Intermolecular Interactions in Nonorganic Crystal Engineering

DARIO BRAGA*

Dipartimento di Chimica G. Ciamician Università degli Studi di Bologna, Via F. Selmi 2, Bologna, Italy

FABRIZIA GREPIONI[†]

Dipartimento di Chimica, Università di Sassari, Via Vienna 2, 07100 Sassari, Italy

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ABSTRACT

The utilization of noncovalent interactions to construct molecular crystals is evaluated in the context of inorganic and organometallic crystal engineering. The attention is focused on hydrogen-bonding interactions involving metal complexes in which the metal atoms participate in the bonding either directly or as ancillary systems. The role of ionic charges is discussed. It is shown, inter alia, that reproducible and transferable crystal synthesis strategies based on charge-assisted hydrogen bonds can be devised to build periodical supermolecules.

"*The important thing in Science is not so much to obtain new facts as to discover new ways of thinking about them*" — W. L. Bragg

Introduction

The chemistry of the last two decades of the twentieth century has been largely dominated by the endeavor to master secondary noncovalent bonding. This has determined a substantial shift of interest, from a focus on atoms and bonds between atoms to a focus on molecules and *bonds between molecules*, and has involved all areas of chemistry, from biochemistry to organic, organometallic, and physical chemistry, to encompass the thriving area of materials chemistry.[1] The logical implications of this change in intellectual focus are easy to grasp. In chemistry courses, we teach students that the energy required to break or form a two-electron covalent bond is of the order of 10^2 kJ mol^{-1}, an energy equivalent to blasting molecules apart if compared with the tiny energies required to break noncovalent interactions. Noncovalent syntheses evolve through formation and rupture of secondary interactions between component subunits (whose covalent skeletons

Dario Braga is Associate Professor of General and Inorganic Chemistry at the University of Bologna. He received the Raffaello Nasini Prize from the Italian Society of Chemistry in 1988 for his studies on solid-state dynamic processes, and the FEDERCHIMICA Prize for 1995 for his research on intermolecular interactions in organometallic systems. His major current interests are in crystal engineering and in organometallic solid-state materials chemistry. He is Scientific Editor of the RSC electronic journal *CrystEngComm*, and a member of the Dalton Council and of the Research Observatory of the University of Bologna.

Fabrizia Grepioni is Associate Professor of General and Inorganic Chemistry at the University of Sassari. She was awarded the 1997 Raffaello Nasini Medal from the Inorganic Chemistry Division of the Italian Society of Chemistry. Her scientific interests are in the fields of inorganic and organometallic structural chemistry and crystal architectures, intermolecular interactions and hydrogen bonding in organometallic materials, and the engineering of organic–organometallic crystals.

Chart 1. A Molecular Crystal Is a Periodic Supermolecule

PARADIGM	AGGREGATE
Non-Covalent Interactions	Supermolecule
Periodicity	Crystal
Periodic Non-Covalent Interactions	Molecular Crystal ≡ Periodic Supermolecule

are not affected). Hence, the energy scale is fundamentally different.[2,3] Small ΔH values often imply a very difficult battle against entropy—a battle that can only be won by cooperativity if supramolecular aggregation becomes thermodynamically spontaneous.

If the utilization of noncovalent interactions is taken as the paradigm of supramolecular chemistry, and periodicity as the paradigm of the crystalline state, the exploitation of periodically distributed noncovalent interactions is the paradigm of molecular crystal engineering (see Chart 1). On this basis, molecular crystals can be viewed as periodic supermolecules, *solid supermolecules*, in which approximately Avogadro's number of molecules interact via a plethora of noncovalent interactions which generate *collective* physical and chemical properties via self-recognition and self-organization.[4] For instance, naive as it may appear, one may consider that the properties of the various polymorphic forms of ice, resulting from hydrogen bond aggregation of water molecules, are different from those of an isolated water molecule in the vapor phase, which, in turn, are different from those of liquid water. The snowflake in Figure 1 is an example of an extraordinarily elegant supramolecular aggregate of water molecules.

Before proceeding, a topological distinction needs to be made between molecular crystal engineering, where the building blocks are clearly recognizable molecular or ionic species, and coordination[5] and covalent[6] crystal engineering, which often utilize building blocks that do not exist as separate entities. Coordination crystal engineering, in particular, can be seen as periodic coordination chemistry, as the ligand-to-metal bonding capacity is projected in two or three dimensions to form extended networks ("coordination polymers") by using polydentate ligands.[5]

A second broad difference arises from the energies involved in the construction of the different types of crystalline materials. Even though there is a continuum of intermediate energetic situations (*Natura non facit saltus*) between those depicted in Figure 2, the construction of covalent networks[6] (e.g., synthetic zeolites, intercalates, etc.) usually requires larger energies than those required to prepare coordination networks or to assemble molecular crystals. Clearly, control, reproducibility, and transferability of the small energies involved in the building-up sequences of molecular crystals by means of noncovalent interactions constitute extremely challenging (hence fascinating) study subjects.

* To whom correspondence should be addressed. E-mail: dbraga@ciam.unibo.it; http://catullo.ciam.unibo.it.
† E-mail: grepioni@ssmain.uniss.it.
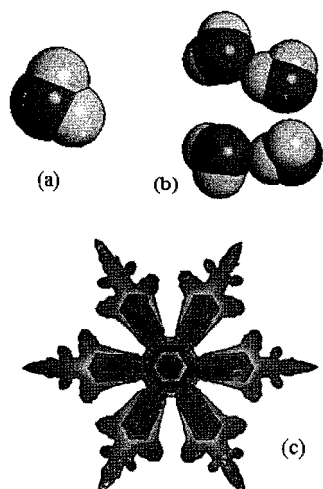
FIGURE 1. Space-filling representation of (a) a gas-phase water molecule, (b) a water aggregate, and (c) the elegant supramolecular arrangement of water molecules via O—H- - -O interactions in a snowflake.
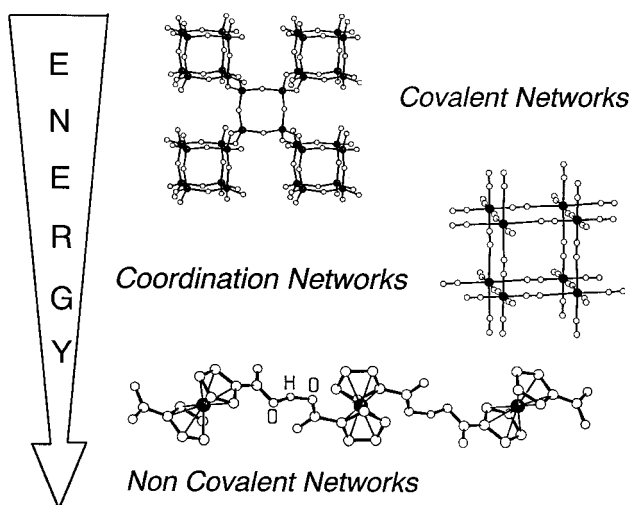
FIGURE 2. Simplistic energy scale from covalent, to coordination, to noncovalent networks.

In the following we will use the term *intermolecular* as a synonym for *noncovalent*, with this encompassing all types of secondary interionic or intermolecular interactions that do not imply two-electron σ-bonds (e.g., electrostatic, EL, hydrogen bond, HB, and van der Waals, vdW, interactions).

Molecular crystal engineering is therefore supramolecular solid-state chemistry, and crystal engineers concentrate their efforts on developing synthetic strategies aimed at the preparation of periodic supermolecules. These *crystal-oriented* synthetic strategies do not differ, in essence, from classical chemical experiments in which molecules are *imagined*, synthetic routes *devised*, products *characterized*, and their properties *measured*. The step forward arises from the idea of being able to devise and/or control collective crystal properties by embedding into the molecular building blocks specific recognition and binding sites (building block functionalization) that may lead to the target supramolecular aggregation. Common chemical procedures are required to synthesize the build-

ing blocks and to encode the desired supramolecular functionality (for instance, the oxidation of a methyl group to a —COOH group destined for intermolecular hydrogen-bonding) prior to supramolecular aggregation.

From an Organic to an Inorganic View of Crystal Engineering: The Role of Metal Atoms

The development of a *molecule-based* solid-state chemistry has been much slower in the inorganic and organometallic fields than in the organic field. One can say that supramolecular inorganic chemistry[7] and the corresponding inorganic branch of molecular crystal engineering are still in their infancy.[8] This is a limitation, of course, but also a great potential for new discoveries.

The aim of this Account is three-fold: (i) to outline the effect of metal atoms on intermolecular interactions in the solid state, (ii) to point out some relevant analogies and differences in cases where no metals are involved compared to those where they are involved, and (iii) to examine some controversial aspects arising from the utilization of directional intermolecular interactions in the Coulombic field generated by ionic transition metal complexes and their counterions in the solid state. The ultimate objective of this Account is to stimulate research interests in the use of coordination and organometallic complexes as building blocks in the synthesis of novel molecular materials. It should be mentioned, before proceeding, that many pioneers prepared inorganic/organometallic molecular or ionic crystals *with a purpose* long before crystal engineering began to grow and become a booming field of research.[9,10]

While there is an extraordinarily abundant literature on organic solid-state chemistry, considerably less is available on inorganic or organometallic molecular solids even though organometallic and coordination complexes form, at the beginning of the year 2000, 55% of all structures in the Cambridge Structural Database.[11] It is sufficient to look at the periodic table to appreciate the potential inherent in the utilization of metal atoms. The properties of metal-containing materials, such as coordination compounds, metal clusters, organometallic complexes, etc., depend on the electronic nature of the metals as well as on the characteristics of the ligands. The ligands are, in general, organic molecules or fragments, which, in most cases, retain the original intermolecular bonding capacity upon metal coordination, because this coordination does not affect the peripheral atoms or atomic groups. Chart 2 summarizes, with a didactic aim, some of the most common supramolecular uses of coordination complexes. Clearly, structural and electronic properties interact to give a broad range of exploitable functions.

Directionality and Strength Are Essential To Assemble Building Blocks. The Hydrogen Bond Is the Interaction of Choice

Directionality is a prerequisite of reproducibility, only if the topological properties of a given interaction persist in different structural environments; i.e., on passing from

Chart 2. Selection of Supramolecular Functions Arising from the Utilization of Metal Coordination and Metal Atom Electronic Properties

Structural/Electronic Properties	→	Potential Supramolecular Functions
Ligand structure and co-ordination geometry →		Preorganization in space of non-covalent links
Electronics of the ligand-to-metal bonding →		Tuning of ligand polarity and acid/base behavior
Metal atom variable oxidation states and/or non-neutral ligands	→	Ionic species and 'charge assistance' to intermolecular bonds
Size and shape of the complexes	→	Template construction of host-guest systems
Electron rich metals	→	Intermolecular HB acceptors
Electron deficient metals	→	Intermolecular electron density acceptors

Chart 3. Strong Donor/Acceptor Groups Such as —COOH (1), —CONHR Amido (2), and —OH (3) Form the Same Type of HB Interactions Whether as Part of Organic Molecules or as Part of Metal-Coordinated Ligands

one solid supermolecule to another, the interaction is useful in the construction of new solids. This concept is elaborated in the idea of supramolecular synthons put forward by Desiraju.[12] The interaction that best combines strength and directionality is the hydrogen bond (HB). For this reason HB interactions are widely exploited in molecular crystal engineering.

What is a hydrogen bond? The long list of definitions collected by Aakeröy and Seddon[13] clearly shows that there is no unique answer to this question. For the purposes of crystal engineering, Etter's elaboration[14] of Linus Pauling's definition of a bond is probably the most appropriate: "a hydrogen bond is an interaction that directs the association of a covalently bound hydrogen atom with one or more other atoms, groups of atoms, or molecules into an aggregate structure that is sufficiently stable to make it convenient for the chemist to consider it as an independent chemical species". The focus is on the concepts of "directed" association and stability.

For most purposes, however, the HB can be described as a stable interaction of essentially electrostatic nature between an X—H donor and a Y acceptor, being X and Y electronegative atoms or electron-rich groups.[15] The HB interaction is generally stronger (if not much stronger) than the strongest vdW interaction. H—Y and X—Y separations shorter than vdW contact distances and X—H—Y angles that tend to linearity are considered diagnostic of the presence of strong HBs.[16] In these cases the length/strength analogy is believed to hold; i.e., the shorter the acceptor—donor distance, the stronger the bond. While the vdW cutoff criterion is quite useful to discover strong HBs (but an acritical application of this relationship has been recently questioned; see below),[17] it is certainly not sufficient when dealing with weak and very weak HB interactions. As discussed by Jeffrey and Saenger:[16] "the use of a van der Waals distance cutoff criterion carries the wrong implication that hydrogen bonds become van der Waals interactions at longer distances" and overlooks the essentially electrostatic nature of the interaction. While vdW interactions fall off very rapidly (r^{-6}), electrostatic interactions follow an r^{-1} dependence (assuming primarily monopole—monopole and monopole—dipole interactions). Thus, HBs can be stabilizing at distances much greater than the sum of vdW radii. In terms of energy, HB interactions span a large interval, ranging from tiny energies (ca. 10 kJ/mol in the
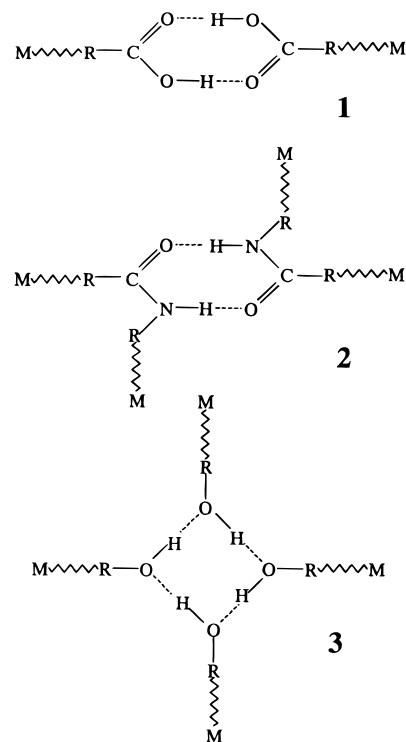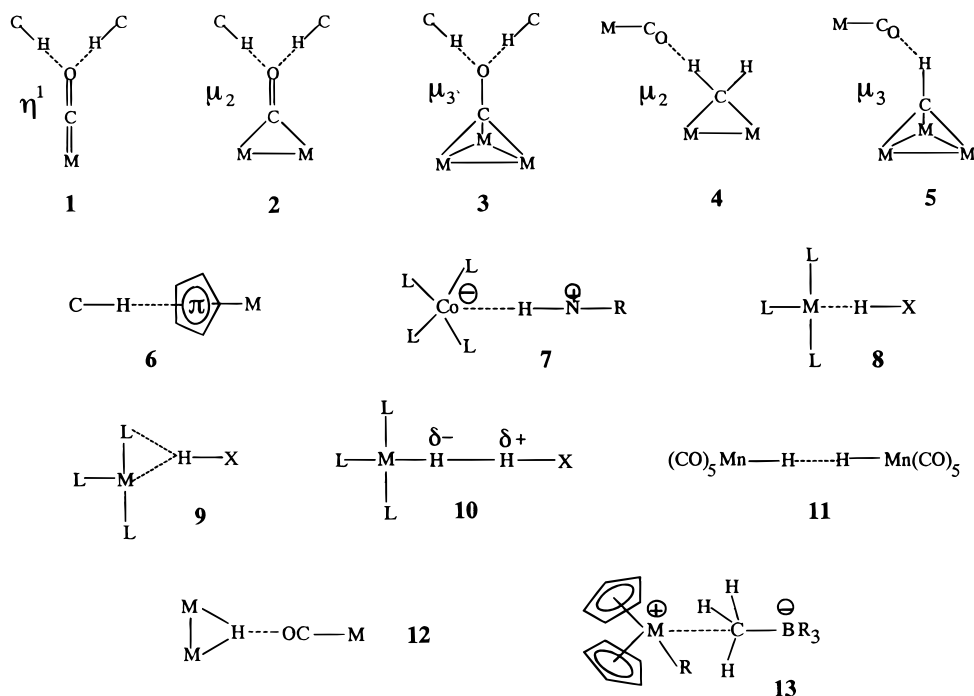
case of C—H- - - O, vide infra) to large values when the acceptor is an anion (ca. 120—130 kJ/mol in the case of O—H- - - $O^{(-)}$).[13,16]

Strong donor/acceptor groups such as —COOH and —OH systems, as well as primary —$CONH_2$ and secondary —CONHR amido groups, form essentially the same type of HB interactions whether as part of organic molecules or as part of metal-coordinated ligands (see Chart 3). This is not surprising, as hydrogen bonds formed by such strong donor and acceptor groups are at least 1 order of magnitude stronger than most noncovalent interactions and are most often already present in solution. In addition to these strong bonds, and the plethora of weaker (e.g., C—H- - - O, C—H- - - N, C—H- - - π, etc.) "organic"-type HB interactions, the presence of metal atoms in molecular building blocks generates *new* types of interactions which are characteristic of inorganic and organometallic systems. This subject has been recently reviewed,[8] and we need only to briefly summarize some key observations.

The most important "nonorganic" types of HB interactions are summarized in Chart 4. For example, the almost ubiquitous CO ligand is able to interact with weak C—H donors. The basicity of the ligand is a function of the coordination mode (whether terminal, μ_2-CO, μ_3-CO) and of the type of metal.[18] Ligand—metal coordination can be used to vary the polarity of metal-bound HB donors in C—H- - - O bonds, e.g., methylidyne (μ_3-CH) and methylene (μ_2-CH_2) ligands. Benzene, arene, and cyclopentadienyl ligands, as well as alkenes and alkynes commonly found in coordination chemistry, behave as weak acceptors in CH— π interactions.[19] The HB acceptor behavior

Chart 4. Nonorganic HB Interactions Involving Ligands[a]

η^1 **1** μ_2 **2** μ_3 **3** μ_2 **4** μ_3 **5**

C—H·······(π) —M   **6**

7   **8**

9   **10** $(CO)_5Mn$—H······H— $Mn(CO)_5$ **11**

12   **13**

[a] Terminal (**1**), edge-bridging (**2**), and face-bridging (**3**) CO ligands; methylene μ_2-CH_2 (**4**) and methylidyne (μ_3-CH) (**5**); an example of −CH−π interaction involving a metal-coordinated Cp ligand (**6**); HB involving electron-rich metal atoms, charge-assisted $[Co(CO)_4]^-$−$[H−NR_3]^+$ (**7**) and neutral (**8**); IMH involving electron-rich metal atoms and main group elements $L_2(M−L)$- - -$H−X$ (**9**); electrostatic (**10**) and "covalent" dihydrogen bonding (**11**); metal− "hydride" donation to CO ligands (**12**); and IPA involving unsaturated electron-deficient metal atoms (**13**).

of metal atoms is, obviously, very distinctive of coordination complexes. Formation of classic three-center, four-electron HBs with electron-rich metal centers has been observed with all traditional hydrogen-bonding donor groups,[20] in particular when carbonyl anions, e.g., [Co(CO)$_4$]$^-$, interact with amino cations.[21] On the other hand, when an electron-rich metal atom is bound to an electron-rich main group atom (e.g., M−S, M−O, M−Cl, etc.), *intermolecular multicenter heteroacceptor* (IMH) interactions are formed between the HB donor and the whole electron-rich system, thus recalling the accepting behavior of multiple bond systems in X−H- - -π interactions. Another intriguing type of interaction that has no parallel in the neighboring organic chemistry field is the *dihydrogen bond* formed between a metal-bound terminal hydrogen and a second hydrogen bound to an electronegative main group element, viz., M−H- - -H−(C,N,O,S).[22] In a few cases, two metal atoms may be involved, viz., M−H- - -H−M, thus forming a weak intermolecular *covalent* dihydrogen bond interaction.[23] For instance, in the case of the β-form of HMn(CO)$_5$, extended Hückel and DFT calculations have demonstrated that the Mn−H- - - H−Mn interaction can be described as a greatly weakened interatomic H−H bond, with a binding energy of ca. 5 kJ mol^{-1}.

Besides acting as bases, transition metal atoms can also manifest Brønsted acidity and behave as HB donors. M−H donors, usually belonging to metal clusters, may form intermolecular M$_n$−H- - -OC−M$_n$ interactions with suitable acceptors such as the CO ligand unless sterically obstructed. The existence of M−H$^{\delta+}$- - - Y$^{\delta-}$, X−H$^{\delta+}$- - - M$^{\delta-}$, and M−H$^{\delta+}$- - - H$^{\delta-}$—Y interactions reflects the great

electronic variation along the transition series from electron-deficient to electron-rich metals.[8] Thus, it is not surprising that, if C−H σ-bonds can form *intra*molecular *agostic* interactions by donating electron density to an electron-deficient transition metal atom,[24] the analogous *inter*molecular M- - -(H−X) (X = C, N, O) interactions also occur.[23] These *intermolecular pseudoagostic* (IPA) interactions are usually, though not always, associated with the presence of tight ion pairs formed by electron-deficient metal cations and counterions carrying methyl or phenyl groups, e.g., $[(\eta^5\text{-}C_5R_5)_2MR][R_3B(CH_3)]$, the prototypical example being the adduct $[(\eta^5\text{-}C_5Me_5)_2ZrMe][(C_6F_5)_3\text{-}BMe]$.[25]

It should be pointed out that other interactions, beside HB, are sufficiently strong and selective to be of use in crystal engineering applications: (i) graphitic-like π-stacking of metal-bound arene ligands is a recurrent motif in crystalline environments;[26] (ii) closed-shell atoms form strong intermolecular interactions[27] with energies of the order of 10−40 kJ mol^{-1}, i.e., weaker than covalent bonds but stronger than most vdW interactions; and (iii) intermolecular hypervalent interactions involving heavy p-block elements form extended networks in the solid state with many geometrical features in common with HB interactions.[28]

Since "new" interactions are being discovered, or rediscovered, almost daily, this section cannot be exhaustive. Having ourselves contributed to such "interaction harvesting", we feel that some cautionary words are in order. Very weak interactions, falling in the fluctuations of the crystal structure energetics—those due, for instance, to motion of atoms or atomic groups—may be useless in

design strategies because they are too feeble to control crystal construction. It is dangerous to focus exclusively on pairwise interactions, as one may forget that it is the overall balance of interactions, some acting at short-range only and some acting at very long range, that accounts for cohesion in molecular crystals.[29] Only strong pairwise interactions (e.g., O−H− O, but also Cl−Cl or Au−Au) may stand out of the noise and act as true packing directors.[27,28] Preservation (or preformation) of robust intermolecular bonds often leads to molecular packings that do not correspond to the best vdW energy. This is, for instance, the case with water and accounts for the absorption of ca. 6 kJ mol^{-1} upon melting.[30] This energy is required to break about 10% of the O−H− O bonds from the HB scaffolding of ice, hence determining the lower density of ice with respect to that of liquid water.

One further point of concern arises from the customary "frozen" picture of molecules in crystals, and from the consequent "frozen" perception of the network of intermolecular interactions. When a fluxional molecule or ion is taken from the solution or gas phase into the solid state, its geometry is distorted along soft deformational paths, and its rotations and vibrations, though restricted, often persist to a very large extent. Large-amplitude oscillations and full-scale reorientational motions are often observed in plastic crystals. The deformation on passing from vacuum to the solid state is particularly dramatic in the case of supermolecules held together by intermolecular interactions; simple examples are the NH$_3$- - - BH$_3$ Lewis acid/base system or the acetic acid dimer CH$_3$COOH- - - CH$_3$COOH, where the distinction between inter- and intramolecular structures is not so straightforward.[31] In these cases the solid-state structure of the molecular aggregate does not correspond to the vacuum or solution structure, because the supramolecular bonding energies are low enough to be significantly perturbed by intermolecular interactions. Distortions and dynamics are obviously significant in the case of flexible coordination compounds: structural nonrigidity of the building blocks needs to be taken into account in devising crystal engineering strategies, since molecular and crystal structures may affect each other in an often unpredictable manner.

Charge-Assisted Hydrogen Bonds Can Be Successfully Used To Build Periodical Supermolecules

One of the *tools* available to the inorganic crystal engineer is the possibility of combining ionic charges and noncovalent interactions in devising new solids. Although ionic building blocks are commonly used in organic crystal engineering,[4] it is a fact that the neutral or charged nature of the ligands combined with the variable oxidation states of metal atoms make possible the observation of the same *synthon* in both neutral and ionic environments, a much less frequent situation in organic chemistry.

Since the HB has a fundamentally electrostatic nature, the presence of ionic charges on the building blocks can be exploited to strengthen the interaction. *Charge as-*
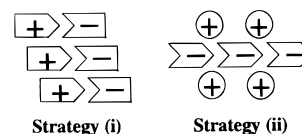
Chart 5

INTERACTION	STRENGTH	DIRECTIONALITY	PATTERN
Coulombic interaction	GOOD	POOR	
Hydrogen bond	POOR	GOOD	
Hydrogen bond within a Coulombic field	GOOD	GOOD	

Chart 6. Anion−Cation Pairing and Anion Self-Assembly in Strategies (i) and (ii), Respectively
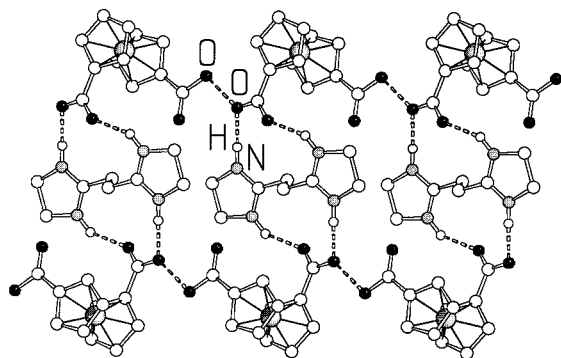
Strategy (i)   Strategy (ii)

sistance to HB is the enhancement of donor and acceptor systems' polarity (whether atoms or groups of atoms) by utilizing cationic donors and anionic acceptors instead of neutral systems, i.e., X−H$^{(+)}$− Y$^{(-)}$ rather than X−H− Y.[32] The favorable location of ionic charges enhances proton acidity *and* acceptor basicity. It should be kept in mind, however, that "acidity" and "basicity" are *relative* concepts and cannot be transferred *tout-court* to the solid state; other factors may change the polarity of the X−H bond and/or the nucleophilicity of the Y acceptor.

Charge-assisted HBs are widely employed to obtain predefined crystalline architectures.[4] The reason is manifold: (i) they are easily obtained in crystal synthesis via proton transfer in acid−base reactions (see below); (ii) the use of ions permits a much greater choice of components, which, in the case of transition metal complexes, may possess not only different topologies but also different bonding and electronic characteristics; and (iii) they *combine* HB directionality with the strength of Coulombic forces (see Chart 5). Indeed, Coulombic forces between anions and cations are much stronger than ion−dipole or dipole−dipole forces but lack directionality and are, therefore, less useful as design tools.

There are essentially two distinct strategies (see Chart 6) that utilize acid−base reactions to construct crystals on the basis of charge-assisted HBs:[4]

(i) The base forms charge-assisted X−H$^{(+)}$− Y$^{(-)}$ bonds. This is achieved, for instance, with nitrogen-containing bases (amines, aminidines, etc.) which are protonated upon reaction with polycarboxylic acid molecules, e.g., RCOOH + NR$_3$ → RCOO$^{(-)}$- - - $^{(+)}$HNR$_3$, leading to formation of strong N−H$^{(+)}$− O$^{(-)}$ interactions, hence on anion−cation pairing in the solid state. Depending on the acid: base stoichiometric ratio, N−H$^{(+)}$- - - O$^{(-)}$ and O−H- - - O$^{(-)}$ HB interactions may be present simultaneously.

(ii) The base *cannot form* HB interactions with the acid moiety. This is the case of the reaction between polycarboxylic acids with inorganic or organometallic hydroxides that do not carry strong acceptor/donor hydrogen bond groups. Partial deprotonation of the −COOH groups leads to self-assembly of acid anions via O−H- - -O$^{(-)}$ and $^{(-)}$O−H- - -O$^{(-)}$ interactions, while anions and cations may be linked via a profusion of weak C−H- - -O bonds.

FIGURE 3. Charge-assisted N—(H)$^{(+)}$- - -O$^{(-)}$ interactions link the organometallic anions $[(\eta^5\text{-}C_5H_4COOH)(\eta^5\text{-}C_5H_4COO)Fe^{II}]^-$ to the dication $[C_7H_{20}N_4]^{2+}$ while the anions form chains via $^{(-)}$O—H- - -O$^{(-)}$ interactions. Only H$_{(NH)}$ atoms are shown for clarity.

Strategy (i) has been extensively used in the field of organic chemistry.[4] A recent example of its application to organometallic systems has been obtained in collaboration with Hosseini.[33] If the dicarboxylic acid $[(\eta^5\text{-}C_5H_4\text{-}COOH)_2Fe^{II}]$ is reacted with the bis-amidine $[C_7H_{18}N_4]$ in a stoichiometric ratio of 2:1, the aggregate $[C_7H_{20}N_4]^{2+}\text{-}\{[(\eta^5\text{-}C_5H_4COOH)(\eta^5\text{-}C_5H_4COO)Fe^{II}]_2\}^{2-}$ is obtained (Figure 3). Formation of the complex requires proton transfer from the organometallic acid to the organic base, leading to the formation of N—H$^{(+)}$ hydrogen bond donor groups, and hence to N—H$^{(+)}$- - -O$^{(-)}$ interactions. Because of the stoichiometric ratio, the diacid is mono-deprotonated so that aggregation occurs via both cation−anion N—H$^{(+)}$- - -O$^{(-)}$ and interanion $^{(-)}$O—H- - -O$^{(-)}$ interactions.

Strategy (ii) requires the use of bases that do not compete in HB formation. We have shown that the organometallic hydroxides $[(\eta^5\text{-}C_5R_5)_2Co^{III}]^+[OH]^-$ and $[(\eta^6\text{-}C_6R_6)_2Cr^I]^+[OH]^-$ (R = H, Me, etc.) can be prepared in situ from the corresponding neutral species $[(\eta^5\text{-}C_5R_5)_2Co^{II}]$ and $[(\eta^6\text{-}C_6R_6)_2Cr]$ and can then be used to construct a variety of new supramolecular salts via templated assembly of the acid anions.[34] Target supramolecular arrangements can also be obtained by using organometallic polycarboxylic acids, such as $[(\eta^5\text{-}C_5H_4COOH)_2Fe^{II}]$ and $[(\eta^5\text{-}C_5H_4COOH)_2Co^{III}]^+$ (see Chart 7).

A recent example of deliberate *engineering* of a supramolecular arrangement with target magnetic properties is provided by crystalline $[(\eta^6\text{-}C_6H_6)_2Cr^I]^+[HC_4O_4]^-$, obtained by reacting squaric acid (3,4-dihydroxy-3-cyclobutene-1,2-dione, $H_2C_4O_4$) with $[(\eta^6\text{-}C_6H_6)_2Cr^I]$.[35] Because of its flat shape and small dimensions, the squarate anion $[HC_4O_4]^-$ was a likely candidate for intercalation between the flat benzene ligands of the paramagnetic cation $[(\eta^6\text{-}C_6H_6)_2Cr^I]^+$. Such intercalation, if achieved, would then lead to the formation of one-dimensional $D^+A^-D^+A^-$ structures comprised of alternating cation donors (D) and anion acceptors (A).[11] Indeed, the anion self-assembles into chains linked by $^{(-)}$O—H- - -O$^{(-)}$ interactions and intercalates between the benzene ligands forming the superstructure shown in Figure 4 ($\pi-\pi$ distance 3.38 Å). The presence of a charge-transfer transition was detected in the reflectance spectrum, while magnetic measurements showed that the weak, but ap-

Chart 7. Target Structures and Choice of Building Blocks for Strategies (i) and (ii)

Target structures	Building blocks
	Diamagnetic $[(\eta^5\text{-}C_5H_5)_2Co]^+,[(\eta^5\text{-}C_5Me_5)_2Co]^+$ Paramagnetic $[(\eta^6\text{-}C_6H_6)_2Cr]^+,[(\eta^-C_6H_5Me)_2Cr]^+$
Chiral Anionic Frameworks	Enantiomerically Pure Polycarboxylic Acids (e.g. L-tartaric, L-*trans*-acotinic acid)
Mixed Metal and Mixed Valence Superstructures	Organometallic Polycarboxylic Acids e.g. $[(\eta^5\text{-}C_5H_4COOH)_2Fe]$ or $[(\eta^5\text{-}C_5H_4COOH)_2Co]^+$
Charge Transfer and π Stack Magnetic Interactions	Flat Enediolones (e.g. squaric $H_2C_4O_4$, croconic $H_2C_5O_5$ acids)
Honeycomb Type Anionic Frameworks	Polycarboxylic Acids and Diones (e.g. D,L-tartaric, phthalic, trimesic acids, cyclohexanedione $H_8C_6O_2$ etc.)
Nanoporous Materials with Channelled Structures	Hydrated and Anhydrous Forms of the Zwitterion $[(\eta^5\text{-}C_5H_4COOH)(\eta^5\text{-}C_5H_4COO)Co]$
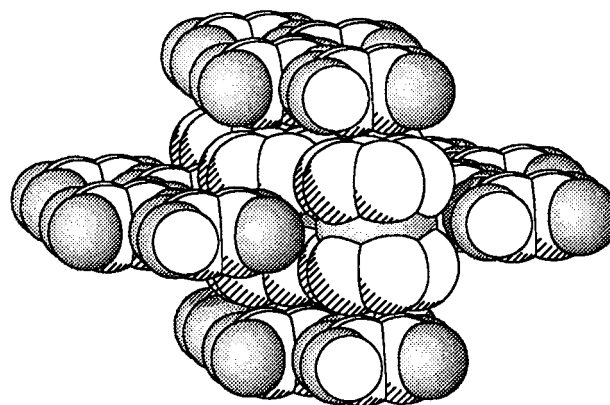
FIGURE 4. Space-filling representation of a row of cations $[(\eta^6\text{-}C_6H_6)_2Cr^I]^+$ surrounded by chains of $[HC_4O_4]^-$ anions joined by $^{(-)}$O—H- - -O$^{(-)}$ interactions.

preciable, antiferromagnetic interaction between the $S = ^1/_2$ of the $[(\eta^6\text{-}C_6H_6)_2Cr]^+$ cations could be attributed to the anion−cation π-stacking interaction. The magnetic susceptibility with temperature (χT) of ca. 0.5 emu K mol^{-1} was significantly higher than that expected for one unpaired electron of the $[(\eta^6\text{-}C_6H_6)_2Cr]^+$ cation. The hydrogen squarate chains thus have the double function of providing the structural framework and of transmitting the magnetic interaction between the paramagnetic cations.

Chart 7 provides further examples of target organometallic structures prepared by us[33−35] according to the two strategies.

On the Effect of Ionic Charges on Noncovalent Interactions

It has been pointed out that the terms attraction and repulsion should be used to refer to forces acting between atoms and molecules, while the terms stabilization and destabilization should be used to refer to energies.[29] It is consequential that stabilizing interactions can be efficacious even in the presence of repulsive forces, as well as the opposite, viz., destabilizing interactions may be observed in the presence of attractive forces. An appreciation of this conceptual distinction is crucial to the understand-
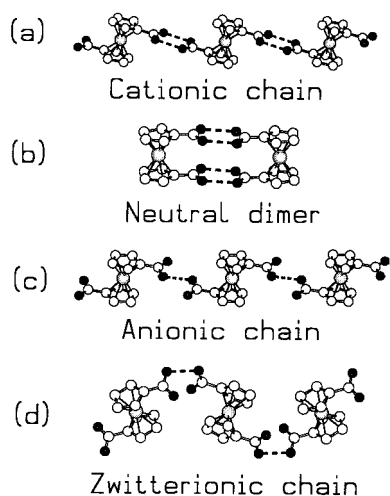
FIGURE 5. Comparison of the geometries and O- - -O separations (in brackets) in a selection of neutral, charged, and zwitterionic metallocene diacids: (a) the *cationic* chain in crystalline [(η^5-C$_5$H$_4$-COOH)$_2$Co^{III}]$^+$[PF$_6^-$] and (b) the *neutral* dimer in [(η^5-C$_5$H$_4$COOH)$_2$Fe^{II}], [O- - -O = 2.600(2) and 2.606(2) Å, respectively]; (c) the *anionic* chain in [(η^5-C$_5$H$_4$COO)(η^5-C$_5$H$_4$COOH)Fe^{II}]$^-$[(η^5-C$_5$H$_5$)$_2$Co^{III}]$^+$ and (d) the neutral chain formed by the *zwitterion* in [(η^5-C$_5$H$_4$COO)(η^5-C$_5$H$_4$-COOH)Co^{III}] [O- - -O = 2.453(3) and 2.456(2) Å, respectively].

ing of the effect of ionic charges on the nature of pairwise noncovalent interactions, particularly when the ions carry the same charge. While charge assistance is easy to understand in the case of a HB between a cationic donor and an anionic acceptor (e.g., N—H$^{(+)}$- - -O$^{(-)}$ as in strategy (i) above), the situation is more problematic when both donor and acceptor carry the same charge (e.g., $^{(-)}$O—H- - -O$^{(-)}$ as in strategy (ii)). In the latter case, one may expect HB chains formed by ions of the same sign to be unstable with respect to dissociation because of the dominant electrostatic repulsion between like charges. Besides the examples discussed above, organometallic compounds provide an ample variety of situations from which some insight can be gained. Figure 5 shows the HB interaction geometries in a selection of neutral, cationic, anionic, and zwitterionic chains of cobalt and iron dicarboxylic acid complexes. A comparison between (a) the *cationic* chain formed by [(η^5-C$_5$H$_4$COOH)$_2$Co^{III}]$^+$ and (b) the *neutral dimer* present in crystalline [(η^5-C$_5$H$_4$COOH)$_2$-Fe^{II}], and between (c) the chain formed by the *anionic* species [(η^5-C$_5$H$_4$COO)(η^5-C$_5$H$_4$COOH)Fe^{II}]$^-$ and (d) the neutral *zwitterion* [(η^5-C$_5$H$_4$COO)(η^5-C$_5$H$_4$-COOH)Co^{III}], demonstrates that the difference in O- - -O separations (see caption of Figure 5) between COOH- - -OC(OH) and COOH- - -$^{(-)}$OOC interactions does not depend on the neutral or ionic nature of the complex. The presence of shorter O- - -O separations in cases (a) and (b) with respect to those in (c) and (d) suggests that, at least in the solid state, proton removal from COOH groups, whether belonging to a neutral or cationic acid, "leaves" the extra electron localized on the deprotonated group. A possible rationale for this observation is that the electron localization allows full advantage to be taken of the stabilizing contribution arising from the electrostatic ($\delta+$)$-$($\delta-$) component of the interaction, even in the case

of building blocks carrying the same charge. It may be argued that the stabilization cannot offset the dominating repulsive forces between like charges and is not sufficient per se to keep the anions together in the absence of counterions. This problem, however relevant to the understanding of supramolecular bonding, may be found somewhat academic by experimentalists, because the precondition "in the absence of the counterions" is physically meaningless in the solid state where the *heteroionic* $+/-$ attractions necessarily overcompensate for the *homoionic* $+/+$ and $-/-$ repulsions and guarantee crystal cohesion.

A structural analysis focused on selected groups of interactions in ionic crystals is often a misleading approach, since short intermolecular distances are often a *consequence* of other truly relevant interactions, such as those between ions in crystalline salts. The implications of the above are quite relevant: (i) even though the *stabilizing* contribution of the HB interaction is small, the directionality is fully operative (see Charts 5 and 6), and (ii) the common assumption that the intermolecular separation between atoms or groups of atoms reflects the strength of the *local* interaction is not directly transferable from neutral to ionic environments. Similar considerations may be applied to other noncovalent interactions, e.g., π-stacking. At the same time, the fact that noncovalent interactions within an electrostatic environment retain exactly the same directionality features as the original neutral interactions becomes a powerful tool in crystal engineering, where reproducible crystal-directed synthetic strategies are sought and ionic materials are often preferable to molecular ones (for their solubility, thermal stability, etc.).

Conclusions and Outlook

There are, in our opinion, three main circumstances that are responsible for the birth (or rebirth) of molecular crystal engineering as a "stand-alone" science:

(i) the appropriate scientific environment provided by the success of supramolecular chemistry[1] and the consequent shift of interest from a molecular-based chemistry to the chemistry of molecular aggregates;

(ii) the progress in computing and diffraction tools that make it possible to tackle on a reasonable time scale theoretical and experimental problems of great complexity, such as those associated with complex molecular solids, interdigitated networks and supramolecular aggregates; and

(iii) the desire for more utilitarian objectives for the chemical sciences, such as those provided by materials chemistry, as a consequence of diffuse funding restrictions for fundamental studies.

This is true across all traditional subdivisions of chemistry, namely organic, inorganic, biological, and organometallic chemistry. The utilization of noncovalent interactions involving metal atoms (i.e., a rather large portion of the periodic table) is probably where the new frontier

lies. Metal atoms may allow us not only to exploit new topologies, hence to achieve new crystal architectures, but also to achieve *fine-tuning* of target supramolecular properties with distinct nonorganic characteristics. The utilization of noncovalent interactions in the presence of ions may also allow preparation of robust, often water-soluble, inorganic molecular materials. Even the smallest progress in the understanding and mastering of these features will represent a substantial step ahead in the development of reproducible inorganic crystal engineering strategies.

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