Langmuir
Letter
pubs.acs.org/Langmuir

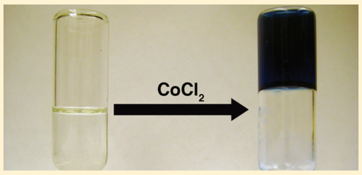
General Approach to Low-Molecular-Weight Metallogelators via the Coordination-Induced Gelation of an L-Glutamate-Based Lipid

Robert E. Bachman,* Anthony J. Zucchero, and Jamie L. Robinson

Department of Chemistry, The University of the South, 735 University Avenue, Sewanee, Tennessee 37383, United States

Supporting Information

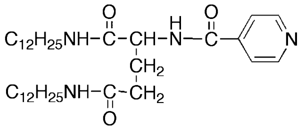
ABSTRACT: A twin-tailed glutamate-based lipid with a pyridine headgroup was prepared in good yield using standard amide coupling and protection/deprotection chemistry. The resulting Lewis basic lipid gels a wide array of hydrocarbon solvents at a critical gelation concentration (C_g) of 0.3 wt %. The gelation of more polar solvents, such as ethanol, THF, dichloromethane, and chloroform, occurs with a C_g of between 2 and 5 wt %, demonstrating the importance of hydrogen bonding interactions in gel formation. The importance of hydrogen bonding in this system was also demonstrated by IR observation of the amide bands, which show a substantial shift upon gelation. Solutions of this new organogelator with concentrations below C_g rapidly form gels upon the introduction of a wide variety of metal salts or complexes, providing a convenient general method for the preparation of metallogelators. Spectroscopic evidence suggests that the enhanced gelation seen in the metal-containing systems can be explained by a cross-linking of gel fibril aggregates similar to those formed by the unmetalated gelator.



Over the last two decades, there has been a rapidly growing exploration of molecular gels, which are composite viscoelastic materials that spontaneously self-assemble when a small amount (typically <2 wt %) of an appropriate low-molecular-weight gelator (LMWG) is introduced into either water or an organic solvent.[1] Interest in these materials is driven at a fundamental level by the desire to understand the self-assembly processes responsible for gel formation. Moreover, given the fine control that chemists have over molecular structure, gelation represents an elegant bottom-up approach to the fabrication of structures on the nanoscale as well as on larger organizational scales.[2] Given their unique ability to organize structure across several length scales, LMWGs have been suggested to have numerous, diverse, practical applications, including low-dimensional conductors, membrane filters, drug-delivery vehicles, and sensors.[1,2]

Although countless organic LMWGs have been identified,[1] metal-containing systems have only more recently begun to receive significant attention.[3] The incorporation of metal centers into gelators permit the design of materials that possess properties—magnetism, color, catalytic activity, and redox behavior—that are difficult to achieve in organic systems. Typically the metallogels (metal-containing gels) prepared to date have been created using preformed metal complexes of organic gelators.[3,4] Alternatively, multitopic ligands have been used to form gels via the in situ construction of coordination polymers.[3,5] In contrast, only a few reports of coordination-induced in situ gelation by discrete complexes have appeared to date,[6] and these systems have typically been designed to function with a single metal species. Inspired by this initial work, we have undertaken an effort to develop ligand systems capable of forming gels with a wide selection of metal fragments via in situ coordination to form discrete metal complexes. Our design strategy is based on the elegant modular approach to glutamate-based gelators developed by Ihara and co-workers,[7] which includes a single example of a metal-based gelator.[8] In this letter, we report the preparation of a new LMWG that incorporates a Lewis basic pyridine headgroup (**L**). This lipid is capable of forming organogels in a variety of hydrocarbon solvents at concentrations of as low as 0.3 wt % (~4 mM). Additionally, the gelation ability of **L** is greatly enhanced by its in situ coordination to a wide variety of metal centers. As such, the synthesis of **L** provides a general approach to the formation of a wide array of metallogels via coordination-induced gelation.

L =



The Lewis basic lipid (**L**) was prepared in three steps from CBZ-protected glutamic acid using standard amide coupling and deprotection chemistry (Scheme 1).[7,9] Both the intermediate CBZ-protected glutamate lipid and **L** readily gel a variety of solvents, allowing purification via washing of the crude solid followed by a gelation/filtration step. The amine intermediate was purified by recrystallization from ethanol. Typical reaction yields for each of the three steps were between 85 and 97%, with much of the variability due to handling losses (Supporting Information).

Organogels of **L** can be formed with a critical gelation concentration (C_g) of approximately 0.3 wt % (~4 mM) in both aromatic and selected aliphatic hydrocarbon solvents (Table 1). The resulting gels may be characterized as

Received: September 12, 2011
Revised: November 17, 2011
Published: December 5, 2011

Scheme 1. Synthesis of L

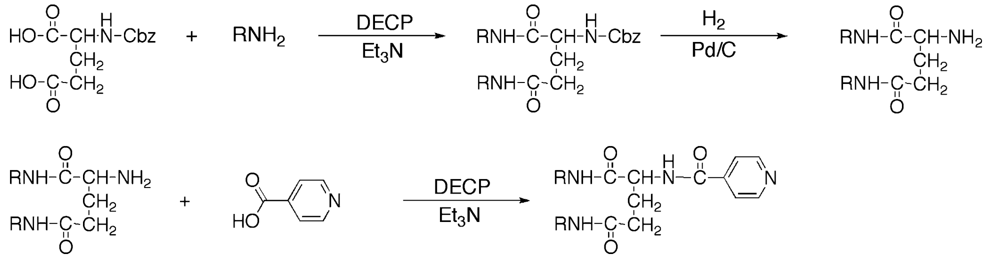


Table 1. Critical Gel Concentration (CGC) in the Weight Percentage for L in a Variety of Solvents

solvent	CGC (%)	solvent	CGC (%)
benzene	0.3	EtOH	3
toluene	0.3	$CHCl_3$	5
xylene	0.3	CH_2Cl_2	5
mesitylene	0.3	THF	5
tetrahydronapthalene	0.3	acetone	ppt/pg[a]
cyclohexane	0.3	Et_2O	insol
silicone oil	0.3	CH_3CN	insol
MeOH	3	H_2O	insol

[a] ppt/pg: precipitation with partial gel formation. insol: the gelator does not dissolve even under extended heating.

transparent to translucent, with the most transparent gels forming in aromatic solvents (Figure 1). Initial X-ray scattering experiments on dried xerogel samples show only broad features indicative of an essentially amorphous fiber structure.

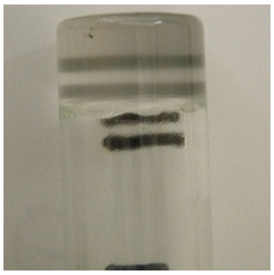


Figure 1. Typical gel formed from 0.5 wt % **L** in toluene with cooling in a water bath. Lines drawn on the background paper help to show the high degree of translucency in these gels. The lines behind the gel are of the same length as the two below the gel but are magnified by the curvature of the vial.

Aromatic hydrocarbon gels with [**L**] between 0.5 and 1 wt % are robust and stable at room temperature for longer than a month. Gels with [**L**] < 0.5 wt % slowly exclude solvent to produce a stable gel with [**L**] higher than that initially formulated along with a small amount of solution. The gel–sol transition temperature (T_g) of mesitylene gels was found to increase rapidly at low [**L**], increasing from 34 °C at 0.3 wt % to 55 °C at 1 wt %. Doubling [**L**] to 2 wt % has much less of an impact, increasing T_g by only 7 °C to 62 °C. At [**L**] > 2 wt %, **L** partially precipitates upon cooling rather than forming a homogeneous gel.

Gels of **L** can be formed in a variety of polar solvents as well, but with a C_g that is at least an order of magnitude higher than that required for hydrocarbons (Table 1). However, sealed solutions of **L** with [**L**] < C_g form optically transparent self-supporting gel masses upon standing for several days without measurable evaporation of the solvent. The isolation of these gelatinous masses by decantation followed by drying returns a composition close to the measured C_g value for that solvent. (e.g., 5 wt % vs a measured C_g = 3 wt % for ethanol). This finding is consistent with the tendency, noted above, for gels formed at or near C_g in hydrocarbon solvents to exclude solvent as they age to reach a higher, and presumably more stable, fiber to immobilized solvent ratio.

The solution ^{1}H NMR spectra of **L** depend on both the concentration and the solvent used. At higher concentrations (~1 wt %, ~25 mM) in $CDCl_3$, the amide signals occur at 8.55, 7.05, and 5.94 ppm. On the basis of the coupling patterns (Supporting Information), we assign these peaks to isonicotinamide linkage and the two lipid amide linkages. The strong upfield shift of one of the lipid amide signals is consistent with the presence of a strong intramolecular hydrogen bonding interaction, most likely involving the N–H group of one dodecyl tail with the carbonyl linkage of the other tail.[10] The isonicotinamide signal migrates downfield with decreasing concentration, reaching approximately 10 ppm at [**L**] ≤ 0.25 wt %, and the other signals show little change in chemical shift but become steadily broader. The differing behavior of these signals suggests that **L** aggregates in solution via an intermolecular hydrogen bonding interaction involving the isonicotinamide group at concentrations well below C_g. It also suggests that deaggregation leads to a higher degree of fluxionality in the hydrogen bonding between the lipid amide linkages. This picture is further supported by spectra taken in hydrogen bond donor and/or acceptor solvents, such as ethanol and THF. These spectra show a significant downfield shift of the lipid amide signals to 8.24 and 8.11 ppm as the hydrogen bonding is disrupted and the environments of the amide groups become more similar.

Taken as a whole, the NMR data suggests that the aggregation of **L** begins to occur well below C_g and that the self-assembly process depends on both intra- and intermolecular hydrogen bonding interactions, which are likely assisted by the van der Waals packing of the aliphatic chains. The significance of such alkyl chain packing in gel formation has been elegantly demonstrated by Weiss and co-workers.[11] This model is also supported by IR spectral data, which shows a strong red shift of both the N–H (3436 to 3298 cm^{-1}) and amide (1664 and 1557 to 1635 and 1522 cm^{-1}) bands upon gelation.[12] The tendency of **L** to aggregate in solution well below C_g also explains the spontaneous formation of gel masses noted above.

Although no gelation was observed for mixtures of 1 wt % **L** in CH_2Cl_2, the addition of half a molar equivalent of a soluble Ag(I) salt, such as $AgBF_4$ or $AgSbF_6$ (2:1 **L**/Ag(I)) leads to instantaneous gelation, presumably induced by the coordination of two molecules of **L** to one Ag^+.[6b,13] The room-temperature CGC for this **L**/Ag^+ system was estimated to be 0.5 wt % using a dilution/thermal isotropization/regelation/inversion protocol. This result indicates that the metal complexation enhances the gelation ability of **L** by 10-fold, as measured by CGC, relative to free **L** in CH_2Cl_2.

The ^1H NMR spectra of very dilute (≤0.3 wt %) solutions with a nominal composition of L_2Ag^+, in either $CDCl_3$ or CD_2Cl_2, show broad signals in the aromatic region at 8.85 and 8.50 ppm. This downfield shift of the pyridine resonances (versus 8.75 and 7.74 ppm for free **L**) is consistent with the binding of a silver ion to the basic nitrogen atom of the pyridine moiety. Similar shifts are seen for the aromatic signals of non-gel-forming species **L**AuCl and [**L**CH_3]OTf, which appear at 8.95 and 8.71 ppm and at 8.92 and 8.51 ppm, respectively. The proposed formula of $[L_2Ag]^+$ is also supported by viscometry measurements on sub-C_g samples. Although the addition of any amount of Ag^+ results in increased viscosity compared to that of solutions of **L**, the viscosity reaches a maximum near a ligand/metal ratio of 2:1. However, the relative broadness of this curve, along with the broad aromatic signals observed in the ^1H NMR, allows for the possibility of a dynamic system consisting of a mixture of species with differing L/M ratios.

The metal-induced gelation of solutions of **L** is a general phenomenon. The addition of a variety of metal salts or complexes (Table 2) to 1 wt % solutions of **L** in CH_2Cl_2, $CHCl_3$, or THF results in essentially instantaneous gelation (Figure 2). Although it is reasonable to expect differing ideal stoichiometries for such a wide array of metal species (e.g., one might expect a 4:1 ratio for Ni(II)[14]), a 2:1 **L**/metal ratio was maintained in these experiments to facilitate comparison. As can be seen in Table 2, the gelation behavior was independent of the identity of the counterion for all Ag(I) salts examined. In contrast, a significant counterion dependence was observed for the Cu(II) salts. Although the origin of this difference remains somewhat unclear, two hypotheses seem viable. First, the anions employed in the Ag(I) case are essentially noncoordinating and so do not compete with the gelator ligand for metal binding. Second, the more variable coordination geometry and number of Cu(II) may require a different **L**/metal ratio than 2:1 to achieve gelation. It is also possible that both of these factors can be operative simultaneously. Studies to explore more fully both the generality of this gelation process and its dependence on variables such as the counterion identity and **L**/metal ratio are ongoing.

Table 2. Results of Coordination-Induced Gelation in CH_2Cl_2 for the Metal Salt or Complex Examined

metal salt	gelation?[a]	metal salt	gelation?[a]
$AgBF_4$	G	$NiCl_2{\cdot}6H_2O$	G
$AgSbF_6$	G	CuBr	G
$AgNO_3$	G	$Cu(NO_3){\cdot}2.5H_2O$	G
$ZnCl_2$	G	$CuBr_2$	S
$CdCl_2$	G	$Cu(OAc)_2$	S[b]
$CoCl_2$	G	$FeCl_2$	S
$SnCl_2{\cdot}2H_2O$	G	$FeCl_3$	S
$Pd(PhCN)_2Cl_2$	G	thtAuCl	sol

[a] G: gel stable to inverstion. sol: solution only. S: semigel—a significant increase in viscosity but not complete immobilization upon inversion. [b] Decreasing the solvent volume by approximately 66% led to the formation of a gel.

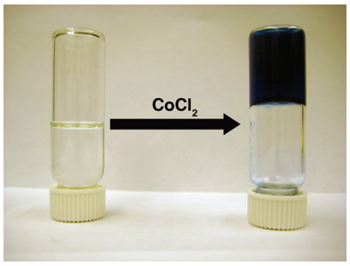


Figure 2. Addition of 0.5 equiv of $CoCl_2$ to a 1 wt % solution of **L** in THF produces instantaneous gelation of the system. The C_g in this system is 0.5 wt %.

Attempts to induce gelation in 1 wt % ethanolic solutions failed; however, the resulting solutions spontaneously form gel masses analogous to those seen for pure **L**, suggesting that gelation in ethanol should be possible at higher concentrations. Additionally, the removal of ethanol provided powders that readily formed metallogels upon swelling with toluene or other hydrocarbon solvents, providing an alternative method for producing metallogels of metal salts with limited solubility in solvents such as CH_2Cl_2.

The IR spectra of the metallogels, regardless of the solvent used for preparation, look essentially identical to gels and xerogels prepared from pure **L**, with the N−H band at ~3300 cm^{-1} and the amide bands at 1635 and 1530 cm^{-1}. This would seem to indicate that the hydrogen bonding network responsible for the formation of the gel fibers in the metallogels is essentially identical to that of free **L**.

In trying to understand the mechanism for coordination-induced gelation, it is also worth noting that fragments capable of binding to a single unit of **L**, such as AuCl or CH_3^+, do not induce gelation. Furthermore, enhanced gelation is independent of whether the fragment linking the **L** moieties carries a charge (e.g., Ag^+ vs $CoCl_2$). Indeed, the overall pattern of behavior summarized in Table 2 supports the idea that coordination-induced gelation by metal−**L** complexes is the result of physically linking two or more **L** units, independent of the geometry of the linkage. This latter point is clearly demonstrated by the deep blue color of the cobalt-containing gel, consistent with a tetrahedral geometry at the metal center[15] and a "bent" cross-link as opposed to the linear cross-link present for the Ag^+ system. This model is consistent with the recent report by Lam and Yam that uses Ag^+ to cross-link Re(I)-acetylide moieties and induce gelation.[6a] This interpretation is also supported by SEM images of xerogels of free **L** (1 wt % in toluene) and both the **L**/Ag^+ and **L**/$CoCl_2$ metallogel systems (1 wt % in CH_2Cl_2) (Figure 3). Although the change in the gelation solvent and the resulting different drying regimes are certainly confounding variables in these measurements, the SEM images reveal subtle differences in the gel morphology. All three samples appear to be composed of fiberlike structures, which further aggregate into the 2D motifs common in LMWG systems.[1a,2a,4] However, whereas xerogels of free **L** typically collapse to tangled mats of fibers upon drying, the metal-containing systems generate robust, porous 3D structures. Additionally, the fiber dimensions in the metal-containing gels are typically larger than in the metal-containing sytems, indicative of higher-order aggregation as would be expected in the case of cross-link formation.

From a macroscopic perspective, our model for the enhanced gelation seen in the presence of metal ions is equivalent to the formation of cross-links between preassembled gel fibrils of **L**

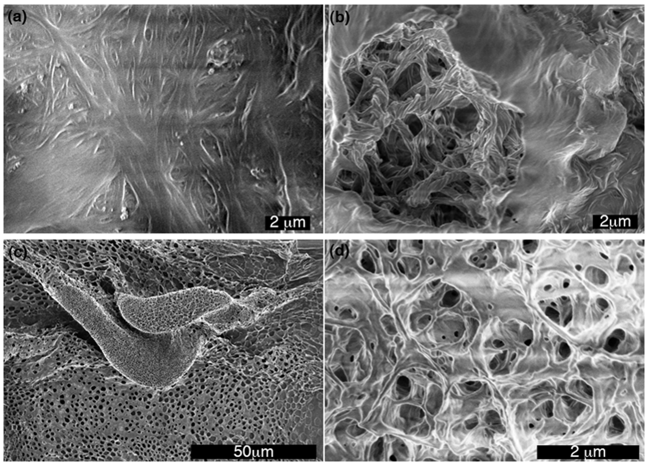


Figure 3. SEM images of xerogels formed from the following gels: (a) 1 wt % **L** in toluene, (b) 2:1 **L**/$CoCl_2$ at 1 wt % **L** in CH_2Cl_2, and (c) 2:1 **L**/Ag^+ at 1 wt % **L** in CH_2Cl_2. (d) Higher magnification of the loop feature near the top of c.

similar to those seen in gels formed by **L** alone. This interpretation is consistent with our initial attempt to prepare gelators of 2,2′-bipyridine with two glutamate lipid units appended. The characterization of these materials has proven to be an intractable problem because of their strong propensity to gel essentially any solvent at extremely low concentrations.

In summary, we have used a modular and general synthetic route to prepare a new Lewis base gelator capable of binding a wide array of metal fragments in situ, with a concomitant increase in the gelation ability. This approach to metallogel formation represents a general and completely modular approach to the preparation of gels containing essentially any metal ion. Significantly, the data collected to date suggest that the metal ions are located on the exterior of the gel fibrils. This structural arrangement should allow preformed xerogels of **L** to act as metal ion sorbents from aqueous environments or the gaseous aerosols. Additionally, the metal ions in these metallogels should be chemically accessible via the solvent-filled pores, allowing for the possibility of further chemical modification or reactivity.[16] These possibilities, as well as the preparation of other Lewis base derivatized gelators, are currently under investigation.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Complete synthesis and spectral information for **L** and experimental protocols for gel formation and T_g and viscometery measurements. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: rbachman@sewanee.edu.

■ ACKNOWLEDGMENTS

We thank the Research Corporation Cottrell College Scholars Fund (CC5549), the Jesse Ball duPont Foundation, and The University of the South for their financial support of this work. Gunnar Glasser of the Max Planck Institute for Polymer Research is acknowledged for his assistance with the acquisition and interpretation of the SEM images.

■ REFERENCES

(1) (a) Weiss, R. G., Terech, P., Eds. *Molecular Gels: Materials with Self-Assembled Fibrillar Networks*; Springer: Dordrecht, The Netherlands, 2006. (b) Ajayaghosh, A.; Praveen, V. K.; Vijayakumar, C. *Chem. Soc. Rev.* **2008**, *37*, 109−122. (c) Sangeetha, N. M.; Maitra, U. *Chem Soc. Rev.* **2005**, *34*, 821−836.

(2) (a) Fages, F. *Angew. Chem., Int. Ed.* **2006**, *45*, 1680−1682. (b) Hirst, A. R.; Smith, D. K. *Chem.—Eur. J.* **2005**, *11*, 5496−5508. (c) van Esch, J. H.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2000**, *39*, 2263−2266.

(3) (a) Piepenbrock, M.-O. M.; Lloyd, G. O.; Clarke, N.; Steed, J. W. *Chem. Rev.* **2010**, *110*, 1960−2004. (b) Llusar, M.; Sanchez, C. *Chem. Mater.* **2008**, *20*, 782−820.

(4) (a) Tam, A. Y.-Y.; Wong, K. M.-C.; Zhu, N.; Wang, G.; Yam, V. W-W. *Langmuir* **2009**, *25*, 8685−8695. (b) Tam, A. Y.-Y.; Wong, K. M.-C.; Yam, V. W-W. *J. Am. Chem. Soc.* **2009**, *131*, 6253−6260. (c) Tam, A. Y.-Y.; Wong, K. M.-C.; Wang, G.; Yam, V. W-W. *Chem. Commun.* **2007**, 2028−2030. (d) Cameral, F; Ziessel, R.; Donnio, B.; Bourgogne, C.; Guillon, D.; Schmutz, M.; Iacovita, C.; Bucher, J.-P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2659−2662. (e) Shirakawa, M.; Fujita, N.; Tani, T.; Kaneko, K.; Ojima, M.; Fujii, A.; Ozaki, M.; Shinkai, S. *Chem.—Eur. J.* **2007**, *13*, 4155−4162. (f) Cardolaccia, T.; Li, Y.; Schanze, K. *J. Am. Chem. Soc.* **2008**, *130*, 2535−2545. (g) Shirakawa, M.; Fujita, N.; Tani, T.; Kaneko, K.; Shinkai, S. *Chem. Commun.* **2005**, 4149−4151.

(5) (a) Weng, W.; Beck, J. B.; Jamieson, A. M.; Rowan, S. J. *J. Am. Chem. Soc.* **2006**, *128*, 11663−11672. (b) Iyer, P. K.; Beck, J. B.; Weder, C.; Rowan, S. J. *Chem. Commun.* **2005**, 319−321. (c) Zhao, Y. Q.; Beck, J. B.; Rowan, S. J.; Jamieson, A. M. *Macromolecules* **2004**, *37*, 3529−3531. (d) Miravet, J. F.; Escuder, B. *Chem. Commun.* **2005**, 5796−5798.

(6) (a) Lam, S.-T.; Yam, V. W-W. *Chem.—Eur. J.* **2010**, *16*, 11588−11593. (b) King, K. N.; McNeil, A. J. *Chem. Commun.* **2010**, *46*, 3511−3513. (c) Liu, Q.; Wang, Y.; Li, W.; Wu, L. *Langmuir* **2007**, *23*, 8217−8223.

(7) (a) Hachisako, H.; Murata, Y.; Ihara, H. *J. Chem. Soc., Perkin Trans. 2* **1999**, 2569−2577.

(8) (a) Ihara, H.; Sakurai, T.; Yamada, T.; Hashimoto, T.; Takafuji, M.; Sagawa, T.; Hachisako, H. *Langmuir* **2002**, *18*, 7120−7123. (b) Takafuji, M.; Sakurai, T.; Yamada, T.; Hashimoto, T.; Kido, N.; Sagawa, T.; Hachisako, H.; Ihara, H. *Chem. Lett.* **2002**, 548−549.

(9) (a) Jintoku, H.; Sagawa, T.; Sawada, T.; Takafuji, M.; Hachisako, H.; Ihara, H. *Tetrahedron Lett.* **2008**, *49*, 3987−3990. (b) Ihara, H; Yoshitake, M.; Takafuji, M.; Yamada, T.; Hachisako, H. *Liq. Cryst.* **1999**, *26*, 1021−1027.

(10) Escuder, B.; Martí, S.; Miravet, J. F. *Langmuir* **2005**, *21*, 6776−6787.

(11) (a) Abdallah, D. J.; Sirchio, S. A.; Weiss, R. G. *Langmuir* **2000**, *16*, 7558−7561. (b) Abdallah, D. J.; Weiss, R. G. *Langmuir* **2000**, *16*, 352−355.

(12) (a) Liang, G.-B.; Desper, J. M.; Gellman, S. H. *J. Am. Chem. Soc.* **1993**, *115*, 925−938. (b) Gellman, S. H.; Dado, G. P.; Liang, G.-B.; Adams, B. R. *J. Am. Chem. Soc.* **1991**, *113*, 1164−1173.

(13) See, for example, (a) Dorn, T.; Fromm, K. M.; Janiak, C. *Aust. J. Chem.* **2006**, *59*, 22−25. (b) Aakeroy, C. B.; Beatty, A. M. *Cryst. Eng.* **1998**, *1*, 39−49.

(14) Bachman, R. E.; Whitmire, K. H.; Mandal, S.; Bharadwaj, P. K. *Acta Cryst. C* **1992**, *48*, 1836−1837.

(15) Kuriowa, K.; Shibata, T.; Takada, A.; Nemoto, N.; Kimizuka, N. *J. Am. Chem. Soc.* **2004**, *126*, 2016−2021.

(16) (a) Li, Y.; Liu, M. *Chem. Commun.* **2008**, 5571−5573. (b) Xue, P.; Lu, R.; Li, D.; Jin, M.; Tan, C.; Bao, C.; Wang, Z.; Zhao, Y. *Langmuir* **2004**, *20*, 11234−11239.