Miquel Àngel Cuevas-Diarte
Harry A. J. Oonk *Editors*

Molecular Mixed Crystals

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Molecular Mixed Crystals

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Part I
Introductory Part

Chapter 1
Introduction

M. À. Cuevas-Diarte and H. A. J. Oonk

Abstract This chapter is an introduction to the book Molecular Mixed Crystals – a monograph on mixed crystals, and on a limited extent on stoichiometric compounds, formed between molecular substances. The emphasis is on the structural and thermophysical properties of binary systems. Summaries of the chapters are presented, and a view is given of the REALM – the network in which the authors of the chapters have joined their forces.

1.1 Scientific Setting

This book, in the first place, is a monograph on *molecular alloys—mixed crystals* of the substitutional type between two or more molecular substances. In addition, and to a limited extent, attention is given to *molecular compounds—stoichiometric complexes* (Chaps. 10 and 11).

The emphasis is on binary systems and their structural and thermophysical properties as a function of composition, temperature, and pressure.

Within this context, the book is a treasury of information: crystal structures; polymorphic changes; heat effects of melting and transition; thermodynamic mixing properties; phase diagrams; empirical relationships; and the like.

Apart from its scientific significance, the book is a reflection of almost half a century of concerted research, carried out by the *REALM*: *Réseau Européen sur les Alliages Moléculaires (European Network on Molecular Alloys)*; see below.

Right from its start, the philosophy of the *REALM* has been to study *families of systems* rather than a number of isolated ones. Such a family consists of systems of which the composing pure components are from a chemically coherent group. For instance, one can think of the family of the *n*-alkanes.

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The study of families of systems has been enormously fruitful. Several empirical relationships have been established: between different thermodynamic mixing properties; and also between thermodynamic mixing properties and exo-thermodynamic parameters. In particular parameters that are related to the structural mismatch between the components of the binary systems.

The book is intended to become and to be a reference point for everyone interested in *mixed crystals* in general, and *molecular mixed crystals* in particular.

1.2   About the Chapters

Including this Introduction chapter, the book has 13 chapters. Chapters 2–13 fall into three sections: (A) Introductory Part (Chaps. 2–4); (B) Facts and Features (Chaps. 5–11); and (C) Applications (Chaps. 12 and 13). The following is a short characteristic of each of the chapters, to begin with Chap. 2.

(A)   Introductory Part

2.   *Molecular homeomorphism and crystalline isomorphism*
     Haget Y., Chanh N. B., Oonk H. A. J., Cuevas-Diarte M. À.

In order to form mixed crystals of the substitutional type between two substances A and B, the component molecules A and B must be similar in size and shape. The measure of similarity is expressed by the *coefficient of molecular homeomorphism.* In order to form a *continuous series* of mixed crystals, the component substances must be *isomorphous.* The chapter starts with an historical overview and ends with a precise statement of the conditions for isomorphism.

3.   *Thermodynamics*
     Oonk H. A. J., Calvet T. and Jacobs M. H. G.

Much of the research, detailed in the chapters ahead, has been carried out on *binary* systems under *isobaric* conditions. The investigations have revealed that the thermodynamic mixing properties of the mixed crystalline state comply with a relatively simple *thermodynamic model*—with three system-dependent parameters. In the text, the model is detailed, and a demonstration is given of its power, which, at the same time, is surprising and outstanding.

4.   *Polymorphism*
     Rietveld I. B., Céolin R. and Tamarit J. Ll.

Molecular substances, as a rule, manifest themselves in more than one crystalline form. And it may happen that two members of a given family, under given conditions of temperature and pressure, do not adopt the same form. Polymorphism, for that matter, is a fascinating and at the same time complicated phenomenon. For the treatment of the polymorphism of a given substance, it is a *sine qua non* to take into account the influences of temperature *and* pressure. The chapter starts with an historical overview.

(B)   Facts and Features

5.   *Aromatics*
       van der Linde P. R. and Oonk H. A. J.

This is the first of seven chapters in which the outcome is summarized of a large number of studies on a large number of (families of) systems.

A start is made with the *family* of the *para*-dihalobenzenes, including the key system *para*-dichlorobenzene + *para*-dibromobenzene. The family of the dihaloben-zenes is followed by the *group* of the 2-*R*-substituted naphthalenes, which falls apart into two *subfamilies*. The naphthalene group includes naphthalene itself ($R = $ H) and the substances with $R = $ F, Cl, Br, SH, CH$_3$, OH. In addition, a number of isolated systems are treated, one of them being *trans*-azobenzene + *trans*-stilbene. Especially, worth mentioning is the melting behavior of mixed crystalline samples prepared by *zone leveling*. And evidence is given of an *extra attractive effect* between substituted methyl and substituted halogen.

6.   *Chains*
       Mondieig D., Moreno-Calvo E. and Cuevas-Diarte M. À.

Starting from a simple aliphatic hydrocarbon chain, a study has been made of the effect on structural properties caused by the incorporation of an increasing number of *hydrogen bonds*. In reality, this comes down to investigations into the struc-tural characteristics—including polymorphism—and the phase behavior of binary mixtures in the following groups of substances: the *n*-alkanes; the 1-alkanols; the α,ω-alkanediols; the alkanoic acids; and the alkanedioic acids. The results that have been obtained clearly show that two 'parameters' have a crucial influence on the structural and thermodynamic properties. These are (i) the *parity* (odd vs. even) of the carbon chain; and (ii) the aim at realizing as many as possible *hydrogen bonds*.

7.   *Plastic crystals*
       Tamarit J. Ll., Barrio M., Pardo L. C. and Négrier P.

This chapter describes binary systems that involve components with at least one orientationally disordered (plastic-crystalline) phase. Ordered and disordered molec-ular alloys are described for two families that differ from one another as regards their molecular interactions (hydrogen bonds vs. van der Waals). In addition, special atten-tion is given to the relationship between stable and/or metastable polymorphs and the pressure–temperature phase diagram for pure components.

8.   *Liquid crystals*
       Salud J. and López D. O.

The tricritical and the reentrant nematic behaviors are two of the most relevant features of the Smectic A (SmA)-to-Nematic (N) phase transition in binary mixtures of liquid crystals. Both of these concepts are studied from a theoretical and an experi-mental point of view for some two-component systems whose members are calamitic liquid crystals belonging to the alkylcyanobiphenyl (nCB) or alkoxycyanobiphenyl

(nOCB) series, n being the number of the carbon atoms in the alkyl or alkoxy chain, respectively.

9.   *Enantiomers*
      Oonk H. A. J. and Rietveld I. B.

Only in exceptional cases, a pair of enantiomers do form a series of mixed crystals. The most well-known of the exceptions is the system *laevo*rotatory carvoxime + *dextro*rotatory carvoxime; its properties are discussed in some detail. Also, attention is given to recent work on the polymorphism of optically active drugs.

10.   *Complexes*
       Marbeuf A. and Mikaïlitchenko D.

In certain cases, two molecular substances A and B, having a high degree of *molecular homeomorphism*, give rise to the formation of a *complex* AB, rather than producing a series of *mixed crystals*. Complexes are formed when short-range Van der Waals forces are overruled by long-range coulomb forces or by hydrogen bonds. Two groups of binary systems have been studied: (i) the group of benzene and benzene derivatives, and (ii) the group of naphthalene and naphthalene derivatives.

11.   *Triacylglycerols*
       Bayés-Garcia L., Cuevas-Diarte M. À. and Calvet T.

Triacylglycerols (TAGs) are the main components of edible fats and oils. TAGs are widely employed in cosmetics and pharmaceutical formulations. TAGs exhibit a complex pattern of polymorphism. In this chapter, an account is given of their polymorphic crystallization and transformation behavior—and so from pure TAG components to more complex lipid systems. Special attention is given to the effects caused by the application of dynamic thermal treatment. These effects are the key to the design of end products that have the physical properties required for them.

(C)   Applications

12.   *Phase change materials*
       Cuevas-Diarte M. À. and Mondieig M.

Apart from a purely scientific interest in molecular mixed crystals, the REALM continuously has been interested in finding applications—especially in the field of *phase change materials* for thermal protection and storage of thermal energy. The central actors are the heat of melting of the material and the *thermal window*, which is the temperature range in which the change from solid to liquid takes place. Applications are possible in the range of temperature from −50 to +200 °C. The composition of the material is one of the parameters that can be used to tune the thermal window to the desired temperature.

13.   *Crystallization of molecular mixed crystals*
       Schaftenaar H. P. C., Matović M. and Los J. H.

The crystallization of mixed crystals from a liquid mixture of the components is a complex event. Mass-transport and heat-transport limitations prevent the crystallizing system from adopting through and through thermodynamic equilibrium: *equilibrium phase diagrams* are making place for *kinetic phase diagrams*. The theoretical background of non-equilibrium crystallization is the main subject of the chapter.

1.3 About the REALM

The member groups of the REALM are from the Université de Bordeaux (UBx), the Universitat de Barcelona (UB), the Universitat Autonoma de Barcelona (UAB), the Universitat Polytecnica de Catalunya (UPC), and Utrecht University (UU).

The origin of the REALM goes back to about 1973 as a cooperation of crystallographers from UBx, UB, and in 1981 from UAB. Starting from 1984, thermodynamic expertise was brought in by physical chemists from UU. From 1988, the network was extended by physicists from UPC interested in plastic crystals, and their colleagues studying liquid crystals.

Starting with the Université de Bordeaux, the following is an enumeration of names of the people, who have contributed to the research of mixed crystals, during their whole (scientific) career, or for a short period of time as a Ph.D. student.

Université de Bordeaux. Yvette Haget, Nguyen Ba Chanh, Louis Bonpunt, Jany Housty, Alain Marbeuf, Denise Mondieig, Philippe Négrier, Valérie Métivaud, François Michaud, Abdou Belaaraj, Didier Mikaïlitchenko, Fazil Rajabalee, Philippe Espeau, Laurence Robles, Gabin Gbabode.

Universitat de Barcelona. Miquel Àngel Cuevas-Diarte, Teresa Calvet, Mercedes Aguilar, Esperança Tauler, Manuel Labrador, Lourdes Ventolà, Màrius Ramírez, Evelyn Moreno, Xabier Novegil, Raquel Cordobilla, Raúl Benages, Laura Bayés, Mercé Font-Bardia.

Universitat Autonoma de Barcelona. Eugènia Estop, Xavier Alcobé, Angel Alvarez.

Universitat Politècnica de Catalunya. J. Muntasell; Josep Lluís Tamarit, David López, Maria del Barrio, Josep Salud, Luis Carlos Pardo. Guests from University Paris Descartes: René Céolin, Ivo Rietveld.

Utrecht University. Harry Oonk; Cees van Miltenburg, Kees de Kruif, Hans Kolkert, Harrie Govers, Aad van Genderen, Paul van Ekeren, Jan Huinink, Tjibbe Kuipers, Gerrit van den Berg, Koos Blok, Michel Jacobs, Ineke van Ginkel, Joke Bouwstra, Mark van Bommel, Wybe van der Kemp, Peter van der Linde, Margot Vlot, Hannah Gallis, Marija Matovič. Guests: Jan Los, Harald Schaftenaar, Günter Figurski.

1.4 Audience

The book addresses itself to an audience interested in mixed crystals in general, and molecular mixed crystals in particular—from a point of view of crystallography, thermodynamics and phase theory, and physical chemistry in general.

Dedication

We gratefully dedicate this book to Yvette Haget and Nguyen Ba Chanh, who are the founding scientists of our line of research–the research on molecular alloys that started in Bordeaux and then fanned out to Barcelona, Utrecht, and Paris. Their scientific skills and their amiability have inspired us and all of our colleagues mentioned above.

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Chapter 2
Molecular Homeomorphism and Crystalline Isomorphism

Y. Haget, N. B. Chanh, H. A. J. Oonk, and M. À. Cuevas-Diarte

Abstract In order to form mixed crystals of the substitutional type between two substances A and B, the component molecules A and B must be similar in size and shape. The measure of similarity is expressed by the coefficient of molecular homeomorphism. In order to form a continuous series of mixed crystals, the component substances must be isomorphous. The chapter starts with an historical overview and ends with a precise statement of the conditions for isomorphism.

2.1 Background and Controversy

Since ancient times, humanity has recognised the importance of composition in the physical and chemical properties of materials. As early as the third century BC, Archimedes used scientific methods to determine the composition of a sword and established a linear relationship between variations in specific weight and composition in the chrome-silver system. He was the first scientist to establish a correlation between a physical property and composition in a continuous series of solid solutions.

For a long time, discoveries were limited to other fields of science, and it was not until the end of the eighteenth and beginning of the nineteenth centuries that significant advances were made in the field of the composition of solid materials with the emergence, towards the end of the century, of the study of phase diagrams.

It was during this period that the most serious controversies arose. In 1800, Proust asserted that compounds could be characterised by the constant proportions of their

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elements, whilst in 1803, Berthollet claimed that these elements could be combined in any proportion [1].

The controversy ended in 1870 with the publication of the research carried out by an American physicist, Gibbs, on phase equilibrium, where it became apparent that the debate was simply a question of terminology. Proust was correct as regards stoichiometric compounds, whereas Berthollet was right as regards *mixed crystals*.

Great strides were also made in the field of the natural sciences. The seventeenth century witnessed the seminal syntheses of botanical information, the appearance of binomial nomenclature by genus and species, and the development of a new systematics.

It was during the eighteenth century that the first attempts to classify minerals were made, provoking one of the most serious debates in the study of solid materials, between mineralogists and chemists. For the former, the observation of crystalline forms was fundamental, whilst, for the latter, it was chemical analysis which determined the mineral species.

Regardless of these differences, a mineral species was defined as "an assemblage of substances with the same composition", although many cases were known to exist where the proportions of the constituent parts were variable within determined limits. Thus, in 1782, Bergman [2] produced a mineral classification scheme based on chemical characteristics. One year later, Romé de Lisle [3] reported the first findings on *isomorphism*, heralding the discovery of isomorphic mixtures with his demonstration that copper sulphate and ferrous sulphate can be mixed to produce crystallisation. His work laid the foundations of modern crystallography.

Later, in 1810, the renowned chemist Berzelius [4] produced a new, more methodical classification scheme; his stoichiometric laws were based on the number of saline constituents identified by chemical analysis. He observed that each salt possessed two groups of constituent oxides, one acid and the other basic, whilst the water of crystallisation was neutral. Based on these observations, he defined two important laws: the "rule of oxides" and the "law of unitary oxygen". With the first, he established that the oxygen of the acid component was equal to or a multiple of the basic component, whilst with the second, he stated that the oxygen of the constituent oxide was a unit, or that the oxygen of each of the other constituents was a multiple. He then used the defined proportions to determine the different species.

Many mineralogists, such as Pusch in 1815 [5] and Hausmann in 1911 [6], were opposed to this classification scheme, considering it anti-mineralogical since certain constituents might be essential chemically but not mineralogically, in other words, they did not produce sufficient differences in external characteristics to justify separation into different species. A purely stoichiometric approach frequently distinguished separate species which a mineralogist considered simply varieties of the same substance.

In contrast, for mineralogists such as Wérner in 1774 [7], the fundamental criterion was crystalline form. In 1801, Haüy [8], the leading figure in crystallography at the beginning of the nineteenth century, combined his knowledge of crystallography, physics and geometric calculations to arrive at the conclusion that crystallisation was the most reliable criterion for distinguishing between different species. A mineral

species consisted of a collection of substances whose constituent molecules were very similar and composed of the same elements in the same proportions. Haüy established the principle according to which two minerals of a different composition could not have the same form, unless one of them was what was called a borderline form (cube, octahedron, regular tetrahedron and rhombic dodecahedron).

Crystallographers maintained that substances whose forms derived from the same crystal system belonged to the same species, whilst chemists argued that a species was formed by substances with the same composition. It was Haüy who, due to his great prestige, ended the debate in 1809 when he asserted that all the substances identified by mineralogists as belonging to the same species frequently presented considerable variations in composition. These differences in composition were explained by the assumption of the existence of mixtures which had combined with the truly constituent parts.

Haüy established the fundamental basis of crystallography, and his opinions received widespread acceptance in the period. To add an interesting anecdote, following the French Revolution, his condition of priest was respected, and he was allowed to continue wearing his clerical clothing [9].

This concept of species entered into contradiction with the tradition represented by Berthollet, who asserted that in order to establish that a constituent molecule belonged to a species, and that the composition of the latter was constant, Haüy would be obliged to consider all the differences which analysis had shown to be present in minerals with the same form as a heterogeneous substance. In earlier studies, Vauquelin [10], in 1797, and Leblanc in 1801 [11] had observed considerable variations in the proportions of the constituents of salts, without finding a corresponding difference in their crystalline form.

In fact, concerned by the relationship between chemical composition and crystal structure, Haüy implicitly acknowledged the principle of the continuity of solid materials, but confused the constituent molecule with the chemical molecule. It would be necessary to wait for Delafosse and the concept of the unit cell before Haüy's tenets progressed further.

In 1818, Beudant [12] had observed that by mixing a small quantity of ferrous sulphate hydrate with zinc sulphate hydrate, he obtained crystals with the rhombohedron shape of ferrous sulphate hydrate. He conducted many experiments, mixing this sulphate with zinc and copper sulphate hydrate and studying the form the crystallisation took. He reached the conclusion that even in small quantities one component could have a great impact on the properties of the compound, and that ferrous sulphate could take many different forms depending on the type and proportions of salts with which it was mixed. In some cases, when two substances were mixed, one imprinted its crystalline form on the other, whereas in others, the results could only be explained in terms of a combination of the two compounds, giving rise to a particular kind of composition with crystals that presented the forms of both substances.

In a later study of 1858, Delafosse [13] referred to the law established by Beudant, based on his observations of the crystals of different carbonates and some other salts. According to this law, the angles of a mixed crystal would have an intermediate value

between the initial products and they would be proportional to the quantity of each of them.

According to Beudant, the form of the carbonates was explained by the presence of small quantities of calcium carbonate, undetected in chemical analyses. Using his reflective goniometer, in 1812, Wollaston [14] found small differences in the angles of these forms, which had not been acknowledged by Haüy for crystallographic reasons. These authors considered the substances identical. It was in this context, in 1819, that the first study by Mitscherlich [15] appeared on diverse sulphates—previously studied by Beudant—phosphates, arsenates and ferrous and calcium carbonates.

This great German scientist had first studied Oriental languages, turning later to medicine and combining his medical studies with the study of ancient Persian texts. Shortly afterwards, he became interested in chemistry, and in 1818, he began to work in the field of crystallography. He observed that the crystals of potassium phosphate and potassium arsenate were almost identical in form. At the same time, he demonstrated that the sulphates of different metals (Fe, Co, Mn, Cu, Zn, Ni and Mg) could crystallise with the same form when they had the same quantity of water of crystallisation. One year later, he met Berzelius and moved to his laboratory in Stockholm where he conducted the research which would lead him to his formulation of isomorphism, and his confrontation with Haüy. On his return to Germany, he continued his brilliant research career, eventually becoming a professor at the University of Berlin. In 1832, he extended the research he had carried out in Sweden, broadening it to include other compounds. He became member of the Berlin Academy of Science and directed his own laboratory.

He conducted innumerable studies in inorganic chemistry, ranging from synthesis of new acids to determining the vapour density of numerous substances. His achievements were no less notable in the field of organic chemistry: synthesis of benzene and derivatives of the same, determination of its chemical formula, etc. His formulations comprised the forerunners of Berzelius' theory of catalysis. He was the first to demonstrate the existence of the phenomenon that we know as dimorphism. He established that $NaH_2PO_4 \cdot H_2O$ and $NaH_2AsO_4 \cdot H_2O$ normally exist in two different forms, and furthermore, that phosphate could present in a form identical to that of arsenate. He also developed methods for analytical organic and inorganic chemistry. Lastly, he was interested in geology and mineralogy, particularly, in the synthesis of minerals based on the fusion of silicon with various metal oxides.

In his study of 1821 [16], by this time immersed in the chemistry of Berzelius, Mitscherlich examined the composition-form relationship of various phosphorous and arsenic acid salts. It was in this article that the term isomorphs appeared for the first time: "…An equal number of atoms combined in the same way produce the same crystalline forms, and these do not depend on the chemical nature of the atoms but on their number and form of combination". The chemical elements could be classified into groups, and he named those elements pertaining to the same group, isomorphs. The small differences in the angles of the crystals of isomorphic substances were due to their chemical affinity. He clearly and explicitly stated that the fundamental tenet of isomorphic substances was that they could crystallise in any proportion.

It should be noted that Mitscherlich used Berzelius' theory of stoichiometry to conduct his studies, that is, he based his work on the case of type $A_{1-x}B_xC$, ionic crystals, where an anion (C) accepted a metallic cation (A) or another cation (B) or a mixture of both.

Isomorphism was defined by three properties; *analogous form* or identical crystalline form, *analogous chemistry* and, lastly, the possibility of *syncrystallisation* occurring in any proportion.

These results contradicted the axiom established by Haüy, according to which a given substance was characterised by the angles of its crystals. Nevertheless, the law established by Mitscherlich was enormously helpful to Berzelius in determining the atomic weight of elements, and later, in clarifying the composition of many minerals where crystallography appeared to contradict chemical analysis (pyroxenes and amphiboles, for example).

The discovery of isomorphism showed that Haüy's proposal was too absolute and imprecise, but it did not demolish it totally, since in the examples which best fitted the definition of isomorphism, their chemical differences translated into differences in the value of the crystal angle. However, this was not appreciated at the time. Similarity of crystalline form refers to the external form of crystals, namely, their morphology. Nevertheless, the parametric relationship was determined during this period, and this enabled scientists to suggest hypotheses about the content of crystal unit cells. In 1980, Melhado [17] provides an extensive description of the events and controversies of this period.

Haüy always maintained his opposing stance, despite the fact that Mitscherlich always accorded him respect: on observing that Haüy's law did not hold true, for example, he remarked of the law that this was not general. During the debate which ensued, Mitscherlich had no direct contact with Haüy, as reflected by the fact that the debate was conducted entirely through letters between Haüy and Berzelius, with the latter always affirming his support for the work of Mitscherlich.

2.2 Isomorphism After Mitscherlich

After Mitscherlich, the idea of isomorphism rapidly began to lose its currency, being relegated to the position of a control criterion for determining atomic weights, and research in the fields of chemistry and mineralogy began to diverge.

Nevertheless, some scientists continued to show great enthusiasm for the subject of isomorphism: following the line of research initiated by Beudant's law, Kopp, in 1843 [18] demonstrated that isomorphic substances had an approximately equal molecular volume (relationship between molecular weight and specific weight), and that the true characteristic of the isomorphism of two compounds was the ability to form mixed crystals. Towards the end of the century, Retgers stated a generalisation concerning the proportionality of the physical properties of mixed crystals with respect to composition, and later, Vegard applied the generalisation to crystal parameters.

During the same period, another author, Laurent, in 1845 [19], stated that two substances from different systems could be isomorphs. In contrast, in 1848, Pasteur [20, 21] did not agree since this would not fulfil an essential condition of crystallisation, namely that maximum occupation of the space should occur, and that total syncrystallisation in this case could only arise if *dimorphism* was present. He would appear to have been the first to speak of *isodimorphism*: the phenomenon that each of two substances A and B can crystallise in two different forms, such that each of the forms of A is isomorphous with one of the forms of B.

A new concept was introduced by Delafosse in 1851 [22], plesiomorphism. For this author, isomorphism implied that the composition of substances could be reduced to a single formula. Similarity between crystalline forms was the consequence of a pre-existing similarity in molecular type. He distinguished two kinds of isomorphism, that of Mitscherlich, which preserved the crystallographic system, and that of Laurent, in which compounds belonged to different systems.

Faced with the wide variety of examples in which the three conditions defined by Mitscherlich were not fulfilled, each author gave priority to a different condition. For some, the essential characteristic was similarity in crystalline form, whilst for others this was merely a reflection of analogous chemistry, and the existence of mixed crystals was simply a consequence of the first two. Still others affirmed that it was this latter characteristic which truly demonstrated that two compounds were isomorphs.

Another name which stands out in the study of isomorphism is that of Groth, who in 1870 [23] studied the relationship between crystalline form and chemical composition in derivatives of benzene and naphthalene. His research led him to conclude that for some atoms and groups of atoms, substitution by hydrogen did not modify the shape of the structure except in one direction, and he named this phenomenon *morphotropism*. The conditions on which the appearance of morphotropism was dependent included: (1) the morphological properties of the substituting atom, (2) the chemical nature of the compound in which the substitution took place, (3) the crystal system and (4) the relative position of the atom or group of atoms.

Numerous studies were carried out during this period on the physical and chemical properties of mixed crystals. Of interest was the research conducted by Baumhauer in 1870 [24] concerning corrosion figures, in which he stated that in isomorphic substances, these figures would have the same position and form on the corresponding faces.

In 1811, Arago [25] discovered the polarisation of light, enabling him to use optics as a means of research. Special mention should be made of the optical study by Sénarmont in 1851 [26] of isomorphic compounds and their alloys. Bodländer, in 1860, [27] determined the proportionality between composition and rotatory power, forming a straight line when represented graphically; in 1880, Schuster [28] observed that the angle of extinction presented continuous variation according to composition. In 1886, Wyrouboff [29] carried out numerous optical studies of isomorphism, basing his research on the idea that, according to Mitscherlich, isomorphism was the property of certain substances with a similar chemical composition and geometric shape, according to which they would crystallise together in any proportion. He examined

the meaning of geometrical symmetry, and proposed a difference of angles of 2–3°. He rejected those cases where, although possessing a strong similarity in terms of chemical composition and crystal parameters, the substances belonged to different crystal systems. He established the law of variation in the optical axis angle of mixed biaxial crystals according to their chemical composition. Of particular note was his work on dimorphism in neutral thallium and ammonium racemates and tartrates, in which he found that although there were no common faces in their crystalline forms, they crystallised in all proportions. Today, we know that a single group can present various external forms.

The same year, in 1886, Mallard [30] was to reject this definition of isomorphism. He proposed the term *syncrystallisation* to refer to the property of crystallising together, and relegated isomorphism to an etymological definition of the word, that is, to the more or less close similarity between crystalline forms.

Towards the end of the nineteenth century, in 1889, an extraordinary and well-structured study by Retgers [31] appeared, in which he reported extensive research on isomorphism. After examining many cases, above all those which were unclear, he concluded that the true expression of the isomorphic character of two compounds was similarity of form and chemical composition, together with the property of producing an intimate mixture, demonstrated by the *continuity of all properties*, both chemical and physical (specific weight, elasticity coefficients, thermal and electrical constants, etc.). It was necessary to diversify research methods and focus on those properties which presented marked differences in pure salts. Chemical and crystalline similarities alone were extremely elastic characteristics, given that they were subject to gradation (for example, the substitution of one atom for others of lower valency, of equivalent elements, similarity in crystal face angles, position and development of faces, etc.). He employed variation in specific volume (the inverse of specific weight) according to composition expressed as a weighted fraction to determine the presence of isomorphism and isodimorphism. In the former case, this variation was a straight line, whilst in the latter, two straight, non-parallel lines were obtained. Discontinuity could be present in both cases, but whereas in the first, the two parts of the straight line would be a prolongation of each other, in the second this regularity did not appear. This representation enabled isomorphism to be distinguished from isodimorphism with relative ease. Isomorphism implied chemical and crystalline similarity, where two compounds could yield homogeneous mixed crystals. Substances which presented the first two properties but not the third he described as morphotropic, and those which only presented similarity in form, isogonic. Morphotropy described changes in form due to successive chemical substitutions. He suggested that the study of isomorphism should be based on mixed crystals rather than on comparison of pure products.

2.3 Thermodynamic Theory of Mixed Crystals: Solid Solutions

It was a period in which both an important qualitative leap and great progress was made: for the sake of brevity, only three important advances will be mentioned. Gibbs' theory of phase equilibrium [32] was widely accepted in the scientific community. In his research, he defined the concepts of phase, components and the conditions for thermodynamic stability of mixtures, and also established the basis for a classification of phase diagrams. These bases enabled Van der Waals, and later, in 1899, Roozeboom [33] to derive all possible phase diagrams in more depth.

Le Chatelier explained the possibility of determining phase diagrams using thermal techniques, measuring the fusion point of mixtures with a thermocouple.

In 1898, Van't Hoff [34] established that properties such as miscibility between two substances would depend on pressure and temperature conditions and could change according to these conditions. As regards isomorphic mixtures, he introduced the term *solid solutions*, widely used nowadays, and stated that isomorphism existed even in those cases in which two compounds did not mix in all proportions. Similar to the solubility of liquids, in solid state, the ability to mix depended on temperature, and it was possible that at a given temperature partial miscibility would become total in compounds with the same crystalline form. The term solid solution was explained through analogy with the theory of solutions developed by this same author; the solid constituent assimilated with the solvent in higher proportions, whilst in the solute it was present in a lower proportion.

A period commenced in which studies of mixed systems, and above all of metal alloys, multiplied, and the concept of *eutectic systems* emerged (from the Greek, eutektos, "easily melting").

At the beginning of the twentieth century, in 1905, Tammann [35] published a series of articles on metallic diagrams, in which he presented an exhaustive analysis of cooling curves, using these as the basis for constructing the diagrams.

In his book on crystallography published in 1909, Wallerant [36] dedicated various chapters to isomorphism. Using examples, he conducted a separate analysis of each of the three conditions necessary for compounds to be defined as isomorphs, concluding that the existence of two of these conditions did not inevitably imply that of the third, and stated that before converting a definition into law, more detailed study was required. This text constituted an exhaustive compilation of all that was known at the time, and also presented an analysis of the characteristics of compounds known as isomorphs: crystalline form, exfoliation, optical properties, crystallisation from saturated solutions, etc. In none of these cases evidence was found of a common behaviour.

As regards the property of syncrystallisation, he summarised the ideas on solutions proposed by Van't Hoff and described the methods for obtaining solid solutions and possible phase diagrams.

All the physical properties of mixed crystals analysed varied continuously with composition, and it was precisely this continuity which distinguished them from a

chemical combination. As for their structure, Van't Hoff did not agree with those authors who believed they were composed of alternate layers of pure compounds, nor those who, based on Bravais' theory, claimed that some of the molecules from one of the substance's unit cells were replaced by the molecules of the second, since according to this author, they would lose their symmetry. He saw the edifices of isomorphic mixtures as individual edifices, rather than more or less intimate mixtures of two edifices. The elementary particles of pure compounds would have the same number of similarly arranged molecules, and by substituting the elementary particles, it would be possible to pass from one crystalline edifice to another.

Wallerant thus defined the existence of a continuous series of mixed crystals between two isomorphic compounds in the strictest sense of the word. Where the elementary particles of two substances did not contain the same number of molecules, or these were arranged differently, two series of crystals would necessarily be produced; isomorphism was no more than a theoretical concept which provided an easy explanation for the relationship between two substances susceptible to being mixed in order to crystallise.

2.4 Isomorphism Following the Discovery of X-Ray Diffraction and the Atomic Structure of Crystals

In 1912, the discovery by Max Von Laue and his collaborators Friedich and Knipping of X-ray diffraction by crystals demonstrated that it was possible to determine the atomic order of solids, heralding a new phase in the development of a theory of mixed crystals. The application of X-ray diffraction to a microcrystalline powder discovered by Bragg and Debye was rapidly adopted to determine phase diagrams.

With this new technique, it became possible to discover the number of system phases and to determine both the crystal parameters of the same and their dependence on composition. However, despite the information it provides, this technique is not routinely used these days to determine phase diagrams, often yielding partial information of the same. Throughout this book, it will be observed how diffraction can constitute an indispensable technique for demonstrating the presence of a given phenomenon and complementing the information obtained with other analytical techniques.

With a simple structure, it was possible to determine the position of the atoms and calculate interatomic distances. Resolving structures held great interest for mineralogists since, as we have seen, they looked to the isomorphism of structures to provide an explanation for the numerous regularities observed in geochemistry. It was found that many minerals could be explained as solid solutions.

One of the first to apply X-ray diffraction to the study of mixed crystals was Vegard in 1917 [37]. As we saw earlier, some authors, such as Retgers, believed that these were simple mechanical mixtures formed by fine, homogeneous and alternating layers of the constituent compounds. However, the studies of Wulf in 1906 [38],

Grossner in 1907 [39] and Tutton in 1910 [40] demonstrated that the difference in molecular volume of the constituents played a fundamental role in the formation of mixed crystals, and that these were the consequence of a more intimate union of the components.

Vegard studied the diffraction spectra of solid solutions of KBr-KCl and KCl-NH_4Cl (all three of which are cubic) and compared them with those of their components. He demonstrated that these mixed crystals were homogeneous substances rather than being composed of different layers, since they each produced single reflections situated between the respective values of the constituents. He formed an empirical law from his experimental results: the *linear variation of the crystal parameters* of alloys according to composition. As we will see later, the most frequent case was continuous variation of these parameters, but presenting deviation in linearity. Today, we know that Vegard's general rule is, in fact, the exception.

In a chapter of his book "Leçons de Cristallographie" of 1926, Friedel [41] undertook an extensive analysis of the three properties given as an indispensable condition for the existence of isomorphism: *homeomorphism*, or the close similarity between crystalline forms, total or partial syncrystallisation and identical chemical composition, except for the replacement of certain elements. For a long time, it was believed that the first two characteristics implied the third, and that syncrystallisation was a sign of identical chemical composition. However, nowadays, we know that this is not the case; even when isomorphic series, in the strict sense of the word, exist (for example, silicates, carbonates and oxides), there are numerous examples where only two of the three conditions are fulfilled. Homeomorphism and syncrystallisation can occur without identical chemical composition (for example, the substitution of the $Si^{4+} Na^{1+}$ group by the $Al^{3+} Ca^{2+}$ group in the plagioclases); homeomorphism and identical formulas can occur without syncrystallisation (between RbCl and NaCl); syncrystallisation occurs without homeomorphism, interpreted as isodimorphism, or that the compounds share a common multiple unit cell; and homeomorphism can occur with or without syncrystallisation whilst showing chemical analogies between the compounds (for example, the notable homeomorphism between NO_3Na and CO_3Ca, in the form of calcite, which do not syncrystallise).

Homeomorphism is best defined by determining unit cells and crystal parameters. In the majority of cases, species which syncrystallise have a similar type of structure and are strictly homeomorphic; when they do not syncrystallise, it is due to a difference in molecular volume and, consequently, in parameters.

In a compound series, when the differences in volume and parameters increase, syncrystallisation ceases to be possible, although not abruptly so; rather, the two compounds syncrystallise only in determined proportions, giving rise to a gap similar to that which occurs in isodimorphism. It would appear that any difference in crystal parameters of below 10% is not prohibitive.

As regards the structure of solid solutions, Friedel was perhaps the first to speak of random substitution. He found that mixed crystals are statistically homogeneous, and X-ray diffraction gives an average of all the periods.

Subsequent development of these techniques facilitated the discovery of the *superstructure* phenomenon, which emerges when a disordered solid solution is cooled,

and the first theories describing the phenomenon began to be formulated. The appearance of high-temperature X-ray cameras led to the systematic study of metal alloy structures.

The introduction of computing, neutron diffraction, electronic microscopy, etc., and the diversity of materials and fields of study (metals, ceramics, polymers, biological complexes, etc.) have both increased and become more specialised. It is neither possible here to enumerate them all here, but rather to examine certain specific aspects in the history of science which are most directly related to the subject matter in question. The following paragraphs will focus on the field of organic compounds, and more precisely, on molecules with a low molecular weight.

2.5   Isomorphism in Organic Compounds

The first organic system, between oleic acid and margaric acid, was studied in 1823 by Chevreul [42]. Other systems (fatty acids, urea, etc.) were studied with the aim of establishing a relationship between their properties and their composition.

In the previous section, mention was made of the work conducted by Provostaye in 1841 [43], Laurent in 1841 [44] and Groth in 1870 [23], in the study of the modifications to benzene and naphthalene crystalline forms, among others, brought about by the substitution of an atom.

Particular mention should be made of those scientists who continued the line of research initiated by Retgers. In the nineteenth century, these directed their efforts to the study of isomorphism, determining binary diagrams among the para-dihalogen derivatives of benzene. The work of Bruni and Gorni of 1900 [45, 46], Küster in 1905 [47] and Nagornow in 1911 [48], among others who will be mentioned in later chapters, demonstrated that these derivatives, when disubstituted with chlorine or bromine, possessed the same symmetry and a similar parametric relationship.

Numerous phase diagrams were also obtained using thermal analysis methods in the field of organic chemistry at the beginning of the twentieth century. Examples would include the research of Efrenov of 1913 [49], Smits in 1923 [50] and Timmermans in 1936 [51].

At this time, organic molecules were considered atomic systems with a determined configuration. Attempts to establish a relationship between phase diagrams and molecular structures led to nothing until information about organic crystal structure was obtained by X-ray diffraction. In general, organic compounds present low symmetry; the crystal unit cells contain few molecules but many atoms in general positions. As a consequence, the structure can only be determined from single crystals, which in many cases are difficult to obtain, and by employing sophisticated methods to analyse the diffractograms.

2.6 Geometric Model of Molecular Compounds

Following the discovery of the structure of penicillin, great strides were made from 1940 onwards in the study of the structure of organic molecules.

A few years later, in 1957, Kitaigorodskii [52] laid the foundations of modern organic crystal chemistry. In brief, he established two empirical rules: molecules are arranged in a crystal in such a way as to occupy the *minimum space* whilst presenting *maximum symmetry*. In this dense packing model, the form and size of molecules are described by geometric criteria (bond length, bond angles and intermolecular distances, determined using known structures).

This packing is characterised by the molecular coordination number; in many crystalline substances, this is twelve. It should also be stressed that all organic crystals are composed of successive layers, each of which is characterised by the partial coordination number of six. Where the intermolecular distances and the bond angles are known, molecular volume (V_o) can be determined; with this, the crystal unit cell volume (V) and its content (Z), it is possible to determine the *packing coefficient* (K) of organic structures.

$$K = Z \cdot V_o / V \tag{2.1}$$

Kitaigorodskii observed that this coefficient K varies between 0.6 and 0.8.

2.7 Coefficients of Molecular Homeomorphism and Crystalline Isomorphism

According to Kitaigorodskii [53], one condition necessary to form a true solid solution, that is, for one molecule to substitute another is the possibility of forming a large number of contacts between these molecules. In other words, a high packing index is required: the replacement of one molecule for another should not alter the intermolecular distances by more than 0.4 or 0.5 Å.

In contrast to what occurs in inorganic chemistry—where a *spherical* atom/ion is substituted by another—the isomorphism between organic molecules is only approximate. For that reason, we prefer to use the term *molecular homeomorphism* rather than molecular isomorphism. In Kitaigorodskii's view, there are three types of *molecular homeomorphism*:

- *Homeomorphism by atomic substitution*: the molecules only differ from one another in the substitution of an atom. In many cases, isomorphic crystals are formed. An example would be the series of *para*disubstituted benzene derivatives.
- *Homeomorphism by radical substitution*: the molecules differ from one another in a radical of much smaller dimensions than the rest of the molecule. Here, it is difficult to know to what extent such homeomorphism will imply crystalline

isomorphism. Included within this group is the ß-substituted naphthalene series, where ß is equal to OH, NO_2, NH_2.

- *Homologous homeomorphism*: is found in those series whose members only differ in the length of one of their axes, for example, the aliphatic and paraffin series.

Kitaigorodskii [54] proposed a coefficient, ε_k, to quantify the *degree of molecular homeomorphism*. This coefficient—the *coefficient of molecular homeomorphism*—is defined by superimposing two molecules in such a way that the included, or common, volume Γ is maximised, and where the excluded volume is Δ.

The coefficient is given by the following expression, in which the subscript "k" is from Kitaigorodskii:

$$\varepsilon_k = 1 - \Delta / \Gamma \tag{2.2}$$

The closer the value of ε_k is to 1, the more similar the molecules are in form and size.

Kitaigorodskii attempted to relate geometric similarity with degree of miscibility, "we can assume that the volume ratio plays a decisive role in solid-state solubility" [52]. The numerous phase diagrams determined by Timmermans [51] demonstrate that there is no miscibility when $\varepsilon_k < 0.8$, whilst extensive miscibility indicates that $\varepsilon_k > 0.9$. Kraftchenko compared those molecular sections which are more or less flat and similar in form for various systems in which diphenyl sulphide intervenes with anthracene, phenanthrene, etc. He found that solubility was continuous when ε_k is >0.95.

In the case of the degree, the coefficient of molecular homeomorphism, a geometric comparison is made between two *molecules.*

In a similar way, one can make a geometric comparison between the *crystalline cells* of two isomorphous crystals and introduce the *coefficient of crystalline isomorphism* [55, 56]. The coefficient of crystalline isomorphism, ε_m, is defined as

$$\varepsilon_m = 1 - \Delta_m / \Gamma_m \tag{2.3}$$

2.8   Updating the Concept of Isomorphism

To conclude this chapter, we consider the three cases that are represented by the sections (*a*), (*b*) and (*c*) in Fig. 2.1 [57, 58]. The three sections pertain to binary systems, and each section consists of three parts: on top the isobaric solid–liquid phase diagram; in the middle, the representation of a certain property P (such as molar volume, or one of the unit cell parameters) as a function of composition and for a given temperature (T_1); and at the bottom, the isothermal section, for $T = T_1$, of the molar Gibbs energies of solid solutions as a function of composition.
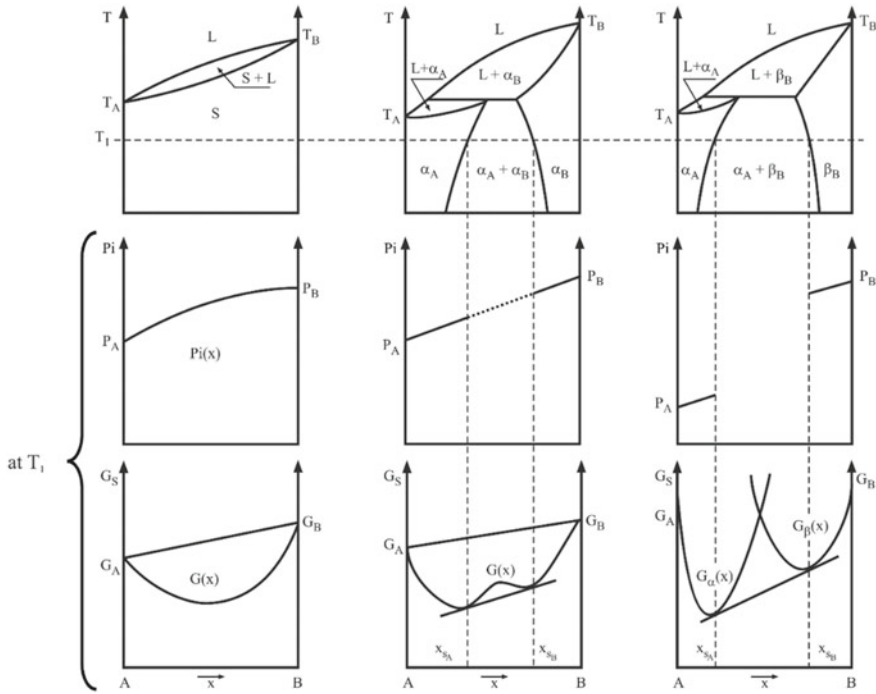
Fig. 2.1 Three cases of binary systems in which the molecules of the substances A and B can replace one another in the crystal lattice. Case (*a*): the solids A and B are isomorphous and form solid solutions in all proportions; case (*b*): the solids A and B are isomorphous but do not form solid solutions in all proportions; case (*c*); the solids A and B are not isomorphous, and, as a consequence, do not form solid solutions in all proportions

In all three cases, the molecules of the substances A and B have a degree of molecular homeomorphism elevated enough to replace one another in the crystal lattice.

2.8.1 Case (a)

Solid A and solid B are isomorphous, and together they form solid solutions in all proportions. In the middle part of Fig. 2.1a, it is shown that the value of a property *P* is represented by a continuous, smooth curve between the values of *P* of the pure solids A and B.

The other way round, the notion that the values of *P* be represented by a continuous curve is a condition *sine qua non* for isomorphism [58].