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Reversible sol–gel transition of a tris–urea gelator that responds to chemical stimuli

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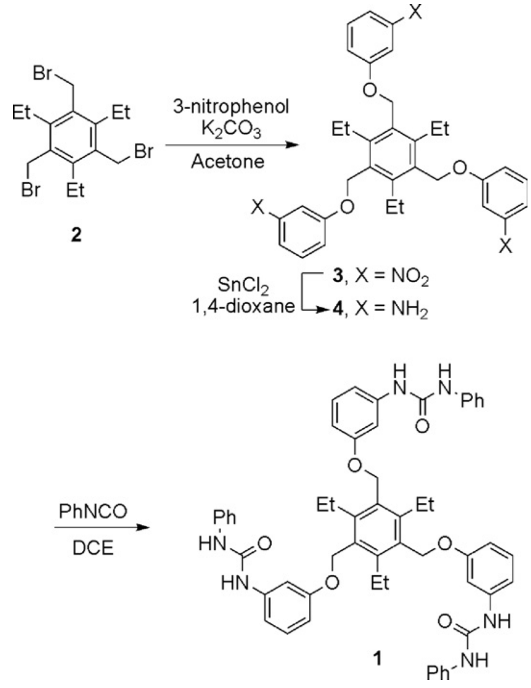
Abstract—Tris–urea **1** functioned as a low-molecular-weight gelator for a variety of polar organic solvents. An acetone gel of **1** became a homogeneous solution in response to the addition of anions. The minimum amount of anion necessary for the gel–sol transition was specific to the anion species. A linear relationship was demonstrated between the amount of anion required and the total binding constant of **1** with the anion. Re-gelation occurred by addition of $BF_3{\cdot}OEt_2$ and with ultrasound irradiation of the acetone solution of **1** and F^-.

Researches on low-molecular-weight gelators have been paid much attention in recent years.[1] Reversible sol–gel transitions in gelators responsive to various stimuli such as light,[2] redox,[3] counter ions,[4] and pH[5] have been achieved by various designs of gelators. Molecular recognition by designed artificial host molecules has received much attention in recent decades.[6] Tripodal structures with binding cavities have widely investigated as synthetic receptors for anions,[7] sugars,[8] and other species.[9] Sol–gel transitions responsive to chemical stimuli can be achieved by introduction of an artificial host molecule into a low-molecular-weight gelator. Indeed recently, the aggregation of urea or pyromellitamide gelators was inhibited by anion binding.[10] We report here that a C_3-symmetric tris–urea gelator **1** showed reversible sol–gel transition in response to chemical stimuli.

Tris–urea **1** was synthesized in three steps from 1,3,5-tris(bromomethyl)-2,4,6-triethylbenzene (**2**) as shown in Scheme 1. Trinitro compound **3** was prepared by the reaction of **2** with 3 equiv of 3-nitrophenol. Nitro groups of **3** were reduced with tin chloride in 1,4-dioxane solvent to afford triamine **4**. The target tris–urea **1** was obtained by the reaction of **4** with phenyl isocyanate.



Scheme 1. Synthesis of tris–urea **1**.

Keywords: Gels; Host–guest chemistry; Phase transitions; Self-assembly; Ureas.

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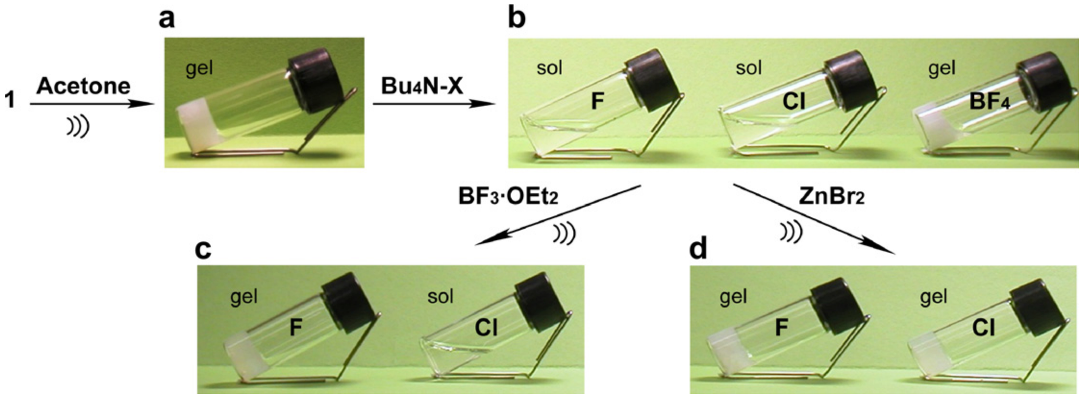

Figure 1. Photographs of acetone gel of **1** responded to chemical stimuli: (a) acetone gel of **1** (2.0 wt %); (b) acetone gel of **1** (2.0 wt %) containing (from left) 1.1 equiv of TBAF, 1.7 equiv of TBACl, and 10 equiv of $TBABF_4$; (c) $BF_3{\cdot}OEt_2$ (1.0 equiv for TBA salt) mixture after sonication of **1** and TBAF (left) or TBACl (right) in acetone; (d) $ZnBr_2$ (1.0 equiv for TBA salt) mixture after sonication of **1** and TBAF (left) or TBACl (right) in acetone.

An acetone suspension of **1** formed a translucent gel after brief sonication[11] (critical gelation concentration: CGC = 1.5 wt %) (Fig. 1a). Once formed the gel was stable at ambient temperatures for at least several months without crystallizing or melting. Cooling of a thermally dissolved acetone solution of **1** resulted in precipitation and no gel formation. Ultrasound irradiation may cause desolvation of **1** and trigger the gelation. Brief sonication of mixtures of tris–urea **1** and polar organic solvents including diethyl phthalate (CGC = 2.0 wt %), MeOH (CGC = 2.0 wt %), and THF (CGC = 5.0 wt %) also resulted in gel formation. However, mixtures of **1** and non-polar solvents such as hexane, toluene, and dichloromethane did not form gels. Scanning electron microscopy (SEM) images of a xerogel prepared by freeze-drying of acetone or MeOH gels showed intertwining nanofibers (see Supplementary data). Fibrous aggregates would primarily form from self-complementary hydrogen bonding of urea moieties. Neither tris–amide (**5**) nor tris-*N*-methyl urea (**6**) derivatives gave gels (Fig. 2). FT-IR spectroscopy of a sample of xerogel of **1** had a peak assigned to the carbonyl stretching at 1645 cm^{-1}. Compared with the carbonyl stretching peak of amorphous **1** (1655 cm^{-1}), the peak was shifted to a lower wave number ($\nu_{\text{amorphous}} - \nu_{\text{gel}} = 10\ \text{cm}^{-1}$) (see Supplementary data). The shift provides evidence for the existence of intermolecular hydrogen bonds of **1** in the gel.[12]

An acetone gel of **1** (2.0 wt %) formed a homogeneous solution on addition to the gelator of F^- (n-$Bu_4N^+F^-$) in excess (⩾1.1 equiv) (Fig. 1b). Addition of less than 1.1 equiv of F^- caused partial disintegration of the gel. Completion of this phase transition took 12 h at room temperature, 2 h at 45 °C, and less than 5 min at room temperature with sonication. Experiments on phase transitions of an acetone gel of **1** (2.0 wt %) were performed using a range of anions (n-$Bu_4N^+X^-$). The minimum amount of halide ions required for complete gel–sol phase transition increased with the size of ionic radius. The amounts were 1.7 equiv, 2.0 equiv, and 2.9 equiv for Cl^-, Br^- and I^-, respectively (Fig. 1b). As disintegration of gel is principally caused by anions, approximately 1.7 equiv of Me_4NCl, Et_4NCl, and n-Pr_4NCl were required for a complete gel–sol phase transition similar to that with n-Bu_4NCl. Addition of 1.6 equiv of AcO^- also resulted in a homogeneous solution. A white suspension was obtained when phosphate $H_2PO_4{}^-$ was mixed with an acetone gel of **1**. It is noteworthy that addition of $BF_4{}^-$ never caused complete phase transition of the gel, and 10 equiv of $BF_4{}^-$ caused slight melting of the gel (Fig. 1b).

The variation in the amount of anions required for complete gel–sol phase transition should be based on the differential binding constants of **1** and the anions involved. Titration experiments of **1** with a range of anions were carried out by using ^1H NMR in acetone-d_6. Data from titration experiments were analyzed using the curve-fitting program HypNMR.[13] Titration results of halide ions and AcO^- were fitted with **1**:anion stoichiometry of 1:3. The total binding constant ($\log\beta_{13}$) for F^- was calculated at 11.61 ($\log K_{11} = 5.05$, $\log K_{12} = 3.45$, $\log K_{13} = 3.11$) and the estimated error was ±21%. In the case of F^-, coexistence of deprotonation of the urea moiety may be responsible for such a large error.[14] The other values of $\log\beta_{13}$ were calculated at 10.23, 8.81, 7.44, and 9.78 for Cl^-, Br^-, I^-, and AcO^-, respectively, with errors less than 10%. A linear correlation was demonstrated between $\log\beta_{13}$ and the minimum amount of anion required for complete gel–sol transition (Fig. 3).

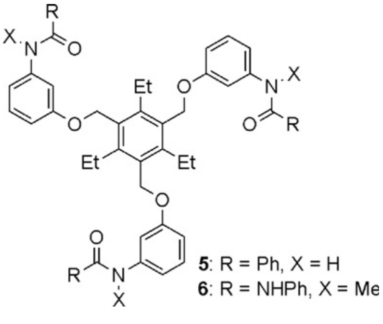

Figure 2. Structure of tris–amide and tris-*N*-methylurea **5** and **6**.

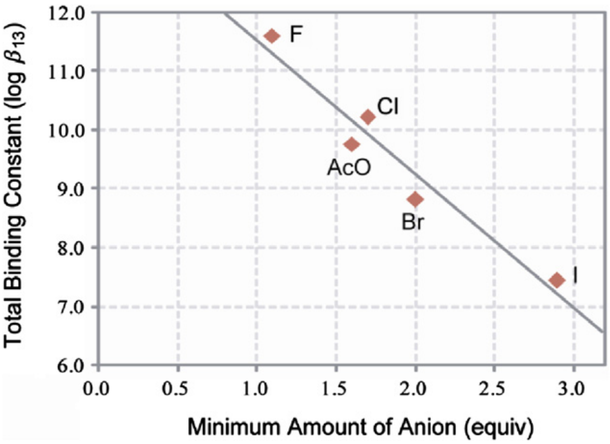

Figure 3. Plot of total binding constants of **1** with anions in acetone-d_6 and minimum amount of anions required for the complete gel–sol transition.

Self-aggregation of the gel could be reversed by anion recognition. Titration results for BF_4^- were curve-fitted with a **1**:anion stoichiometry of 1:1, and the smallest binding constant ($\log K_{11} = 1.27$) for BF_4^-, which could not cause the gel–sol transition.

An additional focus was on re-gelation in solutions where gel disintegration had occurred through the addition of anions. Specific re-gelation would enable identification of the anions involved. The reaction of a fluoride ion with boron trifluoride gave a tetrafluoroborate ion[15] which did not cause disintegration of the gel. Addition of boron trifluoride etherate ($BF_3{\cdot}OEt_2$) to the acetone solution of **1** and F^- caused re-gelation after brief sonication (Fig. 1c). This sol–gel phase transition could be repeated at least four times.[16] The other acetone solution of **1** and anions were attempted to re-gelate by adding $BF_3{\cdot}OEt_2$. Re-gelation was also proceeded in the solution including AcO^- after sonication. Homogeneous solutions remained unchanged with added $BF_3{\cdot}OEt_2$ for the solutions involving Cl^-, Br^-, or I^- (Fig. 1c). Further experiments showed that $ZnBr_2$ acted as a non-specific chemical stimulus for re-gelation of an acetone solution of **1** and anions. In contrast to $BF_3{\cdot}OEt_2$, $ZnBr_2$ re-gelated all solutions containing F^-, Cl^-, Br^-, I^-, or AcO^- (Fig. 1d).

In conclusion, we have demonstrated that tris–urea **1** acts as low-molecular-weight gelators for a variety of polar organic solvents, and that reversible sol–gel transitions occur in response to chemical stimuli. These findings may lead to a simple and convenient anion detection method based on the principles of molecular recognition.

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Supplementary data

Experimental details and spectroscopic data can be found in the PDF format. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.10.090.

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16. Five times phase transition from gel to solution by adding fluoride ion produce a slight insoluble precipitate, but, regelation by addition of $BF_3 \cdot OEt_2$ was achieved.