Organogels from Carbohydrate Amphiphiles

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Gluconamides can be easily functionalized to give a variety of compounds that form organogels with a high viscosity. *N*-*n*-octyl-D-gluconamide-6-benzoate gelates a large variety of organic solvents, including 1,2-xylene, chloroform, ethyl acetate, and ethanol, to form gels which are, in some cases, stable even above the boiling point of the pure solvent. The 2-methoxy, 6-imidazolyl, 6-acetyl, and 6-cyclohexanoyl derivatives also show gelation, but the 2,4;3,5-dimethylene-protected derivatives do not. Detailed ^{1}H NMR, IR, and X-ray powder diffraction studies reveal that the molecules of most gelators are packed in a head-to-tail fashion. If there is, however, the possibility to form *inter*-layer hydrogen bonds, as in the case of *N*-*n*-octyl-D-gluconamide or *N*-*n*-octyl-D-gluconamide-6-(3-pyridyl carboxylate), the molecules are packed head-to-head. Some gluconamides, e.g., those with aliphatic substituents, express their molecular chirality in the supramolecular structures, whereas others, in particular those containing a large aromatic substituent on carbon atom C^6, yield nonchiral aggregates, probably due to interfering $\pi-\pi$ stacking interactions of the substituents. DSC experiments show that the formation of the gels is an entropy-driven process.

Introduction

Assemblies of molecules held together by noncovalent interactions are currently receiving great interest.[1] The behavior of supramolecular assemblies is to some extent comparable to that of macromolecules, as repetitive units linked to each other by either noncovalent or covalent bonds can both give a network resulting in a gellike structure. A difference, however, is that gels obtained from supramolecules can be disintegrated by addition of a cosolvent or by raising the temperature, whereas network structures obtained from macromolecules disintegrate only by breaking chemical bonds.

Amphiphiles consisting of a carbohydrate headgroup[2] to which an aliphatic alkyl chain is connected by an amide function are known to form fibrous aggregates upon dispersion in water.[3−5] *N*-*n*-octyl-D-gluconamide **1** (Chart 1) is known to yield a highly viscous gel in aqueous solutions. Using transmission electron microscopy (TEM) in combination with image analysis,[6] differential scanning calorimetry (DSC),[7] and NMR,[8] it was proposed that this gel consists of helices of intertwined micellar strands.[9] The self-assembly of **1** into helices has been ascribed to the formation of an intermolecular hydrogen bonding network in which, during the aggregation, water molecules are squeezed out.[3,10] Various proposals regarding the packing arrangement of the gluconamide molecules in the aggregates have been put forward, viz., head-to-tail[11] as found in the crystal structure[12] of **1** and head-to-head[13] which is seen more commonly for amphiphilic molecules in water.

Variations in the headgroup were found to affect the type of clustering of *N*-alkylaldonamides more than incorporation of a diacetylene function in the alkyl chain.[6a,14] Gluconamide **1** has also been reported to gelate in 1,2-xylene,[6] forming bilayer scrolls, but this organogel was found to be very unstable.[6] Unfortunately, **1** is scarcely soluble in common organic solvents such as acetone, chloroform, and dioxane and is, therefore, not an ideal molecule for an extensive study of its gelation effects in organic solvents.

Gelation in organic solvents has so far been observed for a large variety of compounds,[15] viz., lecithins,[16] cholesterol derivatives,[17] peptides,[18] two-component gelling agents,[19] calixarenes,[20] semifluorinated *n*-alkanes[21] or silanes,[22] phenols,[23] urea compounds,[24] tetra-alkylammonium salts,[25] and glucosamides.[26] Despite the fact that a relatively broad range of compounds display gelation,

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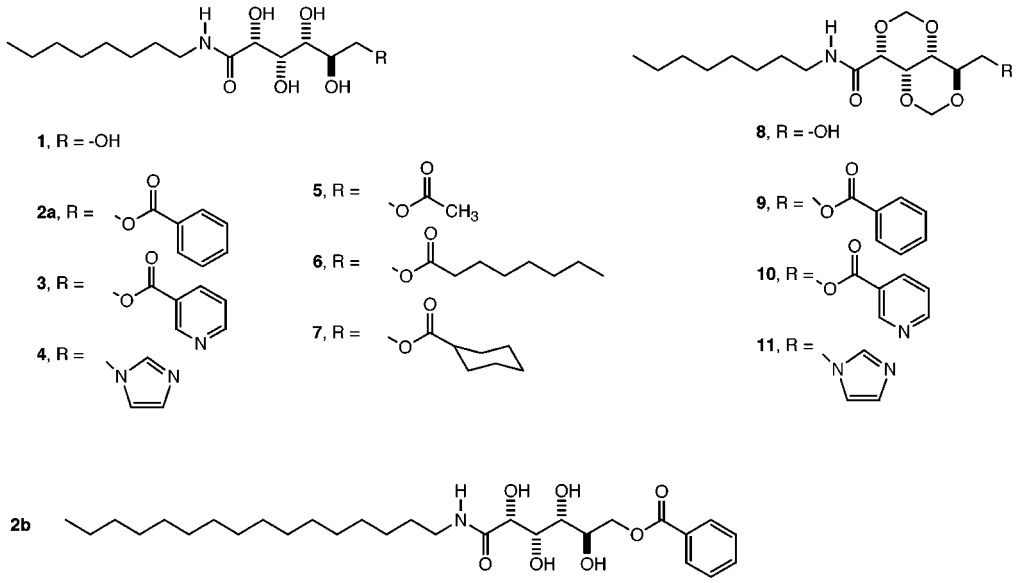
Chart 1



no rules of thumb for the design of such compounds have been given in the literature. This contrasts the situation for the classical amphiphilic compounds where such rules have been proposed.[27] Some factors, however, are known to stimulate gelation behavior, viz., the possibility to form hydrogen bonds (as found in amide[19] and urethane[18c] gels) and a rod-shaped geometry of the building block.[17b]

As part of our program aimed at the design and synthesis of supramolecular structures from carbohydrate amphiphiles and, more particularly, the fine-tuning of these structures,[5] we prepared the *N*-*n*-octylgluconamide benzoate ester **2a**. To our surprise, **2a** formed gels at low concentrations in common organic solvents such as chloroform, ethyl acetate, and acetone.[28] Stimulated by this finding, we decided to study the organogel-forming properties of *n*-alkyl-D-gluconamides in more detail. To probe the influence of a nitrogen donor site in the aromatic headgroup, compounds **3** (pyridyl group) and **4** (imidazolyl group) were synthesized. These compounds, as well as the benzoate ester (**2a**), are aromatic compounds and can display $\pi-\pi$ stacking interactions. We also synthesized a series of gluconamides functionalized with aliphatic esters, viz., the acetyl ester **5**, the octanoyl ester **6**, and the cyclohexanoyl ester **7**. The 2,4;3,5-dimethylene gluconamides **8**−**11** all have their secondary hydroxyl groups protected but contain the same functional groups as **1**, **2a**, **3**, and **4** (hydroxyl, benzoyl, 3-pyridyl, and imidazolyl, respectively). Compound **12** (Chart 2) and its benzoyl and acetyl analogues **13** and **14** are special in the sense that they contain a methoxy group on the carbon atom C^2; this prohibits 1,3-*syn*-diaxial interactions[6a,8b,13,29] between the OH functions on C^2 and on C^4, which are believed to induce a bend in the glucon headgroup leading to a sickle type conformation.[29] We also prepared **15**, which contains two *N*-*n*-octyl-D-gluconamide moieties linked together at the headgroups via a terephthalate spacer. While **6** can be called a reversed bolaamphiphile, **15** fits the "gemini surfactant" description[30] with the two carbohydrate moieties acting as noncharged polar groups. For this compound, inverted bilayer structures with both alkyl chains facing the solvent may be expected.[31] Finally, to study the effect of modification of the chirality of the carbohydrate moiety, the galactonamides **16** and its benzoyl analogue **17** were also synthesized and studied.

Experimental Section

Syntheses. Chemicals were used as obtained from the supplier except for the solvents, which were distilled before use and dried on 3 or 4 Å Mol Sieves. Pyridine was distilled

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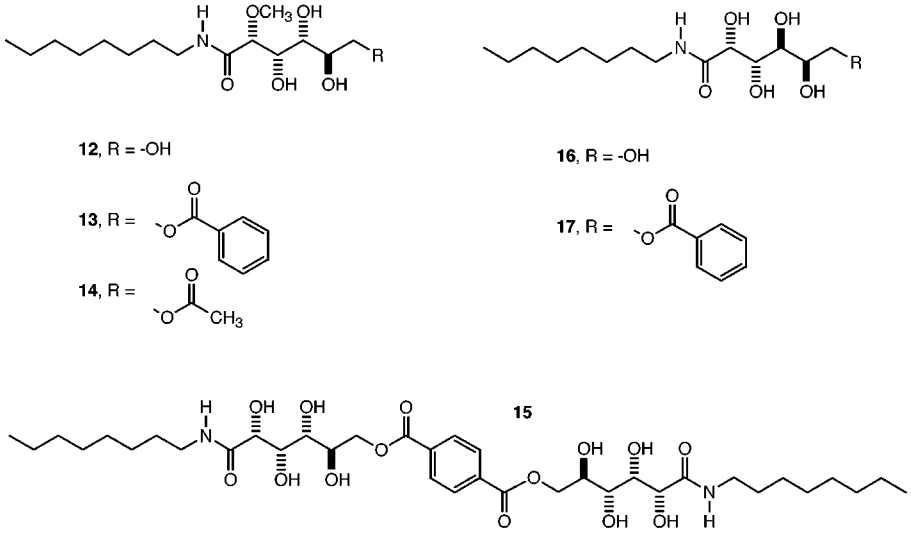
Chart 2



from CaH_2. Melting points were determined as the average of the onset and the top of the melting peaks of DSC thermograms. ^{1}H NMR spectra were recorded at 90 or 400 MHz; ^{13}C NMR spectra at 90 or 110 MHz.

The synthesis of compound **1** has been described by Pfannemüller et al.[3]

***N*-*n*-Octyl-D-gluconamide-6-benzoate (2a).** Benzoyl chloride (1.31 g, 9.29 mmol, 1.08 equiv) was dissolved in 5 mL of pyridine and added dropwise to a cooled (ice bath) and stirred gelated solution of 2.650 g (8.62 mmol) of *N*-*n*-octyl-D-gluconamide (**1**) in 40 mL of pyridine. The apparatus was purged with dried nitrogen gas for a period of 2 h while stirring, during which the temperature was raised from 0 to 60 °C. The resulting clear yellow mixture was poured into 600 mL of saturated $NaHCO_3$/ice water. The precipitate was purified by column chromatography (silica gel, eluent $CHCl_3$/MeOH 95:5, v/v), yield 3.22 g (7.83 mmol, 90%): mp 145.9 °C; IR (KBr) 3660−3030 cm^{-1} broad (OH), 1720/1703 (C=O, ester, probably more than one conformation in the solid state, only one peak in THF solution), 1722, 1666 (amide I), 1546 (amide II); ^{1}H NMR (DMSO-d_6) δ 8.014 ppm (d, 2H), 7.636 (2 d, 1H), 7.516 (t, 2H), for the carbohydrate skeleton protons see Table 3, 3.063 (9 peaks, 2H), 1.397 (t, 2H), 1.226 (broad s, 10H), 0.842 (t, 3H); EI-MS *m*/*z* 412 $(M + H)^+$, 156 $(C_8H_{17}-NHC=O)^+$, 105 $(ArC=O)^+$, 77 (C_6H_5). Anal. Calc for $C_{21}H_{33}NO_7$: C, 61.30; H, 8.08; N, 3.40. Found: C, 61.22; H, 7.97; N, 3.40.

Procedures analogous to that for the synthesis of **2a** were followed for the syntheses of ***N*-*n*-hexadecyl-D-gluconamide-6-cyclohexanoate (2b)** from the hexadecyl analogue of **1** and benzoyl chloride, ***N*-*n*-octyl-D-gluconamide-6-(3-pyridyl)-carboxylate (3)** from **1** and nicotinic acid chloride, ***N*-*n*-octyl-D-gluconamide-6-octanoate (6)** from **1** and octanoyl chloride, and ***N*-*n*-octyl-D-gluconamide-6-cyclohexanoate (7)** from **1** and cyclohexanoyl chloride. Details are given in the Supporting Information.

6-Deoxy-6-(1-imidazolyl)-*N*-*n*-octyl-D-gluconamide (4). Tosyl chloride (2.26 g, 11.8 mmol) dissolved in 10 mL of pyridine was added dropwise to a stirred gelated solution of 3.26 g (10.8 mmol) of *N*-*n*-octyl-D-gluconamide in 25 mL of pyridine which was cooled in an ice bath. The reaction was carried out in a dry nitrogen atmosphere. After 1 h of stirring at room temperature and subsequent reaction overnight in the refrigerator, 7.72 g (76.2 mmol, 7 equiv) of acetic acid anhydride was added. After 24 h of stirring, the clear solution was poured into a mixture of saturated $NaHCO_3$ and ice. The precipitate was collected and dried in vacuo. According to ^{1}H NMR and IR, 6-deoxy-6-tosyl-*N*-(octyl)-D-gluconamide tetraacetate was formed. The crude product was used without further purification to avoid deterioration. The tosylate group was substituted by an imidazole group in a high-pressure reaction vessel using 3.01 g (4.79 mmol) of the tosylate and 0.65 g (9.58 mmol, 2 equiv) of imidazole in 7.5 mL of $CHCl_3$, reaction conditions: 15 kbar, 50 °C, 40 h. The intermediate product, 6-deoxy-6-(1-imidazolyl)-*N*-(octyl)-D-gluconamide tetraacetate, was purified by column chromatography (silica, eluent Et_3N/MeOH/EtOAc 1:5:95, v/v/v), yield 0.66 g (1.26 mmol, 26.4%). The acetate groups were removed by treating 0.664 g (1.26 mmol) of this compound with 3.9 mg of NaOMe in 60 mL of MeOH (0.05 equiv of NaOMe with respect to the imidazole compound). The deprotected product was purified by recrystallization from EtOAc; yield after deprotection was quantitative: mp 104 °C; IR (KBr) 3640−3020 cm^{-1} (OH, broad), 3149, 3119 (=C−H), 1646 (amide I), 1540 (amide II); ^{1}H NMR (CD_3-OD, 400 MHz) δ 7.697 ppm (s, 1H), 7.184 (s, 1H), 6.971 (s, 1H), 4.326 (double d, 1H, J_{5-6a} = 3.65 Hz, J_{6a-6b} = 14.22 Hz), 4.176 (d, 1H, J_{2-3} = 2.36 Hz), 4.067, 4.063 (double d, 1H, J_{6b-5} = 7.08 Hz), 3.875 (5 peaks, 1H), 3.492 (double d, 1H, J_{4-5} = 8.52), 3.218 (9 peaks, 2H), 1.309 (t, 2H), 0.899 (t, 3H). No satisfactory mass spectrum (EI or CI) could be obtained. Anal. Calcd for $C_{17}H_{31}N_3O_5 \cdot H_2O$: C, 54.38; H, 8.86; N, 11.19. Found: C, 54.36; H, 8.55; N, 10.49.

***N*-*n*-Octyl-D-gluconamide-6-acetate (5).** Acetic acid anhydride (1.03 g, 10.1 mmol, 1.01 equiv) was dissolved in 15 mL of pyridine and added dropwise to a stirred (partly gelated) solution of 3.07 g (10.0 mmol) of *N*-*n*-octyl-D-gluconamide in 60 mL of pyridine at room temperature. The reaction vessel was purged with dry nitrogen. After 2 h of stirring, the solvent was evaporated at elevated temperature. The crude product was purified by column chromatography (silica gel, eluent $CHCl_3$/MeOH 9:1, v/v) and recrystallized from EtOAc, yield 0.40 g (1.14 mmol, 11%, not optimized): mp 130.1 °C; IR (KBr) 3650−3030 cm^{-1} broad (OH), 1736 (C=O, ester), 1640 (amide I), 1550 (amide II); ^{1}H NMR (DMSO-d_6) δ 7.598 ppm (t, 1H), for the carbohydrate skeleton protons see Table 3, 3.053 (9 peaks, 2H), 1.994 (s, 3H), 1.389 (t, 2H), 1.227 (broad s, 10H), 0.846 (t, 3H); EI-MS *m*/*z* 350 $(M + H)^+$, 276 $(C_8H_{17}-NHCO-(CHOH)_4)^+$, 156 $(C_8H_{17}-NHC=O)^+$, 43 $(CH_3C=O)^+$. Anal. Calcd for $C_{16}H_{31}NO_7$: C, 55.00; H, 8.94; N, 4.01. Found: C, 54.57; H, 9.01; N, 4.41.

2,4;3,5-Dimethylene-*N*-*n*-octyl-D-gluconamide (8). 2,4;3,5-Dimethylene-D-gluconic acid[32] (20.0 g, 85.4 mmol) was dissolved in 150 mL (10.7 equiv) of octylamine and stirred in a nitrogen atmosphere at 95 °C for 2 days. The solution was diluted with ethyl acetate, and after one night in the refrigerator, a white precipitate was formed which was filtered and additionally washed with *n*-hexane. After purification by column chromatography (silica, eluent EtOAc), the white product was washed with *n*-hexane again, yield 21.8 g (65 mmol, 77%) of white crystals: mp 99.0 °C (after additional

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recrystallization from water); IR (KBr) 3486 cm^{-1} (OH), 3330 (NH), 1660 (amide I), 1550 (amide II), 1180, 1109, 1094 and 1064 (ketal), 1038 (C−OH); IR ($CHCl_3$ solution) 3629 (OH), 3426 (NH), 1675 (amide I), 1543 (amide II), 1043 (C−OH); ^1H NMR (400 MHz, $CDCl_3$, assignments were made by irradiation on the OH proton and subsequent simulation) δ 6.601 ppm (t, 1H, J = 5.76 Hz, NHCO), 5.257 (d, 1H, J = 6.45, H^{7a}), 5.082 (d, 1H, J = 6.20, H^{8a}), 4.958 (d, 1H, H^{8b}), 4.822 (d, 1H, H^{7b}), 4.236 (t, 1H, J_{2-3} = 2.18, H^2), 4.136 (d, 1H, J_{3-4} = 0.82, H^3), 4.014 (double d, 1H, J_{5-6a} = 6.20, J_{5-6b} = 5.78, H^5), 3.890 (7 peaks, 1H, J_{6a-6b} = −11.43, J_{6a-OH} = 6.46, H^{6a}), 3.978 (5 peaks, 1H, J_{6b-OH} = 4.11, H^{6b}), 3.780 (s, 1H, H^4), 3.292 (q, 2H, J = 6.73, $-CH_2-$NHCO), 2.877 (double d, 1H, OH), 1.513 (m, 2H, $-CH_2-CH_2-$NHCO), 1.260 (m, 10H, $CH_3-(CH_2)_5-$), 0.869 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 110 MHz) δ 167.372 ppm, 92.150, 88.587, 77.506, 76.104, 71.439, 67.748, 59.926, 39.110, 31.724, 29.322, 29.148, 26.723, 22.576, 14.030; EI-MS m/z 332 $(M + H)^+$, 302 $(M-CH_2OH)^+$, 156 $(CH_3-(CH_2)_7-NHCO)^+$, 85 (cyclic $-O-CH=CH-CH^+-O-CH_2$). Anal. Calcd for $C_{16}H_{29}NO_6$: C, 57.99; H, 8.82; N, 4.23. Found: C, 57.94; H, 8.68; N, 4.26.

2,4;3,5-Dimethylene-*N*-*n*-octyl-D-gluconamide-6-benzoate (9). Benzoyl chloride 0.85 g (5.93 mmol, 2 equiv) was dissolved in 10 mL of chloroform and added dropwise to a stirred solution of 0.83 g (2.49 mmol) of 2,4;3,5-dimethylene-*N*-*n*-octyl-D-gluconamide (**8**) and 0.26 g (2.55 mmol) of triethylamine in 20 mL of chloroform, which was placed in an ice bath. The reaction vessel was purged with dried nitrogen gas. After stirring overnight at room temperature and refluxing for an additional 2 h, the mixture was washed with water, and the compound was purified by recrystallization from ethyl acetate, yield 0.50 g (1.15 mmol, 46%, not optimized): mp 148.0 °C; IR (KBr) 3285 cm^{-1} sharp (NH), 1719 (C=O, ester), 1660 (amide I), 1549 (amide II): ^1H NMR ($CDCl_3$) δ 8.042 ppm (d, 2H), 7.590 (t, 1H), 7.464 (t, 1H), 6.552 (t, 1H), 5.276 and 4.833 (2 times d), 5.059 and 5.002 (2 times d, 2H), for the carbohydrate skeleton protons see Table 3, 3.309 (q, 2H), 1.510 (m, 2H), 1.262 (broad s, 10H), 0.875 (t, 3H); EI-MS m/z 435 $(M)^+$, 156 $(C_8H_{17}-NHC=O)^+$, 105 $(C_6H_5C=O)^+$, 77 $(C_6H_5)^+$. Anal. Calcd for $C_{23}H_{33}NO_7$: C, 63.43; H, 7.64; N, 3.22. Found: C, 63.43; H, 7.56; N, 3.22.

2,4;3,5-Dimethylene-*N*-*n*-octyl-D-gluconamide-6-(3-pyridyl) carboxylate (10) was prepared from **8** and 3-pyridinecarboxylic acid chloride by a procedure analogous to that described for compound **9**. Details are given in the Supporting Information.

6-Deoxy-6-(1-imidazolyl)-2,4;3,5-dimethylene-*N*-*n*-octyl-D-gluconamide (11). This compound was synthesized from **8** via its tosylate. To a solution of 15.0 g (45.26 mmol) of **8** in 150 mL of anhydrous pyridine, which was placed in an ice bath, was added dropwise 9.8 g (51 mmol, 1.1 equiv) of tosyl chloride dissolved in 50 mL of pyridine, under a nitrogen atmosphere. After an additional hour of stirring, the orange solution was stored overnight in the refrigerator. The product, 6-tosyl-2,4;3,5-dimethylene-*N*-*n*-octyl-D-gluconamide, was precipitated by pouring the pyridine solution into a mixture of saturated $NaHCO_3$ solution and ice. The solid material was filtered off, dried in vacuo, and used without any further purification, yield 19.065 g (39.26 mmol, 86.7%): mp 116.6 °C; IR (KBr) 3398 cm^{-1} (NH), 1680 (amide I), 1531 (amide II), 1359 and 1176 (S=O); ^1H NMR (90 MHz, $CDCl_3$) δ 7.793 ppm (d, 2H), 7.368 (d, 2H), 6.599 (t, 1H), 5.230 (d, 1H, J = 6.3 Hz), 4.896 (d, 1H, J = 6.8 Hz), 4.786 (d, 2H), 4.215 (m, 3H), 4.074 (s, 2H), 3.670 (s, 1H), 2.467 (s, 3H); EI-MS m/z 485 $(M)^+$, 314 $(M-OTs)^+$, 156 $(C_8H_{17}-NHCO)^+$, 155 $(SO_2-C_6H_4-CH_3)^+$, 85 (cyclic $-O-CH=CH-CH^+-O-CH_2$). Anal. Calcd for $C_{23}H_{35}NO_8S\cdot 0.5\ H_2O$: C, 55.85; H, 7.34; N, 2.83; S, 6.48. Found: C, 55.63; H, 7.16; N, 2.98; S, 6.27.

6-Tosyl-2,4;3,5-dimethylene-*N*-*n*-octyl-D-gluconamide (1.13 g, 2.32 mmol) and 0.50 g (7.28 mmol) of imidazole were dissolved in 7.5 mL of chloroform and brought under high pressure (15 kbar) at 50 °C for 2 days. The solution was washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and further purified by column chromatography (silica, eluent Et_3N/MeOH/EtOAc 1:10:89, v/v/v) followed by recrystallization from diluted aqueous NaOH (pH = 8), yield 0.58 g (white needle-shaped crystals, 1.52 mmol, 65.6%): mp 134.5 °C; IR (KBr) 3332 cm^{-1} (NH), 3142 (=C−H), 3097 (=C−H), 1667 (amide I), 1545 (amide II), 1187, 1103, 1095 and 1068 (ketal), 993 (=C−H); IR ($CHCl_3$ solution), 3426 (NH), 1676 (amide I), 1543 (amide II); ^1H NMR (400 MHz, $CDCl_3$, assignments were made by irradiation on proton H^4 and recording a COSY spectrum (8 K, det. F2; 512 K, evol. F1). The spectra did not result in a clear assignment; after recording temperature-dependent experiments in combination with simulation, however, the chemical shifts and J-couplings could be determined unambiguously: δ 7.513 (s, 1H, N=CH−N), 7.105 (s, 1H, $-CH_2-N-CH=CH-N=$), 6.965 (s, 1H, $-N-CH=CH-N=$), 6.530 ppm (t, 1H, J = 5.76 Hz, NHCO), 5.226 (d, 1H, J = 6.50 Hz, H^{7a}), 5.016 (d, 1H, J = 6.19 Hz, H^{8a}), 5.053 (d, 1H, H^{8b}), 4.754 (d, 1H, H^{7b}), 4.330 (double d, 1H, J_{6a-5} = 5.50 Hz, J_{6a-6b} = −15.30 Hz, H^{6a}), 4.219 (m, 1H, J_{5-4} = 1.20 Hz, H^5), 4.211 (m, 1H, J_{6b-5} = 10.00, H^{6b}), 4.180 (d, 1H, J_{3-4} = 1.00, H^3), 4.130 (d, 1H, J_{2-3} = 2.00 Hz, H^2), 3.530 (t, 1H, H^4), 3.306 (double d, 2H, $-CH_2-$NHCO), 1.736 (crystal water), 1.509 (m, 2H, $-CH_2-CH_2-$NHCO), 1.261 (m, 10H, $CH_3-(CH_2)_5-$), 0.877 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.641 ppm, 137.389, 135.342, 129.780, 91.932, 88.003, 77.177, 75.006, 71.118, 66.743, 44.563, 39.008, 31.616, 29.253, 29.040, 28.913, 26.631, 22.470, 13.935; EI-MS m/z 380 $(M - H)^+$, 225 $(M-CH_3-(CH_2)_7-NHCO)^+$. Anal. Calcd for $C_{19}H_{31}N_3O_5\cdot 0.5\ H_2O$: C, 58.44; H, 8.62; N, 10.76. Found: C, 58.68; H, 8.18; N, 10.65.

2-Methoxy-*N*-*n*-octyl-D-gluconamide (12). To a mixture of 4.14 g (13.5 mmol) of *N*-*n*-octyl-D-gluconamide (**1**) and 1.11 g (19.7 mmol, 1.5 equiv) of powdered KOH in 35 mL of DMSO was added dropwise 1.76 g (13.9 mmol, 1.03 equiv) of dimethyl sulfate (*Caution! toxic and carcinogenic!*) dissolved in 15 mL of DMSO. After the reaction mixture was stirred for 4 h, ethanol was added to inactivate the excess of dimethyl sulfate. Prior to evaporation of DMSO, the excess KOH was neutralized with 1.30 g (21.7 mmol) of acetic acid anhydride. The residue was purified by column chromatography (silica, eluent $CHCl_3$/MeOH 93:7, v/v), yield 0.61 g (1.9 mmol, 14%): mp 129.2 °C; IR (KBr) 3660−3060 cm^{-1} broad (OH), 1656 (amide I), 1564 (amide II); ^1H NMR (DMSO-d_6) δ 7.840 ppm (t, 1H), for the carbohydrate skeleton protons see Table 3, 3.260 (s, 3H), 3.057 (m, 2H, 2H), 1.398 (t, 2H), 1.230 (broad s, 10H), 0.844 (t, 3H); EI-MS m/z 321 $(M + H)^+$, 276 $(C_8H_{17}-NHCO(CHOCH_3)-(CHOH)_3CH_2OH)^+$, 260 $(C_8H_{17}-NHCO(CHOCH_3)(CHOH)_2)^+$, 230 $(C_8H_{17}-NHCO(CHOCH_3)CHOH)^+$, 156 $(C_8H_{17}-NHC=O)^+$. Anal. Calcd for $C_{15}H_{31}NO_6$: C, 56.05; H, 9.72; N, 4.36. Found: C, 56.04; H, 9.79; N, 4.42.

2-Methoxy-*N*-*n*-octyl-D-gluconamide-6-benzoate (13) was synthesized by a procedure analogous to that described for compound **2a**, using **12** and benzoyl chloride, and a workup and purification procedure similar to that described for compound **5**. **2-Methoxy-*N*-*n*-octyl-D-gluconamide-6-acetate (14)** was synthesized by a procedure analogous to that described for compound **5**, using **12** and acetic anhydride, and a workup and purification procedure similar to that for compound **7**. **Di-(6-*N*-*n*-octyl-D-gluconamide)-terephthalate (15)** was synthesized by a procedure analogous for that described for compound **2a**, using **1** and terephthaloyl dichloride. Details are given in the Supporting Information.

***N*-*n*-Octyl-D-galactonamide (16).** The synthesis and characterization of this compound has been described in the literature.[6a] The analytical data (^1H NMR, IR, and elemental analysis) were satisfactory.

***N*-*n*-Octyl-D-galactonamide-6-benzoate (17)** was synthesized by a procedure similar to that described for compound **2a**, starting from **16** and benzoyl chloride. Details are given in the Supporting Information.

Physical Measurements

Determination of T_{gel}. A typical procedure for preparation of the organogels was as follows. In a test tube, approximately 0.5 mL solvent was added to 5 mg of powdered sample. The tube was closed and gently heated, in most cases until the mixture started to boil. Subsequently, the mixture was vortexed until a clear solution was obtained. Hereafter, it was

Table 1. Gelation Behavior of Gluconamides in Organic Solvents[a]

compd	protected[b]	substituent[c]	*n*-hexane	1,2-xylene	$CHCl_3$	EtOAc	EtOH
1	no	OH	I	G	I	I	R
2a	no	aromatic	I	G	G	G	G
3	no	aromatic	I	R	I	R	S
4	no	aromatic	I	T	G	R	S
5	no	aliphatic	I	G[d]	G[d]	R	S
6	no	aliphatic	I	S	T	R	R
7	no	aliphatic	I	G	G	G	S
8	methylene (2×)	OH	R	T	S	S	S
9	methylene (2×)	aromatic	R	S	S	S	S
10	methylene (2×)	aromatic	R	S	S	S	S
11	methylene (2×)	aromatic	I	R	S	S	S
12	C^2 methoxy	OH	I	G	S	S	S
13	C^2 methoxy	aromatic	I	R	S	S	S
14	C^2 methoxy	aliphatic	I	R	S	S	S
15	no	(dimeric)	I	I	I	I	I
16[e]	no	OH	I	I	I	I	R
17[e]	no	aromatic	I	T	T	R	R

[a] G: the compound gelates the solvent resulting in a high viscosity mixture upon cooling. S: compound dissolves without gelation. I: the compound is insoluble even after prolonged heating. R: compound recrystallizes upon cooling within 1 h. T: upon cooling, a turbid mixture with slightly increased viscosity is obtained, but no gel is formed. [b] Protection of the hydroxyl groups. [c] Substituents on the C^6 of the carbohydrate skeleton. [d] Gel with low viscosity. [e] Galactonamide derivatives.

allowed to cool to room temperature. When the gel had a viscosity high enough to turn the test tube upside down without damaging the structure, the sol-to-gel temperature was determined according to a method described in the literature.[33] A glass ball was placed on top of the gel and the test tube was subsequently placed in a thermostated water bath and heated at 1.5 °C/min. The temperature at which the ball started to fall through the gel was denoted as T_{gel}.

DSC Measurements. The thermograms were recorded on a Perkin-Elmer DSC 7 instrument using closed stainless steel cups. The gelator (0.5 mg) was placed in the cups, and 50 μL of solvent was added with the help of a pipet. After sealing, the cups were heated to 20 °C above the boiling point of the solvent before the first run was recorded. The scan speed for both the heating and cooling runs was 5 °C/min. At least two heating and two cooling runs per sample were recorded. Loss of solvent during the runs was checked by weighing the cups before and after the measurements. No weight loss was observed in any case. For the calibration of the instrument, cyclohexane and indium samples were used. The thermograms of the samples without solvent were recorded in 30 μL aluminum pans. Calibration was carried out with zinc and indium samples (scan speed of 5 °C/min.)

Electron Microscopy. Electron micrographs were recorded on TEM Philips EM201 and TEM JEOL JEMCXII instruments. The gels were transferred to carbon-coated 150 mesh copper grids; after 30 s of acclimatization, the excess material was removed and the grids were covered with Pt deposited at an angle of 45° prior to examination.

X-ray Powder Diffraction. X-ray powder diffractograms were recorded on a Philips PW1710 powder diffractometer with a Ni filtered Cu source (40 KV, 55 mA, $\lambda = 1.54060$ Å). The 1% (weight/volume) gels were transferred to a silicon sample holder and rapidly dried under high vacuum.

FT-IR Spectra. FT-IR spectra were recorded on a BioRad Digilab Division (FTS-25) instrument. The gels and solutions were measured between NaCl windows and corrected for the solvents. Solid samples were measured as KBr pellets.

Results

Gelation Behavior. Compounds **1**−**17** were studied with regard to their gelation behavior in five organic solvents. The gels obtained were either clear or slightly turbid. Those possessing a viscosity so high that the test tube could be turned upside down without damaging the structure are denoted as (G) in Table 1. Gels displaying this behavior could be made from the gluconamide (**1**), the benzoate (**2a**), the cyclohexanoate (**7**), and the C^2 methoxy protected derivative **12**. The gels obtained from the imidazole and acetate derivatives **4** and **5** showed a significantly higher viscosity than expected for a solution or a vesicular dispersion but were not as viscous as the aforementioned gels; they are earmarked as (T).

Compound **1** dissolved only in very polar solvents such as water and ethanol, or in less polar organic solvents at very high temperature, e.g., in 1,2-xylene at 144 °C. Introduction of substituents at C^6 was found to lead to an increase in solubility. Both aromatic and aliphatic substituents on carbon atom C^6 gave soluble products, which sometimes crystallized (e.g., from ethyl acetate) but in most cases formed gels (see Table 1). When all (**8**−**11**) or just one (at C^2, **12**−**14**) of the secondary hydroxyl groups of the gluconamide was protected, the compounds became too soluble, and in most cases no gels or turbid mixtures were formed upon cooling (except **8** and **12** in 1,2-xylene). *n*-Hexane turned out not to be a suitable solvent for the formation of organogels. Even **6** and **15** did not dissolve in this solvent, despite their relatively hydrophobic character. In fact, the octyl derivative **6** was hardly soluble in any solvent; only in boiling chloroform could a clear solution be obtained, which turned cloudy and viscous but did not form a firm gel. The gemini surfactant **15** was insoluble in almost every solvent except DMSO, in line with the strong intermolecular interactions in the solid phase of this compound (mp 203 °C, dec). Introduction of a benzoate group at C^6 in the gluconamide in **2a** resulted in gelation of almost every solvent. Placing the benzoyl function on the galactonamide framework (**17**) resulted in an increase of the solubility of the compound, but unlike the gluconamide derivative, there was hardly any gelation observed. In 1,2-xylene and chloroform only, gels with very low tensile strengths were formed. Open-chain galactonamides do not have a bent headgroup like that of gluconamides. In the case of compound **16**, this resulted in a complete insolubility in most organic

(33) Takahashi, A.; Sakai, M.; Kato, T. *Polym. J.* **1980**, *12*, 335.

Table 2. Temperatures at Which the Gel of the Benzoate Derivative 2a Vanishes in Various Solvents[a]

solvent	T_{gel} (°C)[b]	polarization index[c]	bp (°C)[d]
water	R	9.0	100
methanol	17	6.6	65
ethanol	28	5.2	79
acetonitrile	50	6.2	82
acetone	28	5.4	56
dioxane	15	4.8	101
chloroform	66	4.4	62
ethyl acetate	42	4.3	77
tetrahydrofuran	S	4.2	66
dichloromethane	43	3.4	40
toluene	101	2.3	111
ether	I	*e*	35
n-hexane	I	*e*	69
benzene	95	*e*	80
1,2-xylene	102	*e*	144

[a] Determined by the Takahashi method, see ref 33. [b] Explanation of symbols, see footnotes of Table 1. [c] Polarization index according to Snyder, see ref 34a. [d] Boiling points of the pure solvents. [e] Polarization index not known.

solvents. The low-tensile gel, which can be prepared at low concentrations in water, has been reported to contain helically twisted ribbons.[6a]

All gels were thermoreversible, i.e., they turned into clear, low-viscosity solutions upon heating and gelation returned after cooling. The temperature at which the gel vanishes, the so-called the gel-to-sol temperature, denoted as T_{gel}, was determined for the benzoate derivative **2a** in a variety of solvents (Table 2). There was no clear correlation of T_{gel} with any of a variety of physical constants of the solvent, e.g., polarization index according to Snyder,[34a] Rohrschneider constants,[34b] dielectrical constants, surface tension, or boiling points.

In contrast to the gels of **1** in water and in 1,2-xylene where precipitation occurred after a couple of days,[6,7] the gels of **2a** in different solvents were very stable and did not change over a period of several months. TEM on an aged sample in chloroform showed exactly the same texture as TEM carried out on a freshly prepared sample. The stability of the gel was only affected by raising the temperature. In some cases (chloroform, dichloromethane, and benzene, see Table 2), the T_{gel} of **2a** exceeded the boiling point of the solvent. Boiling only occurred upon decomposition of the gel (boiling at T_{gel}).

Elongation of the alkyl chain length from *n*-octyl to *n*-hexadecyl as in compound **2b** resulted in a slower gelation process. Only after 1 day of conditioning at ambient temperature was a gel in chloroform was formed, considerably slower than the time required for the octyl derivative **2a**, which gelated within several minutes upon cooling. This effect has also been reported for aqueous gels of unsubstituted *N*-*n*-alkyl-D-gluconamides, which tend to crystallize with a rate depending on the length of the alkyl chain,[3] and in gels of maltobionamides, of which the fibers of the long-chain compounds are not as regularly oriented as those of the short-chain ones.[3]

DSC Measurements. To obtain information about the enthalpy changes that accompany the formation and collapse of the gels, DSC experiments were carried out with compound **2a**. Both the heating and cooling curves showed very broad peaks in all cases, indicating that the transitions took place gradually. This can be attributed to the relatively low degree of ordering that is present in the gel compared to that of crystalline structures, which normally give sharp peaks (e.g., crystal−crystal transitions or melting). Although the large peak width reduced the accuracy of the thermograms,[35] certain trends could still be distinguished.

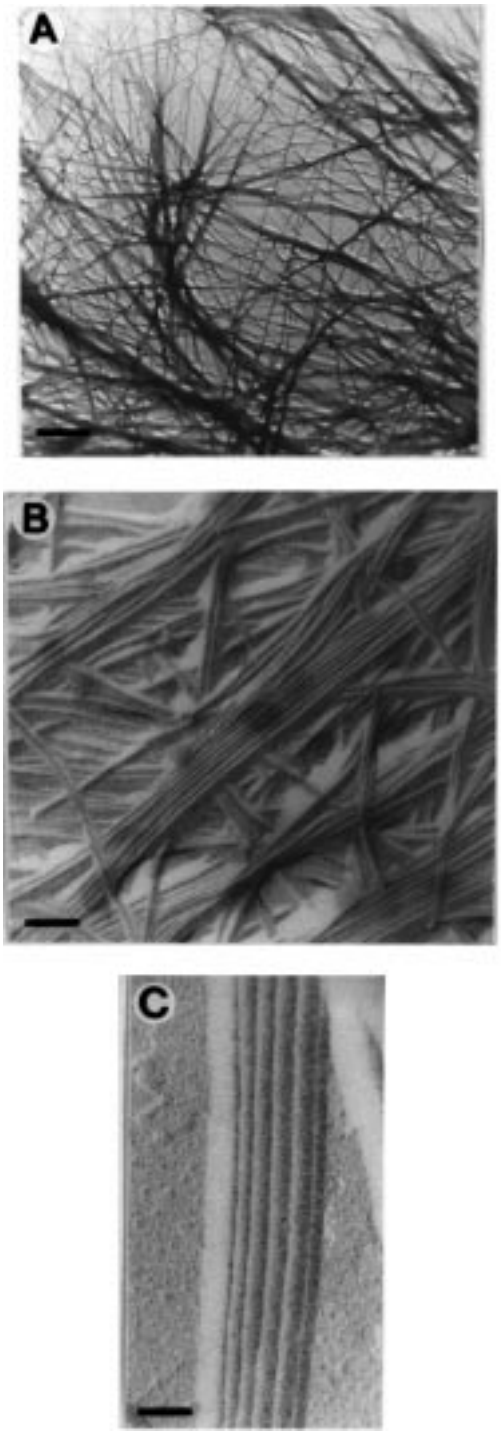

Figure 1. TEM pictures of a gel of **2a** in chloroform (Pt shadowing). (A) Network of fibers; bar is 1.6 μm. (B) Bundles of whisker-type fibers; bar is 268 nm. (C) Intertwined bundles of fibers; bar is 200 nm.

(34) (a) Snyder, L. R. *J. Chromatogr.* **1974**, *92*, 223. (b) Snyder, L. R. *J. Chromatogr. Sci.* **1978**, *16*, 223.

(35) The average of the onset and the top value of the peak from the heating curves were used as T_{gel} values. The T_{gel} values determined from the DSC thermograms were similar to the T_{gel} values as determined by the glass ball method; deviations were observed only for the aromatic solvents.

Figure 2. Microscopic picture of a gel prepared from **2a** in chloroform. The gel was placed between crossed polarized filters.

The ΔH(gel) values were measured in several solvents. Thermograms of gels made from compound **2a** showed that in chlorinated solvents ΔH(gel) is much lower (dichloromethane, − 19; chloroform, −21 kJ/(mol gelator)) than in aromatic solvents (benzene, −44; toluene, − 37; 1,2-xylene, −38 kJ/(mol gelator)). In the case of ethanol, an even lower ΔH(gel) value was observed (+14 kJ/(mol gelator)). This is probably due to the fact that ethanol can accept and donate hydrogen bonds and hence disturb the *inter*-molecular hydrogen-bonding network of **2a**. It would have been of interest to study gels in other solvents that are either H-bond donating or H-bond accepting. As to the former class, compound **2a** dissolved in DMSO or THF but, unfortunately, remained dissolved upon cooling, and gelation in dioxane was too slow (2 days) for accurate DSC measurements. As to the latter, **2a** did not dissolve at all in water, and gelation in methanol again was too slow (16 h) for accurate DSC recording. For comparison, we recorded the energy transfer that takes place when the aqueous gel of **1** is dissolved. The energy transfers of **1** in water and **2a** in ethanol are in the same range (+11 and +14 kJ/(mol gelator), respectively).

We also measured ΔH(gel) values for a number of gelators in the same organic solvent, viz., 1,2-xylene. The ΔH(gel) upon disruption of the gels, amounting to −42, −38, and −38 kJ/(mol gelator) for **1**, **2a**, and **12**, respectively, was found to be nearly independent of the gelator type. Even the galactonamide derivative **17** (ΔH(gel) −37 kJ/(mol gelator)) did not deviate from this trend, although this compound formed a turbid mixture instead of a highly viscous gel.

Electron Microscopy. The high viscosity of the gels suggests that network structures are formed from the gluconamides. This was investigated by TEM (Pt shadowing). In the following the TEM pictures obtained for the various compounds are discussed in some detail.

Gluconamides with Aromatic Substituents on C[6]. Benzoate Derivatives 2a and 2b. The TEM pictures of the organogels formed from the benzoate derivative **2a** showed a network of whisker-type fibers (see Figure 1A, TEM picture of a gel from **2a** in chloroform). Despite the relatively low concentration (1% w/v), the network is finely meshed, which explains the fact that the gel is rigid and can exist above the boiling point of the solvent without collapsing. The fibers are often bundled like the strings in a rope (see Figure 1B), but neither the individual fibers nor the bundles of fibers showed chirality. Apparently, in contrast to **1** in water, the chirality of the headgroup of **2a** is not expressed in the supramolecular structure. The fibers have an average diameter of 31 nm and hence must be composed of more than one monolayer or bilayer (2.4 and 4.9 nm, respectively, as estimated from CPK models) or must be hollow. From the TEM micrographs, it cannot be distinguished if the rodlike structures of **2a** are hollow tubes or solid rods. The aspect ratio (length to width) of the fibers was very high, viz., up to 500. Unlike the T_{gel} and ΔH(gel) values, the shapes of the textures did not depend on the solvent. Micrographs recorded from gels of **2a** in ethyl acetate, ethanol, or 1,2-xylene all showed fiberlike structures with the same dimensions as those seen for **2a** in chloroform.

The ordering present in the gels could also be observed by a polarizing microscope, as shown in Figure 2 for the gel from **2a** in chloroform. It is clear from this figure that the gel does not contain small crystalline parts in a matrix of nonordered solvent molecules but is ordered throughout the sample. The magnification of the light microscope was too low to distinguish the fibers that were observed by TEM.

In electron micrographs of gels of **2b**, two aggregation forms could be discerned: cigarlike rolled up multilayers (see Figure 3A) and whisker-type fibers (see Figure 3B)

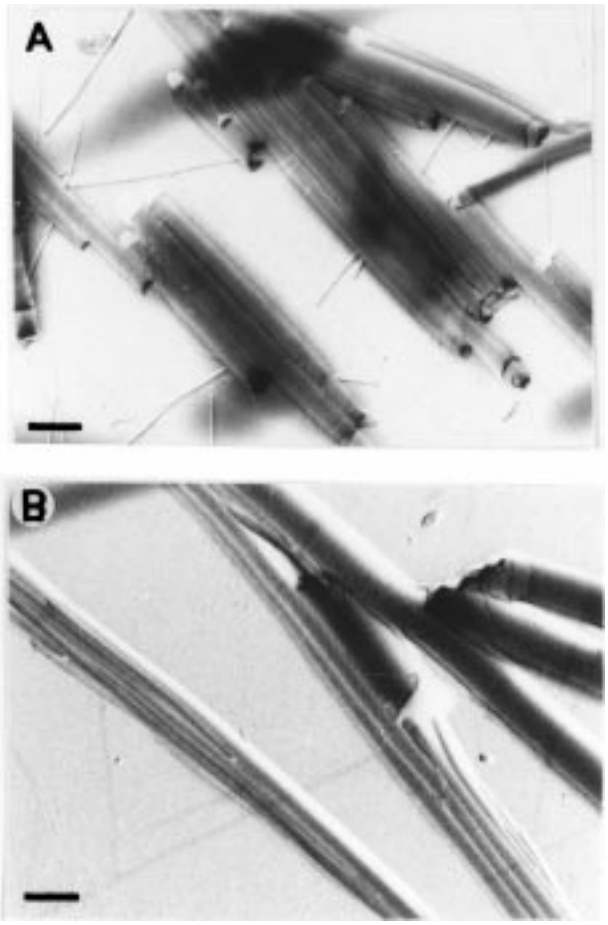

Figure 3. TEM pictures of a gel of **2b** in chloroform (Pt shadowing). (A) Cigar-like tubes from rolled-up multilayers; bar is 1.12 μm. (B) Whisker-type fibers and cigar-like tubes; bar is 450 nm.

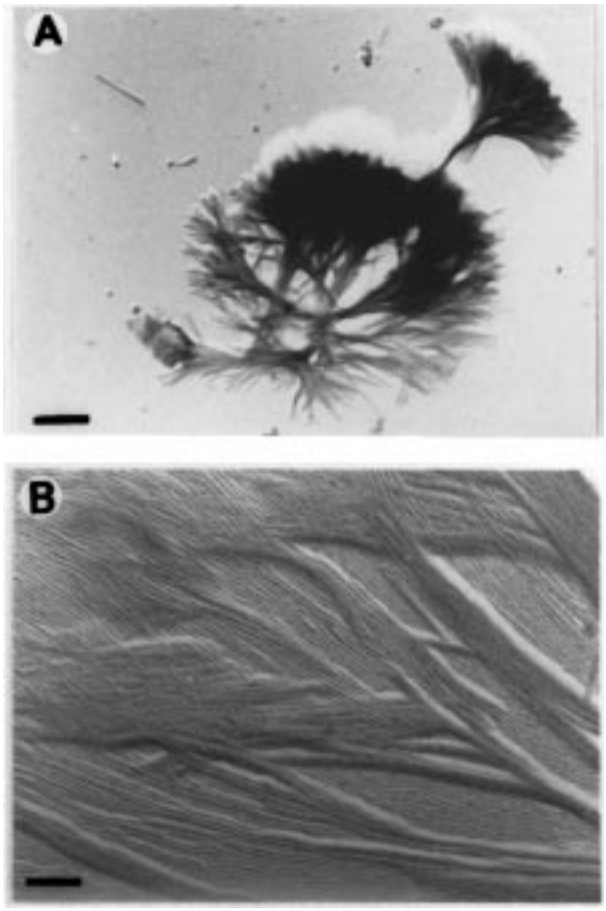

Figure 4. TEM pictures of a gel of **3** in 1,4-dioxane. (A) Overview, bar is 570 nm. (B) Visible are rods which are built up from fibers (Pt shadowing); bar is 170 nm.

which were also present in gels of **2a** in chloroform (see Figure 1B). The multilayered cigarlike structures had diameters ranging from 200 to 500 nm, whereas the fibers had a much smaller average diameter of 65 nm. These fibers must either consist of several layers or be hollow, because the estimated monolayer thickness is only 3.1 nm.

3-Pyridine-carboxylate Derivative 3. A TEM picture of a gel of **3** in dioxane showed fiberlike structures which assembled to form larger rodlike aggregates (the diameter of the fibers was approximately 10 nm, and the average diameter of the rods was 40 nm, see Figure 4). Gluconamide **2a** also formed rodlike structures of approximately 30 nm, but the finer fibers of 10 nm as observed in the gels of pyridinecarboxylic acid ester **3** were absent in the gels of the former compound. Chiral suprastructures such as chiral twists or helical ropes were not observed for compound **3**.

Imidazolyl Derivative 4. TEM pictures of the gels of **4** in chloroform revealed the presence of twisted ribbonlike structures (see Figure 5A). The direction of the twist was similar for all ribbons. For comparison, we also studied the aggregation behavior of **4** in aqueous solution. The imidazole group of **4** has a pK_a of 7.02[36] and will be partly protonated in neutral water. Upon dissolution in Tris-buffered (pH = 8.5) water, compound **4** slowly formed a gel in which the same type of twisted ribbons were present as in the gel in chloroform, pointing to a similarity in molecular arrangement. Staining of the samples with uranyl acetate resulted in micrographs with relatively contrast-rich regions (Figure 5B), possibly indicating that the most hydrophilic parts of **4** are in direct contact with the aqueous phase and the uranyl acetate. Aggregation of **4** in water was found to be much slower than aggregation in chloroform or in dichloromethane. The clear solution of neutral **4** in water gelated only after 1 day, whereas the clear solution of **4** in chloroform gelated within 1 h. Dissolving **4** in acetic acid/sodium acetate buffered (pH = 4.5) water resulted in a clear solution without the formation of any aggregates.

Gluconamides with Aliphatic Substituents on C^6. Acetyl Derivative 5. The aqueous gel of acetyl derivative **5** had a lower viscosity than the gel obtained from **1** in water or from **2a** in chloroform. Electron micrographs of **5** in water showed the presence of multilayered ribbons, which rolled up to give helices (not shown). In chloroform, similar types of chiral aggregates were present (see Figures 6A,B). This would suggest that the way compound **5** aggregates is solvent independent. Apparently, small hydrophobic groups (imidazolyl in **4**, see above, and acetyl in **5**) allow the gluconamides to form gels in both water and chloroform and do not disturb their packing, resulting in expression of the molecular chirality in the superstructures.

***n*-Octanoyl Derivative 6.** Micrographs of a turbid mixture of the *n*-octanoyl derivative **6** in chloroform

(36) R. J. H. Hafkamp, Ph.D. Thesis, University of Nijmegen, 1996.

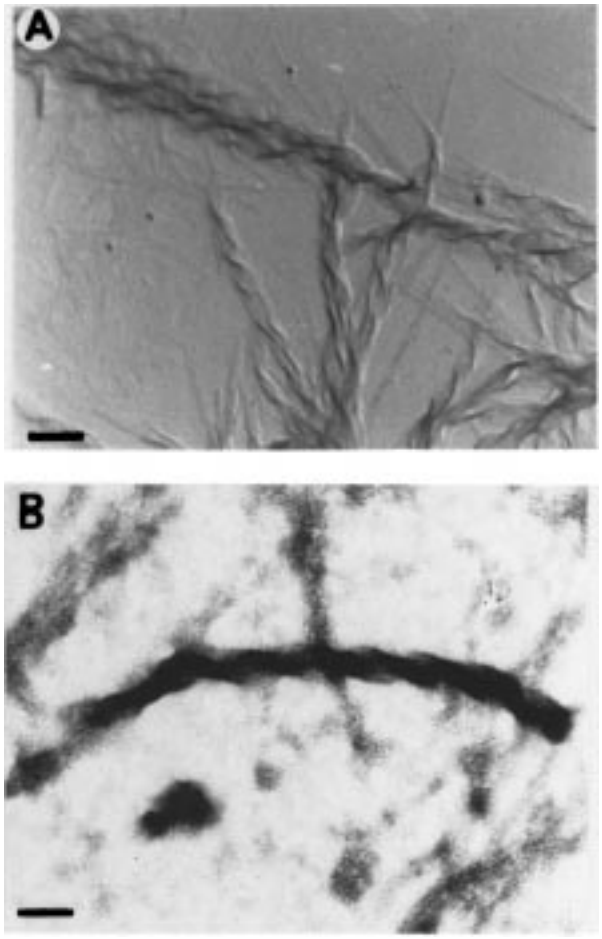

Figure 5. TEM pictures of **4**. (A) Gel in chloroform. Visible are twisted ribbons (Pt shadowing); bar is 310 nm. (B) Gel in Tris-buffered solution, pH 8.5 (negative staining with $U(OAc)_2$, 1%). Visible are twisted ribbons; bar is 100 nm.

showed helical superstructures with an average diameter of 35 nm (Figure 6C) but with a much smaller aspect ratio (maximum 13) than the superstructures obtained from, e.g., **1** in water and **5** in water or chloroform. The observed helices originate from amorphous droplets of material and do not form a network as was observed for, e.g., **2a** in chloroform. This explains why **6** does not form a *rigid* gel.

Cyclohexanoyl Derivative 7. In benzene and ethyl acetate, cyclohexanoyl derivative **7** forms gels in which fiberlike structures are present (Figure 7A). These fibers are not so well defined as those obtained from **2a** in ethyl acetate, 1,2-xylene, or chloroform. They intertwine to form bundles. Many fibers have at both ends a remarkable knob-shaped enlargement (see Figure 7A,B). Careful inspection of the fibers reveals that they are helical and very tightly wound (see Figure 7C). The knobs at the end of the fibers can be interpreted as hairpins where the fibers turn back. Although the cyclohexanoyl substituent in **7** is very bulky and comparable in size to the benzoate group in **2a**, it does not prevent the formation of chiral aggegates as the latter group does. Cyclohexane rings probably can stack in an orientation that fits the packing directed by the glucon group. Similar conclusions were drawn from the X-ray structure of (1*S*,2*S*)-1,2-bis(D-gluconamido)cyclohexane,[37] which has a hydrogen-bonding network with exactly the same connectivity as compound **1**.[12]

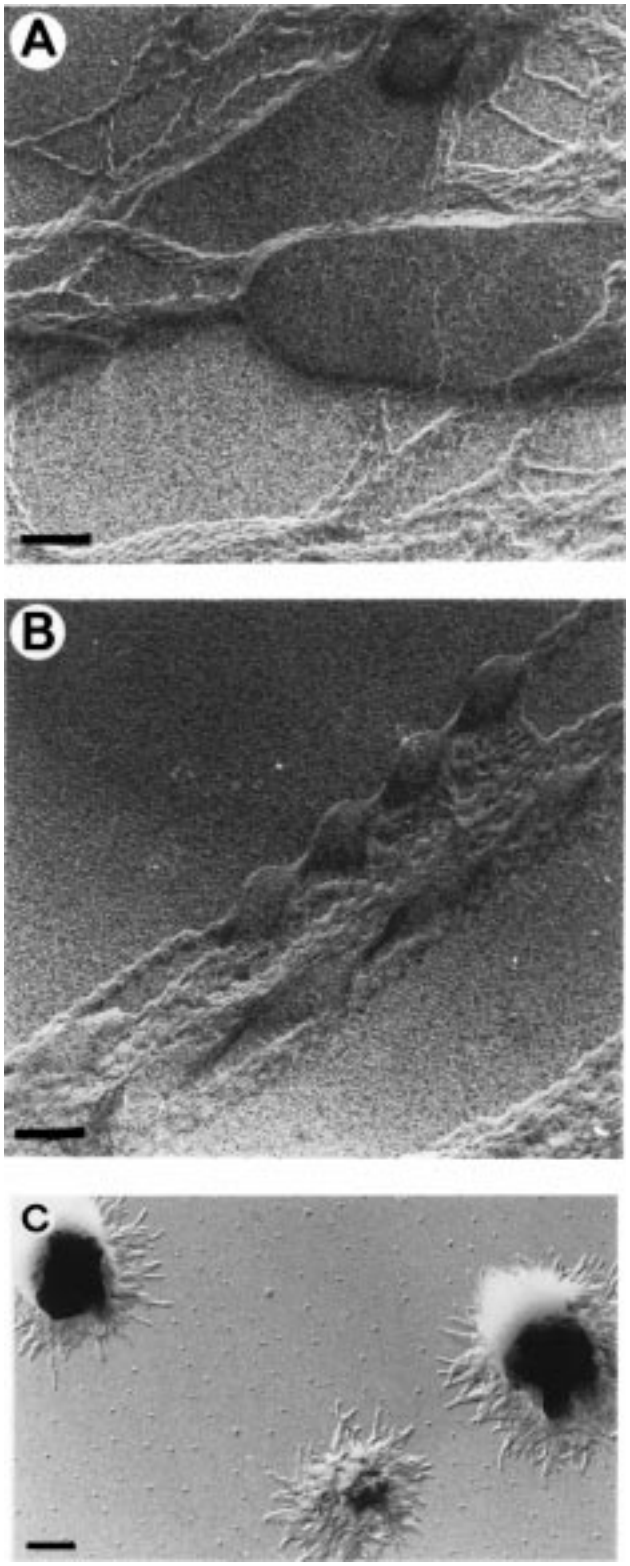

Figure 6. TEM pictures of gels of **5** and **6** in chloroform (Pt shadowing). (A) Flat ribbons of **5** which twist to give a helix; bar is 210 nm. (B) Helix of **5**, which changes into a twisted ribbon and back into a helix; bar is 150 nm. (C) TEM picture of a gel of **6** in chloroform (Pt shadowing). Helices are shown which originate from an amorphous droplet; bar is 100 nm.

(37) André, C.; Luger, P.; Nehmzow, D.; Fuhrhop, J.-H. *Carbohydr. Res.* **1994**, *261*, 1.

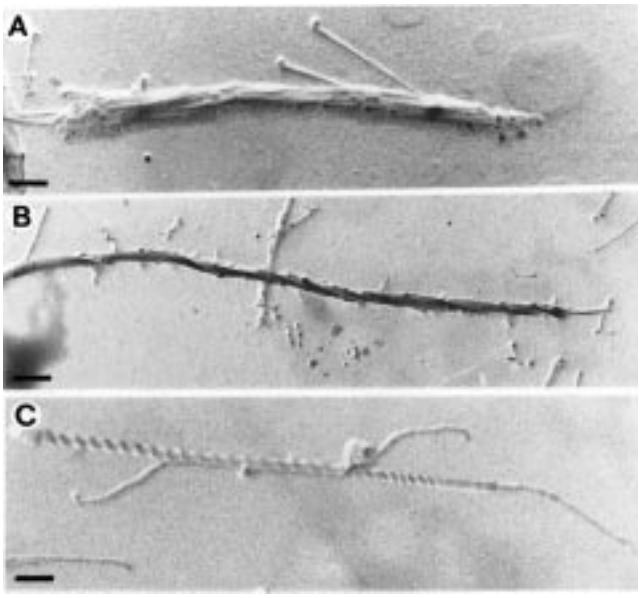

Figure 7. TEM pictures of a gel of **7** in ethyl acetate (Pt shadowing). (A) Several fibers are visible that are twined to form a rope; bar is 550 nm. (B) Fibers with knobs at their ends; bar is 350 nm. (C) Helically wound fiber. The winding gets tighter at the end of the fiber to the extent that a helical structure can no longer be detected; bar is 275 nm.

Gluconamides without C^6 Substituents. The gluconamides with methylene protected secondary OH groups and substituents on C^6 (**8**−**11**) and the gluconamides with a C^2 methoxy group and a C^6 substituent (**13** and **14**) did not form gels or turbid mixtures in organic solvents and were therefore not investigated with electron microscopy.

***N*-*n*-Octylgluconamide 1.** Gluconamide **1** forms gels in water, 1,2-xylene, and pyridine. The gel in pyridine is only stable at temperatures below 10 °C. The type of aggregates displayed by **1** is solvent dependent: in water, helices are generated;[3] in 1,2-xylene, scrolls;[6a] and in pyridine, fibers (see Figure 8A). The fibers have an average diameter of 31 nm. We cannot explain why in pyridine the chirality is not expressed in the aggregate structure.

C^2-methoxy Derivative 12. In water, **12** crystallizes within 15 min. When a freshly prepared solution, however, is dried, stacked bilayers are observed by TEM (see Figure 8B). A highly viscous gel is formed in benzene, which shows fiberlike structures under the electron microscope (see Figure 8C). These fibers have an average diameter of 22 nm and are similar to those formed by **2a** in organic solvents, e.g., ethyl acetate. The above-mentioned fibers and bilayers do not show any chirality.

NMR Study. The type of chiral superstructures formed by the gluconamides seems to be determined by the steric constraints of the carbohydrate headgroups and their opportunity to form extended hydrogen-bonding patterns,[13,38] which in turn depends on the conformations of the carbohydrate headgroup. To investigate what the headgroup conformations of the gluconamides were, we tried to perform a solid state ^{13}C NMR study[13,39,40] of the gels of **2a** in both chloroform and methanol. Unfortunately, the gels were too unstable under the conditions of high spin rates required for the measurements, and consequently this approach was abandoned. Although in solution the conformations of the carbohydrate headgroups can be different from those in the crystalline or gel state, we decided to compare the solution ^1H NMR spectra of the C^6-substituted derivatives of gluconamide **1** (viz., **2**−**5**, **7**) with that of **1** itself. For comparison, the

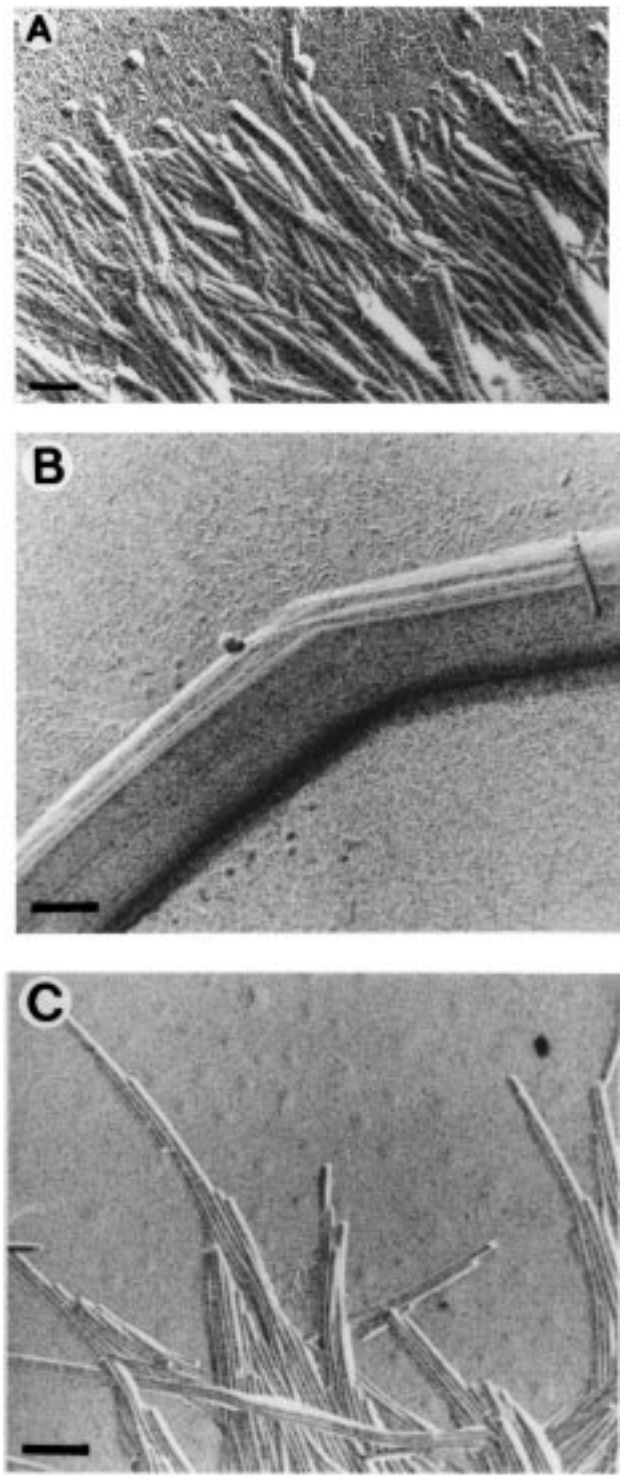

Figure 8. TEM pictures of **1** and **12** (Pt shadowing). (A) Rods formed in gels of **1** in pyridine; bar is 90 nm. (B) Multilayers formed from **12** in water; bar is 170 nm. (C) Whisker-type of fibers formed from **12** in a gel in benzene; bar is 210 nm.

(38) Fuhrhop, J.-H.; Schnieder, P.; Rosenberg, J.; Boekema, E. *J. Am. Chem. Soc.* **1987**, *109*, 3387.
(39) Fuhrhop, J.-H.; Fritsch, D. *Acc. Chem. Res.* **1986**, *19*, 130.
(40) Svenson, S.; Kirste, B.; Fuhrhop, J.-H. *J. Am. Chem. Soc.* **1994**, *116*, 11969.

Table 3. ^{1}H NMR Data of Gluconamide Derivatives[a]

	compound								
	1	**2a**	**3**	**4**[b]	**5**	**7**	**12**	**14**	**11**
2-H	3.956	2.994	4.021	(4.176)	3.952	3.945	3.609	3.607	4.159
3-H	3.877	3.900	3.957	(4.067)	3.844	3.831	3.761	3.758	4.279
4-H	3.440	3.582	3.606	(3.492)	3.456	3.448	3.264	3.285	3.740
5-H	3.462	3.819	3.860	(3.875)	3.669	3.657	3.426	3.641	4.342
6-H	3.558	4.420	4.467	(4.326)	4.177	4.158	3.548	4.171	4.563
6′-H	3.348	4.205	4.265	(4.063)	3.909	3.916	3.317	3.880	4.271
J_{2-3}	3.60	4.20	4.00	(3.65)	3.90	4.10	5.95	6.10	1.50
J_{3-4}	2.30	2.50	2.40	(2.35)	2.70	2.55	2.40	2.15	
J_{4-5}	8.50	8.50	8.45	(8.50)	8.20	8.35	8.30	8.55	
J_{5-6}	2.80	2.55	2.35	(2.45)	2.65	2.55	3.25	2.40	6.25
$J_{5-6'}$	5.50	6.15	6.35	(7.10)	6.85	6.35	6.20	6.75	7.05
$J_{6-6'}$	11.20	11.35	11.25	(14.20)	11.30	11.30	11.05	11.35	11.85

[a] Spectra were recorded in DMSO-d_6 after addition of a small amount of D_2O. Chemical shifts and *J*-couplings were checked by simulation with GeNMR (ref 41). [b] Solvent CD_3OD instead of DMSO-d_6.

Table 4. Comparison of the Coupling Constants of the Carbohydrate Skeleton Protons of Gluconamide Derivatives in Different Solvents

	2a			**6**			**12**		
	DMSO-d_6	CD_3OD	D[a]	DMSO-d_6	CD_3OD	D[a]	DMSO-d_6	CD_3OD	D[a]
J_{2-3}	4.20	3.70	0.50	3.90	3.20	0.70	5.95	5.55	0.40
J_{3-4}	2.50	2.40	0.10	2.70	2.40	0.30	2.40	2.40	0.00
J_{4-5}	8.50	8.40	0.10	8.20	8.40	0.20	8.30	8.20	0.10
J_{5-6}	2.55	2.40	0.15	2.65	2.50	0.15	3.25	3.25	0.00
$J_{5-6'}$	6.15	5.85	0.30	6.85	6.30	0.55	6.20	5.95	0.25
$J_{6-6'}$	11.35	11.55	−0.20	11.30	11.35	−0.05	11.05	11.10	−0.05

[a] $D = J$ in DMSO-d_6 − J in CD_3OD.

C^2 methoxy derivatives **12** and **14** and the methylene protected derivative **11** were also measured. To simplify the coupling patterns, the hydrogen atoms of the hydroxyl groups were exchanged by deuterium through addition of D_2O.

The proton signals and *J*-couplings of **2**−**5**, **7**, **11**, **12**, and **14** are listed in Table 3. Examination of the *J* values shows that for all compounds J_{3-4} is between 2.1 and 2.7 Hz and J_{4-5} is in the range of 8.2−8.6 Hz. In the literature,[13,29] the J_{3-4} and J_{4-5} coupling constants for **1** in DMSO-d_6 have been reported to be 3.40 and 3.00 Hz, respectively, on the basis of NMR simulations,[13,29] leading to the conclusion that the molecule has a sharp bend at C^4 giving it a so-called $_4G^+$ conformation.[13] From our measurements and simulations[41] with compound **1** in DMSO-d_6, we obtained different values for the *J*-couplings, viz., $J_{3-4} = 2.30$ Hz and $J_{4-5} = 8.50$ Hz, which are more in line with those found for the ester and imidazole derivatives (**2**−**5**, **7**). According to our measurements and calculations based on the values of J_{3-4} and J_{4-5}, the percentage *anti* conformation[42] (explanation below) for the H−C^4−C^5−H bond is such that it results in only a very small bend at C^4, which is in contrast with the above-mentioned $_4G^+$ conformation model suggested in the literature.[13] We also note that the J_{2-3} (3.60 Hz) value is slightly smaller than the value previously reported[13] for **1** (J_{2-3} 4.50 Hz), but this may be due to an effect of the added D_2O. Since the solvent may have a strong influence on the conformation of the gluconamide, we measured the ^{1}H NMR spectra of **2a**, **5**, and **12** in CD_3OD also. Except for the J_{2-3} coupling constant, we did not observe any significant difference in *J*-couplings between the samples measured in DMSO-d_6 (with a small amount of D_2O) and those measured in CD_3OD, see Table 4. The gluconamide group is a flexible moiety and therefore not amenable to a strict determination of the dihedral angles between adjacent hydrogen atoms using the modified Karplus relation described by Altona.[43] As, however, there is a difference in vicinal *J*-coupling when the hydrogen atoms are in the *syn* or in the *anti* position, it is possible to make a rough estimate of the percentages of *anti* conformations (P_{anti}) present in the molecules, using eq 1.[44]

$$\text{anti} = \frac{J_{obs} - (J_{60°} + J_{-60°})/2}{J_{anti} - (J_{60°} + J_{-60°})/2} \qquad (1)$$

The results of these calculations are presented in Table 5. It is clear from this table that substitution on C^6 (compare **1**, **2**, **4**, and **5**) does not lead to large deviations in the overall conformation of the glucon unit. This confirms the hypothesis that, despite C^6 substitution, the conformation of the carbohydrate part of the headgroup is only slightly affected. Hence, the packing of the gluconamides in the aggregates must in principle be similar for the unsubstituted (**1**) and the C^6-substituted compounds. In the case of the larger aromatic substituents (**2a** and **3**), however, additional $\pi-\pi$ stacking interactions may play a role, as discussed above. The C^2 methoxy derivative **12** shows an increase in the percentage *anti* conformation around C^2-C^3. This means that a large bend is present in the carbohydrate headgroup at C^2 (the larger P_{anti}, the bigger the bend), which reduces the overall length of the molecule. This decrease in length is also observed in the powder diffractograms (see below).

(41) GeNMR NMR simulation program: Budzelaar, P. H. M. *IvorySoft;* Amerbos 30, NL-1025 ZV Amsterdam, The Netherlands.

(42) A dihedral angle between vicinal hydrogen atoms of 180° corresponds to 100% *anti* position, see ref 29.

(43) Haasnoot, C. A. C.; Leeuw, de F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783.

(44) Hoffman, R. E.; Rutherford, T. J.; Mulloy, B.; Davies, D. B. *Magn. Res. Chem.* **1990**, *28*, 458.

Table 5. Observed Vicinal *J*-Couplings in DMSO-d_6 and Calculated *J*-Couplings According to the Modified Karplus Relation[a]

	substituent		J_{obs} (Hz)	60°	180°	−60°	P_{anti} (%)
1	none	J_{2-3}	3.60	0.54	9.57	4.02	18
		J_{3-4}	2.30	4.03	9.72	0.54	0
		J_{4-5}	8.50	2.27	9.57	2.29	85
		J_{5-6}	2.80	0.90	10.68	5.02	0
		$J_{5-6'}$	5.50	3.07	10.68	2.84	33
2a	C^6 benzoyl	J_{2-3}	4.20	0.54	9.57	4.02	26
		J_{3-4}	2.50	4.03	9.72	0.54	3
		J_{4-5}	8.50	2.27	9.58	2.29	85
		J_{5-6}	2.55	0.90	10.68	5.02	0
		$J_{5-6'}$	6.15	3.07	10.68	2.84	41
4	C^6 imidazolyl	J_{2-3}	(3.65)[b]	0.54	9.57	4.02	19
		J_{3-4}	(2.35)[b]	4.03	9.72	0.54	1
		J_{4-5}	(8.50)[b]	2.24	9.42	2.30	87
		J_{5-6}	(2.45)[b]	1.58	10.96	4.53	0
		J_{5-6}	(7.10)[b]	2.59	10.96	3.52	51
5	C^6 acetyl	J_{2-3}	3.90	0.54	9.57	4.02	22
		J_{3-4}	2.70	4.03	9.72	0.54	6
		J_{4-5}	8.20	2.27	9.58	2.29	81
		J_{5-6}	2.65	0.90	10.68	5.02	0
		J_{5-6}	6.85	3.07	10.68	2.84	50
12	C^2 methoxy	J_{2-3}	5.95	0.67	9.66	3.96	49
		J_{3-4}	2.40	4.03	9.72	0.54	2
		J_{4-5}	8.30	2.27	9.57	2.29	83
		J_{5-6}	3.25	0.90	10.68	5.02	4
		$J_{5-6'}$	6.20	3.07	10.68	2.84	42

[a] See ref 43. The percentage *anti* conformation (P_{anti}) was calculated with eq (1). [b] Spectrum recorded in CD_3OD.

The major *d*-spacing for **12** is 1.8 Å smaller than the spacing for **1**.[45] The aggregate structure of **12** appeared to be solvent dependent (vide infra). A possible explanation is that solvent molecules are incorporated in the superstructures. This is feasible because the packing of the amphiphiles is relatively loose due to the large bend at C^2.

X-ray Powder Diffraction. X-ray powder diffraction (XRD) experiments were carried out to relate the measured periodicities to the lengths of the gluconamide derivatives and in particular to decide if the molecules in the gels were packed in a head-to-head or head-to-tail manner (Figure 9). Estimates for the lengths of the gluconamide derivatives were obtained by the molecular modeling program Quanta-Charm, starting from the coordinates of the crystal structure of **1**,[12] varying the $C^6(H^6)-O^6(C=O)$ torsion angle, and using the maximum values obtained after these variations as the predicted *d*-value (Table 6).

Fuhrhop and co-workers[13a] have shown that **1** can adopt more than one rigid conformation, depending on the preparation of the sample. Whereas lyophilized **1** seems to display a head-to-head packing of the molecules (d = 36 Å),[13a] a head-to-tail packing (d = 17.9 Å) is observed upon crystallization from methanol,[13a] in line with the crystal structure.[12] In the present work, we found that organogels of **1** in pyridine[46] and in 1,2-xylene have head-to-head packings (*d*-spacings of 36.2 and 35.9 Å, respectively), whereas our powder diffraction studies on lyophilized **1** revealed a head-to-tail packing[47] (see Table 6, entries 1−3). On the basis of our XRD and EM studies, we propose that the packing of **1** is solvent dependent. It is a remarkable fact that most of the gels prepared from gluconamides with substituents on C^6 are packed in a head-to-tail manner (Table 6). There is an analogy with the behavior of the corresponding galactonamides: the lyophilized aqueous gel of the nonsubstituted derivative **16** showed a head-to-head packing, whereas the benzoyl-substituted compound **17** displayed a head-to-tail packing.

The pyridyl ester **3** and the imidazole gluconamide derivative **4** are packed in head-to-head geometries. These head-to-head packings may be a result of the

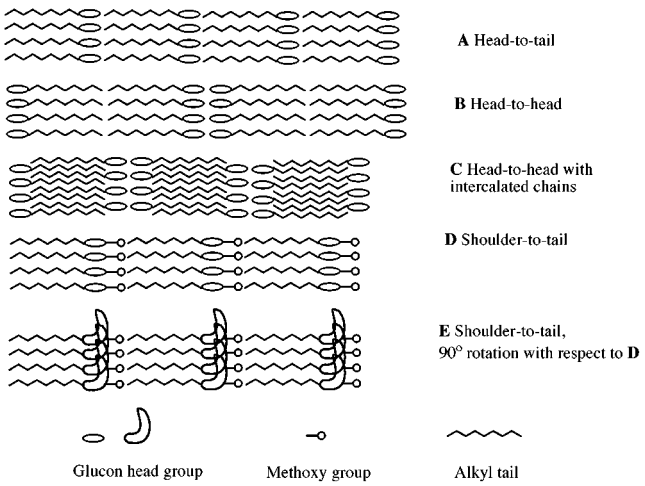

Figure 9. Several packing arrangements of amphiphilic gluconamides: (A) head-to-tail; (B) head-to-head; (C) head-to-head with intercalated chains; (D) and (E) shoulder-to-tail packing as proposed for the C^2 methoxy gluconamide **12**. D and E are different projections in which the layers are rotated by 90°.

Table 6. *d*-Spacings for Gluconamide Derivatives Which Gelate in Organic Solvents[a]

compound	substituent	predicted monolayer thickness (Å)	measured periodicity (Å)
1	none	17.9	16.1[b]
1 (pyridine)	none	17.9	36.2
1 (1,2-xylene)	none	17.9	35.9
2a (ethanol)	C^6 benzoate	24.7	(24.3)[c]
2a (chloroform)	C^6 benzoate	24.7	23.3
2a (1,2-xylene)	C^6 benzoate	24.7	24.4
2b	C^6 benzoate	34.9	31.6
3	C^6 3-pyridyl-carboxylate, ester	23.0	43.2
4	C^6 imidazolyl	21.1	26.3
5	C^6 acetate	21.8	21.3
6	C^6 octanoate	29.4	27.5
7	C^6 cyclohexanoate	25.1	24.0
12	C^2 methoxy	17.9	16.0
16[d]	none	37.0[e]	37.2[b]
17[d]	C^6 benzoate	25.3	23.9

[a] Predicted values were calculated with Quanta-Charm starting from the crystal structure of **1** (see text). The measured values were obtained from powder diffraction measurements (XRD). [b] Lyophilized from the gel in water. [c] Recrystallized from EtOH. [d] Galactonamides. [e] Value obtained from ref 13.

(45) *d*-Spacing for **1** as obtained from the crystal structure, 17.9 Å; for **12** as obtained from a rapidly dried gel in benzene (see also Table 6).

(46) The gel in pyridine is only formed at low temperatures <0 °C and at concentration >10% w/v.

(47) The gel was rapidly freeze-dried in a vacuum desiccator over P_2O_5.

Table 7. Wavenumbers (cm^{-1}) for the Hydroxyl Group and Amide IR Absorptions of Gelating Gluconamide Derivatives in the Solid State (KBr), Gel State, and Dioxane Solution

		hydroxyl groups				amide bonds	
1	KBr	3532	3389	3358	3314	1646	1528
	1,2-xylene gel	3508		3327		1654	1545
	solution[a]					1669	1527
4	KBr	3500	3424	3366		1646	1541
	chloroform gel		3375	3323		1635	1550
	solution[a]					1674	1532
12	KBr		3416	3348	3248	1656	1564
	1,2-xylene gel		3408	3341	3282	1655	1564
	solution[a]					1676	1530
2a	KBr	3521	3446	3368	3309	1631	1552
	1,2-xylene gel	3512	3439	3355	3270	1633	1544
	toluene gel	3509	3449	3355	3160	1643	1548
	chloroform gel	3510	3444	3361	3246	1626	1548
	solution[a]					1678	1531

[a] In dioxane.

presence of water molecules, which link the nitrogen atoms of the pyridyl and imidazolyl groups in two successive layers. We have observed such intercalating water molecules in the crystal structure of the corresponding bis-methylene protected compound **11**.[36] The imidazole compound **4** probably forms bilayers in which the alkyl chains are interdigitized (Figure 9C). This can be concluded from the measured periodicity, which is larger than the predicted thickness of a monolayer but smaller than the thickness of a bilayer (Table 6). As an alternative explanation for this periodicity, tilting of the monolayers may be considered. We think that bilayers with interdigitizing alkyl chains are more likely, however, as such bilayers were also found to be present in the crystal structure of the imidazole gluconamide **11**.[36]

The periodicity measured for the C^2-methoxy gluconamide **12** suggests that the molecules of this compound are arranged in a head-to-tail packing (Table 6). From the NMR study we know, however, that a large bend is present in the molecule at C^2, which will affect the packing. We believe, therefore, that molecules of **12** are packed like spoons in a box and that the methyl groups of the methoxy substituents are touching the tails of nearby layers (see Figure 9). This packing is more likely than a packing in which the C^6 ends of the headgroups touch the termini of the alkyl chains. We propose the name "shoulder-to-tail" packing for this type of arrangement of the molecules.

IR Experiments. The observation that the methylene-protected gluconamides **8**−**11** do not form gels (see Gelation Behavior) suggests that an intermolecular hydrogen-bonding network is necessary for gel formation. The possible existence of such a network in the gels was investigated by FT-IR spectroscopy. The wavenumbers of hydroxyl functions, the amide groups, and the ester groups of compounds **1**, **2a**, **4**, and **12** in the gel state were compared to those in solution and in the solid state (crystalline compound or powder). The results are compiled in Table 7.

The ν(O−H) peaks of compounds **2a** and **12** in the gel state were relatively sharp and even sharper than those in the solid samples, whereas the ν(O−H) peaks of **1** and **4** were relatively broad, resembling the solution spectra. This indicates that the H-bonding network in the case of compounds with a head-to-tail packing, **2a** and **12**, is more defined in the gels than in the solid state. There appears to be no well-defined H-bonding network involving the hydroxy groups in gels of compounds with a head-to-head packing (**1** and **4**). The positions of the amide peaks in the spectra measured in solution were almost identical for all compounds, including **12**, which has an amide function located next to a bulky substituent, viz., the methoxy group on C^2. We conclude that differences in absorption or frequency between the solution and the solid or gel state can be attributed to differences in hydrogen-bonding patterns.

When going from the solid (crystalline) state to the gel state (1,2-xylene), the amide I band of **1** shifted to a higher wavenumber, whereas it remained in the same position for the benzoate **2a** and the methoxy derivative **12**. This reflects the packing as determined by XRD, which is always head-to-tail for **2a** and **12** but changes from head-to-tail in the solid state to head-to-head in the gel for **1**. The IR spectra show that in the latter case the amide carbonyl band is stronger due to a weaker hydrogen bond. The amide I vibration of imidazolyl compound **4**, however, which was shown by XRD to be packed in a bilayer with interdigitized alkyl chains, shows a shift toward a *lower* wavenumber when going from the solid to the gel state, together with a shift to a *higher* wavenumber for the amide II band. This suggests that a change in hydrogen-bonding partners for the carbonyl and N−H in the amide functionality occurs, resulting in stronger and weaker H bonds for the carbonyl and N−H, respectively, in the gel.

The wavenumbers of both the amide I and II bands for **1** increase when going from the solid to the gel states, which indicates a change in hydrogen-bonding pattern resulting in stronger and weaker hydrogen bonds to the carbonyl and N−H functions, respectively. The value for the gel is the same as that reported[13] for **1** packed in bilayers in lyophilized fibers. A similar situation exists for **2a**, where the wavenumber for the amide II band in the gel state is lower than that in the crystalline state but still considerably higher than that in solution. This suggests that the N−H group in the gel state is involved in a weaker H bond than in the solid state, while the strengths of the H bonds to the carbonyl group in the gel and the solid state are the same. It is possible that the carbonyl groups in the gel state and the solid state do not form H bonds with the amide N−H functions. Instead, one of the hydroxyl groups of an adjacent molecule may function as a hydrogen-bond donor to the amide carbonyl group. Unfortunately, we do not have further support for this hypothesis.

The wavenumbers of the amide I and II bands in compound **12** (C^2 methoxy) are similar for the gel state and the solid state, indicating a related packing. Powder diffraction and ^{1}H NMR suggested that the molecules are in an unusual "head-to-shoulder" monolayer packing. However, the amide I wavenumbers are more comparable to those of a bilayer arrangement (cf. Table 7, compound **1** in the gel state and **1** in the solid state). The high value for the wavenumber of the amide II band of **12** is remarkable, especially when its position is compared with that in other spectra of samples for which packing in monolayers is proposed, viz., **1** in the solid state, and that of **2a** in the gelated state. The wavenumbers of the amide II band in solution are similar for all of these compounds,

which means that the differences have to be induced by the different orderings. The strong bend causing the unusual head-to-shoulder packing of **12** may prohibit an ordering of the amide functions as observed for **2a**. The packing is less tight than the head-to-head packing of **1** in the gel state.

Surprisingly, the IR frequencies of the gluconamides in the gel state depend on the type of solvent in which the gel is made. For instance, in the case of **2a**, the difference in wavenumbers of the amide I bands of the gel in chloroform and in toluene is substantial (see Table 7), although the suprastructures formed from **2a** in these solvents appear to be the same by TEM. The ester carbonyl vibration for **2a** shows a splitting in chloroform (1727 and 1702 cm^{-1}), which is absent in toluene (1717 cm^{-1}), suggesting that in the former gel more than one packing arrangement of the gluconamides is present. In one of the packing geometries, the ester probably is in a non-H-bonded arrangement, because the value of one of the wavenumbers is close to that in dioxane solution (1722 cm^{-1}). The splitting of the ester vibrations is also observed in the solid state, which suggests that the fibers in the gel have a similar packing as in the solid state.[48]

Discussion

The formation of gels from the gluconamides presented here is a fascinating phenomenon, especially if one realizes that this process occurs at concentrations as low as 1% w/v. Molecular dynamics calculations which we carried out using the Quanta-Charm program revealed that only 24 chloroform molecules can make close contact with **2a**, forming a 4 Å shell around the gelator. In a 1% w/v gel of **2a** in chloroform, the ratio of solvent to gelator molecules, however, is over 500. Apparently, not all solvent molecules have to be in close contact with the gelator for solvent gelation to occur.[49]

With exception of the *n*-octylate derivative **6**, all gluconamides that produce gels form fibers with a high aspect ratio. These fiber structures are found throughout the gel. Sometimes the same types of texture are formed in a variety of solvents, as shown for the benzoate derivative **2a**. In other cases, the textures very much depend on the solvent, as in the case of compound **1**, which forms helical fibers in water,[3] multilayered sheets in 1,2-xylene,[6] and rodlike structures in pyridine. The failure of the *n*-octyl mannonamide, gulonamide, or talonamide to produce chiral structures in gels in 1,2-xylene has been ascribed to a lack of solvation of the carbohydrate groups.[6a] The carbohydrate part of the benzoate derivative **2a** is probably also shielded from the solvent, because in the gels in chloroform, ethyl acetate, ethanol, and 1,2-xylene, no helical but whisker-type fibers are formed. Such whisker-type fibers have also been described in the literature.[50]

Comparing the aggregation behavior of the C^6-substituted gluconamides, we may conclude that the size and, more importantly, the shape of the substituent determine the transfer of chirality from the molecular to the supramolecular level. Gluconamide moieties form hydrogen bonds, which normally force the molecules to adopt a chiral packing,[3,6,8,11,12] even in the case of a substituent at C^6. When the C^6 substituents are aromatic groups, however, $\pi-\pi$ interactions may partly overrule the hydrogen-bonding scheme, resulting in a loss of the chirality of the assembly. The imidazole group in compound **4** is probably too small to display strong $\pi-\pi$ interactions, and the carbohydrate moiety can still direct the aggregation pattern, resulting in chiral suprastructures. Aliphatic substituents such as the acetyl group in **5** and the cyclohexanoyl group in **7** cannot give $\pi-\pi$ stacking, and hence the carbohydrate moiety regulates the aggregation process, resulting in chiral assemblies. Compounds with a C^6 substituent (**2a**, **4**, and **5**) yield aggregates of which the structure is not controlled by the type of solvent. Compounds without a C^6 substituent (**1** and **12**) form solvent-dependent-type aggregates. A possible explanation for this behavior is that in the latter case solvent molecules are incorporated in the aggregates, whereas in the former case the aggregates are free of solvent.

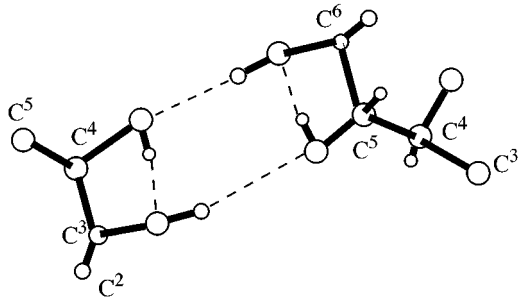

Figure 10. Representation of a four-membered homodromic H-bond cycle found in the crystal structure of compound **1**.[12]

DSC measurements showed that the type of solvent has a larger effect on the ΔH of gelation than the type of gelator. Although the types of aggregates that are formed are the same for each solvent, indicating that the cohesive forces that lead to the supramolecular structures are independent of the solvent, the heat transfer and the gelation temperature are dependent upon the solvent and not on the gelator. The energy transfer measured therefore is a gain in entropy and not an enthalpy effect. We may conclude that the formation of the organogels is a process which is determined by the entropy.

As shown above, IR spectra, in particular in the region of the OH stretching vibrations, can give valuable information on the packing of the gluconamide molecules in the gel state. This information cannot always be obtained from the amide vibrations. The differences in amide wavenumbers are relatively small for the various systems (Table 7b), and the peaks do not sharpen up going from the solution to the gel state. The trends in the shifts, however, can help clarify variations in the hydrogen-bond patterns in the gel and solid state and can provide insight in the way the molecules are packed, e.g., head-to-head, head-to-tail, or shoulder-to-tail.

From the crystal structure of **1**,[12] it is known that this molecule forms (homo)dromic hydrogen-bond cycles which involve the hydroxyl groups on the carbon atoms C^6, C^5, C^4 and C^3. These cycles extend within the layers (see Figure 10). After substitution with an ester or imidazole function, the compound lacks the hydroxyl on the C^6 atom

(48) Crystal structures that have been solved include *N*-*n*-octyl-D-gluconamide **1** (see ref 11), *N*-*n*-dodecyl-D-gluconamide (see Vollhardt, D.; Gutberlet, T.; Emrich, G.; Fuhrhop, J.-H. *Langmuir* **1995**, *11*, 1, 2661), and *N*-trideca-5,7-diyne-D-gluconamide (see André, C.; Luger, P.; Fuhrhop, J.-H. *Carbohydr. Res.* **1994**, *230*, 31).

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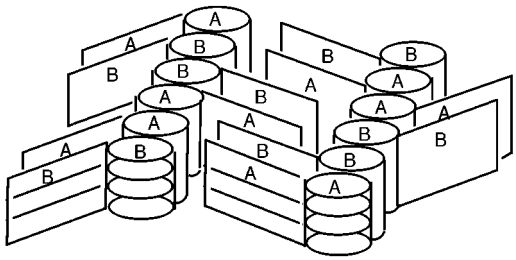

Figure 11. Crystal packing of the 6-deoxy-*N*-*n*-alkyl-D-gluconamide molecules.

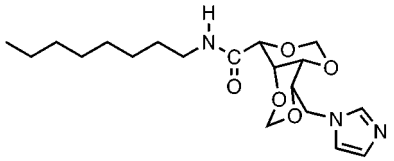

Figure 12. Schematic drawing of the *cis*-decalin structure in 6-deoxy-6-(*N*-imidazolyl)-2,4;3,5-dimethylenegluconamide.

and is no longer able to form such hydrogen-bond cycles. In *N*-*n*-octyl-6-deoxy-D-gluconamide, in which the terminal CH_2OH is converted into a CH_3 group, a homodromic hydrogen-bond cycle cannot be formed either. This molecule contains hydrophobic CH_3 groups on both ends and therefore is comparable to the organogel-forming compounds **2**−**7**. The crystal structure of this deoxy gluconamide has been reported.[51] It appears to crystallize in a packing that deviates from the normal head-to-head or head-to-tail arrangement. The asymmetric crystal consists of molecules with two significantly different conformations (A,B). The headgroups are packed in a AABBAABB fashion, whereas the tails are packed in a ABABABAB manner (see Figure 11). Although a similar type of packing may be expected for our molecules, XRD showed that **2**−**7** pack differently (see Table 6). Powder diffraction, ^{1}H NMR, and IR experiments have revealed that one of the gluconamides (**12**) described in this paper exhibits another yet unknown type of packing, viz., a shoulder-to-tail packing.

The head-to-tail packing of the amphiphiles in the aggregates is quite unusual.[12,52] Gluconamide **1** shows in the crystalline state a head-to-tail packing, but this is changed into a head-to-head packing in the gel state (both in water and in organic solvents).[13] This kind of rearrangement is also known for the thermotropic liquid crystalline (LC) system since *N*-*n*-undecyl-D-gluconamide also changes to a head-to-head packing in the smectic phase.[53] Upon entering the LC phase,[54] the gluconamide molecules are proposed to retain a "core" of stacked alkyl chains rather than a network of hydrogen-bonded carbohydrate moieties.[55] A study of the thermotropic LC properties of the C^6-substituted gluconamides would have been of interest to get more insight in the binding interactions of the head-to-tail packed molecules, because **2a**, **2b**, and **5**−**7** retain their head-to-tail packing in the supramolecular aggregates. Unfortunately, **2a** and **5**−**7** exhibited no thermotropic LC behavior. For comparison, the longer-chain derivative **2b** was also tested, but this compound showed no thermotropic LC behavior.

The compounds with the protected hydroxyl groups (**8**−**11**) do not show gelation behavior. This may be explained by the fact that the hydrogen-bonding capacities of the sugar headgroups are removed and probably also the fact that there is no rotational freedom around the C^2−C^3, C^3−C^4 or C^4−C^5 bonds. The headgroups in **8**−**11** are more or less fixed in a *cis*-decalin structure (see Figure 12). Glycocholic acid derivatives also contain a *cis*-decalin structure and are reported to form micelles upon dispersion in water.[56] These molecules do not give gels. Cholesterol derivatives, on the contrary, have a *trans*-decalin structure and exihibit strong gelation behavior.[17] This *trans*-decalin structure is more flat than that of *cis*-decalin and therefore will lead to a better packing of the molecules. This may explain why compounds **8**−**11** do not form organogels and cholesterol derivatives do.

The gluconamides with a methoxy group on C^2 and an additional group on C^6 (**13** and **14**) are readily soluble in, e.g., chloroform, ethyl acetate, and 1,2-xylene, without any gelation upon cooling. The lack of formation of organogels by the compounds that have their C^2 hydroxyl groups blocked is probably due to a strong bend in the headgroup caused by the methoxy group at C^2. This strong bend may prevent the tight packing needed for aggregation in organic solvents. The exceptional behavior by compound **12** (C^2 methoxy and C^6 hydroxyl), which forms a gel, is not yet fully understood.

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Supporting Information Available: Full syntheses and characterizations of compounds, including subjective NMR assignments (30 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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