The Use of Laminar Inorganic Salts to Make Organic Molecules Display New Properties at the Supramolecular Level in the Solid State

E Brunet, H M H Alhendawi, M Alonso, C Cerro, L Jiménez, O Juanes, M J Mata, A Salvador, M Victoria, E Rodríguez-Payán and J C Rodríguez-Ubis
Department of Organic Chemistry, Faculty of Sciences
Universidad Autónoma de Madrid, 28049-Madrid (Spain)
E-mail: ernesto.brunet@uam.es

Abstract. The design of porous solids of controlled molecular geometry for umpteen applications is a challenge of enormous technological and scientific importance. The placing of organic molecules between the layers of certain inorganic salts leads to enduring solid materials where the confinement makes the organic molecules change their properties or even display new ones at the supramolecular level. Past and ongoing results of our research group concerning the chemistry of metal phosphates/phosphonates are reviewed in relation with recognition, chemically-driven porosity changes, chiral memory and supramolecular chirality, luminescence signaling, photoinduced electron-transfer, gas storage and drug confinement.

1. Introduction
One of the goals of the 4th International Symposium on Atomic Technology (Kobe, November 2009) is to offer solutions to the still unresolved Feynman’s controversial query already stated some fifty years ago [1]: “What would the properties of materials be if we could really arrange the atoms (molecules) the way we want them?” The main objective of our research group is to provide a chemical, conceptual and practical rationale to humbly defy Feynman’s challenge.

In general, the design of supramolecular materials is aimed along those lines and the literature contains many smart processes to achieve that, such as sol-gel chemistry [2], self-assembly [3], film making (Langmuir-Blodgett, etc.) [4], and the use of classical porous materials like zeolites, among many other approaches [5]. Yet, Feynman also conjectured “What could we do with layered structures with just the right layers?” Along the years we have found that zirconium phosphate, a versatile layered inorganic salt, acts as a carving board where organic compounds can be covalently attached by low-temperature hydrothermal reactions to form 3D structures with properties and potential applications only limited by the imagination of the researcher. In particular, our project’s objective is the preparation of nanostructured materials with predictable structure, based on organic-inorganic supramolecular lattices, insoluble and thermally stable, with specific functions like i) recognition; ii) chemically-driven porosity changes; iii) chiral memory and supramolecular chirality; iv) luminescence signaling; v) photoinduced electron-transfer; vi) gas storage; and vii) drug confinement. In this paper we shall present a brief overview of our findings in these fields.

2. Tools for the construction: Zirconium Phosphate (ZrP)
Figure 1 shows the two most common allotropic forms of this layered inorganic salt [6]. In the alpha form one may discover a single kind of phosphates bonded thru three oxygen atoms to three different

---

1 To whom any correspondence should be addressed.
metals, each of the latter being hexa-coordinated. Every phosphate points an acidic OH group towards the interlayer region. In turn, the gamma phase contains two different kinds of phosphates, one internal (green tetrahedrons) using all oxygen atoms to bond four different Zr, and another kind (blue tetrahedrons) placed on the upper and lower external surfaces, bonded to only two Zr atoms and directing two acidic OH groups towards the interlayer space. The salt ZrP is very versatile [7], especially the gamma-phase, because the surface phosphates may be topotactically replaced (i.e. preserving the layered structure) by other phosphorous functions like organic phosphonates of any kind: rigid or flexible, polar or non-polar, chiral or non-chiral or with any conceivable chemical function (Figure 2). In the case of using diphosphonates, the final structure ends up as a pillared 3D arrangement of inorganic lamellae covalently bonded to each other by appropriate organic moieties. The topotactic exchange may be multiple, either simultaneously performed by mixing different phosphorous derivatives or in sequence, by adding one after another. We thus have to our disposal a set of conceptual and practical tools to designing organic-inorganic materials of any imaginable nano-scaled structure whose arrangement can be predicted with quite reasonable accuracy.

3. Recognition

Various crown ethers of different sizes, containing one or two phosphonate groups, where exchanged within the layers of gamma-ZrP [8]. The resulting set of materials was treated with methylphosphonate to further exchange the remaining surface phosphate groups. Competitive experiments (Figure 3) showed that the recognition abilities towards alkaline ions, exerted in the solid-liquid interface by the confined crowns, were very different to those commonly exhibited in solution. Furthermore, the second phosphate/methylphosphonate exchange completely altered the crowns’ response to the ions, thus showing that the nature of the whole matrix structure is crucial in the overall recognition process.

4. Chemically-driven porosity changes

Diphosphonates derived from polyethyleneglycol chains of different lengths (from di- to hexa-ethyleneglycol) were prepared and exchanged at 25% level into gamma-ZrP [9]. The corresponding pillared materials (Figure 4) were thus formed, bearing the general molecular formula of Zr[PO₄]₀.75[H₃PO₄]₀.25[HO₂(P(CH₂)₉(OCH₂CH₂O)₉(CH₂)₉PO₄]₀.125 (n = 2 to 6). The remaining surface phosphonates [(H₂PO₄)₀.75] were quantitatively replaced by hypophosphite [(H₂PO₂)₀.75] leading to two sets of materials, polar/polar (polar columns and polar surface phosphates) and polar/non-polar (polar columns and non-polar surface hypophosphites). Figure 5 summarizes the observed variation of
interlayer distance (as measured by DRX) when the materials containing pentaethylenglycol diphosphonate (n = 5), as a representative example, were treated with methylamine in aqueous dispersion. It may be seen that the polar/polar material steadily augmented its interlayer distance with the increasing amount of intercalating amine. When no amine is present, the polar columns interact by hydrogen bonding with the surface phosphates and the layers are compressed to one another. The amine reacts with the surface phosphates and progressively disrupts the web of hydrogen bonding interactions, thus making the columns to stand up. The overall porosity of the material is thus heavily increased by the mild acid-base reaction. In the case of the polar/non-polar material the increase of interlayer distance occurs all of a sudden, within a very narrow pH range. The replacement of the surface phosphates by hypophosphite greatly diminishes the overall acidity of the material, the only acidic OH groups being those of the phosphonates. In the absence of amine, the polar columns still can establish O…H-P hydrogen bonds with the surface hypophosphite groups. When sufficient amount of amine is present, the few remaining acidic OH groups are quickly neutralized and the methylammonium ions act as wedges that pull the columns to suddenly rise. Therefore, the interlayer distance is doubled and the porosity is on the whole profoundly changed. To the best of our knowledge, this odd behaviour in the solid state, responding to a simple acid-base reaction in the solid-liquid interface, has never been observed before [10].

![Figure 4](image1.jpg)  
**Figure 4.** Animated molecular model of Y-ZrP exchanged with pentaethylenglycol diphosphonate with variable interlayer distance (see text).

![Figure 5](image2.jpg)  
**Figure 5.** Interlayer distance variation with pH of the indicated materials (see text).

5. Supramolecular chirality and chiral memory

When we performed molecular models of the materials described in the previous section, we realized that to fit the largest achieved interlayer distance, the polyethylenoxa columns had to be helicoidally arranged. This is not surprising since polyethyleneglycols are known to attain that conformation in aqueous solution. Yet, what makes a notable difference is that in our materials, the polyethylenoxa columns are covalently attached by both ends to the inorganic layers, thus conferring them a supramolecular order. Therefore, assuming the necessary conditions are established, the P/M helicity of the chains could be somewhat directed to render a certain degree of homochirality which could be detected by simple optical rotation measurements. Figure 6 outlines the experiments aimed to that observation. Dispersions of 5 mg in 10 mL of 1:1 water/acetone of either native Y-ZrP or exchanged at 25% with hexaethylenglycol diphosphonate (n = 6; cf. molecular formula in previous section) displayed no sizeable optical rotation. However, when optically pure (+)-phenethylamine was intercalated in the material containing hexaethylenglycol, a relatively large value of optical rotation was measured. We then smoothly replaced the enantiomerically pure amine by hexylamine and the optical rotation kept showing through. In absence of any (+)-phenethylamine, as shown by pertinent NMR experiments, the only source of optical activity should be the homochirality of the polyethylenoxa columns that was arranged by the concourse of the chiral amine and was maintained.
when the latter was replaced by the achiral one. This is an expression of supramolecular chiral memory; no similar cases can be found in the literature [11].

We wonder what would happen if the chiral influence were intrinsic to the polyethylenoxa chains. To this end, we prepared enantiomerically pure diphosphonates derived from the addition of $R$-glycidol to diethyl vinylphosphonate and subsequent epoxide aperture with hexaethyleneglycol (Scheme 1). The topotactic exchange of this diphosphonate into $\gamma$-ZrP was performed at 25% level and the material was positively characterized using the usual techniques. It occurred to us that the conformation of the polyethylenoxa chains attached to the inorganic layers could be changed if amines of appropriate length were intercalated. Figure 7 summarizes the results. As expected, interlayer distance steadily increased with the length of the amine. Molecular modelling showed that the organic chains are continuously changing their conformation from compressed random coiling at the shortest layer separation to stretched zigzag arrangement at the largest basal spacing. Optical rotation measured in 1:1 water/acetone dispersion passed through a maximum value when hexylamine was intercalated and the resulting interlayer distance allowed for the columns to be in their most ordered helicity, as the molecular models strongly suggested.

In our opinion this experiment clearly proved that chirality can be created at the supramolecular level in the solid state and finely tuned by mild reactions in the solid-liquid interface. There are no examples in the literature achieving this effect in such a clear-cut manner [12].

6. Luminescence signalling
The building of molecular systems able to display the strong luminescence of lanthanide metals is very active a field in chemistry [13]. To accomplish it two stringent conditions have to be met: i) a suitable organic chromophore should absorb light and efficiently transfer energy to the metal (antenna effect); ii) the coordination sphere of the metal should be free of water molecules because the OH oscillators easily quench metal emission. The white powder of \( \gamma \)-ZrP does not absorb visible light and remains reasonably transparent in the UV region. On the other hand, the pillared materials described in the previous section with polyethylenoxa columns may constitute an excellent spider web to enshroud the oxygenphlic lanthanide metals and isolate them within the solid matrix. Acid-base reactions with the surface phosphates may be taken as the driving force to intercalate suitable chromophores in the organic-inorganic lattice. Figure 8 schematizes part of the achieved results.

**Figure 8.** The lanthanide emission was only observed when ethylenopol-yoxa columns, the 2,2'-bipiridyl and the metal were confined within \( \gamma \)-ZrP. **Figure 9.** Exchanged \( \gamma \)-ZrP with chromophores derived from bis-triazolylpyridine and phenylterpyridine, showing the characteristic emission of Eu\(^{3+}\) and Tb\(^{3+}\).

In electronics terms the composite behaves as a triple AND gate because, for the metal luminescence to take place, it is necessary the gathering of the three components: lanthanide metal, polyethylenoxa columns and 2,2'-bipyridyl as sensitizer. These materials may find a number of different applications either in solid or in the solid-liquid interface. More sophisticated chromophores are being tried (Figure 9) and preliminary results showed the pursued strong luminescence of the metals [14].

**7. Photoinduced electron transfer**

There is no fundamental principle running against the possibility of attaining the proper arrangement of chemical components on a surface to accomplish long-lived photoinduced electron transfer [15], the first step in either the achievement of artificial photosynthesis or the construction of efficient solar cells. Inorganic \( \gamma \)-ZrP may constitute an excellent carving board to realize that goal. We have attached to it phosphonate derivatives of the Ru\(^{III}\)(bpy)\(_3\) complex, well known by its excellent light-absorption and electron-donor properties, and placed side-by-side to it different electron donor acceptors ranging from relatively simple viologens to more elaborated fullerene derivatives. Figure 10 contains some molecular models of these complex structures which were positively characterized by the usual techniques [16].
Figure 10. Idealized arrangement of electron-donor Ru\textsuperscript{II}(bpy)\textsubscript{3} and electron acceptors (fullerene derivatives or viologens) on the simplified surface of γ-ZrP.

The first important observation was that the phosphorescence emission of the Ru\textsuperscript{II}(bpy)\textsubscript{3} complex was heavily quenched by the presence of the electron-acceptor species, suggesting that the pursued electron transfer took place. Very recently, flash photolysis revealed some of these materials to have outstanding properties in that the separation of charges is long lived and the initially thought inert inorganic layer resulted semiconducting thus driving the separated electrons and/or holes along the material [17]. Additional results showed that these powders can be arranged as solar cells with promising efficiency [18].

8. Gas storage

Hydrogen is a very appealing energy vector - the release of its energy does not involve the noxious carbon dioxide. Yet, environmental-friendly production and safe storage/transportation methods must be devised if hydrogen is to be efficiently used as the clean energy carrier of the future. Although there are already many reasonably useful technical approaches, neither of the two problems is nowadays at a level of resolution which would make the use of hydrogen routinely possible. Concerning hydrogen storage, it may be attained among other procedures by physisorption in porous matrices [19]. We conjectured whether appropriate matrices based on γ-ZrP could serve the latter purpose. The thorough revision of the literature allows one to find numerous organic, inorganic and hybrid systems in which the storage of hydrogen has been tested, from the delusive carbon nanotubes to the very cleverly designed systems with almost unbelievable specific surface areas higher than 5000 m\textsuperscript{2}/g. The analysis of the different available structures points to the conclusion that a large accessible volume is desirable but by means of micropores or ultramicropores and therefore presenting a large internal contact surface to the elusive hydrogen molecules. Some interesting theoretical studies and experimental ones on zeolites also point to the benefit of having polarizing centers, namely small cations as for instance Li\textsuperscript{+}. Also the presence of transition metals with open coordination sites appears to be important. We believe that our set of tools (Figure 2) might allow us to design appropriate materials for hydrogen storage. Figure 11 summarizes our rationale and the best achieved results [20].

Figure 11. Phosphonate-exchanged ZrP materials for hydrogen storage (see text).

The attachment of polyphenyl or polyphenylethynyl diphosphonates to either α- or γ-ZrP led to materials with slit-like ultramicropores of different length. Further exchange reactions led to polar or non-polar groups at both ends of the pores. This set of materials allowed us to check for a large...
number of different arrangements. The best results were obtained with the material named $\alpha$T60Li, $\alpha$-ZrP with 60% of terphenyldiphosphonates, the remainder phosphates bearing Li$^+$ as counterions. At 800 Torr and 77K, 1.7% w/w of hydrogen could be stored and the Department of Energy goal for 2010 (45 g of hydrogen per L of material) can be attained at 1.8 atm at 77K (Figure 11).

9. Drug confinement
Confinement of drugs into molecular matrices might be a good solution to their slow release at particular locations on the body [21]. We have preliminary studies where it can be shown that the erythromycin family antibiotics can intercalate into $\gamma$-ZrP, the driving force being the acid-base interaction between the amine group(s) of the organic compound and the acidic surface phosphates. The measurement of the interlayer distance vs. the stoichiometry of the reactants (Figure 12) shows that mono- and bilayers of erythromycin derivatives may be enclosed between the inorganic lamellae. More detailed studies will follow.

Figure 12. Intercalation of antibiotics of the erythromycin family (X = CO, R = H, erythromycin A; R = Me, clarithromycin; X = MeN-CH$_2$, R = H, azithromycin). The interlayer distance indicates the formation of mono- and bilayers of antibiotic between the inorganic lamellae at low and high stoichiometric ratio of the reactants, respectively. The x-ray crystal structure of clarithromycin and an ideal model of the bilayer are presented.

10. Conclusion
It has been our aim to show, within the limited length of this communication, the enormous possibilities that the building of organic-inorganic 3D structures does have in numerous fields of either basic or applied research. In particular, the use of ZrP allows the construction of rather complex composites where the confinement of the organic molecules confers them new and unexpected properties at the supramolecular level.

Acknowledgement
This work has been performed under the indirect support of ERCROS-Farmacia S.A. to which we are highly indebted. Unfortunately, we do regret that the financial backing from the Ministry of Science and Education of Spain has just ceased despite the generous grants received in the near past (MAT2002-03243, MAT2006-00570) and the more than reasonable results so far achieved.

References
[1] Feynman R 1960 Eng. Sci., 22-36.
[2] Walcarius A and Collinson M M 2009 Ann. Rev. Anal. Chem. 2 121-143.
[3] Hunter C A and Anderson H L 2009 Angew. Chem., Int. Ed. 48 7488-7499; Kharlampieva E, Kozlovskaya V and Sukhishvili S A 2009 Adv. Mater. 21 3053-3065; Liu Y and Yan H 2009 Science 325 685-686.
[4] Yang J and Yan D 2009 Chem. Soc. Rev. 38 2634-2645.
[5] Farrusseng D, Aguado S and Pinel C 2009 Angew. Chem., Int. Ed. 48 7502-7513.
[6] Alberti G, Murcia-Mascaros S and Vivani R 1994 Mat. Sci. Forum 152-153; Vivani R, Alberti G, Costantino F and Nocchetti M 2007 Microp. Mesop. Mat. 107 58-70.
[7] Alberti G, Costantino U, Dionigi C, Murcia-Mascaros S and Vivani R 1995 Supram. Chem. 6 29-40; Clearfield A and Costantino U 1996 Comprehensive Supramolecular Chemistry 7 107-149; Olivera-Pastor P, Maireles-Torres P, Rodriguez-Castellon E, Jimenez-Lopez A, Cassagneau T, Jones D J and Roziere 1996 J Chem. Mat. 8 1758-1769.
[8] Brunet E, Huelva M and Rodriguez-Ubis J C 1994 Tetrahedron Lett. 35 8697-8700; Brunet E, Huelva M, Vazquez R, Juanes O and Rodriguez-Ubis, J C 1996 Chem. Eur. J. 2 1578-1584.
[9] Alberti G, Brunet E, Dionigi C, Juanes O, Mata M J, Rodriguez-Ubis J C and Vivani R 1999 Angew. Chem., Int. Ed. 38 3351-3353.
[10] Brunet E, Mata M J, Juanes O and Rodriguez-Ubis J C 2004 Angew. Chem., Int. Ed. 43 619-621; Brunet E, Mata M J, Alhendawi H M H, Cerro C, Alonso M, Juanes O and Rodriguez-Ubis J C 2005 Chem. Mat. 17 1424-1433.
[11] Brunet E 2002 Chirality 14 135-143.
[12] Brunet E, Mata M J, Juanes O, Alhendawi, H M H, Cerro C and Rodriguez-Ubis J C 2006 Tetrahedron: Asym. 17 347-354; Brunet E, Juanes O and Rodriguez-Ubis J C 2009 J. Mex. Chem. Soc. 53 154-161.
[13] Brunet E, Juanes O and Rodriguez-Ubis J C 2007 Cur. Chem. Biol. 1 11-39.
[14] Brunet E, Mata M J, Juanes O and Rodriguez-Ubis J C 2004 Chem. Mat. 16 1517-1522; Brunet E, Alhendawi, H M H, Juanes O, Jimenez L and Rodriguez-Ubis J C 2009 J. Mat. Chem. 19 2494-2502.
[15] Hoertz P G and Mallouk T E 2005 Inorg. Chem. 44 6828-6840.
[16] Brunet E, Alonso M, Mata M J, Fernandez S, Juanes O, Chavanes O and Rodriguez-Ubis J C 2003 Chem. Mat. 15 1232-1234; Brunet E, Alonso M, Cerro C, Juanes O, Rodriguez-Ubis J C and Kaifer A E 2007 Adv. Funct. Mat. 17 1603-1610.
[17] Brunet E, Alonso M, Quintana M C, Atienzar P, Juanes O, Rodriguez-Ubis J C and Garcia H 2008 J. Phys. Chem. C 112 4029-4032.
[18] Teruel L, Alonso M, Quintana M C, Salvador A, Juanes O, Rodriguez-Ubis J C, Brunet E and Garcia H 2009 Phys. Chem. Chem. Phys. 11 2922-2927.
[19] Brunet E, Cerro C, Juanes O, Rodriguez-Ubis J C and Clearfield A 2008 J. Mat. Sci. 43 1155-1158.
[20] Brunet E, Alhendawi H M H, Cerro C, Mata M J, Juanes O and Rodriguez-Ubis J C 2006 Angew. Chem., Int. Ed. 45 6918-6920.
[21] Salonen J, Kaukonen A M, Hirvonen J and Lehto V-P 2008 J. Pharm. Sci. 97 632-53.