Topotactic Reactions in Networks

Designing Permeable Molecular Crystals That React with External Agents To Give Crystalline Products**

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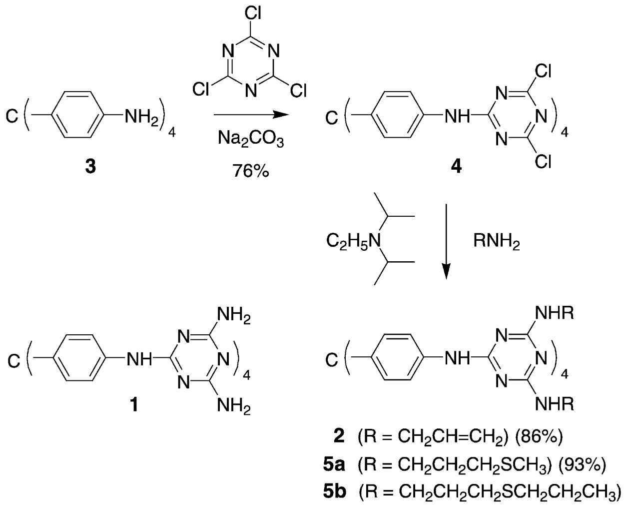
Topotactic reactions,[1] which convert single crystals of starting compounds directly into single crystals of products, are elegant and potentially useful processes that have fascinated solid-state chemists for many years. Unfortunately, such reactions are very rare. Mobility in solids is restricted, so known topotactic reactions in molecular crystals typically involve intramolecular processes or require that all necessary co-reactants be present within the solid, held in close proximity, and oriented properly.[2,3] These prerequisites can sometimes be satisfied by laborious crystal engineering, but new ways to devise topotactic reactions are needed. Here we describe a general strategy based on the use of permeable molecular crystals that are specifically designed to let external agents enter, react, and produce single crystals of new substances, with retention of the original crystalline architecture. Moreover, we show that such topotactic processes can be made to cross-link molecular crystals covalently, thereby capturing temporary supramolecular constructs as permanent crystalline macromolecular replicas.

Our strategy is related to the technique of isomorphous replacement in protein crystallography, a largely empirical process in which protein crystals are treated with agents that diffuse though water-filled channels in the crystal and bind at sites not normally determined in advance. We felt that single crystals of much smaller molecules might be made to react quantitatively with external agents at predetermined sites, thus providing a rational route to new substances in crystalline form. At present, such reactions are exceedingly rare, have been discovered by accident rather than by design, and involve only the smallest possible reactants.[3,4]

Suitable permeable molecular crystals can be made by an approach that has been called molecular tectonics.[5] This approach relies on the programmed association of special sticky molecules called tectons (derived from the Greek word for builder) that form directional interactions with neighbors according to well-established motifs. Such molecules do not typically crystallize in normal close-packed arrays; instead, they tend to form open networks filled with potentially mobile guests.[6] Tectonic networks held together by multiple hydrogen bonds are normally robust enough to allow the original guests to be exchanged or even partially removed without the loss of crystallinity, which renders their interiors accessible to various reagents.[7]

Initial experiments showed that in the porous hydrogen-bonded network formed by tecton **1** (Scheme 1), -NH_2 groups not used in intertectonic hydrogen bonding lie in guest-filled channels.[8] We reasoned that -NHR groups in substituted derivatives would be located similarly, thus making the substituents accessible to external agents. To test this hypothesis, we synthesized octaallyl derivative **2** by the route summarized in Scheme 1. X-ray diffraction established that tecton **2** crystallizes from dioxane in the tetragonal space



Scheme 1. Tecton **1** and the synthesis of tectons **2** and **5a** in solution.

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group $I4_1/a$ to give the network represented by Figures 1 and 2. Each tecton forms a total of 16 hydrogen bonds with four neighbors, which results in a robust noninterpenetrated network with diamondoid connectivity.[9,10]

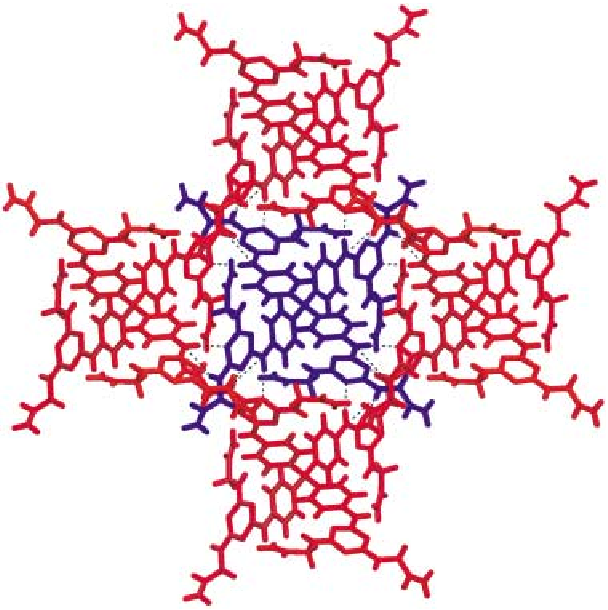

Figure 1. View along the *c* axis of the crystal structure of tecton **2** showing a single tecton (blue) and the four neighbors (red) with which it forms hydrogen bonds (-----).

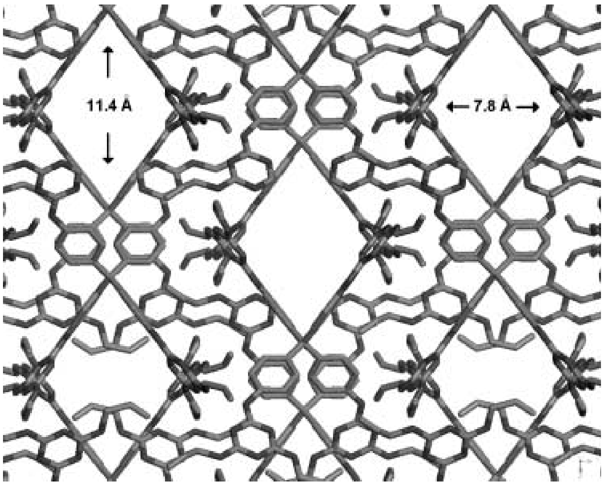

Figure 2. View along the *b* axis of the crystal structure of tecton **2** showing the cross sections of helical channels. Hydrogen atoms and some allyl groups (upper channels) have been removed for clarity.

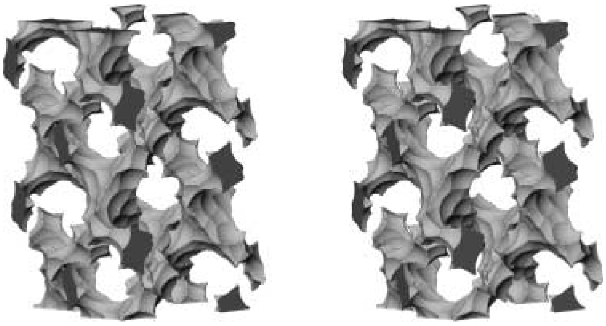

Figure 3. Stereoscopic representation of the channels in the structure of tecton **2**.[13] The image shows a 1 × 1 × 2 array of unit cells with the *c* axis vertical. The outsides of the channels appear in light gray, and dark gray is used to show where the channels are cut by the boundaries of the array. The surface is defined by the possible loci of the center of a sphere of diameter 3 Å as it rolls over the surface of the ordered tectonic network.

Dioxane occupies nearly 40 % of the volume of the crystals,[11,12] which have the composition **2**·6 dioxane, as determined by X-ray crystallography and ^{1}H NMR spectroscopy of dissolved samples. The guests fill interconnected helical channels that have a rhomboid cross section of approximately 7.8×11.4 Å^2 at the narrowest points (Figure 2). The channels themselves are represented by the surface shown in Figure 3.[13] In principle, guests diffusing inside the crystals can reach any point within the channels by multiple redundant pathways. As planned, the channels also include the allyl groups of tecton **2**.

When single crystals of tecton **2**·6 dioxane of dimensions $0.5 \times 0.5 \times 0.5$ mm were treated with excess toluene at 25 °C for 24 h, they remained transparent and morphologically unchanged, continued to exhibit uniform extinction between crossed polarizers, and showed closely similar unit-cell parameters when studied by single-crystal X-ray diffraction. However, analysis of dissolved samples by ^{1}H NMR spectroscopy established that the initial guest, dioxane, had been replaced completely by toluene. As a result, these crystals are well designed to allow a suitable reagent to enter by diffusion and react predictably with the exposed allyl groups without changing the architecture of the network, thereby yielding isostructural crystals of a new substance.

This possibility was tested by placing single crystals of tecton **2** in degassed toluene in a quartz vessel, then exposing them to CH_3SH and irradiating them with a medium-pressure Hg lamp at 25 °C for 40 h. Under these conditions, photochemical solid-state addition of thiol to the allyl groups occurred to give thioether **5a**,[14,15] in which 70–85 % of the allyl groups had reacted, as measured by ^{1}H NMR spectroscopy of dissolved samples. Moreover, the process proved to be topotactic. The resulting crystals were morphologically unchanged, remained transparent, and continued to exhibit uniform extinction between crossed polarizers. X-ray diffraction confirmed that thioether **5a** had been formed isostructurally as single crystals belonging to the tetragonal space group $I4_1/a$, with unit-cell parameters similar (± 9 %) to those of precursor **2**.

A larger thiol ($CH_3CH_2CH_2SH$) also reacted topotactically in high yield with crystals of tecton **2** to give isostructural single crystals of thioether **5b** with similar (± 2 %) unit-cell parameters. In contrast, thiols that were too large to enter the channels in crystals of tecton **2** reacted negligibly under similar conditions, presumably because only the surfaces of the crystals are accessible. For example, photochemical additions of 3,5-dimethylbenzenethiol and 2,4,6-trimethylbenzylthiol proceeded only to the extent of ≈3%. Such control experiments established that the observed solid-state photochemical additions to tecton **2** do not occur by a sequence of dissolution, reaction in solution, and subsequent recrystallization. The mass spectrum of thioether **5a** obtained topotactically showed the expected statistical distribution of molecules with reacted and unreacted allyl groups, which suggests that addition occurs relatively homogeneously throughout the crystal. A bimodal distribution, which would arise if addition occurred exclusively near the surface to leave an unreacted core, was not observed.

A sample of thioether **5a** prepared independently in solution by treating intermediate **4** (Scheme 1) with 3-methylthio-1-propanamine could be crystallized from CH_3OH/THF. In this case, the structure proved to be the same as the one obtained topotactically in the solid state. In other cases, however, we expect new polymorphs to be formed. Our strategy for devising topotactic reactions in porous crystals has two notable advantages: 1) It delivers single crystals of new compounds in polymorphic forms that are predetermined, based on the structure of the starting material, and 2) these polymorphs may be impossible to obtain by direct crystallization of the product, either because other polymorphs are favored or because crystallization does not occur at all.

A long-sought goal in supramolecular chemistry is covalent capture,[16] in which ordered structures formed reversibly by self-assembly are converted into analogues joined permanently by covalent bonds. Molecular tectonics allows predictable covalent capture to occur in the solid state by using permeable crystals with internally exposed reactive groups that can be cross-linked by external agents. This strategy extends conceptually related polymerizations, such as the cross-linking of porous protein crystals[17] and coordination complexes joined by metals,[18] to the realm of small molecular monomers and the production of single crystals of well-defined polymers.[19]

Single crystals of tecton **2**·6 dioxane were exposed to a series of liquid dithiols $HS(CH_2)_nSH$ and irradiated under standard conditions. The resulting materials proved to be insoluble in DMSO, hot aqueous HCl, and CF_3COOH, even after crushing to expose internal surfaces. This result indicates that extensive cross-linking had taken place. When $HSCH_2CH_2SH$ was used as the cross-linker, detailed studies of the resulting polymer by solid-state ^{13}C NMR spectroscopy and Raman spectroscopy confirmed the addition of the thiol to the allyl groups.[20] Remarkably, cross-linking of crystals of tecton **2** by both $HSCH_2CH_2SH$ and $HSCH_2CH_2CH_2SH$ occurred topotactically to give isostructural single crystals of the macromolecular products. Detailed single-crystal X-ray crystallographic analysis of the products confirmed directly that cross-linking had occurred and showed that each molecule of tecton **2** becomes joined not to its immediate hydrogen-bonded neighbors but to those somewhat farther away (Figure 4).

Despite close architectural similarity, the covalently cross-linked materials are vastly more stable than their hydrogen-bonded supramolecular precursor. In particular, variable-temperature X-ray powder diffraction established that the polymer derived from $HSCH_2CH_2SH$ loses its crystallinity only when it decomposes irreversibly above 200°C, whereas the precursor loses crystallinity at 25°C by spontaneous loss of included solvent. The topotactic cross-linking we observe in single crystals of tecton **2** has two unique characteristics: 1) Polymerization occurs in three dimensions to give a single crystalline macromolecular object, and 2) the composition of the product crystals is different from that of the starting crystals. In contrast, previously observed topotactic polymerizations have occurred in one direction to yield crystals with the same composition consisting of multiple copies of linear macromolecules.[2]

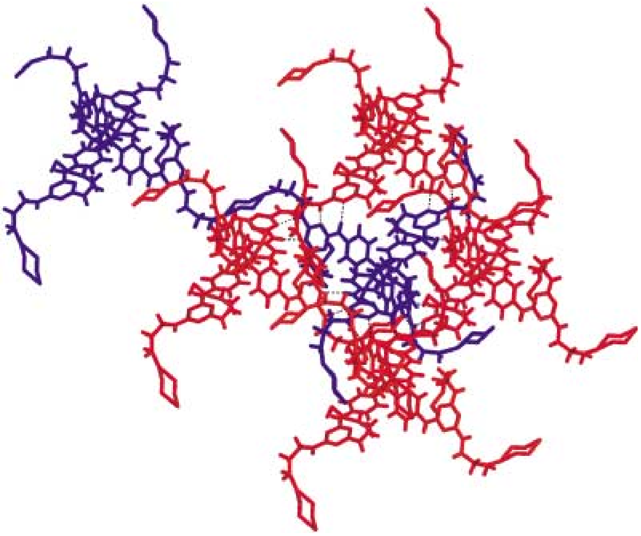

Figure 4. Structure of the macromolecule obtained by cross-linking crystals of tecton **2** with $HSCH_2CH_2SH$, as viewed approximately along the *c* axis. The image shows a central unit derived from tecton **2** (blue), four neighboring units (red) joined by hydrogen bonds (-----), and one of the farther units (also in blue) to which the central unit has been linked covalently.

These observations demonstrate how molecular tectonics, by allowing the design of robust porous networks with reactive interiors, can give access to new molecular and macromolecular materials with predictably ordered structures that would be difficult or impossible to obtain by conventional methods.

Experimental Section

X-ray structural analyses: Data were collected at 173 K using a Bruker SMART 1000 CCD diffractometer with $Mo_{K\alpha}$ radiation ($\lambda = 0.71070$ Å). Intensities were integrated using SAINT[21] and corrected for absorption and other effects using SADABS.[22] Structures were solved and refined using the SHELX suite of programs.[23]

Crystal data for tecton **2**·6 dioxane: crystal size 0.15 × 0.20 × 0.30 mm, tetragonal, space group $I4_1/a$, $a = b = 23.0674(6)$, $c = 16.1892(6)$ Å, $V = 8614.4(4)$ Å^3, $Z = 4$. Least-squares refinement of 273 parameters based on 1759 reflections with $I > 2\sigma(I)$ (out of 2269 reflections) gave $R_1 = 0.0795$, $wR_2 = 0.230$, and GOF = 1.076.

Crystal data for thioether **5a** (as obtained from crystals of tecton **2**): crystal size $0.08\times0.15\times0.20$ mm, tetragonal, space group $I4_1/a$, $a=b=20.988(2)$, $c=16.816(3)$ Å, $V=7407.6(16)$ Å^3, $Z=4$. Least-squares refinement of 214 parameters based on 865 reflections with $I>2\sigma(I)$ (out of 1976 reflections) gave $R_1=0.1210$, $wR_2=0.389$, and GOF = 1.306.

Crystal data for the product of cross-linking crystals of tecton **2** with $HSCH_2CH_2CH_2SH$: crystal size $0.15\times0.30\times0.30$ mm, tetragonal, space group $I4_1/a$, $a=b=23.233(16)$, $c=16.274(17)$ Å, $V=8785(13)$ Å^3, $Z=4$. Least-squares refinement of 182 parameters (with 192 restraints) based on 462 reflections with $I>2\sigma(I)$ (out of 688 reflections) gave $R_1=0.1888$, $wR_2=0.461$, and GOF = 1.766.

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