Gelling Agents to Harden Organic Fluids: Oligomers of α-Amino Acids

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Oligomers of L-valine, L-isoleucine, L-phenylalanine and L-glutamate ester form thermoreversible hard gels in a wide variety of organic fluids; the gelation is characterized by minimum gel concentration, thermodynamic parameters, FTIR and CD spectroscopy.

Some small molecules form huge macromolecule-like aggregates and cause thermoreversible gelation where weak bonding interactions are involved in establishing the network. These compounds have practical value for hardening oil spilled on water, used cooking oils or foods containing mobile unsaturated fatty acids. Interest also lies in molecular aggregate chemistry. Various compounds are known as low-molecular-mass gelling agents for hardening organic fluids.[1]

We have studied thermoreversible physical gels, the driving forces of which are intermolecular hydrogen bonding and van der Waals interactions.[1] Three features are important in developing oil-gelling agents: the existence of intermolecular interactions intertwining of the aggregate, and the presence of some factor to prevent the transformation from metastable gel to a crystalline state. In the present study, we focused on oligo(α-amino acid)s, which are especially promising for gelling agents, because they have plural amide bonds to act as hydrogen-bonding sites and they are known not to crystallize easily.

Oligo(α-amino acid)s were prepared by decarboxylation of the corresponding *N*-carboxyanhydrides[2] of α-amino acids in the presence of an alkylamine. The degree of oligomerization was determined from the relative intensities of appropriate peaks in the NMR spectra. A procedure for studying gel-formation ability is as follows: weighed oligo(α-amino acid) was mixed with organic fluid (2 cm^3) in a septum-capped tube and the mixture was heated until the solid dissolved. The resulting solution was cooled at 25 °C for 2 h and then the gelation was checked visually. Gelation was considered successful if the cooled solution formed a nearly transparent mass that could be inverted without apparent flow. Gel was usually formed after a few minutes and remained stable for several months.

H $\{$NH–CH(R)–C(O)$\}_n$ NHC_mH_{2m+1}

1 R = $CHMe_2$, n = 5.0, m = 18
2 R = CHMeEt, n = 5.0, m = 18
3 R = CH_2Ph, n = 5.1, m = 12
4 R = $CH_2CH_2CO_2Me$, n = 4.2, m = 12
5 R = $CH_2CH_2CO_2Et$, n = 3.5, m = 3
6 R = $CH_2CH_2CO_2Et$, n = 6.0, m = 6
7 R = $CH_2CH_2CO_2Et$, n = 5.0, m = 12
8 R = $CH_2CH_2CO_2Et$, n = 5.2, m = 18
9 R = $CH_2CH_2CO_2Et$, n = 10.2, m = 18
10 R = $CH_2CH_2CO_2Et$, n = 20.5, m = 18
11 R = $CH_2CH_2CO_2CH_2Ph$, n = 4.2, m = 12
12 R = $CH_2CH_2CO_2CH_2Ph$, n = 22.6, m = 12

Results for gelation with **1**–**12** are summarized in Table 1. There is no gel formation ability for oligo(glycine) and oligo(L-alanine), the results of which are not given in Table 1. Oligo(L-valine) **1** afforded a highly viscous gel-like fluid in several organic liquids. It is thought that the gel-like fluid is precursor phase to the gel that cannot be converted to gel owing to poor solubility. A very small amount of **1** was dissolved in ethyl acetate, acetone, chloroform and tetrachloromethane upon heating. Oligo(L-isoleucine) **2** was a relatively good gelling agent owing to good solubility upon heating. The striking characteristics of **1** and **2** as gelling agents are to harden high-polar solvents such as DMF and Me_2SO. Oligo(L-phenylalanine) **3** was also found to be a good gelling agent, especially with aromatic molecules. In general, oligo(L-glutamate ester)s dissolved smoothly in organic fluids upon heating. In particular, oligo(γ-methyl L-glutamate) **4** is an excellent agent for hardening various alcohols, at a concentration of 9–19 g cm^{-3} (gelator/alcohol). Comparing the results of oligo(γ-ethyl L-glutamate)s **5**–**8**, it can be said that the hydrophobicity of C-end group has almost no influence on the gelation of organic fluids except for aromatic molecules, for which oligomers **5** and **6** having short-chain alkylamide are appropriate as gelling agents. The results of oligo(γ-ethyl L-glutamate)s **8**–**10** suggest that oligo(γ-ethyl L-glutamate)s having a degree of oligomerization less than 10 are suitable for gelling agents. The same results were also obtained from the comparison of oligo(γ-benzyl L-glutamate)s **11**, **12**. One reason for this is the lowering of solubility of oligomers by the increasing degree of oligomerization another is the difference of conformation in the organic fluid which is discussed below.

The minimum concentrations of oligo(L-phenylalanine) **3** and oligo(γ-methyl L-glutamate) **4** necessary for gelation are plotted *vs.* temperature in Fig. 1. The sol–gel process depends on temperature and the minimum concentration necessary to form the gel increases with increasing the temperature. Using the sol–gel phase diagram, the standard thermodynamic parameters[3] for the sol to gel transition are calculated as follows: ΔH(25 °C) = −23.2 kJ mol^{-1}, ΔS(25 °C) = −21.2 J K^{-1} mol^{-1} for **3** in nitrobenzene, and ΔH(25 °C) = −20.6 kJ mol^{-1}, ΔS(25 °C) = −8.2 J K^{-1} mol^{-1} for **4** in ethanol. These parameters suggest that the enthalpic contribution compensates for the undesirable entropic change for gelation. The present values of ΔH indicate that *ca.* two hydrogen bonds are formed during the gelation.

In Fig. 2, CD spectra of oligo(γ-ethyl L-glutamate)s **8**–**10** in PrOH and $CHCl_3$ are shown. The comparison of the spectra with related CD spectra[4,5] indicates that both **8** and **9** have a β-conformation and **10** has a α-helical conformation in PrOH, on the other hand, **8** exists as a random coil and both **9** and **10** have a β-conformation in $CHCl_3$. Combining the results represented in Table 1 and Fig. 2, it can be concluded that oligo(α-amino acid)s can cause the gelation, if they have a β-conformation which is built up through intermolecular

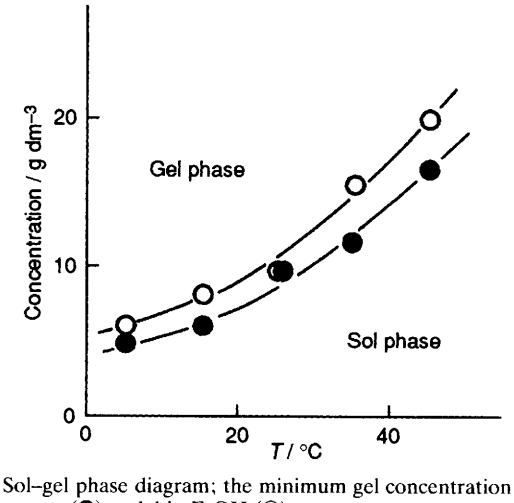

Fig. 1 Sol–gel phase diagram; the minimum gel concentration of **3** in nitrobenzene (●) and **4** in EtOH (○) *vs.* temp.

Table 1 Minimum gel concentration of oligo(α-amino acid) necessary for gelation at 25 °C

Organic fluid	Minimum gel concentration/g dm^{-3} (gelator/organic fluid)											
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
MeOH	30	30	Insol	19	G-like	G-like	G-like	G-like	ppt	G-like	Insol	Insol
EtOH	Insol	28	24	10	14	13	12	17	14	17	Insol	Insol
PrOH	29	17	26	13	13	9	15	11	10	G-like	29	Insol
Oleoyl alcohol	Insol	G-like	G-like	9	11	9	9	10	12	14	12	Insol
EtO_2Et	G-like	15	10	26	16	soln	soln	25	28	Insol	30	9
Acetone	G-like	14	Insol	soln	G-like	soln	soln	soln	28	Insol	soln	G-like
$CHCl_3$	G-like	30	29	soln	soln	soln	soln	soln	27	30	soln	soln
CCl_4	G-like	G-like	30	G-like	soln	G-like	soln	soln	G-like	Insol	G-like	Insol
DMF	9	11	soln	soln	soln	soln	soln	soln	soln	soln	soln	soln
Me_2SO	17	12	soln	soln	soln	soln	soln	soln	soln	soln	soln	soln
Benzene	Insol	soln	18	29	21	20	G-like	G-like	25	G-like	soln	soln
Toluene	Insol	G-like	8	14	26	21	16	G-like	G-like	Insol	26	26
Chlorobenzene	25	15	9	30	12	G-like	soln	soln	soln	G-like	soln	soln
Nitrobenzene	10	9	10	soln	27	soln	soln	soln	17	G-like	soln	soln
Soybean oil	G-like	G-like	21	15	Insol	7	7	8	G-like	Insol	9	Insol
Linoleic acid	G-like	Insol	Insol	G-like	9	7	6	14	9	19	21	Insol
Glyceryl tricaprylate	18	27	30	7	10	9	10	17	soln	Insol	24	Insol
Glyceryl trioleate	Insol	Insol	30	14	G-like	soln	8	10	soln	Insol	6	Insol

Insol = insoluble; soln = solution. G-like = highly viscous gel-like fluid; ppt = precipitation.

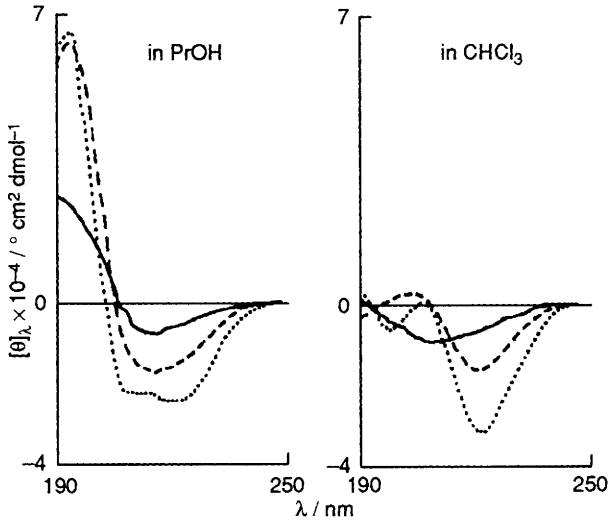

Fig. 2 The circular dichroism of **8–10** in PrOH (*a*) and $CHCl_3$ (*b*) (——) 2.10 g dm^{-3} of **8** in PrOH (dilute gel) and 2.10 g dm^{-3} of **8** in $CHCl_3$ (solution). (- - - -) 1.84 g dm^{-3} of **9** in PrOH (dilute gel) and 1.84 g dm^{-3} of **9** in chloroform (dilute gel). (.....) 1.70 g dm^{-3} of **10** in PrOH (solution) and 1.70 g dm^{-3} of **10** in $CHCl_3$ (dilute gel).

hydrogen bonding. The reason that **10** cannot form the gel in PrOH will be the formation of α-helical conformation, which is constructed by intramolecular hydrogen bonding. In addition, it can be said that oligomers forming a random coil such as **8** in chloroform, do not act as gelling agents.

The β-conformation responsible for the gelation is also supported by FTIR spectra. The FTIR of the chloroform gel of oligo(γ-ethyl L-glutamate) **9** is characterized by bands attributed to intermolecular hydrogen bonding, *i.e.* 3290 (ν_{N-H}), 1665 cm^{-1} ($\nu_{C=O}$ of amide I for β-conformation),[6] and 1625 cm^{-1} ($\nu_{C=O}$ of amide I for β-conformation),[6] whereas the corresponding homogeneous solution containing a small amount of **9** mainly affords bands at 3460 and 1695 cm^{-1} which are assigned to non-hydrogen bonding stretching vibrations.

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