CHEMISTRY

AN ASIAN JOURNAL

www.chemasianj.org

4/06
2011

IYC 2011
International Year of CHEMISTRY

An ACES journal

Supported by:
GDCh Gesellschaft Deutscher Chemiker
ChemPubSoc Europe

WILEY-VCH

DOI: 10.1002/asia.201000560

Supramolecular Synthons in Designing Low Molecular Mass Gelling Agents: L-Amino Acid Methyl Ester Cinnamate Salts and their Anti-Solvent-Induced Instant Gelation

Pathik Sahoo,[a] D. Krishna Kumar,[b] Srinivasa R. Raghavan,[c] and Parthasarathi Dastidar*[a]

Abstract: Easy access to a class of chiral gelators has been achieved by exploiting primary ammonium monocarboxylate (**PAM**), a supramolecular synthon. A combinatorial library comprising of 16 salts, derived from 5 L-amino acid methyl esters and 4 cinnamic acid derivatives, has been prepared and scanned for gelation. Remarkably, 14 out of 16 salts prepared (87.5% of the salts) show moderate to good gelation abilities with various solvents, including commercial fuels, such as petrol. Anti-solvent induced instant gelation at room temperature has been achieved in all the gelator salts, indicating that the gelation process is indeed an aborted crystallization phenomenon. Rheology, optical and scanning electron microscopy, small angle neutron scattering, and X-ray powder diffraction have been used to characterize the gels. A structure-property correlation has been attempted, based on these data, in addition to the single-crystal structures of 5 gelator salts. Analysis of the FT-IR and ^{1}H NMR spectroscopy data reveals that some of these salts can be used as supramolecular containers for the slow release of certain pest sex pheromones. The present study clearly demonstrates the merit of crystal engineering and the supramolecular synthon approach in designing new materials with multiple properties.

Keywords: crystal engineering · gels · supramolecular chemistry · synthon · X-ray diffraction

Introduction

The term "supramolecular synthon" proposed by Desiraju is a well studied and accepted tool in crystal engineering for designing desired supramolecular structures.[1] The concept of a supramolecular synthon is derived from the term "synthon", as defined by Corey,[2] which applies to covalent organic synthesis. The term supramolecular synthon plays the same pivotal role in supramolecular synthesis that synthon does in covalent synthesis. Supramolecular synthons are spatial arrangements of intermolecular non-covalent interactions that frequently occur in supramolecular structures. They can, therefore, be relied upon to generate supramolecular functional materials. To use supramolecular synthons successfully in designing supramolecular structures, it is important that they are robust enough to ensure generality and predictability. Numerous examples of supramolecular structures, wherein supramolecular synthons have been exploited, testify to the power of supramolecular synthons.[3]

Among the various supramolecular functional materials, the low molecular mass weight gelators (LMWGs)[4] are an attractive supramolecular target. LMWGs are able to form gels with various organic (organogel) and aqueous (hydrogel) solvents. In a typical experiment, when a hot solution containing a small amount of LMWG (usually on or slightly above the minimum gelator concentration: MGC) is allowed

[a] P. Sahoo, Dr. P. Dastidar
Department of Organic Chemistry
Indian Association for the Cultivation of Science
2A & 2B Raja S. C. Mullick Road, Jadavpur,
Kolkata-700032, West Bengal (India)
Fax: (+91) 33-2473-2805
E-mail: parthod123@rediffmail.com
ocpd@iacs.res.in

[b] Dr. D. K. Kumar
Present address:
Department of Chemistry
Imperial College
London SW7 2AZ (UK)

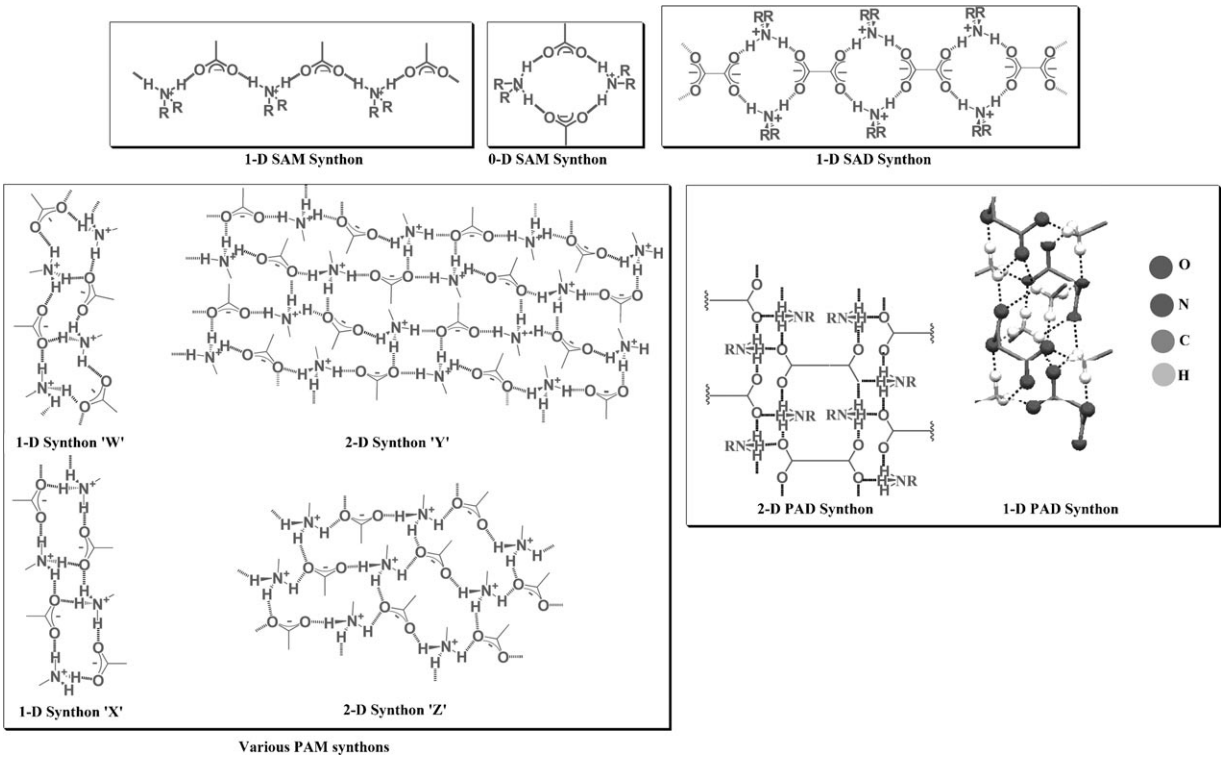
[c] Dr. S. R. Raghavan
Department Chemical & Biomolecular Engineering
University of Maryland
College Park, MD 20742-2111 (USA)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/asia.201000560.

to cool below a critical temperature (the sol–gel temperature), a solid like mass, which is able to hold its own weight upon turning the vial upside down, is formed. This is a visco-elastic material called a gel. Research on LMWGs has witnessed an upsurge because of their various potential applications, such as in structure-directing agents,[5] cosmetics,[6] conservation of artwork,[7] sensors,[8] electro-optics/photonics,[9] catalysis,[10] drug delivery,[11] and biomedical applications.[12] However, designing a gelling agent is challenging. It is believed that gelation is an aborted crystallization process wherein the gelator molecules form self-assembled fibrillar networks (SAFINs)[13] that, furthermore, form hierarchical three-dimensional networks, which self assemble through junction zones.[14] The solvent molecules are then immobilized, owing to the capillary force within such 3D networks of SAFINs, resulting in gel formation. The lack of molecular level understanding of SAFIN and its self-assembled 3D-hierarchical network formation, the interactions involving the targeted solvent with the SAFINs and the wide structural diversity of the known LMWG molecules, make it difficult to plan a strategy to achieve a rational design of gelators.

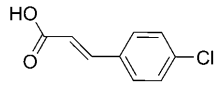
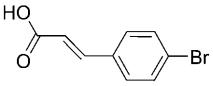
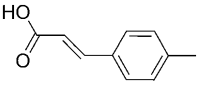
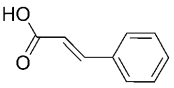
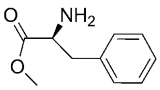
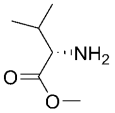
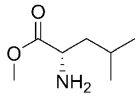
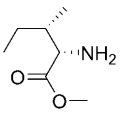
It was proposed a decade ago that 1D-hydrogen-bonding networks promoted gelation whereas 2D and 3D networks either produced weak gels or no gelation at all.[15] This rationale was based on the various microscopic observations of SAFINs that revealed the morphological features of highly branched and/or entangled 1D fibers. It was, therefore, reasoned that anisotropic interactions, such as hydrogen bonding of the gelator molecules that allowed growth in one direction and the lack of such interactions in the other two dimensions, prevented lateral growth resulting in 1D fibers, which may favour SAFIN formation and a resultant gel. The fact that this hypothesis was indeed based on a logical foundation was most explicitly demonstrated by us.[16] It is, therefore, worth looking for a 1D-network forming supramolecular synthon that would allow SAFIN formation, which might eventually promote gelation. The gel-forming supramolecular synthons that we have identified and exploited thus far are secondary ammonium monocarboxylate (**SAM**),[17] secondary ammonium dicarboxylate (**SAD**),[18] primary ammonium monocarboxylate (**PAM**),[19] and primary ammonium dicarboxylate (**PAD**)[20] (Scheme 1). Particularly interesting among them is the **PAM** synthon, which frequently displays 1D-hydrogen-bonding networks (HBN, synthons **W** and **X**, Scheme 1) along with occasional 2D HBNs (synthons **Y** and **Z**, Scheme 1). As both 1D and 2D HBNs are important in gelation, we have been able to exploit the **PAM** synthon to discover a large number of gelling agents.[19]

Herein, we demonstrate how the **PAM** synthon is exploited to reveal easy access to a class of chiral gelators by scanning a combinatorial library of organic salts derived from natural L-amino acid methyl esters and cinnamic acids (Table 1). Synthesis, characterization, and gelation studies of this new class of gelling agent are reported and a structure–property correlation, based on single crystal X-ray diffraction, scanning electron microscopy (SEM), X-ray powder diffraction (XRPD), and small-angle neutron scattering (SANS) data, has been attempted. Interestingly most of the



Scheme 1. Gel-forming supramolecular synthons.

Table 1. Salts formed in the combinatorial library of amino acid methyl esters and cinnamic acid derivatives.

	Cinnamic acid derivatives			
Amino acid methyl esters				
	not reacted	not reacted	**Ala.4MeCin** gelator	**Ala.Cin** gelator
	**Phe.4CLCin** gelator	**Phe.4BrCin** gelator	**Phe.4MeCin** gelator	**Phe.Cin** gelator
	not reacted	not reacted	**Val.4MeCin** gelator	**Val.Cin** gelator
	**Leu.4CLCin** gelator	**Leu.4BrCin** gelator	**Leu.4MeCin** gelator	**Leu.Cin** gelator
	**Ile.4CLCin** nongelator	**Ile.4BrCin** nongelator	**Ile.4MeCin** gelator	**Ile.Cin** gelator

gels could also be formed by anti-solvent induced precipitation techniques at room temperature.

Results and Discussion

Synthesis and Gelation

Organic-salt formation is probably the easiest reaction to perform in chemistry. Within a short period, a large number of organic salts can be prepared with quantitative or near-quantitative yield, which can then be scanned for their gelation behavior. A virtually infinite combination of commercially available acids and amines allows one to prepare a combinatorial library for discovering new classes of gelators.[17d,19a,20b,21] Moreover, charge assisted hydrogen bonding in organic salts is stronger (40–190 kJ mol^{-1}) than normal hydrogen bonding (10–65 kJ mol^{-1}) making them more robust, which is often a requirement for real-life applications.

Thus, we have been focussing our attention on salt-based compounds as potential LMWGs, as this supramolecular approach is definitely advantageous over the time-consuming covalent synthetic approach, which might often lead to frustration in the quest for new gelators. Supramolecular chirality is an important aspect for its role in developing chiral catalysts,[22] chiro-optical switches,[23] helical crystallization of proteins and inorganic replicas,[24] chiral resolution,[25] and so forth, and chiral LMWGs offer such supramolecular systems. To get an easy access to chiral supramolecular systems such as chiral LMWGs, we have decided to exploit the **PAM** synthon in a combinatorial library of organic salts derived from naturally occurring L-amino acid esters and cinnamic acids as potential LMWGs. The salts listed in Table 1 were prepared by reacting free L-amino acid esters with the corresponding cinnamic acids (see the Experimental Section). We have deliberately chosen L-amino acid methyl esters, which have non-functional side chains, and 4-substituted cinnamic acids and cinnamic acid itself as reactants; although L-amino acid methyl esters without functional side chains were chosen to avoid any other strong and directional intermolecular interactions that might interfere and disrupt the formation of **PAM** synthon, 4-substituted cinnamic acids and cinnamic acid itself were selected as they are important moieties in other LMWGs reported by our group.[4a] Moreover, a Cambridge structural database (CSD) search containing cinnamate (without any H attached to the aromatic ring) and C–NH_3^+ as search fragments, resulted in 47 principal hits, of which included 1D **PAM** synthons **W** (18 hits) and **X** (14 hits).[26] Out of 20 combinations involving 5 amino acid methyl esters and 4 cinnamic acids (Table 1), only 16 salts could be formed. These were classified by using FT-IR spectroscopy analysis, the spectra revealed the band for COO^-, $\tilde{\nu}$ = 1638–1644 cm^{-1}. Gelation tests performed with 15 different prototype solvents, which included both polar and non-polar solvents, as well as commercial fuels, such as petrol, revealed that 87.5% of the salts tend to form a gel. Notably, we have limited the gelation study within 4 wt% (w/v) and out of 14 gelator salts, 8 of them showed a minimum gelator concentration within 4 wt%; the rest produced either a gelatinous precipitate or a weak gel. The amino acid side chains and anionic counter parts of the salts seem to have a profound effect on the gelation ability of the gelator salts studied herein, as all the gelator salts in-

Table 2. Gelation data.[a]

Entry	Salts	DMSO	DMF	Methyl salicylate	$PhNO_2$	PhCl	PhBr	PhMe	o-Xylene	*m*-Xylene	*p*-Xylene	1,2-Dichloro benzene	1,2-Dichloro ethane	MeOH	THF	Petrol
1	**Ala.Cin**	S	S	S	S	S	S	S	WG	WG	WG	S	S	S	S	S
2	**Ala.4MeCin**	S	S	S	S	S	S	GP	GP	GP	GP	S	S	S	S	S
3	**Phe.Cin**	S	S	GP	GP	4(41)	4(44)	4(51)	2.1(42)	1.5(44)	2.1(45)	4(50)	S	S	S	WG
4	**Phe.4MeCin**	S	S	S	WG	WG	WG	4(33)	4(50)	4(48)	4(54)	WG	S	S	S	WG
5	**Phe.4CLCin**	S	S	WG	S	_[b]	_[b]	WG	_[b]	_[b]	_[b]	_[b]	_[b]	S	S	PPT
6	**Phe.4BrCin**	S	S	GP	GP	GP	GP	PPT	PPT	PPT	PPT	GP	NC	PC	S	PPT
7	**Val.Cin**	S	S	WG	WG	2.6(37)	2.6(42)	4(53)	WG	WG	WG	WG	WG	S	S	S
8	**Val.4MeCin**	S	S	WG	WG	WG	WG	WG	GP	WG	4(45)	GP	F	S	S	S
9	**Leu.Cin**	S	S	4(48)	4(40)	4(45)	4(45)	3.6(45)	4(55)	1.94(46)	1.96(42)	4(48)	WG	S	S	S
10	**Leu.4MeCin**	S	S	4(61)	WG	1.9(48)	1.9(47)	1.3(42)	1(48)	0.9(47)	0.9(51)	2.6(56)	4(45)	S	S	WG
11	**Leu.4ClCin**	WG	WG	3.94(59)	2.6(57)	WG	3.98(62)	4(59)	4(57)	3.94(65)	4(75)	WG	S	S	S	S
12	**Leu.4BrCin**	S	S	PPT	S	PPT	PPT	GP	PPT	PPT	PPT	PPT	PPT	S	S	PPT
13	**Ile.Cin**	S	S	S	S	S	S	S	WG	WG	WG	S	S	S	S	2.6(57)
14	**Ile.4MeCin**	S	S	3.4(40)	WG	PPT	WG	4(52)	WG	3.8(50)	2.6(48)	4(47)	S	S	S	2.6(61)
15	**Ile.4ClCin**	S	S	PPT	PPT	PPT	PPT	PPT	PPT	PPT	PPT	PPT	PPT	S	S	PPT
16	**Ile.4BrCin**	S	S	PPT	PPT	PPT	PPT	PPT	PPT	PPT	PPT	PPT	PPT	S	S	PPT

[a] Values represent the minimum gelator concentration (MGC) in wt% (w/v); values within parenthesis represent the T_{gel} (gel–sol dissociation temperature, °C); S: soluble; PPT: precipitate; G: gel; WG: weak gel; NC: needle crystals; GP: gelatenous precipitate; PC: plate-shaped crystals; F: fiber. Petrol was obtained from the local petrol station. [b] Not soluble and did not produce gel even after dissolving in MeOH.

volve phenylalanine and leucine-methyl ester, and 4-methyl cinnamic- and cinnamic acid itself are gelators (Table 2). Both cinnamate and 4-methylcinnamate salts of L-leucine are the most versatile gelling agents, as they are able to form stable gels in 9 out of the 15 solvents studied herein; the corresponding salts of L-isoleucine, interestingly, form a gel with commercial fuels, such as petrol. All the gels reported herein display thermo-reversible properties (Table 2).

Table-top rheology[27] was used to assess the thermal stability of the gels in a given solvent. *p*-Xylene was the most frequently gelled solvent used in the present study, the gel–sol dissociation temperatures (T_{gel}) at various concentrations of the gelators were measured by using the dropped-ball method (see the Experimental Section) and the T_{gel} versus [gelator] plot was also examined (see Figure 1a). Analysis of the relationship reveals that T_{gel} steadily increases with the increase in concentration of the gelators. This indicates that the self-assembly process in the gel state is mainly governed by strong intermolecular interactions, such as hydrogen bonding. Further analysis of Figure 1a indicates that **Leu.4MeCin** forms the most thermally stable *p*-xylene gel, whereas **Ile.4MeCin** produces the least stable one. Interestingly, the semilog of the mole fraction of each gelator at each concentration, plotted against $1/T_{gel}$, K^{-1}, reveals a good linear plot and may be compared with the Schroeder–van Laar equation [Eq. (1), Figure 1b]

$$\ln [\text{gelator}] = -(\Delta H_m/RT_{gel}) + \text{constant} \quad (1)$$

in which ΔH_m and T_{gel} are the enthalpy of melting and temperature of the gel–sol transition, respectively. Assuming that the gel melts into an ideal solution and a known amount of gelator is involved in the transition, these gel–sol transitions may be considered as first-order transition. The enthalpy (ΔH_m) values associated with these gel–sol transitions are within the range of 31.6–59.0 kJ mol^{-1}.

Rheology

To evaluate the rheological response, a 4 wt% (w/v) toluene gel of **Phe.Cin** was studied by dynamic rheology; a characteristic gel-like response was found in this case. The elastic modulus **G′** and viscous modulus **G″** are plotted as functions of the angular frequency ω and it is clear from Figure 2 that **G′** is considerably higher than **G″** over the range of frequencies. The gel modulus **G′** is around 91 kPa, which is considerably high, and indicates that **Phe.Cin** is a stiff gel.

Anti-Solvent Induced Gelation

The heating process in gel formation is considered to be a potential impediment in real-life applications. Thus, gelation without heating, wherein the gelator is synthesized in situ, has been reported by us[19b–c] and others.[4z] As gelation is widely believed to be an aborted crystallization process, which may be considered a kind of precipitation that leads to the formation of SAFINs and eventually gel, it is considered worthwhile to use an anti-solvent[28] to induce gelation. For this purpose, two solvent systems, such as $CHCl_3$ or CH_2Cl_2 and alkanes (*n*-pentane, *n*-hexane, cyclohexane, *n*-heptane, *n*-octane) are chosen; although the gelator salts are freely soluble in either $CHCl_3$ or CH_2Cl_2, they are completely insoluble in alkanes. As the solvents $CHCl_3$ or CH_2Cl_2 and alkanes are highly miscible, the alkanes are expected to act as anti-solvents to induce gelation by forcing the gelator salts from their corresponding $CHCl_3$ or CH_2Cl_2 solutions to precipitate out as SAFINs. Interestingly, all the gelator salts that show a reasonable gelation ability (Table 2, entries 3–4,

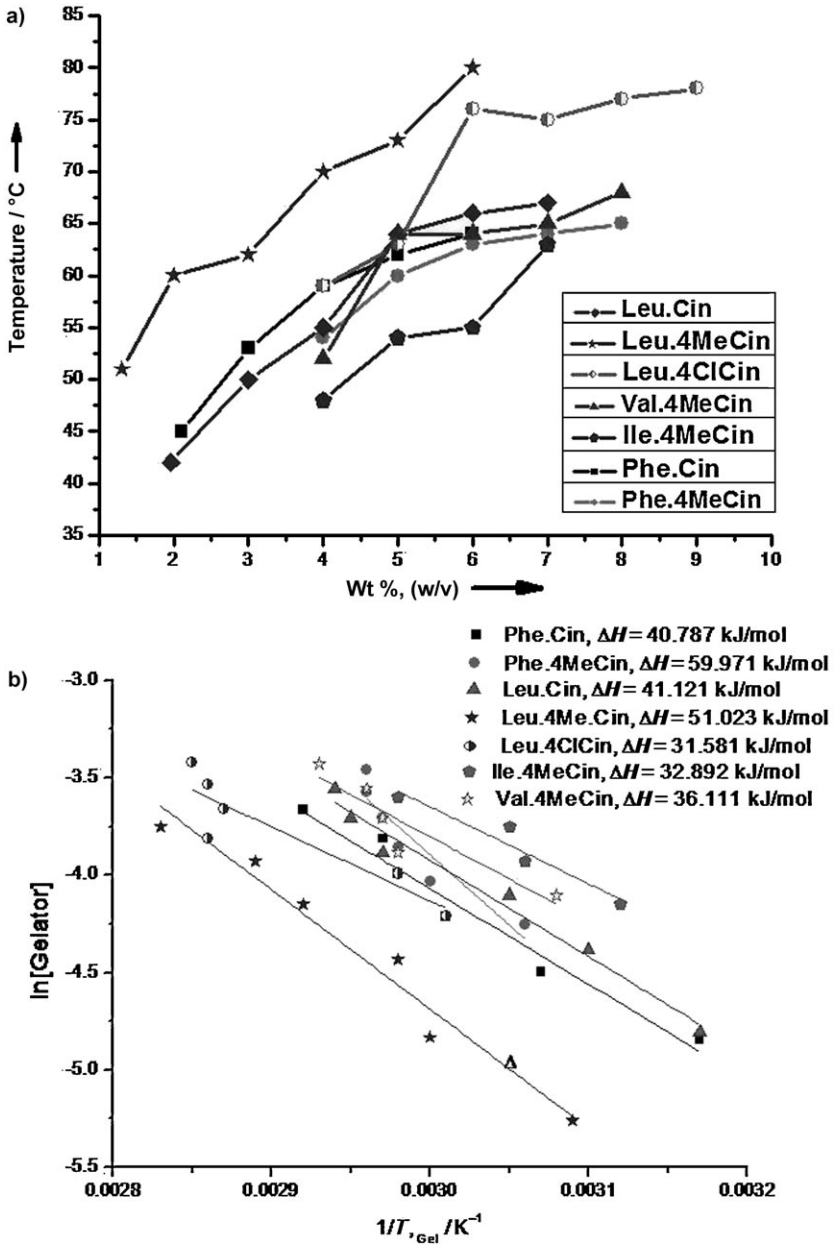


Figure 1. a) T_{gel} vs [gelator] plots of various gels; b) Semilog plot of the mole fraction of the gelators against 1/*T*.

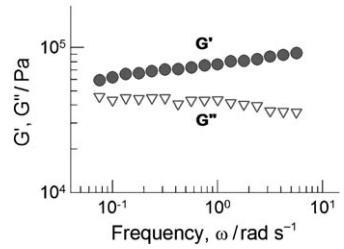


Figure 2. Dynamic rheology at 25 °C of a gel of 4 wt % **Phe.Cin** in toluene. The elastic modulus G′ and the viscous modulus G″ are shown as functions of the angular frequency ω. The strain used was 0.5 %.

7–10, 14,) also display anti-solvent induced gelation. In a typical experiment, 35 mg of a gelator salt was dissolved in 300 μL of $CHCl_3$ or CH_2Cl_2. Then, about 1 mL of the anti-solvent was added to this solution and a gel formed within a few seconds. Microscopic observation reveals the existence of highly entangled crystalline fibers in the gel and a xerogel state for samples prepared under these conventional gelling conditions (Figure 3). The morphological feature of the gel networks prepared under conventional conditions, by using some of the gelator salts, appear to be made of 1D fibers of varying length and thickness. Although most of the cases display a highly entangled, dense network of 1D fibers, the gelator salt **Ile.Cin**, made from a petrol gel, produces highly aligned 1D fibers with a tape-type morphology. The solvent molecules are understandably immobilized in these networks to effect gel formation. Interestingly, the gelator salt **Ala.4MeCin**, which produces only gelateneous precipitates with some of the solvents studied herein, generates a spherulite-like morphology in the dried sample, derived from a toluene solution, indicating that the nature of this salt is more crystalline (Figure 4).

Small Angle Neutron Scattering (SANS)

To study the morphology of the gels, SANS data were obtained on a selected 4 wt % (w/v) gel sample of **Val.Cin** in deuterated toluene. The deuteration of the solvent ensures good contrast between the gelator aggregates and the continuous phase. It is clear from Figure 5 that the intensity (*I*) follows the Porod's law,[29] that is, $I \sim q^{-4}$. This indicates that the sample consists of a two-phase structure with a sharp boundary between the phases. No characteristic size can be discerned within the scattering window. Based on the morphology observed in the SEM micrograph of the 4 wt % toluene xerogel of **Val.Cin** (Figure 4) and the SANS data, it may be concluded that the scattering objects in this gel are fibers with high-aspect ratio. Similar

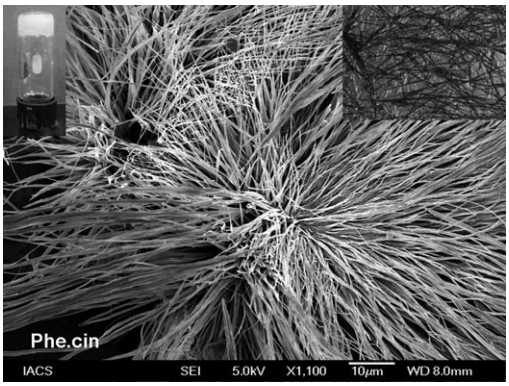


Figure 3. A SEM picture of the gel fibers in the xerogel of **Phe.Cin** in chloroform prepared by anti-solvent (*n*-hexane) induced gelation. Insets: Anti-solvent (*n*-hexane) induced chloroform gel of **Phe.Cin** and the gel fibers seen by using an optical microscope.

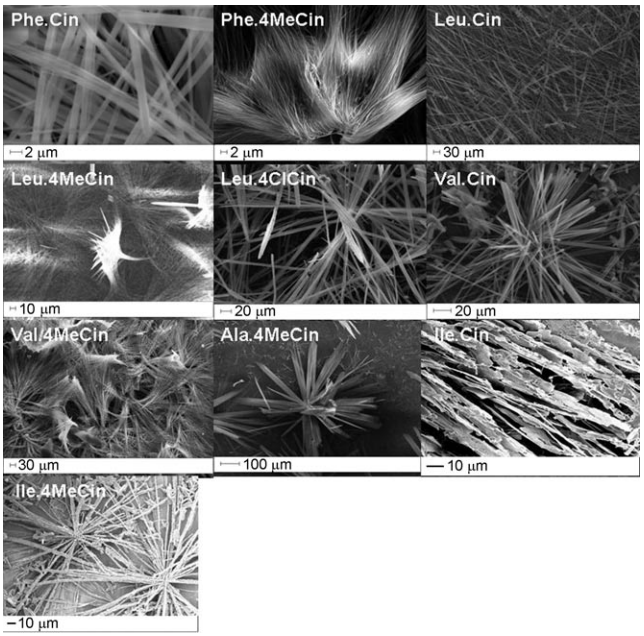


Figure 4. SEM images of the gel fibers in the xerogels (toluene, 4 wt%, w/v); xerogels of **Val.4MeCin** and **Ile.Cin** are prepared from *p*-xylene (4 wt%, w/v) and petrol (1 wt%, w/v), respectively.

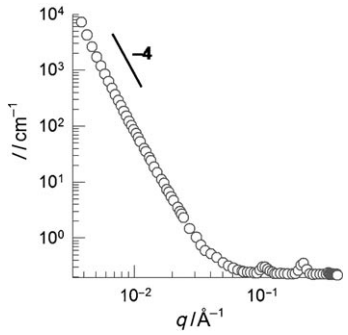


Figure 5. SANS data at 25°C for 4 wt% gel of **Val.Cin** in deuterated toluene.

SANS data are also reported by us for gels of secondary ammonium salts of various bile acids.[17d]

Structure–Property Correlation and Supramolecular Synthons

The chance of showing gelation ability by **PAM** salts is high, as these salts frequently display 1D synthons with occasional 2D **PAM** synthons (Scheme 1). Thus, the fact that 87.5% of the salts of the combinatorial library (Table 1) show a tendency to form gels, clearly support the working hypothesis that 1D HBN promotes gelation, whereas both 2D and 3D HBN produce weak gels or no gelation at all. It was, therefore, worthwhile to investigate the single crystal structures of these gelators to study the supramolecular synthons present herein. Five single crystals of the gelator salts (**Ala.4MeCin**, **Ala.Cin**, **Val.4MeCin**, **Val.Cin**, and **Ile.4MeCin**) of X-ray diffraction quality (Table 3) were examined. All the crystals were obtained by evaporation of a diethyl ether solution of the corresponding salts except **Val.4MeCin**, which was crystallized from a hexane/$CHCl_3$ mixture. All the crystals belong to the non-centrosymmetric orthorhombic space group $P2_12_12_1$ except **Ala.4MeCin**, which crystallizes in the non-centrosymmetric monoclinic space group $P2_1$. The range of carboxyl C–O bond lengths (1.244(3)–1.276(2) Å) in all these salts indicate the carboxylate (COO^-) nature that resulted from complete proton transfer or salt formation. FT-IR analysis reveals bands in the range of $\tilde{\nu}=1640$–$1644\ cm^{-1}$, which also support the presence of COO^- functionality in these salts. Thus, after proton transfer or salt formation, the main hydrogen-bond acceptor and donor are $-COO^-$ and $-NH_3^+$, respectively, and charge assisted N^+–$H\cdots O^-$ hydrogen bonding [$N^+\cdots O^- = 2.689$ (2 Å; $\sphericalangle$ N^+–$H\cdots O^- = 145.5$–$174.7°$] play a crucial role in directing the supramolecular architectures in the crystal structures. Interestingly, in all these crystal structures, the charge assisted hydrogen bonding leads to the formation of 1D **PAM** synthon **X** (Scheme 1). The details of the hydrogen-bonding parameters are given in the Supporting Information. As expected, the ester moiety abstains from any hydrogen-bonding interactions. Notably, in our recent report on a new class of gelator derived from various benzylammonium benzoates,[19c] both 1D **PAM** synthons **W** and **X** along with some 2D HBNs are present in the corresponding crystal structures. In these cases, various substituents on the aromatic ring of the benzoate moiety seem to play a crucial role in determining the final outcome of the supramolecular synthons.

Remarkably, for all the structures in this study the **PAM** synthon **W** was present and various substituents of the anionic moiety and different amino acid side chains do not seem to have any influence on the resultant supramolecular synthon. Although, in the absence of the crystal structures of the other salts in the combinatorial library, it is not possible to comment on the supramolecular synthons present therein, it may be reasonable to believe that 1D supramolecular **PAM** synthons, such as **W** or **X**, might be responsible for the majority of the salts (87.5%) that form gels. Analysis

Table 3. Crystal data.

Crystal parameters	**Ala.Cin**	**Ala.4MeCin**	**Ile.4MeCin**	**Val.Cin**	**Val.4MeCin**
CCDC No	776090	776089	776091	776093	776092
empirical formula	$C_{13}H_{17}NO_4$	$C_{14}H_{19}NO_4$	$C_{17}H_{25}NO_4$	$C_{15}H_{21}NO_4$	$C_{17}H_{24}Cl_3NO_4$
formula weight	251.28	265.30	307.38	279.33	412.72
crystal size [mm]	0.31×0.24×0.16	0.36×0.27×0.18	0.32×0.25×0.16	0.36×0.26×0.18	0.29×0.22×0.15
crystal system	orthorhombic	monoclinic	orthorhombic	orthorhombic	orthorhombic
space group	$P2_12_12_1$	$P2_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
a [Å]	5.6394(8)	8.8677(10)	5.8771(8)	5.8514(6)	6.1743(9)
b [Å]	8.9098(12)	5.7520(7)	14.867(2)	9.3189(9)	18.277(3)
c [Å]	27.051(4)	14.7674(17)	19.325(3)	27.088(3)	18.664(3)
α [°]	90.00	90.00	90.00	90.00	90.00
β [°]	90.00	103.376(2)	90.00	90.00	90.00
γ [°]	90.00	90.00	90.00	90.00	90.00
V [Å^3]	1359.2(3)	732.81(15)	1688.5(4)	1477.1(3)	2106.2(5)
Z	4	2	4	4	4
F(000)	536	284	664	600	864
ν $Mo_{K\alpha}$ [mm^{-1}]	0.091	0.088	0.085	0.091	0.455
T [K]	100(2)	100(2)	100(2)	100(2)	100(2)
R_{int}	0.0276	0.0254	0.0526	0.0386	0.0729
h, k, l	−6/6, −10/8, −33/27	−10/10, −7/7, −18/17	−7/6, −18/18, −23/23	−6/7, −11/11, −32/32	−7/7, −21/21, −21/22
$\theta_{min/max}$ [°]	1.51/26.00	1.42/26.00	1.73/25.82	1.50/25.25	1.56/25.25
reflections collected/unique/ observed [$I>2\sigma(I)$]	7253/1568/1520	5636/1579/1508	17001/1907/1714	10750/1580/1505	15290/2227/1996
data/restraints/parameters	1568/0/162	1579/1/176	1907/0/204	1580/0/185	2227/0/231
goodness of fit on F^2	1.038	1.058	1.062	1.104	1.075
final R indices [$I>2\sigma(I)$]	R_1=0.0334	R_1=0.0341	R_1=0.0327	R_1=0.0506	R_1=0.0677
	wR_2=0.0835	wR_2=0.0847	wR_2=0.0815	wR_2=0.1299	wR_2=0.1383
R indices (all data)	R_1=0.0348	R_1=0.0362	R_1=0.0372	R_1=0.0531	R_1=0.0788
	wR_2=0.0845	wR_2=0.0859	wR_2=0.0838	wR_2=0.1313	wR_2=0.1433

of the X-ray diffraction data reveals that none of the crystals include any solvent molecules in the crystal lattice, except **Val.4MeCin** wherein the lattice-included solvent was chloroform, which does not seem to affect the formation of synthon **W**. The 1D hydrogen bonded chains are packed in parallel fashion along the crystallographic *a*-axis in all the salts, except in **Ala.4MeCin** wherein the chains are packed along the crystallographic *b*-axis. Illustrated in Figure 6 are the various features of the single-crystal structures of these gelator salts.

To find out whether the supramolecular **PAM** synthon **W** is present or not in the SAFINs of the corresponding gels, one has to record good quality XRPD patterns of the gel samples, which is not straightforward, as the gel samples diffract poorly (as a result of the small amounts and their moderate-crystalline nature). The xerogel samples may be considered as reasonably representative, although the formation of other morphs, solvates, and so forth cannot be ruled out. XRPD patterns simulated from the single-crystal data, and experimental-XRPD patterns of the bulk-gelator salt and the corresponding gel, are compared following a method originally proposed by Weiss et al.[30] Depicted in Figure 7 is the comparison of XRPD plots of a few selected gelator salts, obtained under various conditions. It is clear that in the cases of **Val.Cin** and **Ile.4MeCin**, the major peak positions of the XRPD patterns do match quite well and, therefore, it may be concluded that the same supramolecular **PAM** synthon **W** is also present in the corresponding xerogels.

In the case of **Val.4MeCin**, the single crystal structure contains $CHCl_3$ in the lattice and, therefore, the simulated XRPD pattern is quiet different from that of the bulk solid,

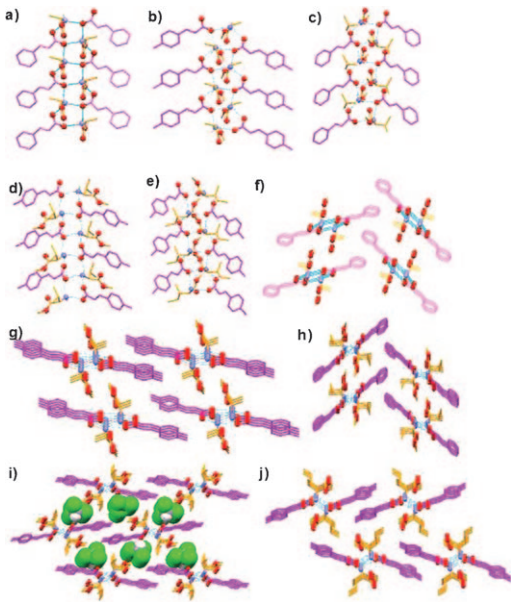


Figure 6. Crystal structure illustrations; a)–e) supramolecular **PAM** synthon **W** found in the crystal structures of **Ala.4MeCin**, **Ala.Cin**, **Val.4MeCin**, **Val.Cin**, and **Ile.4MeCin**, respectively, and f)–j) the parallel packing of the 1D chains in the corresponding crystal structures; lattice included $CHCl_3$ is shown in space filling model.

CHEMISTRY
AN ASIAN JOURNAL

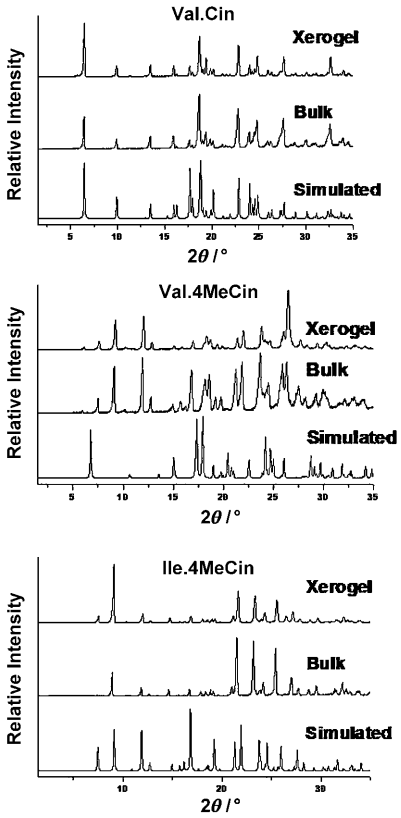


Figure 7. XRPD patterns of some selected gelators under various conditions; the xerogels of **Val.Cin** and **Ile.4MeCin** are prepared from toluene, whereas **Val.4MeCin** is made from *p*-xylene.

which was synthesized from diethyl ether. Interestingly, the XRPD patterns of the bulk solid and the xerogel are near super-imposable, indicating the identical nature of the crystal packing in both the states. However, in the absence of a solvate-free crystal structure of **Val.4MeCin**, it is not possible to comment with certainty on the supramolecular synthon present in the corresponding xerogel or bulk solid.

Organic Salts as Supramolecular Container of Sex Pheromones

It was realized during the course of the current study that three of the L-amino acid methyl esters, namely valine-, leucine-, and isoleucine-methyl esters, are the sex pheromones of certain pests.[31] The ΔpK_a range of the corresponding acids and amines (2.57–3.57) for the prepared salts indicates that these salts could be labile.[32] The volatile L-amino acid methyl ester moieties might be released to the atmosphere thereby making these salts supramolecular, slow release, sex-pheromone containers. Analysis of FT-IR and ^{1}H NMR spectroscopies of **Val.4MeCin** recorded over time, supports this fact (Figure 8); over time a new band at $\tilde{\nu}=1680\,cm^{-1}$ (COOH) emerges and the bands at $\tilde{\nu}=1746\,cm^{-1}$ (C=O of ester) and $\tilde{\nu}=1640\,cm^{-1}$ (COO^-) slowly diminish, indicating the release of the sex pheromone valine methyl ester. A

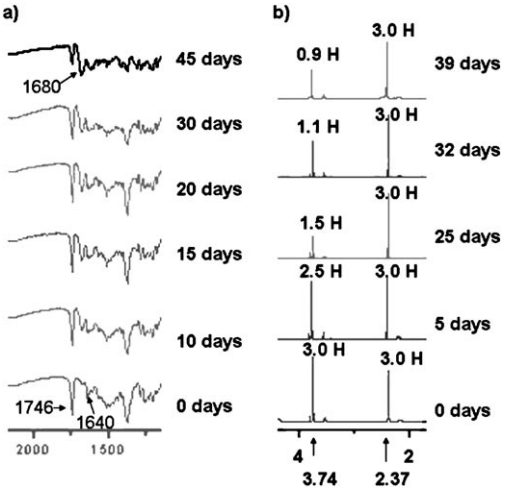


Figure 8. a) FT-IR spectra and b) ^{1}H NMR spectra of **Val.4MeCin** recorded at various time intervals.

similar observation can be made for the ^{1}H NMR spectra; the singlet peak at $\delta=3.74$ ppm for ester methyl protons slowly disappears with time, whereas the corresponding protons of the 4-Me group of the cinnamate moiety remain unchanged.

Conclusions

An easy access to chiral gelators by following a supramolecular synthons-based design strategy has been demonstrated. The fact that 87.5% of the salts prepared herein have the tendency to form moderate to good gels with various solvents clearly emphasizes the power of the supramolecular synthon approach in designing new gelators. The exclusive presence of the 1D **PAM** synthon **W** in the single crystal structures of the five gelator salts and the XRPD studies on some selected gelator salts, indicates that the **PAM** synthon appears to be responsible for the gelation abilities of the salts prepared from various L-amino acid methyl esters and cinnamic acid derivatives. Although the **PAM** synthon provided the required 1D HBN for gelation, the L-amino acid moieties afforded chirality to give easy access to chiral gelators. The anti-solvent induced gelation observed for these gelator salts and the structure–property correlation studies clearly demonstrate that the gelation is indeed an aborted crystallization phenomenon and that the supramolecular information (supramolecular synthon) already embedded in the neat crystal structures might play a crucial role in SAFIN formation, which ultimately leads to the formation of a gel under suitable conditions. However, to improve the strategies for designing LMWGs, detailed understanding is needed of other parameters, such as the nucleation of gel-fiber formation, gel-fiber self assembly leading to SAFIN, and interactions of the SAFINs with the targeted solvents to form a gel. The fact that some of the salts can be used as supramolecular containers for the slow release of pest sex

pheromones is intriguing and clearly emphasizes the merit of crystal engineering in designing materials with multiple properties.

Experimental Section

Materials and Methods

All the chemicals (Aldrich) and solvents (A.R. grade, S.D. Fine Chemicals, India) are commercially available and were used without any further purification. The petrol used in the gelation experiments was purchased from the local market. Microanalyses were performed by using a Perkin–Elmer elemental analyzer 2400, Series II. The FT-IR spectra were recorded by using a Perkin–Elmer Spectrum GX. The powder X-ray patterns were recorded by using a XPERT Philips ($Cu_{K\alpha}$ radiation, $\lambda = 1.5418$ Å) diffractometer. The scanning electron microscopy (FT-SEM) was performed by using a JEOL; JSM-6700F microscope. The single crystal X-ray diffraction data were recorded by using a BRUKER AXS, SMART APEX II.

Preparation of Salts

Amino acid esters, namely glycine methyl ester hydrochloride, alanine methyl ester hydrochloride, valine methyl ester hydrochloride, leucine methyl ester hydrochloride, and phenylalanine methyl ester hydrochloride were purchased from Aldrich. Crude isoleucine methyl ester hydrochloride was prepared by following the literature procedure.[33] Free amino acid methyl ester was prepared by treating the aqueous solution of the corresponding amino acid methyl ester hydrochloride with an aqueous solution of K_2CO_3 (2.0 M) followed by extraction into a diethyl-ether layer, which was subsequently dried over anhydrous Na_2SO_4. The organic layer containing the free amino acid methyl ester was then reacted with the corresponding cinnamic acid derivative and, upon evaporation of the ether layer using an aspirator pump; the corresponding cinnamate salt was isolated and subjected to various physico-chemical analyses (Supporting Information) and gelation tests.

Rheological Studies

Dynamic rheological experiments were performed by using an AR2000 stress-controlled rheometer (TA Instruments). The samples were run at 25 °C by using cone-and-plate geometry (40 mm diameter, 2° cone angle). Frequency sweeps were conducted in the linear viscoelastic regime of each sample, as determined previously by stress-sweep experiments.

Small-Angle Neutron Scattering (SANS)

SANS experiments were carried out by means of the NG-7 (30 m) beamline at NIST in Gaithersburg, MD. Neutrons with a wavelength of 6 Å were selected. Three sample–detector distances were used to obtain data over a range of wave vectors from 0.004 to 0.4 $Å^{-1}$. Samples were studied in 2 mm quartz cells at 25 °C. Scattering spectra were corrected and placed on an absolute scale using NIST calibration standards. The data are shown as plots of the absolute intensity I versus the wave vector $q = (4\pi \sin(\theta/2))/\lambda$, for which λ is the wavelength of incident neutrons and θ is the scattering angle.

Crystal Structures

CCDC 776090 (**Ala.Cin**), 776089 (**Ala.4MeCin**), 776091 (**Ile.4MeCin**), 776093 (**Val.Cin**), and 776092 (**Val.4MeCin**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgements

P.D. thanks CSIR for financial support. P.S. thanks CSIR for SRF fellowships. We acknowledge NIST for facilitating the SANS experiments performed as part of this work.

[1] a) G. R. Desiraju, *Angew. Chem.* **1995**, *107*, 2541; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2311; b) V. R. Thalladi, B. S. Goud, V. J. Hoy, F. H. Allen, J. A. K. Howard, G. R. Desiraju, *Chem. Commun.* **1996**, 401; c) G. R. Desiraju, *Angew. Chem.* **2007**, *119*, 8492; *Angew. Chem. Int. Ed.* **2007**, *46*, 8342; d) G. R. Desiraju, *J. Mol. Struct.* **2003**, *656*, 5.

[2] E. J. Corey, *Pure Appl. Chem.* **1967**, *14*, 19.

[3] a) C. B. Aakeröy, B. M. T. Scott, M. M. Smith, J. F. Urbina, J. Desper, *Inorg. Chem.* **2009**, *48*, 4052; b) P. M. Bhatt, Y. Azim, T. S. Thakur, G. R. Desiraju, *Cryst. Growth Des.* **2009**, *9*, 951; c) R. Banerjee, B. K. Saha, G. R. Desiraju, *CrystEngComm* **2006**, *8*, 680; d) L. S. Reddy, N. J. Babu, A. Nangia, *Chem. Commun.* **2006**, 1369; e) C. B. Aakeröy, J. Desper, J. F. Urbina, *Chem. Commun.* **2005**, 2820; f) D. R. Turner, B. Smith, A. E. Goeta, I. R. Evans, D. A. Tocher, J. A. K. Howard, J. W. Steed, *CrystEngComm* **2004**, *6*, 633; g) F. H. Allen, V. J. Hoy, J. A. K. Howard, V. R. Thalladi, G. R. Desiraju, C. C. Wilson, G. J. McIntyre, *J. Am. Chem. Soc.* **1997**, *119*, 3477; h) D. S. Reddy, Y. E. Ovchinnikov, O. V. Shishkin, Y. T. Struchkov, G. R. Desiraju, *J. Am. Chem. Soc.* **1996**, *118*, 4058; i) D. K. Kumar, A. Das, P. Dastidar, *Cryst. Growth Des.* **2006**, *6*, 216; j) S. Kohmoto, Y. Kuroda, Y. Someya, K. Kishikawa, H. Masu, K. Yamaguchi, I. Azumaya, *Cryst. Growth Des.* **2009**, *9*, 3457; k) R. Thaimattam, C. V. Krishnamohan Sharma, A. Clearfield, G. R. Desiraju, *Cryst. Growth Des.* **2001**, *1*, 103.

[4] a) P. Dastidar, *Chem. Soc. Rev.* **2008**, *37*, 2699; b) M.-O. M. Piepenbrock, G. O. Lloyd, N. Clarke, J. W. Steed, *Chem. Rev.* **2010**, *110*, 1960; c) M. George, R. G. Weiss, *Acc. Chem. Res.* **2006**, *39*, 489; d) N. M. Sangeetha, U. Maitra, *Chem. Soc. Rev.* **2005**, *34*, 821; e) O. Gronwald, E. Snip, S. Shinkai, *Curr. Opin. Colloid Interface Sci.* **2002**, *7*, 148; f) P. Terech, R. G. Weiss, *Chem. Rev.* **1997**, *97*, 3133; g) D. J. Abdallah, R. G. Weiss, *Adv. Mater.* **2000**, *12*, 1237; h) B. G. Bag, G. C. Maity, S. K. Dinda, *Org. Lett.* **2006**, *8*, 5457; i) A. Pal, B. Hajra, S. Sen, V. K. Aswal, S. Bhattacharya, *J. Mater. Chem.* **2009**, *19*, 4325; j) P. Terech, S. Dourdain, U. Maitra, S. Bhat, *J. Phys. Chem. B* **2009**, *113*, 4619; k) G. Palui, A. Banerjee, *J. Phys. Chem. B* **2008**, *112*, 10107; l) C. Vijayakumar, V. K. Praveen, A. Ajayaghosh, *Adv. Mater.* **2009**, *21*, 2059; m) S. Dutta, A. Shome, S. Debnath, P. K. Das, *Soft Matter* **2009**, *5*, 1607; n) A. Pal, B. S. Chhikara, A. Govindaraj, S. Bhattacharya, C. N. R. Rao, *J. Mater. Chem.* **2008**, *18*, 2593; o) R. Ghosh, A. Chakraborty, D. K. Maiti, V. G. Puranik, *Org. Lett.* **2006**, *8*, 1061; p) D. D. Díaz, J. J. Cid, P. Vázquez, T. Torres, *Chem. Eur. J.* **2008**, *14*, 9261; q) A. Dawn, N. Fujita, S. Haraguchi, K. Sada, S. Shinkai, *Chem. Commun.* **2009**, 2100; r) M. Suzuki, K. Hanabusa, *Chem. Soc. Rev.* **2009**, *38*, 967; s) M.-O. M. Piepenbrock, G. O. Lloyd, N. Clarke, J. W. Steed, *Chem. Commun.* **2008**, 2644; t) A. R. Hirst, J. E. Miravet, B. Escuder, L. Noirez, V. Castelletto, I. W. Hamley, D. K. Smith, *Chem. Eur. J.* **2009**, *15*, 372; u) F. Placin, M. Colomès, J.-P. Desvergne, *Tetrahedron Lett.* **1997**, *38*, 2665; v) H. Hopf, H. Greiving, H. Bouas-Laurent, J. P. Desvergne, *Eur. J. Org. Chem.* **2009**, 1868; w) W. Deng H. Yamaguchi, Y. Takashima, A. Harada, *Chem. Asian J.* **2008**, *3*, 687; x) N. Sreenivasachary, J.-M. Lehn, *Chem. Asian J.* **2008**, *3*, 134; y) F. M. Menger, K. L. Caran, *J. Am. Chem. Soc.* **2000**, *122*, 11679; z) M. Suzuki, Y. Nakajima, M. Yumoto, M. Kimura, H. Hirai, K. Hanabusa, *Org. Biomol. Chem.* **2004**, *2*, 1155; aa) A. Ajayaghosh, V. K. Praveen, *Acc. Chem. Res.* **2007**, *40*, 644; ab) A. Ajayaghosh, V. K. Praveen, C. Vijayakumar, *Chem. Soc. Rev.* **2008**, *37*, 109.

[5] a) K. J. C. van Bommel, A. Friggeri, S. Shinkai, *Angew. Chem.* **2003**, *115*, 1010; *Angew. Chem. Int. Ed.* **2003**, *42*, 980; b) H. Basit, A. Pal, S. Sen, S. Bhattacharya, *Chem. Eur. J.* **2008**, *14*, 6534; c) S. Ray, A. K. Das, A. Banerjee, *Chem. Commun.* **2006**, 2816; d) G. Gun-

diah, S. Mukhopadhyay, U. G. Tumkurkar, A. Govindaraj, U. Maitra, C. N. R. Rao, *J. Mater. Chem.* **2003**, *13*, 2118.
[6] A. Wynne, M. Whitefield, A. J. Dixon, S. Anderson, *J. Dermatol. Treat.* **2002**, *13*, 61.
[7] E. Carretti, L. Dei, in *Molecular Gels. Materials with Self-Assembled Fibrillar Networks* (Eds.: G. Weiss, P. Terech), Springer, Dordrecht, The Netherlands, **2005**, chap. 27, p. 929.
[8] a) K. Murata, M. Aoki, T. Nishi, A. Ikeda, S. Shinkai, *J. Chem. Soc. Chem. Commun.* **1991**, 1715; b) J. J. D. de Jong, L. N. Lucas, R. M. Kellogg, J. H. van. Esch, B. L. Feringa, *Science* **2004**, *304*, 278.
[9] a) T. Kato, *Science* **2002**, *295*, 2414; b) A. Ajayaghosh, V. K. Praveen, C. Vijayakumar, S. J. George, *Angew. Chem.* **2007**, *119*, 6376; *Angew. Chem. Int. Ed.* **2007**, *46*, 6260; c) A. Ajayaghosh, C. Vijayakumar, V. K. Praveen, S. Santhosh Babu, R. Varghese, *J. Am. Chem. Soc.* **2006**, *128*, 7174.
[10] F. Rodriguez-Llansola, J. F. Miravet, B. Escuder, *Chem. Commun.* **2009**, 7303.
[11] K. Y. Lee, D. J. Mooney, *Chem. Rev.* **2001**, *101*, 1869.
[12] Z. Yang, G. Liang, L. Wang, B. Xu, *J. Am. Chem. Soc.* **2006**, *128*, 3038.
[13] *Molecular Gels. Materials with Self-Assembled Fibrillar Networks*; (Eds.: R. G. Weiss, P. Terech), Springer, Dordrecht, The Netherlands, **2005**.
[14] a) P. Terech, E. Ostuni, R. G. Weiss, *J. Phys. Chem.* **1996**, *100*, 3759; b) P. Terech, I. Furman, R. G. Weiss, *J. Phys. Chem.* **1995**, *99*, 9558, and references therein.
[15] R. Luboradzki, O. Gronwald, M. Ikeda, S. Shinkai, D. N. Reinhoudt, *Tetrahedron* **2000**, *56*, 9595.
[16] a) A. Ballabh, D. R. Trivedi, P. Dastidar, *Chem. Mater.* **2003**, *15*, 2136; b) D. R. Trivedi, A. Ballabh, P. Dastidar, *Chem. Mater.* **2003**, *15*, 3971; c) D. R. Trivedi, A. Ballabh, P. Dastidar, B. Ganguly, *Chem. Eur. J.* **2004**, *10*, 5311.
[17] a) D. R. Trivedi, P. Dastidar, *Cryst. Growth Des.* **2006**, *6*, 2114; b) D. R. Trivedi, P. Dastidar, *Cryst. Growth Des.* **2006**, *6*, 1022; c) D. R. Trivedi, A. Ballabh, P. Dastidar, *J. Mater. Chem.* **2005**, *15*, 2606; d) P. Dastidar, S. Okabe, K. Nakano, K. Iida, M. Miyata, N. Tohnai, M. Shibayama, *Chem. Mater.* **2005**, *17*, 741.
[18] a) D. R. Trivedi, A. Ballabh, P. Dastidar, *Cryst. Growth Des.* **2006**, *6*, 763; b) A. Ballabh, D. R. Trivedi, P. Dastidar, *Cryst. Growth Des.* **2005**, *5*, 1545; c) P. Sahoo, D. K. Kumar, D. R. Trivedi, P. Dastidar, *Tetrahedron Lett.* **2008**, *49*, 3052.
[19] a) A. Ballabh, D. R. Trivedi, P. Dastidar, *Chem. Mater.* **2006**, *18*, 3795; b) D. R. Trivedi, P. Dastidar, *Chem. Mater.* **2006**, *18*, 1470; c) U. K. Das, D. R. Trivedi, N. N. Adarsh, P. Dastidar, *J. Org. Chem.* **2009**, *74*, 7111.
[20] a) A. Ballabh, D. R. Trivedi, P. Dastidar, *Org. Lett.* **2006**, *8*, 1271; b) P. Sahoo, N. N. Adarsh, G. E. Chacko, S. R. Raghavan, V. G. Puranik, P. Dastidar, *Langmuir* **2009**, *25*, 8742.
[21] K. Nakano, Y. Hishikawa, K. Sada, M. Miyata, K. Hanabusa, *Chem. Lett.* **2000**, 1170.
[22] F. Rodríguez-Llansola, J. F. Miravet, B. Escuder, *Chem. Commun.* **2009**, 7303.
[23] a) P. Guo, L. Zhang, M. Liu, *Adv. Mater.* **2006**, *18*, 177; b) H. Goto, E. Yashima, *J. Am. Chem. Soc.* **2002**, *124*, 7943; c) Y. Li, T. Wang, M. Liu, *Soft Matter* **2007**, *3*, 1312.
[24] a) H. Ihara, M. Takafuji, T. Sakurai in *Encyclopedia of Nanoscience and Nanotechnology*, *Vol. 9* (Ed.: H. S. Nalwa), American Scientific Publishers, Stevenson Ranch, CA, **2004**, pp. 473; b) A. Brizard, R. Oda, I. Huc, *Top. Curr. Chem.* **2005**, *256*, 167; c) J. M. Schnur, *Science* **1993**, *262*, 1669.
[25] J. Bunzen, U. Kiehne, C. Benkhäuser-Schunk, A. Lützen, *Org. Lett.* **2009**, *11*, 4786.
[26] CSD version 5.31 (November 2009).
[27] S. R. Raghavan, B. H. Cipriano, in *Molecular Gels. Materials with Self-Assembled Fibrillar Networks* (Eds.: G. Weiss, P. Terech), Springer, Dordrecht, The Netherlands, **2005**; Chap. 8, p. 241.
[28] For example, anti-solvent induced drug nanoparticle precipitation is described in M. E. Matteucci, M. A. Hotze, K. P. Johnston, R. O. Williams III, *Langmuir* **2006**, *22*, 8951.
[29] a) G. Porod, *Kolloid Z.* **1951**, *124*, 83; b) G. Porod, *Kolloid Z.* **1952**, *125*, 51.
[30] E. Ostuni, P. Kamaras, R. G. Weiss, *Angew. Chem.* **1996**, *108*, 1423; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1324.
[31] a) A. Zhang, P. S. Robbins, W. S. Leal, C. E. Linn, Jr., M. G. Villani, W. L. Roelofs, *J. Chem. Ecol.* **1997**, *23*, 231; b) S. Nojima, P. S. Robbins, G. A. Salsbury, B. D. Morris, W. L. Roelofs, M. G. Villani, *J. Chem. Ecol.* **2003**, *29*, 2439.
[32] S. Mohamed, D. A. Tocher, M. Vickers, P. G. Karamertzanis, S. L. Price, *Cryst. Growth Des.* **2009**, *9*, 2881.
[33] M. Bodanszky, A. Bodanszky, *The Practice of Peptide Synthesis*, *2nd Revised Ed.*, Springer, Berlin, **1994**.

Received: August 12, 2010
Published online: October 21, 2010

CHEMISTRY
AN ASIAN JOURNAL

Supporting Information

Supramolecular Synthons in Designing Low Molecular Mass Gelling Agents: L-Amino Acid Methyl Ester Cinnamate Salts and their Anti-Solvent-Induced Instant Gelation

Pathik Sahoo,[a] D. Krishna Kumar,[b] Srinivasa R. Raghavan,[c] and Parthasarathi Dastidar*[a]

asia_201000560_sm_miscellaneous_information.pdf

Analytical data of the compounds synthesized

Phe.Cin phenyl alanine methyl ester cinnamate – mp 110°C, Anal. Calc. For $C_{19}H_{21}NO_4$: C, 69.71; H,6.47; N,4.28. Found: C, 69.66; H,6.47; N, 4.64%. FT-IR (KBr): 3472, 2925, 2672, 2145, 1745 (>C=O of ester), 1639 (COO^-), 1524, 1496, 1450, 1385, 1323, 1290, 1245, 1209, 1081, 986, 883, 850, 780, 753, 718, 702, 587, 513, 442 cm^{-1}. ^1H NMR (CD_3OD) (200MHz) δ = 7.575-7.496 (m, 3H), 7.377-7.195 (m, 8H), 6.490 (d, 16.2, 1H), 4.008 (t, 1H, J = 6.80Hz), 3.722 (s, 3H), 3.188-2.979 (m, 2H).

Phe.4MeCin phenyl alanine methyl ester 4-methylcinnamate: mp 118°C, Anal. Calc. For $C_{20}H_{23}NO_4$: C,70.36; H,6.79; N,4.10. Found: C, 70.63; H,6.78; N, 3.89%. FT-IR (KBr): 3755, 3449, 2950, 2370, 2112, 1752 (>C=O of ester), 1641 (COO^-), 1536, 1443, 1387, 1289, 1220, 1088, 1034, 989, 817, 742, 705, 527, 492, 421 cm^{-1}. ^1H NMR (CD_3OD) (200MHz) δ = 7.589- 7.181 (m, 10H), 6.424 (d, 1H, J = 16.2), 4.02-3.93 (m, 1H). 3.723 (s, 3H), 3.179-2.953 (m, 2H). 2.348 (s, 3H)

#**Phe.4ClCin** phenyl alanine methyl ester 4-chlorocinnamate: mp 106°C, FT-IR (KBr): 3474, 2951, 2360, 2123, 1748 (>C=O of ester), 1642 (COO^-), 1538, 1493, 1443, 1408, 1377, 1287, 1226, 1086, 985, 948, 923, 828, 730, 702, 659, 596, 535, 496, 450, 420cm^{-1}. ^1H NMR (CD_3OD) (200MHz) δ = 7.571-7.201 (m, 10H), 6.488 (d, 1H, J = 16.2 Hz), 4.050 (t, 1H, J = 6.7 Hz), 3.736 (s, 3H), 3.208-2.994 (m, 2H).

Ala.4BrCin alanine methyl ester 4-bromocinnamate mp 110°C, Anal. Calc. For $C_{19}H_{20}BrNO_4$: C,56.17; H,4.96; N,3.45. Found: C,56.22; H,4.69; N, 2.85%. FT-IR (KBr): 3469, 2953, 2658, 2118, 1742 (>C=O of ester), 1641 (COO^-), 1532, 1490, 1441, 1405, 1385, 1288, 1234, 1209, 1072, 1009, 985, 849, 820, 726, 701, 634, 535, 488, 428 cm^{-1}. ^1H NMR (DMF-d7) (300MHz) δ = 7.908-7.790 (m, 5H), 7.496-7.368 (m, 5H), 6.831 (d, 1H, J = 16.02,), 3.843 (t, 1H, J = 6.63Hz), 3.805 (s, 3H), 3.162- 2.970 (m, 2H).

Leu.Cin leucine methy lester cinnamate mp. 114-118°C, Anal. Calc. For $C_{16}H_{23}NO_4$: C,65.51; H,7.90; N,4.77. Found: C,65.31; H,7.83; N, 5.24%. FT-IR (KBr): 3489, 2961, 2872, 2185, 1753 (>C=O of ester), 1640 (COO^-), 1615, 1495, 1375, 1269, 1245, 1188, 1127, 1093, 1016, 986, 881, 829, 776, 721, 689, 585, 539, 440 cm^{-1}. ^1H NMR ($CDCl_3$) (300MHz) δ = 7.702 (d, 1H, J = 15.933Hz), 7.545-7.523 (m, 2H), 7.387-7.369 (m, 3H), 6.456 (d. 1H, J = 15.93 Hz), 3.797-3.665 (m, 4H), 1.849-1.553 (m, 3H), 0.959- 0.927 (m, 6H).

#**Leu.4MeCin** leucine methyl ester 4-methylcinnamate mp. 132-134°C, FT-IR (KBr): 3484, 2956, 2872, 2361, 2341, 2175, 1749 (>C=O of ester), 1641 (COO^-), 1569, 1514, 1482, 1440, 1413, 1377, 1272, 1251, 1193, 1126, 1092, 1044, 1019, 987, 881, 856, 820, 775, 711, 646, 539, 525, 494, 441 cm^{-1}. ^1H NMR ($CDCl_3$) (300MHz) δ = 7.674 (d, 1H, J = 15.96), 7.378 (d, 2H, J = 7.98), 7.138 (d, 2H, J = 7.89Hz), 6.336 (d, 1H, J = 15.96Hz), 3.786-3.660 (m, 4H), 2.314 (s, 3H), 1.836-1.432 (m, 3H), 0.910-0.846 (m, 6H).

Leu.4ClCin leucine methyl ester 4-chlorocinnamate mp. 136 -140°C, Anal. Calc. for $C_{16}H_{22}ClNO_4$: C,58.62; H,6.76; N,4.27. Found: C,58.31; H,6.41; N, 4.32 %. FT-IR (KBr): 3487, 2961, 2928, 2873, 2363, 2174, 1752 (>C=O of ester), 1643 (COO^-), 1612, 1523, 1493, 1407, 1375, 1268, 1244, 1192, 1128, 1088, 1015, 985, 887, 828, 732, 662, 538, 496, 453 cm^{-1}. ^1H NMR (CD_3OD) (300MHz) δ = 7.55-7.36 (m, 5H), 6.49 (d, J = 16.2Hz, 1H), 3.80 (s, 1H), 3.31-3.29 (m, 1H), 1.76-1.61 (m, 3H), 0.99-0.95 (m, 6H)

Leu.4BrCin leucine methyl ester 4-bromocinnamate mp. 126° C. Anal. Calc. for $C_{16}H_{22}BrNO_4$: C, 51.62; H, 5.96; N, 3.76. Found: C,52.63; H, 6.27; N, 4.05 %. FT-IR (KBr): 3485, 2955, 2929, 2872, 2359, 2171, 1749 (>C=O of ester), 1643 (COO^-), 1614, 1521, 1490, 1405, 1379, 1270, 1228, 1127, 1072, 1010, 985, 885, 823, 728, 633, 536, 490, 440 cm^{-1}. ^1H NMR (CD_3OD) (300MHz) δ = 7.46-7.32 (m, 5H), 6.43 (d, 1H, J = 18 Hz), 3.71 (s, 3H), 3.24-3.22 (m, 1H), 1.70-1.48 (m, 3H), 0.91-0.87 (m, 6H).

Val.Cin valine methyl ester cinnamate mp. 118°C, Anal. Calc. for $C_{15}H_{21}NO_4$: C, 64.50; H,7.58; N,5.01. Found: C, 64.56; H, 7.57; N, 4.81%. FT-IR (KBr): 3475, 2972, 2937, 2172, 1743 (>C=O of ester), 1642 (COO^-), 1612, 1531, 1448, 1379, 1290, 1233, 1114, 1053, 986, 883, 845, 774, 720, 689, 586, 536, 485, 420 cm^{-1}. ^1H NMR ($CDCl_3$) (300MHz) δ = 7.713 (d, 1H, J = 15.96Hz), 7.547-7.526 (m, 2H), 7.391-7.381 (m, 3H), 6.454 (d, 1H, J = 15.96), 3.746 (s, 3H), 3.529 (d, J = 4.62, 1H), 2.184-2.123 (m, 1H), 1.01 (d, 3H, J = 6.6 Hz), 0.96 (d, 3H, J = 6.6)

Val.4MeCin valine methyl ester 4-methylcinnamate mp. 116-12 2°C, Anal. Calc. for $C_{16}H_{23}NO_4$: C,65.51; H,7.90; N,4.77. Found: C, 65.08; H, 7.78; N, 4.83%. FT-IR (KBr): 3473, 2969, 2360, 2145, 1746 (>C=O), 1640 (COO^-), 1514, 1440, 1375, 1287, 1259, 1205, 1110, 1052, 991, 884, 852, 821, 774, 746, 708, 525, 494, 430 cm^{-1}. ^1H NMR ($CDCl_3$) (300MHz) δ = 7.71 (d, 1H, 15.9 Hz), 7.43 (d, 2H, J = 8.1 Hz), 7.19 (d, 2H, J = 8.1), 6.39 (d, 1H, J = 15.9 Hz), 3.75 (s, 3H), 3.53 (br s, 1H), 2.37 (s, 3H), 2.22-2.14 (m, 1H), 1.02 (d, 3H, J = 6.9), 0.97 (d, 3H, J = 6.9 Hz)

Ala.Cin alanine methyl ester cinnamate mp. 104°C, Anal. Calc. for $C_{13}H_{17}NO_4$: C,62.14; H,6.82; N,5.57. Found: C, 61.19; H, 6.36; N, 5.42 %. FT-IR (KBr): 3490, 3025, 2957, 2822, 2742, 2613, 2360, 2177, 1752 (>C=O of ester), 1643 (COO^-), 1616, 1549, 1495, 1449, 1378, 1287, 1249, 1222, 1122, 1071, 1028, 983, 908, 884, 843, 779, 755, 722, 689, 585, 538, 484, 415 cm^{-1}. ^1H NMR ($CDCl_3$) (300MHz) δ = 7.690 (d, 1H, J = 15.9 Hz), 7.558-7.526 (m, 2H), 7.396-7.375 (m, 3H), 6.479 (d, 1H, J = 15.9 Hz), 3.907 (m, 1H), 3.765 (s, 3H), 1.53 (d, 3H, J = 7.11 Hz)

Ala.4MeCin alanine methyl lester 4-methylcinnamate mp. 118-122°C, Anal. Calc. for $C_{14}H_{19}NO_4$: C,63.38; H,7.22; N,5.28. Found: C, 63.35; H, 6.94; N, 5.16 %. FT-IR (KBr): 3492, 3008, 2638, 2359, 2185, 1754 (>C=O of ester), 1644 (COO^-), 1547, 1495, 1377, 1285, 1222, 1123, 1033, 987, 910, 884, 845, 819, 755, 708, 523, 496 cm^{-1}. ^1H NMR ($CDCl_3$) (300MHz) δ = 7.709 (d, 1H, J = 15.96 Hz), 7.452 (d, 2H, J = 7.92 Hz), 7.210 (d, 2H, J = 7.83 Hz), 6.422 (d, 1H, J = 15.93), 3.915 (q, 1H, J = 7.09). 3.76 (s, 3H), 2.392 (s, 3H), 1.539 (d, 3H, J = 7.11 Hz)

Ile.Cin isoleucine methyl ester cinnamate mp. 92°C, Calc. for $C_{16}H_{23}NO_4$: C,65.51; H,7.90; N,4.77. Found: C,65.53; H,8.01; N,5.34 %. FT-IR (KBr): 2970, 2359, 2167, 1750 (>C=O of ester), 1641 (COO^-), 1619, 1521, 1496, 1449, 1379, 1287, 1249, 1199, 1151, 1107, 1083, 1025, 991, 912, 882, 846, 775, 717, 688, 585, 536, 484, 439 cm^{-1}. ^1H NMR ($CDCl_3$) (300MHz) δ = 7.671 (d, 1H, J = 15.93Hz), 7.490-7.459 (m, 2H), 7.334 -7.314 (m, 3H), 6.387 (d, 1H, J= 15.96 Hz), 3.663 (s, 3H), 3.568 (d, 1H, J = 3.63 Hz), 1.845 (br, 1H), 1.428-1.166 (m, 3H), 0.935-0.806 (m, 6H).

Ile.4MeCin isoleucine methylester p-methylcinnamate mp. 106-108°C, Calc. for $C_{17}H_{25}NO_4$: C,66.43; H,8.20; N,4.56. Found: C,67.02; H,8.07; N,4.68 %. FT-IR (KBr): 3482, 2973, 2933, 2735, 2640, 2155, 1749 (>C=O of ester), 1638 (COO^-), 1570, 1515, 1491, 1413, 1375, 1288, 1251, 1200, 1159, 1102, 1084, 1022, 992, 970, 882, 849, 820, 777, 747, 708, 649, 524, 494, 441 cm^{-1}. ^1H NMR ($CDCl_3$) (300MHz) δ = 7.69 (d, 1H, J = 15.72 Hz), 7.430 (d, 2H, J = 7.77 Hz), 7.190 (d, 2H, J = 7.59 Hz), 6.404 (d, 1H, J = 15.81 Hz), 3.738 (s, 3H), 3.584 (br s, 1H), 2.372 (s, 3H), 1.872 (br, 1H), 1.465-1.217 (m, 3H), 0.984-0.894 (m, 6H).

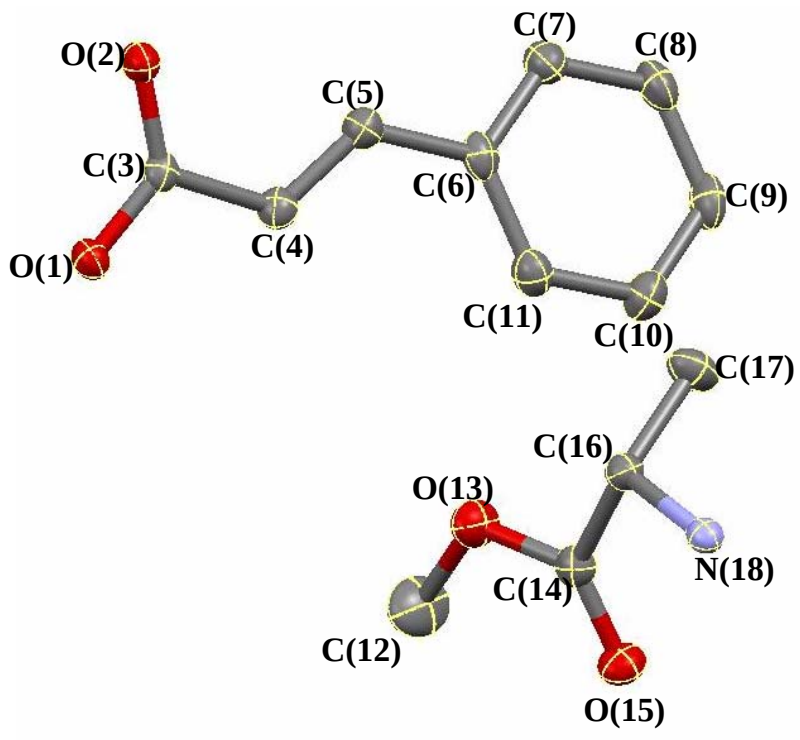
Ile.4ClCin isoleucine methylester p-chlorocinnamate mp. 108-110°C, Calc. for $C_{16}H_{22}ClNO_4$: C,58.62; H,6.76; N,4.27. Found: C,58.94; H,6.19; N,3.92 %. FT-IR (KBr): 3477, 2970, 2934, 2362, 2148, 1748 (>C=O of ester), 1643 (COO^-), 1613, 1520, 1492, 1407, 1374, 1283, 1250, 1229, 1199, 1088, 1014, 987, 883, 827, 788, 731, 660, 536, 496, 452 cm^{-1}; ^1H NMR (CD_3OD) (300 MHz) delta = 7.55-7.35 (m, 5H), 6.49 (d, 1H, J = 1599 Hz), 3.77 (s, 3H), 3.72 (t, 1H, J = 4.50 Hz), 1.88-1.83 (m, 1H), 1.52-1.24 (m, 2H), 0.98-0.93 (m, 6H). .

Ile.4BrCin isoleucine methyl ester 4-bromocinnamate mp. 108-110°C, Calc. for $C_{16}H_{22}BrNO_4$: C,51.62; H,5.96; N,3.76. Found: C,51.14; H,5.46; N,3.51 %. FT-IR (KBr): 3482, 2968, 2636, 2364, 2194, 1907, 1749 (>C=O of ester), 1640 (COO^-), 1567, 1491, 1441, 1404, 1371, 1318, 1281, 1225, 1168, 1105, 1072, 1008, 983, 909, 876, 821, 791, 747, 723, 682, 633, 537, 489 cm^{-1}. ^1H NMR (CD_3OD) (300 MHz) delta = 7.54-741 (m, 5H), 6.50 (d, 1H, J = 15.90), 3.77 (s, 3H), 3.71 (d, 1H, J = 4.50), 1.88-1.82 (m, 1H), 1.52-1.24 (m, 2H), 0.98-0.92 (m, 6H).

[#] The elemental analysis for these two particular salts happened to be inconsistent presumably due to the fact that the cationic moieties of all these salts reported herein were found to be labile as detailed ^1H NMR and FT-IR studies on one of the selected salts namely **Val.4MeCin** established.

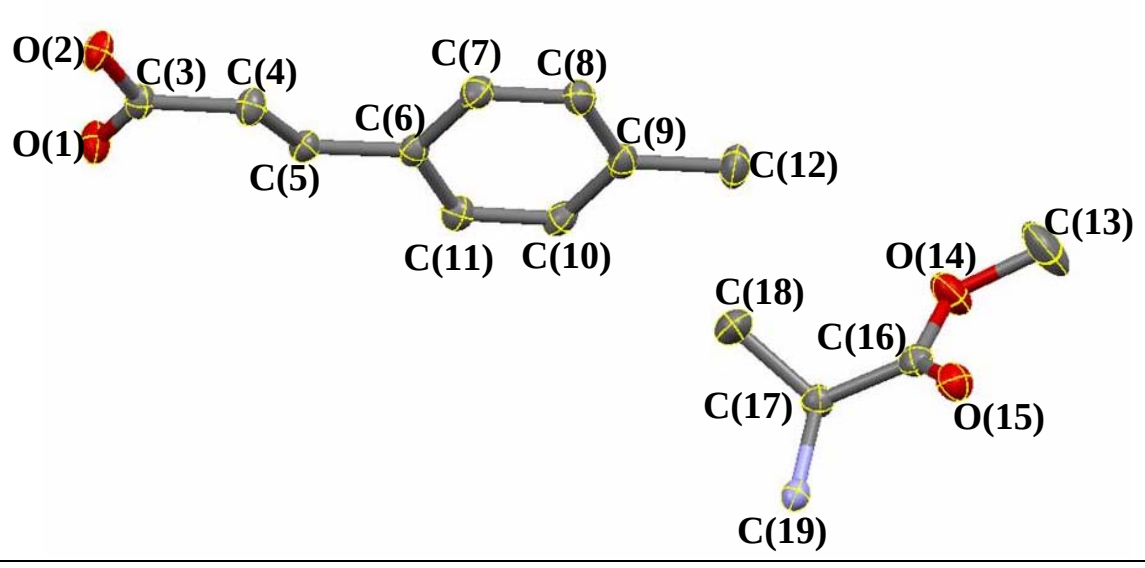
Molecular Plots and Hydrogen Bonding Parameters for the compounds

Compound: Ala.Cin



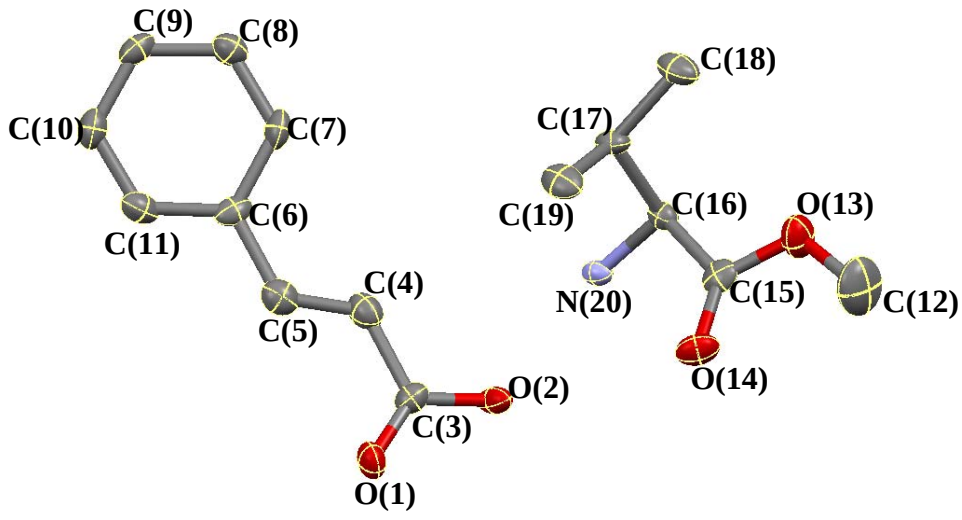
D*—H···*A	***D*—H**	**H···*A***	***D*···*A***	***D*—H···*A***
Ala.Cin				
N18—H18A···O1[i]	0.91	2.00	2.8023 (17)	146
N18—H18B···O1[ii]	0.91	1.81	2.706 (2)	167
N18—H18C···O2[iii]	0.91	1.84	2.7137 (19)	161
Symmetry codes: (i) *x*+1/2, −*y*+3/2, −*z*; (ii) *x*, *y*−1, *z*; (iii) *x*+1, *y*−1, *z*				

Compound: Ala4Me.Cin



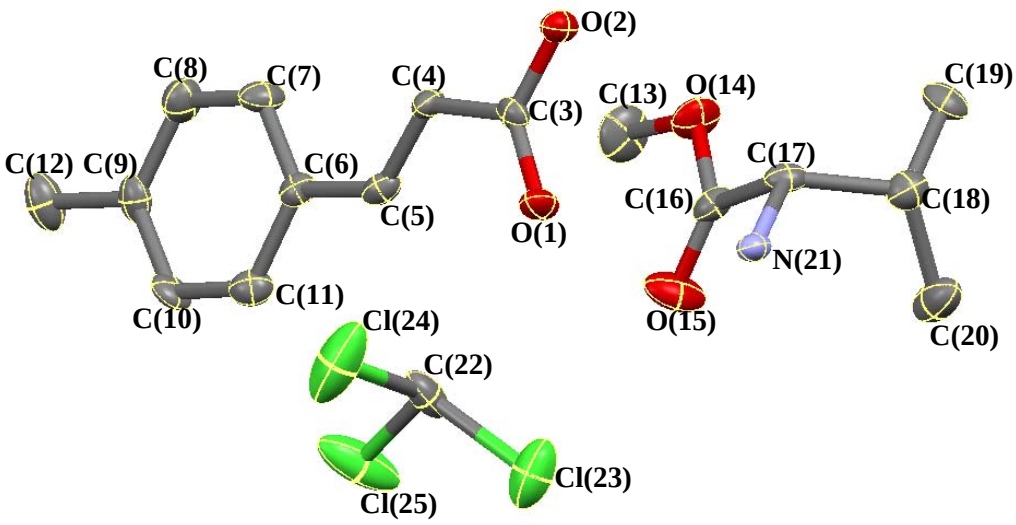
Ala4Me.Cin				
N19—H19A···O2[i]	0.91	1.98	2.794 (2)	149
N19—H19B···O2[ii]	0.91	1.82	2.717 (2)	168
N19—H19C···O1[iii]	0.91	1.81	2.689 (2)	162
Symmetry codes: (i) *x*+1, *y*, *z*+1; (ii) −*x*, *y*−1/2, −*z*+1; (iii) −*x*, *y*+1/2, −*z*+1				

Compound: Val.Cin



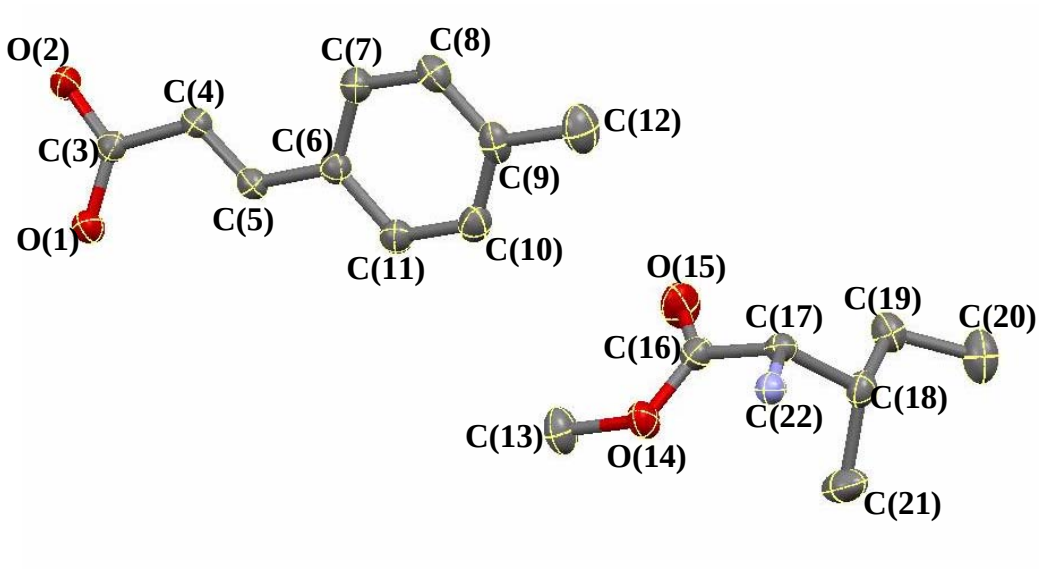
Val.Cin				
N20—H20A···O2	0.91	1.88	2.763 (4)	162
N20—H20B···O2^{i}	0.91	1.95	2.788 (3)	153
N20—H20C···O1^{ii}	0.91	1.85	2.753 (4)	173
Symmetry codes: (i) *x*−1/2, −*y*+1/2, −*z*+2; (ii) *x*−1, *y*, *z*.				

Compound: Val.4MeCin



Val4MeCin				
N21—H21A···O1	0.91	1.82	2.722 (6)	169
N21—H21B···O2^{i}	0.91	1.86	2.733 (5)	159
N21—H21C···O2^{ii}	0.91	1.91	2.752 (6)	152
Symmetry codes: (i) *x*+1/2, −*y*+3/2, −*z*+2; (ii) *x*+1, *y*, *z*				

Compound: Ile.4MeCin



Ile4MeCin				
N22—H22A···O2[i]	0.89	1.91	2.789 (2)	169
N22—H22B···O1[ii]	0.89	1.82	2.703 (2)	175
N22—H22C···O2[iii]	0.89	1.93	2.782 (2)	158
Symmetry codes: (i) *x*−1/2, −*y*+1/2, −*z*+1; (ii) *x*−1, *y*+1, *z*+1; (iii) *x*, *y*+1, *z*+1				