

Mesoscopic-scale sheet-like assembly: critical role of inter-tape hydrogen bonds in the organogel formation and gel–liquid crystal transition of an alkylsilylated deoxyguanosine–dodecane system

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2'-Deoxy-3',5'-bis-*O*-(octyldiisopropylsilyl)guanosine (**1**) showed a good gelation ability for non-polar solvents like alkanes. Atomic force microscopy of the organogel showed the formation of mesoscopic-scale sheet-like assemblies, whose width and height were 50–300 and 2.5 nm, respectively. From the IR spectral analysis and crystallographic data of reference compounds, the gel was shown to have a structural hierarchy with different levels of hydrogen bonds, *i.e.*, a one-dimensional tape motif with double hydrogen bonds between guanine units and a mesoscopic-scale sheet-like assembly with hydrogen bonds between adjacent tape motifs. Formation of the sheet structure was shown to be essential for the gelation process. On heating, the concentrated 1–dodecane (37–63 wt%) gel showed gel (G)–lamellar liquid crystal (L)–isotropic fluid (I) phase, and the G–L transition was ascribed to the cleavage of the inter-tape hydrogen bonds.

Introduction

Structural hierarchy is found in highly ordered protein structures and other biological systems, which offer excellent examples for the design and construction of macroscale structures by self-assembly through non-covalent bonds.¹ Though tapes, ribbons, and other types of nanometre-scale supramolecular assemblies have been the subjects of intense studies in a variety of fields such as crystal engineering, colloid chemistry, and polymer chemistry,² for relatively few is known the mode of self-assembly of the nanometre-scale assemblies into macroscale structures. Recently, increasing numbers of novel low-molecular-weight organogelators have been reported because of their thermoreversibility, chemical sensitivity, and diversity of their mesoscopic-scale structures.^{2,3} These gelators are fatty acid derivatives,⁴ steroid derivatives,⁵ amino acid derivatives,⁶ or organometallic compounds.⁷ Macroscale gelation is generally ascribed to the development of networks of nano- to micrometre-scale rigid fibres in organic liquids at relatively low concentrations, but formation of the fibrous networks is not well understood at the molecular level.

In our effort to develop artificial nucleoside-based supramolecular materials,⁸ we observed that some of the alkylsilyl derivatives of guanosine caused gelation of organic solvents. We report here a novel nucleoside-based gelator, 2'-deoxy-3',5'-bis-*O*-(octyldiisopropylsilyl)guanosine (**1**), and molecular-level, mesoscopic-scale, and macroscale structures of the 1–dodecane organogel. Through these studies, the structural hierarchy within the gel and the role of the inter-tape hydrogen bonds in the gelation process will be clarified.

Experimental

Measurements

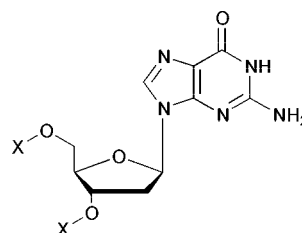
¹H-NMR spectra of the samples were recorded on a JEOL AL400 spectrometer operated at 400 MHz. Temperature-controlled IR spectra were measured on a Perkin-Elmer 1600 spectrometer with a Shimadzu PDT-3 heating control system. Thermal properties of the samples were analysed with a Rigaku

DSC 8230 or a Perkin-Elmer Pyris 1 DSC. For atomic force microscope (AFM) observation of a gel sample, a silicon wafer was pressed onto the gel surface,⁹ and the transferred gel was subjected to a tapping-mode AFM observation using a JEOL JSPM-4200. A Nikon EC600POL and a Mettler FP-900 thermosystem were used for temperature-controlled polarised photomicroscopy. X-Ray diffraction (XRD) patterns were measured with a Rigaku RINT2000 diffractometer (Cu-K α) in the range $1.5^\circ < 2\theta < 30^\circ$, and crystallographic data were corrected by a MAC Science DIP Lab imaging plate system. All structures were solved by direct methods and refined by full matrix least squares on F^2 by SHELX-97.¹⁰

Materials

Reactions of guanosine with the corresponding trialkylsilyl chlorides according to the method of Ogilvie *et al.*¹¹ gave 2'-deoxy-3',5'-bis-*O*-(octyldiisopropylsilyl)guanosine (**1**, Scheme 1), 2'-deoxy-3',5'-bis-*O*-(*tert*-butyldiphenylsilyl)guanosine (**2**), and 2'-deoxy-3',5'-bis-*O*-(triisopropylsilyl)guanosine (**3**) in fair to good yields.

Compound 1. Purified by silica gel column chromatography (Merck silica gel 60, chloroform–ethanol = 14 : 1, v/v). White solid (mp 143.0–144.3 °C). ¹H-NMR (400 MHz, CDCl₃) 0.5–1.5 (62H, m), 2.00 (1H, m), 2.35 (1H, m), 2.50 (1H, m), 3.78 (2H, m), 4.01 (1H, d), 4.62 (1H, d), 6.09 (2H, br), 6.24 (1H, t), 7.75 (1H, s), 11.98 (1H, br). Anal. Calcd for C₃₈H₇₃N₅O₄Si₂: C, 63.35; H, 10.2; N, 9.7%. Found C, 63.55; H, 10.6; N, 9.9%.



Scheme 1 Chemical structures of trialkylsilyl guanosine.

Table 1 Minimum gelation concentration of **1** at 25 °C

Solvent	Minimum concentration/wt%
Dodecane	0.6
Hexane	1.0
Cyclohexane	4.3
Benzene	No gelation
Ethyl acetate	No gelation
Acetone	No gelation
Ethanol	No gelation

Compound 2. Recrystallised from dimethylformamide. Colourless needles [mp > 220 °C (decomp.)].¹²

Crystal data. C₄₂H₄₉N₅O₄Si₂, *M* = 744.04, orthorhombic, *a* = 9.5300(1), *b* = 11.0750(1), *c* = 39.4220(3) Å, *U* = 4160.79(7) Å³, *T* = 100 K, space group *P*2₁2₁2₁, *Z* = 4, μ(Cu–Kα) = 1.54 mm⁻¹, 40833 reflections measured, 7002 unique (*R*_{int} = 0.032) which were used in all calculations. The final *R* indices, *R*₁ = 0.0658, *wR*₂ = 0.1885 (all data).†

Compound 3. Recrystallised from ethanol. Colourless plates [mp > 205 °C (decomp.)].¹³

Crystal data. C₂₈H₅₃N₅O₄Si₂, *M* = 579.92, monoclinic, *a* = 17.0140(4), *b* = 11.2140(3), *c* = 18.4050(4) Å, β = 112.716(2)°, *U* = 3239.19(14) Å³, *T* = 100 K, space group *P*2₁, *Z* = 4, μ(Cu–Kα) = 1.54 mm⁻¹, 28374 reflections measured, 8328 unique (*R*_{int} = 0.031) which were used in all calculations. The final *R* indices, *R*₁ = 0.0552, *wR*₂ = 0.1535 (all data).†

Results

Formation of organogel

The deoxyguanosine derivative **1** having a relatively long octyl group at the silyl centre was obtained as a white solid, and did not crystallise from common solvents. When a small amount of **1** was dissolved in hexane by heating, a transparent organogel was obtained after cooling the solution to room temperature. No gelation was observed in solvents like chloroform, acetone, or ethanol. The minimum concentration of **1** required for gelation of the solvent was determined by the inversion method described by Hanabusa *et al.*,¹⁴ and the results are summarised in Table 1. The novel nucleoside derivative **1** was shown to serve as a good gelator for non-polar solvents.

The DSC curve of the **1**-dodecane gel (3 wt%) showed only one endothermic peak at 60 °C on heating, and the gel became an isotropic fluid. However, the **1**-dodecane gel at higher concentration (37–63 wt%), where the **1**-dodecane molar ratio was 1:7–1:3, showed two endothermic peaks. A typical example of the gel (41 wt%) is shown in Fig. 1(a), in which peaks are observed at 75.2 (–3.0 J g⁻¹) and 94.6 °C (–2.2 J g⁻¹). A polarised photomicrograph of the sample at the temperature between the first and second peaks showed a lamellar liquid crystal (L) texture (Fig. 2),¹⁵ and the sample became an isotropic liquid (I) above the second peak. The same L phase was also observed during the cooling process, and repeated heating confirmed the process to be reproducible. Thus, the **1**-dodecane system at higher concentrations showed a thermotropic liquid crystalline phase (G) and the isotropic liquid phase. The phase diagram of the **1**-dodecane system is shown in Fig. 1(b).

†CCDC reference numbers 153735 and 153736. See <http://www.rsc.org/suppdata/jm/b1/b105000c/> for crystallographic files in .cif or other electronic format.

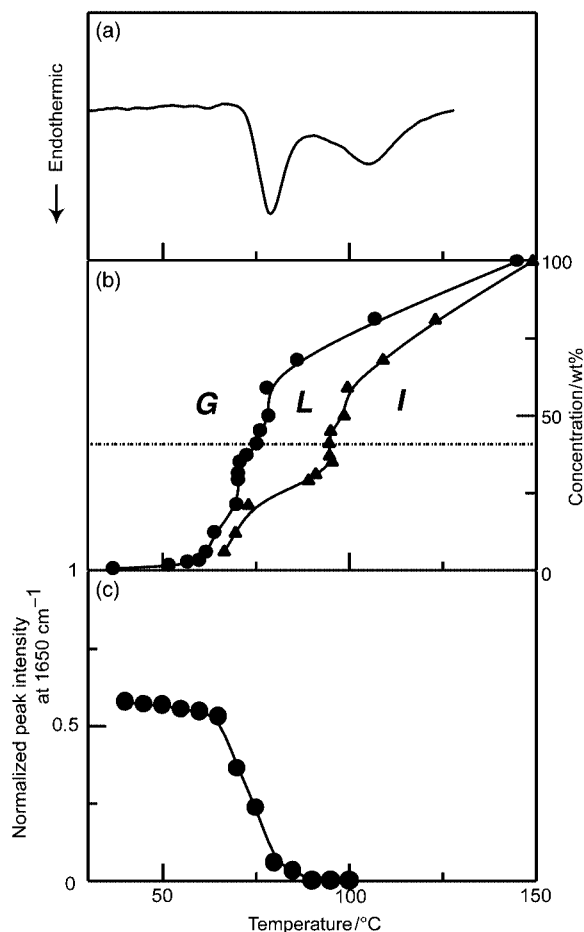


Fig. 1 Thermal properties of the **1**-dodecane system. (a) DSC curve of the sample of the **1**-dodecane system (41 wt%), (b) phase diagram of the **1**-dodecane system, and (c) normalised peak intensity of the deformation mode of 2-NH₂ group at 1650 cm⁻¹ (*I*₁₆₅₀/(*I*₁₆₅₀ + *I*₁₆₂₉)) in the temperature-controlled IR spectra of the **1**-dodecane system (41 wt%).

Mesoscopic-scale and molecular level analyses of the **1**-dodecane gel structure

To clarify the mesoscopic-scale structure of the **1**-dodecane gel, an AFM image of the gel transferred onto a silicon wafer was directly observed. In the AFM image (Fig. 3), mesoscopic-scale sheet-like structures instead of fibrous structures were clearly observed. The depth profile along the line in the image showed that the height of the sheets was 2.5 ± 0.2 nm but their width was as large as 50–300 nm. A concentrated gel (41 wt%) showed further extended and piled sheet-like assemblies, but the height of the sheets was practically unchanged. No sheet structures were found in the AFM image of the sample in the L

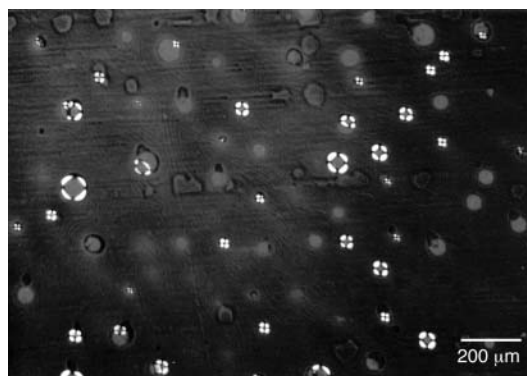


Fig. 2 Polarised photomicrograph of the **1**-dodecane (41 wt%) sample in the liquid crystalline phase at 85 °C.

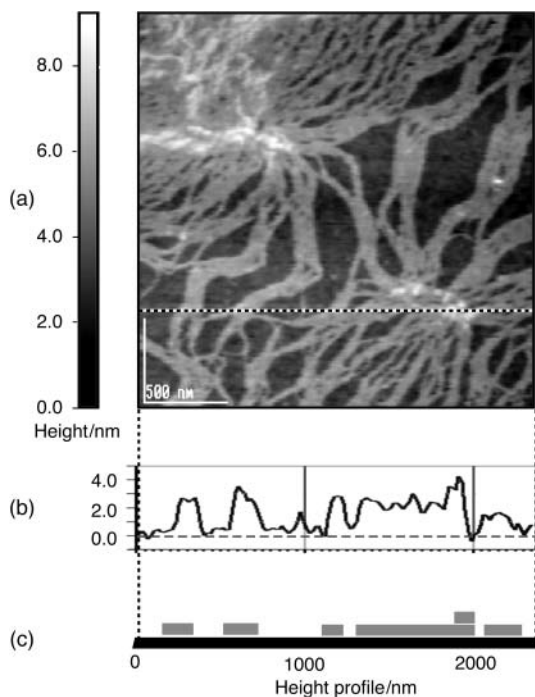


Fig. 3 (a) AFM view of the 1-dodecane (5 wt%) sample. (b) Depth profile along the line in the image. Height from the silicone surface is shown in nm. (c) Schematic view of the depth profile.

state, indicating that the mesoscopic-scale sheet-like assembly is responsible for gelation.

To understand the gel structure at the molecular level, we examined the stretching and deformation modes of the 2-NH₂ group on the guanine ring in the temperature-controlled IR spectra of the 1-dodecane system and two reference compounds (Fig. 4). The IR spectrum of a reference compound having bulky *tert*-butyldiphenylsilyl groups,¹⁶ 2'-deoxy-3',5'-bis-*O*-(*tert*-butyldiphenylsilyl)guanosine (**2**), showed a free NH stretching peak at 3495 cm⁻¹ in addition to the hydrogen-bonded peaks at lower wavenumber, and an in-plane deformation peak was observed at 1629 cm⁻¹. In the crystal of **2**, formation of the hydrogen-bonded tape motif by two

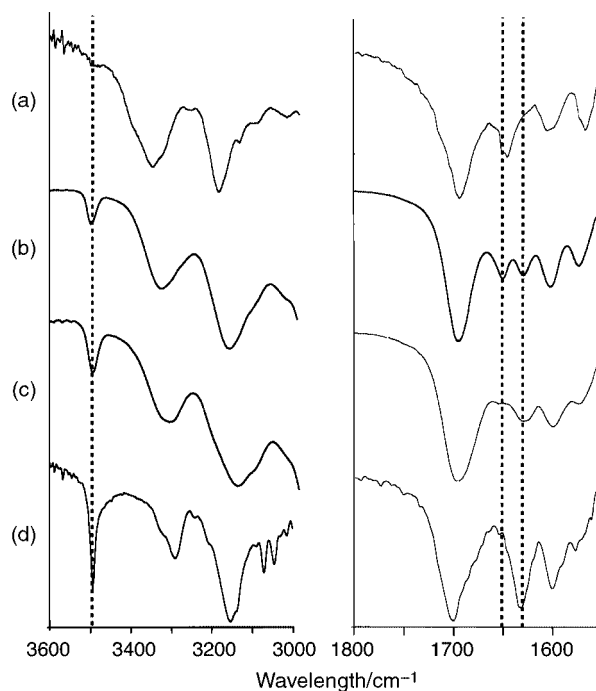


Fig. 4 Temperature-controlled IR spectra of the 1-dodecane sample (41 wt%) and two reference compounds. From the top, (a) the reference compound **3**, (b) the 1-dodecane sample in the gel phase at room temperature, (c) the 1-dodecane sample in the liquid crystalline phase at 85 °C, and (d) the reference compound **2**. Broken lines from the left show 3495, 1650, and 1629 cm⁻¹.

hydrogen bonds from 2-NH₂ to 6-C=O and from 1-NH to 7-N of the guanine units was noticed (Fig. 5(a)). The same hydrogen-bonded tape motif has been found for many guanine derivatives.¹⁷ In this hydrogen-bonding mode, one of the hydrogen atoms of 2-NH₂ was not involved in the hydrogen-bond network of the tape motif, and this explained the presence of the free NH stretching peak in the IR spectra. The 1-dodecane sample (41 wt%) in the L state on heating also showed the free NH stretching and deformation peaks at 3495 and 1629 cm⁻¹, respectively, and the spectral pattern was

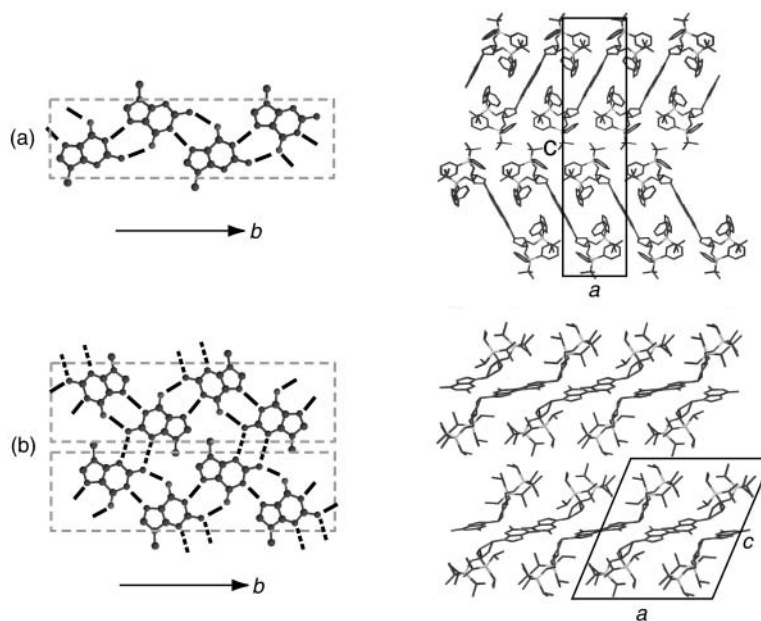


Fig. 5 Crystal structures of (a) **2** and (b) **3** (for clarity, hydrogen atoms are omitted). Hydrogen-bonding patterns of the guanine moieties are shown at the left side of each figure. Interatomic distance of hydrogen-bonding, (a): D···A(Å), N1···N7ⁱ 2.80, N2···O6ⁱ 2.88 ($i = 2 - x, y - 1/2, 3/2 - z$), (b): D···A(Å), N1···N7ⁱ 2.94, N2···O6ⁱ 3.13, N51···N57ⁱⁱ 2.79, N52···O56ⁱⁱ 2.99, N2···N53ⁱⁱⁱ 3.06, N52ⁱⁱⁱ···N3 3.09 ($i = -x, y - 1/2, 1 - z$, $ii = 1 - x, y + 1/2, 1 - z$, $iii = x, y - 1, z$).

almost identical to that of the crystal of **2**. Therefore, formation of the same hydrogen-bonded tape motif was indicated in the L state of the **1**-dodecane sample. However, the sample in the gel state showed only a weak free NH stretching at 3495 cm^{-1} , and an additional deformation peak appeared at 1650 cm^{-1} . The IR spectrum of the other reference compound, 2'-deoxy-3',5'-bis-*O*-(triisopropylsilyl)guanosine (**3**), having less bulky triisopropyl groups compared to those of **2**, showed the deformation peak at 1650 cm^{-1} and no free NH stretching peak at all. Since the deformation peak was known to shift to a higher wavenumber by hydrogen bonding with a H-acceptor,¹⁸ the result suggested that the 2-NH₂ group formed an additional hydrogen bond. Indeed, the crystal structure of **3** confirmed the formation of additional double inter-tape hydrogen bonds between 2-NH₂ and 3-N of the two guanine-bases located at the adjacent tapes. These additional inter-tape hydrogen bonds led to formation of the two-dimensional hydrogen-bonded sheet assemblies having 1.69 nm thickness (Fig. 5(b)). Since the spectral pattern of the **1**-dodecane gel could be reproduced by superposition of those of **2** and **3**, partial formation of similar inter-tape hydrogen bonds in the gel was indicated. The IR spectrum of the **1**-dodecane gel at lower concentration (5 wt%) showed essentially the same pattern. Therefore, the resultant sheet-like assembly in the gel was observed by AFM. Since **1** has a longer alkyl chain compared to **3**, the observed thickness of 2.5 nm for the sheet-like structure of **1** is acceptable. A schematic view of the mesoscopic-scale sheet-like assembly in the gel is given in Fig. 6.

Normalised intensities of the deformation peak at 1650 cm^{-1} ($I_{1650}/(I_{1650} + I_{1629})$) as a function of temperature are also shown in Fig. 1(c). The disappearance of the deformation peak at 1650 cm^{-1} during the G-L phase transition indicated that cleavage of the inter-tape hydrogen bond on heating caused the G-L phase transition. The results indicated that formation of the sheet assemblies by the inter-tape hydrogen bonds was essential for the gelation process.

Gel structure studied by XRD

XRD patterns of the **1**-dodecane gel samples at 41 and 60 wt% at ambient temperature showed sharp diffraction peaks at the small angle region, and the spacings calculated from these peaks were 4.0 and 3.2 nm, respectively. The observed spacing of the gel was larger than the thickness of the sheet assembly. Since a higher dodecane content increased the spacing, the gel is suggested to have a layer structure composed of the hydrogen bonded sheet-like assemblies and dodecane which was incorporated in between the sheet assemblies.

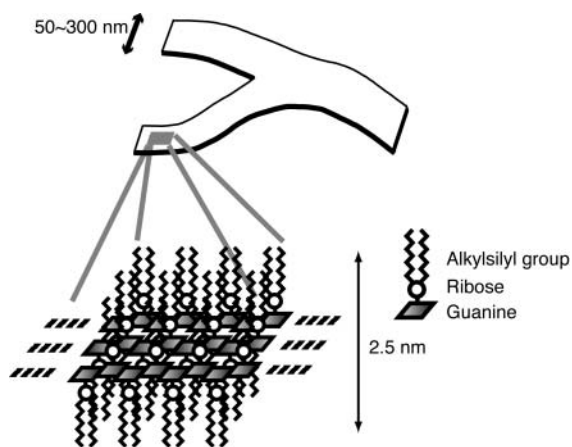


Fig. 6 Schematic view of the mesoscopic scale sheet-like assembly of the **1**-dodecane gel.

Discussion

Structure of the **1**-dodecane gel

Immobilization of a large quantity of liquid by small amounts of low-molecular-weight gelators has attracted a wide range of interest, and organogels are the subject of recent work not only in supramolecular and colloid chemistry but also because of future applications as novel supramolecular materials.³ In this context, a molecular level understanding of organogel structure is essential. Electron micrographs of gels have revealed the formation of mesoscopic-scale fibrous networks of self-assembled gelators, and gelation is attributed to these fibrous networks in most cases. Only recently, however, formation of sheet assemblies was reported by van Esch *et al.* and Jung *et al.*,¹⁹ and little is known as to the sheet-like assemblies in gel structures. In this study, we clearly showed formation of the mesoscopic-scale sheet-like assemblies in the **1**-dodecane gel, and confirmed that the sheet formation was essential for macroscale gelation. Solvent molecules are indicated to exist in between the sheet structures.

Formation of nanometre-scale tape, ribbon, and cylindrical motifs by hydrogen bonding interaction has been known from the molecular level. However, the development of fibrous networks by aggregation of the hydrogen-bonded motifs should be explained in order to understand the gelation process. A recent report by Simmons *et al.*²⁰ has successfully elucidated the structure of a fibre bundle on the 20–100 nm scale from the 2.1 nm scale cylindrical motifs, but connection of the fibres to form the networks was not clear enough. It is pointed out that the structure of the junction is the important subject to be studied.³ We clarified the structure of the 50–300 nm scale sheet assembly on the molecular level showing that the sheet assembly was formed by the additional inter-tape hydrogen bonds between nanometre-scale hydrogen-bonded tape motifs. The AFM image (Fig. 3) clearly showed that splitting and stitching of the sheet assemblies led to formation of networks of the sheet assemblies. Therefore, the junction formation of the sheet assemblies is explained by cleavage of the inter-tape hydrogen bonds, offering a molecular-level understanding of the network formation. The sheet assemblies may form a three dimensional network, though no information is available from the AFM image of the gel transferred onto the silicone surface.

It is interesting to note that the tape motifs within the sheet assemblies are not fully connected by the inter-tape hydrogen bonds. Though it is difficult to estimate quantitatively, the relative intensities of the peaks at 1650 and 1629 cm^{-1} in the IR spectrum of the gel suggested that a considerable portion of the guanine units did not participate in the inter-tape hydrogen bonds. Since the width of the sheet in the **1**-dodecane gel (5 wt%) shown in Fig. 3 was 50–300 nm, the tape motif located at the edge of the sheet comprised only a small part. Therefore, the inter-tape hydrogen bonds were not fully but partially formed even inside of the sheet assemblies.

Structural hierarchy in the gel

The **1**-dodecane gel is shown to have structural hierarchy by different levels of hydrogen bonds, *i.e.*, the tape motif by the double intra-tape hydrogen bonds and the sheet-like assembly by the double inter-tape hydrogen bonds. The unique thermal behaviour of the **1**-dodecane gel is ascribed to this structural hierarchy. Above the first endothermic peak, the inter-tape hydrogen bonds were cleaved but the intra-tape hydrogen bonds were retained. The rigid nature of the hydrogen-bonded tape motif and the flexible nature of the alkylsilyl side chains might allow alignment of the mesogenic tape motifs, and the gel-to-liquid crystalline phase transition took place on heating. A similar liquid crystalline phase of a lipophilic deoxyguanosine derivative in hydrocarbon solvents was reported recently

by Gottarelli *et al.*,^{17,21} and formation of the same hydrogen-bonded guanine tape motif was indicated.

In conclusion, we demonstrated that the molecular-level inter-tape hydrogen bond led to formation of the mesoscopic-scale sheet-like assembly in the 1-dodecane system, which caused macroscopic gelation of the system. We are further extending the study to design and control the hierarchical structures of artificial nucleoside-based materials.

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