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Organogel or polymer gel; facilitated gelation of a sugar-based organic gel by the addition of a boronic acid-appended polymer†

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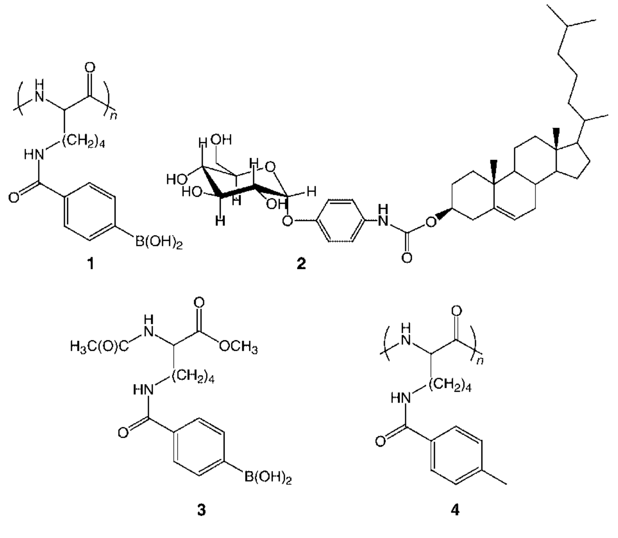
The combination of boronic acid-appended poly(L-lysine) 1 and sugar-based gelator 2 yields a novel organo-polymer gel, consisting of vesicles held together by polymer molecules.

The assembly of certain low-molecular weight compounds (gelators) into complex, three-dimensional networks in which organic solvent molecules are confined, leads to the formation of organic gels.[1] Polymer gels, on the other hand, have three-dimensional structures created by cross-linked covalent bonds.[2] Hence, they are generally more robust than organic gels, however, they lack the characteristic, excellent thermo-reversibility inherent to organogels.[3] Recently, several groups have been able to improve the robustness of hydrogen-bond-based,[3,4] as well as cholesterol-based[5] gels by polymerization of the gelator molecules. Feringa *et. al.*[6] have shown that increased thermostabilization of methacrylate-containing cyclohexane-based gels can be achieved by *in situ* polymerization. In our group, the introduction of multi-point hydrogen bonding sites into cholesterol-based gelators, and the utilization of metal–ligand interactions in sugar-based gelators have resulted in a remarkable stabilization of these gel systems.[7] Moreover, polymerization of a bis(diacetylene)-containing gelator also improves gel stabilization.[3] Thus, combination of polymers with low-molecular weight gelators is a new and interesting concept which can lead to more robust gel systems.

In this paper we show how the gelating capability of cholesterol–saccharide conjugate gelator **2** is facilitated by the addition of boronic acid-appended poly(L-lysine)[8] **1** (Scheme1), in a DMSO–H_2O mixture. Moreover, the formation of the gel is shown to be pH-reversible due to the intrinsic properties of the boronic acid–sugar interaction governing the gelation process. Furthermore, transmission electron microscopy (TEM) images[9] of the gel revealed a remarkably novel superstructure consisting of a network of polymer-coated vesicles, held together by boronic acid-appended poly(L-lysine) molecules. This contrasts with most other gels that show structures consisting of fibrous networks. On the basis of TEM and dynamic light scattering (DLS) measurements, a mechanism for gel formation is proposed.



Scheme 1

Compounds **1** and **2** were synthesized according to literature procedures[7b,8] and utilized to perform the gel test.[10] To a solution of **2** in DMSO (90 μL) was added a solution of **1** in water (20 μL) at pH 11.5 to favor the boronic acid–sugar interaction.[11] After heating, the system was allowed to cool in order to grow the organogel. This procedure was repeated at several concentrations of **2**, maintaining the concentration of **1** constant (1.8 mmol dm^{-3}), which yielded a maximum T_{gel} of 58 ± 3 °C at a concentration ratio of polymer to gelator of approximately 1 : 6 (Fig. 1). In good agreement with these results, a maximum T_{gel} of 62 ± 3 °C was observed, at a polymer to gelator ratio of approximately 1 : 5 by varying the concentration of **1** while maintaining the concentration of **2** constant (10.6 mmol dm^{-3}). Compound **2** has previously been shown to form gels with many solvents.[7b] However, since it did not form a gel in DMSO–H_2O (9 : 2 v/v) in the absence of **1**, the addition of the latter expands the gelation capabilities of **2** to more polar solvents. To investigate the role of both the poly(L-lysine) chain and the boronic acid moiety in the gelation process, reference compounds **3** and **4** were used respectively (Scheme 1).† Gelation tests carried out with **3** or **4** (1.8 mmol dm^{-3}) and

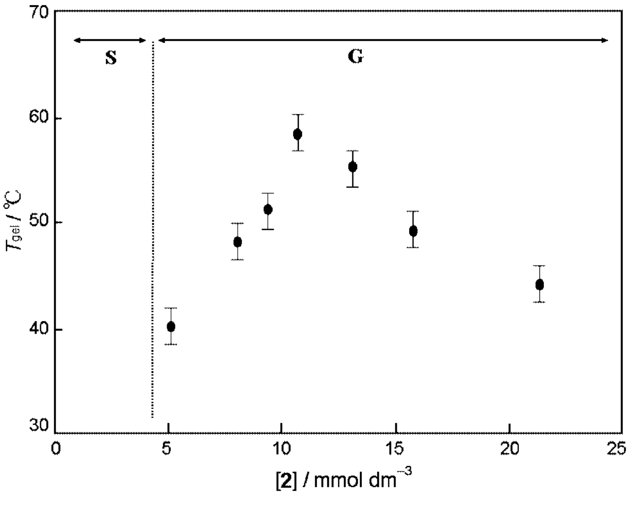


Fig. 1 Concentration dependence of the T_{gel} of **1** (1.8 monomer unit mmol dm^{-3}) upon addition of **2** in DMSO–H_2O (9 : 2 v/v). S: solution, G: gel.

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† Electronic supplementary information (ESI) available: experimental details and synthesis of compounds **3** and **4**. See http://www.rsc.org/suppdata/cc/b1/b102436c/

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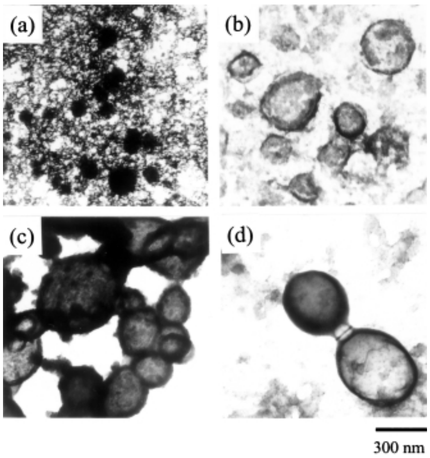
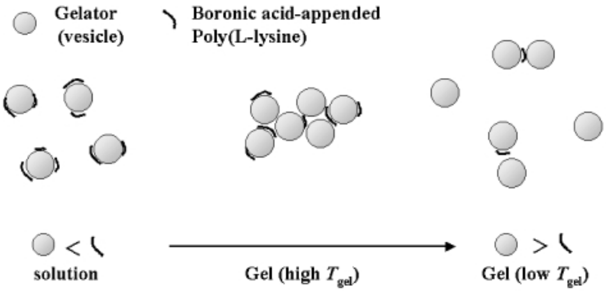


Fig. 2 TEM images of a 10.6 mmol dm^{-3} solution of **2** (a); a solution of **1** (1.8 mmol dm^{-3}) and **2** (2.6 mmol dm^{-3}) (b); a gel of **1** (1.8 mmol dm^{-3}) and **2** (10.6 mmol dm^{-3}) at $T_{\text{gel}} = 58 \pm 3$ °C (c); and a gel of **1** (1.8 mmol dm^{-3}) and **2** (15.9 mmol dm^{-3}) at $T_{\text{gel}} = 44 \pm 3$ °C (d).



Scheme 2

gelator **2** (0–21 mmol dm^{-3}) did not result in gel formation, indicating that both the poly(L-lysine) chain, and the boronic acid moiety are a prerequisite for gelation to occur. Under alkaline conditions, the boronic acid moiety of **1** can interact with the glucopyranosyl moiety of **2**, forming covalent bonds with the 4,6-diol of the saccharide,[12] thus creating a connection between the polymer (**1**) and the gelator (**2**). Under acidic conditions (pH 5), on the other hand, the addition of **1** to a solution of **2** did not cause gel formation. The gelation behavior of this particular system is obviously pH dependent, since it relies on the boronic acid–saccharide interaction for gel formation.

To shed light on the mechanism of gel formation, TEM was employed (Fig. 2). In sample (a), containing only compound **2** (10.6 mmol dm^{-3}), monodisperse colloidal particles with diameters of approximately 50–100 nm, can be observed.[13] In sample (b), representative of gelator **2** (2.6 mmol dm^{-3}) plus polymer **1** (1.8 mmol dm^{-3}) in the solution state, slightly larger (200–400 nm in diameter), monodisperse vesicles are present. However, in sample (c), representative of the gel state with a high T_{gel} (**1**: 1.8 mmol dm^{-3}, **2**: 10.6 mmol dm^{-3}), no individual structures are present, but only a network of vesicles can be observed. In sample (d), representative of the gel state with a low T_{gel} (**1**: 1.8 mmol dm^{-3}, **2**: 15.9 mmol dm^{-3}), similar features as in sample (b) can be observed. To obtain a more accurate evaluation of the dimensions of the vesicles observed by TEM, DLS measurements were carried out.[14] The average diameters of the features observed in samples (a)–(d) are 121, 302, 2140, and 495 nm, respectively. The high average diameter observed for sample (c) could correspond to either very large vesicles present in solution, or to aggregates of smaller vesicles. In light of the TEM results (see Fig. 2c), the latter is more viable.

From the results presented, a mechanism for gel formation can be proposed (Scheme 2). In the presence of a large excess of **1** with respect to **2**, the gelator can form vesicles which are completely coated by the polymer, giving rise to individual vesicles (Fig. 2b). As a consequence, gel formation is not observed at high concentrations of **1** with respect to **2**. When the concentration of gelator is increased and the ratio of polymer to gelator is approximately 1 : 6, the number of vesicles increases and the amount of **1** is not sufficient to completely coat all the vesicles (Scheme 2). Therefore, aggregation of the gelator vesicles occurs, giving rise to an extended network of vesicles held together by polymer molecules and thus, the formation of the gel is observed (Fig. 2c). When the concentration of gelator **2** is increased even further, the amount of polymer **1** present in the system is not sufficient anymore for the formation of an extended network of vesicles (Scheme 2). Under these conditions, only dimers can still be observed in the TEM images and T_{gel} decreases.

In contrast to most gel structures that have been reported so far, consisting of fibrous networks running through the gels,[1,15] an assembly of vesicles of gelator **2** held together by polymer **1** is at the basis of this particular gel. Remarkably, the building blocks of this novel gel structure are polymer-coated gelator vesicles, which assemble into a superstructure, the gel, whilst maintaining the identity of vesicles. The gel cannot be defined as a polymer gel since the polymer chain length is far too short (100–200 nm, if fully stretched) to allow cross-linking of polymer chains by vesicles. One can thus regard the gelation as being induced by the 'cross-linking' of vesicles by polymers, but not by the 'cross-linking' of polymers by vesicles. Studies are currently underway to further elucidate the more detailed mechanism of gel formation proposed in this paper and to investigate the possibilities of utilizing poly(L-lysine)-based polymers for the formation of robust gels useful in aqueous systems.

Notes and references

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10 To a solution of gelator **2** in DMSO, was added a solution of polymer **1** in H_2O at pH 11.5 (NaOH). The solution containing **1** and **2** was then heated until all components dissolved and allowed to cool slowly to form the gel. Here, T_{gel} is defined as the temperature at which the gel appears.

11 The DMSO–H_2O (9 : 2 v/v) solution was the only one in which both compounds **1** and **2** dissolve simultaneously.

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14 Dynamic Light Scattering: diameter and diffusion coefficient measurements were carried out on a Photal Otsuka Electronics VLS-70 super dynamic light scattering spectrophotometer (light source: Ar). Samples for DLS were diluted 10 times with respect to the samples used for gel formation.

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