Novel saccharide–pyridine based gelators: selective gelation and diversity in superstructures†

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A series of *N*-glycosylamine based organogelators were synthesized from 4,6-*O*-protected saccharides introducing pyridylamines. The gelation properties of these compounds were studied in regard to their molecular structure by scanning electron microscopy, differential scanning calorimetry, FT-IR spectroscopy and quantum chemical calculations.

Introduction

The gelation of various fluids by low molecular weight organic compounds is an interesting field and fascinates a wide variety of scientists and such organic compounds have structures possessing at least one heterocyclic component. Heterocyclic compounds[1,2] and their saccharide derivatives[3] exhibit various applications as a result of their structures. Sugars, being biocompatible, are certainly attractive chemical candidates for making organogels. Saccharide based gelators are at a better advantage owing to the existance of rich carbohydrate chemistry that can be used to bring requisite molecular designs.[4] In most of the saccharide based gelators, hydrogen bonding, π–π, dipole–dipole and CH–π interactions are important for their gelation property[5] though there are cases where the gelation is dependent on hydrophobic and hydrophilic properties of the gelator.

Organogels are thermoreversible and viscoelastic materials with low molecular weight gelators in organic solvents.[6] Gelation of organic solvents is believed to proceed through the self-assembly of the gelator molecules. In addition to the non-covalent interactions present between the gelator molecules, their affinity for the solvent molecules is also an important factor in the gelation process. Though there exist several reports on sugar organogelators in recent literature,[7] to our knowledge this is the first report on *N*-glycosylamines containing heterocyclic derivatives, as efficient gelators.

In the present case, hydrogen bonding, π–π stacking interaction and London dispersion forces seem to play an important role in the self assembly. In order to obtain further insight into the structure–function relationship of sugar-based organogelators, we have generated a library of sugar derivatives that contain a heterocyclic moiety linked to pyridylamines.

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Results and discussion

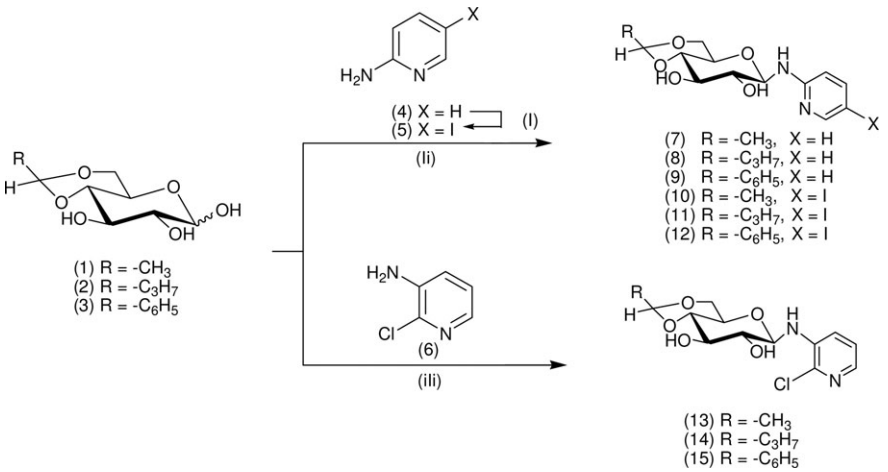
Synthesis of *N*-glycosylamines

4,6-*O*-Protected-D-glucose derivatives (**1–3**) were synthesised and characterised by adopting literature procedures.[8] Except for 5-iodo-2-aminopyridine all other aromatic amines were purchased from Sigma-Aldrich and used without further purification. 5-Iodo-2-aminopyridine (**5**) was synthesised by treating 2-aminopyridine (**4**) with iodine in DMF at room temperature (Scheme 1). The reactants were chosen to have desired functional groups, such as a primary amine in the aromatic moiety and active hydroxyl group in the 4,6-*O*-protected-D-glucose. *N*-glycosylamine compounds (**7–15**) were identified through spectral techniques. During the synthesis of different *N*-glycosylamines using partially protected saccharides,[9] gel formation was observed and this observation prompted us to go for the study of the gelation property of pyridine-containing saccharide compounds (**7–15**) (Scheme 1). Though the precursor saccharide, 4,6-*O*-protected-D-glucopyranose has been shown to exist as a mixture of both the α and β anomers in DMSO-d_6 based on spectral studies, the corresponding *N*-glycosylamines, **7–15** exist only in the β-anomeric form. Coupling constants observed in ^{1}H NMR spectra supported these observations (see ESI,† Table S1).

Gels and gelation properties

Generally, heterocyclic and aromatic compounds possesing alkyl and amide substitutions exhibit gelation.[10] It is known that the presence of pyridyl moieties leads to better solubility in polar as well as nonpolar solvents, suggesting that this moiety has greater affinity towards solvent molecules. All gel samples were prepared by dissolving the gelator to a solvent, in such a way it forms a homogenous solution. The solution was allowed to cool to room temperature, whereby the gel formed. The gelation ability of the *N*-glycosylamines (**7–15**) has been carried out by using the test tube inversion method.[11]

The study includes nine different pyridine based saccharide derivatives (**7–15**) in 21 different polar and nonpolar organic solvents and the results of the gelation tests are summarised in Table 1. In general, protecting groups, such as, ethylidene, butylidene and benzylidene present on the D-glucose moiety led to remarkable change in the gelation process. The gelating ability of these compounds follows



Scheme 1 Synthesis of *N*-glycosylamines, **7–15**. *Reagents and conditions*: (i) 2-aminopyridine (**4**), I_2, DMF, rt, 50% (ii) 2-aminopyridine (**4**), 5-iodo-2-aminopyridine (**5**), ethanol, rt, 23–69%; (iii) 3-amino-2-chloropyridine (**6**), ethanol, rt, 60–71%.

Table 1 Gelation ability of *N*-glycosylamine derivatives in different organic solvents: G = good gelator, P* = partial gelator, S = solution, S* = slightly soluble, P = precipitation, I = insoluble. Minimum concentration of gelation = 2.0% for **7**, **8**, **9**, **10**, **12**,**13** and **15**; 1.0% for **11** and 1.5% for **14**

Solvent	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
Hexane	I	I	I	I	I	I	I	I	I
C_6H_6	I	P	I	P	P*	I	S*	P	P*
$NO_2C_6H_5$	S*	S*	S	G	G	G	P*	S	G
CCl_4	P	P	I	I	I	I	I	I	I
i-PrOH	P	P	P	P	P*	P	P	P	S
$CHCl_3$	S*	P	I	P	G	S*	S*	S*	P
$CH_3C_6H_5$	S*	P	P	P	P*	I	S*	P*	I
1,2-DCB	S*	S*	S	P*	G	P*	G	G	P*
Et_2O	S*	I	I	P	P	I	I	I	I
1,2-DCE	S*	S*	I	G	P*	S*	S*	S*	P
MeOH	P	P	P	P	P*	S*	S	S	S
EtOH	P	P	P*	P	P*	S*	S	S	S
Acetone	P	P	P	P	P	S*	S*	S*	I
DMF	S	S	S	S	S	S	S	S	S
DMSO	S	S	S	S	S	S	S	S	S
EtOAc	P	P	P	P	P*	I	S	S	I
THF	S	P	P	S	S	I	S	S	S
CH_3CN	S*	S*	S	S	G	S*	P	P	P*
o-Xylene	S*	S*	S*	P	S*	P	P	P	I
m-Xylene	S*	S*	S*	P	S*	P	P	P	I
p-Xylene	S*	S*	S*	P	S*	P	P	P	I

the order, **11** > **10** > **14** > **15** > **13** > **12** > **9**. *N*-Glycosylamine, **11** was able to gelate at a minimum gel concentration (MGC) of 1%, similarly compound, **14** undergoes gelation at a minimum concentration of 1.5%, but *N*-Glycosylamines **10**, **12**, **13** and **15** exhibited gelation only at a minimum concentration of 2%.

The gelation ability of the organogelators significantly depend on the presence of alkyl and the heterocyclic groups. Greater gelating ability of butylidene protected *N*-glycosylamines (**11** and **14**), is due to higher London dispersion forces[11] existing between the alkyl chain groups. Such interactions are expected to be less in ethylidene protected *N*-glycosylamines (**7**, **10** and **13**) and the corresponding gelation would be low. However, in benzylidene protected *N*-glycosylamines (**9**, **12** and **15**) the π–π stacking interactions seem to be largely responsible for their gelation properties. These results support that partially protected *N*-glycosylpyridylamines with butylidene and benzylidene moieties have greater ability to undergo gelation compared to the ethylidene derivatives. However, the structural differences in aminopyridine moieties of compounds, **7**, **8**, **9**, **13**, **14** and **15** compared to **10**, **11** and **12** leads to poorer gelation property owing to the disruption of π–π interaction. The presence of significant involvement of London dispersion forces and the structural arrangement that enhances the π–π interactions are chemical factors responsible for greater gelation ability of *N*-glycosylpyridylamine, **11**.

Among the various polar and nonpolar solvents used for gelation of *N*-glycosylpyridylamines (**7–15**), 1,2-dichlorobenzene (1,2-DCB) and nitrobenzene were found to be the best solvents for the gelation process which may be attributed to a strong solute–solvent interaction. Partially protected *N*-glycosylamines *viz*., **10**, **12** and **15** were found to be good organogelators in nitrobenzene, whereas **13** and **14** performed

well in 1,2-DCB. However, *N*-glycosylamine, **11** acts as an efficient organogelator in both solvents.

Xerogel structure

In order to obtain insight into the aggregation mode at the microscale SEM studies were performed. An SEM image of compound **9** [Fig. 1(a)] which gives a partial gelator in ethanol, exhibited a fibrous network with crosslinking.[12] Elongated rod like structures were observed for compound **12** [Fig. 1(d)] and these kinds of structures were most likely to result from a strongly anisotropic growth process and are indicative of directional intermolecular interactions. The SEM image of *N*-glycosylamine **15** [Fig. 1(f)] shows short and thick lamellar aggregated morphology. *N*-Glycosylamine **10** [Fig. 1(g)], which forms a partial gelator in 1,2-DCB, forms a fibrous network morphology. Fibrous aggregated morphologies observed for compounds, **9**, **11**, **13** and **14** [Fig. 1(a)–(c), (e), (i) and (h)] may be due to the presence of a higher number of solvent molecules than for the lamellar (**15**) [Fig. 1f] or rod (**12**) like structures. These results can be attributed to a higher void volume (2.36 μm) observed for the former as compared to the latter (1.74 μm). These different morphologies should emanate from differences in interfacial free energy or attachment energies in the stated solvents.

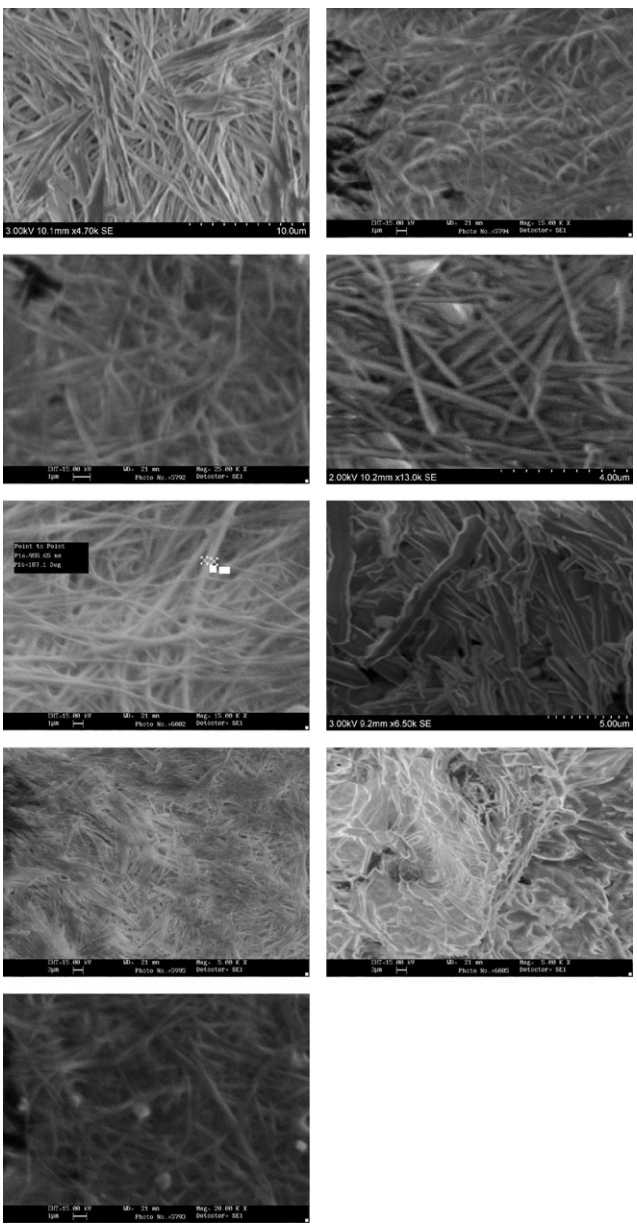


Fig. 1 SEM images for (a) **9** (ethanol), (b) **11** (nitrobenzene), (c) **11** (1,2-dichlorobenzene), (d) **12** (nitrobenzene), (e) **13** (1,2-dichlorobenzene), (f) **15** (nitrobenzene), (g) **10** (1,2-dichlorobenzene), (h) **14** (1,2-dichlorobenzene), (i) **13** (nitrobenzene).

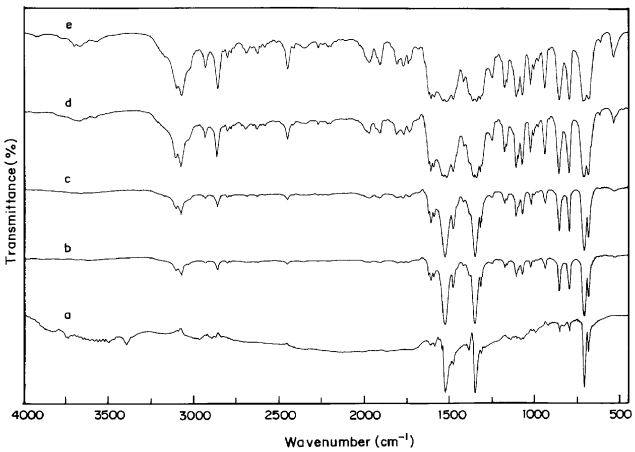


Fig. 2 Solution FT-IR spectra of compound **11** in nitrobenzene: (a) 0.1 M, (b) 0.01 M, (c) 0.001 M, (d) 0.0001 M, (e), 0.0005 M.

It is well known that hydrogen bonding plays an important role in the formation of organogels. FT-IR experiments were carried out to further explore the gelation of *N*-glycosylamine **11** in 1,2-dichlorobenzene (see ESI,† Fig. S2). The FT-IR spectra of the *N*-glycosylamine **11** in the gel phase shows a N–H stretching band at 3000 cm^{-1} and bending band at 1510 cm^{-1}. In the case of the solid phase the N–H stretching band appears at 3375 cm^{-1} and bending band at 1585 cm^{-1}. The red shift observed in the gel phase can be attributed to an increase in intramolecular hydrogen bonding. Based on FT-IR studies, it is reasonable to deduce that the amine in *N*-glycosylamines form hydrogen bonds in the gel phase.[13]

In order to obtain insight into the involvement of functional groups *viz*., Gly-NH, Sac-OH in the aggregation phenomena, we recorded solution FT-IR spectra (500–4000 cm^{-1}) for **11** in nitrobenzene solvent [Fig. 2]. As the concentration of the sample in the solution decreases, the peaks appearing in the region around 1600 cm^{-1} get more sharpened and also a greater number appear. This may be due to the involvement of the Gly-NH group in the hydrogen bonding, as was confirmed from the quantum mechanical calculations below.

Thermoanalysis

The thermal properties of the organogelators have been analysed using differential scanning calorimetry (DSC). DSC data obtained for **12** and **15** are shown in Fig. 3. The melting point and enthalpy of organogelator **12** in the solid phase are 192.4 °C and $\Delta H = 98.22$ J g^{-1} and in gel phase the values are 136.1 °C and 61.23 J g^{-1}. The organogelator, **15** shows melting

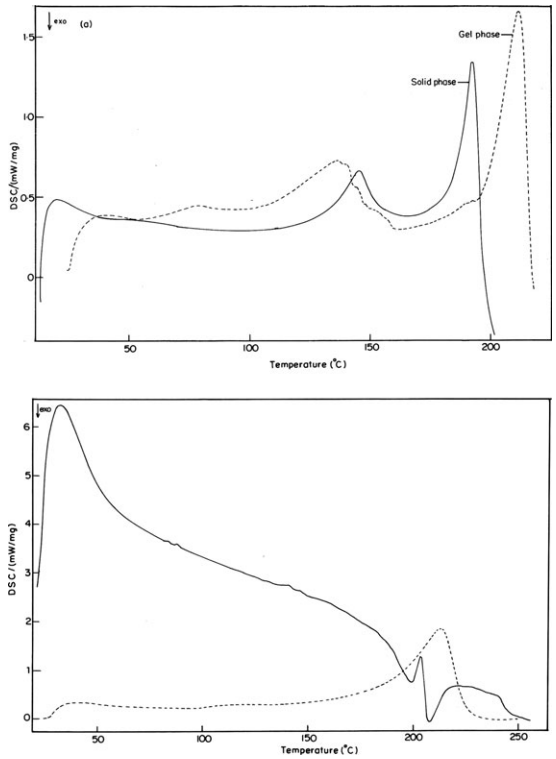


Fig. 3 DSC spectra: (a) **12** (nitrobenzene); (b) **15** (nitrobenzene): (—) solid phase, (---) gel phase.

Table 2 Thermodynamic parameters for sol–gel transition

Gelator	Solvent	MGC (%)	T_{gs}/°C	ΔH/J g^{-1}
12	Nitrobenzene	1	136.1	61.23
15	Nitrobenzene	1	212.8	267.1

point and enthalpy in solid and gel phase at 202.9 °C (ΔH = 22.4 J g^{-1}) and 212.8 °C (ΔH = 267.1 J g^{-1}), respectively. These results indicate that organogel **15** is more stable in the solid phase.[14,15] Endotherms at 200 °C correspond to solvent peak. The results of DSC experiments are summarized in Table 2.

In the case of compound **12** in nitrobenzene T_{gs} of gel phase was found to lower than the solid phase while for compound **15** the T_{gs} of gel phase was found to be greater than that of solid phase. These results indicate that the gel phase of *N*-glycosylamine **12** has greater thermal stability than its corresponding solid phase, whereas for *N*-glycosylamine **15**, the solid phase has greater thermal stability than its corresponding gel phase. Though both *N*-glycosylamines **12** and **15**, have different tendencies of thermal stability, they both show similar minimum gelator concentration (Table 2).

Computational studies

In the present study, quantum chemical calculations were carried out in an attempt to probe the various types of intermolecular interactions responsible for the aggregation/gelation properties of molecules **7–15**. All the calculations are done using the G98W suite of programs.[16] Optimized

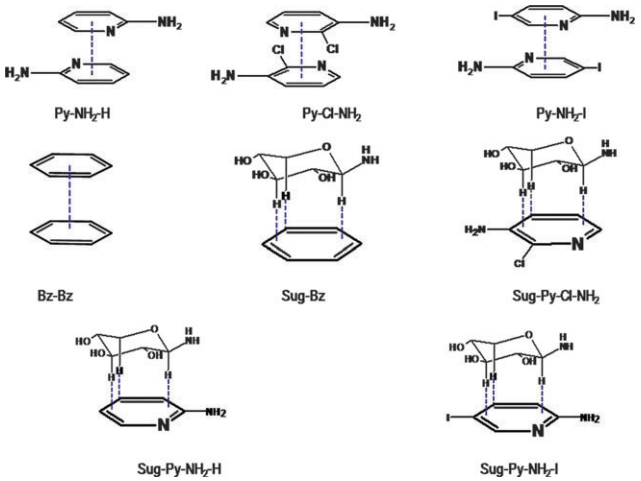


Fig. 4 Various possible interactions that are observed through molecular modelling for *N*-glycosylamines reported in the present study.

geometries of **7–15** (see ESI,† Fig. S4) were characterized as minima on the potential energy surface by frequency calculations. The experiments have shown that π–π interactions are the major source of interaction (see ESI,† Fig. S3). Therefore calculations were focussed to provide support to these observations concerning the interaction region for π–π and CH–π type of interactions in all the molecules. Due to computational limitations, only the active regions (Fig. 4) are considered for calculation at MP2 level of theory. The 6-31G* basis set is used for all the calculation except for iodine containing molecules where the MIDIX basis set was employed. The stabilization energies (SEs) are obtained using the equation, SE = $-[(E_{complex} - E_{monomer\ 1} + E_{monomer\ 2})]$, where $E_{complex}$, $E_{monomer\ 1}$ and $E_{monomer\ 2}$ are the total energies of complex and monomers.

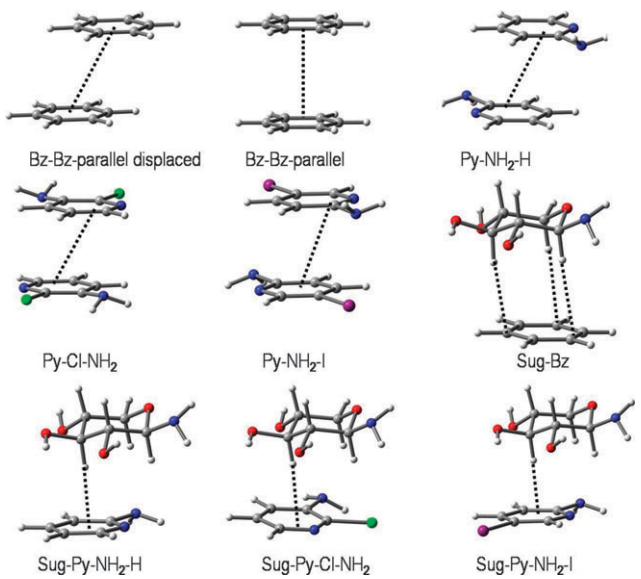


Fig. 5 Optimized geometries of various interactions obtained from MP2 level of theory using 6-31G* and MIDIX basis sets: grey = C, blue = N, red = O, white = H, green = Cl, pink = I.

The SEs are corrected for basis set superposition error (BSSE) using the method adopted by Boys and Bernardi[17] (see ESI,† Table S5 for more details). The optimized geometries provided in Fig. 5 clearly shows that π–π stacked interactions are in parallel displaced conformation.

Superimposing the calculated structure with the complete molecule in appropriate manner results in the possible aggregation model supported by stacking interactions. Fig. 6–9 clearly demonstrates the aggregation of the molecules into superstructures.

Molecular electrostatic potential (MESP)[18] maps are highly useful to identify different hydrogen-bonding regions in a molecule. MESP topographies of molecules **7–15** were calculated using B3LYP/6-31G* method (see ESI,† Fig. S6, which presents MESP maps obtained at ±0.04 au isosurface value).[19] These maps indicate that oxygen atoms of the carbohydrate moiety are rich in electron density and therefore could play a major role in the formation of hydrogen bonds. Although calculations were not performed on other types of intermolecular interactions such as London dispersion forces, and halogen–halogen interactions, *etc.*, we neglect the role of such interactions in the aggregation of the molecules.

Models for different aggregation modes of these compounds have been proposed as shown in Fig. 6–9. While π–π and hydrogen bonding interactions dominate in ethylidene protected *N*-glycosylamines (**7**, **10**, **13**) it is the π–π and London dispersion forces that dominate in butylidene protected *N*-glycosylamines (**8**, **11**, **14**). The hydrogen bonding between the amines also contribute to their mode of gelation.

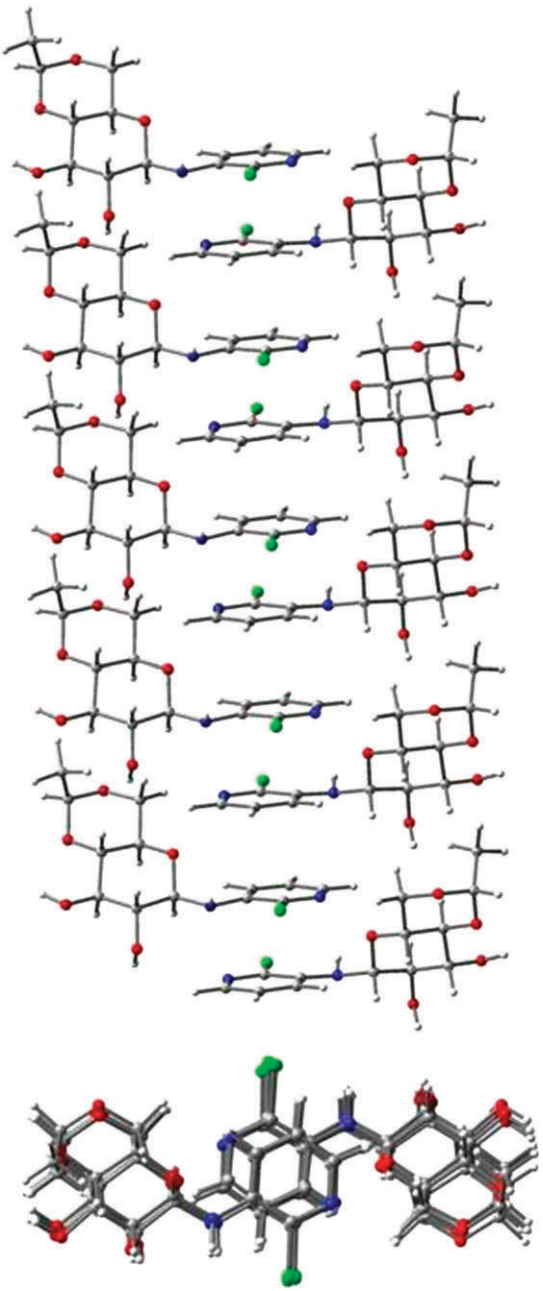


Fig. 6 Aggregation mode of ethylidine protected *N*-glycosylamines (**7**, **10** and **13**), where π–π stacking interaction between the pyridine moieties is observed.

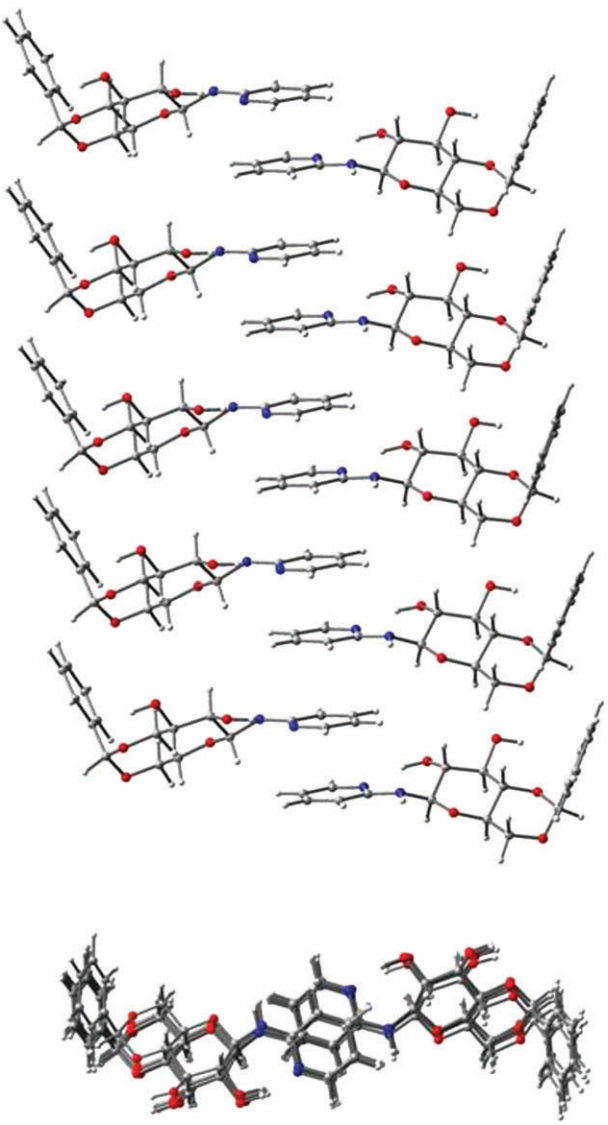


Fig. 7 Aggregation mode of benzylidine protected *N*-glycosylamines (**9**, **12** and **15**).

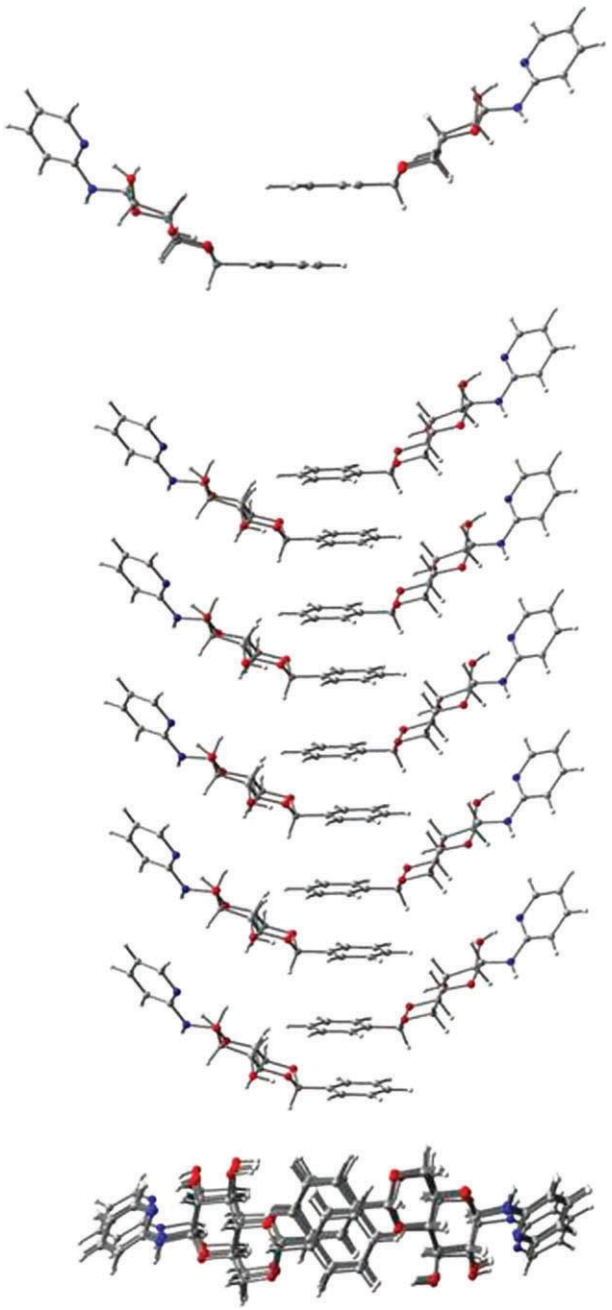


Fig. 8 (i) π–π Stacking interaction observed between the adjacent aromatic rings of benzylidene protected *N*-glycosylamines (**9**, **12** and **15**). (ii) Aggregation of the molecules when benzylidene protected *N*-glycosylamines show π–π stacking interaction between the aromatic rings.

As shown in Fig. 7, benzylidene protected *N*-glycosylamines (**9**, **12**, **15**) exhibit π–π stacking interactions between the heterocyclic moiety and aromatic group. In aromatic nonpolar solvents, the self assembly of the gelator molecules is favoured by rigid hydrogen bonds that lead to highly ordered one-dimensional aggregates. In polar solvents, the molecular assembly leads to one-dimensional aggregates mediated by solvophobic effects and dipole–dipole interactions.

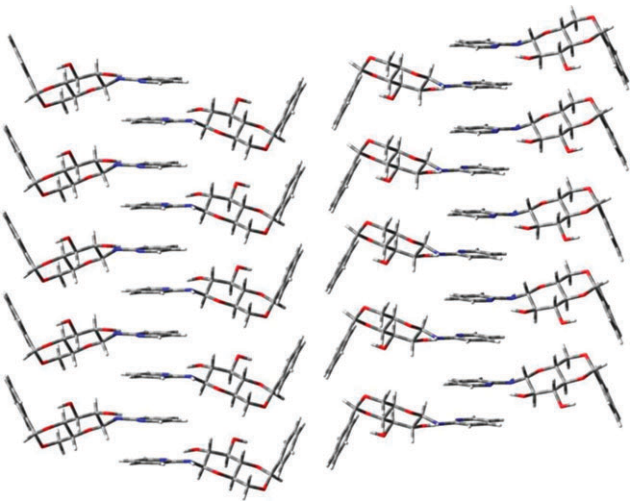


Fig. 9 Aggregation mode of benzylidine protected *N*-glycosylamines (**9**, **12** and **15**) where π–π stacking interaction between both the adjacent aromatic rings and adjacent pyridine moieties are considered.

Conclusions

In summary, a novel class of *N*-glycosylamine containing heterocyclic derivatives have been synthesised and characterised. These compounds have been found to be good organogelators. The morphology of the gels shows a strong dependence on the solvent, showing fibrils in nitrobenzene and entangled fibres in 1,2-dichlorobenzene. The presence of different protecting groups results in a change in the gelating ability of these derivatives.

Experimental

Spectral characterizations

Compounds. NMR spectra were recorded with Bruker Avance 300 (300 MHz). The solvent peak in ^{1}H NMR and ^{13}C NMR was adjusted to 7.5 and 77.23 ppm for $CDCl_3$ and 2.5 and 39.51 ppm for DMSO-d_6, respectively. FT-IR studies were carried out using Perkin Elmer PE257 IR spectrometer. Polarimeter studies were carried out using Rudolph-Autopol II digital polarimeter.

Thermoanalysis. Thermal transitions for gels were determined on a NETZSCH DSC 204. The measurements were carried out under nitrogen atmosphere using 50 μL sealed aluminium sample pans. The temperature calibration of DSC was made using two standard materials (*n*-decane, indium) and energy calibration by an indium standard (28.45 J g^{-1}). Each sample was heated from 25 to 300 °C with a heating range of 20–25 °C min^{-1}. sample weights of 3–28 mg were used in measurements.

Microscopy. The gels were imaged with HITACHI-S-3400W scanning electron microscope. The samples were gold coated in such a way the gold coating was <1 nm thick on average.

Synthesis of 5-iodo-2-aminopyridine (5). To a solution of 2-aminopyridine (**4**) in dry DMF 5.6 gm (0.022 mol) of iodine was added and stirred at room temperature for about 2 h. The

reaction was then monitored through thin layer chromatography. Soon after the completion of the reaction, the reaction mixture was transferred into a solution containing 1 g of sodium metabisulfate in 10 ml of a dilute cold aqueous ammonia solution. Compound **5** was extracted using ethyl acetate and then washed with brine solution, dried over anhydrous sodium sulfate, filtered, and concentration of the resultant solution gave brown solid product 5-iodo-2-aminopyridine (**5**). Yield: 1.2 g (50%); mp 126–130 °C; ^{1}H NMR ($CDCl_3$); δ 8.16 (s, 1H, Ar-*H*), 7.56 (m, 1H, Ar-*H*), 6.29 (d, 1H, J = 8.7 Hz, Ar-*H*); ^{13}C: δ 157.3 (1C, Ar-*C*), 153.7 (1C, Ar-*C*), 145.4 (1C, Ar-*C*), 110.9 (1C, Ar-*C*), 77.8 (1C, Ar-*C*).

Synthesis of *N*-glycosylamines 7–15. A typical synthetic procedure for the synthesis of compounds (**7–15**) is as follows.

To a solution of 1 mol of 4,6-*O*-ethylidene-β-D-glucopyranose, (**1**) in 10 ml of ethanol, was added 1.2 mol of 2-aminopyridine (**4**). The reaction was then stirred at room temperature and the reactants dissolved within 5–10 min. In certain cases the undissolved reactants were heated slightly at a temperature of 50 °C. The reaction was thereby followed through TLC. The crystalline product which separates was filtered off and dried under vacuum.

Synthesis of gels of 7–15. General procedure for the preparation of gels.

Compounds **7–15** (*ca.* 0.1 g) was placed in a glass vial and 0.5 ml of organic solvent was added. The gelator in the organic solvent was heated. The solution was then allowed to cool to room temperature whereby the gel formed.

Spectral characterization

Abbreviations, Sac, Ar, Ano, Ace and Gly correspond to the saccharide, aromatic, anomeric, acetal and glycosidic groups, respectively.

4,6-*O*-Ethylidene-*N*-pyridyl-β-D-glucopyranosylamine, 7. Yield: 0.94 g (69%); mp 220–224 °C; $[\alpha]_D^{30}$ −90.74 (*c*, 1.0, DMSO); ^{1}H NMR (DMSO-d_6), δ 8.05 (d, 1H, J = 3.9 Hz, Ar-*H*), 7.40–7.46 (m, 1H, Ar-*H*), 6.56–6.65 (m, 2H, Ar-*H*), 6.46 (d, 1H, J = 7.8 Hz, Gly-N*H*), 5.09 (t, 1H, J = 9.3 Hz, Ano-*H*), 4.91–5.02 (m, 2H, Sac-O*H*), 4.1–4.13 (m, 1H, Ace-*H*), 3.7–3.3 (m, 6H, Sac-*H*), 1.34 (d, 3H, –C*H*$_3$). ^{13}C (DMSO-d_6): δ 157.2 (1C, Ar-*C*), 147.3 (1C, Ar-*C*), 136.9 (1C, Ar-*C*), 113.7 (1C, Ar-*C*), 107.8 (1C, Ar-*C*), 98.8 (1C, Ace-*C*), 66.7–83.6 (6C, Sac-*C*), 20.0 (1C, –*C*H$_3$).

4,6-*O*-Butylidene-*N*-pyridyl-β-D-glucopyranosylamine, 8. Yield: 0.86 g (65%); mp 198–200 °C; $[\alpha]_D^{30}$ −99.22 (*c*, 1.0, DMSO); ^{1}H NMR (DMSO-d_6), δ 8.01 (d, 1H, J = 3.9 Hz, Ar-*H*), 7.44 (m, 1H, Ar-*H*), 7.03 (d, 1H, J = 9.3 Hz, Gly-N*H*), 6.53–6.61 (m, 2H, *Ar*-*H*), 5.23 (d, 1H, J = 5.1 Hz, Sac-O*H*), 5.10 (d, 1H, J = 5.1 Hz, Sac-O*H*), 5.04 (t, 1H, J = 8.7 Hz, Ano-*H*), 4.55 (t, 1H, J = 4.8 Hz, Ace-*H*), 4.00–4.04 (m, 1H, Sac-*H*), 3.09–3.45 (m, 5H, Sac-*H*), 1.51 (m, 2H, –C*H*$_2$), 1.35 (m, 2H, –C*H*$_2$), 0.88 (t, 3H, J = 7.2 Hz, –C*H*$_3$). ^{13}C (DMSO-d_6), δ 157.8 (1C, Ar-*C*), 147.3 (1C, Ar-*C*), 137.1 (1C, Ar-*C*), 113.4 (1C, Ar-*C*), 108.4 (1C, Ar-*C*), 101.2 (1C, Ace-*C*), 35.9–82.9 (6C, Sac-*C*), 30.6 (1C, –*C*H$_2$), 17.1 (1C, –*C*H$_3$), 13.8 (1C, –*C*H$_2$). FT–IR (KBr, cm^{-1}): ν 3328, 2948, 2881, 1604, 1446 cm^{-1}.

4,6-*O*-Benzylidene-*N*-pyridyl-β-D-glucopyranosylamine, 9. Yield: 0.61 g (48%); mp 202–206 °C; $[\alpha]_D^{30}$ −98.71 (*c*, 1.0, DMSO); ^{1}H NMR (DMSO-d_6), δ 7.25–8.00 (m, 5H, Ar-*H*), 6.58–6.67 (m, 4H, Ar-*H*), 6.52 (d, 1H, J = 9 Hz, Ano-*H*), 6.4 (d, 1H, J = 9 Hz, Gly-N*H*), 5.16–5.44 (m, 2H, Sac-O*H*), 4.44 (s, 1H, Ace-*H*), 3.6–4.1 (m, 6H, Sac-*H*). ^{13}C (DMSO-d_6): δ 127.6–157.6 (5C, Ar-*C*), 101.1–126 (6C, Ar-*C*), 81.2 (1C, Ace-*C*), 61.6–71.1 (6C, Sac-*C*).

4,6-*O*-Ethylidene-*N*-(5-iodopyridyl)-β-D-glucopyranosylamine, 10. Yield: 1.2 g (60.9%); mp 176–180 °C; $[\alpha]_D^{30}$ −94.82 (*c*, 1.0, DMSO); ^{1}H NMR (DMSO-d_6): δ 8.18 (s, 1H, Ar-*H*), 7.72 (d, 1H, J = 2.4 Hz, Ar-*H*), 7.68 (d, 1H, J = 2.4 Hz, Ar-*H*), 7.28 (d, 1H, J = 9 Hz, Gly-N*H*), 6.41 (d, 1H, J = 8.7 Hz, Ano-*H*), 5.26 (d, 1H, J = 5.4 Hz, Sac-O*H*), 5.11 (d, 1H, J = 5.7 Hz, Sac-O*H*), 5.01 (t, 1H, J = 9 Hz, Ace-*H*), 4.7 (d, 1H, J = 5.1 Hz, Sac-*H*), 3.93–3.98 (m, 2H, Sac-*H*), 3.09–3.46 (m, 3H, Sac-*H*), 1.23 (d, 3H, J = 5.1 Hz, –C*H*$_3$). ^{13}C (DMSO-d_6): δ 156.8 (1C, Ar-*C*), 152.7 (1C, Ar-*C*), 144.5 (1C, Ar-*C*), 111.2 (1C, Ar-*C*), 98.5 (1C, Ar-*C*), 82.6 (1C, Ace-*C*), 66.9–80.4 (6C, Sac-*C*), 20.3 (1C, –*C*H$_3$).

4,6-*O*-Butylidene-*N*-(5-iodopyridyl)-β-D-glucopyranosylamine, 11. Yield: 1.02 g (69%); mp 160–164 °C; $[\alpha]_D^{30}$ −89.51 (*c*, 1.0, DMSO); ^{1}H (DMSO-d_6): δ 8.18 (s, 1H, Ar-*H*), 7.72 (d, 1H, J = 8.4 Hz, Ar-*H*), 7.31 (d, 1H, J = 8.7 Hz, Ar-*H*), 6.49 (d, 1H, J = 8.7 Hz,Gly-N*H*), 5.30 (d, 1H, J = 4.7 Hz, Sac-O*H*), 5.16 (d, 1H, J = 5.4 Hz, Sac-O*H*), 5.01 (t, 1H, J = 8.7 Hz, Ano-*H*), 3.96 (t, 1H, J = 5.4 Hz, Ace-*H*), 3.08–3.24 (m, 6H, Sac-*H*), 1.51–1.53 (m, 2H, –C*H*$_2$), 1.35–1.39 (m, 2H, –C*H*$_2$), 0.88 (t, 3H, J = 6.9 Hz, –C*H*$_3$). ^{13}C (DMSO-d_6), δ 156.8 (1C, Ar-*C*), 152.7 (1C, Ar-*C*), 144.5 (1C, Ar-*C*), 125.6 (1C, Ar-*C*), 111.3 (1C, Ar-*C*), 101.4 (1C, Ace-*C*), 67.3–82.6 (6C, Sac-*C*), 35.9 (1C, –*C*H$_2$), 17.1 (1C, –*C*H$_3$), 13.8 (1C, –*C*H$_2$). FT-IR (KBr, cm^{-1}): ν 3375, 2956, 2869, 1585, 1446 cm^{-1}.

4,6-*O*-Benzylidene-*N*-(5-iodopyridyl)-β-D-glucopyranosylamine, 12. Yield: 0.4 g (23%); mp 182–186 °C; $[\alpha]_D^{30}$ −84.61 (*c*, 1.0, DMSO); ^{1}H NMR (DMSO-d_6), δ 7.33–8.12 (m, 5H, Ar-*H*), 6.28–6.97 (m, 3H, Ar-*H*), 6.96 (d, 1H, J = 6 Hz, Ano-*H*), 5.25 (d, 1H, J = 6 Hz, Gly-N*H*), 4.52–4.92 (m, 2H, Sac-O*H*), 4.27 (s, 1H, Ace-*H*), 2.06–3.07 (m, 6H, Sac-*H*). ^{13}C (DMSO-d_6), δ 126–147.4 (5C, Ar-*C*), 80.9–113.4 (6C, Ar-*C*), 76.7 (1C, Ace-*C*), 61.2–73.7 (6C, Sac-*C*).

4,6-*O*-Ethylidene-*N*-(2-chloropyridyl)-β-D-glucopyranosylamine, 13. Yield: 1.08 g (71%); mp 184–186 °C; $[\alpha]_D^{30}$ −88.74 (*c*, 1.0, DMSO); ^{1}H NMR (DMSO-d_6), δ 7.73 (s, 1H, Ar-*H*), 7.31 (d, 1H, J = 7.5 Hz, Ar-*H*), 7.24 (d, 1H, J = 3.6 Hz, Ar-*H*), 5.86 (d, 1H, J = 6.6 Hz, Gly-N*H*), 5.38 (s, 1H, Ace-*H*), 4.71 (d, 1H, J = 4.5 Hz, Sac-O*H*), 3.99 (d, 1H, J = 5.4 Hz, Sac-O*H*), 3.18–3.44 (m, 7H, Sac-*H*), 1.24 (d, 3H, J = 3.6 Hz, –C*H*$_3$). ^{13}C (DMSO-d_6), δ 139.3 (1C, Ar-*C*), 137.6 (1C, Ar-*C*), 136.1 (1C, Ar-*C*), 123.8 (1C, Ar-*C*), 120.6 (1C, Ar-*C*), 98.5 (1C, Ace-*C*), 66.8–84.6 (6C, Sac-*C*), 20.3 (1C, –*C*H$_3$). FT-IR (KBr, cm^{-1}): ν 3423, 3269, 2893, 1589, 1521 cm^{-1}.

4,6-*O*-Butylidene-*N*-(2-chloropyridyl)-β-D-glucopyranosylamine, 14. Yield: 0.94 g (64%); mp 154–158 °C; $[\alpha]_D^{30}$ −96.86 (*c*, 1.0, DMSO); ^{1}H NMR (DMSO-d_6), δ 7.73 (d, 1H, J = 4.2 Hz, Ar-*H*), 7.31 (d, 1H, J = 7.8 Hz, Ar-*H*), 7.20–7.24 (m, 1H, Ar-*H*), 5.86 (d, 1H, J = 7.2 Hz, Gly-N*H*), 5.34 (d, 1H, J = 4.5 Hz, Sac-O*H*), 5.32 (d, 1H, J = 3.9 Hz, Sac-O*H*), 4.64 (t, 1H, J = 7.5 Hz, Ano-*H*), 4.56 (t, 1H, J = 4.8 Hz, Ace-*H*), 4.00–4.04 (m, 1H, Sac-*H*), 3.15–3.45 (m, 5H, Sac-*H*); 1.49–1.54 (m, 2H, –CH_2), 1.35–1.4 (m, 2H, –CH_2), 0.90 (t, 3H, J = 7.2 Hz, –CH_3). ^{13}C (DMSO-d_6), δ 139.3 (1C, Ar-*C*), 137.6 (1C, Ar-*C*), 136.1 (1C, Ar-*C*), 123.8 (1C, Ar-*C*), 120.6 (1C, Ar-*C*), 101.3 (1C, Ace-*C*), 66.8–84.6 (6C, Sac-*C*), 36.92 (1C, –CH_2), 17.0 (1C, –CH_3), 13.7 (1C, –CH_2). FT-IR (KBr, cm^{-1}): ν 3342, 2948, 2877, 1589, 1512 cm^{-1}.

4,6-*O*-Benzylidene-*N*-(2-chloropyridyl)-β-D-glucopyranosylamine, 15. Yield: 0.85 g (60%); mp 220–224 °C; $[\alpha]_D^{30}$ −98.64 (*c*, 1.0, DMSO); ^{1}H NMR (DMSO-d_6), δ 6.97–7.16 (m, 5H, Ar-*H*), 6.61–6.67 (m, 3H, Ar-*H*), 6.96 (d, 1H, J = 6 Hz, Ano-*H*), 6.82 (d, 1H, J = 6 Hz, Gly-N*H*), 4.53–5 (m, 2H, Sac-O*H*), 4.38 (s, 1H, Ace-*H*), 3.15–4.11 (m, 6H, Sac-*H*). ^{13}C (DMSO-d_6), δ 126–136.7 (5C, Ar-*C*), 92.7–123.1 (6C, Ar-*C*), 81.2 (1C, Ace-*C*), 61.7–72.7 (6C, Sac-*C*).

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