A carbene-modified carbohydrate amphiphile as new low-molecular mass gelator for organic solvents
Gunnar Bühler, Martinus C. Feiters, Roeland J. M. Nolte, Karl-Heinz Dötz

In recent years the interest in molecules that form supramolecular structures by self-assembly via non-covalent interactions has increased considerably. The formation of such supramolecular aggregates may give 3-dimensional networks, which can lead to solvent gelation. In contrast to macromolecular networks these supramolecular aggregates can be disintegrated easily by adding a co-solvent, application of mechanical stress, or heating, because no chemical bonds need to be broken.

The work of Fuhrhop and others has shown that amphiphiles bearing a polar carbohydrate headgroup connected to an alkyl chain by an amide functionality can form various supramolecular aggregates in aqueous media. Some derivatives of this type of alkyl aldonamides are excellent gelators for a variety of organic solvents.

Our ongoing interest in carbohydrate-functionalized transition metal carbene complexes prompted us to synthesize pentacarbonyl[\(\text{D-gluc-o-hex(N-octylamino)-1-yldien}\)]chromium 4 (scheme 1), the closest organometallic analogue of \(N\)-octyl-D-gluconic amide.

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\text{Scheme 1. Synthesis of glucose-based chromium carbene complex 4}
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The pentacarbonyl chromate adds to the pentaacetylated gluconic acid chloride to form an anionic acyl complex which undergoes subsequent O-methylation to form carbene complex 3. The aminocarbene complex 4 is formed by aminolysis followed by deprotection under basic conditions (see experimental part). Only the Z-isomer is formed with regard to the restricted rotation about the carbene carbon-nitrogen bond, as was confirmed by comparison of NMR data of 4 with studies published by Fischer.

The exchange of the carbonyl-oxygen atom in \(N\)-octyl-D-gluconic amide, which tends to play an important role in the aggregation of the organic analogue, for the bulky, apolar pentacarbonylchromium-fragment leads to an increased solubility of the resulting carbene complex 4 in organic solvents; on the other hand 4 is almost insoluble in water.
Furthermore the exchange does, however, not affect the ability of 4 to gelate organic solvents. Metal carbene 4 forms gels upon heating (70–75°C) followed by cooling to room temperature within several minutes in chloroform, dichloromethane, benzene, toluene and mixtures of this solvents. The yellow gels in chloroform are more or less turbid, depending on the concentration of 4, which ranges from 0.35 to 1.3 wt%, and the cooling rate. If the solutions are cooled rapidly (see experimental part), turbid gels are formed within a few seconds, if cooled slowly the gels appear clear. At higher concentrations some non-dissolved solid remains in the gel. The gels formed in chloroform are quite stable towards mechanical agitation and no visible change could be determined after storage for several weeks at room temperature. The gel-to-solution phase transition temperatures (Tgel) of gels formed upon slow cooling were determined using the “falling ball method”[6] (see experimental part) for various concentrations and are shown in table 1. The Tgel values observed for rapidly cooled, turbid gels were about 5-10°C lower. The gels of 4 in benzene and toluene at concentrations of about 1 wt% are not very stable against mechanical agitation and sometimes precipitation with loss of gelation was observed within several hours. With the addition of chloroform to benzene or toluene (wt/wt up to 1:4 chloroform:benzene/toluene) more rigid gels are formed at concentrations starting from 0.5 wt%. Again these yellow gels are more or less turbid (vide ante), depending also on the concentration of 4 and the amount of chloroform. The Tgel values are listed in table 1, again slowly cooled gels are more stable. Even without heating, the solvent mixtures (wt/wt 1:1 chloroform:benzene/toluene) are gelled on standing over night at room temperature while most of compound 4 remains undissolved. These clear gels appear only slightly yellow due to the low concentration of 4 and are less stable against mechanical agitation than heated samples of higher concentrations.

<table>
<thead>
<tr>
<th>Solvent(mixture)</th>
<th>Tgel at 1wt%</th>
<th>Tgel at 0.7wt%</th>
<th>Tgel at 0.5wt%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHCl₃</td>
<td>48-54⁷</td>
<td>45-51</td>
<td>30-32</td>
</tr>
<tr>
<td>CHCl₃/C₇H₈ 1:1</td>
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<tr>
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<td>68</td>
<td>53-54</td>
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</tr>
<tr>
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<td>no gel</td>
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<tr>
<td>CHCl₃/C₇H₈ 1:3</td>
<td>63-67</td>
<td>57-59</td>
<td>no gel</td>
</tr>
</tbody>
</table>

Table 1: Tgel values for various solvent(mixtures) at various concentrations

a) wt/wt, b)1.3 wt%

Electron microscopy (SEM and TEM) can be applied to dried samples of gels of 4 without metal shadowing or sputtering because the electron density of chromium provides enough contrast. In all samples of the mentioned gels the micrographs show dense networks of long fibres, which explains the gel’s rigidity. In TEM micrographs of Pt-shaded (shadowing at an angle of 45° allows the heights of the aggregates to be determined) samples prepared from gels in chloroform and dichloromethane the aggregates appear to be flat with a maximum height of about 13 nm, but most of the tape-like fibres do not show a shadow at all, indicating that the heights of the aggregates is less than the resolution of the TEM (< 3-4 nm). Furthermore the height of the
aggregates is independent of width, which varies from 16 nm to more than 200 nm (figure 1A). Micrographs of an aged gel (2 weeks at 4°C) showed identical structures. TEM micrographs of gels of 4 in mixtures of benzene or toluene and chloroform (various concentrations and amount of chloroform, with or without Pt-shadowing at 45°) reveal the presence of long hollow tubules, which are mostly linear but could also be strongly bent (figure 1C). The tubules appeared to be flat probably due to a loss of solvent from the inner space under vacuum conditions. The diameter of the tubules varies from 80 nm to 120 nm. Furthermore tube-like aggregates can be seen in combination with rolled-up flat layers as tubules pre-stages (figure 1D,E). SEM micrographs of gel samples (Au/Pd sputtering, figure 1B) confirm the existence of dense networks. On some samples drop-like aggregates as centres of fibres can be seen, in which the aggregates cover large areas with a dense, cloth-like film. Electron micrographs of gels of 4 in pure benzene or toluene could not be obtained due to their limited mechanical stabilities.

Figure 1: A) TEM, gel in CHCl₃, 0.78 wt%, Pt-shadowing at 45°, bar is 2 μm; B) SEM, gel in benzene/chloroform 1:1, 0.71 wt%, bar is 1μm; C) TEM, gel in toluene/chloroform 1:1, 0.74 wt%, bar is 500 nm; D) TEM, gel in benzene/chloroform 1:3, 0.89 wt%, bar is 400 nm; E) SEM, gel in toluene/chloroform 1:1, 0.74 wt%, Pd/Au sputtering, bar is 200 nm.

All reported gels are thermo reversible as checked by several heating-cooling cycles between 75°C and room temperature. After addition of a suitable solvent (here methanol) the gels were disintegrated and no indication of decomposition of 4 was seen in IR-spectra of the resulting solutions.
In a series of temperature dependent CD-experiments on a $4 \times 10^{-3}$ M gel in chloroform a thermoreversible CD-effect was detected (figure 2). At temperatures below $T_{gel}$ the effect was strong whereas it disappeared gradually on heating to about 50° C. After the third heating cycle a change of sign was observed from positive to negative as the effect reappeared gradually on cooling the sample. This could be an indication of the formation of chiral supramolecular structures, for example curved mono- or bilayers that are formed from the flat fibres observed by electron microscopy in this solvent. At higher temperatures these ordered structures were destroyed. A similar change of sign has been reported previously by Shinkai et al. for azobenzene-appended cholesterol derivatives and was found to depend on the cooling speed of heated solutions of the gelator molecule.\[7\]

Figure 2: top panel: CD, lower panel UV-VIS: a) originally prepared gel at 25° C; b) after heating to 50° C; c) after cooling to 25° C; d) after 2nd heating to 55° C and cooling to 25° C.

Temperature dependent $^1$H-NMR experiments of gels in CDCl$_3$ (0.7 wt%), CD$_2$Cl$_2$ (0.8 wt%) and a mixture of CDCl$_3$/C$_6$D$_6$ (1:1, 0.8 wt%) showed a strong broadening of all signals at room temperature, including the solvent signal. With increasing temperature the width of all signals decreased more or less. At temperatures slightly below the boiling point of the solvent some signals of the alkyl chain and the solvent were well resolved, whereas all other signals kept a strong broadening. Even though all samples appeared as clear solutions at this temperatures and spinning conditions, this suggests that even at high temperatures molecules are still aggregated, but with lower order as indicated by the free rotation of the alkyl chains.
IR-spectra of solutions of 4 in methanol show three carbonyl absorption bands with peaks at 2053 cm\(^{-1}\) (\(A_1\)), 1968 cm\(^{-1}\) (\(B_1\)) and a broader band at 1930-1920 cm\(^{-1}\) (\(A_{12} + E\)) that are typical for amino substituted pentacarbonylchromium complexes of formal C\(_{4v}\) symmetry. IR-spectra of chloroform gels of 4 showed two additional strong absorptions at 1889 and 1878 cm\(^{-1}\), the other bands shift to 2055 cm\(^{-1}\) (\(A_1\)), 1976 cm\(^{-1}\) (\(B_1\)) and the broad band sharpens with its peak at 1926 cm\(^{-1}\). With decreasing concentrations of 4 the gels turn to highly viscous fluids and finally to solutions and corresponding IR-spectra showed the gradual decrease of the additional bands (1889 and 1878 cm\(^{-1}\)), while the other bands shifted to end in a solution spectra similar to the above mentioned. Similar results were obtained by heating a gel to 55° C, cooling the sample to caused the additional bands to re emerge (figure 3). Furthermore the absorptions of hydrogen bonded OH- and/or NH- groups (3200 – 3500 cm\(^{-1}\)) disappear with continuous dilution or heating.

The observed effects are probably due to molecular packing on fibre formation, causing a degradation of symmetry with the rotation of the pentacarbonylchromium-moiety around the metal-carbene carbon bond being hindered. Furthermore there is evidence of one or more carbonyl ligand being involved in intermolecular hydrogen bonding, as the effect is depending on the concentration of 4. The observed shifts can be related to reported effects of lewis-acid adducts with carbonyl ligands of metal complexes,[8] though the values are smaller due to weaker interactions with hydroxyl protons.

Figure 3: IR-spectra of a gel in CHCl\(_3\), 1.0 wt% at various temperatures:

a) 25°C; b) 40° C; c) 55°C; 25°C (cooled).
The self-assembly of 4 is probably a result of hydrogen bonding between the hydroxyl groups of the carbohydrate head group, furthermore the proton of the amino substituent is known to have an influence as a hydrogen bond donor-site. X-ray structure analysis would be helpful to find out which hydroxyl groups are possibly involved and to construct a model of aggregation. So far all our efforts to obtain suitable crystals of 4 failed and thus all possibilities for the formation of mono- and/or bilayers must be considered.

In conclusion, we have shown that 4 is an efficient gelator for some organic solvents and solvent mixtures. Different aggregates are formed, depending on the solvent (mixture) and on the cooling-rate. To our best knowledge 4 is the first gelator molecule bearing a transition metal carbon bond to be reported. The implementation of metal centres by direct bonding to a gelator molecule may give access to compounds with interesting properties. Imaginable is the application of such compounds in chemically reactive gels for supramolecular catalysis. The immobilization of the metal centre might facilitate work up and separation processes. In addition a chiral environment formed by supramolecular aggregates could possibly induce stereoselectivity. Further investigations are going on to provide a more detailed insight in the process of self-assembly of 4 and related compounds.

Experimental part:

All metal organic reactions were carried out under argon atmosphere and in dry reaction vessels. All solvents were distilled, dried and stored under argon on mole sieve 4 Å. Silica gel (0.063 – 0.200 mm) was used as stationary phase for column chromatography, which was degassed in vacuum and stored under argon before use.

For the preparation of the gel samples the solvents (quality p.a.) were saturated with argon by pump, freeze and thaw and stored on mole siev 4 Å. About 8 mg of 4 were filled into a screw cap tube and the solvent was added via syringe in an argon filled glove box. The exact concentration was determined by differential weighting. 4 was dissolved by heating in an oil-bath (75°C) or a heat-gun under continuous shaking. Afterwards the samples were cooled down rapidly in an 5°C water bath or slowly in a water bath starting from 60°C by 1°C per minute. The samples for SEM/TEM where left to cool down on air.

For the determination of T_{gel} a glass ball (r=1.5 mm, weight = 36 mg) was placed on the gel surface and the samples were heated in a water bath at 0.3°C per minute. As soon as the ball started subsiding the gel, the corresponding temperature was denoted as T_{gel}. TEM/SEM-experiments were carried out on JEOL-JEM 1010/JEOL-JSM 6330F microscopes. All pictures were taken digitally. For sample preparation carbon coated copper grids (mesh 200 or 150) were laid on the gels surface for a short time followed by drying in vacuum. For this the gel samples were partly destroyed by hardly knocking the tube on the table , to provide a “print” of the inner sphere of the gel. This work was carried out in an argon filled glove box.

The NMR-experiments were carried out on a BRUKER DRX 500. The gels were prepared in the NMR-tubes under argon atmosphere.

The CD-experiments were carried out on a JASCO J-720 Spectropolarimeter. The gel was inserted into a thermo-adjustable 0.2 mm quartz sample cell via syringe.
The synthesis of compounds 1 to 3 has been published previously (see [4a] and references therein).

Pentacarbonyl[D-gluco-hex-(N-octylamino)-1-yliden]chrom 4: In a Schlenk-tube 3 (2.56 g, 4.29 mmol) was dissolved in a mixture of methanol (20 mL) and dichloromethane (20 mL) and cooled to −78 °C. n-Octylamine (0.71 mL, 4.3 mmol) was dissolved in dichloromethane and added via syringe. The reaction mixture was stirred for 0.5 h and heated slowly to −40 °C. At this temperature most of the dichloromethane was removed in vacuum. Afterwards a saturated solution of ammonia in methanol was added (50 mL) and the reaction mixture was left to reach room temperature. After 6 h of stirring the solvent and excess ammonia were removed in vacuum and the resulting brown syrup was purified by column chromatography (silica gel, dichloromethane, change to dichloromethane/methanol 8:1, -5 °C) to provide 4 as a yellow solid (1.04 g, 2.16 mmol, 50 %). ^1H-NMR (CD$_3$OD, 500 MHz): δ = 5.07 (s, 1H), 4.56 (s, 1 H), 3.81 (m, 1 H), 3.92 (t, $^3$J(H,H) = 7.4 Hz, 2 H), 3.79 (dd, $^3$J(H,H) = 10.9 Hz, $^3$J(H,H) = 3.0 Hz, 1 H), 3.71 (m, 1 H), 3.65 (dd, $^3$J(H,H) = 10.9 Hz, $^3$J(H,H) = 5.8 Hz, 1 H), 1.79 (p, $^3$J(H,H) = 7.4 Hz, 2 H), 1.47 (m, 2 H), 1.42 − 1.28 (m, 8 H), 0.92 (t, 3 H) ppm; $^{13}$C-NMR (CD$_3$OD, 125 MHz): δ = 264.59, 223.98, 219.52, 87.82, 76.61, 73.05, 68.89, 64.71, 53.71, 32.92, 30.38, 30.35, 30.23, 27.74, 23.68, 14.81 ppm; FAB-MS: m/z : 371 [M$^+$ - 4 CO].