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Self-Assembly Based on the Cyanuric Acid–Melamine Lattice¹

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Received May 7, 1990

Reaction of cyanuric acid (CA) with melamine (M) forms a stable, insoluble 1:1 complex CA·M.³ We, and others, believe that CA·M has a local structure represented by the lattice **1**.⁴ We have started a program in the design and synthesis of three-dimensional supramolecular assemblies based on the hydrogen-bonding pattern of CA·M. This program is an extension of the strategy of molecular self-assembly that has been highly successful in forming quasi-two-dimensional monolayers on solid supports.⁵

(1) Supported by the National Science Foundation (Grants CHE-88-12709 to G.M.W. and DMR 86-14003 to the Harvard University Materials Research Laboratory).

(2) NIH Training Grant Predoctoral Fellow, 1987–1988.

(3) Kazuo, M.; Hironobu, K.; Koichiso, Y.; Junichi, N. *Jpn. Kokai Tokkyo Koho* **1979**, 79, 588.

(4) Ostragorich, G.; Bacaloglu, R. *Timisoara, Studii Cercetari Stiint. Chim.* **1962**, 9, 273–289. Finkel'shtein, A. I.; Rukevich, O. S. *Zh. Prikl. Spektrosk.* **1983**, 38, 327–330. The X-ray powder pattern of CA₃·M₃ is consistent with our proposed structure. Zerkowski, J.; Graham, R.; Whitesides, G. M., unpublished results. For the crystal structure of CA·M·3HCl, see: Wang, Y.; Wei, B.; Wang, Q. *J. Crystallogr. Spectrosc. Res.* **1990**, 20, 79–84.

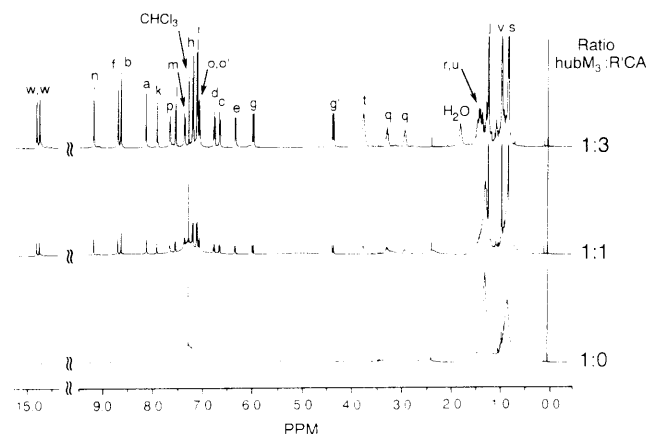
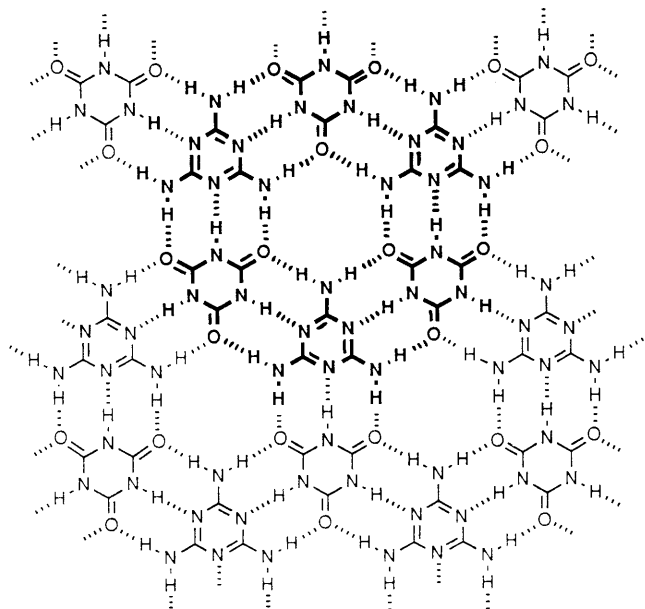


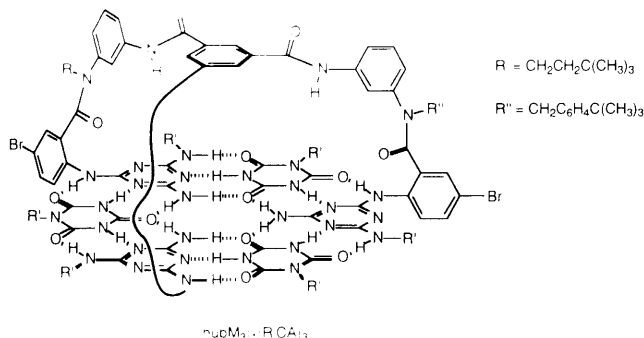
Figure 1. Spectra of ^1H NMR titration of hubM_3 (500 MHz, 10 mM in CDCl_3) with $\text{R}'\text{CA}$. The peak assignments are shown at the top of the figure.

Scheme 1. Self-Assembly of hubM_3 with $\text{R}'\text{CA}$ To Give a Supramolecular 1:3 Complex^a

We set as our first objective the preparation of a soluble, stable derivative of the cyclic hexamer CA_3M_3 (see the boldfaced section in **1**). To promote the formation of this structure, we preorganized the three M units by connecting them covalently to a central "hub", using "spokes" conformationally compatible with the desired CA_3M_3 structure.⁶ Here we report that the tris(melamine) hubM_3 (**2**) reacts with neohexyl cyanurate ($\text{R}'\text{CA}$, **3**) in CHCl_3 and forms a well-defined 1:3 complex $(\text{hubM}_3)_1(\text{R}'\text{CA})_3$ (Scheme 1).⁷

We monitored the titration of hubM_3 (10 mM in CDCl_3) with solid aliquots of $\text{R}'\text{CA}$ by ^1H NMR spectroscopy (Figure 1). The spectrum of uncomplexed hubM_3 (bottom trace) has resonances that are broadened by self-association and restricted rotation around the amide and RNH -triazine bonds. At intermediate points in the titration, the spectrum shows resonances for the $(\text{hubM}_3)_1(\text{R}'\text{CA})_3$ complex against a background of uncomplexed hubM_3 . The resonances for the complex are sharp because it is locked into a single conformation and exchange between the complex and hubM_3 in solution is slow on the NMR time scale. As the titration proceeds, the intensities of the resonances for $(\text{hubM}_3)_1(\text{R}'\text{CA})_3$ increase until the 1:3 stoichiometry is reached, and beyond this point there is no further change in the spectrum.^{8,9}

The peak assignments for $(\text{hubM}_3)_1(\text{R}'\text{CA})_3$ are shown at the top of Figure 1. Two features support the assigned structure: First, several methylene protons (g, g' and q, q') of hubM_3 are diastereotopic in $(\text{hubM}_3)_1(\text{R}'\text{CA})_3$ and thus appear as two separate resonances. Second, the two imide N-H protons (w and



^a The third spoke of $(\text{hubM}_3)_1(\text{R}'\text{CA})_3$ has been drawn schematically for the sake of clarity. The groups R' and R'' were chosen to add solubility to the complex and to provide centers easily analyzed by ^1H NMR spectroscopy.

w') of $\text{R}'\text{CA}$ are in different hydrogen-bonding environments and thus appear as separate resonances in the complex even though they are identical in uncomplexed $\text{R}'\text{CA}$. NOESY studies are also consistent with the proposed structure. We observed NOEs between (i) the *tert*-butyl protons of $\text{R}'\text{CA}$ (v in Scheme 1) and the adjacent aromatic protons of hubM_3 (l and m) and (ii) the methylene and *tert*-butyl protons of $\text{R}'\text{CA}$ (t and v) and the adjacent *tert*-butyl protons of hubM_3 (s). In the $(\text{hubM}_3)_1(\text{R}'\text{CA})_3$ complex these groups are close together.

Several other methods support the 1:3 stoichiometry, $(\text{hubM}_3)_1(\text{R}'\text{CA})_3$. Vapor pressure osmometry (VPO) indicated a MW of 2720¹⁰ (calculated for $(\text{hubM}_3)_1(\text{R}'\text{CA})_3 = 2733$) over the concentration range 2–16 mM in CHCl_3 at 37 °C. Titration of hubM_3 (0.1 mM in CH_2Cl_2) with $\text{R}'\text{CA}$ monitored by UV spectroscopy indicated a 1:3 complex. The complex is also stable enough to withstand chromatography. Reverse-phase TLC (eluted with 5% 2-propanol in CH_2Cl_2) gave three spots: a major spot

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(6) The importance of preorganization is clearly illustrated in the work of Rebek, Cram, and others. Rebek, J., Jr. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 245–255 and references therein. Bryant, J.; Ericson, J.; Cram, D. *J. Am. Chem. Soc.* **1990**, *112*, 1255–1256. Hydrogen-bonding networks have been used in many imaginative approaches to the construction of structurally defined, noncovalent complexes. Etter, M. *Acc. Chem. Res.* **1990**, *23*, 120–126.

(7) All new compounds gave satisfactory ^1H NMR (500 MHz), ^{13}C NMR (125 MHz), and mass spectra.

(8) We have examined the complexation of hubM_3 with a number of other cyanuric and barbituric acid derivatives. These compounds also seem to lead to complexes analogous in structure to $(\text{hubM}_3)_1(\text{R}'\text{CA})_3$, although some of them contain up to 10% of other hydrogen-bonded species. We believe these other hydrogen-bonded species to be conformational isomers of a symmetrical 1:3 complex (Scheme 1) in which one of the M units has been flipped 180° with respect to the plane of the CA_3M_3 ring. These isomers have a dissymmetric arrangement of the three "spokes".

(9) $\text{R}'\text{CA}$ alone has low solubility in CDCl_3 . Beyond the 1:3 stoichiometry the $\text{R}'\text{CA}$ in excess of that required to form $(\text{hubM}_3)_1(\text{R}'\text{CA})_3$ does not go into solution.

(10) The values of three separate determinations were MW = 2670, 2640, 2850.

for the complex $(\text{hubM}_3)_1(\text{R}'\text{CA})_3$ (R_f 0.35–0.45) and minor spots for uncomplexed hubM_3 (R_f 0.15–0.30) and uncomplexed $\text{R}'\text{CA}$ (R_f 0.0).¹¹

These data establish the composition and structure of $(\text{hubM}_3)_1(\text{R}'\text{CA})_3$. Preorganization, i.e., joining the three melamine units by using the 1,3,5- $\text{C}_6\text{H}_3\text{R}_3$ hub and spokes conformationally compatible with the desired structure (Scheme 1), is an important factor contributing to the stability of the complex. Reaction of monomeric derivatives of M and CA in solution forms complexes having approximately the correct molecular weight for $\text{CA}_3\cdot\text{M}_3$ by VPO,¹² but crystallization of these complexes yields extended linear structures.¹³ The apparent solution molecular weight in these systems may represent a true cyclic hexamer $\text{CA}_3\cdot\text{M}_3$ or an average of linear and cyclic oligomers.

Acknowledgment. NMR instrumentation was supported by National Science Foundation Grant CHE-84-10774. Mass spectra were obtained by Dr. Andrew Tyler (Harvard University Mass Spectrometry Facility) using instrumentation provided by JEOL (USA) Inc. We thank Professor Robert Cohen (MIT, Chemical Engineering) for the loan of the vapor pressure osmometer and for helpful discussions.

(11) We have not obtained crystals of the 1:3 complex that are suitable for X-ray diffraction.

(12) VPO indicated a MW of 2710 for a 1:1 mixture of *N,N'*-bis(4-*tert*-butylphenyl)melamine and 3,3,3-triphenylpropyl cyanurate (calculated for $(\text{N,N}'\text{-bis}(4\text{-}i\text{-tert}\text{-butylphenyl)melamine)}_1(\text{3,3,3-triphenylpropyl cyanurate})_3 = 2370$) over the concentration range 6–20 mM in CHCl_3 at 37 °C. The MW estimated by VPO depends strongly on concentration at lower concentrations.

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