) where the sol phase changes into the gel phase, (2) the gel-sol phase transition temperature (T_{gel}), and (3) the gelation versatility for various solvents. Property (1) has frequently been reported and several ''supergelators'' which can gelate the solvents at less than 1 wt% have been reported.[6] Property (2) has also been studied and the ''thermally-stable galators'' which have T_{gel} higher than their solvent boiling points have been reported.[7] On the other hand, property (3) has been left much less developed and in fact, there is no systematic guideline for the design of such gelators. In this paper, we have made a new approach to property (3) using pyridine-containing cholesterols. It is known that pyridine shows versatile solubility in both polar and apolar solvents (including water and cyclohexane). This suggests that the pyridine moiety in gelators would play a role to keep the affinity with solvent molecules. With this idea in mind we designed pyridine-containing cholesterol-based gelators **1–3**, expecting their versatile gelation ability for many organic solvents.

Compounds **1** (mp 192–193 °C),[8] **2** (mp 211–214 °C), and **3** (mp 199–200 °C) were synthesized by the reaction of cholesteryl chloroformate with the corresponding aminopyridine in the presence of triethylamine and identified by ^{1}H NMR and MALDI TOF mass spectral evidence and elemental analyses.

The gelation ability of **1–3** was tested for 19 different solvents with 10 g dm^{-3} (19.7 mmol dm^{-3}) as a standard concentration. The results are summarized in Table 1. Compound **2** shows 8 ''S'' marks (soluble at 10 g dm^{-3}) and 8 ''P'' marks (soluble at reflux temperature but precipitate at 25 °C). Hence, it is either too soluble or too crystalline. Compound **3** makes 12 solvents gelatinous, but 10 solvents among them gel only partially, as shown with ''PG''. Presumably, **3** tends to form microcrystalline particles. On the other hand, compound **1** can gel 10 solvents at 10 g dm^{-3}, 15 solvents at 25 g dm^{-3}, and 16 solvents at 35 g dm^{-3}. The results clearly support the view that **1** is a unique gelator possessing property (3). With respect to ''property(1)'', methanol, acetonitrile, and diphenyl ether gel even at 5.0 g dm^{-3}, indicating that **1** has a character of ''supergelator''. The T_{gel} values determined at 10 g dm^{-3} in diphenyl ether were 100 °C for **1** and 67 °C for **3**. The results indicate that **1** has even a character of property (2).

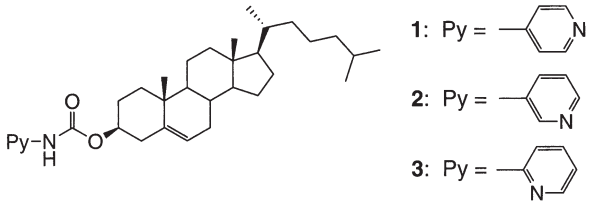

Table 1. Gelation properties of the compound **1–3** at rt[a]

Solvent	State[b]		
	1	**2**	**3**
n-Hexane	G	P	PG
Cyclohexane	G	S	PG
n-Octane	G	P	PG
Benzene	G[e]	S	S
Toluene	G[d]	PG	S
p-Xylene	G	S	S
THF	S	S	S
Anisole	G	G	S
Diphenyl ether	G[c]	S	G
Methanol	G[c]	P	PG
Ethanol	G[d]	P	PG
1-Butanol	G[d]	S	PG
Ethyl acetate	G	P	PG
Acetone	G	P	PG
CH_3CN	G[c]	P	PG
$CHCl_3$	S	S	S
DMF	G[d]	S	PG
DMSO	G[d]	P	G
H_2O	I	I	I

[a]Concentration of the compound is 19.7 mmol dm^{-3} (10 g dm^{-3}). [b]G: gel, PG: partial gel, P: precipitation, S: solution, I: insoluble when heated. [c]Gel at 5.0 g dm^{-3}. [d]Gel at 25 g dm^{-3}. [e]Gel at 35 g dm^{-3}.

It is not yet clear what is the origin of the difference between **1** and others. When the cholesterol moieties form a one-dimensional stacking column, the pyridine moieties are helically arranged, like a spiral staircase, around the cholesterol column (See graphical abstract).[9–11] Pyridine has a dipole running from 4-C to 1-N. In the one-dimensional columnar aggregate of **1**, therefore, the dipoles are arranged in a radial fashion around the central cholesterol column. This aggregation mode may be effective to maintain the gel stability and to suppress the undesired further coagulation. As expected, the well-developed network structure composed of fine fibrils was observed in the

TEM picture (Figure 1).

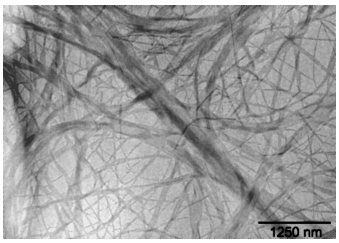

Figure 1. TEM image of the *p*-xylene gel of **1** (10 g dm^{-3}).

Here, it occurred to us that the gelation ability may be improved by a metal-pyridine interaction. Judging from the aggregation mode (See graphical abstract), this effect is particularly expected for **2** because a pyridyl nitrogen on **2** is perpendicularly oriented to the radius of the columnar aggregate[12] and two nitrogen atoms in the neighboring pyridyl groups arranged along the helical staircase can face each other approximately in 180°. We extensively investigated the influence of added metal ions (Pt(II), Cd(II), Co(II), Cu(II), Ni(II), Zn(II), Pd(II), etc.) on the gelation ability of **1**–**3** and found that the positive effect appears in the combination of **2** and Ag(I). As shown in Figure 2, the T_{gel} values for **3** (10 g dm^{-3}) in diphenyl ether are less affected by added AgOTf. This is due to the poor coordination ability of the 2-pyridyl group. The T_{gel} values for **1** sharply lowered at low AgOTf concentration region and then flattened at around 80 °C. On the other hand, the sol solution of **2** in the absence of AgOTf is changed into the gel at [AgOTf]/[**2**] = 0.02–0.06 and results in the precipitate above [AgOTf]/[**2**] = 0.06. When the **2** concentration is enhanced to 15 g dm^{-3}, the T_{gel} maximum appears at around [AgOTf]/[**2**] = 0.05.

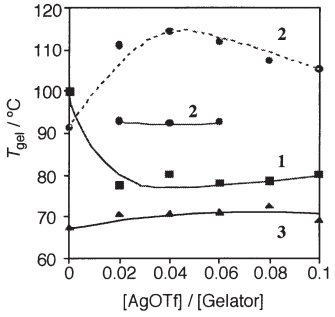

Figure 2. Plots of T_{gel} vs [AgOTf]/[**1**, **2**, or **3**] in diphenyl ether: [**1**, **2**, or **3**] = 10 g dm^{-3} for the solid line, [**2**] = 15 g dm^{-3} for the dotted line. In [**2**] = 15 g dm^{-3}, the system became sol below [AgOTf]/[**2**] = 0.02 whereas it became precipitate above [AgOTf]/[**2**]=0.06.

To obtain evidence for the Ag(I)-pyridine interaction in the gel phase we measured the ^{1}H NMR (600 MHz) spectra for gelatinous **2** (30 g dm^{-3} (59.2 mmol dm^{-3})) and **2** + AgOTf (11.8 mmol dm^{-3}) in benzene-d_6 at 25 °C. The particular difference between the two spectra is the down-field shift of the pyridyl 2-H from 8.141 ppm in the absence of AgOTf to 8.165 ppm in the presence of AgOTf. Further interesting is a morphological change induced by added AgOTf (Figure 3). In the absence of AgOTf, rod-like clusters are recognized. In the presence of AgOTf, on the other hand, the fibrillar aggregates are recognized. It is clear,

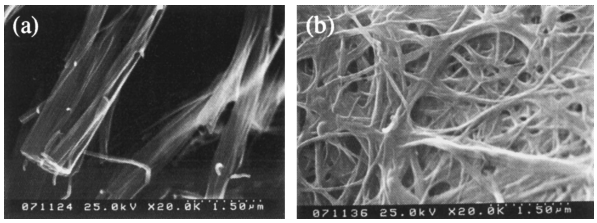

Figure 3. SEM images of the xerogels prepared from (a) **2** (30 g dm^{-3}; 59.2 mmol dm^{-3}) + benzene gel and (b) **2** + AgOTf (11.8 mmol dm^{-3}) + benzene gel.

therefore, that Ag(I) interacts with the 3-pyridyl nitrogens in **2** and changes the morphology into the fibrillar one suitable to the gel formation.

In conclusion, the present study demonstrated that pyridine, which a priori shows the versatile solubility in various solvents, is useful to design the versatile gelator based on the chlolesterol skeleton. Furthermore, their morphologies and gel stabilities can be modified by added Ag(I). We believe that further structural modifications (introduction of a spacer group between pyridine and cholesterol, quaternization of the pyridyl groups, etc.) will lead to further exploitation of new functionalized gelators.

References and Notes

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12 Energy-minimized structures of **1**–**3** are calculated by MM2 using Discover 3/Insight II 98.0.