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Chapter

Polymorphism and Supramolecular Isomerism: The Impasse of Coordination Polymers

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Abstract

The chapter presented hereafter, outlines the narrow link between chemistry and crystallography that impelled the identification of *polymorphism* and provided a priceless grounding to understand structure-properties relationship. It was initially conceived for organic substances but actually embraced by metal–organic products, especially in the study of coordination polymers. All of the technologic advances have provided profound insights on the control of crystal structures formation revealing that any applied stimulus over a substance can undergo a structural transformation. This has led to the implementation of several methodologies in the industrial and academic segment shedding light on the source of hitherto, not well understood results.

Keywords: polymorphism, pseudopolymorphism, solvates, transition metals, organic linkers, crystal structures

1. Introduction: historical perspective

The intrinsic awareness in structure-properties relationship of solids was firstly introduced on the study of minerals and inorganic compounds and has been preserved over time [1]. Within this frame, the first step on the polymorphism phenomenon was unknowingly given by Klaproth [2] in 1788 identifying three different crystalline phases of calcium carbonate (calcite, vaterite and aragonite). In 1819, Mitscherlich commenced his research on phosphates and arsenates of potassium (KH_2PO_4 and KH_2AsO_4) and established their complete morphological similarity, noting that *they crystallize in similar forms*. His subsequent results with the corresponding potassium salts ($NH_4H_2PO_4$ and $NH_4H_2AsO_4$) confirmed that observation and led him to pose that *there do exist bodies of dissimilar chemical composition having the same crystalline form*. He not only recovered the work of Whollaston with orthorhombic carbonates and sulfates of barium, strontium and lead, who already noticed this phenomenon in 1812 but also, extended to rhombohedral carbonates of calcium, magnesium, iron and manganese, and to sulfates of iron, copper, zinc, magnesium, nickel and cobalt. Curiously, he also evinced the basis of *seeding* at realizing that *having two substances both able to crystallize in various forms, the presence of one during the crystallization of the other will force the crystallization of the latter in the same form*. Then, he moved to Stockholm with Berzelius with whom he delved deeply into phosphates and arsenates and forged the concept of

isomorphism. Last but not least, he reported two distinct crystallized forms of sulfur in 1826 demonstrating *a clear case of an element which could be made to crystallize in two different systems of symmetry at will, by merely changing the crystallization conditions.* Therefore, Mitscherlich was identified as the one who took the first step towards the rise of *polymorphism* [3]. Shortly after, in 1824, the contradictory results garnered by Liebig [4] and Wöhler [5] during their research on silver fulminate and silver cyanate triggered the conflict which led them to be colleagues and to pose the following dilemma: *can two compounds with the same composition have different physical properties?*. Their results evinced two Ag salts with the same composition but different physical properties, which did not go unnoticed by Wöhler's master Berzelius, who merged these results with those of Mitscherlich. It is unclear who was the first to conceive the notion of *polymorphism* but this crucial period of 1820–1832 was mainly drawn by Mitscherlich [6–8] who shed light on this phenomenon, even though the concept was still vague. It was during these years when Berzelius [9] proposed the concept of *isomerism* (1831–1832) and it took until 1832 for Wöhler and Liebig [10] to report the first case of *polymorphism* in an organic compound. The awareness of *isomerism* set the beginning of structural chemistry, broadening the knowledge and understanding of organic structures.

Since observation was the essential tool to identify *polymorphism*, this research drastically changed with the accessibility and wide spreading use of the microscope, but it was not until 1839 when Frankenheim [11] introduced the first principles defining *polymorphism* and *a postriori*, Mallard [12] set the structural basis of *polymorphism* in 1876, relating differences in physical properties with different arrangements. One of the most remarkable contribution during this period was the "Rule of steps" or "Law of successive reactions" from Ostwald [13] in 1897. He pointed that during a succession of polymorphic forms, those appeared later are generally more stable. Despite not being considered a rule, it is still valid as a general observation. But the two major queries raised by Buerger and Bloom [14] in 1937 were still unanswered: what causes the formation of different phases of a substance and which factors determine them?.

The narrow link between crystallography and *polymorphism* was forged by Tamman [15] in 1926 and settled with the first polymorphic X-ray crystal structure determination of an organic compound, resorcinol, published by Robertson and Ubbelohde [16] in 1939. Despite this achievement, the next decades passed without a better understanding of *polymorphism,* being underrated until 1965 when McCrone [17] conducted a comprehensive study in which he defined a polymorph as: "*a solid crystalline phase of a given compound resulting from the possibility of at least two different arrangements of the molecules of that compound in the solid state*" and published a review in 1969 about the importance of such phenomenon in the pharmaceutical outlook [18]. Since the introduction of the term *allotrope* by Berzelius in 1841, *Polymorphism* had been taken with *allotropy* on the same meaning. But, it was not until the 1990s, when Sharma [19] and Reinke [20] set the differences between them: *polymorphism* occurs in chemical compounds while *allotropy* occurs in chemical elements. This work was crowned *a posteriori* by Dunitz's [21, 22] crystal description contribution.

In the 1970s, the works of Schmidt [23] and Paul and Curtin [24, 25] grounded the flourish of solid-state chemistry and precede the breakthrough of conceiving polymorphism. They served as inspiration to Bernstein and Desiraju, who laid the foundation for recent supramolecular chemistry. In 1978, Bernstein [26] changed the landscape of *polymorphism* by rationalizing the study of crystal packing forces on molecular conformations of polymorphs and later in 1990, together with Etter [27–30], applied their graph set descriptors and provide guidelines to understand polymorphic transformations [31]. Bernstein compiled most of this historical

results in his book "*Polymorphism in Molecular Crystals*", which the authors encourage reading [32]. Likewise, Desiraju achieved substantial progress in this field during his studies of structure-properties relationship of organic solids mainly of pharmaceutical interest, emphasizing and aiming its importance in this industry as reflected in his book "*Crystal Engineering: A Textbook*" [33]. Both channeled their polymorphism vision in terms of supramolecular chemistry.

During 1990s, computational chemistry went hand in hand, achieving methodologies capable to reproduce experimental results and enabling even crystal structure predictions. The first attainment was obtained by using Williams' software [34] that met the main handicap hitherto, the identification of lattice energy minimums. Subsequent years, many computational approaches were developed facing with computer-generated structures for prediction, to the extent that in 1999 a collaborative workshop held at the Cambridge Crystallographic Data Centre (CCDC) [35] brought together the benchmark computational groups of this period to provide an objective assessment of the possibilities of crystal structure prediction. The results gathered in this event were clearly summarized *a posteriori* in a paper published by Lommerse [36]. Further advances on prediction methods accuracy as well as the implementation of Density Functional Theory (*DFT*) and Machine Learning (*ML*) can be found in Spark's review [37].

Despite the basis of polymorphism were already defined at the end of the twentieth century, the increasing advances on X-ray diffraction techniques and crystallization methods afforded the determination and analysis of metal–organic structures, especially *coordination polymers*. *Polymorphism* of metal–organic complexes was still unexplored and these new class of materials, from which polymorphic structures grew exponentially, required classification and awareness. This impasse was encouraged by renowned researchers as Sharma [38], Ciani [39], Rogers [40] and Zaworotko [41]. In this regard, the same Zaworotko was who published a review in 2001 emphasizing the difference between *polymorphism* and *supramolecular isomerism* and underlined the link between them in organic and metal–organic networks [42].

2. Types and borders: from organic to metal–organic

During the early stages of polymorphism, the lack of crystallographic tools conditioned the understanding and therefore, classification of the different polymorphic forms, but the exponential advances in this field provided perhaps too many concurrent data to bring it together and form a unique mindset. It was not until 1965 when McCrone [17] gathered the knowledge hitherto and set a more excluding definition of polymorphism. The inclusion or not of hydrated forms and solvates have been discussed since the rise of polymorphism, but be that as it may, he ventured to propose their exclusion from polymorphic forms and to avoid the use of *pseudopolymorphism* to define them. This assertion was underpinned by Bernstein [32] in 2002, even if actually it is a wide spread term, probably because of its acceptance by the pharmaceutical industry [43] from its regulatory and patentability point of view. Since the aim of this chapter is not about *pseudopolymorphs* we therefore, decided to exclude this term to refer to solvates and hydrates, which can lead to undesirable misunderstandings. In 2012, Desiraju, Karpinski, Thaper and Zaworotko [44] defined *cocrystals* as *solids that are crystalline single-phase materials composed of two or more different molecular and/or ionic compounds generally in a stoichiometric ratio which are neither solvates nor simple salts*. As well as *salts* that are *any of numerous compounds that result from replacement of part or all of the acid hydrogen of an acid by a metal or a radical acting like a metal;*

an ionic or electrovalent crystalline solid. Instead, *solvates* have one component, commonly a solvent, which is liquid by itself and *hydrates* are a particular case of *solvates*, containing water as solvent. A deeper discussion on *pseudopolymorphism* can be found in references [45–47].

Until the beginning of the twenty-first century, the polymorphs' classification was settled from the perspective of crystal packing forces and introduced *conformational* and *packing polymorphism* to sort the examples hitherto. *Coordination polymers* are infinite repeating coordination entities composed of organic molecules serving as linkers and metal ions as nodes [48]. Their main classification is based on dimensionality which is the number of directions in which the array is extended. Therefore, they can be divided into one-, two- or three-dimensional. The rise of this field befell in 1961 when Bailar [49] firstly introduced the term *coordination polymers*. Distinction between polymorphs and other forms as solvates, hydrates or cocrystals in organic structures was well defined, but in the case of metal–organic structures, in particular *coordination polymers,* this classification was not sufficient.

Numerous structures which were not truly polymorphs (solvent molecules were present in the lattice), but neither were solvates, started to rise at the end of the twentieth century. This new domain required the borders to be clarified and established. Yet, these rigid structures were thought to be less disposed to suffer structural variations but some examples were gathered in works of Janiak [50] with Zn(II) poly(pyrazolyl)borates, Ciani [39] with Ag(I) and 4-cyanopyridine, Zaworotko [41, 51] with Co(II) and pyridyl containing linkers, Ripmeester [52] with Cu(II) and a diketone and Rogers [40] with Hg(II) and tetrapyridylporphyrines. Thus, *supramolecular isomerism* was invoked to merge those different types of structures (mainly coordination polymers) assembled from identical building blocks. In this impasse, Zaworotko [42] strongly contributed to shed light upon this ambiguity in his review of 2001. He defined *supramolecular isomerism* as "*...the existence of more than one type of network superstructure for the same molecular building blocks...*" and pointed that polymorphs are a particular case of supramolecular isomers "*...polymorphs can therefore be regarded as being supramolecular isomers of one another but the reverse is not necessarily the case*". This assertion should be clear before classifying metal–organic structures.

Henceforth, *supramolecular isomerism* was divided into *structural* (regarding the formation of different networks *inter alia* ladder, brickwall, 3D frame, herringbone, bilayer or Lincoln logs), *conformational* (relying on the flexibility of the ligands) and a new class named *catenane* (promoted by interpenetration), being polymorphic forms a certain condition of them. A schematic representation highlighting such division is depicted in **Figure 1**. At that time, *structural isomerism* was focused on the particular case of *architectural isomers* [41], understood as variations of the connectivity of the ligands between two structures, sharing the same composition as a result of ligand conformations [53]. In particular, to those cases in which the accommodation of different solvent guest molecules promoted the change in the spatial disposition of the organic linkers.

In this direction, Robin and Fromm [48] in 2006 described *supramolecular isomerism* as the ability of a substance to arrange into one or several network superstructures by different molecular or supramolecular assemblies with the inherent condition that organic linkers and metal ion remain the same and this metal ion retains an equal coordination sphere. They also reported several examples of a new subclass of structural supramolecular isomers named as *ring opening*. Recently, Zhou [54] has provided the specific term *framework isomers* to define supramolecular isomerism in MOFs, in which solvent occluded molecules are trivial.

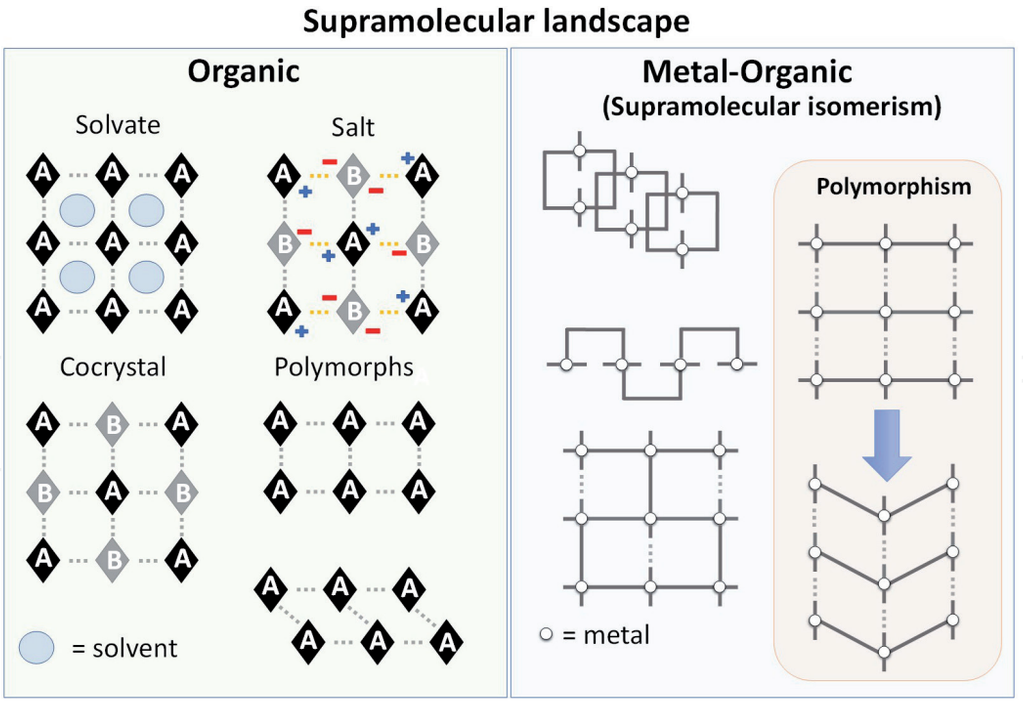


Figure 1.
Schematic representation of the structural relationship between the different architectures among organic and metal–organic compounds.

3. Thermodynamic vs. kinetic factors: formation and transformation of polymorphs

A brief summary of fundamental thermodynamics principles is required prior to understand their relevance on *polymorphism*. Despite ideal systems are not viable, the definition of boundaries within this phenomenon based on simple laws could be achieved with a sufficient accuracy to be useful. It is essential to stress that the result of any structural change will be reflected as a change on the properties of the system. Since energy changes are empirically measurable, they are a pragmatic way to face *polymorphism* and led these energy differences to be a useful descriptor. The identification of the relative intensities within the different forms of energy displays whether exchanges of energy between two polymorphs will occur. Remarkably, this allows to induce energetic modifications, by an external stimulus, only on a selected form of energy to establish relationships in a linear manner.

The quantity of energy a system exchanges with environs is named *enthalphy* and is referred to as *H*. Taking a chemical reaction as the case study, the character of the energetics involved in it, is represented as the *enthalpy of reaction,* which is the difference in enthalpies between products and reactants. This concept is useful to determine the direction in which energy will flow but such information is not conclusive to establish *spontaneity*. Hence the introduction of the notion of *entropy* (*S*) is essential. It is a way to represent the organization of a system approached as the degree of disorder and it is measured in terms of entropy changes of the system. Using both terms, *Gibbs free energy* (*G*) provides further insights into *spontaneity* at constant temperature and pressure.

To understand the relative stability of the different polymorphs within a given system as well as their transformations, the energy/temperature diagrams (E/T) introduced by Buerger in 1951 [55] are the most valuable approach, being capable to encapsulate much data in a single representation. It is based on the *G* equation:

$$G = H - TS \quad (1)$$

As a general representation, the diagram on **Figure 2a** displays how these terms evolve at increasing temperature. Since the term *TS* is more significantly affected by temperature than *H*, its effect on *G* becomes intense as the temperature of the system raises and thus, *G* of the system tends to decrease. The energy of a transformation undergone within a polymorphic system, under conditions of constant temperature and pressure, are defined by:

$$\Delta G = \Delta H - T\Delta S \quad (2)$$

Within a series of polymorphic forms their crystal lattices are unique *per se*, so despite their *G* at a certain temperature could be equal (*isoenergetic* forms), the values of *H* and *S* will be different (**Figure 2b**). If isoenergetic forms are present, there is a crossing point between the two *G* value curves in the E/T diagram, named *transition point* (*t.p.*), which to be useful is to be placed below the *melting point* (*m.p.*). In such a scenario, if the formation of these polymorphs is allowed by kinetic factors, both forms coexist and can be formed as *concomitant polymorphs* (*vide infra in Section 5*).

For instance, considering a case study as the one represented in **Figure 2b**, containing two polymorphic forms (*dimorphic*) named as *A* and *B*, a brief analysis of this E/T diagram can provide some useful data. Below the *t.p.* (blue region) form *A* is the most thermodynamically stable as its lower *G* value states. Within this region, its transformation into form B is related to an increase in *H* and it is defined as an *endothermic* transition. At the *t.p.* both forms have the same *G* ($\Delta G = 0$), which applied to Eq. (2) is set that $\Delta H = T\Delta S$, where $\Delta H = H_B - H_A$ and $\Delta S = S_B - S_A$. All these equations allow to quantify the entropic change of a polymorphic transformation once the enthalpic variation $(\Delta H_{t,B\leftrightarrow A})$ is experimentally determined (see Section 4.1). Above the *t.p.* (green region), within this range of temperature and before the change of state at the *m.p.*, form *B* is the thermodynamically stable and therefore, transformation from *A* to *B* is associated with a decrease in *H* (*exothermic* process). After defining these borders, one can infer the proper conditions in which the formation of one polymorph is favored instead of the other.

Considering that theoretical thermodynamic relations applied to systems undergoing phase transformation are bounded by experimental data, more empirical concepts were developed to better represent these changes. Consequently, the terms *Enantiotropism* and *Monotropism* were defined to meet this requirement. The former refers to those systems presenting a reversible transformation before the *m.p*. when heated above or cooled below the *t.p.* Contrarily, *Monotropism* sets that only one polymorph is the more thermodynamically stable over the entire range

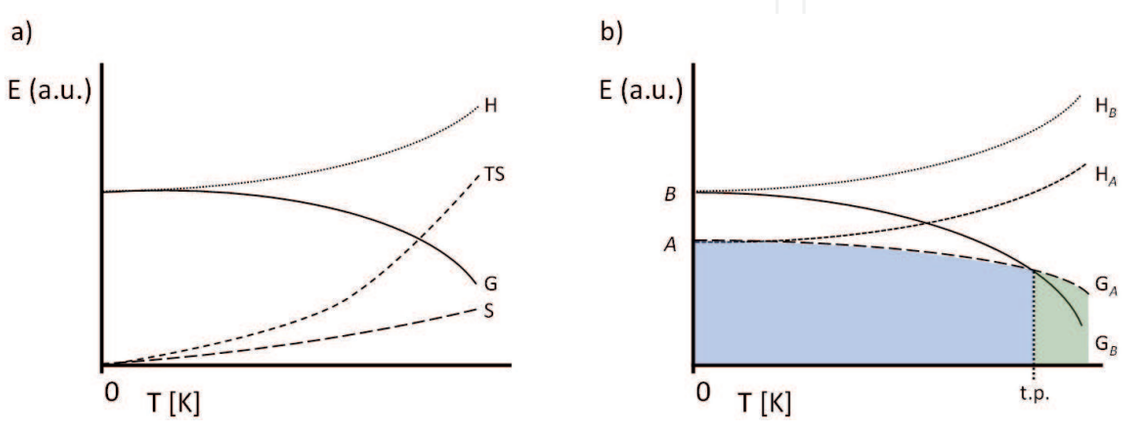


Figure 2.
(a) Progression of the terms G, S, TS and H at increasing temperature. (b) Representation of the evolution of H and G variables in a dimorphic system (polymorphs A and B) at increasing temperature.

of temperatures until the *m.p*. Both examples are illustrated in **Figure 3a** and **b**, respectively.

The incorporation of energetics associated with the liquid state into the E/T diagram, enthalpy (H_{liq}) and free energy (G_{liq}), ease to parse their behavior and classification. If the crossing points between the G_{liq} curve and the *G* curves of both *A* and *B* are after the *t.p.*, they are said to be *enantiotropes*. The absence of crossing points between *A* and *B* before their *m.p.* classify them as *monotropes*. The terms $\Delta H_{f,}B$ and $\Delta H_{f,}A$ are the energy that *B* or *A* require to change into liquid state, respectively.

Burger and Ramberger [56] in 1979, pioneered in the development of many experimental rules to empirically establish the nature of this relationship between polymorphic forms and their applicability was exemplified with 113 substances [57]. All giving fundamental knowledge to determine the proper conditions to control their formation: Heat-of-transition, Heat-of-fusion, Entropy-of-fusion, Phase transformation reversibility, Enthalpy of sublimation, Heat-capacity, Infrared, Solubility and Density rules. Among them, the most applied are Heat-of-transition and Heat-of-fusion rules. The former being based on using Differential Scanning Calorimetry (DSC) to identify the endothermic or exothermic character of the transition. If this rule cannot be applied, Heat-of-fusion rule, which rely on the determination of the *m.p.*, states that the relation is *enantiotropic* when the higher melting polymorph has the lower enthalpy of fusion while *monotropic* systems are defined by the higher melting polymorph having the higher enthalpy of fusion. Detailed explanation on the application of them could be found in Burger publication [57] or in the more recent Brittain's review [58].

Crystallization is the process related with nucleation and growth of a crystal structure. This process is, in principle, directed by thermodynamic factors that tend to reach the structure with a lower lattice energy. However, the crucial stage is supersaturation which is determined by kinetics, in particular, by the rate of nucleation and thus, the first structure to be formed is the one with preferred nucleation. Therefore, a metastable form can grow despite being unfavored by thermodynamic factors. Subsequently, this form can be converted into a more thermodynamically stable by solution or solid state-mediated phase transformation. This successive phase change was identified and proposed as the *Law of States* by Ostwald [13].

To avoid common mistakes in ascribing the nature of the *nucleation* process, Mullin [59] divided it into *primary*, in which any crystalline matter is directing the process, and *secondary*, pertaining to the circumstances of nucleation generated in the vicinity of crystals, previously nucleated or intentionally placed, a methodology known as *seeding* (*vide infra* in Section 4.2). Furthermore, secondary nucleation can be classified as *homogeneous* if it is spontaneous or *heterogeneous* if it is induced by foreign particles.

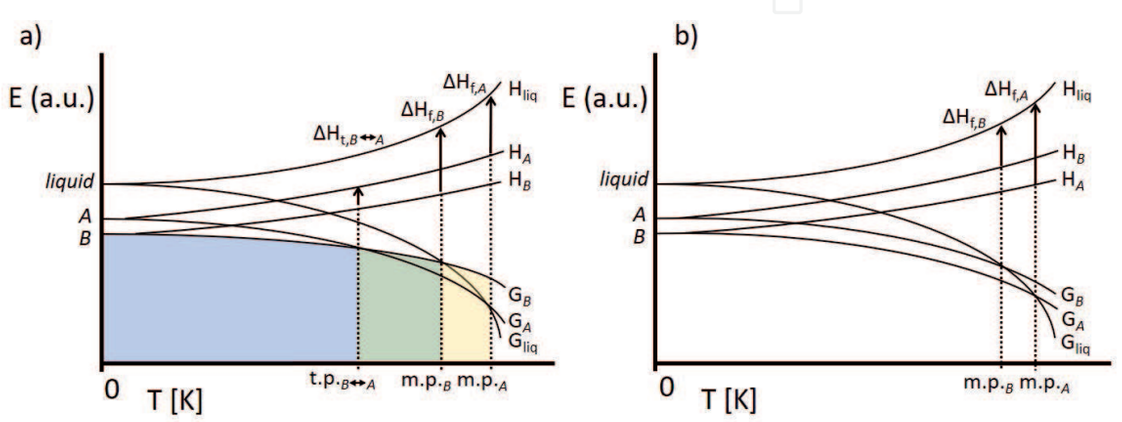


Figure 3.
E/T diagrams of (a) enantiotropic and (b) monotropic dimorphic systems.

Solid-state phase transformations are usually promoted by an external stimulus in the form of mechanical work or temperature. They are thought to be related with intrinsic defects, whether coming from the original structure or being caused by mechanical stress, which commence and propagate the formation of the new phase. The most studied transformations are those based on order–disorder changes, mainly promoted by temperature variations. *Disordering* processes arise from increasing temperature whereas *ordering* processed are observed at decreasing temperature. An excellent analysis of such phenomena with the most relevant examples were summarized by Dunitz and Bernstein [60].

The reversibility of these changes could not be evident or even accessible since *hysteresis* plays a crucial role. It is the lagging of the transition behavior respect to the applied stimulus. Therefore, it is possible to need heating or cooling beyond the *t.p.* to let the phase change occurs and even with the sufficient high degree of *hysteresis* is conceivable to avoid transformation [61]. Although ideal reversibility is often desired, control of hysteresis [62] also leads to unique properties [63], often advantageous to the application of these materials, only achievable by a precedent transformation. *Hysteresis* phenomenon is associated to *structural fatigue* [64–66], which means the rise of structural changes in the crystalline material as dislocations as well as to a different nucleation with different energy barriers from one to another [67]. Further concerns regarding the basis of this topic can be addressed reading Flanagan's publication [68].

Overall, since crystallization is a competitive process between minimizing lattice energy (thermodynamic) and reaching supersaturation (kinetic), the achievement of non-minimal energetically stable forms allows to the transformation into lower energetic forms after reaching the activation barrier.

4. Strategies to identify and achieve polymorphs and the influence on their properties

4.1 Identification of polymorphs

The identification of polymorphism had been, in the vast majority of cases, a matter of chance, but this all changed as a result of the efforts of many scientists in the field. The first tool of recognition was visual observation inasmuch as it was the most affordable and accessible technique. Since it is not a strict approach, however, it is often useful to detect anomalies. In particular, observation of crystalline materials through optical microscopy can allow to differentiate between two crystal *habits* (their characteristic external shape), because this shape is governed by its molecular packing and intermolecular interactions (internal structure). Notwithstanding that more than a century has passed, it is still a routinely used technique, even if optical microscopy is being superseded by Scanning Electron Microscopy (SEM), which allows more accurate surface topology and morphology analysis. The closely related Transmission Electron Microscopy (TEM) was not appropriate for this kind of materials even given its uniqueness. It could collect structural and dynamic data from single crystals in a bulk powder and therefore, have remarkable benefits compared to any other. Unfortunately, the high energy applied to the samples caused strong damages precluding their characterization. Over years, researchers intended to reduce the applied voltage, seeking for this technique to be applicable by minimizing sample damage and improving cameras and detector technologies. This was especially aimed to the study of metal organic frameworks (MOFs), one of the most emerging topics with fundamental need to understand structure-properties relationship. Hence, breakthrough developments

in characterization techniques as cryogenic-TEM (cryo-TEM) [69] and High-Resolution TEM (HR-TEM) [70] paved the way to structural features at the nanometric scale as well as recent improvements for *in situ* measurements *inter alia* hot stage TEM, liquid cell TEM (LCTEM) [71] or environmental TEM (ETEM) [72] enabled to observe the dynamics of these systems. Advanced 3-dimensional electronic techniques as automated electron diffraction tomography (ADT) [73] and Rotation Electron Diffraction (RED) [74] were able to gather sufficient data for *ab initio* structure elucidation and thus succeeded where conventional diffraction techniques failed [75].

Despite all these advances, the most valuable technique has been and remains, single-crystal X-ray diffraction (SC-XRD). Only neutron diffraction is tantamount, being capable to collect specific and accurate data of atomic positions, bond distances, and angles [76]. Thus, serving as a complementary technique to SC-XRD. However, one must consider the possibility of temperature driven single-crystal to single-crystal transformations since a growing number of examples have been reported in the literature. Careful inspection of temperature effects on the sample is to be required. The generally used condition in SC-XRD is about 100 K which can undergo the phase transformation. If such events are not assured, one could fail at drawing conclusions of property changes from structural differences.

Although SC-XRD provides complete information about atom positions and structural packing, the growth of suitable crystals for structure determination is sometimes a laborious and very time-consuming task or even not attainable. Often, but nowadays less and less, it is not thought to be part of the endeavors of a chemist. That is why structural studies goes hand in hand with Powder X-Ray diffraction (PXRD), which is in many cases more available and can reflect any structural difference between SC-XRD and the bulk powder. But one must not forget that after ensuring no phase transformation, SC-XRD and neutron diffraction are the unique unambiguous techniques while the rest requires to be combined to successfully identify *polymorphism*. Recent advances in diffraction methodologies have enabled to improve PXRD characterization. For instance, variable temperature-PXRD and variable temperature-SC-XRD not only ease to determine differences in crystalline materials but also allow to trace phase transformations being subject to temperature changes.

Solid-state spectroscopic techniques are also a complementary tool during the identification of structural differences. Sometimes these changes are not evident but, in many cases, subtle structure modifications are reflected in the spectra. The most marked differences observable by Fourier Transformation Infrared Spectroscopy-Attenuated Total Reflectance (FTIR-ATR) [77] or Raman spectroscopies [78] usually appears in the fingerprint region since it is unique for a substance. In the case of polar molecules, transitions associated with rotation can be measured in absorption or emission by microwave or far infrared spectroscopies [79]. Also solid-state Nuclear Magnetic Resonance (SS-NMR) [80] as well as solid-state Ultraviolet–Visible absorption (SS-UV–Vis) [81] and fluorescence [82] have proven to be fruitful techniques to identify polymorphism and phase transformations. The recording of SS-NMR data can be improved by using Schaefer and Stejskal [83] experiments, in which high power heteronuclear decoupling, cross polarization (CP) and magic-angle spinning (MAS) are combined. Careful attention should be paid during MAS since the required high spinning rates generate mechanical stress and local heating, thus favoring conditions for transformations. *Isotopomeric polymorphs* [84] have also been identified, albeit in a lesser extent.

Solid-state Electron spin resonance (ESR) also known as Electron Paramagnetic Resonance (EPR) can be used only for materials containing paramagnetic metal

ions or structures in which those metal ions have been embedded. Copper(II) but also cobalt(II) are the archetypal metals for this technique and there already exist examples incorporating Cu(II) into the structures of templated materials [85]. More sophisticated variations include variable-temperature magnetic-susceptibility and variable-temperature solid-state EPR measurements. An increasingly common strategy combines them in the study of single-ion magnets (SIMs), a type of single-molecule magnets (SMMs). This EPR analysis is not easily available since it is preferably implemented with a synchrotron radiation source [86]. The magnetic evaluation of SIMs is performed in solid state so the structural differences between polymorphic forms promoted by conformational changes could lead to a dramatic alteration of the magnetic properties [87]. This effect is marked in Clathrochelates, a special class of structurally rigid cage metal complexes [88].

Last but not least, thermoanalytical techniques *inter alia* hot stage microscopy (also known as thermal microscopy), Thermogravimetric analysis (TGA), Differential Thermal Analysis (DTA) and Differential Scanning Calorimetry (DSC), are widely used to characterize both polymorphism as well as phase transformation phenomena. They are usually combined to maximize the efficiency of the data collection as TG-DTA or DSC-TGA, among others.

During hot stage microscopy, the sample is subjected to heating and cooling processes under polarized light. It provides *m.p.* data as well as, if it occurs, the reversible or irreversible character of the transition. TGA method is used to determine the thermal stability of the products and as previously mentioned, it is commonly combined with DTA. By the use of a thermobalance, it is capable to measure weight losses during temperature changes. It is especially useful to determine desolvation temperatures and thermal stability ranges but it is less accurate to quantify these transitions. The most appropriate technique to track phase transformations with quantitative data is DSC.

DSC is routinely used to measure the difference in the amount of heat required to increase the temperature of the sample respect to a reference. It is divided into power compensation DSC and heat-flux DSC methods. The quantification of the $\Delta H_{t,B\leftrightarrow A}$ enables to identify its exo- or endothermic character, as well as the determination of reversible or not transitions provides essential data about the *enantiotropic* or *monotropic* behavior. DSC has not been deeply exploited yet for metal–organic materials but this practice is inevitably set to change. In particular, it is increasingly used in the study of breathing metal–organic frameworks (MOFs) [89] or solid-state phase transformations in Zeolitic imidazolate frameworks (ZIFs) [90].

Evidence of *polymorphism* can also be confirmed by nanoindentation or by optical properties as refractive index (n) or the identification of an interference figure caused by birefringence, which is the presence of different n and mainly depends on crystallographic orientations [91]. Once *polymorphism* has been identified and characterized, the proper conditions to isolate or to only reach one polymorphic form are to be established, avoiding the presence of mixtures and undesired products.

4.2 Screening and isolation of polymorphic forms

There are significant factors determining the formation of polymorphs *inter alia* molecular structure, chemical composition, energetic differences and experimental conditions (solvent, additives, pH, temperature and pressure). What should be clear is that the different polymorphic forms of a given structure can be selectively reach either by crystallization from the melt or solution, or by solid-state transformation. Crystallization approach has been the most widely studied heretofore but awareness of hitherto ignored solid-state transformations has led to value their tantamount importance. The solution-mediated approach is based on the proper

adjustment of the crystallization process and involves much more control of the polymorphs forming conditions. Instead, the advances in solid-state characterization techniques have triggered a significant increase of polymorphism studies allowing traceability of such conversions. This is especially the case of *coordination polymers* and MOFs, optimal materials for polymorphism study because of their flexibility and capability to accommodate structural modifications without the breaking of bonds.

The first step in polymorphs screening is to determine the phase space of a substance and the boundaries of stability for the different forms as well as identifying, if it is the case, interconversion. Defining the most stable phase is recommended since, unless modulating external factors dictate otherwise, that form would be the result. The occurrence of polymorphs and their transformations are confined to what is known as *occurrence domains* that encompass all the conditions in which the targeted crystal forms originate. Early studies carried out by Sato [92] on stearic acid delved deeply into the dependence of temperature and supersaturation on solvent polarity. Is in those regions with *domain* overlap where polymorphic transformations can occur, bearing in mind that the *domain* is not unique for one crystallographic form.

The many attempts to control the formation of a desired form have supplied us of a vast number of methods to selectively achieve it through crystallization or solid-state phase transformation. Most of the old and recent methods have been compiled in **Figure 4**. Further details about fundamental crystallization methods are found in Hulliger's review [93].

Over all of the difficulties of achieving isolated polymorphs, to identify the conditions to reach isolated forms is an essential task. When dealing with a polymorphic mixture scenario, the initial way of facing it, is the use of common crystallization methods as those mentioned before. However, crystallization of less stable forms is often intricated and therefore, it requires the design of more robust strategies *inter alia* high-pressure crystallization, spray-drying, crystallization from a melt or crystallization from a quenched amorphous phase. They give sometimes

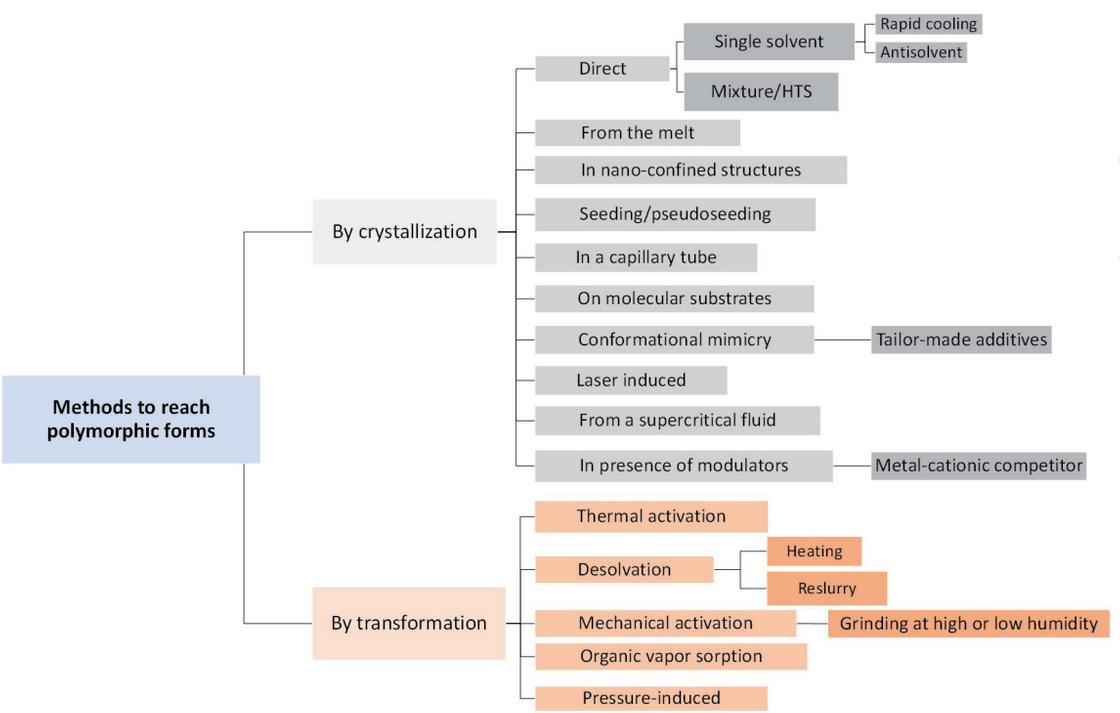


Figure 4.
Classification of the different methods to achieve polymorphic forms by crystallization or transformation.

satisfactory results, but their major drawback is the lack of control in the formation of a single product. Hence, the use of additives and substrates was implemented as template though a limited triumph, considering that only thermodynamic aspects are contemplated and kinetic factors have a determinant role in nucleation. Subsequent methods as application of external fields, surface templating, selective nucleation by supersaturation control and nucleation temperature or seeding experiments emerged, but there is still a need for their improvement.

It is nevertheless important to note again that MOF materials are themselves appropriate candidates for filing structural modifications, since the predefined preferences of the organic linkers combined with those of the metal ions result in a restricted range of potential structures. This is strongly reflected in the common formation of isostructural products although they combine different linkers and metal ions. Such a controllable way of structure design is therefore adequate to identify new strategies for the isolation of different crystalline phases. Currently, throughout all the advances in MOFs design, *polymorphism* and *isomerism* awareness has driven the seeking of selective crystalline phase formation methods. For instance, in the case of mixed-metal MOFs, in which the addition of more than one metal ion disrupts the predefined structural formation, the selective phase formation has been achieved by the incorporation of guiding organic linkers or even metal ions to template the structural assembly. There was already consciousness of *polymorphism* and *isomorphism* in chromium(III) terephthalate MOFs [94], but

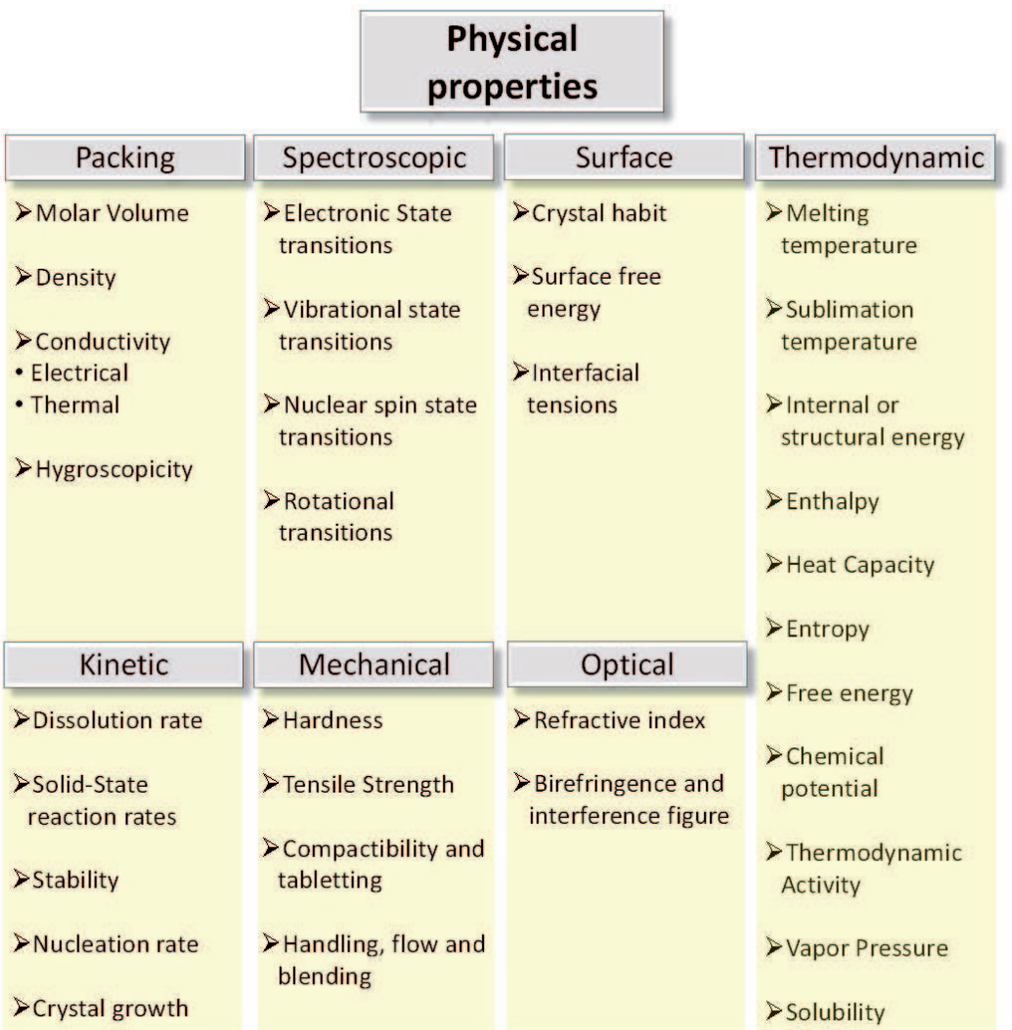


Figure 5.
Properties likely to be altered by polymorphic modifications.

the strategies to reach them were lacking. In 2018, Bureekaew [95] controlled the formation of this family of MOFs by using iron(III) metal-cationic competition, which served as *modulator* during crystallization. Likewise, Užarevic [85] demonstrated a rapid and selective way of controlling *polymorphism* in this family of MOFs by a mechanochemical approach using additives.

4.3 Properties

Become aware of a difference in the properties of a unique sample or two sample which in principle, are to be identical is the commencement of most *polymorphism* studies. One important aspect to be considered, sometimes careless, is the manipulation of the samples before the measurements. It is widely reported that a routinely sample treatment as grinding can undergone phase transformation. Even this subtle stimulus can provoke changes in the sample with the consequent incongruent results, thus hampering their correct analysis. These changes produced by polymorphic modifications could range from slight differences to dramatic alterations of the target properties and those which have raised more interest are listed in **Figure 5**.

5. The special cases: concomitant, vanishing (or disappearing) and intergrowth polymorphism

The terms *Vanishing or disappearing polymorphs* were renowned during the second half of the twentieth century by referring to the evolving nature of some crystal forms over time that caused their unrepeatability. In the course of the subsequent years, researchers realized that every crystal form can be repeated being the finding of the proper conditions (control over nucleation and crystal growth) the main trouble.

Within the polymorphism landscape, the presence of mixtures of crystalline phases has brought a profound attention whereby, many efforts were devoted to the understanding of such circumstances. Reproducibility and purity have always been a requisite for chemists, so such demonstration of lack of control led them to seek to comprehend and identify the source of these phenomena. These two closely related special cases, named as *Concomitant* and *Vanishing* polymorphs, refers to a condition describing all the forms involved. *Concomitant* polymorphs are those simultaneously formed at the exactly same conditions. This assertion is not trivial since many factors contribute to the crystallization process. The case of *vanishing* or *disappearing* polymorphs describes the formation of a metastable phase which undergoes transformation into a more thermodynamically stable one. This phenomenon is quite thorny since as mentioned, reproducibility of the results is often intricated. Such conversions can be found by redissolution of the former crystal or in solid-state. In the solution-mediated process, the formation and disappearing of a metastable product can be quenched by *seeding*. A crucial statement is to be noted, once seeds of one polymorph are formed, the other form will no longer be formed. By using this criterion, seeding *crystallites* of the desired polymorph will lead to the growth of its crystals, even though it is a metastable form [60]. This method allows to avoid both undesirable cases, *concomitancy* and *vanishing*, if phase-pure materials are to be achieved. *Vanishing* by solid-state transformations is even less evident, indeed, any slight appliance of an external stimuli can promote this phase change and routinely sample treatments required for many characterization techniques as grinding, milling or pressure and temperature changes could be sufficient to trigger it. Both phenomena have probably been less reported than occurs and just a curious point is that the first recognized example of *polymorphism* in an organic substance

described by Wöhler [10] the *dimorphism* of benzamide, that was also the first precedent of *concomitancy*.

The critical point describing *concomitant* and *vanishing* polymorphs is based on the same kinetic/thermodynamic factors, better understandable by the mentioned E/T plots and promoted by the kinetic govern. In fact, *concomitancy* is dependent on where from the diagram the polymorphs are growing. Having this data, one can also design a strategy to favor the nucleation of one polymorphic form instead of the other.

Identification of concomitant polymorphs is as always, initially assessed by visual recognition. Thus far, careful inspection during hot-stage microscopy has been the most reliable method. Differences in crystal habit and variable melting point suggesting crystalline mixtures could provide a clue as to trace *concomitancy*. Also broadening signals in solid-state NMR or FTIR-ATR may be a symptom of this.

Reported cases of *vanishing* polymorphs in metal–organic compounds are in large part still unfathomed. The phenomenon of *concomitant* polymorphs is equally meager being only few examples reported hitherto. Oliver [96] in 2012 reported the special case of two Cd(II) coordination polymers concomitantly formed from which the less stable form was subsequently identified as a disappearing polymorph. Both products crystallize in the monoclinic crystal system but the stable form (2) exhibited a C_2/c space group and bigger unit cell parameters than the vanishing form (1), which displayed a P2/c space group. Their main dissimilarity was the slightly different orientation of the dipicolinate ligands (**Figure 6**), which improved the inter-chain π···π interactions in the structure of the stable form and provoked a different packing.

In the case of organic structures, several examples can be found in literature. Chalcones are a class of natural products widely used in medicinal chemistry. For instance, the (E)-3′-dimethylamino-nitrochalcone has demonstrated *concomitant polymorphism*, easily detectable by the different colors associated to each form [97].

In spite of topologically flexible MOFs as ZIFs and other azolates are prone to manifest *polymorphism*, the scarce monitoring of *in situ* structure formation thwart its recognition. An example of concomitant polymorphism has been recently reported by Sánchez and Fernández [98] with two Pt(II) metallosupramolecular polymers. Both products were formed by self-assembly of monomeric units but

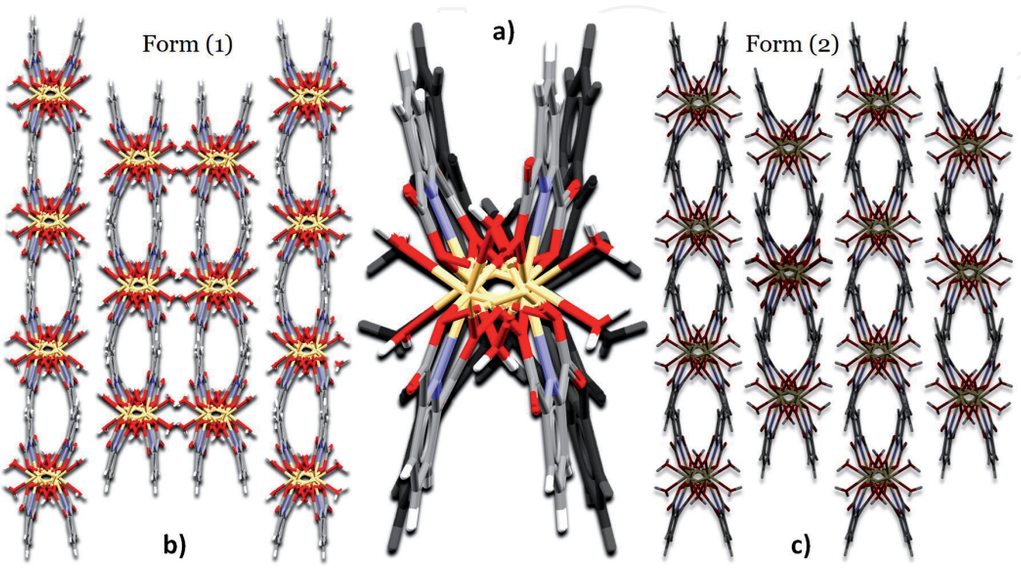


Figure 6.
(a) Overlapping representation of the two Cd(II) polymeric chains in the two polymorphs. Different disposition of dipicolinate ligands: front chain (1) and back chain in dark (2). (b) c axis view of the packing of the less stable form 1 and (c) a axis view of the packing of the more stable form 2 [96].

differed in presenting slipped or pseudoparallel packings. In 2020, a new study from Hanusa and Friščić [99] identified the presence of a *disappearing* polymorph during the formation of two different Hg(II) imidazolate ($Hg(Im)_2$) phases, synthesizing a new layered structure (*sql*) with the consequent disappearing of a previously reported interpenetrated dense phase (*dia*) $Hg(Im)_2$ [100]. Both forms exhibited an orthorhombic crystal system but having evident structural differences driven by an *agostic* interaction (C-H··Hg) in the *sql* form. The *dia*-$Hg(Im)_2$ contained tetrahedral Hg(II) nodes in a Pbca space group and cell parameters of a = 14.5899(3) Å; b = 10.8076(2) Å; c = 9.8200(2) Å while the *sql*-$Hg(Im)_2$ form presented a tetrahedral *see-saw* geometry in the space group $P2_12_12$, with a = 9.4089(4) Å, b = 7.6414(3) Å, c = 5.3625(2) Å. The transient nature of the *dia* form was tracked by PXRD during the mechanochemical synthesis of *sql* form, being inaccessible to reach *dia* form as a final product.

Intergrowth polymorphism was firstly reported by Bond, Boese and Desiraju [101] in 2007 during a study about the doubtful crystalline forms of aspirin and the related difficulties of its structural refinement. It was conceived *to refer to the existence of distinct structural domains within a single crystal of a compound*. When analyzing the one-dimensionally diffuse diffraction data, using Bürgi [102] method, they noticed some diffuse streaks between the Bragg reflections. Considering the reported results of Bürgi, this would be associated with the presence of a less ordered domain. Careful inspection of such results led them to identify two differently ordered domains in the same crystal of aspirin. They also demonstrated by a nanoindentation study in 2014, a bimodal mechanical response depending on which of the crystal faces were measured [103]. From the metal–organic perspective, there had already been examples reported by Ciani of *coordination polymers* of cobalt(II) *intergrowth supramolecular isomers* [104] and copper (II) *intergrowth polymorphs* [105] due to the presence of conformational non-rigid linkers.

6. Interest of polymorphism in organic and metal–organic structures

Polymorphism has an implicit interest since it represents a special situation for the study of structure-properties relationship with limited number of variables as well as provides essential information to understand and control the crystalline inception. The special case of *concomitant polymorphs*, is in turn, an even more worthwhile situation. From a unique reaction, one could establish direct relations between structure modifications and properties. They are also benchmark products for computational analysis as well as for verification of structure-prediction softwares. All this beneficial knowledge can be fruitfully employed throughout the industrial and academic landscape.

6.1 Industrial interest

In the industrial field, stability and purity are mandatory equal for organic and metal–organic materials. Properties of organic solids reflected in their processability and storage as well as solubility and dissolution rates are directly related with bioavailability of a drug and hence are of prime interest to the pharmaceutical industry. For instance, an important concern in the manufacturing, storage and transport of energetic materials is that polymorphic modifications alter the energetics and safety risks associated to them. A representative case is 1,3,5,7-tetranitro-1,3,5,7-tetrazocane (HMX), in which higher compact crystal packings lead to the safer form [106]. In addition, *polymorphism* has relevant commercial impact in the patenting of drugs [107] as in the renowned case of Ranitidine, a drug for the treatment of stomach and

intestines ulcers. The subsequent discovery of the polymorphic form 2, having an easier manufacturing procedure, after the patenting of form 1, originated a lengthy court process [108]. *Concomitant* polymorphs are regularly found in industrial precipitation processes in the pharmaceutical and fine-chemicals sectors as in the case of L-histidine, to which anti-solvent crystallization became an inevitable proceeding [109]. *Coordination polymers* has special interest for waste water treatment, protective coatings and fluorescent chemosensors [110]. For instance, in MOFs the thermo-mechanical stability is crucial to move towards the industrial segment. Among the most promising applications, those of industrial interest are adsorption, separation, purification and catalysis. They are being exhaustively tested to supersede, by improved performance, the extensively exploited zeolitic molecular sieves, activated carbon and base metal oxides [111]. Furthermore, ZIFs materials have exhibited remarkable efficiency in separation of olefin/paraffin mixtures [112] and emerged as appropriate candidates to adsorb and retain radioactive iodine [113]. All of these applications depend on the structural arrangement of the materials and thus, control over crystal structure formation is imperative.

6.2 Academic interest

The interest of *polymorphism* in *coordination polymers* lies on the always present structure-properties relationship. The exact control of their structural arrangement is reflected in the achievement of the desired chemical and physical properties. Despite being known as promising functional materials their modular nature can result in polymorphic forms and thus, hampering their application. This is emphasized in applications demanding a high selectivity as enantiomeric separation, gas storage, sensing, molecular recognition, ionic exchange [114], heterogeneous catalysis [115] or non-linear optics. The rise of MOFs, a remarkable case of ordered coordination polymers with potential voids and permanent porosity was driven by the breakthrough of the archetypal MOF-5 [116]. Their main attribute is the controlled porosity to which the formation of cages allows their controlled use in such applications. Currently research is devoted to study structural transformations in Zr-based MOFs. Also a particular family of MOFs essentially constructed with zinc(II) or cobalt(II) metal ions, the Zeolitic Imidazolate Frameworks (ZIFs), have been explored for their superior thermal and chemical stability but as zeolites, the ZIF family displays rich polymorphism [117]. The $Zn(Im)_2$ itself can accommodate 18 polymorphic forms, being essential towards its application the finding of controlled synthesis as the recently established template-mediated route [118]. As afore mentioned, there has been evidence in the recent cases of Cd(II) *coordination polymers* or especially in the ZIF material *dia*-$Hg(Im)_2$ of the undesirable scenario of *vanishing polymorphs.* In the latter case, the formation of the more stable form has hampered the obtention of the 3D structure being superseded by the new layered *sql*-$Hg(Im)_2$. These examples demonstrate the dormant resemblance of metal–organic materials with such well known phenomenon in organic compounds. Another important subject are phthalocyanines, being copper phthalocyanine the model compound. They revolutionized color printing offering a better economic remedy but facing polymorphic troubles since their discovery. Subtle alterations of their crystal packing which is based on π···π interactions, acutely influences the absorption properties with the consequent color change from blue to red [119]. *Intergrowth polymorphism* and *intergrowth supramolecular isomerism* in coordination polymers has also been promoted by flexible linkers and several examples have been reported hitherto mainly with d^{10} metal ions [120]. This ability to present different properties available in a single crystal open new possibilities for materials design.

7. Conclusions

The perspective of *polymorphism* was primarily based on organic substances until the beginning of the twenty-first century. The increasing advances on solid state characterization, especially *in situ* measurements, benefited the rise of metal–organic structure and its awareness on polymorphic modification. Currently, the ease of tracking structural transformations of dynamic materials has brought to promising insights into the understanding and control of *polymorphism*.

Acknowledgements

J.P. acknowledges financial support from the CB615921 project, the CB616406 project from "Fundació La Caixa" and the 2017SGR1687 project from the Generalitat de Catalunya. F.S.F. acknowledges the PIF pre-doctoral fellowship from the Universitat Autònoma de Barcelona.

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References

[1] Wells AF. Structural inorganic chemistry. Fifth Edi. Nature. Oxford, UK: Clarendon Press; 1989. p. 294-315

[2] M.H. K. Phosphorsäure, ein Bestandtheil des Apatits. Arch f Miner Geognosie u Hüttenkd. 1798;1:294-300.

[3] Tutton AEH. The work of Eilhardt Mitscherlich and his discovery of isomorphism. In: The natural History of Crystals. First Edit. London, UK: Kegan Paul; 1924. p. 70-97.

[4] Gay-Lussac JL, Liebig J. Analyse du Fulminate d'Argent. Ann Chim Phys. 1824;25:285-311.

[5] Wöhler F. Poggendorffs Ann. Phys. Chem. 1824;1:117-24.

[6] Mitscherlich E. Sur la relations qui existe entre la forme cristalline et les proportion chimiques. Ann Chim Phys. 1820;14:172-90.

[7] Mitscherlich E. Sur la relation qui existe entre la forme cristalline et les proportions chimiques, I. Mémóire sure les arseniates et les phosphates. Ann Chim Phys. 1822;19:350-419.

[8] Mitscherlich E. Über die Körper, welche in zwei verschiedenen krystallisieren Formen. [Considering the materials which can crystallize in two different crystal forms]. Abhl Akad Berlin. 1823;43-8.

[9] Ihde JI. The Development of Modern Chemistry. New York, USA: Dover Publications Inc.; 1984. p. 170-173.

[10] Wöhler F, Liebig J. Untersuchungen über das Radikal der Benzoesäure [Investigations of the radical of benzoic acid]. Ann der Pharm. 1832;3:249-82.

[11] Frankenheim ML. Ueber die Isomerie. Prakt Chem. 1839;16:1-14.

[12] Mallard E. Explication des phenomes optiques anomaux. Ann Mines. 1876;10:60-196.

[13] Ostwald W. Studien über die Bildung und Umwandlung fester Körper 1. Abhandlung: Übersättigung und Überkaltung. Zeitschrift für Phys Chemie Int J Res Phys Chem Chem Phys. 1897;22:289-330.

[14] Buerger MJ, Bloom MC. Crystal Polymorphism. Zeitschrift für Krist - Cryst Mater. 1937;96:182-200.

[15] Tammann GHJA. The states of aggregation: The changes in the state of matter in their dependence upon pressure and temperature (translate by F.F. Mehl). First Edit. New York, USA: Van Nostrand; 1926. p. 116-157.

[16] Robertson JM, Ubbelohde AR. Structure and thermal properties associated with some hydrogen bonds in crystals, II. Thermal expansion. Proc R Soc London Ser A Math Phys Sci. 1939;170:241-51.

[17] McCrone WC. Polymorphism. In: Fox D, Labes M., Weissberger A, editors. Physics and Chemistry of the Organic Solid State. Volume 2. New York, USA: Wiley Interscience; 1965. p. 725-67.

[18] Haleblian J, McCrone W. Pharmaceutical applications of polymorphism. J Pharm Sci. 1969;58:911-29.

[19] Sharma BD. Allotropes and polymorphs. J Chem Educ. 1987;64:404-7.

[20] Reinke H, Dehne H, Hans M. A discussion of the term "Polymorphism." J Chem Educ. 1993;70:101.

[21] Dunitz JD. Phase transitions in molecular crystals from a chemical

viewpoint. Pure Appl Chem. 1991;63:177-85.

[22] Dunitz JD. Thoughts on crystals as supermolecules. In: The crystal as a supramolecular entity Perspectives in supramolecular chemistry. Desiraju GR, editor. Chichester, UK: Wiley; 1996. p. 1-30.

[23] Schmidt GMJ. Photodimerization in the solid state. Pure Appl Chem. 1971;27:647-78.

[24] Paul IC, Curtin DY. Thermally Induced Organic Reactions in the Solid State. Acc Chem Res. 1973;6:217-25.

[25] Paul IC, Curtin DY. Reactions of Organic Crystals with Gases. 1975;187:19-26.

[26] Bernstein J, Hagler AT. Conformational Polymorphism. The Influence of Crystal Structure on Molecular Conformation. J Am Chem Soc. 1978;100:673-81.

[27] Etter MC. Encoding and Decoding Hydrogen-Bond Patterns of Organic Compounds. Acc Chem Res. 1990;23:120-6.

[28] Etter MC, MacDonald JC, Bernstein J. Graph-set analysis of hydrogen-bond patterns in organic crystals. Acta Crystallogr Sect B. 1990;46:256-62.

[29] Etter MC. Hydrogen bonds as design elements in organic chemistry. J Phys Chem. 1991;95:4601-10.

[30] Bernstein J, Etter MC, Macdonald JC. Decoding Hydrogen-bond Patterns. The Case of lminodiacetic Acid. J Chem Soc, Perkin Trans 2. 1991;1989-91.

[31] Bernstein J, Davis RE, Shimoni L, Chang N -L. Patterns in Hydrogen Bonding: Functionality and Graph Set Analysis in Crystals. Angew Chemie Int Ed English. 1995;34:1555-73.

[32] Bernstein J. Polymorphism in Molecular Cystals. New York, USA: Oxford University Press Inc.; 2002. p. 19-27.

[33] Desiraju, Gautam R.; Vittal, Jagadese J.; Ramanan A. Crystal Engineering: A Textbook. Singapore: World Scientific Publishing Co. Pte. Ltd.; 2011. p. 99-130.

[34] Williams DE. PCK83, QCPE Program 548; Quantum Chemistry Program Exchange. Bloomington, IN: Chemistry department, Indiana University; 1983.

[35] Groom CR, Bruno IJ, Lightfoot MP, Ward SC. The Cambridge structural database. Acta Crystallogr Sect B Struct Sci Cryst Eng Mater. 2016;72:171-9.

[36] Lommerse JPM, Motherwell WDS, Ammon HL, Dunitz JD, Gavezzotti A, Hofmann DWM, et al. A test of crystal structure prediction of small organic molecules. Acta Crystallogr Sect B Struct Sci. 2000;56:697-714.

[37] Graser J, Kauwe SK, Sparks TD. Machine Learning and Energy Minimization Approaches for Crystal Structure Predictions: A Review and New Horizons. Chem Mater. 2018;30:3601-12.

[38] Sharma CVK. Crystal Engineering - Where Do We Go from Here? Cryst Growth Des. 2002;2:465-74.

[39] Carlucci L, Ciani G, Proserpio DM, Sironi A. Interpenetrating Diamondoid Frameworks. J Chem Soc, Chem Commun. 1994;2755-6.

[40] Krishnamohan Sharma C V., Broker GA, Rogers RD. Polymorphous one-dimensional tetrapyridylporphyrin coordination polymers which

structurally mimic aryl stacking interactions. J Solid State Chem. 2000;152:253-60.

[41] Hennigar TL., MacQuarrie DC., Losier P, Rogers RD., Zaworotko MJ. Supramolecular Isomerism in Coordination Polymers: Conformational Freedom. Angew Chemie Int Ed English. 1997;36:972-3.

[42] Moulton B, Zaworotko MJ. From molecules to crystal engineering: Supramolecular isomerism and polymorphism in network solids. Chem Rev. 2001;101:1629-58.

[43] Polymorphism S. Guidance for industry. ANDAs: Pharmaceutical Solid Polymorphism. Chemistry, Manufacturing and Controls Information [Internet]. 2007. Available from: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm072866.pdf

[44] Aitipamula S, Banerjee R, Bansal AK, Biradha K, Cheney ML, Choudhury AR, et al. Polymorphs, salts, and cocrystals: What's in a name? Cryst Growth Des. 2012;12:2147-52.

[45] Nangia A, Desiraju GR. Pseudopolymorphism: Occurrences of hydrogen bonding organic solvents in molecular crystals. Chem Commun. 1999;605-6.

[46] Seddon KR. Pseudopolymorph: A polemic. Cryst Growth Des. 2004;4:1087.

[47] Nangia A. Pseudopolymorph: Retain this widely accepted term. Cryst Growth Des. 2006;6:2-4.

[48] Robin AY, Fromm KM. Coordination polymer networks with O- and N-donors: What they are, why and how they are made. Coord Chem Rev. 2006;250:2127-57.

[49] J. C. Bailar J. "Coordination Polymers," A Chapter in "Inorganic Polymers, An International Symposium,." In London: The Chemical Society; 1961. p. 51-66.

[50] Janiak C, Hemling H. Linkage lsomerism in bis[hydrotris(1,2,4-triazolyl)borato]zinc from a molecular chelate complex to a three-dimensional co-ordination polymer. J Chem Soc, Dalt Trans. 1994;2947-52.

[51] Biradha K, Zaworotko MJ. supramolecular isomerism and polymorphism in dianion salts of pyromellitic acid. Cryst Eng. 1998;1:67-78.

[52] Soldatov D V., Ripmeester JA, Shergina SI, Sokolov IE, Zanina AS, Gromilov SA, et al. α- And β-bis(1,1,1-trifluoro-5,5-dimethyl-5-methoxyacetylacetonato)copper(II): Transforming the dense polymorph into a versatile new microporous framework. J Am Chem Soc. 1999;121:4179-88.

[53] Swift JA, Pivovar AM, Reynolds AM, Ward MD. Template-directed architectural isomerism of open molecular frameworks: Engineering of crystalline clathrates. J Am Chem Soc. 1998;120:5887-94.

[54] Makal TA, Yakovenko AA, Zhou HC. Isomerism in metal-organic frameworks: "Framework isomers." J Phys Chem Lett. 2011;2:1682-9.

[55] Buerger MJ. Phase Transformations in Solids. Smoluchowski R, Mayer JE, Weyl WA, editors. New York, USA: Wiley; 1951. p. 183-211.

[56] Burger A, Ramberfer R. On the Polymorphism of Pharmaceuticals and Other Molecular Crystals. I. Mikrochim Acta. 1979;72:259-71.

[57] Burger A, Ramberger R. On the polymorphism of pharmaceuticals and

other molecular crystals. II. Mikrochim Acta. 1979;72:273-316.

[58] Brittain HG. Computational methodologies: Toward crystal structure and polymorph prediction. In: Polymorphism in Pharmaceutical Solids. Second Edi. New York, USA: CRC Press; 2016. p. 52-75.

[59] Mullin JW. Crystallization. Fourth Edi. Oxford, UK: Butterworth Heinemann; 2001. p. 181-189.

[60] Dunitz JD, Bernstein J. Disappearing Polymorphs. Acc Chem Res. 1995;28:193-200.

[61] Richardson MF, Yang Q -C, Novotny-Bregger E, Dunitz JD. Conformational polymorphism of dimethyl 3,6-dichloro-2,5-dihydroxyterephthalate. II. Structural, thermodynamic, kinetic and mechanistic aspects of phase transformations among the three crystal forms. Acta Crystallogr Sect B. 1990;46:653-60.

[62] Iasco O, Boillot ML, Bellec A, Guillot R, Rivière E, Mazerat S, et al. The disentangling of hysteretic spin transition, polymorphism and metastability in bistable thin films formed by sublimation of bis(scorpionate) Fe(II) molecules. J Mater Chem C. 2017;5:11067-75.

[63] Goodwin CAP, Ortu F, Reta D, Chilton NF, Mills DP. Molecular magnetic hysteresis at 60 kelvin in dysprosocenium. Nature. 2017;548:439-42.

[64] Eggeler G, Hornbogen E, Yawny A, Heckmann A, Wagner M. Structural and functional fatigue of NiTi shape memory alloys. Mater Sci Eng A. 2004;378:24-33.

[65] Norfleet DM, Sarosi PM, Manchiraju S, Wagner MFX, Uchic MD, Anderson PM, et al. Transformation-induced plasticity during pseudoelastic deformation in Ni-Ti microcrystals. Acta Mater. 2009;57:3549-61.

[66] Straka L, Drahokoupil J, Veřtát P, Kopeček J, Zelený M, Seiner H, et al. Orthorhombic intermediate phase originating from {110} nanotwinning in Ni50.0Mn28.7Ga21.3 modulated martensite. Acta Mater. 2017;132:335-44.

[67] Zhang Z, James RD, Müller S. Energy barriers and hysteresis in martensitic phase transformations. Acta Mater. 2009;57:4332-52.

[68] Flanagan TB., Park C-N., Oates WA. Hysteresis in solid-state reactions. Prog Solid State Chem. 1995;23:291-363.

[69] Patterson JP, Xu Y, Moradi MA, Sommerdijk NAJM, Friedrich H. CryoTEM as an Advanced Analytical Tool for Materials Chemists. Acc Chem Res. 2017;50:1495-501.

[70] Liu L, Chen Z, Wang J, Zhang D, Zhu Y, Ling S, et al. Imaging defects and their evolution in a metal–organic framework at sub-unit-cell resolution. Nat Chem. 2019;11:622-8.

[71] Lyu J, Gong X, Lee SJ, Gnanasekaran K, Zhang X, Wasson MC, et al. Phase Transitions in Metal-Organic Frameworks Directly Monitored through in Situ Variable Temperature Liquid-Cell Transmission Electron Microscopy and in Situ X-ray Diffraction. J Am Chem Soc. 2020;142:4609-15.

[72] Parent LR, Pham CH, Patterson JP, Denny MS, Cohen SM, Gianneschi NC, et al. Pore Breathing of Metal–Organic Frameworks by Environmental Transmission Electron Microscopy. J Am Chem Soc. 2017;139:13973-6.

[73] Kolb U, Mugnaioli E, Gorelik TE. Automated electron diffraction tomography - A new tool for

nano crystal structure analysis. Cryst Res Technol. 2011;46:542-54.

[74] Wan W, Sun J, Su J, Hovmöller S, Zou X. Three-dimensional rotation electron diffraction: Software RED for automated data collection and data processing. J Appl Crystallogr. 2013;46:1863-73.

[75] Wang B, Rhauderwiek T, Inge AK, Xu H, Yang T, Huang Z, et al. A Porous Cobalt Tetraphosphonate Metal–Organic Framework: Accurate Structure and Guest Molecule Location Determined by Continuous-Rotation Electron Diffraction. Chem - A Eur J. 2018;24:17429-33.

[76] Hutchison IB, Bull CL, Marshall WG, Urquhart AJ, Oswald IDH. Pressure-induced polymorphism of caprolactam: A neutron diffraction study. Molecules. 2019;24:2174.

[77] Smokrović K, Muratović S, Karadeniz B, Užarević K, Žilić D, Dilović I. Synthon Robustness and Structural Modularity of Copper(II) Two-Dimensional Coordination Polymers with Isomeric Amino Acids and 4,4′-Bipyridine. Cryst Growth Des. 2020;20:2415-23.

[78] Fan WW, Cheng Y, Zheng LY, Cao QE. Reversible Phase Transition of Porous Coordination Polymers. Chem - A Eur J. 2020;26:2766-79.

[79] Hoffman AEJ, Vanduyfhuys L, Nevjestić I, Wieme J, Rogge SMJ, Depauw H, et al. Elucidating the Vibrational Fingerprint of the Flexible Metal-Organic Framework MIL-53(Al) Using a Combined Experimental/ Computational Approach. J Phys Chem C. 2018;122:2734-46.

[80] Dudek MK, Kazmierski S, Kostrzewa M, Potrzebowski MJ. Solid-State NMR Studies of Molecular Crystals. In: Annual Reports on NMR Spectroscopy. Elsevier Ltd; 2018. p. 1-81.

[81] Shin CH, Huh JO, Lee MH, Do Y. Polymorphism-induced dual phosphorescent emission from solid-state iridium(III) complex. J Chem Soc Dalt Trans. 2009;6476-9.

[82] Quartapelle Procopio E, Mauro M, Panigati M, Donghi D, Mercandelli P, Sironi A, et al. Highly emitting concomitant polymorphic crystals of a dinuclear rhenium complex. J Am Chem Soc. 2010;132:14397-9.

[83] Schaefer J, Stejskal EO. Carbon-13 Nuclear Magnetic Resonance of Polymers Spinning at the Magic Angle. J Am Chem Soc. 1976;98:1031-2.

[84] Zhou J, Kye YS, Harbison GS. Isotopomeric polymorphism. J Am Chem Soc. 2004;126:8392-3.

[85] Karadeniz B, Žilić D, Huskić I, Germann LS, Fidelli AM, Muratović S, et al. Controlling the Polymorphism and Topology Transformation in Porphyrinic Zirconium Metal-Organic Frameworks via Mechanochemistry. J Am Chem Soc. 2019;141:19214-20.

[86] Nehrkorn J, Holldack K, Bittl R, Schnegg A. Recent progress in synchrotron-based frequency-domain Fourier-transform THz-EPR. J Magn Reson. 2017;280:10-9.

[87] Novikov V V., Pavlov AA, Nehrkorn J, Nelyubina Y V. Influence of Polymorphism on the Magnetic Properties of Single-Molecule Magnets According to the Data of EPR Spectroscopy in the Terahertz Range. Russ J Coord Chem Khimiya. 2020;46:756-61.

[88] Voloshin Y, Belaya I, Krämer R. Cage Metal Complexes. Clathrochelates Revisited. Cham, Switzerland: Springer Nature; 2017. p. 231-317.

[89] Schneemann A, Bon V, Schwedler I, Senkovska I, Kaskel S, Fischer RA. Flexible metal-organic

frameworks. Chem Soc Rev. 2014;43:6062-96.

[90] Longley L, Li N, Wei F, Bennett TD. Uncovering a reconstructive solid–solid phase transition in a metal–organic framework. R Soc Open Sci. 2017;4.

[91] Thompson JR, Katz MJ, Williams VE, Leznoff DB. Structural Design Parameters for Highly Birefringent Coordination Polymers. Inorg Chem. 2015;54:6462-71.

[92] Sato K, Boistelle R. Stability and occurrence of polymorphic modifications of the stearic acid in polar and nonpolar solutions. J Cryst Growth. 1984;66:441-50.

[93] Hulliger J. Chemistry and Crystal Growth. Angew Chemie Int Ed English. 1994;33:143-62.

[94] Carson F, Su J, Platero-Prats AE, Wan W, Yun Y, Samain L, et al. Framework isomerism in vanadium metal-organic frameworks: MIL-88B(V) and MIL-101(V). Cryst Growth Des. 2013;13:5036-44.

[95] Tanasaro T, Adpakpang K, Ittisanronnachai S, Faungnawakij K, Butburee T, Wannapaiboon S, et al. Control of Polymorphism of Metal-Organic Frameworks Using Mixed-Metal Approach. Cryst Growth Des. 2018;18:16-21.

[96] Kukovec BM, Venter GA, Oliver CL. Structural and DFT studies on the polymorphism of a cadmium(II) dipicolinate coordination polymer. Cryst Growth Des. 2012;12:456-65.

[97] Hall SR, Hall CL, Guo R, Potticary J, Cremeens ME, Warren SD, et al. Color differences highlight concomitant polymorphism of chalcones. Cryst Growth Des. 2020;20:6346-55.

[98] Langenstroer A., Kartha KK., Dorca Y, Droste J, Stepanenko V, Albuquerque RQ., et al. Unraveling Concomitant Packing Polymorphism in Metallosupramolecular Polymers. J Am Chem Soc. 2020;141:5192-200.

[99] Speight IR, Huskić I, Arhangelskis M, Titi HM, Stein RS, Hanusa TP, et al. Disappearing Polymorphs in Metal–Organic Framework Chemistry: Unexpected Stabilization of a Layered Polymorph over an Interpenetrated Three-Dimensional Structure in Mercury Imidazolate. Chem - A Eur J. 2020;26:1811-8.

[100] Masciocchi N, Ardizzoia GA, Brenna S, Castelli F, Galli S, Maspero A, et al. Synthesis and ab-initio XRPD structure of group 12 imidazolato polymers. Chem Commun. 2003;3:2018-9.

[101] Bond AD, Boese R, Desiraju GR. On the polymorphism of aspirin: Crystalline aspirin as intergrowths of two "polymorphic" domains. Angew Chemie - Int Ed. 2007;46:618-22.

[102] Bürgi HB, Hostettler M, Birkedal H, Schwarzenbach D. Stacking disorder: The hexagonal polymorph of tris(bicyclo[2.1.1]hexeno) benzene and related examples. Zeitschrift fur Krist. 2005;220:1066-75.

[103] Mishra MK, Desiraju GR, Ramamurty U, Bond AD. Studying microstructure in molecular crystals with nanoindentation: Intergrowth polymorphism in felodipine. Angew Chemie - Int Ed. 2014;53:13102-5.

[104] Carlucci L, Ciani G, Proserpio DM. A new type of entanglement involving one-dimensional ribbons of rings catenated to a three-dimensional network in the nanoporous structure of $[Co(bix)_2(H_2O)_2](SO_4)\cdot 7H_2O$ [bix = 1,4-bis(imidazol-1-ylmet. Chem Commun. 2004;4:380-1.

[105] Carlucci L, Ciani G, Proserpio DM, Spadacini L. Supramolecular isomers in the same crystal: a new case

involving two different types of layers polycatenated in the 3D architecture of $[Cu(bix)_2(SO_4)]\cdot 7.5H_2O$[bix=1,4-bis(imidazol-1-ylmethyl)benzene]. CrystEngComm. 2004;6:96-101.

[106] Liu G, Gou R, Li H, Zhang C. Polymorphism of Energetic Materials: A Comprehensive Study of Molecular Conformers, Crystal Packing, and the Dominance of Their Energetics in Governing the Most Stable Polymorph. Cryst Growth Des. 2018;18:4174-86.

[107] Braga D, Brammer L, Champness NR. New trends in crystal engineering. CrystEngComm. 2005;7:1-19.

[108] Bernstein J. Polymorphism and Patents from a Chemist's Point of View. In: Polymorphism: in the Pharmaceutical Industry. Hilfiker R, editor. Weinheim, Germany: Wiley-VCH; 2006. p. 369-72.

[109] Roelands CPM, Jiang S, Kitamura M, ter Horst JH., Kramer HJM., Jansens PJ. Antisolvent Crystallization of the Polymorphs of L-Histidine as a Function of Supersaturation Ratio and of Solvent Composition. 2006;6:955-63.

[110] Sunday NF. Emerging Trends in Coordination Polymers and Metal-Organic Frameworks: Perspectives, Synthesis, Properties and Applications. Arch Org Inorg Chem Sci. 2018;1:39-51.

[111] Czaja AU, Trukhan N, Müller U. Industrial applications of metal–organic frameworks. Chem Soc Rev. 2009;38:1284-93.

[112] Hartmann M, Böhme U, Hovestadt M, Paula C. Adsorptive Separation of Olefin/Paraffin Mixtures with ZIF-4. Langmuir. 2015;31:12382-9.

[113] Bennett TD, Saines PJ, Keen DA, Tan JC, Cheetham AK. Ball-milling-induced amorphization of zeolitic imidazolate frameworks (ZIFs) for the irreversible trapping of iodine. Chem - A Eur J. 2013;19:7049-55.

[114] Kitagawa S, Kitaura R, Noro SI. Functional porous coordination polymers. Angew Chemie - Int Ed. 2004;43:2334-75.

[115] Biradha K, Goswami A, Moi R. Coordination polymers as heterogeneous catalysts in hydrogen evolution and oxygen evolution reactions. Chem Commun. 2020;56:10824-42.

[116] Li H, Eddaoudi M, O'Keeffe M., Yaghi OM. Design and synthesis of an exceptionally stable and highly. Nature. 1999;402:276-9.

[117] Widmer RN, Lampronti GI, Chibani S, Wilson CW, Anzellini S, Farsang S, et al. Rich Polymorphism of a Metal-Organic Framework in Pressure-Temperature Space. J Am Chem Soc. 2019;141:9330-7.

[118] Tu M, Kravchenko DE, Xia B, Rubio-Giménez V, Wauteraerts N, Verbeke R, et al. Template-mediated control over polymorphism in the vapor-assisted formation of zeolitic imidazolate framework powders and films. Angew Chemie Int Ed. 2021;60:1-7.

[119] Erk, Peter; Hengelsberg H. Applications of Phthalocyanines. In: The Porphyrin Handbook. Kadish KM, Smith KM, Guilard R, editors. San Diego, California, USA: Academic Press; 2003. p. 118-22.

[120] Caradoc-Daviesa PL, Hanto LR, Henderson W. Coordination polymers and isomerism; a study using silver(I) and a π-stacked ligand. J Chem Soc Dalt Trans. 2001;2749-55.