

Controlling the assembly of hydrogen-bonded supramolecular polymers by the strategy of molecular tectonics*

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Abstract: Studies of how hydrogen bonding can be used to control molecular association continue to yield exciting discoveries in supramolecular chemistry. A simple way to make molecules that associate predictably is to link carefully selected cores to functional groups that form multiple hydrogen bonds according to reliable patterns. Bifunctional molecules constructed according to this strategy can associate to form linear aggregates robust enough to warrant the name supramolecular polymers, even though the bifunctional monomers are joined only by hydrogen bonds. More complex molecules with multiple hydrogen-bonding sites can be devised so that neighbors are held in predetermined positions, giving crystalline solids with predictable architectures and properties not previously seen in other materials. Initial studies of the ability of such compounds to associate in solution and in the molten state suggest that hydrogen-bonded networks can be purposefully designed to create novel partially ordered liquid materials, including liquid crystals, gels, and fluids with unusual rheological properties.

INTRODUCTION

Use of hydrogen bonding to direct molecular association

Biological chemistry provides magnificent illustrations of the potential of hydrogen bonding to control molecular recognition and association. Among the most striking examples are (1) formation of the double helix of DNA, directed by hydrogen bonding of pairs of complementary heterocyclic rings; (2) the creation of α -helices, β -sheets, and other periodic structures from peptide chains, controlled by hydrogen bonding of CO and NH groups in the main chain; and (3) binding and stabilization of transition states by the active sites of enzymes, typically involving complex arrays of hydrogen-bonded groups. Of the properties that give hydrogen bonds a special role as structuring elements in biological chemistry, their directionality, strength, and reversible formation are particularly important [1].

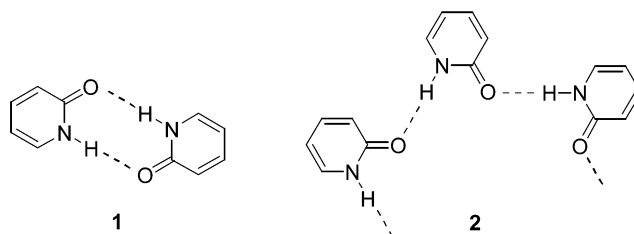
Such biological examples have provided a powerful incentive for researchers to explore molecular association more broadly, and they have helped give birth to the field of supramolecular chemistry and ensure that it continues to expand rapidly, decades after its creation by the pioneering work of

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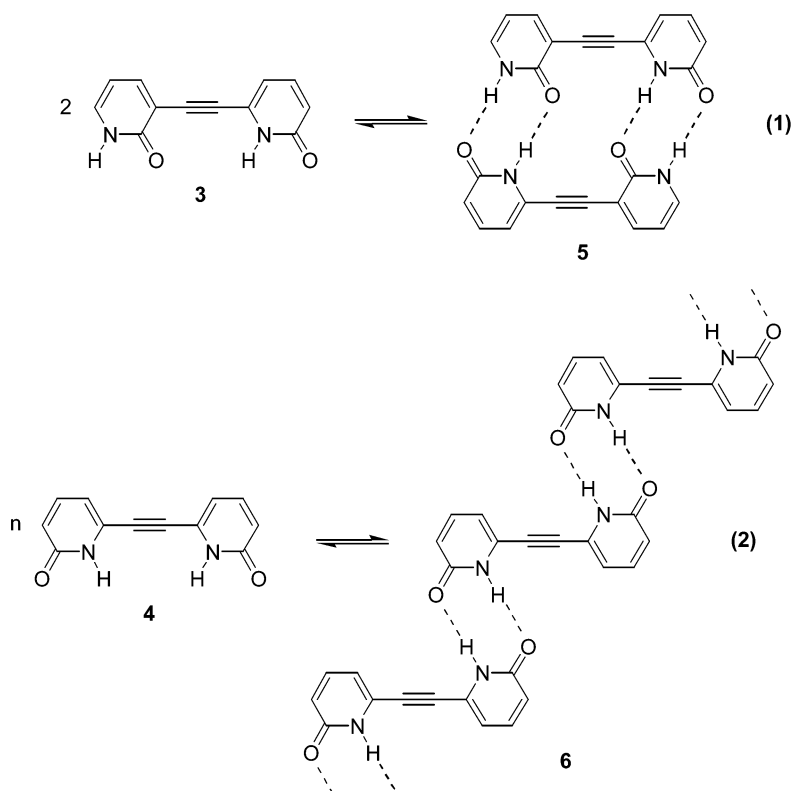
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Cram, Lehn, and Pedersen [2]. Among the fundamentals of this field is the notion that certain functional groups frequently encountered in chemistry form hydrogen bonds according to established patterns and can therefore be used to control association with a degree of rationality. For example, 2-pyridinones are known to self-associate by hydrogen bonding in solution and in the solid state to form cyclic dimers **1** or chains **2**. However, such association is relatively weak because each molecule takes part in only two hydrogen bonds; in addition, multiple motifs are possible, making aggregation hard to control and predict.



We recognized that these shortcomings of simple functional groups can be alleviated or even eliminated by devising more complex units able to form larger numbers of hydrogen bonds, or by simply joining multiple copies of simple groups to carefully selected cores. For example, in a widely cited paper published more than 15 years ago [3], we showed how two 2-pyridinone groups can be grafted to an acetylenic spacer to create dipyridinones **3** and **4**, thereby doubling the enthalpy of association per molecule. Moreover, this strategy simultaneously controls the selectivity of association by creating unique linear patterns of sites that donate (D) or accept (A) hydrogen bonds. In particular, dipyridinone **3** incorporates a quadruple DADA pattern, which is self-complementary and thereby permits formation of cyclic dimer **5** in solution and in the solid state (eq. 1). In contrast, the quadruple ADDA pattern of



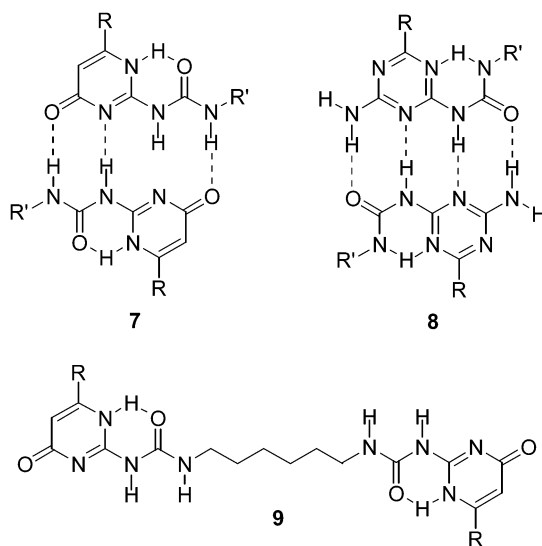
hydrogen-bonding sites in dipyridinone **4** is not self-complementary, and oligomeric chains **6** are produced (eq. 2). As summarized in the following two sections, this initial work has helped stimulate further development of two exciting new fields of research in supramolecular chemistry: supramolecular polymers [4,5] and molecular tectonics [6–11].

Hydrogen-bonded supramolecular polymers

Modifying covalent polymers by intentionally introducing hydrogen-bonding groups has proven to be a productive strategy in macromolecular chemistry for controlling assembly and altering rheological properties. In pioneering research of this type, de Lucca Freitas and Stadler grafted self-associating hydrogen-bonding groups at random positions along poly(butadiene) chains [12]. They confirmed that inter-chain hydrogen bonding created a thermoreversible network, and they established that the rheological properties of the modified polymer changed as a function of the number of hydrogen-bonding sites introduced.

In a significant extension of our earlier studies of dipyridinones **3** and **4**, Meijer and coworkers devised elegantly simple ways to make a variety of new quadruple linear hydrogen-bonding motifs [13], and other groups have also constructed related arrays of hydrogen-bonding sites designed to control association [14–16]. Of particular note are self-complementary DDAA arrays such as those found in dimers **7** of ureidopyrimidinones, which generally give stronger association than related DADA motifs such as those in dimers **8** of ureidotriazines.

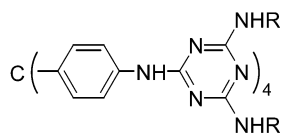
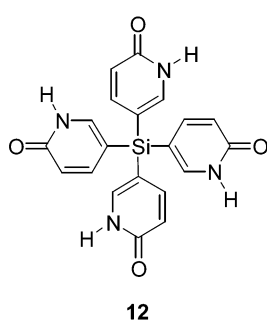
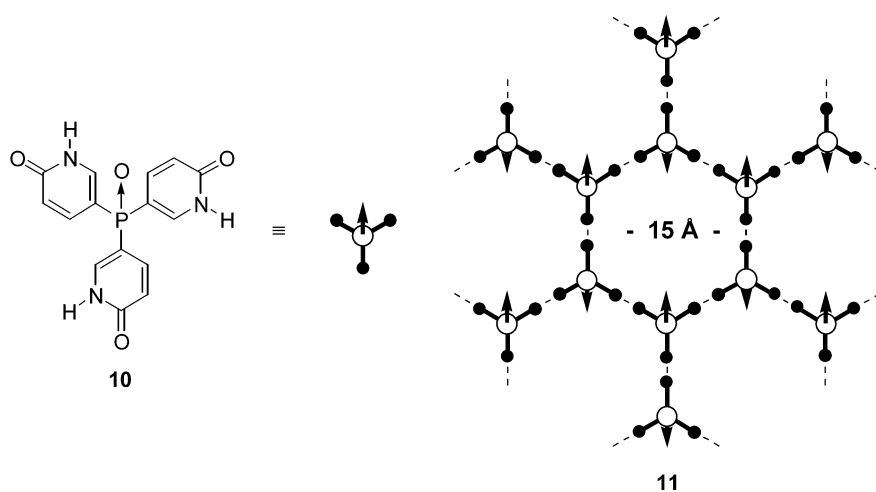
In subsequent work, Meijer and coworkers made a notable contribution to supramolecular chemistry by connecting strongly self-associating quadruple hydrogen-bonding arrays to various spacers to create well-defined bifunctional derivatives [4,5]. For example, bis(ureidopyrimidinone) **9** is designed to form robust linear aggregates. Such aggregates are joined reversibly by noncovalent bonds, not irreversibly by covalent bonds. Nevertheless, the noncovalent bonding is typically strong enough to ensure that aggregates have long lifetimes and incorporate large numbers of bifunctional monomers. As a result, it is proper to refer to the aggregates as supramolecular polymers [4,5]. Placing extended hydrogen-bonding arrays at the ends of polymer chains creates telechelic derivatives with significantly altered rheological properties. For example, Sijbesma, Meijer, and coworkers have found that a telechelic derivative of poly(ethylene/butylene) made by adding ureidotriazine end groups is a soft elastic solid, whereas the unmodified copolymer is a viscous liquid under the same conditions [17].



Molecular tectonics

Our study of dipyridinones **3** and **4** was also the starting point for the development of a potentially general strategy for controlling molecular association, which we have called *molecular tectonics* [6]. This strategy is based on special sticky molecules called *tectons* (from the Greek word for builder), which are strongly predisposed to associate according to well-established motifs. Their association is best controlled by noncovalent interactions that are well defined, directional, and predictable, such as selected arrays of hydrogen bonds. Once synthesized, tectons associate to produce ordered aggregates by a process of programmed self-assembly. For example, self-complementary dipyridinone **3** was designed to form a simple dimer by zero-dimensional assembly, as observed. In contrast, non-self-complementary isomer **4** was designed to form polymeric chains by one-dimensional assembly, again as observed.

We recognized that control of assembly in higher dimensions could be achieved by attaching multiple sticky sites to increasingly more complex cores. For example, crystallization of tripyridinone **10** is directed by normal hydrogen bonding of the pyridinone rings to give stacks of corrugated sheets **11** [18], as planned, and tetrapyridinone **12** generates a three-dimensional network with diamondoid connectivity [9,19]. In favorable cases such as these, the strategy of molecular tectonics can be used to place neighboring molecules in predetermined positions, giving ordered networks with predictable architectures and properties. Because the sticky sites and cores can both be varied broadly, molecular tectonics has wide scope for creating new ordered materials by design.



13a (R = H)

13b (R = CH₂CH=CH₂)

13c (R = (CH₂)₅CH₃)

13d (R = (CH₂)₇CH₃)

13e (R = (CH₂)₈CH₃)

13f (R = (CH₂)₉CH₃)

13g (R = (CH₂)₁₁CH₃)

Initial studies of molecular tectonics have emphasized its usefulness as a rational method for engineering crystals [6–11]. Of particular note is the observation that the strong predisposition of tectons to form directional interactions normally keeps them from crystallizing as close-packed structures. Instead, tectonic association typically produces porous networks that include other molecules as guests. Remarkably, networks with high porosity can be formed even from tectons constructed by attaching sticky sites to highly flexible cores [20,21]. Other recent highlights of our studies of molecular tectonics are summarized below:

Crystal engineering with sub-nanometric precision

The molecular structures of individual tectons can be altered logically to create series of isostructural networks that have been expanded or contracted predictably on the sub-nanometric scale. For example, rational expansion of networks built from tectons derived from tetraphenylmethane can be achieved by replacing the central carbon atom with silicon, thereby incorporating longer Si–C bonds in place of C–C bonds [7].

Hydrogen-bonded networks with exceptional porosity and robustness

Tectons built from cores with shapes that are intrinsically resistant to close packing can generate networks with exceptional porosity. For example, a tecton derived from spirobifluorene yields crystals in which 75 % of the volume is accessible to guests [8], and the guests can be exchanged in single crystals without loss of crystallinity. This is the highest porosity ever observed in networks constructed from small molecules.

Highly deformable crystals

The silyl core of tecton **12** can act as a locus of structural deformation, allowing single crystals to withstand changes of dimension of at least 30 % without loss of crystallinity [9]. The special resilience of these crystals appears to be due in part to the incorporation of highly flexible Si nodes in an otherwise robust network maintained by multiple hydrogen bonds.

Rational topotactic reactions of crystalline solids with external agents

Tectons can be designed to give permeable crystals that react with external agents to give single crystals of new compounds with retention of the original crystalline architecture [10,11]. Moreover, crystals can be cross-linked covalently by this strategy, thereby capturing temporary supramolecular constructs as permanent crystalline macromolecular replicas. For example, monothiols small enough to diffuse into single crystals of tecton **13a** can undergo efficient photoaddition to exposed allyl groups, thereby producing single crystals of the corresponding thioethers. Similar exposure of single crystals to suitable dithiols provides single crystals of a cross-linked macromolecule.

These discoveries confirm that molecular tectonics is a fruitful strategy for making crystalline solids with properties not previously observed in other materials. Also of significant interest, but so far little studied, is the possibility that extensive tectonic association may occur in liquid phases to create partially ordered materials with novel features, including liquid crystals, gels, and fluids with unusual rheological properties. An initial exploration of the potential of molecular tectonics in these areas is summarized below.

RECENT RESULTS

As expected, tecton **13a** crystallizes to form a porous three-dimensional network held together by hydrogen bonding of triaminotriazine groups according to established motifs [10,11]. Similarly, crystallization of octaallyl derivative **13b** gives a porous diamondoid network in which each tecton forms a total of 16 hydrogen bonds with four neighbors [10]. The relatively low solubility and high melting points of tectons **13a–b** prevented us from studying their association in solution or in the molten state. However, we reasoned that derivatives with longer alkyl substituents would show a similar tendency to form extensively hydrogen-bonded networks but would have significantly higher solubilities and lower

melting points, thereby facilitating studies of their association in liquid phases. Straightforward modifications of the routes used to synthesize tectons **13a–b** allowed us to prepare the series of octaalkyl derivatives **13c–g**, with straight alkyl chains ranging from six to twelve carbons in length.

We expected compounds **13c–g** to exist as hydrogen-bonded supramolecular polymers in the solid state, to associate reversibly to form less extensively hydrogen-bonded networks in the melt, and finally to form increasingly less viscous fluids at higher temperatures. Measurements using modulated differential scanning calorimetry have been carried out to establish how T_g varies with chain length in the series of compounds **13c–g**. In addition, their rheological behavior has been studied in steady-state and dynamic modes to reveal how viscosity depends on chain length. The viscosity of conventional linear polymers is known to increase linearly with molecular weight, and the viscosity of dendrimers increases with molecular weight according to a power law. Significant deviations from these patterns of behavior establish that compounds **13c–g** behave neither like dendrimers nor like conventional linear polymers, but rather form a novel class of materials. The results of our detailed study of compounds **13c–g** have been submitted for publication [22].

CONCLUSIONS

Studies of how hydrogen bonding can be used to control molecular association continue to yield exciting discoveries in supramolecular chemistry. A simple way to make molecules that associate predictably is to link carefully selected cores to groups that form multiple hydrogen bonds according to reliable patterns. Bifunctional molecules constructed according to this strategy can associate to form linear aggregates robust enough to warrant the name supramolecular polymers, even though they are joined only by hydrogen bonds. More complex molecules with multiple hydrogen-bonding sites can be devised so that neighbors are held in predetermined positions, giving crystalline solids with predictable architectures and properties not previously seen in other materials. Initial studies of the ability of such compounds to associate in solution and in the molten state suggest that hydrogen-bonded networks can be purposefully designed to create novel partially ordered liquid materials, including liquid crystals, gels, and fluids with unusual rheological properties.

REFERENCES

1. G. A. Jeffrey and W. Saenger. *Hydrogen Bonding in Biological Structures*, Springer, New York (1991).
2. J.-M. Lehn. *Supramolecular Chemistry. Concepts and Perspectives*. Wiley-VCH, Weinheim, Germany (1995).
3. Y. Ducharme and J. D. Wuest. *J. Org. Chem.* **53**, 5787 (1988).
4. L. Brunsveld, B. J. B. Folmer, E. W. Meijer, R. P. Sijbesma. *Chem. Rev.* **101**, 4071 (2001).
5. D. C. Sherrington and K. A. Taskinen. *Chem. Soc. Rev.* **30**, 83 (2001).
6. M. Simard, D. Su, J. D. Wuest. *J. Am. Chem. Soc.* **113**, 4696 (1991).
7. J.-H. Fournier, T. Maris, J. D. Wuest, W. Guo, E. Galoppini. *J. Am. Chem. Soc.* **125**, 1002 (2003).
8. J.-H. Fournier, T. Maris, J. D. Wuest. *J. Org. Chem.*, ASAP Article, DOI: 10.1021/jo0348118 (2003).
9. O. Saied, T. Maris, J. D. Wuest. *J. Am. Chem. Soc.* **125**, 14956 (2003).
10. P. Brunet, E. Demers, T. Maris, G. D. Enright, J. D. Wuest. *Angew. Chem., Int. Ed.* **42**, 5303 (2003).
11. E. Le Fur, E. Demers, T. Maris, J. D. Wuest. *Chem. Commun.* 2966 (2003).
12. L. L. de Lucca Freitas and R. Stadler. *Macromolecules* **20**, 2478 (1987).
13. R. P. Sijbesma and E. W. Meijer. *Chem. Commun.* 5 (2003).
14. L. J. Prins, D. N. Reinhoudt, P. Timmerman. *Angew. Chem., Int. Ed.* **40**, 2382 (2001).
15. E. A. Archer, H. Gong, M. J. Krische. *Tetrahedron* **57**, 1139 (2001).

16. C. Schmuck and W. Wienand. *Angew. Chem., Int. Ed.* **40**, 4363 (2001).
17. J. H. K. K. Hirschberg, A. Ramzi, R. P. Sijbesma, E. W. Meijer. *Macromolecules* **36**, 1429 (2003).
18. N. Malek, T. Maris, J. D. Wuest. Manuscript in preparation.
19. X. Wang, M. Simard, J. D. Wuest. *J. Am. Chem. Soc.* **116**, 12119 (1994).
20. D. Laliberté, T. Maris, J. D. Wuest. *J. Org. Chem.* In press.
21. D. Laliberté, T. Maris, A. Sirois, J. D. Wuest. *Org. Lett.* **5**, 4787 (2003).
22. D. Boils-Boissier, M.-È. Perron, F. Monchamp, H. Duval, T. Maris, J. D. Wuest. *Macromolecules*. Manuscript accepted for publication.