

## Commentary

### Supramolecular chemistry

William L. Jorgensen

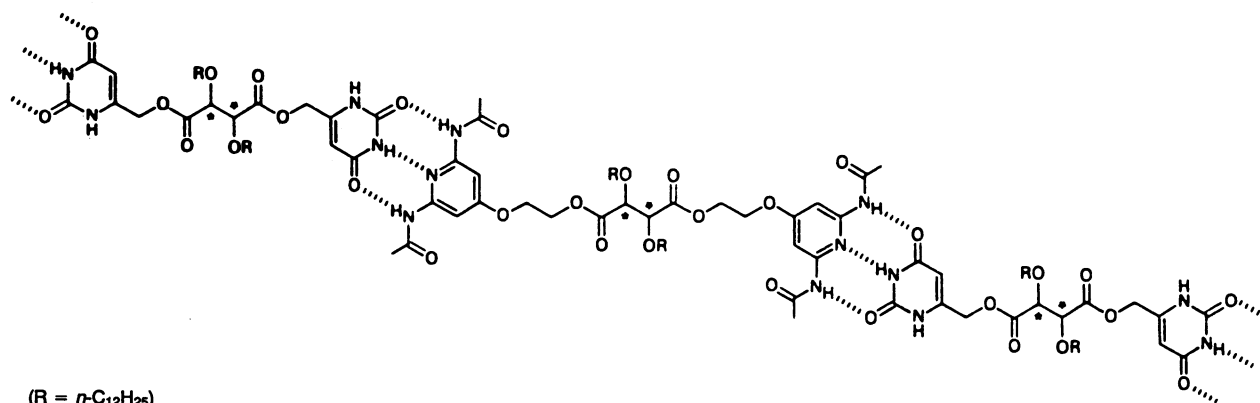
Department of Chemistry, Yale University, New Haven, CT 06511-8118

Supramolecular chemistry is a broad emerging field that features molecular assemblies built-up from components interacting through specific noncovalent interactions (1, 2). The efforts in the area extend from the studies of molecular recognition and bioorganic host–guest chemistry over the last 25 years that have extensively characterized the nature and variability of fundamental noncovalent interactions, particularly hydrogen bonding

The latter work is significantly extended in a recent paper by Lehn and coworkers (8). It has been demonstrated (9) that ditopic complementary components based on 2,6-diaminopyridine (P) and uracil (U) with tartaric acid (T) derivatives as spacers yield supramolecular polymers through triple hydrogen bonding.

The tartaric acid can have L, D, or *meso* stereochemistry to yield compo-

helical strings by winding multiple filaments. Naturally, the DP<sub>2</sub> + DU<sub>2</sub> mixture was found to give the same progression based on left-handed helical constituents. Other interesting observations were made; for example, racemic solutions of LP<sub>2</sub> + LU<sub>2</sub> + DP<sub>2</sub> + DU<sub>2</sub> yielded separate subdomains with either left- or right-handedness, presumably caused by separation of the D and L components. Thus, growth of the triple



and ion complexation. A major goal is the rational design of self-assembling supramolecular systems with desired structures and properties. This requires a much enhanced understanding of the relationships between molecular geometry, intermolecular interactions, and macroscopic characteristics. Pursuit of this fundamental knowledge can be expected to be accompanied by the development of valuable catalysts, molecular electronic components, and photochemical devices.

Activities in supramolecular chemistry are widespread. The last year or two have yielded some truly novel structures, for example, a trefoil knot (3), an  $\alpha$ -cyclodextrin necklace (4), “molecular mecano” rotaxanes and catenanes (5), self-replicating molecules (6), and molecular tapes and a rosette (7). All along, a leading center for both concept and practice has been Jean-Marie Lehn’s group (1). Lehn and his coworkers have done much to define the field and to demonstrate the potential for the creation of useful imaginative materials. Their work on molecular wires, synthetic ion channels, double-stranded copper helicates, and self-assembling mesogenic complexes reflects only some of their seminal contributions (1).

nents designated LP<sub>2</sub>, DP<sub>2</sub>, MP<sub>2</sub>, LU<sub>2</sub>, DU<sub>2</sub>, and MU<sub>2</sub>. The 1:1 mixtures (LP<sub>2</sub> + LU<sub>2</sub>) and (MP<sub>2</sub> + MU<sub>2</sub>) were found to display thermotropic mesophases over a broad range from below room temperature up to 250°C. However, x-ray diffraction revealed different structures for the two mesophases; the results supported a triple-helix superstructure formed from three strands of the LP<sub>2</sub> + LU<sub>2</sub> polymer, whereas the MP<sub>2</sub> + MU<sub>2</sub> mixture appears to assemble into polymeric strands in a zig-zag arrangement. Further structural characterization of the mixtures has now been carried out with electron microscopy. The mixtures were deposited on carbon-coated grids and the chloroform solvent was evaporated. Variations in the concentrations of the solutions allowed analysis of small aggregates to multilayer assemblies of the hydrogen-bonded polymers.

At low concentration, the LP<sub>2</sub> + LU<sub>2</sub> mixture forms aggregates, which do extend into right-handed triple-helical filaments at higher concentration. Further increase in concentration results in lateral association of the filaments, likely accompanied by alkyl side chain entanglement, and also the formation of super-

helices selects the stereochemically compatible components and local spontaneous resolution occurs. In contrast, the achiral MP<sub>2</sub> + MU<sub>2</sub> mixtures only yielded aggregates with amorphous structure under the same conditions.

Lehn and coworkers (8) provide a striking example of the elegantly complex structures that can be built by supramolecular assembly of complementary chiral components. The chirality of the tartaric acid units becomes amplified into the helicity of the triple-stranded filaments, which is amplified again by further association into macroscopic fibers with specific textures. Though this progression is exciting to witness, it is also humbling in the unanswered questions that it raises. The association of the TP<sub>2</sub> + TU<sub>2</sub> units by triple hydrogen bonding to form mesogenic supramolecular polymeric strands is understandable from numerous precedents on such complexations and the structures of mesogenic compounds. But, that is about it. The driving force for organization of the L strands into the triple-helical filaments in preference to other structures is unclear, as is the origin of the difference between the L and M structures. The atomic-level

structure of the helices is unknown. The amplification of the L or D stereochemistry into the right- and left-handedness of the helices is also currently unexplained. Molecular modeling of the helices could be illuminating for the last two issues. It might also help provide an explanation for the curious observation that 1:1 (DP<sub>2</sub> + LU<sub>2</sub>) and (LP<sub>2</sub> + DU<sub>2</sub>) mixtures only yield right-handed and left-handed helical strands, respectively; i.e., the TU<sub>2</sub> unit controls the helical twist. A related issue includes better understanding of the B → Z transition for DNA.

Overall, there is no question that many more studies of supramolecular assembly are essential to help build the data base needed for the emergence of algorithms governing the steps from intermolecular

complexation to macroscopic structure. The central problems here are closely related to those in predicting the structures of proteins and organic crystals. Sufficiently accurate and general computational tools are not yet available to calculate *a priori* the structures of such assemblies. Improvements will come from extensive integration of computation and experiment. This will be a productive direction for the next decade and beyond along with development of the great potential of supramolecular systems.

1. Lehn, J.-M. (1990) *Angew. Chem. Int. Ed. Engl.* **29**, 1304–1319.
2. Schneider, H.-J. (1991) *Angew. Chem. Int. Ed. Engl.* **30**, 1417–1436.
3. Sauvage, J.-P. (1990) *Acc. Chem. Res.* **23**, 319–327.
4. Harada, A., Li, J. & Kamachi, M. (1992) *Nature (London)* **356**, 325–327.
5. Anelli, P. L., Ashton, P. R., Ballardini, R., Balzani, V., Delgado, M., Gandolfi, M. T., Goodnow, T. T., Kaifer, A. E., Philp, D., Pietraszkiewicz, M., Prodi, L., Reddington, M. V., Slawin, A. M. Z., Spencer, N., Stoddart, J. F., Vicent, C. & Williams, D. J. (1992) *J. Am. Chem. Soc.* **114**, 193–218.
6. Feng, Q., Park, T. K. & Rebek, J., Jr. (1992) *Science* **256**, 1179–1180.
7. Zerkowski, J. A., Seto, C. T. & Whitesides, G. M. (1992) *J. Am. Chem. Soc.* **114**, 5473–5475.
8. Gulik-Krzywicki, T., Fouquey, C. & Lehn, J.-M. (1993) *Proc. Natl. Acad. Sci. USA* **90**, 163–167.
9. Fouquey, C., Lehn, J.-M. & Levelut, A.-M. (1990) *Adv. Mater.* **2**, 254–257.