

Review

Isosymmetric Phase Transitions in Crystals: From Subtle Rearrangements to Functional Properties

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Abstract

Isosymmetric phase transitions (IPTs) represent a rare class of solid-state transformations in which substantial structural reorganization occurs without a change in crystallographic symmetry. These phenomena, though subtle, can have a profound impact on the physical and functional properties of materials, offering novel opportunities for property tuning without chemical modification. This review provides a comprehensive overview of the experimental and computational methods used to detect and characterize IPTs, including single-crystal and powder X-ray diffraction, Raman and FT-IR spectroscopy, differential scanning calorimetry, and advanced simulation techniques such as density functional theory, molecular dynamics, and crystal structure prediction. Special emphasis is placed on correlating local structural rearrangements—such as hydrogen-bond reconfiguration, polyhedral tilting, and molecular fragment reorientation—with macroscopic thermodynamic signatures. A broad selection of examples from the literature is discussed, covering molecular crystals, coordination compounds, organic functional materials, simple salts, and inorganic oxides, with detailed tables summarizing pressure- and temperature-induced IPTs. The review also analyses the primary factors that trigger IPTs, particularly temperature and pressure, and examines their role in governing structural stability and transformation pathways. By combining structural, spectroscopic, and thermodynamic perspectives, this work aims to consolidate the understanding of IPT mechanisms and to highlight their significance for the design of responsive crystalline materials.

Keywords: isosymmetric phase transition; solid-state transformation; high-pressure crystallography; temperature-induced transition; hydrogen bonding; X-ray diffraction; Raman spectroscopy; density functional theory; molecular dynamics; crystal structure prediction



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1. Introduction

Solid state phase transitions affect the structural behavior of materials, influencing their physical, chemical, and functional properties. Of note within this category of phenomena are isosymmetric phase transitions (IPTs) that have attracted increasing attention recently. Unlike the other types of polymorphic transformations, IPTs involve reconfiguration of the crystal lattice without changing its overall symmetry. For example, in the pharmaceutical field, where polymorphism and solid-state transformations impact drug efficacy and manufacturability, understanding isosymmetric transitions is particularly

significant. Emerging studies suggest that IPTs could provide innovative pathways for tuning the solubility, mechanical properties, and bioavailability of medicinal compounds without the need for demanding chemical modifications.

The aim of this review is to present the current knowledge on the isosymmetric phase transition and methods employed for the analysis and understanding of this phenomenon. First part of this article briefly describes the physicochemical methods used to analyze the IPT. In the second part chosen examples are presented in more detailed way, supported by a table concluding the reported cases. Finally, the typical conditions at which the IPT occur and factors that trigger such transformations are analyzed.

This review is intended as a broad overview of isosymmetric phase transitions across various classes of materials. The primary focus is on the experimental and computational methods applied to their investigation, and on the external factors that trigger such transitions. The selected case studies serve to illustrate these approaches and phenomena rather than to provide exhaustive analyses of each individual system. Readers seeking complete crystallographic and thermodynamic datasets are referred to the original publications cited throughout the text.

2. Isosymmetric Phase Transition

An isosymmetric phase transition (IPT) is an uncommon and fascinating class of structural transitions in crystalline materials. In this review, we adopt a broad definition of IPTs as transformations that preserve the crystallographic space group, regardless of the magnitude of structural rearrangement. In this context, IPTs may involve very subtle changes—such as minor molecular rotations, conformational shifts, or small hydrogen-bond adjustments—as well as the extensive reorganization of molecular packing, as in the α/β -resorcinol system [1]. The latter demonstrates that space-group retention can accompany substantial changes in intermolecular arrangements, which remain mechanistically and thermodynamically distinct from symmetry-breaking phase transitions.

The key characteristic of an IPT is therefore not the scale of structural change, but the invariance of the space group. Structural similarity can vary greatly and should be assessed using molecule-by-molecule overlays, the analysis of the topology of interaction networks, and thermodynamic signatures. This broad definition allows the inclusion of both “strict” IPTs, where changes are minimal, and “extensive” IPTs, where reorganization is large but still occurs without symmetry reduction [2]. The traditional methods of symmetry analysis and group–subgroup relations fail to detect these transitions, where they constitute a subtle yet significant anomaly in solid-state physics and crystallography. Because no symmetry breaking occurs, classical Landau theory cannot fully describe their thermodynamic nature. In this review, we distinguish strict IPTs (space group and Wyckoff scheme unchanged) from pseudo-isosymmetric transitions, where minimal symmetry lowering (e.g., Z' change under a pseudosymmetric relationship) accompanies a first-order rearrangement that preserves the topology of interactions and yields close structural overlays, and we focus solely on this first group.

The key characteristic of an IPT is a rearrangement of its internal degrees of freedom. These may emerge as rotations and tilts of coordination polyhedra, cooperative distortions of hydrogen-bonding frameworks, or reorientations of molecular fragments within the crystal structure. As an example, neutron diffraction and Raman spectroscopy studies of biurea demonstrated a pressure-induced IPT, marked by a rapid decrease in unit cell volume and reconfiguration of intermolecular interactions at around 0.6 GPa [3]. Similarly, in ammonium bicarbonate, in situ synchrotron X-ray diffraction revealed that biaxial compression of a “double-wine-rack” hydrogen-bond network may trigger an IPT with highly anisotropic elastic responses [4].

In addition to molecular systems, IPTs have been observed in inorganic structures, such as rare-earth orthoferrites (RFeO_3). The driving mechanism here is the competition between oxygen coordination shells surrounding the rare-earth cation and the softening of particular phonon modes. Experimental data showed changes in lattice parameters and octahedral distortions without any alteration in space group symmetry, hence offering definitive evidence of an IPT [5]. Covalent organic frameworks have demonstrated the ability to undergo IPT under pressure, demonstrating remarkable phenomena such as negative linear compressibility and breathing effects, which present promising opportunities for adjustable and adaptable functional materials [6].

Overall, IPTs are a unique and under explored class of phase transitions that present a challenge for conventional classification schemes. By maintaining macroscopic symmetry while allowing hidden microscopic reorganizations, they uncover new dimensions of structure–property interactions in materials. Their occurrence in several material classes, from basic molecule crystals to complex oxides and frameworks, underscores their universality and promise for technological applications, including responsive materials, sensors, and pressure-adaptive systems. Concurrently, their complex nature makes them challenging to detect experimentally and to predict computationally, emphasizing the necessity of ongoing methodological innovation in computational modeling, spectroscopy, and crystallography. It should be noted that the retention of the same space group is a necessary but not sufficient condition for classifying a transformation as strictly isosymmetric. Structural similarity must be assessed using molecule-by-molecule overlays, analysis of the topology of interaction networks, and thermodynamic signatures. For example, in the α/β -resorcinol system, both phases crystallize in the same space group ($\text{Pna}2_1$), yet their molecular packing differs substantially, making them structurally distinct despite apparent symmetry retention [1].

3. Methods Used to Analyze IPTs

The study of IPTs involves an experimental and theoretical challenge, as these transitions include significant structural reorganizations without a change in crystallographic symmetry. Therefore, conventional symmetry-based methods are insufficient, and exploration into combinations of complementary techniques that can capture both local and long-range effects is required. Diffraction techniques, particularly X-ray diffraction (XRD), are pivotal among experimental approaches, as they provide direct structural information and facilitate the confirmation of space-group invariance. Spectroscopic methods, such as Raman and Fourier-Transform Infrared (FT-IR), are similarly significant as they reveal vibrational abnormalities and local reorganizations. Thermal techniques like differential scanning calorimetry (DSC) provide thermodynamic evidence of first-order behavior, hence supporting the classification of these transitions.

Computational methods like molecular dynamics (MD) and density functional theory (DFT) are crucial for simulating IPT mechanisms and investigating the delicate energetic balance among competing phases. Crystal structure prediction (CSP) enhances these capabilities by mapping potential isosymmetric polymorphs and predicting changes under diverse thermodynamic conditions. Collectively, experimental and theoretical methodologies establish an effective framework that enables the accurate identification, characterization, and mechanistic comprehension of IPTs.

3.1. X-Ray Diffraction

XRD is a fundamental method utilized to examine crystalline structures and has long been recognized as the main method for analyzing structural phase transitions. Its role is particularly important in IPTs as these transitions are defined by subtle structural

reorganizations within the same crystallographic framework [7]. XRD techniques provide an accurate measurement of unit-cell dimensions, bond lengths, coordination environments, and atomic positions, making them essential for confirming that an observed transition is genuinely isosymmetric.

Differentiating between transformations that are truly isosymmetric and those that involve undetected or very subtle symmetry changes is one of the primary challenges in IPT research. This is particularly relevant for first-order transitions, where sudden discontinuities in structural parameters are to be expected [8]. Under variable temperature or pressure, XRD presents direct evidence of such discontinuities in lattice constants or unit-cell volumes, additionally at the same time confirming the lack of change in space group symmetry. By combining XRD with other techniques such as Raman spectroscopy or calorimetry, researchers may support their classification of a transition as an IPT [2]. Two main XRD-based methods are utilized in IPT studies: powder X-ray diffraction (PXRD), which is particularly effective for high-pressure and high-temperature analysis, and single-crystal X-ray diffraction (SCXRD), which is considered the standard for atomic-scale structural resolution.

3.1.1. Powder X-Ray Diffraction

PXRD enables the observation of changes in unit-cell dimensions and diffraction peak positions when external stimuli are applied. Despite the fact that PXRD does not offer the same level of atomic precision as single-crystal methods, it is highly effective in identifying discontinuous variations in lattice constants and unit-cell volumes. An excellent example of applying PXRD in IPT research is the analysis of orthopyroxene ($\text{Mg}_2\text{Si}_2\text{O}_6$), a silicate mineral significant in geology, where high-temperature synchrotron powder X-ray diffraction (HTXRD) showed a discontinuous change in unit-cell parameters at around 1230 K. The transition was classified as an IPT, driven by bond-switching mechanisms between Mg atoms and coordinated O atoms, and confirmed by MD simulations [9]. As another example, studies of sulfamic acid under pressure using synchrotron PXRD revealed sudden distortions in lattice parameters between 10.2 and 12.7 GPa, which is consistent with pressure-induced IPT involving hydrogen-bonding motif rearrangements [10].

PXRD is especially suitable for diamond anvil cell studies, capable of achieving pressures above tens of gigapascals. In such settings, PXRD facilitates the identification of compressibility anomalies, negative linear compressibility, and abrupt volume collapses, which are structural characteristics often linked to IPTs [5,11]. Therefore, whereas PXRD is incapable of directly detecting minor atomic displacements or molecular reorientations, its usefulness lies in recognizing macroscopic lattice anomalies and mapping phase boundaries.

3.1.2. Single Crystal X-Ray Diffraction

SCXRD is the most conclusive technique for identifying IPTs, as it provides knowledge of the arrangement of atoms within the unit cell. In contrast to PXRD, which offers averaged structural data, SCXRD can identify minor anisotropic displacements, molecular reorientations, hydrogen-bond rearrangements, or octahedral tilts. As a strictly isosymmetric, SCXRD-resolved example, L-histidine exhibits reversible pressure-induced IPTs wherein the space group is retained while discontinuous changes in unit-cell metrics and hydrogen-bond geometry occur; SCXRD, PXRD, and Raman jointly confirm the first-order nature without symmetry breaking [12]. This level of precision could not have been achieved only with powder techniques, highlighting the essential role of SCXRD in identifying IPT.

SCXRD is especially significant in high-pressure crystallography, since its capacity to identify anisotropic lattice distortions and coordination-shell rearrangements provide conclusive evidence for IPTs. In studies of rare-earth orthoferrites, SCXRD showed dis-

tortions in octahedral environments and abnormalities in lattice parameters indicative of an IPT mechanism driven by coordination–shell interactions [5]. By detecting minor yet abrupt changes, SCXRD offered the most accurate evidence that a structural transition occurred without symmetry breakdown. The primary limitations of SCXRD are its quality requirements for a sample, which needs to be well-formed single crystals and presenting technical difficulties under extreme pressures or temperatures.

In summary, SCXRD is the most important method for IPT study. Its unmatched atomic-level resolution enables researchers to definitively confirm that a structural transition, despite severe distortions and reconfigurations, maintains the overall crystallographic symmetry. When integrated with other methods, SCXRD establishes the conclusive structural basis for investigating IPTs.

3.2. Spectroscopic Methods

3.2.1. Raman Spectroscopy

Raman spectroscopy is a widely used spectroscopic technique employed in the investigation of IPTs, due to its exceptional sensitivity to lattice vibrations, phonon anomalies, and local bonding configurations. As IPTs maintain global crystallographic symmetry, conventional diffraction methods may not always disclose the full extent of structural reorganization. However, Raman spectroscopy can identify discontinuities in vibrational frequencies, mode splitting, and intensity alterations that indicate local atomic or molecular rearrangements, including molecular fragment reorientations, hydrogen-bond reorganizations, or polyhedral tilting.

A notable example is the pressure-induced IPT in sulfamic acid, where integrated Raman and synchrotron XRD analyses demonstrated a structural transition occurring between 10.2 and 12.7 GPa and Raman spectra exhibited abrupt alterations in NH_3^+ and SO_3^- vibrational modes, indicative of hydrogen bond reorganization [10]. Similarly, Raman spectroscopy detected phonon anomalies at 327 K and 347 K in $[(\text{C}_3\text{H}_7)_4\text{N}]_2\text{Zn}_2\text{Cl}_6$, which corresponded to two reversible IPTs involving the order–disorder processes of the organic cations. These anomalies were subsequently confirmed by calorimetry [13]. Raman spectroscopy used in analysis of fluorene up to 9 GPa revealed a reversible IPT involving molecular stacking rearrangement, with changes in intermolecular mode frequencies reflecting structural stiffening [14]. Raman spectroscopy is also valuable for its capability to detect IPTs across various temperature ranges. In $(\text{NH}_4)_3\text{GeF}_7$, variable-temperature Raman studies revealed symmetry-preserving structural reorganizations linked to ammonium ion ordering, exhibiting significant alterations in lattice vibrational modes, while GeF_6^{2-} groups remained mostly unaffected [15].

In summary, Raman spectroscopy is important for IPT research due to its ability to directly detect vibrational discontinuities and investigate local lattice dynamics. While it cannot independently verify symmetry invariance, Raman spectroscopy, when combined with XRD and calorimetry, offers essential spectroscopic evidence of the first-order nature of IPTs (Figure 1).

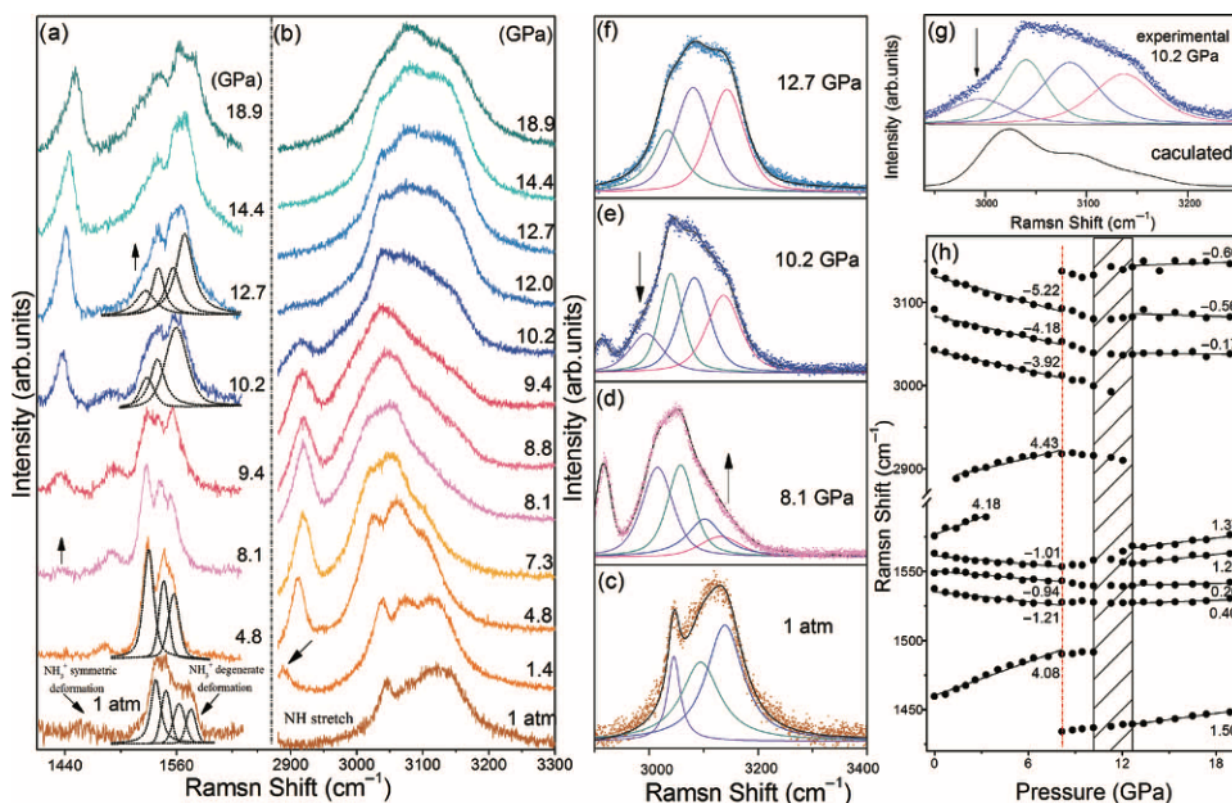


Figure 1. Representative high-pressure Raman spectra of NH_3^+ -related modes in sulfamic acid: (a) deformation of NH_3^+ , (b) N–H stretching, (c–f) decompositions of the N–H stretching region for clarity, (g) comparison of calculated and experimental N–H stretching modes, and (h) pressure dependence of peak positions for these NH_3^+ related modes. The vertical dotted line marks the beginning of changes in Raman spectra. The shadow represents the phase-transition region. Linear fits are conducted for clarity, and the neighboring numbers represent the slopes of the respective modes. The unit is $\text{cm}^{-1}/\text{GPa}$. Reprinted from [10] with the permission of AIP Publishing.

3.2.2. Fourier-Transform Infrared Spectroscopy

FT-IR spectroscopy [16], a commonly used vibrational technique, which provides comprehensive data on the local bonding environment in crystalline materials and facilitates the investigation of IPTs. In contrast to Raman spectroscopy, which is more sensitive to lattice and low-frequency modes, FT-IR primarily describes intramolecular vibrations, including the stretching and bending of polar functional groups. This method is sensitive to discontinuous shifts in absorption bands associated with O–H, N–H, or C=O stretching, which are IPT's fingerprints in hydrogen-bonded molecular crystals. For instance, the abrupt changes in the vibrational signature of hydrogen bonds can be used to directly trace order–disorder processes in ammonium-based salts or organic–inorganic hybrids, even in the absence of diffraction–detectable symmetry lowering.

The applicability of FT-IR to IPT research is demonstrated by several case studies. A conformational IPT was identified in oleic acid through the use of combined FT-IR and XRD investigations, which highlighted discontinuous changes in the arrangement of the olefinic chain. The transition was characterized by a splitting and intensity change in the C–H and C=C stretching bands, indicating molecular reorientation [17]. In another case, variable temperature FT-IR spectroscopy of $(\text{NH}_4)_3\text{GeF}_7$ revealed abrupt shifts in N–H stretching frequencies that were associated with ammonium ion reordering consistent with an IPT [15]. Although FT-IR alone cannot confirm that a transition is isosymmetric, its sensitivity to molecular vibrations makes it essential in multi-method studies.

3.3. Differential Scanning Calorimetry

DSC is a commonly used thermal analysis method that measures the heat flow resulting from structural changes as a function of temperature or time. In the analysis of IPTs, DSC is of importance since it offers thermodynamic confirmation of structural reconfigurations that transpire without alterations in crystallographic symmetry. Because many IPTs are first-order in nature, they are usually accompanied by sudden enthalpic changes, which appear as sharp endothermic or exothermic peaks in DSC traces, despite the lack of symmetry-breaking signs in diffraction data [18].

DSC has demonstrated significant value when utilized combined with diffraction and spectroscopic techniques. In the organic–inorganic hybrid crystal $[(C_3H_7)_4N]_2Zn_2Cl_6$, DSC identified significant calorimetric anomalies at 327 K and 347 K, indicating two reversible IPTs associated with the order–disorder dynamics of organic moieties. The transitions were concurrently identified by Raman spectroscopy, underscoring the efficacy of DSC as a supplementary method for investigating latent heat effects [13]. Similarly, calorimetric results from hydrogen-bonded molecular systems such as biurea supported pressure-induced IPTs, with sudden heat flow anomalies corresponding to intramolecular hydrogen bond reorganization [3].

In summary, DSC offers the thermodynamic validation of IPTs by identifying enthalpy changes associated with structural reorganizations that are undetectable through symmetry analysis. Although it cannot independently confirm the isosymmetric nature of a transition, when integrated with diffraction and spectroscopy methods, it provides conclusive evidence for the first-order nature of IPTs and continues to be an important tool in their analysis.

3.4. Computational Methods

3.4.1. Density Functional Theory

DFT has become known as a fundamental theoretical method in the analysis of IPTs, enabling the accurate assessment of the relative stability of competing structures with the same symmetry. Due to the absence of symmetry breaking, the experimental detection of IPTs is often difficult, and DFT offers essential assistance by modeling energetic landscapes, structural aberrations, and electronic contributions to stability.

DFT calculations in molecular crystals have recreated pressure-induced IPTs, such as the chlorothiazide transition, in which simulations demonstrated that entropic and pressure effects stabilize one polymorph over another [2]. As another example study on Na_3MnF_6 showed that orbital reorientation and pressure-induced Jahn–Teller distortions can stabilize alternate monoclinic forms, which explains the microscopic origin of the IPT [19].

In addition to static optimization, DFT, combined with phonon computations or ab initio molecular dynamics (aiMD) [20], has been utilized for strongly correlated systems like cerium and contributed to capturing the electronic balance that drives the α – γ transition [21]. These examples show that DFT not only confirms empirically observed IPTs but also offers a mechanistic understanding of their driving mechanisms, ranging from hydrogen-bond reorganizations to orbital reconstructions.

3.4.2. Molecular Dynamics Simulations

MD simulations have become recognized as a significant computational method for IPTs, enabling direct observation of atomic-scale dynamics in response to external stimuli like temperature and pressure. In contrast to static methods like geometry optimization, MD explicitly incorporates thermal vibrations, entropy, and transient bond rearrangements, proving it particularly effective at identifying the dynamic pathways of IPTs. This is especially significant as IPTs often entail subtle local reorganizations, such as bond

shifting or molecule reorientation, which cannot be effectively described by diffraction techniques alone.

An excellent example is the study of orthoenstatite ($\text{Mg}_2\text{Si}_2\text{O}_6$), where MD simulations replicated a first-order IPT at about 1230 K. The transition displayed abrupt changes in unit-cell parameters and Mg–O coordination shifts, which was consistent with synchrotron PXRD analysis [9]. Further studies confirmed similar high-temperature IPTs in orthopyroxenes by extended MD protocols, demonstrating the maintenance of structural stability across extensive compositional ranges [8]. In molecular systems, calcite (CaCO_3) has functioned as a model for MD analysis of order–disorder IPTs, where simulations demonstrated significant rotations and flipping of carbonate groups under temperature and pressure, resulting in discontinuous structural reorganizations [22].

MD may be combined with electronic structure calculations to enhance predictive precision. For instance, aiMD employed on chlorothiazide effectively replicated its pressure-induced IPT, demonstrating that real-time simulations can capture structural rearrangements not anticipated by static DFT alone [2]. These integrated methods show the versatility of MD as a method for both verifying experimental findings and revealing hidden structural pathways that may be thermodynamically accessible yet challenging to observe under laboratory conditions.

In summary, MD simulations offer essential insights into the mechanisms of IPTs by describing entropic contributions, transient atomic movements, and the dynamics of structural reorganization. Although they cannot substitute for diffraction or spectroscopy in confirming symmetry invariance, they are essential for developing a mechanistic comprehension of how IPTs occur at the atomic level.

3.4.3. Crystal Structure Prediction

CSP methods have gained recognition in the study of IPTs, as they facilitate the systematic identification of alternative structures that maintain the same space-group symmetry while differing in atomic arrangements or molecular conformations. In contrast to experimental methods, which are restricted to laboratory-accessible settings [23], CSP can reveal metastable or hidden polymorphs that could form under pressure, temperature, or entropic stabilization. This is especially significant in IPT research, where diffraction methods alone may fail to show the complete polymorphic landscape. CSP generally combines global search algorithms, including evolutionary or random sampling techniques, along with energetic ranking derived from force-field methods or quantum-mechanical calculations, so creating a strong predictive framework.

The applicability of CSP in IPT research is seen in numerous studies. A significant case is molecular oxygen at megabar pressures, where *ab initio* CSP revealed two energetically competing monoclinic phases with equal symmetry. The subtle change in stability among these polymorphs offers a microscopic explanation for the isosymmetric ϵ – ζ transition [24]. In intermetallic compounds like Zr_2Cu , CSP-guided DFT simulations predicted a pressure-induced IPT marked by a discontinuous alteration in axial ratio and volume collapse [25]. These examples demonstrate how CSP enables researchers to detect and explain IPTs across several material categories, including minerals, molecular solids, and metallic alloys.

Overall, CSP offers a predictive framework for the identification of potential IPTs and the comprehension of their underlying energetic competition. Although it is unable to independently confirm the occurrence of an IPT, CSP enables researchers to identify hidden polymorphic landscapes and predict structural reorganizations in an extensive range of crystalline systems when combined with experimental diffraction data and electronic-structure calculations. The addition of computational crystal engineering into IPT studies underscores its increasing significance in discovering new functional materials.

4. Factors Causing the Phenomenon of IPT

The phenomenon of IPTs is closely associated with the influence of external stimuli that disrupt the internal configuration of crystalline systems. Such stimuli generally function by shifting the balance of intermolecular interactions, adjusting coordination environments, or changing lattice dynamics, leading to structural rearrangements under the same space group conditions. Among the several potential triggers, temperature and pressure are the most fundamental and extensively studied. Both parameters directly impact the energetic stability of competing phases, temperature primarily through entropic contributions and dynamic disorder, and pressure by altering interatomic distances and the compressive forces applied on coordination shells. IPTs often appear as sudden, first-order transitions, resulting in discontinuous alterations in unit cell dimensions, polyhedral distortions, or molecular orientations. These discontinuities are often associated with abrupt changes in macroscopic physical properties, such as dielectric permittivity, compressibility, and elastic responsiveness, highlighting the importance of IPTs within the wider context of solid-state phase transitions [2]. Understanding the influence of temperature and pressure in triggering of IPTs offers significant insight into the microscopic mechanisms that determine structural stability, as well as a conceptual framework for predicting and manipulating these phenomena in functional materials.

4.1. Temperature

Temperature-induced IPTs are significantly affected by changes in vibrational amplitudes, entropy contributions, and the reorientation or ordering of molecular or ionic fragments. Often, the fundamental mechanism is associated with order–disorder phenomena, wherein specific structural components, such as anions or organic cations, reorganize or assume different orientations. Triethylbenzylammonium perchlorate is a well-documented example that exhibited a reversible IPT at approximately 196 K. The transition involved varying orientations of perchlorate anions and modifications in hydrogen-bonding interactions [26]. Similarly, cadmium–dabco coordination complexes underwent temperature-driven IPTs between 100 and 293 K, with torsional distortions of the organic moieties caused sudden changes in molecular conformation [27]. Furthermore, inorganic systems also exhibit temperature-induced IPTs; for instance, in orthopyroxene, HTXRD studies demonstrated a discontinuous alteration in cell parameters resulting from Mg–O coordination rearrangements [8]. These examples demonstrate that thermal energy can serve as a trigger for subtle reorientations and polyhedral adjustments that elude group-theoretical classification yet still induce sudden structural and physical transformations typical of IPTs.

4.2. Pressure

Pressure is another an important factor in the induction of IPTs, since it directly influences interatomic distances, polyhedra coordination, and hydrogen-bonding networks. Under compression, atoms are pushed into new configurations that often result in abrupt alterations in structural parameters. In molecular crystals, pressure-induced IPTs often arise from the reorientation of molecules or functional groups. For example, Biurea underwent a pressure-induced IPT at around 0.6 GPa, which was characterized by intramolecular reorientation and a sudden reduction in unit cell volume [3]. Hydrogen-bonded systems represent another significant class of pressure-sensitive IPTs. Ammonium bicarbonate, for instance, experienced an IPT under biaxial compression due to rearrangements within its “double-wine-rack” hydrogen-bonding structure, resulting in anisotropic compression and the establishment of new hydrogen bonds [4]. In inorganic oxides, pressure-induced IPTs are often associated with the tilting and distortion of octahedral units. This behavior was clearly shown by rare-earth orthoferrites (RFeO_3), which exhibited anomalies in

coordination–shell interactions and lattice parameters under pressure, revealing a hidden IPT [5]. These studies show that pressure-induced IPTs can significantly influence macroscopic mechanical properties, frequently resulting in uncommon events such as anisotropic elasticity or negative linear compressibility. Therefore, they have both fundamental crystallographic significance and potential for technological applications in adaptive and responsive materials.

5. Overview of Documented IPT Cases in Crystalline Materials

This literature review identified around 150 relevant articles on IPTs, based on a systematic search of the Scopus database performed on 3 April 2025. The chronological distribution of these studies indicates a distinct increase in interest over the last years, which is indicative of their escalating scientific significance and the progression of experimental and computational techniques facilitating their identification.

Tables 1 and 2 summarize selected studies on IPTs across various material classes. Significant emphasis has been placed on the experimental methodologies utilized to identify and characterize these transitions, with X-ray diffraction serving as a pivotal method. Although PXRD is extensively utilized, SCXRD is especially significant in IPT research. Its ability to precisely determine atomic positions, resolve anisotropic structural changes, and detect subtle distortions is essential for determining whether a given transition is truly isosymmetric. Consequently, SCXRD has been listed separately from other methods in the tables, as it offers a particularly significant role in the precise identification of IPTs.

Table 1. Summary of selected experimental studies on pressure-induced IPTs.

Name	Pressure Range	Transition Range	Space Group	System	SCXRD	Other Methods	Year	References
Resorcinol (1,3-Dihydroxybenzene)	ambient up to 14.5 GPa	0.5 GPa (α to β) and 5.6 GPa (to γ)	Pna21	Orthorhombic	N	Raman Spectroscopy, PL	2002	[1]
Sulfamic acid	ambient up to 20.1 GPa	10.2 GPa–12.7 GPa	Pbca	Orthorhombic	N	ADXRD, Raman Spectroscopy	2013	[10]
L-Histidine polymorphs	ambient up to 6.60 GPa (form I), ambient up to 6.85 GPa (form II)	4.5 GPa (form I), 3.1 GPa (form II)	P21 (form I), P212121 (form II)	Orthorhombic (form I), Monoclinic (form II)	Y	PXRD, Raman Spectroscopy	2020	[12]
N-isopropylpropionamide	ambient up to 10 GPa	4 GPa	P21/a	Monoclinic	Y	DTA	2015	[28]
Lead Fluoride	ambient up to 75 GPa	10–22 GPa	Pnma	Orthorhombic	N	ADXRD, DFT Calculations	2016	[29]
Lead Fluoride	ambient up to 28 GPa	10 GPa, 9.8–12.9 GPa	Pnam	Orthorhombic	N	ADXRD, Raman Spectroscopy	1998	[30]
Sodium Oxalate	ambient up to 8 GPa	3.8 GPa	P21/c	Monoclinic	N	HRXRD, Raman Spectroscopy	2003	[31]
Paracelsian	ambient up to 32 GPa	3–6 GPa	P21/c (I, II), Pna21 (III), Pn (IV)	Monoclinic (I, II, IV), Orthorhombic (III)	Y	DFT Calculations	2019	[32]
DL-Cysteine	ambient up to 7.90 GPa	0.1 GPa, 1.55 GPa and 6.20 GPa	P21/a	Monoclinic	N	HRXRD, Raman Spectroscopy	2010	[33]
Solid Ammonia	4 GPa–123 GPa	12 GPa	P212121 (for Phase IV and the phase above 12 GPa)	Orthorhombic	Y	Raman Spectroscopy, ND (for ND3)	2006	[34]
Rubrene (5,6,11,12-Tetraphenyl-tetracene)	ambient up to 7.2 GPa	7.1 GPa	P-1	Triclinic	Y	Hirshfeld Surface Analysis; PIXEL method for lattice and intermolecular interaction energy calculations	2014	[35]

Table 1. Cont.

Name	Pressure Range	Transition Range	Space Group	System	SCXRD	Other Methods	Year	References
Biurea	0.01 GPa–3.89 GPa	0.6 GPa–1.5 GPa	C2/c	Monoclinic	N	NPD, Raman Spectroscopy, DFT Calculations, Rietveld Refinement	2019	[3]
Potassium Titanyl Phosphate (KTP)	0.2 GPa–8.2 GPa	5.8 GPa	Pna21	Orthorhombic	Y	High-Raman Scattering	1996	[36]
Copper–Dicyanoaurate Complexes	ambient up to 3.6 GPa	1.2 GPa	P21/c	Monoclinic	Y	Raman Spectroscopy, IR Spectroscopy, UV-vis Absorption Spectroscopy	2022	[37]
Chlorothiazide	0 GPa–6.20 GPa	4.2 GPa	P21/c	Monoclinic	Y	DFT calculations, aiMD Simulations	2021	[2]
Hydroquinone–Formic Acid Clathrate	ambient up to 10.2 GPa	4.25 GPa	R-3	Trigonal	Y	Raman Spectroscopy, DSC, Energy Framework Calculations	2016	[38]
Ammonium Bicarbonate	ambient up to 3.4 GPa	2 GPa	Pccn	Orthorhombic	N	ADXRD, DFT calculations, Raman Spectroscopy	2023	[4]
α -Silver Sulfide	ambient up to 32 GPa	7.5 GPa and 15 GPa	P21/c	Monoclinic	N	DFT Calculations, XRD	2022	[39]
3D Covalent-Organic Framework (NPN-1)	0 GPa–5 GPa	0.14 GPa	P4b2	Tetragonal	N	DFT Calculations, aiMD	2023	[11]
Mixed-Valence Rare-Earth Fullerides	ambient up to 6 GPa	4 GPa	Pcab	Orthorhombic	N	SXRPD, PFY-XAS	2024	[40]
Cobalt Iodate	ambient up to 28 GPa	3.0 GPa and 9.0 GPa–11.0 GPa	P21	Monoclinic	N	Raman Spectroscopy, FT-IR Spectroscopy, DFT Calculations, HPXRD	2021	[41]
Barium Titanate	ambient up to 10 GPa	6 GPa	P4mm (tetragonal) and Pm-3m (cubic)	Tetragonal (at lower pressure) and Cubic (at higher pressure)	N	DFT Calculations	2022	[42]
Zinc Iodate	ambient up to 27.8 GPa	3.4 GPa and 8.9 GPa	P21	Monoclinic	N	HPXRD, Raman Spectroscopy, DFT Calculations	2021	[43]
Caesium Hydroxide	ambient up to 20 GPa	10 GPa	P212121	Orthorhombic	N	DFT Calculations, EDX	2016	[44]
α -Glycylglycine	ambient up to 14.5 GPa	6.7 GPa	P21/c	Monoclinic	N	PXRD, Raman Spectroscopy, DFT Calculations, CSP	2020	[45]
α -Silver Sulfide	ambient up to 32 GPa	7.5 GPa and 16 GPa	P21/c	Monoclinic	N	HPXRD, Raman Spectroscopy, DFT Calculations, Electrical Resistance Measurements	2020	[46]
L-Serine	ambient up to 14.5 GPa	5.3 GPa and 7.8 GPa	P212121	Orthorhombic	Y	HRXRD	2006	[47]
Sodium Manganese Fluoride	ambient up to 4.06 GPa	2.2 GPa $\pm$ 0.5 GPa	P21/n	Monoclinic	Y	Polarized Single-Crystal Optical Absorption Spectroscopy	1998	[48]
Blatter’s Radical	ambient up to 6.07 GPa	5.34 GPa–5.54 GPa	P2 ₁ /n	Monoclinic	Y	DFT calculations	2022	[49]

Table 2. Summary of selected experimental studies on temperature-induced IPTs.

Name	Pressure Range	Transition Range	Space Group	System	SCXRD	Other Methods	Year	References
Dabcodinium chlorochromate chloride	173–296 K	185 K	P21/m	Monoclinic	Y	DSC, Dielectric Measurements	2012	[50]
4-Ethylanilinium hydrogen (2R,3R)-tartrate	123–298 K	186 K	P1	Triclinic	Y	DSC, Dielectric Constant Measurements	2011	[51]
Ibuprofen lysine salt	30–110 °C (30–300 °C)	70–90 °C	P21/n	Monoclinic	N	PXRD, DSC, TGA	2015	[52]
2-nitroanilinium bisulphate	100–300 K	232 K	P-1	Triclinic	Y	FT-IR Spectroscopy, DSC	2020	[53]
Dapsone	60–100 °C	78 °C ± 4 °C	P212121	Orthorhombic	Y	DSC, PXRD	2017	[54]
Triethylbenzylammonium Perchlorate	93–291 K	196 K ± 18 K	Pbca (93 K), Pbcm (291 K)	Orthorhombic	Y	DSC, Dielectric Measurements	2013	[26]
R-Cinacalcet Hydrochloride	room temperature up to 423 K (150 °C)	164.5 °C (437.65 K)	P212121 (form I, III), P1 (form II)	Orthorhombic (form I, III), Triclinic (form II)	Y	DSC, PXRD, FT-IR Spectroscopy, FT-Raman Spectroscopy	2008	[55]
Pyridinium-3-Carboxylic Acid Perchlorate	93 K–298 K	129 K	P21/c	Monoclinic	Y	DSC, Dielectric Measurements	2010	[56]
Lanthanum Gallate	room temperature up to 1100 °C	300–1100 °C	Pnma	Orthorhombic	N	PXRD, Raman Spectroscopy, TEM	2018	[57]
Yttrium manganite	room temperature up to 1403 K	920 K	P63cm	Hexagonal	N	NPD, DTA, Rietveld Analysis	2011	[58]
Yttrium Chromite	321 K–1200 K	900 K	Pmnb	Orthorhombic	N	NPD, DC Magnetization Measurements, Rietveld Refinement, Thermal Expansion Analysis	2020	[59]
Estradiol 17β Valerate (E2V)	room temperature down to 100 K	251.1 K (cooling) and 256.3 K (heating)	P21	Monoclinic	Y	FT-IR Spectroscopy, DSC, ssNMR Spectroscopy	2014	[60]
Potassium Lutetium Phosphate	100 K–293 K	230 K and 130 K	P-3 (at room temperature), P21/m (at 100 K and 200 K)	Hexagonal (at room temperature), Monoclinic (at 100 K and 200 K)	Y	NPD, DSC, Heat Capacity Measurements	2014	[61]
1,4-Diazoniabicyclo[2.2.2]octane-1-acetate-4-acetic Acid Chloride Trihydrate	135 K–298 K	210.7 K (heating) and 180.3 K (cooling) ± 30.4 K.	P21/n	Monoclinic	Y	DSC, Dielectric Measurements	2013	[62]
2-(3,5-Bis(trifluoromethyl)phenyl)-4,5-dihydro-1H-imidazole	100 K–298 K	150 K ± 15 K	P-1	Triclinic	Y	PXRD, DSC, TGA	2024	[63]
Layered Indium Selenide	room temperature up to 350 °C	220 °C (heating) and 190 °C (cooling)	R3m (for α-In2Se3) and P-3m1 (for β-In2Se3)	Rhombohedral	N	DSC, XRD, DFT Calculations, Raman Spectroscopy	2022	[64]
Hexathiocyanate Thulium(III) Anions	160 K–280 K	204.6 K (heating) and 188.7 K (cooling) ± 15.9 K	P-1	Triclinic	Y	DSC, Dielectric Measurements, PXRD	2021	[65]
Orthopyroxene	room temperature up to 1400 °C	1170 °C (both heating and cooling)	Pbca	Orthorhombic	N	SXRPD, Unit Cell Dimension Measurements	2008	[66]
Deuterated 3,5-Pyridinedicarboxylic Acid	15 K–300 K	150 K–200 K	P2 ₁ /n	Monoclinic	Y	DFT Calculations, PXRD, NPD	2011	[67]
4,4'-(Benzo[b]benzo[4,5]thieno[2,3-d]thiophene-2,7-diyl)bis(butan-1-ol) (BTBT-C4OH)	100 K–300 K	200 K	P21/c	Monoclinic	Y	DSC, Thermal Expansion Measurements	2020	[68]
Estradiol 17β Valerate (E2V)	room temperature down to 100 K	251.1 K (cooling) and 256.3 K (heating)	P21	Monoclinic	N	FT-IR Spectroscopy, DFT Calculations	2021	[69]

Table 2. Cont.

Name	Pressure Range	Transition Range	Space Group	System	SCXRD	Other Methods	Year	References
Samarium Fulleride	4.2 K–295 K	32 K	Pcab	Orthorhombic	N	HRXRD, Magnetic Susceptibility Measurements	2003	[70]
CaTiOSiO ₄ — CaTiOGeO ₄ Solid Solution	up to 1123 K	800 ± 25 K	P2 ₁ /a (low temperature), A2/a (high temperature)	Monoclinic	Y	HTXRD, TEM, Spontaneous strain Analysis	2005	[71]
Lutetium Orthoborate	20–1450 °C	1020 °C	C2/c	Monoclinic	N	HTXRD, DSC, TGA, High-temperature Raman Spectroscopy	2020	[72]
Orthoenstatite	300 K–2000 K	1230 K	Pbca	Orthorhombic	N	aiMD Simulations	2004	[9]
Magnesium Aluminum Phosphate Oxide	room temperature up to 1170 °C	485 °C (758 K)	P2 ₁ /c	Monoclinic	Y	HTXRD, DSC, Heat Capacity Measurements	2007	[73]

5.1. Low-Molecular-Weight Organic Compounds

5.1.1. Phenolic Compounds

Resorcinol

The high-pressure phase behavior of resorcinol (1,3-dihydroxybenzene), a hydrogen-bonded molecular solid, was investigated using Raman spectroscopy and photoluminescence up to 14.5 GPa. In addition to the extensively studied isosymmetric $\alpha \rightarrow \beta$ transition at 0.5 GPa, a new disordered high-pressure phase (γ) was discovered at approximately 5.6 ± 0.2 GPa. The γ phase, characterized by weakened and broadened Raman signals, demonstrates reversibility with hysteresis during decompression. Significantly, fast pressurization that bypasses the $\alpha \rightarrow \beta$ transition generates a unique, more ordered phase (δ) above 3 GPa, highlighting the impact of kinetic parameters and loading rate on phase development. This case also illustrates that the retention of the same space group is a necessary but not sufficient condition for a strict IPT; structural overlays and interaction topologies must be examined, as in α/β -resorcinol where Pna2₁ is preserved yet packing differs substantially [74,75].

The appearance of a broad photoluminescence band centered at 2.25 eV in both γ and δ phases indicated the formation of excimer-like states, suggesting a parallel stacking configuration of resorcinol molecules under high pressure. The disorder in the γ phase was attributed to pressure-induced polymorphism rather than amorphization, with the δ phase potentially signifying a crystalline polymorph among various energetically accessible configurations. These findings revealed the complex polymorphic setting of resorcinol under compression, influenced by hydrogen bonding, kinetic limitations, and transformation paths [1].

Hydroquinone–Formic Acid Clathrate

Eikeland et al. have examined the high-pressure characteristics of the hydroquinone–formic acid clathrate (C₆H₄(OH)₂·2HCOOH), a host–guest system of hydroquinone (C₆H₄(OH)₂) frameworks that enclose disordered formic acid (HCOOH) molecules. The researchers employed SCXRD and Raman spectroscopy to investigate the evolution of the crystal structure up to 2 GPa using various pressure-transmitting media (PTMs).

A major finding was the identification of a reversible, pressure-induced IPT at around 1.3 GPa when subjected to compression in a non-penetrating PTM such as Daphne oil. The transition maintained the same space group (P2₁/c) but was marked by a sudden approximately 13% reduction in unit cell volume, signifying a first-order isosymmetric collapse. The structural change arises from a collapse of the hydrogen-bonded framework

due to densification, resulting in the expulsion of formic acid guest molecules from the one-dimensional channels formed by the hydroquinone hydrogen-bonded host framework.

In contrast, when a PTM such as a methanol–ethanol mixture was used—chemically distinct from the aqueous formic acid solvent of crystallization—the structural transition was suppressed. Fluid infiltration helps stabilize the open hydrogen-bonded framework and prevents collapse. This underlines the crucial influence of PTM selection on the pressure-induced structural response [38].

5.1.2. Amino Acids and Their Derivatives

L-Histidine

The pressure-induced structural transition of L-histidine ($C_6H_9N_3O_2$) was examined, focused on its polymorphs α and β . The authors employed HRXRD, complemented by SCXRD and Raman spectroscopy, to monitor the structural response of both polymorphs under escalating pressure up to 7.5 GPa. This comprehensive crystallographic analysis demonstrated that both forms experience reversible IPTs: α -L-histidine at approximately 2.6 GPa and β -L-histidine at around 2.3 GPa.

The transitions entailed important reorientations within the hydrogen-bonding network and rearrangements of molecular packing. The authors asserted that the response is mainly governed by cooperative molecular motions and the reallocation of intermolecular connections, rather than extensive reconstructions of the crystal lattice. The transitions were additionally defined by discontinuities in unit-cell volume and compressibility, substantiating their first-order characteristics.

The research illustrates that even basic amino acids can exhibit complex pressure responses, and that isosymmetric transitions may occur more frequently in biological molecules than previously believed and emphasizes the significance of integrating SCXRD, HRXRD, and vibrational spectroscopy to describe subtle transitions, underscoring the value of high-pressure crystallography in comprehending biomolecular solid-state changes [12].

DL-Cysteine

The complex relationship between temperature and pressure when inducing polymorphic transitions in DL-cysteine ($C_3H_7NO_2S$), an amino acid that has both hydrophilic and hydrophobic characteristics, was analyzed. The authors examined structural behavior at low temperatures (as low as 3 K) and pressures up to 2.6 GPa using a combination of PXRD, infrared spectroscopy (IR), and computational methods. They determined that both temperature and pressure stimuli can induce phase transitions, with particular emphasis on the transition from DL-cysteine-I to DL-cysteine-II.

An IPT was observed, showing that it was caused by internal rearrangements within the crystal rather than a symmetry-breaking. This transition pertains to the reconfiguration of hydrogen bonding interactions—specifically between the $-CH_2SH$ side groups and $N-H\cdots O$ hydrogen bonds—as the molecular packing modifies in response to external stimuli. Furthermore, the same polymorph (DL-cysteine-II) can be obtained through either cooling or compressing the primary DL-cysteine-I phase, underlining the similar structural reactions to thermal contraction and pressure-induced strain.

This study demonstrated that pressure may induce more significant strain changes than temperature, indicating that competing van der Waals and hydrogen bonding interactions determine the polymorphism landscape. These findings align with behaviors previously reported in other amino acids such as glycine and L-alanine (Figure 2) [33].

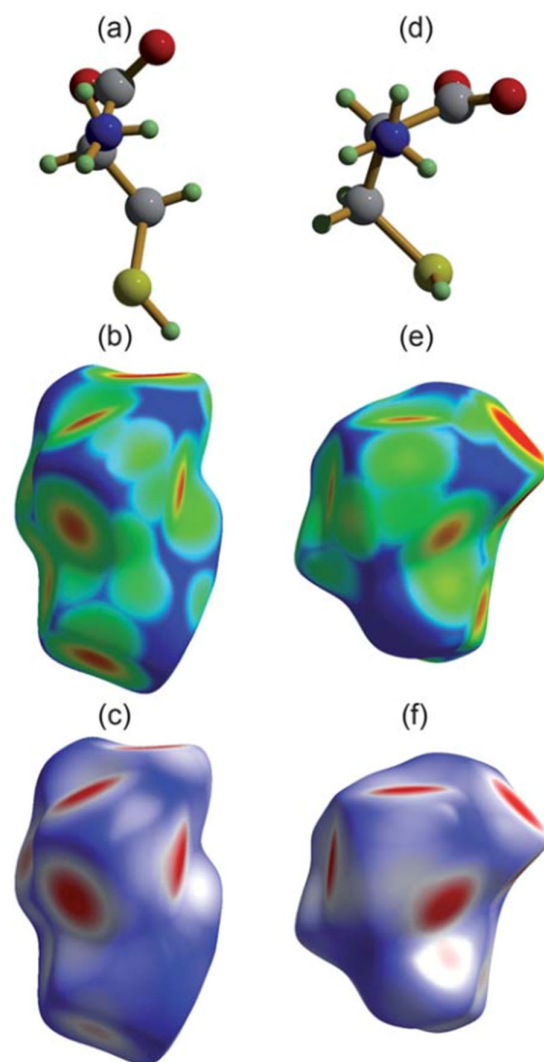


Figure 2. Molecular conformation and Hirshfeld surfaces of DL-cysteine-I at 225 K (a–c) and DL-cysteine-II at 200 K (d–f). Each molecule is shown with the Hirshfeld surface mapped with d_e (b,e); for these series mapped between 1.0 (red) and 2.0 Å (blue)] and d_{norm} [(c,f); mapped between 0.71 (red) and 1.1 Å (blue)], where d_e is the distance to the nearest atom center exterior to the surface and d_{norm} is the normalized contact distance, which takes the van der Waals radii of the atoms into account. Reprinted from [33] with permission from the Royal Society of Chemistry.

L-Serine

The high-pressure behavior of crystalline L-serine was examined using SCXRD and HRXRD within a diamond anvil cell. Two isosymmetric pressure-induced phase transitions were observed: the first transition occurred at 5.3 GPa, resulting in polymorph II, and the second transition at 7.8 GPa, forming polymorph III. The first included only minor changes in unit-cell volume and showed significant modifications in molecule conformation and hydrogen-bond geometry. However, the second showed more significant structural reorganization and changes in packing density. PXRD data confirmed findings, enabling the precise identification of equation-of-state parameters and uncovering minor atomic displacements during the first transition. The integration of single-crystal and powder methods provided an extensive understanding of the compression mechanism, illustrating the gradual adaptation of hydrogen-bond networks under elevated pressure.

The behavior of L-serine is atypical as it has undergone two consecutive isosymmetric transitions, where a minor structural change is followed by a more significant reorganization, which is an unusual occurrence among amino acids under high pressure [47].

α -Glycylglycine

Clarke et al. have examined the high-pressure behavior of α -glycylglycine (α -digly) up to 14.5 GPa, utilizing synchrotron PXRD, Raman spectroscopy, and first-principles-based calculations, which demonstrated a notable change in lattice behavior beyond approximately 6.7 GPa. PXRD analysis revealed a modification in axial compressibility, particularly the strengthening of the c-axis alongside heightened compressibility in the a- and b-axes. This change does not entail a loss of monoclinic $P2_1/c$ symmetry, indicating an IPT. Complementary Raman spectra showed sudden frequency shifts, mode splitting, and changes in pressure coefficients between 6 and 7.5 GPa, especially in the N–H and C–H stretching regions, consistent with a reorganization of hydrogen-bond networks.

USPEX-based structure searches and DFT calculations have revealed multiple potential high-pressure polymorphs. An orthorhombic phase ($P2_12_12_1$) is anticipated to represent the lowest-enthalpy state above approximately 6.4 GPa; however, its simulated diffraction pattern did confirm the experimental results. The most feasible candidate, α' -digly, maintains the $P2_1/c$ symmetry characteristic of the low-pressure phase, yet exhibits subtle structural alterations: bending of the peptide backbone, rotation of the terminal amine group, and a reconfigured hydrogen-bonding arrangement that adds a new C–H $\cdots$ O interaction. These modifications aligned with the experimentally observed changes in axial compressibility. While calculations indicated that α' -digly is more stable only beyond approximately 11.4 GPa, the small energy disparity from α -digly within the 6–9 GPa range, along with recognized computational constraints in modeling hydrogen bonds, confirmed that it is responsible for the observed transition.

The suggested driving force is the relief of strain in short N–H $\cdots$ O hydrogen bonds that approach critical bond-length thresholds under compression, a phenomenon observed in other amino acids as well. The α' -digly structure is chemically different from α -digly because of intramolecular charge redistribution, which potentially affect its reactivity [45].

5.1.3. Amides, Amidines, and Nitrogen-Containing Heterocyclic Compounds

N-Isopropylpropionamide

The P,T phase diagram of N-(isopropyl)propionamide (NiPPA) shows two solid-state transformations within the same molecular system: a low-pressure plastic crystalline (PC)–crystalline (C) transition and a high-pressure isosymmetric crystalline–crystalline transition above ~ 4 GPa. As determined by synchrotron X-ray diffraction, the latter was characterized by strong anisotropic compression, substantial molecular flattening, and isopropyl group reorientation, which resulted in a denser packing of the high-pressure β -form in comparison to the low-pressure α -form. Despite the existence of intermolecular hydrogen bonds in all solid phases, the PC–C boundary, measured at pressures as high as around 400 MPa, produced apparent ΔV and ΔH values that are similar to those of non-hydrogen-bonded analogs. The PC phase is metastable over the entire investigated P–T range, with extended coexistence regions resulting from kinetic effects. The phase diagram highlights the complex interactions between metastability, kinetics, and anisotropic structural responses by demonstrating the uncommon coexistence of a high-pressure isosymmetric transition and a pressure-dependent PC–C transition in the same molecular crystal (Figure 3) [28].

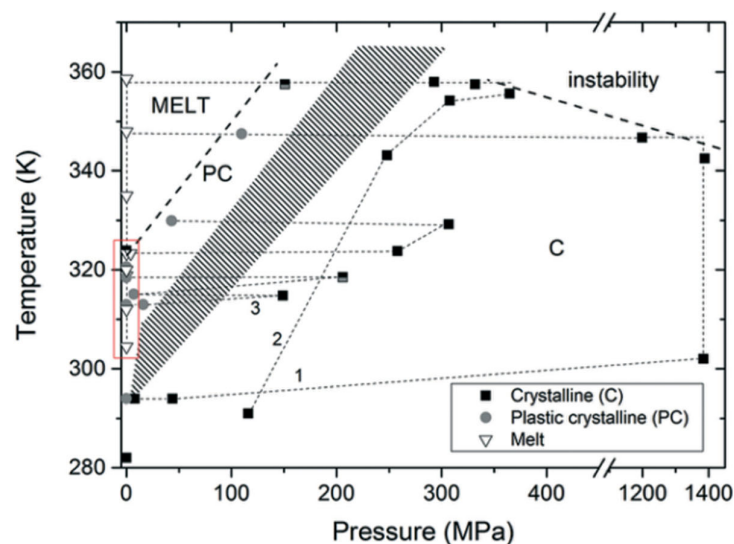


Figure 3. Diagram depicting the P–T trajectories (1, 2, and 3: dotted lines) employed to examine the phase transformation characteristics of NiPPA. The region marked in red illustrates the alteration of the compound subsequent to high-pressure and high-temperature treatment in run 2. It is important to note that the plastic crystalline phase remains metastable across all pressure and temperature levels. The shaded zone denotes the location where a metastable C–PC phase transition is anticipated to transpire. The dashed line in the upper right signifies a crystalline instability that leads to a fast reduction in pressure within the cell and the vanishing of the X-ray diffraction pattern. Reproduced from [28] with permission from the Royal Society of Chemistry.

Biurea

High-pressure neutron diffraction, Raman spectroscopy, and DFT calculations showed that biurea underwent a first-order IPT near 0.6 GPa, accompanied by a ~5% unit-cell volume collapse. The transition was driven by substantial intramolecular reorientation, specifically a change in the torsional angle between the two urea units, together with notable changes in hydrogen-bond geometries. In accordance with a “wine-rack” hinging mechanism, compression caused negative linear compressibility along one principal axis in both phases. Compared to Phase I, Phase II showed a higher density but unexpectedly higher compressibility. Hydrogen-bonding changes were anisotropic: some N–D···O interactions shortened continuously, while others lengthened at the transition, resulting in altered N–N bond characteristics and Raman mode intensity shifts. According to DFT results, Phase I was stabilized at ambient pressure by vibrational zero-point and entropic contributions, while Phase II was favored by static lattice energy. The pV term increased with increasing pressure, shifting stability toward Phase II. The study demonstrated the subtle yet significant impact of vibrational free-energy terms on phase stability under compression, emphasizing their role in stabilizing phases across isosymmetric transitions in molecular crystals [3].

1,4-Diazoniabicyclo[2.2.2]octane-1-acetate-4-acetic Acid Chloride Trihydrate

The 1:1:3 complex of 1,4-diazoniabicyclo[2.2.2]octane-1-acetate-4-acetic acid with chloride ions and water underwent a reversible first-order IPT between 210.7 K (heating) and 180.3 K (cooling), with a thermal hysteresis of 30.4 K. The transition, accompanied by dielectric anomalies, was confirmed by dielectric measurements and DSC. Both the high- and low-temperature structures adopted the monoclinic $P2_1/n$ space group; however, there were notable differences in cell parameters, especially a doubling of the a -axis and unit cell volume upon cooling. A reorganization of hydrogen-bonded anionic chains that were formed between water molecules and chloride ions was the driving force behind the tran-

sition. In the low-temperature phase, two different chain types with varying ring motifs, dihedral angles, and chloride–oxygen arrangements replaced the single chain type that was present in the high-temperature phase. Without significant changes in donor–acceptor distances, these rearrangements were caused by changes in the relative positions of water molecules and chloride ions. The water molecules’ overall crystal symmetry and hydrogen-bond metrics were maintained when they were deuterated, but the thermodynamic and dielectric signatures changed, adding anomalies close to 243 K that were probably caused by isotope effects on proton dynamics. This study showed that IPTs in hydrogen-bonded molecular crystals could be caused by modifications in hydrogen-bond topology rather than symmetry breaking [62].

2-(3,5-Bis(trifluoromethyl)phenyl)-4,5-dihydro-1H-imidazole

The examined imidazole-based single-component molecular crystal, 2-(3,5-bis(trifluoromethyl)phenyl)-4,5-dihydro-1H-imidazole underwent an isosymmetric dynamic disorder-order reversible phase transition at around 150 K with a thermal hysteresis of ~15 K. Variable-temperature PXRD and SCXRD, supported by DSC, demonstrated the transition was driven by rotational disorder in the terminal $-\text{CF}_3$ groups, that became ordered upon cooling. The material showed distinct anisotropic thermal expansion, which was positive (PTE) along the *a*-axis, near-zero (ZTE) along the *b*-axis, and negative (NTE) along the *c*-axis, resulting in uniaxial NTE and biaxial PTE features in both high- and low-temperature phases. Structural analysis revealed that $\text{N}-\text{H}\cdots\text{N}$ hydrogen bonds formed scissor-like motifs, with the *b*-axis hinge explaining the ZTE and scissor-jack-like motion accounting for the axial PTE/NTE. The ordered low-temperature phase was found to be more stable than the disordered high-temperature phase, using the energy framework, lattice, and packing calculations. These results demonstrated that this organic system holds promise for environment-friendly thermoresponsive device applications [63].

5.1.4. Functional Organic Compounds for Electronic and Ionic Applications

Rubrene

A reversible isosymmetric single-crystal-to-single-crystal phase transition was observed in triclinic rubrene(5,6,11,12-Tetraphenyl-tetracene), using high-pressure SCXRD. Anisotropic shortening along the π – π stacking direction of the tetracene cores, along with progressive twisting of phenyl substituents and “scissoring” between phenyl pairs, caused the compression of form I up to 5.91 GPa to result in a ~23% reduction in molecular volume. PIXEL lattice energy calculations and Hirshfeld surface analysis showed that during compression, π – π interactions gradually decreased as $\text{C}-\text{H}\cdots\pi$ contacts increased. The structure changed into form II at 7.12 GPa, losing inversion symmetry and tripling the unit-cell volume. In comparison to the ambient-pressure form, this new conformation had a significant “double twist” of the tetracene backbone and substantial phenyl torsions, resulting in an intramolecular energy penalty of about 70 kJ mol^{−1}. The transition was primarily driven by packing efficiency and a reduction in the PV term, rather than conformational stabilization. When decompressed between 5.0 and 4.0 GPa, the transition was completely reversible without causing crystal deterioration. Structural analysis revealed that whereas compression of form I should enhance charge-transport properties, by decreasing π – π distances, form II may not demonstrate improved mobility due to decreased $\text{C}\cdots\text{C}$ contacts despite its higher density [35].

BTBT-C4OH

Dumitrescu et al. analyzed the temperature-dependent structural evolution of 4,4′-(benzo[*b*]benzo[4,5]thieno[2,3-*d*]thiophene-2,7-diyl)bis(butan-1-ol) (BTBT-C4OH) and

found a rare continuous crossover from positive to negative uniaxial thermal expansion along the monoclinic *b*-axis near 200 K.

SCXRD between 100 and 300 K showed that atomic displacement parameters (ADPs) for all non-hydrogen atoms displayed a distinct slope shift and negative discontinuity at the crossover. All translational tensor eigenvalues were discontinuous at the same temperature, according to rigid-body Translation–Liberation–Screw (TLS) analysis, whereas librational eigenvalues merely changed in slope, which is consistent with a continuous type-0 first-order IPT.

BTBT-C4OH has a staggered herringbone packing and differs from BTBT-C6OH by having shorter side chains, lack of close S⋯S contacts, and weaker anharmonic molecular motion. These characteristics correspond to smaller negative expansion. The crossover was caused by steric compensation between herringbone arranged molecules, where contraction along *b*-axis was induced by increased librational motion and herringbone angle with temperature. This mechanism, which is influenced by chain length, is similar to that in pentacene and BTBT-C6OH. Clear ADP and TLS anomalies and the lack of sudden changes in geometric parameters demonstrated the usefulness of displacement tensor analysis at identifying subtle isosymmetric transitions [68].

2-Nitroanilinium Bisulphate

The crystalline 2-nitroanilinium bisulphate underwent a reversible, first-order IPT at 232 K, which was characterized by abrupt changes in lattice characteristics and marked hysteresis. The transition was driven by a concerted double proton transfer within centrosymmetric (HSO₄)₂ dimers, which reconstructed the R²₂(8) hydrogen-bond ring motif into an alternative configuration without changing the overall donor/acceptor count. A topologically invariant component of the hydrogen-bond network was highlighted by graph-set analysis, which showed a consistent R⁶₆(20) pattern that was maintained throughout the transition. While π – π stacking between aromatic cations strengthened during cooling, structural rearrangements include shifts in ammonium hydrogen-bond acceptors and restructuring of ring patterns (e.g., R²₂(6) to R²₃(8), R⁴₆(16) to R⁴₄(12)). The calorimetric signature of a first-order event was confirmed by DSC measurements, and the typical splitting of bisulphate bending modes was identified by IR spectroscopy, which was consistent with symmetry-preserving structural modifications. Two minima corresponding to different hydrogen-bond arrangements were observed using computational modeling of the relaxed potential energy surface for the (HSO₄)₂ dimer: non-centrosymmetric [H₂SO₄/SO₄^{2−}] and centrosymmetric [SO₄^{2−}/2H⁺/SO₄^{2−}]. The second one exhibited greater geometric distortion while possibly facilitating ion displacement [53].

4-Ethylanilinium Hydrogen (2R,3R)-Tartrate

The homochiral organic salt of ethylanilinium hydrogen (2R,3R)-tartrate underwent a reversible IPT at about 186 K. A configurational order–disorder mechanism was confirmed by calorimetric data, which showed a first-order transition with small thermal hysteresis (0.7 K) and an entropy change ($\Delta S = 0.89 \text{ J K}^{-1} \text{ mol}^{-1}$). Variable-temperature XRD revealed abrupt unit-cell changes and a near-doubling of cell volume. The transition involved extensive reorganization of hydrogen-bond networks and significant phenyl-ring reorientation ($\sim 22^\circ$), meanwhile dielectric measurements revealed no anomaly at accessible frequencies, implying low-frequency ferroelectric behavior. A reversible isosymmetric transition of this kind has never been observed in a homochiral organic salt before (Figure 4) [51].

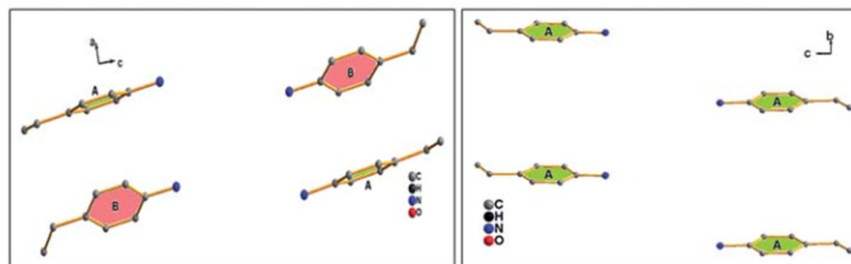


Figure 4. Packing diagrams of 4-ethylanilinium cation moieties in the homochiral organic salt of ethylanilinium hydrogen (2R,3R)-tartrate at 123(2) K (**left**) and 298(2) K (**right**) viewed along the *b* axis and *a* axis, respectively. The hydrogen tartrate anions and all hydrogen atoms were omitted for clarity. Reprinted from [51] with permission from the Royal Society of Chemistry.

Pyridinium-3-Carboxylic Acid Perchlorate

Ye et al. reported a reversible first-order isosymmetric transition in pyridinium-3-carboxylic acid perchlorate at around 129 K. Dielectric measurements and DSC confirmed the transition with a broad hysteresis of about 15 K. SCXRD showed that the unit-cell parameters, particularly the *c* axis and monoclinic angle, change suddenly, which is consistent with a discontinuous character.

The layered structure of the compound is formed by hydrogen-bonded pyridinium-3-carboxylic acid cation chains that are connected together by perchlorate anions. The most noticeable differences between phases were shortened distances between neighboring pyridinium ring planes and a significant displacement of hydrogen-bonded layers. The progressive ordering of the perchlorate anions upon cooling was considered a secondary effect. The reorientation of the pyridinium cations, which strengthened hydrogen bonding and stabilized the low-temperature phase, was found to be the main driving force (Figure 5) [56].

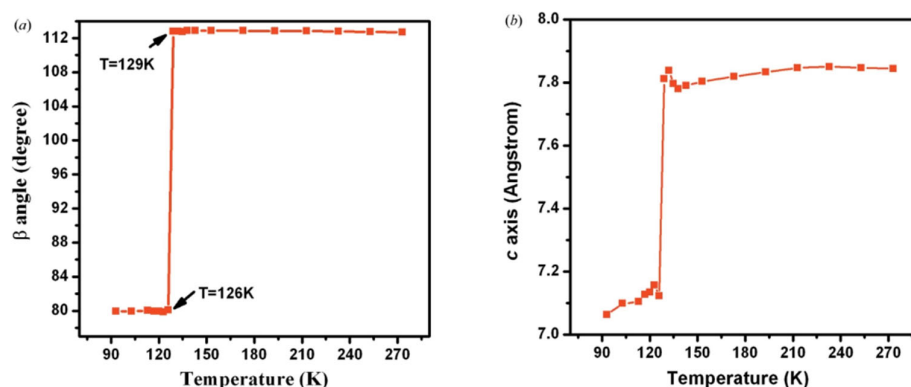


Figure 5. Temperature dependency of the *c* axis (**b**) and angle (**a**) in the 93–273 K range. Reprinted from [56] with the permission from IUCr journals.

5.1.5. Active Pharmaceutical Ingredients

Dapsone

The reversible IPT between dapsone (DDS) polymorphs II and III was observed using thermal analysis, variable-temperature XRD, and intermolecular energy calculations. This first-order solid–solid transition occurred at 78 ± 4 °C, with a low enthalpy of transformation (~ 2 kJ mol^{−1}) and minimal hysteresis, indicating fast kinetics and reversibility. The only differences between the two polymorphs were a relative shift in molecular layers and minor molecular conformations. According to structural analysis, despite being the high-temperature phase, form II adopted a denser packing arrangement than form III.

This is an exception from the density rule that is usually seen in enantiotropically related polymorphic pairings, which was further studied using pairwise intermolecular energy calculations. The results showed that the loss of a strong N–H···O hydrogen bond during the transition from III to II was compensated by increased dispersion contributions, stabilizing the more compact form II. The transition pathway included slight conformational changes and cooperative layer displacements, which was consistent with the transitions' single-crystal-to-single-crystal nature and the low activation barrier indicated by the calorimetric data [54].

Chlorothiazide

Chlorothiazide was found to undergo a pressure-induced IPT at 4.2 GPa. The authors utilized detailed periodic DFT calculations, along with phonon and thermodynamic analyses, to determine whether such a transition could be predicted computationally. The reverse transition (Form II → Form I under decompression) was reproduced using geometry optimization, however the forward pressure-driven process was not captured, which showed that there is a major energy barrier. Nevertheless, the energetic and Gibbs free energy comparisons consistently indicated that Form II was thermodynamically more stable at high pressures, which was consistent with experimental observations. The transition was also demonstrated to be entropy-driven, as evidenced by phonon-derived parameters. Significantly, the conversion of Form I into Form II under pressure was successfully replicated by aiMD simulations, overcoming the kinetic constraints of static optimization and showed the potential of aiMD as a predictive tool for IPTs (Figure 6) [2].

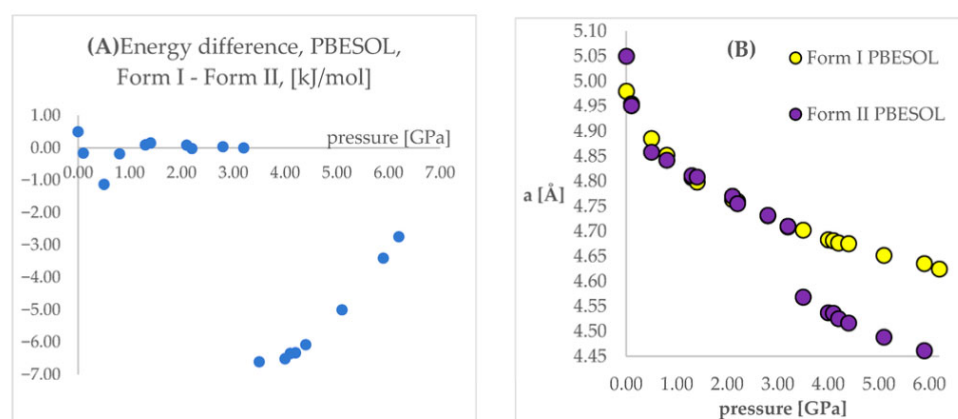


Figure 6. (A) Differences between the energies (Form I–Form II) of the chlorothiazide structures modeled using PBESOL functional, with respect to pressure. (B) The change in unit cell edge “a” length obtained from calculations using PBE TS functional, with respect to pressure. Yellow circles—using Form I as initial; violet circles—using Form II as initial. Reprinted from [2], licensed under CC BY 4.0.

Ibuprofen Lysine Salt

The solid-state behavior of ibuprofen lysine salt was studied using DSC and variable-temperature XRPD, which revealed a fully reversible polymorphic transition near 70 °C. Despite experimental difficulties related to powder data, two crystalline phases, identified as IBL-I (ambient temperature) and IBL-II (high temperature), were structurally described. Both polymorphs showed strong structural similarities in molecular conformation, hydrogen-bonding networks, and packing motifs. The transition was linked to anisotropic lattice strain, specifically an expansion along the b axis and a subtle contraction along the a axis. The extensive hydrogen-bonding structure was maintained throughout the phases, and the molecular rearrangements were confined to conformational shifts within lysine and minor torsional adjustments of the ibuprofen isopropyl group.

According to an analysis of structural strain tensors, the disengagement of interdigitated isopropyl groups, which resulted in a displacing but reversible rearrangement without bond cleavage, was the driving force behind the transition. The event's low enthalpy change ($+2.3 \text{ kJ mol}^{-1}$) was in consistent with the structural disturbances' minor character [52].

R-Cinacalcet Hydrochloride

The polymorphic system of R-cinacalcet hydrochloride displayed a reversible solid–solid transition between form III^o and the high-temperature form I, maintaining the orthorhombic space group (P2₁2₁2₁). The transition took place at 148.5 °C, exhibiting a significant hysteresis of approximately 30 K, as determined through DSC and variable-temperature PXRD. Although symmetry change was not observed, notable structural reorganization was reported. In form III^o, molecular packing was characterized by distinct crankshaft-like chains formed by N–H...Cl[−] hydrogen bonds. Meanwhile, form I showed dynamic orientational disorder of the phenyl moiety, along with minor changes in hydrogen-bond geometry and a rotation of the naphthyl group. The transition maintained the overall lattice structure while allowing for enhanced molecular mobility, representing an example of an IPT triggered by conformational dynamics. Significantly, the transformation was enantiotropic and fully reversible, with form III^o remaining stable below the transition point and form I above it [55].

Estradiol 17 β Valerate

Estradiol 17 β valerate (E2V), an esterified derivative of the natural hormone estradiol, underwent a reversible IPT at 251 K. The structural change was triggered by a significant conformational reorientation of the valerate side chain, which was accompanied by an unusual contraction of the b axis. The first-order and discontinuous nature of the transition was confirmed by DSC, which also showed latent heat and thermal hysteresis that were consistent with an order–disorder mechanism involving the freezing of dynamic disorder in the high-temperature phase.

The discontinuity was verified by the solid-state ¹³C NMR spectra, which showed noticeable spectrum broadening and chemical shift alterations below the transition. The valerate fragment's conformational reconfiguration was confirmed to be the primary structural driver by complementary vibrational spectroscopy, which revealed small but reversible intensity changes in selected infrared bands. The intermolecular hydrogen-bonding network was preserved throughout the transition, despite the noticeable conformational changes [60].

Pandey et al. reported a reversible low-temperature IPT in E2V, which occurred near 250 K and was triggered by subtle reorientations along the valerate side chain. Changes in this chain's torsional angles (ϕ_1 , ϕ_2 , ϕ_3) caused conformational differences between the room- and low-temperature phases and altered hydrogen-bonding patterns. Vibrational spectroscopy and DFT calculations revealed a clear correlation between characteristic infrared bands at 1115, 1200, and 1415 cm^{−1} and the conformational changes in the valerate side chain, serving as transition fingerprints. Potential energy surface scans verified feasible conformers that corresponded to experimental torsional angles, supporting the order–disorder mechanism described by Buerger's classification. Furthermore, E2V maintained agonist activity toward estrogen receptor isoforms, as shown by molecular docking simulations, while the binding energies were modulated by conformational variation across phases [69].

5.1.6. Organic Radicals

Blatter's Radical

High-pressure crystallographic studies of Blatter's radical up to 6.07 GPa revealed a first-order IPT, followed by ongoing structural changes. Compression was highly anisotropic, with the highest strain occurring along the π -stacking direction. Between 3.42 and 5.34 GPa, gradual rotation of the N-phenyl substituent accommodated increasing intermolecular repulsion, serving as a cautionary second-order transition. This rotation underwent a discontinuous jump, indicating the first-order isosymmetric transition, upon further compression to 5.54 GPa. The transition was primarily driven by volume minimization rather than the relief of unfavorable contacts, whereas the triazinyl core's planarity was enhanced, as confirmed by DFT calculations connecting this conformational change to the alleviation of intramolecular H $\cdots$ H strain. The intermolecular coupling was strengthened as π -stacking contacts were shortened by 0.34 Å over the pressure range. Although radical dimerization was not observed, the transition suggested potential consequences for magnetic behavior, including a potential pressure-driven shift toward a diamagnetic ground state and enhanced antiferromagnetic interactions [49].

5.2. Inorganic Compounds and Metal Complexes

5.2.1. Simple Salts and Oxides

Sulfamic Acid

Raman spectroscopy and synchrotron XRD were used to investigate the structural response of sulfamic acid (NH₃⁺SO₃[−]) under high pressure. Results revealed a reversible IPT between 10.2 and 12.7 GPa. The transition was initiated by conformational distortions of the SO₃[−] and NH₃⁺ groups above 8 GPa and was characterized by a discontinuous contraction of the c-axis (~9%), resulting from the sliding of hydrogen-bonded chains along this direction, which rearranged the hydrogen-bonding network and strengthened electrostatic interactions between zwitterionic units. These rearrangements created a tighter packing pattern with decreased compressibility along c. The gradual character of the transition showed kinetic hindrance from short-range electrostatic repulsion, and decompression studies revealed full reversibility. The study established sulfamic acid as a model system for pressure-driven isosymmetric transformations in hydrogen-bonded molecular crystals by connecting anisotropic lattice distortions with molecular conformational changes [10].

Ammonium Bicarbonate

Ammonium bicarbonate (AB) underwent a pressure-induced IPT at approximately 2 GPa, driven by the interaction of its highly anisotropic elastic response and the structure of its hydrogen-bonding network. Synchrotron XRD and Raman spectroscopy demonstrated that compression along the bc-plane was countered by a "double-wine-rack" hydrogen-bonding motif, resulting in atypically rigid mechanical properties of the otherwise soft N–H $\cdots$ O and O–H $\cdots$ O bonds. The biaxial hard compression minimized major distortions in the bc-plane and facilitated quasi-uniaxial contraction along the a-axis, allowing for subtle structural rearrangements that led to the formation of new N–H $\cdots$ O hydrogen bonds between ammonium cations and bicarbonate anions. The lack of peak splitting in both Raman and XRD signatures supported the isosymmetric nature of the transition, indicating that only local hydrogen-bond reconfigurations occurred, rather than a global symmetry reduction [4].

Sodium Oxalate

A reversible first-order IPT in crystalline sodium oxalate (Na₂C₂O₄) was identified at 3.8 GPa, as revealed using high-pressure Raman spectroscopy in diamond anvil cells and

synchrotron PXRD methods. The transition involved abrupt changes in unit-cell parameters, specifically a significant reduction in the monoclinic angle β and a noticeable volume contraction from $176 \text{ \AA}^3$ at 3.6 GPa to $167 \text{ \AA}^3$ at 4.3 GPa. Raman spectra demonstrated significant frequency discontinuities in various vibrational modes, especially in the low-frequency range associated with the translational motions of Na^+ cations. The lack of a soft mode indicated that the transition did not occur through conventional phonon softening. Structural refinements showed that the oxalate anions underwent collective reorientations while largely maintaining their centroid packing. However, the sodium cations exhibited a change in coordination from sixfold ($3\text{O}(1) + 3\text{O}(2)$) to sevenfold ($4\text{O}(1) + 3\text{O}(2)$), with the most significant positional shifts observed for Na^+ . The lattice-dynamics calculations of the elastic constants confirmed structural stability at pressures significantly exceeding the transition point, thereby ruling out elastic instabilities as the driving force (Figure 7) [31].

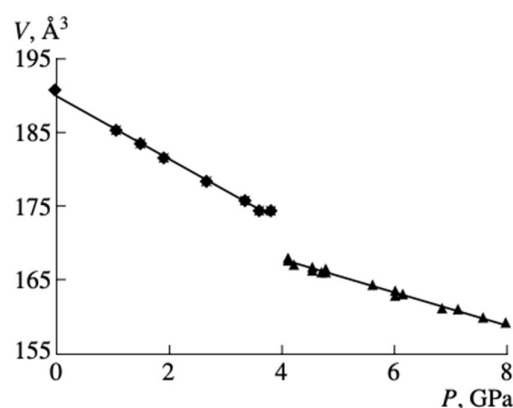


Figure 7. Cell volume of sodium oxalate vs. pressure. Reprinted from [31] with the permission from Pleiades Publishing.

Caesium Hydroxide

The compression behavior of Caesium Hydroxide (CsOH) and Rubidium Hydroxide (RbOH) was investigated computationally, and the results showed a richer sequence of high-pressure phases than had been previously identified. The structural assignment of the RbOH-VI phase has been revised, revealing a tetragonal topology similar to that of KOH-VI , defined by localized square-planar $(\text{OH})_4$ units within a distorted CsCl -like cation framework. This transformation signifies a shift from layered structures to compact three-dimensional hydrogen-bonded networks, characterized by a significant increase in density and spectroscopic signatures indicative of weakened hydrogen bonding. Calculations showed that in CsOH , a pressure-induced IPT occurred around 10 GPa, resulting in the formation of a new phase, CsOH-VII . This phase exhibited a subtle reorganization of kinked one-dimensional OH chains and a reorientation of CsO_5 polyhedra into a three-dimensional network. The enthalpic driving force for this transition was relatively small, indicating sluggish kinetics and accounting for the lack of experimental confirmation, despite the possibility for detection through diffraction signatures. The dimensionalities of RbOH-VI and CsOH-VII , which ranged from localized clusters to extended one- and two-dimensional motifs, demonstrated the unexpected versatility of hydrogen-bond network formation in alkali hydroxides. This flexibility suggests that similar IPTs could occur in other hydrogen-bonded solids, affecting the structural diversity and physical properties of hydrous minerals in mantle conditions (Figure 8) [44].

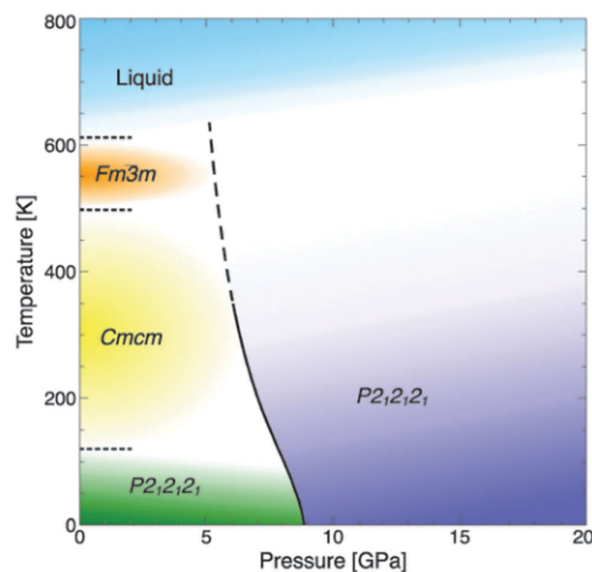


Figure 8. Phase diagram of CsOH, including the calculated transition line CsOH-IVc-VII (solid-dashed line), experimental data at $P = 1$ atm (dotted lines), and estimates for the high-temperature phases' stability fields (colored areas). Reprinted from [44] with the permission from the Royal Society of Chemistry.

Cobalt Iodate

Synchrotron XRD, Raman and IR spectroscopy, and DFT calculations revealed two symmetry-preserving phase transitions in cobalt iodate, $\text{Co}(\text{IO}_3)_2$, at ~ 3 GPa and 9–11 GPa. Both transitions included pressure-induced rearrangements fueled by the iodate ion's stereochemically active lone electron pair. Despite overall volume contraction, the lattice reaction was highly anisotropic, showing an unexpected expansion along the a and c axes, which was explained by the progressive elongation of specific I–O bonds, allowing for the formation of additional coordination environments at high pressure. The calculated vibrational properties and mode symmetries were consistent with the spectroscopic measurements, which showed clear anomalies in phonon frequencies and mode splitting across the transitions. Pressure-volume equations of state were established up to 27 GPa, resulting in bulk modulus values consistent with theoretical predictions. The role of iodine coordination increase in stabilizing isosymmetric high-pressure phases has been highlighted by the comparative analysis with related iodates like $\text{Fe}(\text{IO}_3)_3$ and $\text{Zn}(\text{IO}_3)_2$ [42,44,74,75].

Zinc Iodate

Zinc Iodate ($\text{Zn}(\text{IO}_3)_2$), a metal iodate with stereoactive lone electron pairs on iodine, was analyzed using SCXRD, Raman spectroscopy, and DFT calculations and two reversible IPTs, which occurred in the approximate ranges of 2.5–3.4 GPa and 8–9 GPa were observed. The structural alterations were primarily caused by gradual distortions of the IO_6 polyhedra, including shortening of the long I–O bonds and elongation of the short ones, whilst ZnO_6 octahedra remained stiff. The transitions were accompanied by S-shaped compressions of unit-cell axes and anomalous, nonlinear changes in Zn–O distances, showing that the structural reaction was driven by local polyhedral adjustments. Raman spectra showed mode softening and reversible intensity changes in certain vibrations, indicating a gradual decrease in iodine lone electron pair stereoactivity and a minor reorganization of the coordination environment. The overall connectivity of the crystal structure remained preserved regardless of these significant bond rearrangements, showing that symmetry breaking did not occur the transitions [43].

Magnesium Aluminum Phosphate Oxide

The thermal behavior and polymorphism of MgAlPO_4O , a breakdown product of lazulite, were studied across a wide temperature range using DSC, thermogravimetric analysis, and in situ HTXRD. At 758 K, MgAlPO_4O underwent a reversible IPT, during which minor rearrangements of the AlO_6 and PO_4 polyhedra were observed. The transition involved a discontinuous shift in lattice parameters, resulting in cooperative modifications in bond lengths and angles that improved structural packing efficiency. Thermochemical analysis showed an enthalpic anomaly associated with the transition, suggesting latent heat connected to the framework's reorganization [73].

Dabcodiiium Chlorochromate Chloride

Dabcodiiium chlorochromate chloride was shown to undergo a reversible structural phase transition at around 185 K, as confirmed by sharp DSC peaks with 4.9 K hysteresis and step-like dielectric anomalies. The isosymmetric nature of the transition was confirmed by variable-temperature crystallographic study, which showed that both high- and low-temperature structures remained monoclinic in $P2_1/m$. The a -axis tripled during the transition, while the b , c , and β parameters remained essentially unaltered. According to structural comparison, the transition was primarily driven by a ca. 60° reorientation of one-third of the chlorochromate anions by the rotation of the CrO_3 groups around the Cr–Cl bond with accompanying rotation of a subset of dabcodiiium cations. However, the chloride counterions and hydrogen-bonding networks underwent minimal rearrangement, and the deuterated analog exhibited practically comparable thermal behavior, emphasizing the insignificant role of hydrogen bonding in the transition. The relatively weak dielectric response was explained by the discontinuous nature of the phenomenon, the structural similarity between high- and low-temperature phases, and the lack of notable dipole changes. In summary, these findings determined that the transition was a first-order, temperature-induced IPT dominated by anion reorientation rather than cation ordering (Figure 9) [50].

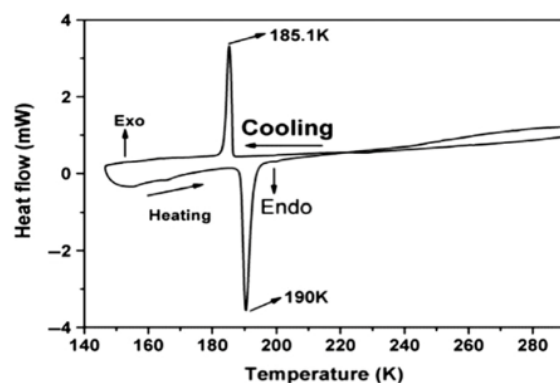


Figure 9. DSC curves displaying sharp peaks near 185 K, evidencing a reversible first-order phase transition. Reprinted from [50] from Elsevier.

5.2.2. Inorganic Fluorides

Lead Fluoride

Stan et al. observed that lead fluoride (PbF_2) compressed up to 75 GPa underwent a continuous isosymmetric transition from cotunnite- to Co_2Si -type phase between 10 and 22 GPa. XRD displayed unusual lattice behavior with significant anisotropy in axial compressibilities but no volume discontinuity. DFT calculations revealed a tenfold environment resembling the Co_2Si -type phase, resulting from progressive bond rearrangements and the development of an additional Pb–F bond.

PbF₂ partially transformed to the 11-coordinated Ni₂In-type phase upon heating above 1200 K, at and over 25.9 GPa; however, it returned to Co₂Si-type phase after the temperature was quenched, indicating a negative Clapeyron slope. Although only partial retention occurred at ambient conditions, near-complete transformation was achieved above 43 GPa at high temperatures. The values of the bulk modulus showed only minor differences in compressibility between the phases.

In contrast to alkaline earth difluorides, PbF₂ showed a unique high-pressure routing, with isosymmetric development dominating its structural response. This results align with predicted patterns for lanthanide and actinide dioxides at megabar pressures, emphasizing the importance of continuous transitions in AX₂ compounds [30,76–79].

High-pressure diffraction studies on orthorhombic PbF₂ revealed a first-order isosymmetric transition near 10 GPa. The cotunnite-type phase (Pnam, Z = 4, CN = 9) changed into a Co₂Si-related structure with the same symmetry but increased coordination (CN = 10). The transition resulted in a small volume collapse (~2%) and anisotropic lattice compression, primarily along the a-axis. Other cotunnite-type dihalides stabilize either monoclinic post-cotunnite or hexagonal Ni₂In phases. PbF₂, on the other hand, followed a different structural path, yielding a third high-pressure configuration in this family. The isosymmetric nature of the transition and its initiation in the minor modifications of the cation coordination environment were confirmed by both Raman data and theoretical calculations [30].

Sodium Manganese Fluoride

A pressure-induced, reversible IPT was observed in Na₃MnF₆ within the range of 1.7–2.2 GPa. Single-crystal diffraction data indicated that the transition was induced by a reorientation of the static Jahn–Teller distortion of Mn(III). At ambient pressure, the elongated axis of the MnF₆^{3−} octahedron was oriented approximately 20° from [001]. Above the transition, this axis rotates to about 70°, directing towards a distinct set of fluorine ligands. The distortion flip was confirmed by polarized optical absorption spectroscopy, revealing significant and fully reversible changes in the polarization of spin-allowed d–d transitions in Mn³⁺ depending on the transition pressure. Compressibility measurements indicated anisotropic lattice responses consistent with the packing of Na⁺ and F[−] layers, implying that the transition reflected a shift from distortions accommodated perpendicular to these layers to orientations within them. The hysteresis of approximately 0.5 GPa represents the first well-described instance of Jahn–Teller distortion reorientation in a Mn³⁺ compound subjected to pressure. The findings highlighted the significance of electronic configuration in stabilizing isosymmetric transformations, in contrast to the lack of a similar transition in isostructural Na₃ScF₆ [48].

5.2.3. Coordination Complexes and Ionic Compounds

Copper–Dicyanoaurate Complexes

A study of Cu–Au supramolecular compounds synthesized from chelating ligands and dicyanoaurate anions revealed architectures defined by aurophilic interactions and distinct responses to external stimuli. One of the five compounds obtained, ((Cu(L1)₂[(μ-CN)Au(CN)])[Au(CN)₂]), has been investigated for pressure–temperature behavior. An isosymmetric distortive phase transition between 1.3 and 1.5 GPa was identified by high-pressure Raman spectroscopy combined with SCXRD. This transition was characterized by anomalous compression and reorganization of Au⋯Au contacts, along with distortions around the Cu(II) coordination environment. However, variable-temperature crystallography up to 343 K revealed only continuous lattice adjustments, emphasizing that pressure is the main factor responsible for initiating structural transformations in these systems. The findings show how subtle aurophilic interactions and Jahn–Teller effect driven distortions collaborate under compression to produce isosymmetric transitions [37].

Hexathiocyanate Thulium(III) Anions

The compound $[(n\text{Bu})_4\text{N}]_3[\text{Tm}(\text{SCN})_6]$ underwent a reversible structural phase transition near 204 K, as confirmed by DSC and temperature-dependent dielectric measurements. The transition included by a significant thermal hysteresis (~ 15.9 K) and an entropy change that was consistent with an order–disorder mechanism. SCXRD confirmed that the transition was isosymmetric. According to structural analysis, the transition was caused by the disordering of the $[(n\text{Bu})_4\text{N}]^+$ cation’s terminal carbon chain, while the $[\text{Tm}(\text{SCN})_6]^{3-}$ anionic framework remained basically intact. The phase transition was accompanied by distinct dielectric anomalies, demonstrating the system’s potential as a switchable dielectric material. The compound also showed solid-state photoluminescence, with a peak emission at 458 nm that was linked to the $^3\text{D}_2 \rightarrow ^3\text{F}_4$ transition of Tm^{3+} (Figure 10) [65].

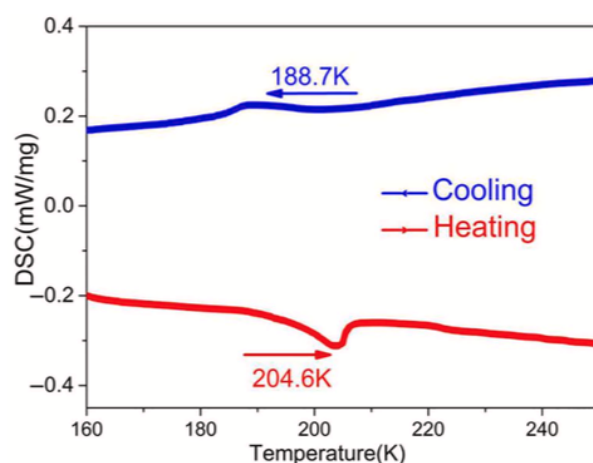


Figure 10. The heat anomalies of compound $[(n\text{Bu})_4\text{N}]_3[\text{Tm}(\text{SCN})_6]$ in the cooling and heating cycle. Reprinted from [65] with permission from Elsevier.

Triethylbenzylammonium Perchlorate

Triethylbenzylammonium perchlorate underwent a reversible first-order IPT at approximately 196 K with a thermal hysteresis of 18 K, as shown by sharp endothermic and exothermic peaks in DSC measurements. In the same temperature range, the dielectric permittivity showed step-like changes, which further supported the discontinuous character of the transition. Variable-temperature SCXRD showed that the crystal structure changed from orthorhombic Pbcm at room temperature to Pbca at low temperature, and the unit cell volume doubled at the same time. The transition is described as isosymmetric by the authors; however, it must be noted that the two space groups are distinct and this classification is based on the preservation of the same orthorhombic point symmetry (D_{2h}) rather than strict space-group identity.

The main structural difference in the phases was the orientation and degree of order of the perchlorate anions, which were highly disordered at higher temperatures but became ordered during cooling. Modifications in the hydrogen-bonding network between cations and anions were also found, implying a cooperative role of weak hydrogen bond interactions in the formation of the low-temperature phase. Thermodynamic analysis revealed changes in entropy that were consistent with an order–disorder mechanism, suggesting that the change was caused by the reorientational dynamics of ClO_4^- anions [26].

5.3. Silicate Minerals and Orthopyroxenes

Paracelsian

High-pressure synchrotron SCXRD analysis of paracelsian ($\text{BaAl}_2\text{Si}_2\text{O}_8$) revealed a sequence of three pressure-induced polymorphic transitions up to 32 GPa. The first transition

that occurred between 3 and 6 GPa was found to be isosymmetric ($P2_1/c \rightarrow P2_1/c$). It was marked through the gradual formation of additional Al–O and Si–O bonds. This anomalous mechanism created three different intermediate states (IIa, IIb, and IIc), underscoring the role of fivefold coordination in the densification of tetrahedral frameworks [32].

Orthoenstatite

MD simulations of orthoenstatite ($\text{Mg}_2\text{Si}_2\text{O}_6$) showed a first-order IPT at ~ 1230 K, producing a distinct high-temperature orthorhombic polymorph with the same space group (Pbca) as the low-temperature form. The transition was characterized by discontinuous changes in unit-cell parameters and volume, which were associated with silicate chain stretching and switching of the M2–O3B bonds. These bonds are links between magnesium cations occupying the M2 crystallographic site in the orthoenstatite structure and the bridging oxygen atoms (O3B) of the silicate chains. Despite their identical symmetry, the two phases showed distinct structural differences, particularly in silicate chain geometry and Mg–O coordination. The simulated high-temperature structure was remarkably close to the results from in situ X-ray studies, indicating the possibility of its existence as a stable phase at high temperature [9].

Orthopyroxene

HTXRD studies on the Ca-bearing orthorhombic pyroxene composition $(\text{Ca}_{0.8}\text{Mg}_{1.8})\text{Si}_2\text{O}_6$ showed a reversible structural transition at approximately 1170°C , with discontinuous changes volume and unit-cell parameters. The transition was determined to be first-order and isosymmetric. The high-temperature orthopyroxene was found to be thermodynamically distinct from the low-temperature orthoenstatite, despite preserving the same crystallographic symmetry [66].

6. Conclusions

The increasing amount of research on IPTs emphasizes the extraordinary structural versatility of crystalline solids in response to external factors like pressure and temperature [79]. The reviewed research papers indicate that IPTs, despite maintaining overall crystallographic symmetry, can lead to significant reorganizations of hydrogen-bond networks, conformational changes, and anisotropic lattice responses. The prevalent theme of these transitions is the delicate balance among local molecular flexibility, cooperative intermolecular interactions, and external constraints, resulting in discontinuous yet symmetry-preserving transformations.

The hydrogen bond reorganization is a primary structural driver in organic compounds. For example, L-histidine and L-serine undergo pressure-induced IPTs, which enable the crystal to accommodate compression without disrupting the space group symmetry due to cooperative changes in hydrogen-bond geometry. In L-serine, two consecutive isosymmetric transitions were observed at 5.3 and 7.8 GPa, demonstrating a rare instance of sequential symmetry-preserving polymorphism [28,48]. Additionally, DL-cysteine revealed that the same isosymmetric polymorph can be reached either by cooling or by compression [33]. This shows that pressure and temperature are both equally effective at reorganizing hydrogen-bonded frameworks.

Conformational flexibility represents another significant mechanism for inducing IPTs. In α -glycylglycine, the bending of the backbone and the rotation of terminal groups at pressures exceeding approximately 6.7 GPa resulted in a reorganized hydrogen-bond network, while maintaining monoclinic symmetry. Computational results indicated the existence of multiple nearly degenerate polymorphs, suggesting that isosymmetric transitions frequently occur in shallow energy landscapes that allow for several closely related structures [45]. A similar mechanism was observed in pharmaceutical systems, for example,

ibuprofen lysine salt and estradiol valerate displayed reversible IPTs driven by side-chain torsional alterations and minor reorganization of hydrogen bonding, which have significant implications for drug formulation and stability [53,60,69].

Dynamic disorder–order processes can be the driving force behind IPTs, in addition to hydrogen bonding. The imidazole derivative 2-(3,5-bis(trifluoromethyl)phenyl)-4,5-dihydro-1H-imidazole demonstrated low-temperature IPT linked to the freezing of CF_3 group rotations, resulting in significant anisotropic lattice behavior, including uniaxial negative thermal expansion [63]. In BTBT-C4OH, a temperature-driven isosymmetric crossover was observed as a transition from positive to negative uniaxial thermal expansion, indicating that IPTs can arise from subtle dynamical rearrangements of herringbone packing [68].

In several reviewed cases, IPTs demonstrated significant anisotropic lattice responses. Biurea underwent a first-order transition at approximately 0.6 GPa, which was characterized by anisotropic modifications of hydrogen bonds and negative linear compressibility in one crystallographic direction [3]. Similarly, $\text{Co}(\text{IO}_3)_2$ and $\text{Zn}(\text{IO}_3)_2$ exhibited IPTs, where iodine polyhedra distortions cause counterintuitive expansions along lattice axes [42,44]. This illustrates how stereoactive lone pairs enable unconventional elastic responses while maintaining symmetry.

The functional consequences are a significant aspect of IPTs. The emergence of disordered and ordered high-pressure polymorphs (γ and δ phases) in resorcinol is determined by the compression rate, with both phases displaying a broad photoluminescence band associated with excimer formation [1]. In rubrene, a high-pressure IPT involved reorganization of π – π and $\text{C-H}\cdots\pi$ contacts, directly influencing charge transport properties [35]. This is an example of how such transitions can modulate the performance of organic semiconductors. In ionic systems, hexathiocyanate thulium(III) salts exhibited IPTs that were associated with cation disordering and were accompanied by strong dielectric anomalies [65]. This suggests that they have the potential for switchable dielectric applications.

Another recurring theme is the role of kinetic effects. Resorcinol is an example of how rapid compression can bypass the $\alpha \rightarrow \beta$ transition, resulting in a distinct ordered phase (δ), whereas slow compression supports the stabilization of a disordered polymorph (γ) [1]. Similarly, the IPT's occurrence in clathrate systems like hydroquinone–formic acid is dependent upon the choice of the pressure-transmitting medium, emphasizing the transitions' sensitivity to external factors [38].

In inorganic compounds, IPTs typically arise from polyhedral distortions and alterations in coordination. PbF_2 underwent an isosymmetric transition from a cotunnite-type to a Co_2Si -type structure at approximately 10 GPa, accompanied by an increase in coordination from 9 to 10 [30]. Na_3MnF_6 experienced a distinctive IPT characterized by a shift in Jahn–Teller distortion axes, illustrating a rare instance in which electronic degeneracy directly drives a transition [48]. These examples highlight that IPTs in inorganic frameworks usually reflect the cooperative modifications of coordination environments, rather than changes in conformation or hydrogen-bond reorganizations.

All together, these examples show that IPTs, while preserving symmetry, constitute varied types of transformations characterized by unique structural factors: hydrogen bonding, conformational dynamics, polyhedral flexibility, dynamic disorder, or electronic effects. They usually generate significant anisotropy in lattice response, exhibit high sensitivity to kinetic conditions, and directly impact functional properties, including optical luminescence, dielectric behavior, electronic transport, and pharmaceutical performance. The evidence indicates that IPTs should not be viewed as uncommon crystallographic anomalies, but as a general structural adaptation strategy employed by various mate-

rials, ranging from simple salts to complex pharmaceuticals, in order to accommodate external stimuli.

Across the surveyed systems, the principal microscopic drivers of IPTs are hydrogen-bond reallocation, conformational torsions, and order–disorder freezing, while their first-order character is evidenced by enthalpy jumps and anisotropic compressibility. These features connect IPTs to shallow energy landscapes and make them attractive for responsive-material design.

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Abbreviations

The following abbreviations are used in this manuscript:

ADXRD	Angle-Dispersive X-ray Diffraction
ADP	Atomic Displacement Parameter
aiMD	Ab Initio Molecular Dynamics
CN	Coordination Number
CSP	Crystal Structure Prediction
DFT	Density Functional Theory
DSC	Differential Scanning Calorimetry
DTA	Differential Thermal Analysis
EDX	Energy-Dispersive X-ray Spectroscopy
FT-IR	Fourier-Transform Infrared Spectroscopy
HRXRD	High-Resolution X-ray Diffraction
IPT	Isosymmetric Phase Transition
IR	Infrared Spectroscopy
MD	Molecular Dynamics
ND	Neutron Diffraction
ssNMR	Solid-State Nuclear Magnetic Resonance
NPD	Neutron Powder Diffraction
NTE	Negative Thermal Expansion
PC	Plastic Crystalline
PFY-XAS	Partial Fluorescence Yield–X-ray Absorption Spectroscopy
PTE	Positive Thermal Expansion
PL	Photoluminescence
PXRD	Powder X-ray Diffraction
SCXRD	Single-Crystal X-ray Diffraction

TEM	Transmission Electron Microscopy
TLS	Translation–Liberation–Screw
TGA	Thermogravimetric Analysis
UV-vis	Ultraviolet–Visible Absorption Spectroscopy
XRD	X-ray Diffraction
XRPD	X-ray Powder Diffraction
ZTE	Zero Thermal Expansion

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