Small Molecular Gelling Agents to Harden Organic Liquids: Alkylamide of *N*-Benzyloxycarbonyl-L-valyl-L-valine

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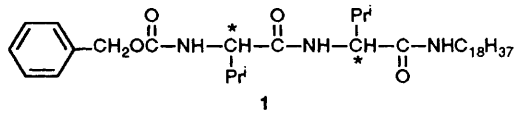
A long-chain alkylamide of *N*-benzyloxycarbonyl-L-valyl-L-valine **1** can cause physical gelation of a wide variety of organic liquids and harden them at very low concentrations; the fourier-transform infra-red (FTIR) spectra, and the thermodynamic parameters, suggest that the gel is built up through intermolecular hydrogen bonding between the N–H and C=O groups of both the amide and urethane bonds; TEM (transmission electron micrographs) of the gels show that the networks consist of numerous fibres.

Previously, we reported that a very small amount of *N*-benzyloxycarbonyl-L-alanine 4-hexadecanoyl-2-nitrophenyl ester can form thermoreversible physical gels in methanol or cyclohexane, for which hydrogen bonding, dipole–dipole, and hydrophobic interactions are involved in establishing the network.[1] In our studies of the simplification of the structure required to cause physical gelation, we have discovered that *N*-benzyloxycarbonyl-L-valyl-L-valine n-octadecylamide is an excellent gelling agent, hardening a wide variety of organic liquids, including alkanes, alcohols, esters, ketones, aromatic molecules, mineral oils and edible oils.

The minimum concentrations of *N*-benzyloxycarbonyl-L-valyl-L-valine n-octadecylamide necessary for gelation are summarized in Table 1. Surprisingly, this compound can form physical gels and harden most organic liquids at very low concentration, except for hexane, tetrahydrofuran, chloroform, and pyridine. Using the sol–gel phase diagram in which the minimum gel concentration is plotted *vs.* temperature, the standard thermodynamic parameters[1] for the sol to gel transition are calculated as follows: ΔH (20 °C) = −36.5 kJ mol^{-1}, ΔS (20 °C) = −66.5 J K^{-1} mol^{-1} for cyclohexane, ΔH (20 °C) = −23.4 kJ mol^{-1}, ΔS (20 °C) = −18.4 J K^{-1} mol^{-1} for methanol, ΔH (20 °C) = −44.8 kJ mol^{-1}, ΔS (20 °C) = −98.7 J K^{-1} mol^{-1} for ethyl acetate, ΔH (20 °C) = −43.9 kJ mol^{-1}, ΔS (20 °C) = −89.5 J K^{-1} mol^{-1} for benzene, and ΔH (20 °C) = −33.9 kJ mol^{-1}, ΔS (20 °C) = −67.4 J K^{-1} mol^{-1} for tetrachloromethane. These parameters indicate that the enthalpic contribution compensates for the undesirable entropic change for gelation. Considering that the ΔH of hydrogen bonding for *N*-methylacetamide[2] in cyclohexane is −15.5 kJ mol^{-1}, the values of ΔH suggest that at least two hydrogen bonds are freshly formed when the gel is built up in organic solvents except protic methanol. Actually, *N*-benzyloxycarbonyl-L-valyl-L-valine n-octadecylamide is able to form three intermolecular hydrogen bonds between N–H and C=O of a urethane and two amide bonds. This is also supported by the fact that the FTIR spectrum of the gel in cyclohexane is characterized by bands attributed to intermolecular hydrogen bonding, *i.e.* 3290 cm^{-1} (νN–H of urethane and amides),



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1690 cm^{-1} (νC=O of urethane) and 1640 cm^{-1} (νC=O of amides).

The gelling abilities of some structurally related molecules **2–11** (non-gel-forming) and **12–17** (gelling forming) have been inspected. None of the related compounds involving glycine, L-alanine, L-leucine, L-proline, L-glutamic acid, or racemic D, L-valine exhibit gelling ability. Benzyloxycarbonyl (Z) and ethoxycarbonyl groups are suitable as the hydrophilic head group, but not the n-dodecyloxycarbonyl example. Furthermore, n-butylamide is not sufficient as a lypophilic tail group. Although *N*-benzyloxycarbonyl-L-valine n-octadecylamide is a gelling agent, the gelling ability is fairly inferior to that of *N*-benzyloxycarbonyl-L-valyl-L-valine n-octadecylamide, taking into account that the minimum gel concentrations are

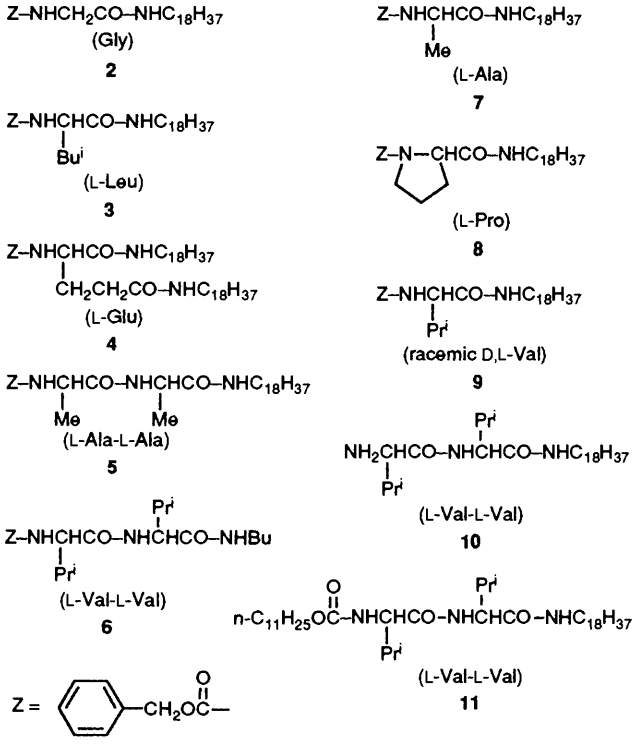
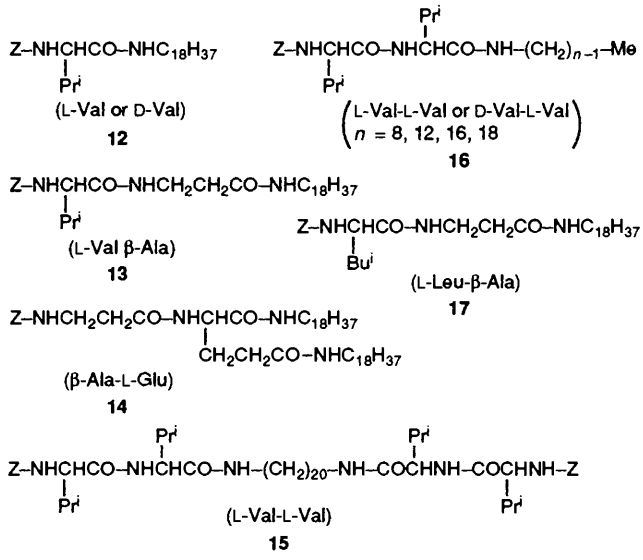


Table 1 Minimum gel concentration of *N*-benzyloxycarbonyl-L-valyl-L-valine n-octadecylamide necessary for gelation at 20 °C

Solvent	Minimum gel concentration g dm^{-3} (gelator/solvent)
Hexane	Insoluble
Cyclohexane	5
Methanol	9
Ethanol	15
Propan-1-ol	15
Propan-2-ol	19
Butan-1-ol	15
Ethyl acetate	8
Acetone	5
Butan-2-one	8
Cyclohexanone	12
Tetrahydrofuran	Isotropic[a]
1,4-Dioxane	18
Benzene	4
Chlorobenzene	4
Nitrobenzene	4
Toluene	14
N,N-Dimethylformamide	18
N,N-Dimethylacetamide	43
Dimethyl sulfoxide	3
Chloroform	Isotropic
Tetrachloromethane	18
Pyridine	Isotropic
Kerosene	4
Light oil	3
Heavy oil	8
Silicone oil	4
Salad oil	2
Soybean oil	2

[a] Isotropic = isotropic-like solution.



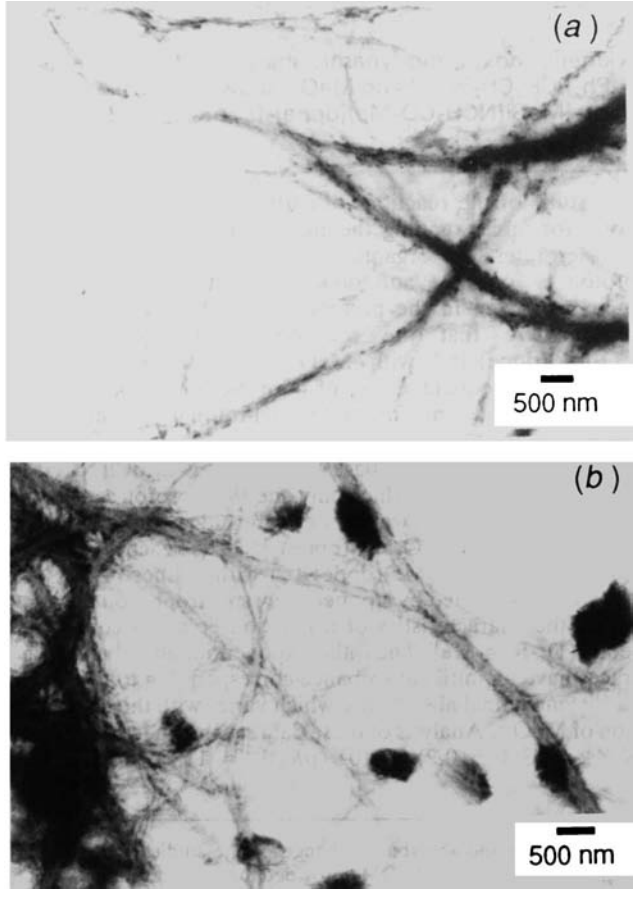


Fig. 1 TEMs of loose gels negatively stained by osmic acid: (*a*); *N*-benzyloxycarbonyl-L-valyl-L-valine n-octadecylamide in ethyl acetate (0.2 g dm^{-3}), (*b*); *N*-benzyloxycarbonyl-L-valyl-β-alanine n-octadecylamide in cyclohexane (0.3 g dm^{-3})

18 g dm^{-3} for cyclohexane, 24 g dm^{-3} for methanol, 19 g dm^{-3} for ethyl acetate and 46 g dm^{-3} for benzene at 20 °C. It is worth noting that the **15** can harden chloroform at 12 g dm^{-3}. About ten groups of small molecular gelling agents are so far known,[3] however, this molecule is, to our knowledge, the first compound that can gel chloroform. From these observations, we concluded: (*i*) Gelling ability strongly depends on the structure of the amino acid residue. (*ii*) Racemic molecules are unsuitable for gelation. (*iii*) The hydrophile–lypophile balance is a significant factor for gelation. (*iv*) Gelling ability is increased when a dipeptide is involved instead of the single amino acid.

The TEM of gels formed by *N*-benzyloxycarbonyl-L-valyl-L-valine n-octadecylamide in ethyl acetate and *N*-benzyloxycarbonyl-L-valyl-β-alanine n-octadecylamide in cyclohexane exhibit the gathering of numerous fibres juxtaposed and intertwined by several long slender aggregations (diameter *ca.* 10–30 nm) (Fig. 1). It can be assumed that the fibre-like aggregations are formed from numerous molecules by intermolecular hydrogen bonding, then they are juxtaposed and interlocked by van der Waals interaction as has been reported for the thermoreversible gelation of polymers,[4] and finally immobilize the organic liquid.

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