

# Molecular Recognition in Lamellar Solids and Thin Films

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“Molecular recognition” describes the selective, and usually noncovalent, binding of a molecule or ion to a complementary host. Such specific associations between molecules are ubiquitous in biology and include the vital functions of catalysis, immune response, transcription, replication, and biochemical signaling. They also lie at the heart of several practical chemical technologies, including chemical sensing, separations, and catalysis.

In light of the important place that molecular recognition holds in chemistry, the design and discovery of better hosts remain a worthy challenge. Historically, this challenge has been taken up by organic chemists, who have elaborated the principles of host–guest chemistry and have synthesized a wide variety of hosts with high affinity and selectivity.<sup>1</sup> It has been correctly noted, however, that molecular recognition by itself is not enough.<sup>2</sup> To be useful, host–guest interactions must operate in concert with other processes. In chemical sensing, for example, the binding event must be coupled to a signal transduction mechanism. Sometimes this can be achieved by using a soluble, small molecule host, as in the case of fluorescent chemosensors.<sup>3</sup> More often, however, some kind of macromolecular scaffolding—a membrane, an electrode, a conducting polymer, to name a few possibilities—is needed to allow the binding event to be detected in the outside world. Similar considerations apply to the design of supramolecular catalysts, in which molecular association must occur near a catalytic center or, in the case of a bimolecular reaction, in such a way as to bring the reactant molecules together.<sup>4</sup> Solids in general present more opportunities for signal transduction and catalysis than do individual organic molecules in solution. The hard part is making solids with molecular specificity.

This Account describes work that our group and others have recently undertaken in the design of lamellar inor-

ganic hosts. The idea behind this research is to combine the best of both worlds: to take inspiration and design from the world of organic host–guest chemistry, and to combine them with materials that have the virtues of crystallinity, ultrahigh surface area, and modular synthesis from easily manipulated metals, ligands, and templates. So far our work has concentrated on problems of chiral separations and small molecule sensing; however, it should be noted that the catalytic and electronic properties associated with inorganic materials might lend themselves readily to other applications, once the design principles of extended inorganic hosts are better elaborated.

## Intercalation Reactions

With crystalline solids, as with molecular hosts, molecular recognition implies accessibility to sites of complementary size, shape, charge, and chemical functionality. Open framework and layered materials provide this kind of access, and both have their own unique advantages. Zeolites and related porous solids contain well-defined void spaces and channels for guest molecules. They select ions and molecules on the basis of size and charge, and to some extent the chemical environment of their cages can be deliberately altered. Zeolites have widely been used as hosts for supramolecular assemblies,<sup>5</sup> and as components of chemical sensors,<sup>6</sup> and these applications have been recently reviewed.<sup>7</sup>

We focus here on lamellar inorganic solids, in which guest molecules access intracrystalline binding sites via intercalation reactions. Normally, intercalation (of graphite, clays, metal dichalcogenides, etc.) is driven by relatively unselective processes, such as oxidation–reduction, ion-exchange, or acid–base reactions. The interlamellar gallery expands to accommodate the guest, and so there is usually little size- or shape-selectivity to the reaction. This poor selectivity is offset by the fact that small changes in composition can translate to easily measured changes in mass, capacitance, electronic conductivity, or optical properties. The lamellar semiconductor  $\text{Mn}_2\text{P}_2\text{S}_6$ , for example, intercalates ammonia with partial charge transfer from the guest molecule. Both the dielectric constant and the electronic conductivity of the solid change dramatically during this process.<sup>8</sup> Thin films of “organoclays,” prepared by pillaring smectite clays with tetra(alkylammonium) ions, sorb benzene and other small hydrophobic molecules. The uptake of these molecules from the vapor phase can be monitored by means of a sensitive mass transducer, such as a quartz crystal microbalance.<sup>9</sup> Likewise, lamellar clay/polymer composites swell and contract as water is added and removed. Changes in humidity can therefore be read from changes in the interference colors of thin films of these materials.<sup>10</sup>

By intercalating or covalently “grafting” to the sheets a molecule which itself acts as a host, one can impart greater selectivity to subsequent guest intercalation reactions. This process, which is shown schematically in

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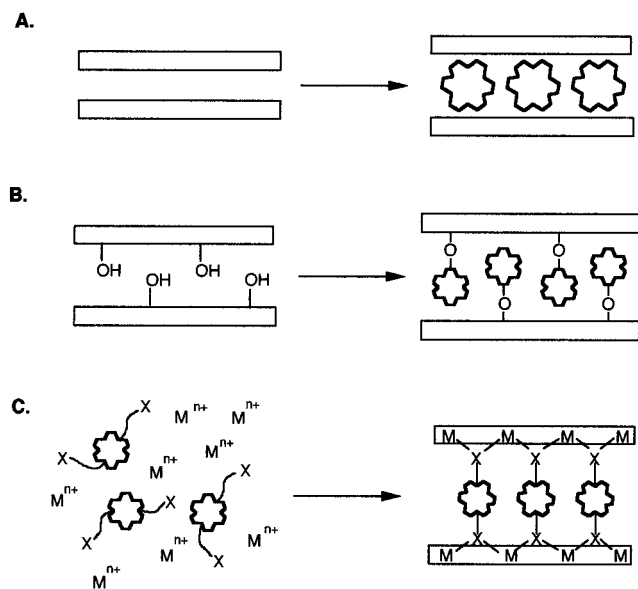


FIGURE 1. Intercalation, grafting, and assembly of layered compounds from host-containing ligands.

Figure 1, is similar to the pillaring of clays by bulky cations. Alternatively, a layered solid can be assembled from appropriate metals and ligands (Figure 1C), the latter containing a pendant host molecule such as a crown ether.<sup>11</sup> The intercalation route is simpler, in the sense that a specific ligand functionality, such as a phosphonate, thiolate, or amine, is not needed. The included host molecule, for example, a metal tris(diimine) complex,<sup>12</sup> cyclodextrin,<sup>13</sup> or enzyme,<sup>14</sup> is bound electrostatically or by van der Waals interactions with the enclosing sheets.

Indirect intercalation methods have proven very useful in cases where the solid and organic host do not react for kinetic or thermodynamic reasons. For example,  $\alpha$ -Zr-(HPO<sub>4</sub>)<sub>2</sub>·H<sub>2</sub>O (abbreviated  $\alpha$ -ZrP) is a lamellar solid acid that can be activated by reaction with base.<sup>15</sup> Figure 2 shows a reaction that has been used in our laboratory to prepare this solid, as well as layered titanates and niobates, for intercalation reactions. The bulky tetra(*n*-butylammonium) ion, TBA<sup>+</sup>, is forced to intercalate by neutralization of some of the interlamellar weak acid sites. Because of its low charge density, TBA<sup>+</sup> will be displaced quantitatively by cations of higher charge density; that is, it is a good “leaving group” for subsequent intercalation reactions. Similar pre-intercalation reactions of zwitterionic bases prepare the solid for intercalation by neutral guests, such as enzymes.<sup>14a</sup> Interestingly, the limit of composition for a stable intercalation compound of TBA<sup>+</sup> and  $\alpha$ -ZrP is approximately Zr(TBA<sup>+</sup>PO<sub>4</sub><sup>-</sup>)<sub>0.5</sub>(HPO<sub>4</sub>)<sub>1.5</sub>. At this composition, a single layer of densely packed TBA<sup>+</sup> ions fills each gallery.<sup>16</sup> If more cations are forced in by addition of excess base, cation–cation repulsions cause delamination of the solid. At an approximate composition Zr(TBA<sup>+</sup>PO<sub>4</sub><sup>-</sup>)<sub>1.0</sub>(HPO<sub>4</sub>)<sub>1.0</sub>, the solid disperses completely in water to make a permanent colloid. This unilamellar colloid, which consists of individual, nanometer-thick  $\alpha$ -ZrP sheets covered on both sides by TBA<sup>+</sup> ions, ultimately decomposes to hydrated zirconium oxide and

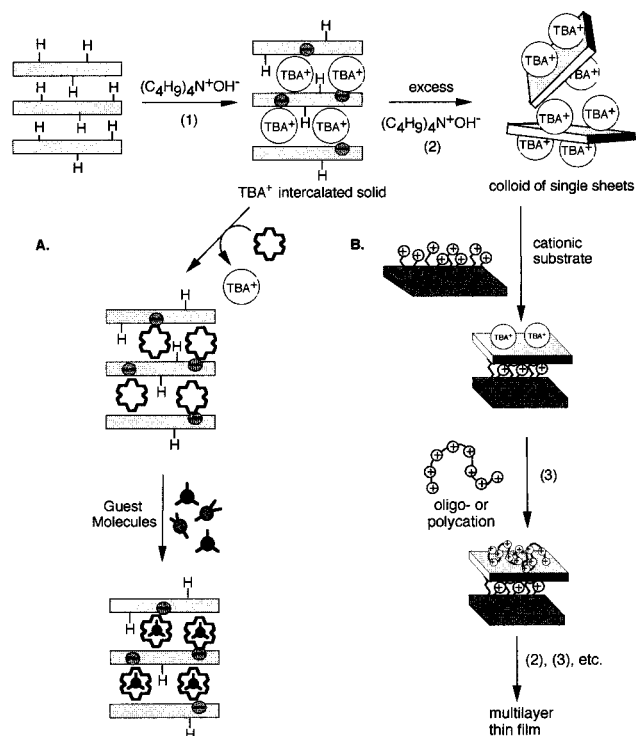


FIGURE 2. Pre-intercalation of lamellar solid acids using TBA<sup>+</sup>OH<sup>-</sup>, intercalation of cationic hosts, exfoliation, and self-assembly of multilayer inorganic polyanion/organic polycation thin films.

aqueous phosphate. The colloids are, however, stable if kept at ice temperature or in the presence of excess phosphate.<sup>17</sup> A variety of other lamellar solids have been dispersed as single-sheet colloids by acid–base and oxidation–reduction reactions.<sup>18</sup>

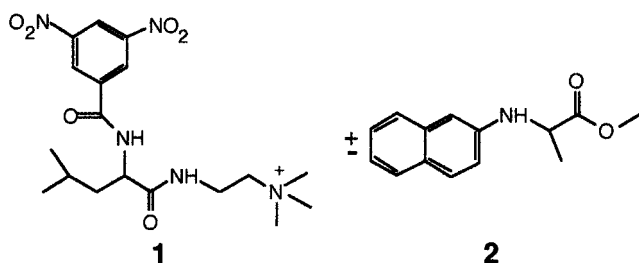
If colloidal  $\alpha$ -ZrP is prepared from neutral amines, the solid can be restacked to form thin films or free-standing membranes, which can then be intercalated by ion-exchange.<sup>19</sup> These films have been studied as protonic conductors,<sup>20</sup> and as active elements of sensors for hydrogen and carbon monoxide.<sup>21</sup> The TBA<sup>+</sup>-containing colloids can be grown as thin films one layer at a time, by dipping suitably prepared substrates alternately into the colloidal suspension and a solution containing oligo- or polycations.<sup>22</sup> Again, cations of high charge density readily displace TBA<sup>+</sup>; the process is also favored entropically by the release of *n* TBA<sup>+</sup> ions from the surface for every *n*-mer adsorbed. This “molecular beaker epitaxy” technique, shown on the right side of Figure 2, allows one to grow an intercalation compound layer-by-layer, with essentially any desired sequence of anionic sheets and polycations.<sup>23</sup> Various surface-sensitive probes (XPS, ellipsometry, AFM, Förster energy transfer) show that the sheets (about 1 nm in thickness and several hundred nanometers in the lateral dimensions) tile the surface densely, and that adsorbed polycations do not desorb or mix in subsequent layer growth steps. The technique represents a useful alternative to covalent layer-by-layer film growth techniques,<sup>24,25</sup> again because no specific functionality, other than positive charge, is needed to incorporate a molecule into a particular layer.

## Chiral Molecular Recognition

In favorable cases, the selectivity and affinity of organic hosts are unimpaired by their inclusion into lamellar solids, and the distinct features of the latter emerge. The most important of these are the very high density of interlamellar binding sites, typically  $10^{-2}$ – $10^{-4}$  mol/g, and molecular recognition effects arising from cooperative interactions of pairs or arrays of intercalated host molecules. In some cases these cooperative effects can be quite spectacular, as in a recent report of “self-replicating” surface multilayer structures.<sup>26</sup>

Chiral intercalation compounds, in particular, illustrate the importance of cooperativity in controlling molecular recognition. The intercalation reaction of clays with metal tris(1,10-phenanthroline) or tris(2,2'-bipyridyl) complexes ( $[M(\text{phen})_3]^{2+}$  or  $[M(\text{bpy})_3]^{2+}$ ;  $M = \text{Fe, Ru, Ni}$ ) is very different, depending on whether a single enantiomer ( $\Lambda$  or  $\Delta$ ) or a racemic mixture is used.<sup>27</sup> In the case of  $[\text{Ru}(\text{bpy})_3]^{2+}$ , the racemate intercalates as a single layer, and the quantity taken up by the clay is consistent with its cation-exchange capacity (CEC). Approximately twice as much of either pure enantiomer is intercalated, as a double layer containing an intervening layer of anions for charge compensation. This unusual behavior can be rationalized in terms of cooperative solid-intercalant interactions (i.e., epitaxial siting and orientation of complexes on the clay surface) which enforce their stereochemistry onto the intercalant layers. Monte Carlo and lattice energy calculations show that the bilayer packing arrangement is only efficient in the case of pure enantiomers.<sup>28,29</sup>

If enantiomeric host molecules that have a higher affinity for complementary guests than for themselves are intercalated, then the solid becomes a useful medium for preparative-scale chiral separations. We investigated this principle by reacting  $\text{TBA}^+$ -intercalated  $\alpha$ -ZrP with the chiral quaternary ammonium cation **1**.<sup>30</sup> Molecules of this type form 1:1 noncovalent complexes enantioselectively with chiral  $\pi$ -donors, such as naphthylamine derivatives.<sup>31</sup> When contacted with a racemic solution of guest **2**, the



host-intercalated solid shows a strong preference for one enantiomer. A preparative-scale separation is effected by filtering the solid, and then desorbing the guest into an appropriate solvent. Figure 3 shows the progressive change in the enantiomeric excess of the solution ( $\text{EE} = \frac{[R] - [S]}{[R] + [S]}$ ) as this extraction process is repeated several times. In the example shown, a solution sample

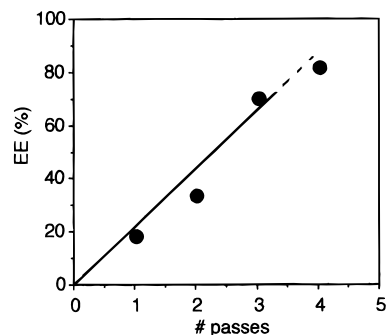


FIGURE 3. Preparative-scale separation of **2** using **1**-intercalated  $\alpha$ -zirconium phosphate.

with 82% EE is separated from the racemate in four batchwise passes. The total mass of chiral intercalation compound (which is recycled in the process) used in this separation was approximately six times that of the purified enantiomer.<sup>32</sup>

Again, the host–guest complexation process is highly cooperative. The binding isotherm is non-Langmuirian, and X-ray diffraction shows that the phase transition from the host-only to the host–guest intercalation compound is first-order, with a rather dramatic 50% expansion of the solid upon intercalation of **2**. This behavior may be understood in terms of Cram’s “preorganization” principle.<sup>33</sup> Accommodation of the guest causes expansion of the interlayer gallery, and there is an associated free-energy penalty. Once a particular gallery is opened, the penalty has already been paid, and further intercalation can occur more easily until the gallery is filled. This cooperative behavior translates into a relatively abrupt change, at a particular guest concentration, to a fully guest-intercalated solid. For some practical applications, such as chromatography, expansion and contraction of the solid phase must be minimized. Langmuirian adsorption of the analyte (i.e., a constant partitioning ratio at low concentration) is also desirable for analytical applications.

This problem can be solved using preorganized hosts, which retain a relatively undistorted binding cavity in the absence of a guest. Zirconium phosphates and phosphonates containing preorganized hosts **3**, **4**, and **5** have been synthesized,<sup>11,13</sup> and the structure of one such compound is shown in Figure 4. However, few binding studies have been carried out with these compounds. Because many interesting chiral analytes are good  $\pi$ -donors, we have focused our efforts on  $\pi$ -acceptor hosts. The achiral cyclophane **6**, which contains a hydrophobic cavity flanked by two  $\pi$ -accepting viologen groups, serves as a good starting point for this work. Stoddart and co-workers found that **6** binds strongly to  $\pi$ -electron-rich molecules, such as tryptophan, indole, and tyrosine, in aqueous solutions.<sup>34</sup> Cyclophane **7** is a derivative of **6** containing the chiral *trans*-1,2-cyclohexanediamine group, which has been proven to be useful in asymmetric synthesis,<sup>35</sup> synthetic receptors,<sup>36</sup> and chiral stationary phases.<sup>37</sup> The

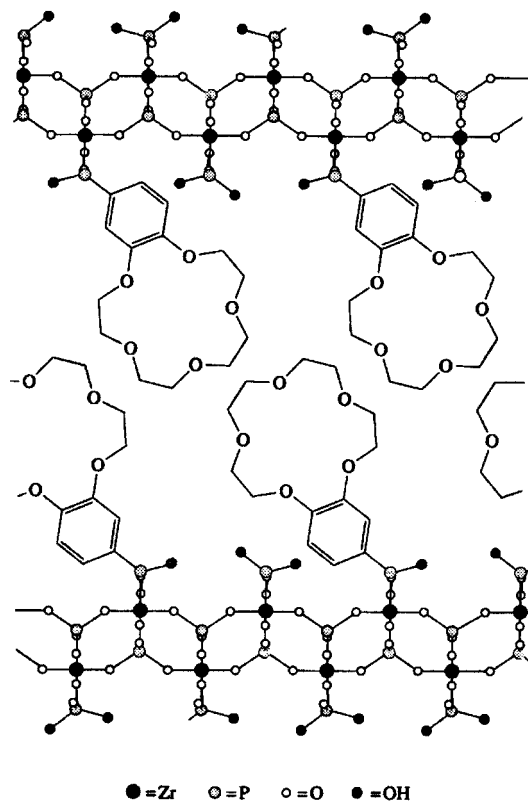
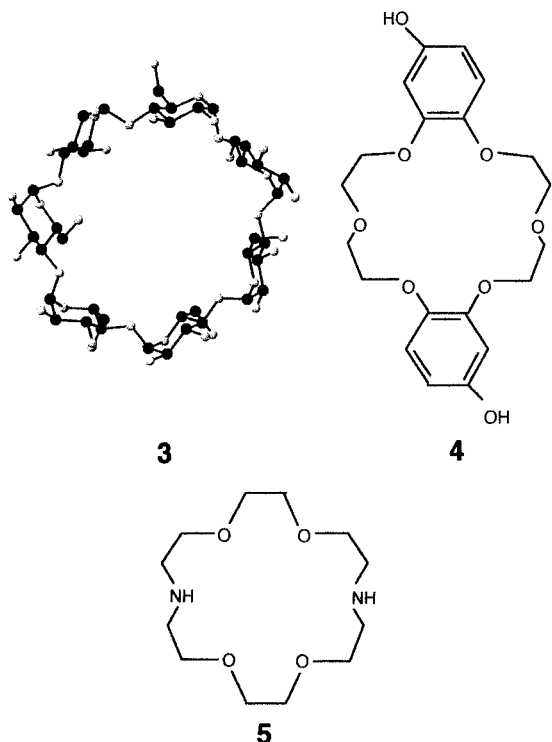


FIGURE 4. Schematic representation of  $\gamma$ -zirconium phosphate pillared by grafted crown ether molecules. Reprinted with permission from Alberti, G. In *Comprehensive Supramolecular Chemistry*; Alberti, G., Bein, T., Eds.; Elsevier: Oxford, U.K., 1996; Vol. 7, Chapter 5.

related host **8** has a binding cavity consisting of viologen and chiral L-tripeptide walls.<sup>38</sup>



These viologen cyclophanes are easily exchanged into  $\text{TBA}^+-\alpha\text{-ZrP}$ , where they act as hosts for intercalation of

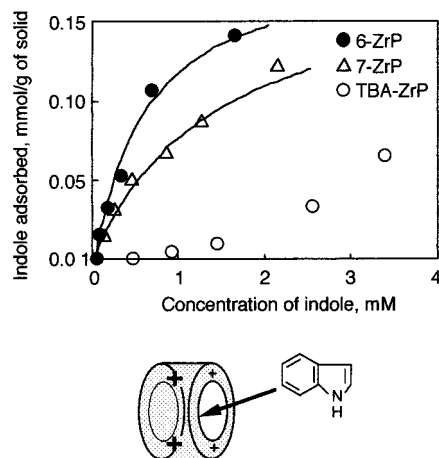
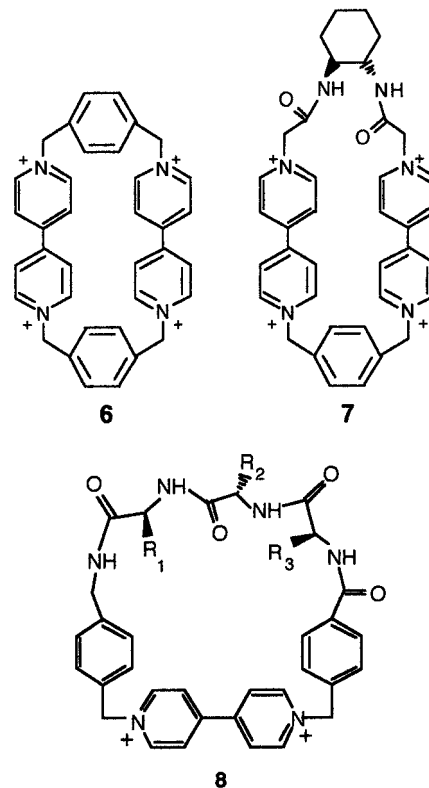


FIGURE 5. Binding isotherms of cyclophane-intercalated  $\alpha$ -zirconium phosphate with indole. Solid lines represent Langmuir isotherm fits to the data. The abscissa represents the concentration of indole at equilibrium.

$\pi$ -donors.<sup>38d</sup> Figure 5 shows binding isotherms for the intercalation of  $\text{TBA}^+-\alpha\text{-ZrP}$ , **6**- $\alpha\text{-ZrP}$ , and **7**- $\alpha\text{-ZrP}$  by



indole. While indole intercalates directly into  $\alpha\text{-ZrP}$ , the upward curvature of the binding isotherm is indicative of strong cooperativity. In contrast, the binding data for the **6**- and **7**-intercalated materials fit well to Langmuir isotherms. X-ray diffraction patterns confirm that there is minimal layer expansion when guest molecules form 1:1 complexes with these intercalated hosts. The indole binding constants for **6** and **7** are higher in water than in the  $\alpha\text{-ZrP}$  intercalation compounds by about a factor of 5. Charge compensation of the viologen groups by the negatively charged sheets may reduce their  $\pi$ -acidity in the intercalation compounds.

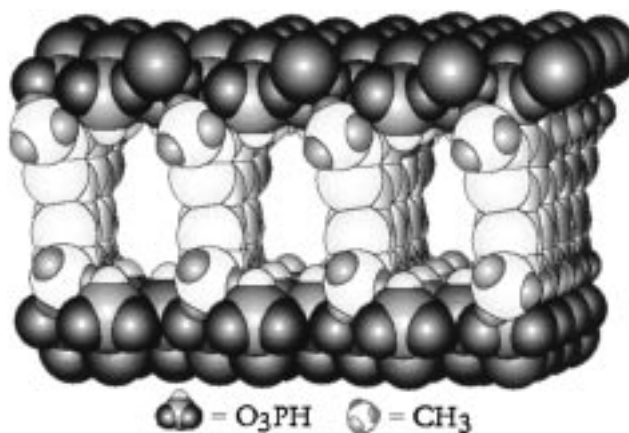
Both **7** and **8** are enantioselective hosts in solution. **7** has binding constants of  $2.1 \times 10^2$  and  $6.2 \times 10^1 \text{ M}^{-1}$  for the L- and D-enantiomers, respectively, of tryptophan methyl ester in aqueous base, i.e., an enantioselectivity ratio of 3.3. The L-Ala-Leu-Val tripeptide cyclophane **8** has an enantioselectivity ratio in excess of 10 for the two enantiomers of DOPA, but a relatively low binding constant ( $4 \times 10^1 \text{ M}^{-1}$ ) for the preferred D-isomer. These binding constants are too low to be useful for chiral separations; to address this problem, chiral hosts with more hydrophobic binding pockets are currently being synthesized. The cyclophane family **8** also presents an opportunity for combinatorial synthesis, and small orthogonal libraries have already been prepared.<sup>38b</sup>

### Pillaring and Template Synthesis of Porous Metal Phosphonates

Phosphonate salts of di-, tri-, and tetravalent metals are typically insoluble lamellar solids, which are crystallized hydrothermally from the appropriate metal salts and phosphonic acids. Simple alkyl- and arylphosphonic acids almost invariably yield dense, nonporous materials. These dense solids are of limited interest for applications involving molecular recognition or catalysis. Early attempts to make open solids by using a mixture of pillaring diphosphonates ( $\text{O}_3\text{P}-\text{R}-\text{PO}_3$ ) and monophosphonates ( $\text{O}_3\text{P}-\text{R}'$ ,  $\text{R}' = \text{H}, \text{OH}, \text{CH}_3$ ) led to apparently porous, poorly crystalline materials.<sup>39</sup> However, subsequent crystallization invariably produced a mixture of dense phases, rather than the less thermodynamically stable mixed phases.<sup>40</sup>

Successful routes to porous metal phosphonates take advantage of the stereochemical constraints imposed on the pendant organic groups by the crystalline, two-dimensional metal–oxygen–phosphorus networks. Each metal ion enforces a particular packing on these organic groups and defines the area available to each. In tetravalent metal phosphonates derived from the  $\alpha$ -ZrP structure, for example,  $24 \text{ \AA}^2$  is available per organic group. Alberti et al. reasoned that by mixing very large pillaring groups with small monophosphonates in a 1:3 ratio, a stable porous solid should form, in which the smaller groups surround the larger ones. The resulting material has a narrow distribution of micropores centered around  $6 \text{ \AA}$ , consistent with the proposed structure shown in Figure 6.<sup>41</sup>

A second approach to porous metal phosphonates, which has perhaps more ready applicability to molecular recognition, is template synthesis. In this case a small molecule (usually water or an alcohol) is coordinated to the metal in the as-synthesized compound. Subsequent thermal or chemical treatment displaces this molecule, in favorable cases leaving all other bonds intact. The topochemical displacement of the template leaves a crystallographically well-defined array of micropores adjacent to vacant metal coordination sites. Binding of guest molecules to these sites is then quite selective in terms of both chemical functionality and molecular shape. This effect was first discovered by Johnson et al., who found



**FIGURE 6.** Computer-generated model of the pillared compound  $\text{Zr}(\text{HPO}_4)_{1.33}(\text{O}_3\text{P}-\text{R}-\text{PO}_3)_{0.33}$ ;  $\text{R} = 3,3',5,5'$ -tetramethylbiphenyl; zirconium atoms are omitted for clarity. Reprinted with permission from Alberti, G. In *Comprehensive Supramolecular Chemistry*; Alberti, G., Bein, T., Eds.; Elsevier: Oxford, U.K., 1996; Vol. 7, Chapter 5.

that vanadyl phosphonates of general formula  $\text{VO}(\text{O}_3\text{-PR})\cdot\text{H}_2\text{O}\cdot\text{BzOH}$  lose BzOH (benzyl alcohol) topochemically upon heating.<sup>42</sup> The process may be reversed by coordination of BzOH or other small alcohols to the vacant sites on the vanadium atoms, and the reaction shows a marked shape selectivity, in that alcohols with branching at the  $\alpha$ -position are excluded. The choice of R groups, which serve as pillars in the structure, allows one to exert very fine control over the juxtaposition of these intercalated alcohol molecules. For example, a recent study shows that excimer formation by intercalated 2-naphthalenemethanol is a strong function of the length of the alkanephosphonate pillars.<sup>43</sup>

### Layer-by-Layer Assembly of Small Molecule Chemical Sensors

We have been interested in exploiting both shape-selective coordination and pillaring features of metal phosphonates in the design of small molecule chemical sensors. This idea was stimulated by the discovery that many of the divalent metal phosphonates  $\text{M}(\text{O}_3\text{PR})\cdot\text{H}_2\text{O}$  ( $\text{M} = \text{Mg}, \text{Zn}, \text{Mn}, \text{Fe}, \text{Co}, \text{Cd}$ ) undergo topochemical loss of water upon heating, to leave an open coordination site at the metal. Most subsequent studies have concentrated on the Zn and Co compounds, which upon dehydration can be intercalated by amines and other basic ligands.<sup>44</sup> In this structure, the R groups surround the metal above and below the metal–oxygen–phosphorus sheets, making a rectangular  $5.2 \times 5.4 \text{ \AA}$  “picket fence” around the open coordination site. Access to this site is further controlled by the size and shape of the R group. With R = alkyl, the effect is similar to that found in  $\text{VO}(\text{O}_3\text{PR})\cdot\text{H}_2\text{O}$ ; i.e., branching at the  $\alpha$ -position inhibits intercalation. For R = phenyl, the binding site is so restricted that only ammonia and water can intercalate from the gas phase.

The excellent shape-selectivity of these intercalation reactions suggested a strong potential for adaptation to chemical sensing. Ammonia, being an important analyte

in a variety of industrial and agricultural activities, was chosen as an initial test case. Micron-thick films of colloidal  $\text{Zn}(\text{O}_3\text{PC}_6\text{H}_5)\cdot\text{H}_2\text{O}$  were grown on the gold electrodes of 5-MHz quartz crystal microbalance (QCM) devices, and were dehydrated thermally to  $\text{Zn}(\text{O}_3\text{PC}_6\text{H}_5)$ , which selectively intercalates ammonia. The QCM device is an extremely sensitive mass transducer, which can detect changes on the order of nanograms, and is particularly well suited to vapor-phase detection.<sup>45</sup> These devices showed a rapid response to gaseous ammonia, consistent with the expected intercalation reaction.<sup>46</sup> Similar devices were prepared from  $\text{Zn}(\text{O}_3\text{PCH}_3)$ , and tested with butylamine isomers. The expected reactivity pattern was observed; i.e., *n*-butylamine gave the largest response, followed by isobutyl- and *sec*-butylamines, followed by *tert*-butylamine.<sup>47</sup> Unfortunately, two problems were immediately apparent with these sensors. First, the roughness of the colloidal films created a high density of unselective sites on particle surfaces, which adsorbed various interferents, such as aliphatic amines and water. Second, the intercalation reaction was irreversible at ambient temperature, so the sensors were "one shot" and required regeneration at 165 °C to liberate the bound amine.

In order to minimize the external surface area of the active elements of these devices, metal bis(phosphonate) thin films were grown layer-by-layer on QCM's, by the sequential adsorption scheme shown in Figure 7.<sup>48</sup> A similar technique had been developed for self-assembly of tetravalent and trivalent metal phosphonate films.<sup>25b,49</sup> However, previous attempts to grow thin films of divalent metal phosphonates had been unsuccessful, because of their slight solubility in water. The solubility of the zinc and copper compounds was reduced by carrying out the adsorption and washing steps in ethanol. To our surprise, good films grew in a small fraction of the time per adsorption cycle (10 min vs several hours) needed to make high-quality zirconium phosphonate films. This behavior may be understood in terms of the higher rate of Ostwald ripening of more soluble materials. Phosphonates of tetravalent elements (Ti, Zr, Hf, Sn, Ce, Th, U) are extremely insoluble in water, reflecting the stability of their metal–oxygen bonds to hydrolysis. This formation of well-ordered monolayers is accelerated by increasing the adsorption temperature,<sup>50</sup> or by lowering the charge on the metal ion. Recent AFM experiments show the evolution of surface roughness of these films with time, and confirm that the slow hydrolysis reaction controls the "annealing" or ripening of an adsorbed metal phosphonate layer.<sup>51</sup>

The problem of reversibility was addressed by using copper(II) phosphonate thin films. While the stoichiometry of the copper phosphonates,  $\text{Cu}(\text{O}_3\text{PR})\cdot\text{H}_2\text{O}$ , is the same as that of the other divalent metal compounds, the Jahn–Teller Cu(II) ion adopts a five-coordinate geometry, in which it is coordinated by four phosphonate oxygen atoms and one water molecule.<sup>52</sup> This leaves an open sixth coordination site, which is reversibly filled by Lewis bases. In addition, the bound water molecule can be

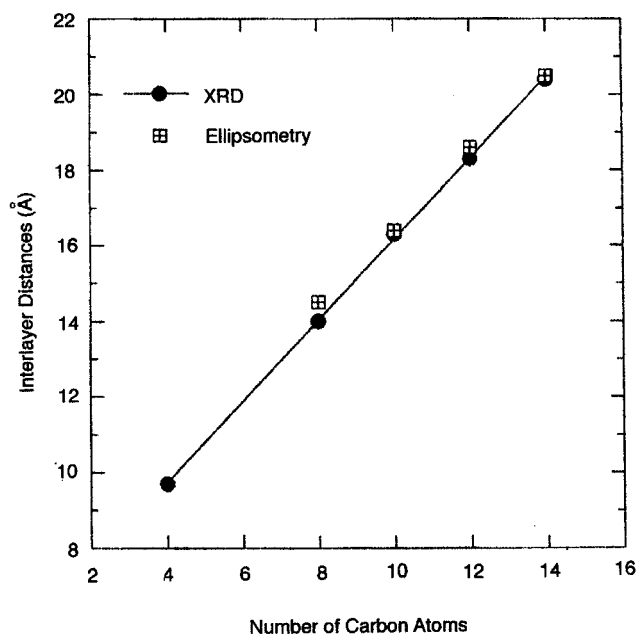
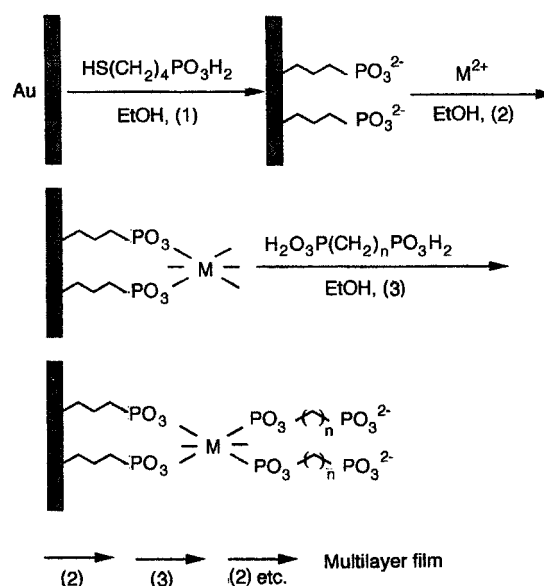
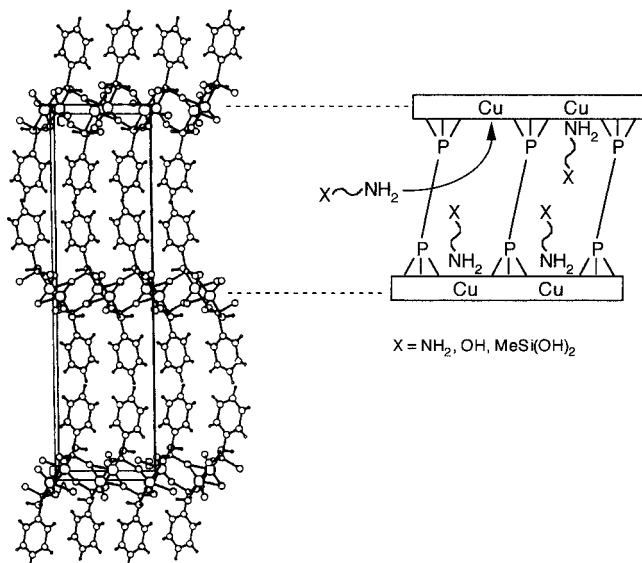


FIGURE 7. Top: Sequence of adsorption steps for self-assembly of divalent metal phosphonate films. Bottom: Comparison of average film thickness change per adsorption cycle, measured by ellipsometry, and layer spacing, determined by X-ray powder diffraction, for  $\text{Zn}_2(\text{O}_3\text{P}(\text{CH}_2)_n\text{PO}_3)\cdot 2\text{H}_2\text{O}$ .

irreversibly displaced by a second basic ligand. X-ray powder diffraction patterns of anhydrous copper 4,4'-biphenylbis(phosphonate),  $\text{Cu}_2(\text{O}_3\text{PC}_6\text{H}_4)_2$ , showed that it had essentially identical in-plane lattice constants to the analogous phenylphosphonate salt (Figure 8). Again, a shape-selective binding site, the dimensions of which are defined by the pillaring bis(phosphonate) ligands, is available in this structure for Lewis bases.

Self-assembled thin films of this material on QCM devices gave strikingly improved performance as an ammonia sensor.<sup>53</sup> With five-layer, 70-Å thick films, two molecules of ammonia bind per Cu atom, one reversibly and the other irreversibly. Binding at the reversible site



**FIGURE 8.** Layer arrangement of  $\text{Cu}(\text{O}_3\text{PC}_6\text{H}_5)\cdot\text{H}_2\text{O}$  as viewed down the  $a$ -axis. Reprinted with permission from ref 52a. Copyright 1992 American Chemical Society. The amine end of the bifunctional receptor molecule coordinates the copper atom, anchoring the functional group X in the binding cavity.

is Langmuirian, and the useful range of the device is ca. 0.05–30%  $\text{NH}_3$  by volume. Larger Lewis bases, such as butylamine isomers, are substantially excluded from the ammonia binding sites, and irreversibly saturate approximately one-third of the available copper sites at the external surface of the film. While the device response is reasonably fast (ca. 90 s for intercalation of 90% of the film by ammonia), it is remarkably slow considering that the film is so thin. At present it is not known whether the transport rate of ammonia (and alkylamines in self-assembled films of  $\text{Cu}_2(\text{O}_3\text{PC}_8\text{H}_{16}\text{PO}_3)$ ) is limited by vertical diffusion through defects, or lateral, intracrystalline diffusion within the pillared galleries.

These materials would be fairly uninteresting as sensor elements if they were limited to the detection of only amines and ammonia. Ideally, one would like a generic sensor design that provides good sensitivity and selectivity, but is easily modified to accommodate a range of interesting analytes. In this context, it is possible to modify the copper binding sites to include an auxiliary functional group X in the cavity, as shown schematically in Figure 8.<sup>54</sup> An amine “hook” anchors the bifunctional receptor molecule to the sheets. By controlling the height of the pillaring groups, as well as the length of the tether joining the amine and X groups, one can create a binding site tailored to the appropriate size and chemical functionality of a particular analyte.

To demonstrate this idea, we designed QCM sensors for carbon dioxide, based on its reactions with alcohols and amines to produce organic carbonates and carbamates, respectively. Bifunctional amines with  $X = \text{OH}$ ,  $\text{NH}_2$ , and  $(\text{CH}_3)_2\text{Si}(\text{OH})_2$  bind in a 1:1 ratio to coordinatively unsaturated copper atoms in  $\text{Cu}_2(\text{O}_3\text{P}(\text{CH}_2)_8\text{PO}_3)$ . Solid-state NMR experiments using  $^{13}\text{C}$ -labeled  $\text{CO}_2$  showed that carbonates and carbamates form rapidly and reversibly

within the interlamellar cavities of the solid. Interestingly, the silanol groups react analogously, binding first one and then a second  $\text{CO}_2$  molecule at higher pressure. In all three cases, the response of the devices to  $\text{CO}_2$  was reversible and similar, in terms of kinetics, sensitivity, and selectivity, to the ammonia sensors made from  $\text{Cu}_2(\text{O}_3\text{PC}_6\text{H}_4^-)_2$  thin films.

## Summary and Outlook

The supramolecular chemistry of solids now represents an area of vigorous chemical research, but it is still relatively unsophisticated when compared with parallel efforts in the world of molecular chemistry. In this Account we have highlighted recent efforts that our group and others have made to unite these two research areas. Using this approach, real progress has been made toward the development of preparative-scale chiral separations media and molecule-specific chemical sensors. Many other applications of these materials and assembly techniques are possible, and some have been described in recent reviews.<sup>55</sup> In terms of molecular recognition, if we take the lead from molecular chemistry, it would seem that unexplored opportunities now exist for the design of “artificial enzymes”<sup>4</sup> and related supramolecular catalysts based on metal phosphates and phosphonates. We now have the tools to pillar these solids reliably and to bind appropriate organic hosts at specific sites. As noted by Professor Alberti, the inorganic scaffolding of these crystalline layer structures serves as a precisely ordered set of “clothes hooks” for organic groups.<sup>11c</sup> Given the large variety of structures already known, each with a different set of lattice spacings between “hooks”, it should be possible to design bifunctional sites that both bind and activate molecules for chemical reactions.

The growing number of examples of lamellar solids incorporating macrocyclic hosts also suggests applications for which the latter have proven useful, particularly in chemical sensing of ions and small molecules and chiral separations. Interesting new possibilities for separations and sensing are also suggested by topologically similar, lamellar hydrogen-bonded networks, which flex to accommodate guest molecules of different sizes within interlamellar voids.<sup>56</sup> Clearly, as the portfolio of available structures continues to expand, and as techniques for assembling them become increasingly sophisticated, these research opportunities in molecular recognition will continue to be developed.

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