Soft Matter



View Article Online

PAPER

Check for updates

Cite this: Soft Matter, 2025, 21, 2124

Stereoisomerism-dependent gelation and crystal structures of glycosylated *N*-methylbromomaleimide-based supramolecular hydrogels[†]

in the crystals of the compounds that showed gelation ability.

Kotoyo Yamashita,^a Akitaka Ito, ^b*^{bc} Masashi Ishida,^d Yuki Shintani,^e Masato Ikeda, ^ef^{ghi} Shingo Hadano,^{adj} Masayuki Izumi ^{adj} and Rika Ochi *^{adj}

In this study, we developed glycosylated *N*-methylbromomaleimide-based supramolecular hydrogels exhibiting colour change along with gel–sol transition and found that the stereoisomerism of the sac-

charide residue affects their gelation ability. Single-crystal X-ray diffraction analysis revealed the molecular packing and hydrogen-bonding networks contributed by the saccharide residues.

Interestingly, it was found that water molecules were incorporated into the hydrogen-bonding network

Received 9th November 2024, Accepted 8th February 2025

DOI: 10.1039/d4sm01325e

rsc.li/soft-matter-journal

Introduction

Low molecular weight (LMW) supramolecular hydrogels¹ formed by self-assembly of LMW amphiphiles (gelators) have attracted increased interest due to their high responsiveness to external stimuli, such as pH,² chemical/biological additives³ and temperature.⁴ The high stimulus responsiveness due to the weak non-covalent interactions (*e.g.* hydrogen-bonding, π - π stacking and hydrophobic interactions) enables the self-assembly of LMW gelators and, therefore, fine-tuning of the

- ^a Graduate School of Integrated Arts and Sciences, Kochi University, 2-5-1, Akebono-cho, Kochi 780-8520, Japan. E-mail: ochi@kochi-u.ac.jp
- ^b School of Engineering Science, Kochi University of Technology, Kami, Kochi 782-8502, Japan

^c Research Center for Molecular Design, Kochi University of Technology, Kami, Kochi 782-8502, Japan

^d Faculty of Science and Technology, Kochi University, 2-5-1, Akebono-cho Kochi 780-8520, Japan

- ^e United Graduate School of Drug Discovery and Medical Information Sciences, Gifu University, 1-1 Yanagido, Gifu 501-1193, Japan
- ^f Department of Chemistry and Biomolecular Science, Faculty of Engineering, Gifu University, 1-1 Yanagido, Gifu 501-1193, Japan
- ^g Institute for Glyco-core Research (iGCORE), Gifu University, 1-1 Yanagido, Gifu 501-1193, Japan
- ^h Center for One Medicine Innovative Translational Research (COMIT),
- Gifu University, 1-1 Yanagido, Gifu 501-1193, Japan
- ⁱ Innovation Research Center for Quantum Medicine, Graduate School of Medicine, Gifu University, 1-1 Yanagido, Gifu 501-1193, Japan
- ^j Research and Education Faculty, Kochi University, 2-5-1, Akebono-cho, Kochi 780-8520, Japan

† Electronic supplementary information (ESI) available: Fig. S1–S11 and cif files. CCDC 2370385. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d4sm01325e

self-assembled structures and non-covalent interactions of LMW gelators is of primary importance. As user-friendly sensing materials that do not require special equipment, LMW hydrogels that exhibit colour change (i.e. chromism) in response to specific external stimuli are useful. However, the number of reports on chromic supramolecular hydrogels is still limited, except for the appearance of a visible absorption band upon complexation with transition metal cations.^{5,6} Our group focuses on supramolecular hydrogel systems based on N-alkyl-2-anilino-3-halogenomaleimide-type chromophores, whose colour changes depending on the molecular assembly state.⁶ For example, glycolipid-type gelators such as glycosylated N-alkyl-2anilino-3-chloromaleimide (MS-AAC-C11-COOH (MS (monosaccharide) = α/β -D-glucose (Glc), α/β -D-galactose (Gal) or α -D-mannose (Man)); Fig. 1A) exhibited chromism from yellow (hydrogel state) to orange (solution state) upon gel-sol transition.^{6a} The hypsochromic shift of the absorption in the hydrogel state compared with the relevant solution (sol) state indicates that



Fig. 1 Chemical structures of glycolipid-type amphiphiles. (A) **MS-AAC-C11-COOH** (previous work)^{6a} and (B) **MS-AAB-Me** (this work).

Paper

the MS-AAC moieties in the gelators were stacked in an H-type arrangement.⁷ In our chromic hydrogel system, the efficient induction of the gelator stacking and self-assembly is an important process. The main factor determining the self-assembly ability of glycolipid-type gelators is the stereoisomerism (epimeric and anomeric isomers) of the saccharide moiety.⁸ The multiple hydroxy groups in the saccharide moiety act as hydrogen-bonding sites, forming a unique hydrogen-bonding network that significantly affects gelation ability and gel stability. Therefore, the elucidation of the hydrogen-bonding network pattern contributed by saccharide residues is expected to provide a useful guide for the molecular design of gelators.

In this study, novel glycolipid-type amphiphiles MS-AAB-Me with a glycosylated N-alkyl-2-anilino-3-bromomaleimide (AAB)based chromophore (Fig. 1B) were designed and synthesised, and the effects of the stereoisomerism of the saccharide moiety on the gelation ability with colour change behaviour were investigated. Furthermore, single crystals of several glycolipids, aGal-AAB-Me, aGlc-AAB-Me and BGlc-AAB-Me, were obtained from aqueous media, and their crystal structures were successfully elucidated by single-crystal X-ray diffraction (XRD) analysis. The molecular packing with hydrogen-bonding networks of a LMW gelator is quite important for the design of LMW gelators.9 There is, however, a trade-off relationship between gelation and crystallisation abilities. Therefore, the single-crystal XRD analysis of the packing mode and hydrogen-bonding networks of LMW gelators is generally difficult, and only one single-crystal XRD analysis of a glycolipid-type gelator has been reported by Hamachi and coworkers.^{9a} The obtained crystal structures of the LMW gelators, in which the saccharide moiety contributes to the hydrogen-bonding networks, are informative for the design of the glycolipid-type LMW gelators.

Results and discussion

Molecular design and synthesis of gelators

MS-AAB-Me amphiphiles (Fig. 1B) possessing a hydrophobic core consisting of an AAB-based chromophore and a hydrophilic monosaccharide (MS) moiety were designed. In our previous study, all the MS-AAC-C11-COOH amphiphiles (Fig. 1A) formed supramolecular hydrogels, and the stereoisomerism of the saccharide moiety had little effect on the gelation ability.^{6a} This phenomenon was thought to be due to the participation of both the carboxy (COOH) group at the end of the flexible C11 chain and the saccharide moiety in the hydrogen-bonding network. In this study, we therefore replaced the COOH-terminated C11 chain with a short methyl (Me) group to reduce the flexibility and hydrophilicity of the Nalkyl moiety. In addition, we expected that the introduction of the Me group would increase the fraction of the saccharide moiety in the molecule, thereby enhancing the effect of the stereoisomerism of the saccharide moiety on the gelation ability. We also changed the halogen species of the chromophore from chlorine to bromine to promote stronger halogenbonding interactions between the bromomaleimide moieties.¹⁰



The molecular library was obtained from 2,3-dibromo-*N*-methylmaleimide (1) and the corresponding 4-aminophenyl pyranoside in good yields, as shown in Scheme 1.

Gelation ability and gel stability

The gelation ability, critical gelation concentrations (CGCs) and gel-to-sol phase transition temperature (T_{gel}) of MS-AAB-Me in 200 mM HEPES-KOH buffer (pH 6.7) were investigated using the tube inversion method¹¹ (Table 1, Fig. 2 and Fig. S1, ESI[†]). The gelation ability can be influenced by the pH and salt strength. Here, HEPES-KOH buffer which is one of Good's buffers with a neutral pH was used. **aGal-AAB-Me**, **BGal-AAB-Me** and ßGlc-AAB-Me formed stable hydrogels above the CGC. In particular, β Glc-AAB-Me showed a high gelation ability (CGC = 0.32 wt%). The transparency and colour of the obtained gels were slightly different from each other (Fig. 2 and Fig. S2, ESI[†]). The αGal-AAB-Me and βGlc-AAB-Me hydrogels were turbid and bright yellow (λ_{max} = 409 nm and 405 nm, respectively), whereas the **\betaGal-AAB-Me** hydrogel was transparent and orange (λ_{max} = 411 nm with a shoulder at 460 nm, Fig. S2B, ESI[†]). The colour difference indicates a difference in molecular packing. In addition, the β Glc-AAB-Me hydrogel also had higher thermal stability (T_{gel} = 81 °C) than α Gal-AAB-Me and β Gal-AAB-Me hydrogels (T_{gel} = 76 and 54 °C, respectively) at the same concentration (2.2 wt%). The gelation and chromism of the hydrogels were thermally reversible (Fig. 3, typically for **βGlc**-AAB-Me). Conversely, aGlc-AAB-Me and aMan-AAB-Me underwent precipitation. These results suggest that the gelation ability is related to the epimeric and anomeric isomerism of

Table 1Gelation ability (G: gel, P: precipitation), critical gelation con-
centrations (CGCs), absorption maxima (λ_{max}) at room temperature
(around 23 °C) and gel-to-sol phase transition temperature (T_{gel}) of MS-
AAB-Me. Conditions: 200 mM HEPES-KOH buffer (pH 6.7)

Entry	Compound		CGC [wt%]	$T_{\mathrm{gel}}{}^a \left[{}^\circ\mathrm{C}\right]$	$\lambda_{\max}^{a,b}$ [nm]
1	αGal-AAB-Me	G	1.7	76	409
2	βGal-AAB-Me	G	1.4	54	411
3	αGlc-AAB-Me	Р	_	_	c
4	βGlc-AAB-Me	G	0.32	81	405
5	αMan-AAB-Me	Р	_	_	c

 a^{a} [MS-AAB-Me] = 2.2 wt%. b^{b} Fig. S2, ESI. c^{c} Not measurable due to sample inhomogeneity.



[**βGal-AAB-Me**] = 1.9 wt%, [**αGlc-AAB-Me**] = 2.0 wt%, [**βGlc-AAB-Me**] = 1.9 wt%, [αMan-AAB-Me] = 2.1 wt% in 200 mM HEPES-KOH buffer (pH 6.7).



Fig. 3 Photographs and schematics of **βGlc-AAB-Me** hydrogel exhibiting reversible thermal gel-sol transition and thermochromism. Condition: [BGlc-AAB-Me] = 1.7 wt% in 200 mM HEPES-KOH buffer (pH 6.7).

the molecules, induced by a difference in the orientation of the hydroxy groups. In addition to hydrogen-bonding, hydrophobic interactions contribute to the self-assembly ability of the molecule. The hydrophobicity of unprotected monosaccharides, based on their solubility in water decreases in the order of Gal > Glc > Man.¹² In practice, α Man-AAB-Me, which has the most hydrophilic saccharide residue, exhibited high solubility and hardly precipitated even at high concentration (<0.80 wt%) compared to its Gal or Glc counterparts (0.25, 0.49, 0.26 and 0.20 wt% for aGal-AAB-Me, BGal-AAB-Me, aGlc-AAB-Me and βGlc-AAB-Me, respectively). These results suggest that the hydrogen-bonding networks and the hydrophobic-hydrophilic balance of the saccharide moiety contribute to the molecular aggregation ability. Furthermore, the compounds bearing β-anomers exhibited higher gelation ability than the corresponding α -anomers with the same epimeric saccharide (Gal and Glc). The theory that the hydrogen-bonding mode of the β -configuration is preferred during the molecular stacking process supports these results.^{8,13}

Morphology of the hydrogels

Insight into the morphology of the self-assembled structures was obtained by transmission electron microscopy (TEM) on the αGal-AAB-Me, βGal-AAB-Me and βGlc-AAB-Me hydrogels (Fig. 4 and Fig. S3, ESI[†] (other views of Fig. 4)). TEM images showed that αGal-AAB-Me (Fig. 4A and Fig. S3A, ESI[†]) and βGal-AAB-Me (Fig. 4B and Fig. S3B, ESI⁺) self-assembled into thin one-dimensional (1D) nanofibers or two-dimensional (2D) nanosheets. On the other hand, ßGlc-AAB-Me self-assembled into longer and thick 1D nanofibers, thereby facilitating the formation of a highly entangled three-dimensional (3D) network (Fig. 4C, D and Fig. S3C, ESI[†]). These conventional TEM images are not cryo-TEM and thus there is the potential influence of the sample preparation process (especially during the drying process) on the observed morphologies. Nevertheless, we speculate that the highly entangled 3D network formed by the



Fig. 4 Representative TEM images of αGal-AAB-Me (A), βGal-AAB-Me (B) and **βGlc-AAB-Me** (C) and (D) hydrogels transferred on an elastic carboncoated grid. The scale bar represents 500 nm. Conditions: $[\alpha Gal-AAB-Me] =$ [BGal-AAB-Me] = [BGlc-AAB-Me] = 2.2 wt% in 200 mM HEPES-KOH buffer (pH 6.7).

longer and thicker nanofibers of BGlc-AAB-Me may be one of the reasons for the stable and mechanically tough hydrogel formation (vide infra).

Rheological measurements of hydrogels

Interestingly, the βGlc-AAB-Me hydrogel prepared at a high concentration (1.4 wt%) showed an agar-like texture. The obtained hydrogel was able to maintain a complex shape, could be held by hand or a toothpick and showed unusually high strength for a supramolecular hydrogel (Fig. 5). Most LMW supramolecular hydrogels do not have mechanical toughness comparable to polymer-based hydrogels, and the lack of mechanical toughness unfortunately limits their usefulness as functional materials. The development of mechanically tough LMW supramolecular hydrogels has therefore become a research objective.¹⁴ Given the above research background, the high strength properties of the βGlc-AAB-Me hydrogel is intriguing and are expected to be useful as functional materials.

The mechanical strength of the αGal-AAB-Me, βGal-AAB-Me and BGlc-AAB-Me hydrogels (1.9 wt%) was evaluated by



Fig. 5 Photographs of **βGlc-AAB-Me** hydrogel prepared at high concentration. Condition: [βGlc-AAB-Me] = 1.4 wt% in 200 mM HEPES-KOH buffer (pH 6.7)

View Article Online

Paper

Paper



Fig. 6 Frequency sweep (*G'* (closed symbols); *G''* (open symbols)) of α Gal-AAB-Me (green data), β Gal-AAB-Me (blue data) and β Glc-AAB-Me (red data) hydrogels. Conditions: [α Gal-AAB-Me] = [β Gal-AAB-Me] = [β Gal-AAB-Me] = [β Glc-AAB-Me] = 1.9 wt% in 200 mM HEPES-KOH buffer (pH 6.7). The measurements were carried out at a strain of 0.20%, 25 °C.

rheological measurements (Fig. 6). The frequency sweep measurements revealed that the storage modulus (*G'*) was greater than the loss modulus (*G''*) throughout the measurement range, demonstrating typical gel properties. The maximum values of *G'* for α **Gal-AAB-Me**, β **Gal-AAB-Me** and β **Glc-AAB-Me** hydrogels were about 13, 4 and 83 kPa, respectively. The *G'* value of β **Glc-AAB-Me** (83 kPa) is remarkably high for LMW supramolecular hydrogels reported so far.¹⁴ One of the factors that may have contributed to the extremely high strength of β **Glc-AAB-Me** is the highly entangled 3D network shown in the TEM observation described above (Fig. 4C, D and Fig. S3C, ESI†). In addition, the stability of the fibre structure may also have contributed. The mechanism behind the high strength of the β **Glc-AAB-Me** hydrogel requires further investigation.

Hydrogen-bonding networks revealed by single-crystal XRD analyses

Diluted solutions of MS-AAB-Me in 200 mM HEPES-KOH buffer (pH 6.7) at concentrations below CGC gave precipitates. Polarized optical microscopic images revealed that all the precipitates except for that of aMan-AAB-Me were micrometre-scale crystals, with *a***Glc-AAB-Me** exhibiting plate-like crystals and the others crystallising in the form of needle-like crystals (Fig. S4, ESI[†]). In addition, single crystals suitable for X-ray structural analysis were successfully obtained for aGal-AAB-Me, aGlc-AAB-Me and β Glc-AAB-Me and the results are shown in Fig. 7 and Fig. S5, ESI[†] (other views of Fig. 7), and the corresponding data are summarised in Table 2. It should be noted that the structures of aGlc-AAB-Me and BGlc-AAB-Me were determined with large errors due to poor crystal quality. Moreover, the structural analysis of the BGal-AAB-Me crystals could not be performed due to a significant loss of crystallinity after collection from the solution. The crystal structure of aGal-AAB-Me is shown in Fig. 7A and Fig. S5A, ESI.† Each unit cell contains two crystallographically equivalent a Gal-AAB-Me molecules and six



Fig. 7 Single-crystal X-ray structures of α Gal-AAB-Me (A), α Glc-AAB-Me (B) and β Glc-AAB-Me (C) (left: overview with 50% ellipsoids, right: schematic illustration). Colour code: grey, carbon; red, oxygen; blue, nitrogen; orange, bromine; white, hydrogen; green, water. Red dots represent hydrogen bonds. The crystallographic data are summarised in Table 2.

water molecules. The water molecules are connected via hydrogen bonds and the individual water molecules are surrounded by the NH and carbonyl groups in the AAB backbone and the hydroxy groups at the 2-, 4- and 6-positions in the α Gal residue. This kind of hydrogen-bonding network, which encapsulates water, is thought to be important for the formation of stable hydrogels. It is also worth noting that the two C-Br···Br angles between two AAB moieties in a unit cell are $177.2(2)^{\circ}$ and $95.3(2)^{\circ}$, suggesting the presence of type-II halogen bonds according to our molecular design. In addition, the AAB moiety is stacked with the AAB moiety of a molecule in the neighbouring unit cell, supporting the hypothesis that the colour change mechanism of this chromic supramolecular hydrogel is due to the formation of H-aggregates.⁷ A similar hydrogen-bonding network with a halogen-bonded and π -stacked AAB system was obtained for the crystal of β Glc-AAB-Me (Fig. 7C and Fig. S5C, ESI[†]). The crystal structure contains 2.5 water molecules per one ßGlc-AAB-Me molecule and the individual water molecules are surrounded by the NH and carbonyl groups in the AAB backbone and the hydroxy groups at the 2-, 4- and 6-positions in the β Glc residue. Furthermore, the hydroxy groups at the 3- and 6-positions also form hydrogen bonds between neighbouring BGlc-AAB-Me molecules. In contrast with the crystal structures of gel-forming αGal-AAB-Me and βGlc-AAB-Me, which contain more than two water molecules, the crystals of αGlc-AAB-Me, which showed no gelation ability, contain no

 Table 2
 Crystallographic data for αGal-AAB-Me, αGlc-AAB-Me and βGlc-AAB-Me

Compound	aGal-AAB-Me	αGlc-AAB-Me	βGlc-AAB-Me
Formula	C ₁₇ H ₁₉ BrN ₂ O ₈ ·3H ₂ O	C ₁₇ H ₁₉ BrN ₂ O ₈	C ₁₇ H ₁₉ BrN ₂ O ₈ ·2.5H ₂ O
Formula weight	513.30	459.25	503.79
Crystal system	Monoclinic	Monoclinic	Triclinic
Space group	$P2_1$	$P2_1$	<i>P</i> 1
a/Å	12.8648(7)	6.0927(6)	9.4507(9)
b/Å	4.7385(2)	7.2170(6)	12.7474(14)
c/Å	18.1370(10)	20.9754(18)	17.6136(11)
a/deg.	90	90	76.759(7)
β/deg.	104.231(5)	95.482(9)	89.921(6)
c/deg.	90	90	88.668(8)
<i>V</i> /Å ³	1071.70(10)	918.09(14)	2065.0(3)
Ζ	2	2	4
Crystal size/mm ³	$0.639\times0.028\times0.021$	0.17 imes 0.053 imes 0.019	0.688 imes 0.032 imes 0.019
T/K	103.15	103.15	103.15
$D_{\rm c}/{\rm g~cm}^{-3}$	1.591	1.661	1.620
F ₀₀₀	528.0	468.0	1034
$\lambda/\text{\AA}$	0.71073	0.71073	0.71073
μ (Mo K α)/mm ⁻¹	1.980	2.289	2.051
$R_1 [I > 2.00\sigma(I)]^a$	0.0353	0.1026	0.1029
R (all reflections) ^{<i>a</i>}	0.0481	0.1299	0.1784
wR_2 (all reflections) ^b	0.0752	0.2580	0.3162
GOF	1.028	1.075	0.945
Number of observations	7763	5291	15 537
Number of variables	3816	3231	10448
CCDC number	2370385		_

water molecule (Fig. 7B and Fig. S5B, ESI[†]). Although the results represent the mode of interaction in the crystalline state and it is questionable whether they fully reflect those in the gel state, we have succeeded in elucidating the hydrogenbonding network pattern in this molecular system. These results suggest that a unique hydrogen-bonding network is formed depending on the stereoisomerism of the saccharide residues, and that this network may determine the properties of the nanostructure that is the component of the hydrogels.^{10a}

To investigate the impact of the hydrogen-bonding networks triggered by the hydroxy groups of the saccharide residues on the formation of the hydrogels, we performed Fouriertransform infrared (FT-IR) measurements for the solventretained aGal-AAB-Me, BGal-AAB-Me and BGlc-AAB-Me hydrogels (Fig. S6, ESI[†]). We prepared the hydrogel samples (1.9 wt%) using distilled water as the solvent instead of the HEPES-KOH buffer to avoid complicatedness of analysis due to the presence of buffer-derived signals. In the 2700–3700 cm^{-1} region, the bending vibrations of the O-H moiety in the saccharide residues and water molecules could be observed. In particular, the βGlc-AAB-Me hydrogel, which showed high gelation ability and crystallised with water molecules, exhibited a strong and narrow band at around 3290 cm⁻¹. Furthermore, the band at $\sim 1640 \text{ cm}^{-1}$ was also narrow compared with that of H₂O. These spectroscopic characteristics strongly suggest the existence of the hydrogen-bonding network in the ßGlc-AAB-Me hydrogel.¹⁵ Similar behaviours were also observed for the aGal-AAB-Me hydrogel, of which the crystal structure was successfully analysed. Thus, the hydrogen-bonding networks between the hydroxy groups of the saccharide residues and water molecules in the hydrogel state were experimentally detected.

Experimental

Generals

Chemical reagents were purchased from Tokyo Chemical Industry Co., Ltd, FUJIFILM Wako Pure Chemical Co., or Watanabe Chemical Industries, Ltd, and used without further purification. Thin layer chromatography (TLC) was performed on TLC silica gel 60F254 (Merck). Column chromatography was performed on silica gel 60 N (Kanto Chemical Co., Inc., spherical neutral, 63-210 µm). ¹H and ¹³C NMR spectra in CDCl₃, CD₃OD, or DMSO- d_6 were recorded on a JEOL ECA500 spectrometer, and chemical shifts were determined by tetramethylsilane (TMS) or residual non-deuterated solvents as an internal reference. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m =multiplet, dd = double doublet, and br = broad. ESI-MS analyses were carried out using a Bruker amaZon SL mass spectrometer. FT-IR spectra (for chemical structure identification of compounds) were recorded on a JEOL FT/IR-4100 spectrometer using KBr pellets in the range of 4000 to 500 cm^{-1} , with a resolution of 4 cm^{-1} .

Preparation of hydrogels

Powders of compounds (typically, 2 mg) were suspended in 200 mM HEPES-KOH buffer (pH 6.7, 20–500 μ L) in a glass screw neck vial, sealed with a polypropylene cap and Teflon packing (Mighty vial, Maruemu, Japan). The suspensions were heated until homogeneous solutions were obtained. The solutions were solidified into hydrogels after incubating for several minutes at room temperature.

Determination of T_{gel} of hydrogels

 T_{gel} was determined by a tube inversion method (Fig. S1, ESI[†]).¹¹ The vial containing the hydrogel (2.2 wt% in 200 mM

Paper

Paper

Measurements of the UV-visible absorption spectra of hydrogels

Hydrogel samples (2.2 wt% in 200 mM HEPES-KOH buffer (pH 6.7)) were heated to form a homogeneous solution. The hot solution (100 µL) was transferred into an assembled quartz cell (path length: 0.1 mm (GL Sciences Inc., cat. no. AB10-UV-0.1 with cell adaptor, GL Sciences Inc., cat. no. CAS-10-1)) and stored at room temperature for 10 min. The absorption spectra at room temperature were recorded using a Shimadzu UV-1280 spectrophotometer.

Rheological measurement of hydrogels

Dynamic frequency sweep experiments were carried out on a TA instruments AR-G2 rheometer using a 20-mm stainless steel parallel plate (the temperature of the plate was controlled at 25 °C by Peltier system) at the gap of 2000 µm. Hydrogel samples (1.9 wt% in 200 mM HEPES-KOH buffer (pH 6.7)) were placed on the plate. Typically, a freshly prepared solution (800 µL) of MS-AAB-Me, as described above in a glass vial, was immediately transferred into a mold, which was prepared by cutting the top off a 20 mL (2 cm diameter) plastic syringe and setting it up vertically with its plunger. The top of the syringe mold was covered with parafilm and allowed to stand for 24 h at room temperature. The hydrogel was ejected and transferred onto the bottom plate of the rheometer by carefully pushing the plunger. All gels exhibited an almost linear viscoelastic regime up to 1.0% strain (frequency: 1.0 rad s^{-1}). Thus, a frequency sweep (0.1–100 rad s^{-1}) was performed under 0.2% strain. The sampling and measurements were according to previously reported methods.9e,16

TEM analysis of hydrogels

Hydrogel samples (2.2 wt% in 200 mM HEPES-KOH buffer (pH 6.7), 5 μ L) were dropped on a copper TEM grid covered by an elastic carbon-support film (20-25 nm) with filter paper underneath and the excess solution was blotted with the filter paper immediately. The TEM grids were washed with $H_2O(5 \mu L)$ three times and dried under a reduced pressure for 6 h prior to TEM observation. The TEM images were acquired using a Hitachi H-7100 (accelerating voltage: 100 kV) equipped with a CCD camera and AMTV600 software.

Single-crystal X-ray diffraction analyses

Powders of compounds (typically, 2 mg) were suspended in 200 mM HEPES-KOH buffer (pH 6.7) in a mighty vial (1.6 wt%, 2.8 wt% and 0.20 wt% for aGal-AAB-Me, aGlc-AAB-Me and BGlc-AAB-Me, respectively). The suspensions were heated until homogeneous solutions were obtained. The solutions were incubated at room temperature for several days to form crystals. One crystal was picked up under an optical microscope, and then, single-crystal XRD measurements were performed

using a Rigaku XtaLAB Synergy-S/Mo system (Mo K α ; λ = 0.71073 Å). X-Ray diffraction data were collected at 103.15 K by a HyPix-600HE photon counting detector and analysed using an Olex2 crystallographic software package.¹⁷ The structure was solved by direct methods (ShelXT¹⁸) and refined through fullmatrix least-squares techniques on F^2 using ShelXL.¹⁹ All nonhydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed at calculated positions and refined "riding" on their corresponding carbon, nitrogen or oxygen atom. The crystal data are summarized in Table 2. Final cif files for all the crystals are listed in the ESI.† Deposition number 2370385 for aGal-AAB-Me, contains the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service https://www.ccdc.cam.ac.uk/structures.

FT-IR measurement of hydrogels

FT-IR spectra of hydrogels were recorded on a Jasco FT/IR-4600 spectrometer with an attenuated total reflectance (ATR) attachment (ATR-PRO-ONE) in the range of 4000 to 500 cm⁻¹, with a resolution of 4 cm⁻¹. Hydrogel samples (1.9 wt% in distilled water) were prepared for the measurement. Spectra of the corresponding powdery samples which were obtained by drying the methanolic solutions and H2O were also measured as references.

Synthesis

Aniline derivatives with a saccharide residue (MS-Ph-NH₂) were synthesized according to previously reported methods.^{8b 1}H NMR spectra of the compounds are shown in Fig. S7-S11, ESI.†

Synthesis of α Gal-AAB-Me. To a solution of 1 (108 mg, 0.4 mmol) in dry N,N-dimethylformamide (DMF, 1 mL) was added aGal-Ph-NH₂ (120 mg, 0.44 mmol, 1.1 equiv.) and N,Ndiisopropylethylamine (DIEA, 77 µL, 0.44 mmol, 1.1 equiv.), and the mixture was stirred at room temperature overnight under ambient atmosphere. The solvent was then evaporated, and residue was washed with diethyl ether and H₂O. The resulting product was dried under vacuum to give aGal-AAB-Me (150 mg, 82%) as a yellow powder. ¹H NMR (500 MHz, CD₃OD): δ = 3.01 (s, 3H), 3.68–3.70 (m, 2H), 3.92–3.97 (m, 4H), 5.49 (d, I = 1.8 Hz, 1H), 7.17 ppm (dd, $I_1 = 8.9$ Hz, $I_2 = 18$ Hz, 4H). ¹³C NMR (125 MHz, DMSO- d_6): $\delta = 24.27$, 53.66, 60.32, 68.03, 68.57, 69.45, 72.33, 77.65, 98.54, 116.60, 126.19, 130.37, 141.93, 155.16, 166.07, 167.89 ppm. LRMS (ESI, positive mode): Calcd. for $[M(C_{17}H_{19}BrN_2O_8) + Na]^+$: m/z = 481.0; found: 481.0. FT-IR (KBr pellet): v = 3355.5, 3031.6, 2958.3, 2935.1, 1762.6, 1712.5, 1658.5, 1508.1, 1446.4, 1388.5, 1311.4, 1226.5, 1149.4, 1091.5, 1037.52, 983.5, 960.4, 860.1, 833.1, 771.4, 740.5, 705.8, 667.3, 582.4, 536.1 cm⁻¹.

Synthesis of BGal-AAB-Me. To a solution of 1 (108 mg, 0.4 mmol) in DMF (1 mL) was added \u03b3Gal-Ph-NH2 (120 mg, 0.44 mmol, 1.1 equiv.) and DIEA (77 µL, 0.44 mmol, 1.1 equiv.), and the mixture was stirred at room temperature overnight under ambient atmosphere. The solvent was then evaporated, and the residue was washed with diethyl ether and H₂O. The resulting product was dried under vacuum to give BGal-AAB-Me

(138 mg, 75%) as a yellow powder. ¹H NMR (500 MHz, CD₃OD): δ = 3.01 (s, 3H), 3.58 (dd, J_1 = 3.5 Hz, J_2 = 9.7 Hz, 1H), 3.68–3.71 (m, 1H), 3.74–3.82 (m, 3H), 3.90 (d, J = 3.5 Hz, 1H), 4.85–4.92 (m, 1H (overlap with water)), 7.14 ppm (dd, J_1 = 8.9 Hz, J_2 = 18 Hz, 4H). ¹³C NMR (125 MHz, DMSO- d_6): δ = 24.25, 53.64, 60.42, 68.16, 70.30, 73.28, 75.53, 77.59, 101.15, 115.72, 126.17, 130.26, 141.90, 155.36, 166.05, 167.88 ppm. LRMS (ESI, positive mode): Calcd. for [M(C₁₇H₁₉BrN₂O₈) + Na]⁺: m/z = 481.0; found: 481.0. FT-IR (KBr pellet): ν = 3509.8, 3371.0, 3239.8, 3016.1, 2946.7, 2881.1, 1762.6, 1712.5, 1654.6, 1616.1, 1508.1, 1442.5, 1384.6, 1307.5, 1234.2, 1137.8, 1083.8, 1052.9, 887.1, 829.2, 744.4, 698.1, 640.3, 574.7, 524.5 cm⁻¹.

Synthesis of a Glc-AAB-Me. To a solution of 1 (108 mg, 0.4 mmol) in DMF (1 mL) was added aGlc-Ph-NH₂ (121 mg, 0.44 mmol, 1.1 equiv.) and DIEA (77 µL, 0.44 mmol, 1.1 equiv.), and the mixture was stirred at room temperature overnight under ambient atmosphere. The solvent was then evaporated, and residue was washed with diethyl ether and H₂O. The resulting product was dried under vacuum to give aGlc-AAB-Me (160 mg, 87%) as a yellow powder. ¹H NMR (500 MHz, CD₃OD): δ = 3.01 (s, 3H), 3.42 (t, *J* = 9.2 Hz, 1H), 3.57 (dd, *J*₁ = 3.5 Hz, J₂ = 9.7 Hz, 1H), 3.64–3.76 (m, 3H), 3.85 (t, J = 9.2 Hz, 1H), 5.48 (d, J = 3.5 Hz, 1H), 7.17 ppm (dd, $J_1 = 9.5$ Hz, $J_2 =$ 15 Hz, 4H). ¹³C NMR (125 MHz, DMSO- d_6): δ = 24.24, 60.73, 69.95, 71.61, 73.06, 73.80, 77.69, 98.20, 116.57, 126.19, 130.46, 141.90, 154.97, 166.05, 167.86 ppm. LRMS (ESI, positive mode): Calcd. for $[M(C_{17}H_{19}BrN_2O_8) + Na]^+$: m/z = 481.0; found: 481.0. FT-IR (KBr pellet): v = 3390.2, 3278.4, 2950.6, 2912.0, 1774.2,1704.8, 1643.1, 1511.9, 1446.4, 1384.6, 1272.8, 1214.9, 1153.2, 1099.2, 1022.1, 929.5, 864.0, 837.0, 528.4 cm⁻¹.

Synthesis of BGlc-AAB-Me. To a solution of 1 (107 mg, 0.4 mmol) in DMF (1 mL) was added βGlc-Ph-NH₂ (120 mg, 0.44 mmol, 1.1 equiv.) and DIEA (77 µL, 0.44 mmol, 1.1 equiv.), and the mixture was stirred at room temperature overnight under ambient atmosphere. The solvent was then evaporated, and residue was washed with diethyl ether and H₂O. The resulting product was dried under vacuum to give ßGlc-AAB-Me (167 mg, 91%) as a yellow powder. ¹H NMR (500 MHz, CD₃OD): δ = 3.01 (s, 3H), 3.44–3.49 (m, 4H), 3.70 (dd, J_1 = 5.8 Hz, $J_2 = 12.0$ Hz, 1H), 3.90 (dd, $J_1 = 2.3$ Hz, $J_2 = 15$ Hz, 1H), 4.86–4.91 (m, 1H (overlap with water)), 7.13 ppm (dd, $J_1 = 9.5$ Hz, $J_2 =$ 15 Hz, 4H). ¹³C NMR (125 MHz, DMSO- d_6): δ = 24.24, 53.63, 60.69, 69.69, 73.25, 76.59, 77.04, 77.54, 100.54, 115.69, 126.14, 130.34, 141.88, 155.24, 166.05, 167.87 ppm. LRMS (ESI, positive mode): Calcd. for $[M(C_{17}H_{19}BrN_2O_8) + Na]^+$: m/z = 481.0; found: 481.0. FT-IR (KBr pellet): v = 3367.1, 3293.8, 2919.7, 1877.3, 1762.6, 1712.5, 1650.8, 1511.9, 1450.2, 1388.5, 1295.9, 1230.4, 1076.1, 1388.5, 1295.9, 1230.4, 1076.1, 1018.2, 891.0, 829.2, 744.4, 644.1, 582.4, 528.4 cm^{-1} .

Synthesis of α Man-AAB-Me. To a solution of 1 (107 mg, 0.4 mmol) in DMF (1 mL) was added α Man-Ph-NH₂ (119 mg, 0.44 mmol, 1.1 equiv.) and DIEA (77 µL, 0.44 mmol, 1.1 equiv.), and the mixture was stirred at room temperature overnight under ambient atmosphere. The solvent was then evaporated, and the residue was purified by column chromatography (SiO₂, CH₂Cl₂/MeOH = 12/1 to 6/1 to 1/1 (v/v)) and was then

evaporated. The residue was washed with diethyl ether. The resulting product was dried under vacuum to give **αMan-AAB**-**Me** (95 mg, 52%) as a yellow powder. ¹H NMR (500 MHz, CD₃OD): δ = 3.01 (s, 3H), 3.58–3.61 (m, 1H), 3.69–3.78 (m, 3H), 3.89 (dd, J_1 = 3.5 Hz, J_2 = 5.70 Hz, 1H), 3.99–4.01 (m, 1H), 5.46 (d, J = 3.5 Hz, 1H), 7.14 ppm (dd, J_1 = 8.7 Hz, J_2 = 16 Hz, 4H). ¹³C NMR (125 MHz, DMSO- d_6): δ = 24.24, 61.04, 66.71, 70.09, 70.67, 75.14, 99.19, 117.83, 126.19, 130.54, 141.88, 154.18, 166.04, 167.85 ppm. LRMS (ESI, positive mode): Calcd. for [M(C₁₇H₁₉BrN₂O₈) + Na]⁺: m/z = 481.0; found: 481.0. FT-IR (KBr pellet): ν = 3394.1, 3293.8, 2939.0, 1712.5, 1643.1, 1508.1, 1446.4, 1384.6, 1303.6, 1226.5, 1122.4, 1060.66, 1022.1, 983.5, 914.1, 887.1, 833.1, 744.4, 675.0, 644.1, 574.7, 505.3 cm⁻¹.

Conclusions

We developed novel glycolipid-type amphiphiles, MS-AAB-Me, and found that the stereoisomerism of the saccharide residue affects their gelation ability. The single-crystal XRD analysis revealed the presence of hydrogen-bonding networks and molecular packing in the crystals of some compounds. Interestingly, water molecules were incorporated into the hydrogenbonding networks in the crystals of the gel-forming compounds. These results indicate that the stereoisomerism of the saccharide residue has a marked effect on the formation of the hydrogen-bonding networks, as well as on the gelation ability and gel stability and are expected to provide important insights not only for the design of glycolipid-type supramolecular hydrogels but also for their application as functional materials. Interestingly, the BGlc-AAB-Me hydrogel prepared at a high concentration (1.4 wt%) showed an agar-like texture and sufficient mechanical toughness for easy handling. The TEM observation suggests that βGlc-AAB-Me can form stable hydrogels by forming a 3D structure with long and thick 1D nanofibers. We would like to investigate the mechanical properties and mechanism in more detail.

Author contributions

Conceptualisation: R. O. and K. Y.; synthesis and structural analysis: K. Y. and M. I. (M. Ishida); data curation (self-assembly properties): K. Y.; single-crystal XRD analysis: A. I.; rheological measurement: Y. S. and M. I. (M. Ikeda); absorption spectra measurements: K. Y.; polarised light microscopy experiments: K. Y. and Y. S.; TEM analysis: S. H. and K. Y.; FT-IR measurement: R. O. and A. I.; supervision: M. I. (M. Ikeda) and M. I. (M. Izumi); writing – original draft: K. Y. and R. O.; writing – review and editing: R. O., A. I., K. Y., M. I. (M. Ikeda), S. H. and M. I. (M. Izumi).

Data availability

The data supporting this article have been included as part of the ESI† and cif files in the Supplementary files. Additional data

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This work was partially supported by the JSPS KAKENHI Grant Number JP20K15416 and JP24K08637 and the Assisted Joint Research Program (Exploration Type and Acceleration Type) of the J-GlycoNet cooperative network, which is accredited by the Minister of Education, Culture, Sports, Science and Technology, MEXT, Japan, as a Joint Usage/Research Center. We would like to thank MARUZEN-YUSHODO Co., Ltd (https://kw.maru zen.co.jp/kousei-honyaku/) for the English language editing.

Notes and references

- 1 (a) L. A. Estroff and A. D. Hamilton, Chem. Rev., 2004, 104, 1201; (b) M. de Loos, B. L. Feringa and J. H. van Esch, *Eur. J. Org. Chem.*, 2005, 3615; (c) R. V. Ulijn and A. M. Smith, Chem. Soc. Rev., 2008, 37, 664; (d) M. Ikeda, R. Ochi and I. Hamachi, Lab Chip, 2010, 10, 3325; (e) A. Dawn, T. Shiraki, S. Haraguchi, S. Tamaru and S. Shinkai, Chem. - Asian J., 2011, 6, 266; (f) S. S. Babu, V. K. Praveen and A. Ajayaghosh, Chem. Rev., 2014, 114, 1973; (g) X. Du, J. Zhou, J. Shi and B. Xu, Chem. Rev., 2015, 115, 13165; (h) B. O. Okesola and D. K. Smith, Chem. Soc. Rev., 2016, 45, 4226; (i) H. Shigemitsu and I. Hamachi, Acc. Chem. Res., 2017, 50, 740; (j) K. Sato, M. P. Hendricks, L. C. Palmer and S. I. Stupp, Chem. Soc. Rev., 2018, 47, 7539; (k) N. Mehwish, X. Dou, Y. Zhao and C.-L. Feng, Mater. Horiz., 2019, 6, 14; (l) T. Shimizu, W. Ding and N. Kameta, Chem. Rev., 2020, 120, 2347; (m) M. Yokoya, S. Kimura and M. Yamanaka, Chem. - Eur. J., 2021, 27, 5601; (n) S. Panja and D. J. Adams, Chem. Soc. Rev., 2021, 50, 5165; (o) D. K. Smith, Soft Matter, 2024, 20, 10.
- 2 (a) S. L. Zhou, S. Matsumoto, H. D. Tian, H. Yamane, A. Ojida, S. Kiyonaka and I. Hamachi, *Chem. – Eur. J.*, 2005, 11, 1130; (b) S. Ray, A. K. Das and A. Banerjee, *Chem. Mater.*, 2007, 19, 1633; (c) A. Shome, S. Debnath and P. K. Das, *Langmuir*, 2008, 24, 4280; (d) J. Nanda, A. Biswas and A. Banerjee, *Soft Matter*, 2013, 9, 4198; (e) T. J. Moyer, J. A. Finbloom, F. Chen, D. J. Toft, V. L. Cryns and S. I. Stupp, *J. Am. Chem. Soc.*, 2014, 136, 14746; (f) B. O. Okesola, Y. Wu, B. Derkus, S. Gani, D. Wu, D. Knani, D. K. Smith, D. Adams and A. Mata, *Chem. Mater.*, 2019, 31, 7883; (g) G. Zhang, J. Li, W. Cai, Y. Kong and Z. Z. Yin, *Microchem. J.*, 2023, 193, 109160.
- 3 (a) M.-O. M. Piepenbrock, G. O. Lloyd, N. Clarke and J. W. Steed, *Chem. Rev.*, 2010, **110**, 1960; (b) J. Hu, G. Zhang and S. Liu, *Chem. Soc. Rev.*, 2012, **41**, 5933; (c) A. Y.-Y. Tam and V. W.-W. Yam, *Chem. Soc. Rev.*, 2013,

42, 1540; (*d*) M. D. Segarra-Maset, V. J. Nebot, J. F. Miravet and B. Escuder, *Chem. Soc. Rev.*, 2013, 42, 7086; (*e*) J. Zhou and B. Xu, *Bioconjugate Chem.*, 2015, 26, 987; (*f*) M. Ikeda, *Polym. J.*, 2019, 51, 371; (*g*) J. Gao, J. Zhan and Z. Yang, *Adv. Mater.*, 2019, 1805798; (*h*) A. N. Shy, B. J. Kim and B. Xu, *Matter*, 2019, 1, 1127; (*i*) R. Kuosmanen, K. Rissanen and E. Sievänen, *Chem. Soc. Rev.*, 2020, 49, 1977; (*j*) S. Kimura, M. Yokoya and M. Yamanaka, *Chem. Lett.*, 2021, 50, 459; (*k*) S. Panja and D. J. Adams, *Chem. – Eur. J.*, 2021, 27, 8928; (*l*) J. Chen, H. Wang, F. Long, S. Bai and Y. Wang, *Chem. Commun.*, 2023, 59, 14236; (*m*) N. Das and C. Maity, *ACS Catal.*, 2023, 13, 5544; (*n*) R. Kubota and I. Hamachi, *Adv. Sci.*, 2024, 11, 2306830.

- 4 (a) D. J. Pochan, J. P. Schneider, J. Kretsinger, B. Ozbaas, K. Rajagopal and L. Haines, J. Am. Chem. Soc., 2003, 125, 11802; (b) K.-S. Moon, H.-J. Kim, E. Lee and M. Lee, Angew. Chem., Int. Ed., 2007, 46, 6807; (c) Z. Chu and Y. Feng, Chem. Commun., 2011, 47, 7191; (d) M. Ikeda, R. Ochi, Y. Kurita, D. J. Pochan and I. Hamachi, Chem. – Eur. J., 2012, 18, 13091; (e) R. Ochi, T. Nishida, M. Ikeda and I. Hamachi, J. Mater. Chem. B, 2014, 2, 1464; (f) S. Xian and M. J. Webber, J. Mater. Chem. B, 2020, 40, 9197; (g) J. P. Fan, F. H. Tao, X. H. Zhang, T. T. Yuan, C. F. Xie, H. P. Chen and H. L. Peng, Colloids Surf., A, 2022, 652, 129839.
- 5 (a) S. Wang, W. Shen, Y. L. Feng and H. Tian, Chem. Commun., 2006, 1497; (b) Z. Qiu, H. Yu, J. Li, Y. Wang and Y. Zhang, Chem. Commun., 2009, 3342; (c) F. Rodriguez-Llansola, B. Escude, J. F. Miravet, D. Hermida-Merino, I. W. Hamley, C. J. Cardinb and W. Hayes, Chem. Commun., 2010, 46, 7960; (d) P. K. Sukul, P. K. Singh, S. K. Maji and S. Malik, J. Mater. Chem. B, 2013, 1, 153; (e) Y. Cai, Y. Shi, H. Wang, J. Wang, D. Ding, L. Wang and Z. Yang, Anal. Chem., 2014, 86, 2193; (f) X. Yu, X. Ge, H. Lan, Y. Li, L. Geng, X. Zhen and T. Yi, ACS Appl. Mater. Interfaces, 2015, 7, 24312; (g) T. Xu, C. Liang, S. Ji, D. Ding, D. Kong, L. Wang and Z. Yang, Anal. Chem., 2016, 88, 7318; (h) T. Yuan, Y. Xu, C. Zhu, Z. Jiang, H.-J. Sue, L. Fang and M. A. Olson, Chem. Mater., 2017, 29, 9937; (i) S. Dhiman, R. Ghosh and S. J. George, ChemSystemsChem, 2019, 1, e1900042; (j) P. Singh, S. Misra, A. Das, S. Roy, P. Datta, G. Bhattacharjee, B. Satpati and J. Nanda, ACS Appl. Bio Mater., 2019, 2, 4881; (k) X. Xu, X. Zhou, L. Qu, L. Wang, J. Song, D. Wu, W. Zhou, X. Zhou, H. Xiang, J. Wang and J. Liu, ACS Appl. Bio Mater., 2020, 3, 7236; (*l*) B. C. Roy and T. S. Mahapatra, *Soft Matter*, 2023, **19**, 1854; (*m*) A.-L. Leistner, M. M. Most and Z. L. Pianowski, *Chem.* – Eur. J., 2023, 29, e202302295.
- 6 (a) R. Ochi, K. Kurotani, M. Ikeda, S. Kiyonaka and I. Hamachi, *Chem. Commun.*, 2013, 49, 2115;
 (b) R. Oosumi, M. Ikeda, A. Ito, M. Izumi and R. Ochi, *Soft Matter*, 2020, 16, 7274; (c) N. Tsutsumi, A. Ito, A. Ishigamori, M. Ikeda, M. Izumi and R. Ochi, *Int. J. Mol. Sci.*, 2021, 22, 1860; (d) Y. Chabatake, T. Tanigawa, Y. Hirayama, R. Taniguchi, A. Ito, K. Takahashi, S. Noro, T. Akutagawa, T. Nakamura, M. Izumi and R. Ochi, *Soft Matter*, 2024, 20, 8170.

- 7 (a) M. Kasha, H. R. Rawls and M. A. El-Bayoumi, *Pure Appl. Chem.*, 1965, 11, 371; (b) F. C. Spano, *Acc. Chem. Res.*, 2010, 43, 429.
- 8 (a) T. Shimizu and M. Masuda, J. Am. Chem. Soc., 1997, 119, 2812; (b) J. H. Jung, S. Shinkai and T. Shimizu, Chem. -Eur. I., 2002, 8, 2684; (c) S. Kiyonaka, S. Shinkai and I. Hamachi, Chem. - Eur. J., 2003, 9, 976; (d) T. Shimizu, M. Masuda and H. Minamikawa, Chem. Rev., 2005, 105, 1401; (e) R. Roytman, L. Adler-Abramovich, K. S. A. Kumar, T.-C. Kuan, C.-C. Lin, E. Gazit and A. Brik, Org. Biomol. Chem., 2011, 9, 5755; (f) S. Datta and S. Bhattacharya, Chem. Soc. Rev., 2015, 44, 5596; (g) M. Delbianco, P. Bharate, S. Varela-Aramburu and Н. Seeberger, Chem. Rev., 2016, 116, 1693; Ρ. (h) T. Tsuzuki, M. Kabumoto, H. Arakawaa and M. Ikeda, Org. Biomol. Chem., 2017, 15, 4595; (i) L. Latxague, A. Gaubert and P. Barthélémy, Molecules, 2018, 23, 89; (*j*) J. Morris, J. Bietsch, K. Bashaw and G. Wang, *Gels*, 2021, 7, 24; (k) A. Brito, S. Kassem, R. L. Reis, R. V. Ulijn, R. A. Pires and I. Pashkuleva, Chem, 2021, 7, 2943; (l) L. Su, S. I. S. Hendrikse and E. W. Meijer, Curr. Opin. Chem. Biol., 2022, 69, 102171; (m) R. Tyagi, K. Singh, N. Srivastava and R. Sagar, Mater. Adv., 2023, 4, 3929.
- 9 (a) S. Kiyonaka, K. Sada, I. Yoshimura, S. Shinkai, N. Kato and I. Hamachi, *Nat. Mater.*, 2004, 3, 58; (b) Y. Wang, L. Tang and J. Yu, *Cryst. Growth Des.*, 2008, 8, 884; (c) M. Ikeda, T. Tanida, T. Yoshii and I. Hamachi, *Adv. Mater.*, 2011, 23, 2819; (d) R. G. Weiss, *J. Am. Chem. Soc.*, 2014, 136, 7519; (e) Y. Shintani, H. Katagiri and M. Ikeda, *Adv. Funct. Mater.*, 2024, 34, 2312999.
- 10 (a) P. Auffinger, F. A. Hays, E. Westhof and P. S. Ho, Proc. Natl. Acad. Sci. U. S. A., 2004, 101, 16789; (b) P. Metrangolo, F. Meyer, T. Pilati, G. Resnati and G. Terraneo, Angew. Chem., Int. Ed., 2008, 47, 6114; (c) F. Meyer and P. Dubois, CrystEngComm, 2013, 15, 3058; (d) A. Mukherjee, S. Tothadi and G. R. Desiraju, Acc. Chem. Res., 2014, 47, 2514; (e) L. C. Gilday, S. W. Robinson, T. A. Barendt, M. J. Langton, B. R. Mullaney and P. D. Beer, Chem. Rev.,

2015, **115**, 7118; (*f*) A. M. S. Riel, R. K. Rowe, E. N. Ho, A.-C. C. Carlsson, A. K. Rappé, O. B. Berryman and P. S. Ho, *Acc. Chem. Res.*, 2019, **52**, 2870; (*g*) L. Turunen and M. Erdélyi, *Chem. Soc. Rev.*, 2020, **49**, 2688.

- 11 C. K. Han and Y. H. Bae, Polymer, 1998, 39, 2809.
- 12 M. C. Gray, A. O. Converse and C. E. Wyman, *Biotechnol. Appl. Biochem.*, 2003, **105–108**, 179.
- 13 R. Roytman, L. Adler-Abramovich, K. S. A. Kumar, T.-C. Kuan, C.-C. Lin, E. Gazit and A. Brik, *Org. Biomol. Chem.*, 2011, 9, 5755.
- 14 (a) Y. Zhang, Z. Yang, F. Yuan, H. Gu, P. Gao and B. Xu, J. Am. Chem. Soc., 2004, 126, 15028; (b) S. E. Paramonov, H.-W. Jun and J. D. Hartgerink, J. Am. Chem. Soc., 2006, 128, 7291; (c) E. T. Pashuck, H. Cui and S. I. Stupp, J. Am. Chem. Soc., 2010, 132, 6041; (d) M. Ikeda, R. Ochi, A. Wada and I. Hamachi, Chem. Sci., 2010, 1, 491; (e) H. Komatsu, M. Ikeda and I. Hamachi, Chem. Lett., 2011, 40, 198; (f) H. Komatsu, S. Tsukiji, M. Ikeda and I. Hamachi, Chem. Asian J., 2011, 6, 2368; (g) J. H. Lee, J. Park, J.-W. Park, H.-J. Ahn, J. Jaworski and J. H. Jung, Nat. Commun., 2015, 6, 6650; (h) S. V. Jadhav, P. Amabili, H.-G. Stammler and N. Sewald, Chem. Eur. J., 2017, 23, 10352; (i) H. Sawada and M. Yamanaka, Chem. Asian J., 2018, 13, 929.
- (a) Y. Shen and P. Y. Wu, J. Phys. Chem. B, 2003, 107, 4224;
 (b) W. Li, B. Sun and P. Wu, Carbohydr. Polym., 2009, 78, 454;
 (c) F. Mashingaidze, Y. E. Choonara, P. Kumar, L. C. du Toit, V. Maharaj, E. Buchmann, V. M. K. Ndesendo and V. Pillay, J. Biomed. Mater. Res., Part A, 2013, 101A, 3616;
 (d) Z. Wang, H. Yang and Z. Zhu, Polymer, 2019, 163, 144.
- 16 A. M. Castilla, M. Wallace, L. L. E. Mears, E. R. Draper, J. Doutch, S. Rogers and D. J. Adams, *Soft Matter*, 2016, 12, 7848.
- 17 O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Crystallogr.*, 2009, **42**, 339.
- 18 G. M. Sheldrick, Acta Crystallogr., Sect. A:Found. Adv., 2015, 71, 3.
- G. M. Sheldrick, Acta Crystallogr., Sect. C:Struct. Chem., 2015, 71, 3.