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# Potential and challenges of engineering mechanically flexible molecular crystals

as challenges faced in predicting/designing mechanically compliant crystalline compounds.

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### 1. Introduction

Crystals are known to exhibit growth, transformation, locomotion, and response to stimuli based on the complexity of their assembly. To address responses, extensive work in understanding the micro and macroscopic changes occurring

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in the crystal as a consequence of thermal, mechanical, and photo-irradiated stimuli has been performed.<sup>1-6</sup> As per the earlier construct, the reputation of molecular crystals as inflexible or brittle entities has now been gradually amended in past two decades.<sup>7-9</sup> With the help of upgraded experimental techniques and computational tools, a detailed exploration of mechanically reconfigurable crystals is emerging. As a result of consistent developments in this area in the past one decade, our understanding of the microscopic mechanism during the process of mechanical deformation,



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to say the least, is progressive. Thereby, for innumerable systems, this exercise has gradually led to the establishment of structure-property relationships, which has further evolved into structure-property-function for unconventional soft crystalline materials.<sup>2,9–11</sup> The research in this field is still in the developmental stage and has led to a basic division with respect to the type of macroscopic response shown by a crystal when subjected to mechanical force, *i.e.*, elastic/ reversible deformation, where the crystal regains/restores its original shape as soon as the force is retrieved and plastic/ irreversible deformation, where the crystal stays in a deformed state and does not restore on its own on the retrieval of force.<sup>7,8,12-14</sup> This categorization can also be distinguished through the range of strain that these two types of response elicit in the stress-strain profile.<sup>15,16</sup> Generally, coordination polymers are known to be rigid and brittle but recent investigations on flexible crystals of such systems have proved to be insightful.<sup>17,18</sup>

This highlight intends to give an overview on recent establishments in the field of mechanically flexible molecular crystals, displaying elastic, plastic, and elastic-plastic deformation on applying force. The main aim is to categorically focus attention on the significance of topology and energetics of intermolecular interactions involved in segregating molecular crystals lying in the spectrum of elastic-plastic materials. This collation is inclusive of organic as well as hybrid (coordination polymer) systems demonstrating mechanical compliance, which could help in aiming at devising a universally applicable model. As discussed further, techniques such as nanoindentation, and flexure test 3-point bending, supported with computational methods such as 3-D elastic mapping, attachment energy, and interaction energy through energy frameworks utilized in specific cases have proved to be highly beneficial to justify the respective mechanical response exhibited by the crystal. Together, it provides examples of the methodological engineering of molecular crystals showing different mechanical responses via derivatization, integrating solvent molecules, or other co-formers in the formation of multi-component phase and navigation through their polymorphs. These can assist in the design and engineering of new organic compounds, coordination polymers and hybrid materials with tunable compliance. In addition, they encompass different molecular compliant crystals exhibiting multi-functional properties. A bird's eye view, on the present state of this field of research, along with challenges faced in elucidating properties exhibited by crystalline systems, is elaborated further.

# 2. Mechanical deformation in molecular crystals

#### 2.1. Elastic deformation

The reversible deformation of an acicular/needle/thin plateshaped crystal under external applied stress refers to elastic bending, *i.e.*, restoration/regaining of the initial shape and size of the crystal as soon as the external force is removed.<sup>12,17</sup> The proposed criteria for elastic characteristics in crystals are the similar chemical interactions along the orthogonal directions, i.e., isotropy in packing, nonavailability of a slip-plane, and interlocked/interdigitated crystalline assembly.<sup>12,13</sup> The collective role of weak interactions is realized to behave as 'structural buffers', which helps in adapting to the induced strain during elastic deformation.<sup>19,20</sup> Desiraju et al. utilized the principle of crystal engineering based on  $\sigma$  and  $\pi$ -hole synthons to design two-component cocrystals with high elasticity.14 These criteria pertain to justify isolated cases and require systematic analysis in a wide variety of compounds, especially in conformationally flexible, non-rigid, and non-stacking molecules. Some of the recent investigations involving crystal engineering approach, includes the derivatization of molecules, co-crystallization, and solvate formation, have now been adapted for inducing and tuning the extent of elasticity in crystals and are collated below.<sup>21</sup>

The mapping of the structural changes associated with the elastic deformation of crystals using micro-focus X-ray radiation (at a synchrotron facility) for elastically bendable, acicular crystals of bis(acetylacetonato)copper(II) [A(I) in Scheme 1] by Worthy et al. contradicted the postulated criteria for the elastic bending of molecular crystals, *i.e.*, (1) molecules connected isotropically by weak and dispersive interactions; (2) crystal packing in which the molecules are interlocked to prevent slippage.<sup>22</sup> The tensile elasticity test of the crystal revealed stretching of 4.4% in length before breaking. On performing sophisticated micro-focus X-ray diffraction experiments on the bent site of the crystals, it was concluded that intermolecular interactions in the  $[Cu(acac)_2]$ crystals are anisotropic with relatively strong  $\pi$ -stacking in one dimension and dispersive interactions in others. It was also observed that the molecules are not interlocked. In response to the mechanical stress exerted on the crystal, the molecules rotate and this rotation facilitates simultaneous compression and expansion along different faces. Hence, the authors suggested that for elastic contortions, the molecules must be able to reorganize reversibly to allow the compression of the crystal along the concave side of the crystal with subsequent expansion along the convex side.

Another methodological study on the coordination polymer of Cd( $\pi$ ) halides [A(II) in Scheme 1] revealed some intriguing points specifically with respect to the design of flexible molecular crystals.<sup>23</sup> With the careful choice of metal ion and ligands interlinked *via* directional but substantially weaker intermolecular interactions, the degree of anisotropy in the structure can be modulated, which can consequently help in tuning the mechanical flexibility. Seven complexes were synthesized by combining CdX<sub>2</sub> (X–Cl, Br, I) with 3 different halopyrazines, which have similar packing as that of cadmium( $\pi$ ) in an octahedral geometry (as the anchoring point), forming 1D polymeric chain with neighboring Cd( $\pi$ ) centers bridged by two halide ions. These 1D chains are interlinked *via* C–H···N/Br in the (001) plane and tapes of the



Scheme 1 Molecules investigated for exhibiting A (I–V, purple)- elastic deformation; B (I–IX, yellow)- plastic deformation; C (I–IV, green)- elastic and plastic in a single crystal; D (I–IV, blue)- distinct compliance for each polymorph; E (I, II, red)- distinct compliance on derivatization; F (I–III, grey)- different mechanical response on forming multi- component systems, relative to the parent compound. The respective article discussing the mechanical deformation corresponding to the molecule is cited in superscript (in blue).

C-X···X-Cd halogen bond in the (010) plane. The supramolecular interactions are different along the two axes but the arrangement of the polymeric chains from two different crystal faces are similar, thereby exhibiting 2D elasticity. A systematic analysis of the crystalline arrangement in these structures elaborated the significance of non-covalent interactions, with distinct differences with respect to the extent of the elasticity. As mentioned in Fig. 1., for the class of compounds showing high (5–7) and moderate (4) elasticity, the halogen bonded tapes were further linked *via* C-H···N hydrogen bonds, which are orthogonal to the length of the crystal. The single crystals for the set of compounds

exhibiting high elasticity had additional C-H···X-Cd hydrogen bonds, which ensures pronounced elasticity. The crystals showing a slight extent of elasticity (1–3) primarily contained halogen-bonded interactions without other orthogonal, structure-directing non-covalent forces. This suggests that the intermolecular interactions, in a plane perpendicular to the length of crystal, play a significant role in tuning the elasticity/reversible flexible bending in crystals.

Calvin Sun and coworkers explored the mechanical response of a single component drug, celeoxib [A(III) in Scheme 1], which responds to mechanical force on its major faces in an elastic manner, *i.e.*, the deformation is reversible in nature.<sup>24</sup>



**Fig. 1** a) Extent of relative elasticity as described by the bending strain ( $\varepsilon$ ); crystals were classified as highly elastic (5–7, green), moderately elastic (4, yellow), and slightly elastic (1–3, red). b) Crystal packing of 6 (representative of 5–7; left), 4 (middle) and 2 (representative of 1–3; right) viewed in the (100) plane; crystal faces (011)/(01–1)/(01–1)/(01–1) are indicated as black lines. Reproduced from ref. 23. With permission from the Wiley-VCH Verlag GmbH & Co. KGaA, Copyright 2018.

This mechanical behavior is justified by a corrugated layer formed between the CEL dimers connected by C-H··· $\pi$  hydrogen bonds, which are interlocked *via* the C-H···O dimer and C-H···F interactions along the (001) plane. This prevents long-range molecular movement and avoids slippage and the presence of multiple dispersive interactions in orthogonal direction allows for 'structural buffering'. The elastic bending mechanistic model predicts inhomogeneous molecular distribution in the lattice of the bent crystal, which is also supported by micro-Raman spectroscopy (as shown in Fig. 2), where the broadening and shifting in the bending modes of the lattice vibrations and aromatic C-H bonds are observed for three different domains, namely, the inner arc, the middle part, and the outer arc.

With progressing work in the field, several elastic bent and/or twisted crystals are also known to show efficacy as optical waveguides, which indicates towards the applicability of flexible crystalline material in the field of optoelectronics.<sup>25</sup> Also, systematic work on the doping of an elastic but non-fluorescent crystal with a highly emissive but poor crystalline material yielded a highly elastic and emissive crystal, which could be utilized as optical waveguides and amplify the spontaneous emission in both the straight and bent states.<sup>26</sup> The mechanical and optical properties of a Schiff base, (E)-1-(4-(dimethylamino)phenyl)iminomethyl-2hydroxyl-napthalene [A(IV) in Scheme 1], were investigated by Zhang and coworkers.<sup>27</sup> The crystal arrangement viewed down the (010) plane represents  $\pi$ - $\pi$  stacking and C-H··· $\pi$ along the needle axis (a-axis) with C-H...O connecting the parallel stacks, which restricts relative slippage. The elastic bending of the crystal is accommodated through expansion and contraction of the outer and inner arcs along the crystal length constituting  $\pi$ -stacks. Together, the optical waveguide property was initially detected from the brighter emission of the crystal tip than the body when irradiated with a UV lamp. The bent crystal was also irradiated at different positions of the crystal using a 355 nm laser and recording the emission spectrum corresponding to each irradiation position at one tip of the crystal, the distance dependent emission spectra was first obtained. The emission spectra at the tip were seen to gradually decrease when the distance between the tip and the irradiated distance increased due to the loss of more emitted light for a longer propagation distance.



Fig. 2 Raman spectra corresponding to the bent and straight crystal of CEL with red and blue circles indicating the point of data collection (inner arc and outer arc, respectively), (a) lattice vibration, and (b) aromatic symmetric in-plane bending  $\delta$ (C–H) modes of inner and outer arc of a bent CEL single crystal, as well as in the non-strained straight orientation. Adapted from ref. 24 with permission from the American Chemical Society, Copyright 2019. https://pubs.acs.org/doi/10.1021/acs.chemmater.9b00040.

Similar to the  $Cu(acac)_2$  elastic crystals, a recent investigation on the formation of the elastic fibril of Ni<sup>II</sup>(salophen) [A(V) in Scheme 1] complex reflected the anisotropic crystalline arrangement of the molecules in the solid state, wherein the molecule adapts a slightly curved shape, which are stacked *via* Ni $\cdots \pi$  and C $\cdots$ O interactions.<sup>28</sup> This 1D column interacts with the adjacent column via C- $H \cdots \pi$  interactions. The anisotropic interaction topology is confirmed via computing the interaction energy between the dimers utilizing the energy frameworks. Micro-focus synchrotron XRD was employed to evaluate the mechanism of elastic bending. The diffraction on the bent section gave elongated diffraction spots, which supports the stretching/ compressing of non-covalent interactions between the molecules with a loss of long-range ordering in the crystals. Simultaneously, the solvate (1.5 chloroform) of the same coordination polymer exhibited brittle behavior as the chloroform molecules sit between the Ni $\cdots \pi$  columns and are stabilized via relatively stronger hydrogen bonds, which inhibits easy deformative-restorative movement of the columns that facilitate elastic bending.

#### 2.2. Plastic deformation

As a result of applying force on a single crystal, irreversible deformation in the crystal results in plastic deformation. The deformation may be a consequence of gliding of layers/ column.<sup>7</sup> With respect to the stress–strain curve, a plastically bendable crystal has to overcome an elastic regime.<sup>15,16</sup> With exception to a few recent cases,<sup>29</sup> a majority of plastically deformed crystals are rationalized on the basis of anisotropic crystal packing with strong and weak interactions orthogonal to each other. This introduced the concept of slip planes, generally constituting weaker interactions with low rugosity, which is believed to aid the mechanical behavior. The plastic bending of crystals is proposed to occur by delamination,

sliding of the crystal layers, and reformation of the weak interactions such as  $\pi$ - $\pi$  interactions, halogen bonds, and van der Waals interactions.<sup>7,8,11,16,30</sup> Based on these criteria, a recent exploration of 1D and 2D plastically bendable twisting into helix, have been exhaustively crystals, investigated. Saha and co-workers elaborated the significance of halogen bonding in hand-twisted helical crystals via the retrosynthesis strategy using supramolecular synthons for substituted benzoates.<sup>31,32</sup> In addition, the evidence of molecular perturbation through IR spectroscopy, micro-Raman, micro-X-ray, and other computational techniques have also been observed.<sup>33,34</sup> The novel cases of plastically deformed crystals, which are restorable, i.e., they can regain their shape and size on exerting force from an appropriate direction and do not undergo delamination or exfoliation, are of utmost importance. Firstly, such systems could help in rationalizing and hypothesizing a suitable model for the plastic response exhibited by the crystal, secondly, they could help in placing such systems suitably in the elastic-plastic spectrum and thirdly, they open up the opportunity to explore phenomenon such as superelasticity, shape memory, and ferroelasticity.35-38 The section below highlights the recent advances that help in gaining an improved perspective with respect to the current state of research for plastically bendable systems.

After extensive work on the mechanical properties of halogenated benzenes<sup>8</sup> and 4-halobenzonitriles,<sup>39,40</sup> Barbour and coworkers investigated 2D plastic bending in 4-bromobenzonitriles [B(I) in Scheme 1], which could twist into helices.<sup>41</sup> The crystalline arrangement was stabilized via  $\pi$ -stacks (Br $\cdots\pi$ ,  $\pi\cdots\pi$ ) perpendicular to the (010) bending face and soft halogen bonds (C–N $\cdots$ Br) parallel to the (010) bending face. Here, the stacking interactions are relatively strong in comparison to other orthogonal van der Waals contacts. The significance of two orthogonal 1D plastic deformations (2D) is that these allow for twisting or helical

deformation. In addition, changes in the melting point due to bending have also been discussed.With studies elaborating the twisting mechanism in molecular crystals,<sup>31,32</sup> an intriguing study conducted by Sun and co-workers on single crystals of caffeine hydrate [B(II) in Scheme 1] showed 2D plastic deformation by the application of mechanical force on the crystal.<sup>42</sup> The investigation elaborates the rationale behind the bending of facets of (011)/(0-1-1) and (01-1)/(0-1-1)(0-11) in the pharmaceutical crystal with exceptional tabletability. The water molecule forms O-H…N with the imidazole of caffeine and catemeric infinite chain with itself along the [100] direction, which also facilitates the stacking of caffeine molecules. The weak C-H…O dimer in one direction and linear C-H···O hydrogen bond interactions in the other direction (approx. 73°) form a 2D molecular arrangement, which is responsible for identical packing in (0-11) and (011) faces, thereby showing 2D plastic mechanical behavior. The higher plasticity and tabletability

for 2D twistable crystals are reasonable to anticipate as it has been observed for 1D plastic crystals that these form a larger bonding area between adjacent particles by undergoing extensive plastic deformation *via* the slip. This was found to be true on comparing the tabletability of this hydrate with other 1D plastic bendable crystals as well.

With a surge in mechanistic exploration of 2D plastic crystals, a different model was proposed by Emmerling and co-workers on the single crystal of 2D plastically deformed crystals of a 1D coordination polymer of  $[Zn(\mu-Cl)_2(3,5-dichloropyridine)_2]_n$  [B(III) in Scheme 1].<sup>43</sup> They suggested that mechanical bending occurs by the displacement of the coordination polymer. The mechanical properties on the (-110) face for the straight and the bent crystal were quantified by AFM force-distance curve. The results of AFM and micro-focus X-ray diffraction show that the single crystallinity remains unchanged at small deformation, whereas, for large deformation, the bent site results in a



**Fig. 3** Vibrational spectra of the linear and bent B(III) crystal. a) Unpolarized Raman spectra collected at different locations in the crystal at different stages of plastic bending. The Raman spectra are displayed alongside the corresponding crystal and the laser spot is indicated as a red dot. The crystals are denoted as: S: straight; OA: outer arc; MA: middle arc; IA: inner arc; and SP: straight part of a bent crystal. b) THz-TD (time domain) spectra collected for the *ca.* 908 bent crystal (blue) and for a straight crystal (black). c) Schematic representation of the spaghetti model for the bending of the coordination polymer. Note that each bundle of straws represents a cluster of CP chains. Reproduced from ref. 43. With permission from the authors, Copyright 2019. Published by Wiley-VCH Verlag GmbH & Co. KGaA.

highly polycrystalline phase. This was further supported *via* micro-Raman and THz-TD spectroscopy, which reflected the loss of long-range order. These experiments showed that the stress of bending is accumulated between the CP chain and not within. As depicted in Fig. 3, a new proposal named the 'Spaghetti model' was proposed, where the initial stress leads to the slippage of the CP chain perpendicular to the bend. Concurrently, a cluster of chains are displaced parallel to the bend and become interwoven and separated on bending. Plastic deformation requires the breaking of interchain CP…CP interactions. This investigation highlighted a different approach towards mechanistic models facilitating plastic bending in crystals.

With different bending models proposed, an extensive investigation conducted by Chopra et al. experimentally supported the slippage mechanism in plastically bendable and recoverable, phase-pure single crystals of N-(3-ethynylphenyl)-3fluoro-4-(trifluoromethyl)benzamide [B(IV) in Scheme 1], which are devoid of delamination on bending.44 Utilizing micro-focus with synchrotron radiation, SEM, bulk and local indentation experiments helped in clarifying the bending mechanism down the (100) face. Through micro-focus X-ray diffraction, the possibility of two slip planes running parallel to the length of the crystal, *i.e.*, the (100) plane with the ethynyl group involved weak interactions and the (200) plane with weak  $CF_3 \cdots CF_3$ interactions, where the slippage predominantly occurs and the CF<sub>3</sub> groups slide past each other and reform via cooperative interchange between the adjacent layers (Fig. 4a-e). With 40 datasets collected across the bent part of the crystal, no phase change was observed and the dimensions are the same as those obtained for the unbent sample, which helps in carving out the state-of-the-art mechanism for restorative plastic deformation in single crystals of the compound (Fig. 4f). In addition, the nanoindentation experiment revealed that the E<sub>ind</sub> and H varies

from 0.62  $\pm$  0.12 GPa, 74.50  $\pm$  5 MPa to 3.97  $\pm$  0.45GPa, 330.3  $\pm$  15 MPa from the bent to the straight region of the crystal, thereby addressing the softer bent region.

An interesting investigation conducted on terephthalic acid [B(V) in Scheme 1] by Naumov and coworkers showed that single crystals of Form II undergo plastic deformation when subjected to pressure on the (010) face.45 The coexistence of two phases in the bent region was confirmed by SEM, AFM, and micro-XRD and helps to establish the mechanism for mechanical as well as the observed additional thermal response, *i.e.*, the exhibition of the shape memory effect. Both forms differ in the relative position of the adjacent layers. Bending occurs due to the gliding of the parallel layers and the re-formation of inter-layer bonds. The application of localized stress induces a partial phase transition and the two-phases coexist in the bent region (Fig. 5b). This plastic deformation does not recover at room temperature. Hence, one phase can be converted to another by heating or cooling, which results in a decrease in the bending angle and the recovery of the straight shape of the crystal, similar to the shape memory effect (Fig. 5a and c). This extensive work carried out on the terephthalic acid crystals provides examples of pressure induced phasetransition in a bending crystal where two phases co-exist and establishes an unreported mechanism of crystal bending.

In recent years, the realm of mechanically deformed crystals has not been limited to one kind of response but has evolved to be applied in the field of photo-luminescence as flexible optical waveguides. Naumov and co-workers crystallized fluorescent 9,10-dicyanoanthracene [B(VI) in Scheme 1], which shows 2D plasticity where weak van der Waals interactions between the  $\pi$ - stacks helps in the smooth movement along the slip planes (001) and (010), and facilitates slippage.<sup>46</sup> In addition to plastic deformation, these act as both active and



**Fig. 4** (a-c) Crystal packing of *N*-(3-ethynylphenyl)-3-fluoro-4-(trifluoromethyl)benzamide, B(IV). Strong N-H···O hydrogen bonds extend along [010]. Ethynyl interactions of type  $C(sp/sp^2)-H\cdots\pi(sp)$ , and  $\pi(sp)\cdots\pi(sp)$  and with weak  $CF_3\cdots CF_3$  and  $C(sp^2)-H\cdots F$  contacts form the bilayers along [100]. (d) The bent crystal used for a mapping study. The yellow arrow shows the area covered by the mapping experiment on the (100) face. (e) Sample diffraction pattern obtained at position 15. (f) Plot of cell axes obtained. It is noted that positions 1–13 and 30–40 were positioned off the edges of the crystal. Reproduced from ref. 44 with permission from The Royal Society of Chemistry, Copyright 2020.

![](_page_7_Figure_2.jpeg)

**Fig. 5** Mechanism of phase transition upon bending and shape-memory effect of a Terephthalic acid crystal (B(V)). (a.) Transformation of the crystal between forms II and I, and the relationship between the unit cells in the two phases. (a1) Transformation between the unit cell orientations of form II and form I viewed normal to the crystallographic faces (0–10) and (010). (a2) Images of the crystal in the two phases with face indices. (a3) Variation in the dimensions and shape of the unit cell shown as different views. (b.) Mechanism of transformation of the two-dimensional crystal lattice (cartoon) during the phase transition induced by the application of local pressure including the structures of the two phases and the molecular orientation in each phase. (b1) The crystal of form II and the schematic of its lattice before bending. The straight crystal of form II can be bent by applying pressure on its (010) or (0–10) face. The lattice here is shown along the crystallographic [100] direction. (b2) The crystal and the schematic of its lattice after bending. The bent crystal is a bimorph with two coexistent phases in the bent region separated by a phase boundary. (c.) Mechanism of the shape-restorative effect. (c1) A bimorph in the kink of the bent crystal, shown with its lattice and unit cell. Unit cell orientations of both form II and form I in the bent region. (c2) Partial restoration of the straight shape of the crystal and schematic representation of the underlying phase transition to form I. Reproduced from ref. 45. With permission from the authors, Copyright 2019. Published by Springer Nature.

passive optical waveguide.<sup>47,48</sup> This material has been established to bent plastically to acute angles without fracturing and transduce light both by transmission and

emission, and the mode of light transduction can be switched by changing the excitation wavelength. This work subtly utilizes the understanding of the crystalline assembly of the compound

to rationalize the mechanical and optical properties exhibited by its single crystal.

Recently, the exploration of irreversible mechanical bending, down the (001) face with a 3-fold enhancement in the fluorescence of the bent crystal of green fluorescent protein chromophore (GFPC) analogue, ethyl[(4Z)-2-methyl-5oxo-4-(2,3,4-trimethoxybenzylidene)-4,5-dihydro-1H- imidazol-1-yl]acetate [B(VII) in Scheme 1], has been carried out by Reddy and co-workers.<sup>49</sup> The structure has  $\pi$ -stacking along the *a*-axis with a possible slip plane along (001), where the methoxy group is stabilized by weaker C-H···O hydrogen bond ( $E_{tot}$  obtained from energy frameworks = -16 kJ mol<sup>-1</sup>). The  $\pi$ -stacks have shown to be affected due to the mutual rotation or splaying upon slippage in case of plastic deformation. Moreover, the molecules are in a different environment upon deformation and the fluorescence of GFPC analogues is known to be sensitive to the environment. Hence, the strained structure is believed to play a significant role in the enhancement of emission of the bent crystal.

With most of the systems under discussion dominated by  $\pi$ - $\pi$  stacking, a disparate investigation on the hydrate of two blockbuster zwitterionic drugs exhibiting plastically bendable faces showed that the presence of  $\pi$ -stacking or an alternation of 2D networks with orthogonal weak dispersive forces are not the ultimate criteria for exhibiting the characteristics of plastic deformation. On reviewing, it was revealed that plastic deformation can occur even in the case of mechanically and chemically interlocked hydrates of compounds, as seen in the case of pregabalin and gabapentin [B(VIII) in Scheme 1].<sup>50,51</sup> For hydrated forms of both the drugs, the zwitterions are arranged along the [010] axis and intercalated by H<sub>2</sub>O so that the double molecular layers of drugs are separated into parallel planes. The strong hydrogen bonds between the drug and the water molecules brings each layer closer and yet prevents interdigitation.

Plastic bending is exhibited on applying a force perpendicular to the *c*-axis, which results in the sliding of successive layers along the *b*-axis. As shown in Fig. 6, the quick breaking and reforming of bonds is expected to occur either between water and zwitterions or dispersion forces between the non-polar layers. As the deformation is not observed in anhydrous drugs with similar packing (excluding strong H-bond between water and zwitterions), therefore, it is safe to state that strong hydrogen bonds between water and zwitterions together with the high mobility of these molecules enables the quick rearrangement of non-covalent interactions, thereby imparting mechanical flexibility to the crystal.

As an advancement in the exploration of irreversibly deformed crystals, a diversification between plastically bendable and plastic crystal was further exemplified by a thorough investigation performed by Reddy and coworkers on globular aminoboranes molecules, namely, BH<sub>3</sub>NMe<sub>3</sub>, BF<sub>3</sub>NMe<sub>3</sub>, and BH<sub>3</sub>NHMe<sub>2</sub> [B(IX) in Scheme 1].<sup>52</sup> Due to the presence of a facile slip plane and restricted rotation across the B-N bond due to the presence of the strong dihydrogen bond, BH<sub>3</sub>NHMe<sub>2</sub> showed 1D plastic bending. This was further corroborated by energy frameworks and the weak dispersive forces amongst the columnar packing of BH<sub>3</sub>NMe<sub>3</sub> and BF<sub>3</sub>NMe<sub>3</sub> are responsible for the observed plastic characteristics, such as the exceptional ductility and malleability of the single crystal. High globularity (G) and low asphericity  $(\Omega)$  also support plasticity in such compounds, which show extensive mechanical deformation such as tensile stretching, twisting, compression, and thinning. Nanoindentation experiments support the softer nature of BH<sub>3</sub>NMe<sub>3</sub> when compared to BH<sub>3</sub>NHMe<sub>2</sub>. Further, PXRD experiments on a thin film made by applying stress to a number of crystals revealed a loss of symmetry from rhombohedral to monoclinic via three-fold rotation for

![](_page_8_Figure_8.jpeg)

Fig. 6 Schematic representation of the crystal packing of (a) pregabalin, (b) pregabalin form I, (c) pregabalin form II. Hydrogen bonding interactions are in green, selected hydrogen atoms have been omitted for clarity. Reproduced from ref. 50. With permission from the authors, Copyright 2019. Published by International Union of Crystallography.

BH<sub>3</sub>NMe<sub>3</sub>. For BF<sub>3</sub>NMe<sub>3</sub>, additional satellite peaks with preserved rhombohedral symmetry were recorded. The SCXRD of the deformed crystal showed elongated Bragg peaks due to large mosaicity. The PXRD fit and reflection statistics from SCXRD reveals the symmetry to be monoclinic for BH<sub>3</sub>NMe<sub>3</sub>. Consequently, after the progressive analysis of data, it was hypothesized that the deformation-induced phase transition of BH<sub>3</sub>NMe<sub>3</sub> is understood as stress dissipation in long range via twinning, where a small finite displacement of molecules from the mean position occurs, which helps in preserving the crystallinity of the sample. On the other hand, in BF<sub>3</sub>NMe<sub>3</sub>, a complex mechanism possibly involves twinning and (3 + 2) structural modulation due to mechanical deformation. This study, along with other such examples, helps in highlighting the potential of plastic crystals with exceptional mechanical plasticity and longrange order.53

#### 2.3. Elastic-plastic deformation

With evolving case studies, an interesting set of systems have surfaced, which can be elastically as well as plastically deformed on either being subjected to varied magnitudes of force or on being subjected to force on different faces of the same crystal. At first, such statements appear to be counterintuitive but on closer inspection, one can suggest that different mechanistic models can evolve with each and every investigation. The earlier criteria of isotropic packing for elastic/reversibly bendable crystals and anisotropic crystalline arrangement for plastically/irreversibly deformed crystals can be remodeled, which could bring forward some unique insights for designing flexible crystals with respect to crystal engineering.

Recently, elastic bending under external moderate stress and plastic bending under excessive stress were exhibited by the single crystals of 4,4'-dibromobenzil [C(I) in Scheme 1], *i.e.*, elasto-plastic crystal.<sup>54</sup> In addition, it also showed room temperature phosphorescence through crystallizationinduced phosphorescence, which gives green emission with band maxima at 514 nm with an average lifetime of 279 µs. The molecule forms chain through  $\pi$ - $\pi$  stacking and C-H···O interactions, which facilitates elastic bending along the (010) plane. The  $\pi$ -stacks provide a structural buffer for easy deformation and recovery. Also, the (-100) plane has type-II Br…Br halogen bonding with C-H…Br interactions, which are arranged in different directions, balancing each other and preventing slippage. Subsequently, the balance of multiple interactions should have several metastable states, *i.e.*, on providing average force, the weak interactions could prevent slippage and show elastic bending, whereas on the application of force with an increased magnitude, these weak interactions promote slippage and exhibit plastic deformation (when elastic strain is over 2.65%). It suggests that the crystalline arrangement should be in the intermediate region of anisotropic and isotropic packing. The emission intensity has an inverse relation with the distance

between the irradiated position and the emitting tip. Hence, the emission was recorded on the bent crystal upon irradiation by a 355 nm pulse laser on different points and it was observed that the optical loss coefficient increased on bending (straight =  $0.285 \text{ dB mm}^{-1}$ , elastic bent =  $0.306 \text{ dB} \text{ mm}^{-1}$ , plastic bent =  $0.307 \text{ dB mm}^{-1}$ ). Thereby, this is the first report where flexible optical waveguide of a phosphorescent crystal is realized in straight, elastically bent, and plastically bent crystals.

These sets of systems also include a co-crystal of conformationally selective e-OH cyclohexanol of vitamin D<sub>3</sub> cyclohexanol with a-OH form of 3α-cholesterol [C(II) in Scheme 1] in 1:2 ratio, which yielded a 3-fold helical hydrogen bond.<sup>55</sup> The major face (001)/(00-1) shows elastic bending, whereas the minor face along the length (100)/(-100)shows plastic bending. The e-OH and a-OH form a helix parallel to the (001) face with vdW interactions between the adjacent helix, which acts as slip planes and allows the gliding of helixes, thereby, facilitating plastic deformation. The backbone of the structure is a 1-D helix of substituted cyclohexanol and these helices are interlocked via weak van der Waals interactions between the alkyl chains, which promotes reversible bending in crystals, thus avoiding any slippage along this direction (as shown in Fig. 7). The packing in the co-crystal was compared with the structure of vitamin D<sub>3</sub>, where the co-crystal exhibits comparitively loose packing, which leads to the structural buffering of terminal alkyl chains and allows the stretching of intermolecular interactions on deformation. The synchrotron X-ray diffraction experiments at the elastically bent site showed dispersed Bragg's peak, indicating a loss of the long-range ordering at the bent site. To test the strategy implemented for designing flexible crystals with 3-fold hydrogen bonded helix consisting of a-OH···e-OH synthon in addition to soft alkyl chains co-crystallized with controlled stoichiometry, vitamin  $D_2$  was co-crystallized with 3 $\alpha$ -cholesterol. The co-crystal constituted the 3-fold helix with the absence of a facile slip plane, which renders elastic mechanical property to the crystal. Hence, the 3-fold helical backbone with/without the availability of alkyl chains may provide plastic/elastic deformation characteristics to the crystal.

Zhang et al., reported another set of keto-enol tautomer, (E)-1-(((3,5- dimethoxyphenyl)imino) methyl)naphthalen-2-ol (sensitive to humidity, C(III) in Scheme 1), where the enol form, CRY-G, shows plastic twisting and elastic bending, whereas the hydrate of keto form, CRY-Y, showcased only elastic bending.<sup>56</sup> The  $\pi$ -stacks along the *b*-axis facilitate inelastic bending by compression and expansion amongst the stacks. The molecule in CRY-Y, consisting of 2 water molecules, is richer in H-bonding with the primary contribution from C-H···O and O-H···O H-bonds. The hydrogen bonding network in the layered structure helps in the synergetic movement of the intra-layer movement, thereby facilitating elastic bending. The higher shear modulus for this form confirms the more difficult molecule slippage along the [100] direction. For CRY-G, twisting generates shearing stress on the cross-section. Spatial

![](_page_10_Figure_2.jpeg)

Fig. 7 A schematic representation of elastic and plastic bending of single crystals of co-crystal of vitamin  $D_3$  and cholesterol and the consequences at different levels of structural hierarchy. Reproduced from ref. 55. With permission from the Royal Society of Chemistry, Copyright 2019.

separation between the  $\pi$ -skeleton can cause long-range slippage along the [001] direction as well as the rotation of the  $\pi$ -skeleton around the central axis along the length of the crystal. The difference lies in the hydrogen bonding network, which makes the intra-layer  $\pi$ -skeleton synergistically move for CRY-G to facilitate plastic twisting as well as elastic bending. Due to the twistable character of CRY-G, it was possible to examine the influence of crystal twisting on the light-polarization property. The experiments were conducted on twisted crystals, demonstrating that the polarization direction of the emitted light can be controlled quantitatively by the twisting angle, which makes them polarization rotators. These innovative systems exhibit an unexplored spectrum of applications, which makes the study in the field of flexible crystals more intriguing.

Another exhaustive study on the single crystals of 2-(3isopropoxyphenyl)benzo[d][1,3,2]dioxaborole[C(IV) in Scheme 1], exhibiting plastic deformation and elastic twisting characteristics along with the propensity of self-healing, was conducted by Naumov and group.57 The (100) face shows plastic bending along with elastic twisting around the long axis [010], where the crystal returns to their original shape after the torque has been removed. The molecules are arranged head-tohead, forming alternating infinite chains interacting through  $\pi$ - $\pi$  interactions, which forms sheets. The force applied on the (100) face allows the gliding of the layers due to the presence of weak interactions between the layers, showcasing plastic behavior, which can be bent-unbent for several cycles. The restorative force at the interface helps in the partial repairing of the crystalline lattice. Subsequently, during elastic twisting, torsional strain is subjected in the [010] direction, *i.e.*, in the direction of  $\pi$ - $\pi$  interaction. As depicted in Fig. 8, a twist causes the stacks to strain as the stacked molecules rotate away from the optimal geometry. On removing the torque, the structure is retrieved by restoring the ideal configuration. The observation of self-healing in single crystals proved to be significant and was further explored. The dynamic nature of the ester bonds, *i.e.*, broken and reformed at room temperature, is well known. The plausible mechanism for self-healing, *i.e.*, metathesis and transesterification, were confirmed *via* several sets of experiments involving ball milling grinding, manual grinding, solution experiment in DMSO-d6, application of uniaxial pressure, and AFM adhesion experiment.

### 3. Tuning of mechanical properties

#### 3.1. Screening for polymorphs

Trimorphs of 4-bromophenyl-4-bromobenzoate [D(I) in Scheme 1] are known to show diverse mechanical properties.<sup>58</sup> Interestingly, the orientation and strength of halogen bonds decides the fate of the crystal. Form II is brittle in nature, whereas form I and III, exhibiting elastic and 2-D plastic deformation (with two bendable faces) as the mechanical response, respectively. Both forms are stabilized *via*  $\pi$ - $\pi$  stacking, which are connected to the other column by type II halogen bonds. In the unidirectional molecular orientation of form I, two chemically different bromines (Br1 attached to the carbonyl side and Br2 attached to the oxygen side of ester) form type I and type II halogen bonds) is aligned perpendicular to the major phase (001) and acts as a structural buffer, which helps in restoring the structure back

![](_page_11_Figure_2.jpeg)

**Fig. 8** Crystal structure of C(IV) and mechanism of plastic bending, elastic twisting, and breaking of its single crystals. During bending, the layers of the molecules slide past each other along the glide planes bound by  $\pi$ - $\pi$  interactions (the closest centroid-to-centroid distances are 3.545(1) and 3.628(1)). The twisting rotates the molecules around the [001] direction, which strains but does not break, the  $\pi$ - $\pi$  interactions. When force is applied in plane of the  $\pi$ - $\pi$  interactions, the crystal breaks. Reproduced from ref. 57. With permission from the Royal Society of Chemistry, Copyright 2020.

after the force is retracted. The  $\pi$ - $\pi$  stack along [010], which is primarily dispersive in nature, helps in accommodating the stress. On the other hand, the structural analysis of form III revealed a 2-D packing where the  $\pi$ - $\pi$  stacks along *a*-axis are connected to type II Br2···Br2 halogen bonds, whereas Br1 forms C-H···Br1 hydrogen bond. It is proposed that the Br2···Br2 halogen bond involved in form III has a relatively smaller magnitude of the  $\sigma$ -hole (108 kJ mol<sup>-1</sup>) as compared to the Br1···Br1 halogen bond (140 kJ mol<sup>-1</sup>) involved in form I. Thus, a relatively weaker strength of the former halogen bond interaction results in a distorted structure, thereby exhibiting plasticity.

Polymorphism in ROY has also been explored extensively in the past and is still being scrutinized.<sup>59,60</sup> Interestingly, a recent exploration includes the investigation of the YN polymorph of ROY [D(II) in Scheme 1], which shows elastic deformation when force is applied on major facets (010)/(0-10), whereas the ON polymorph breaks on the application of force.<sup>61</sup> The difference between both the polymorphs and their respective mechanical behaviors lies in the difference in the conformation across the N–C (thiophene) bond. The elastic strain generated in the YN crystal when bent into an arc of a small radius is ~14.6%, which is comparable to the previously reported highest value observed in 1,4-bis[2-(4methylthienyl)]-2,3,5,6-tetrafluorobenzene. The elastic limit of YN is dictated by the separation distance between the stacking aromatic rings aligned parallel to the bending face with multiple soft ancillary interactions, *i.e.*, C- H···O, C-H···N, and C-H··· $\pi$ , which prevents slippage between the layers parallel to the bending face. The elastic limit of the crystal is increased by the ability of the molecules to accommodate strain by reversible rotation during reversible deformation. On the other hand, the ON polymorph has less twisted conformation, which results in numerous additional weak interactions, thus further stabilizing the  $\pi$ -stacks. Additional ancillary interactions lead to interlocked molecular packing, making the crystal brittle with lower limit of elastic strain.

Similarly, concomitant and conformational trimorphs of 3-((4chlorophenyl)imino)indolin- 2-one, a Schiff's base [D(III) in Scheme 1], showcased distinct mechanical responses.<sup>62</sup> Form I was observed to be brittle due to an interdigitated and highly corrugated structure. However, form II and III showed plastically and elastically deformation, respectively. The distinct mechanical behavior was thoroughly investigated *via* slip layer topology, analyzing the intermolecular interaction energies,

nanoindentation, and Hirshfeld surface analysis. Form II and III have similar 1-D tapes formed via N-H···N and C-H···O hydrogen bonds. The inspection of the topology of form II shows that these tapes are connected to other via weak C-H···Cl bonds, which act as slip planes and are also low in ruggedness. Similarly, form III has antiparallel tapes with a slip layer between the chlorinated phenyl groups pointing in the opposite directions. Through energy frameworks, the lowest total interaction energy for form II and III is -30.6 kJ mol<sup>-1</sup> and -34.7 kJ mol<sup>-1</sup>, respectively, and this corroborates with the presence of facile slip planes. These interaction energies are very close to each other, therefore emphasizing that the energy framework alone is not sufficient for distinguishing mechanical responses and this should be attributed to the difference in the topology of the slip planes, which is further supported by quantifying the mechanical properties through nanoindentation. Here, this case study emphasizes not only on the role of energetics involved along the slip plane but also suggested that the directionality of these interactions plays a significant role in deciding the type and extent of the observed mechanical flexibility in a crystal.

Zhang and co-workers reported another interesting exploration where the tuning of the mechanical compliance and luminescent properties through polymorphism in diaryl  $\beta$ -diketone compound, (Z)-3-(4-(dimethylamino)phenyl)-1-(3fluorophenyl)-3-hydroxyprop-2-en-1-one [D(IV) in Scheme 1], was conducted.<sup>63</sup> The flexible characteristics of each polymorph were explained by the extent of  $\pi$ -overlap in the stacking interactions and modifications in the peripheral weak interactions. All the three forms have highly planar structures due to the formation of strong intra-molecular interactions (C-H···O, O-H···O hydrogen bonds) with minor torsional changes in the fluorophenyl part of the molecule. The CRY-G form shows elastic/reversible deformation due to the crosswise, interlocked structure (primarily stabilized via C-H···O) with molecular stacking constructing the (001)plane. The CRY-O form is observed to be brittle in nature as the overlap due to molecular stacking is higher and the slip plane is absent. The intermolecular interactions are dispersed homogenously in the crystalline assembly. CRY-Y shows evident plastic deformation in crystals with small length/thickness ratio whereas elastic deformation in crystals with higher length/thickness ratio. The (100) plane, which is

also the bendable face, consists of C-H···O and  $\pi$ - $\pi$ interactions that are stacked into layers via C-H…F hydrogen bonds. The packing is anisotropic along the [010] and [001] directions, which are much stronger than those along the [100] directions. The layered structures provide enough space for sliding along the [001] direction. The three-point bending experiment specially clarified the elastic-plastic behavior shown by CRY-Y. The load v/s displacement plot showed that the crystal first underwent elastic deformation and then plastic deformation before breaking (shown in Fig. 9), which is consistent with the packing where C-H…F bonds connecting neighboring stacks prevent molecular sliding up to a certain extent, beyond which the threshold is exceeded and the crystal deforms plastically/irreversibly. Along with the mechanical compliance, CRY-Y and CRY-G can efficiently propagate and amplify light through bent crystal as well. The straight and bent crystals also efficiently help in light transduction with almost similar values of the optical loss coefficient, showing that physical bending does not create extensive defects that could cause optical loss.

Also, this is one of the few reports where CRY-Y and CRY-G are amplified spontaneous emission (ASE)<sup>26</sup> active forms. This has been acknowledged by exciting one end of the crystal with increased pump laser and the amplified emission generated on the tip is recorded, whereas no ASE was exhibited for the CRY-O brittle form.

Probing into such systems reveals the extent of sensitivity, in terms of conformational changes at the molecular level and the geometric-energetic changes in non-covalent interactions involved at the inter-molecular assembly level in exhibiting distinguished mechanical and optical properties.

#### 3.2. Derivatization

As a part of crystal engineering, the derivatization of the base compound with suitable groups has proven to be highly suitable for tuning different properties.

On delving into the mechanical properties of single crystals of semiconducting naphthalene diimide derivatives [E(I) in Scheme 1], Devarapalli *et al.* distinguished macroscopic mechanical responses between highly plastic 1Me, elastically flexible 1Et, and brittle crystals of 1nPr.<sup>64</sup> The work emphasizes on the role of alkyl

![](_page_12_Figure_11.jpeg)

**Fig. 9** (a) Cross-section and microscopic images of faces of CRY-Y; and (b) the displacement-load curve of the three-point bending test for CRY-Y; fluorescence spectra as a function of the pump laser energy of (c) the straight crystal and (d) the elastically bent crystal for CRY-G. [D(IV) in Scheme 1]. Adapted from ref. 63. With permission from the American Chemical Society, Copyright 2020.

side chains in tuning the self-assembly as well as the elastic properties. Though the energy frameworks suggest the possibility of slip planes along the lowest intercolumn interactions for 1Me  $(-47 \text{ kJ mol}^{-1})$  and 1Et  $(-50 \text{ kJ mol}^{-1})$ , the corrugated nature of molecular packing of these planes ruled out the possibility. Hence, the plane consisting of the alkyl chain, *i.e.*, methyl group in 1Me, allows for long-range shear sliding, which facilitates irreversible plastic deformation. On the other hand, the elastic behavior of 1Et is justified by topological interlocking due to the crossover of ethyl group over each other, which inhibits permanent slip and allows small localized molecular displacements that probably cause the tilting of molecules associated with the expansion or contraction of the intermolecular space. In case of brittle 1nPr, the propyl groups have moderate layer cross-over with a large stacking energy (-158 kJ mol<sup>-1</sup>), which makes the stacks rigid and prevents any kind of mechanical deformation. The three-point bending and threepoint flexure experiments were carried out on the single crystal of 1Me, which shows remnant displacement after unloading and is indicative of plastic deformation. On the other hand, 1nPr loads 250 cycles with  $h_{\text{max}}$  of 50  $\mu$ m in each cycle, showing shape recovery during unloading, which is indicative of the occurrence of enhanced elasticity.

Recently, Nath *et al.* analyzed probenecid and its hydrazide/amide derivatives [E(II) in Scheme 1] to delve into the significance of strategical engineering of molecules to tune their mechanical flexibility.<sup>65</sup> Probenecid is shown to exhibit plastic deformation when the force is indented on the (001) face. As shown in Fig. 10, the crystalline assembly consists of 2D layers (in *ab*-plane) formed *via* O–H···O dimeric synthon formed between the –COOH group of the drug and C–H···O hydrogen bonds connecting the molecule to the neighboring molecules. These 2D layers are packed *via* van der Waals interactions amongst the *n*-propyl chains, which facilitates slippage. Similar to this, the hydrazide derivative has 2D layer packing consisting of strong N–H···O dimers formed between the -CONHNH<sub>2</sub> group of molecules, which were further connected to the adjacent ring via N-H…N hydrogen bonds, and the n-propyl chain facilitates slippage. The observations from the microscopy experiment and the visualization of supramolecular assembly were also corroborated via interaction energies computed through energy frameworks, where the intralayer energy (for the 2D layer) is much higher than that of inter-layer energy (stabilized via van der Waals interactions between n-propyl chains), which supports the presence of slip plane in the inter-layer region. The probenecid amide forms centrosymmetric N-H···O dimer, further interconnected via N-H···O forming hydrogen bonded tapes. The n-propyl chains on both sides are interdigitated and unlikely to slip, thereby making the derivative of probenecid amide brittle in nature. Therefore, changes in the mechanical properties were observed as a consequence of the change in the hydrogen bond synthon.

#### 3.3. Designing multi-component systems

Similar to the earlier study by Frawley's Group, another investigation on the crystals of the Pregabalin (SPG) salt with oxalate anion, SPG<sup>+</sup> OX<sup>-</sup>, and Pregabalin salt with salicylate anion, SPG<sup>+</sup> SA<sup>-</sup> [F(I) in Scheme 1], showed plastic deformative characteristics.<sup>66</sup> The anhydrous drug is known to be brittle in nature, whereas these salt crystals show irreversible deformation on applying force. The anion in both the cases acts as a bridge to bring two flexible SPG molecules close with the alkyl groups facing each other, which consequently leads to low rugosity of the slip planes along the slip direction. The interdigitated packing of anhydrous SPG is rearranged *via* strong interactions with the oxalate and salicylate anions, which act as structural buffers that facilitate tight packing amongst the cation and the anion, and also facilitate slipping between the layers. Further, the

![](_page_13_Figure_7.jpeg)

**Fig. 10** The 2D layers of (a) probenecid, (b) probenecid hydrazide, closely pack *via* weak van der Waals interactions between the *n*-propyl chains in an end-to-end fashion. The slip plane across the (001) plane is shaded differently. (c) Probenecid amide forms hydrogen-bonded dimers and these dimers interconnect by forming N-H…O—S and (d) C-H…O—S hydrogen bonds. (e) Interdigitation of *n*-propyl chains in the probenecid amide crystal structure. Adapted from ref. 65. With permission from the American Chemical Society, Copyright 2020.

tableting performance and solubility of the salts and anhydrous forms were compared, which showed a significant enhancement in the solubility and better tabletability of the salts over the anhydrous drug.

An elaborate inquest on elastically bendable organic cocrystal-solvate of caffeine (CAF), 4-chloro-3-nitrobenzoic acid (CNB) and methanol (1:1:1, F(II) in Scheme 1), emphasizes on the experimental exploration required to investigate the mechanical behavior of organic molecular crystals.<sup>12,67</sup> The intriguing results of nanoindentation experiments revealed the high elastic modulus and hardness when the ambient cocrystal was indented on major [(010),  $E = 76.86 \pm 1.30$  GPa, H = 6.92  $\pm$  0.19 GPa] and minor faces [(001),  $E = 64.39 \pm 1.96$  GPa,  $H = 3.23 \pm 0.13$  GPa), is counter-intuitive with respect to general perception relating to all flexible organic crystals as soft. These exceptionally high values are comparable to certain metals, such as aluminum, with nearly half the density. The micro-XRD structural analysis revealed doublesided stacked comb-like interlocked structures with the 0D O-H…N hydrogen bond in the CAF-CNB dimer along with weak C-H…O hydrogen bonds forming a zipper network. The zipper locking resists the movement of molecules along the direction of the planes as well as orthogonal to their length, thus preventing slippage and resulting in reversible deformation. Consequently, the experiments revealed that on applying force on the major face of the crystal, there is long-

![](_page_14_Figure_6.jpeg)

**Fig. 11** Crystal packing and schematic representation of the resistance to external load. (a) Geometry and packing of the comb-like tapes (bluegreen shades) viewed along *c*-axis and (b) along *b*-axis. The zipper-like conformation of the comb-like tapes resists deformation by knuckling, sliding, and compression against external load on the (010) and (001) faces. Inset of (a) shows the atom labels with intermolecular interactions. Reproduced from ref. 67. With permission from the authors, Copyright 2019. Published by Springer Nature.

range redistribution of stress as the volume of the bent region decreased, whereas that of the straight part expanded. The strained regions of the bent portion of the crystal, *i.e.*, Mo (outer), Mm (middle), and Mi (inner), show anisotropic changes in intermolecular interactions. The results obtained from micro-X ray diffraction experiment, which were corroborated with micro-IR and micro-Raman results, establish the weakening of the C-H···O hydrogen bond, which is involved in the CNB-CAF dimer, from Mo to Mi due to the overall lattice perturbation, on account of anisotropic stress dissipation. Subsequently, the intermolecular interaction energy was computed via energy frameworks and comparisons were made amongst the ambient and bent crystals (Mo, Mm, and Mi), which showed a decrease in the stability of the CAF-CNB interactions in the stressed crystals. Similarly, the overall weakening of the intra-tape interactions consisting of CAF-CAF interactions was observed. The Etot for  $\pi$ -stacks among the CNB-CNB and CAF-CAF pairs showed strengthening in the strained region (refer to Fig. 11). This suggests that the stability lost by strained hydrogen-bonds has been compensated by  $\pi$ -stacking.

Crystal engineering, via the cocrystallization of 4-amino azobenzene (AAB, F(III) in Scheme 1) with different coformers, was utilized to tune the photomechanical bending, the photochromic responses, as well as mechanical deformation. Five different co-formers, namely, 3-amino-4methylpyridine (AMP), 4-pyrrolidin-1-ylpyridine (PYP), 4,4-bipyridine (BIP), 1,2-bis(4-pyridyl)ethane (BPE), and 4-(1naphthylvinyl)pyridine (NPE), yielded cocrystals.<sup>68</sup> The photomechanical bending was due to the trans-to-cis isomerization of azobenzene.<sup>69</sup> Different photomechanical responses such as bending towards or away from the light source were attributed to the dihedral angle between the AAB molecule and the dominant faces, i.e., co-crystals consisting of the AAB molecule with larger dihedral angles have greater chances of bending away from the light source and vice versa. With respect to mechanical deformation, AAB-NPE and AAB-BIP were compared to reveal elastic and plastic deformation in the crystals. The crystalline assembly of AAB-NPE consists of crisscross packing in the herringbone style between AAB and NPE via N-H···N hydrogen bonding (down the (10-1) face), supported via extensive interactions such as N-H $\cdots\pi$ , C-H $\cdots\pi$ , and C-H $\cdots$ N interactions. These dispersive interactions interlock without slip the planes with  $\pi$ - $\pi$  stacking parallel to the dominant face (10-1). In case of the AAB-BIP co-crystal, the crystal underwent a small range of elastic bending and then irreversible plastic deformation on increasing the force exerted on the crystal. This is due to the presence of fewer dispersive interactions (C-H···  $\pi$ , C-H···N) joining the molecular stacks of AAB, BIP, which could adapt to significant compression/expansion of the lattice during the bending process. Further, the absence of the interlocked assembly of molecules, with an evident slip plane, constituting the C-H···N interactions, facilitates plastic deformation on triggering more external force on the crystal.

# 4. Utilization of computational methods to rationalize the mechanical response

Computational techniques for understanding the structuremechanical properties relationship in organic crystals can help to predict or design crystals with desired mechanical properties.<sup>70</sup> The preliminary step for understanding the structure-mechanical relation includes the visualization and analysis of crystalline assembly, which helps in segregating diverse mechanical responses with respect to different synthons involved in crystal packing.<sup>7,65,71</sup> In addition, inputs from the "energy frameworks" help in distinguishing the synthons in terms of energetics and help in rationalizing the individual/collective role of inter-molecular interactions.72,73 The decomposition of energy along with topological analysis helps in establishing the role of specific intermolecular interactions in exhibiting the mechanical response, such as slip planes for irreversible shearing/gliding of planes in plastic crystals and buffer/elastic regions in elastic crystals. Simultaneous quantitative layer topological analysis helps in predicting the slip planes based on molecular sliding on the basis of layer separation, rugosity, interdigitation/crossovers, presence of orthogonal layers, and dimensionality of the hydrogen bonding network.<sup>74,75</sup> Additional support from attachment energy and 3D elasticity matrices, which gives the calculated Young's modulus, shear modulus, Poisson's ratio, etc., are of extreme importance in delineating the reason for a crystal exhibiting flexible characteristics.70,75

The concoction of various computational methods for predicting the mechanical properties of a-oxalic acid anhydrous (OAA) and dihydrate (OAD) performed by Wang et al. revealed the dire need for implementing different computational methods in support of the experimental techniques.<sup>70</sup> The computation of the attachment energy, energy frameworks, and elasticity matrices suggested the (10-1) and (100) planes in OAD and OAA to be facile for slip, respectively. On the other hand, topological analysis, ToposPro, and attachment energy computed for OAA suggested the (200) plane to be acting as a slip plane. The predicted order of crystal plasticity and slip planes by various computational methods were not in agreement, which suggested that relying on any single computational method may not be a practical choice. To determine the accuracy of prediction, the tabletability, powder compaction, and compressibility of both forms were determined experimentally. The OAD form was found to be more plastic than OAA, which contradicts the results deduced from simple structure visualization. Higher plasticity was supported by better compressibility and thereby, lower porosity (with higher bonding area and bonding strength). The experimental (nanoindentation, 18.8 ± 0.96GPa) and computational (DFT-D method, 19-20 GPa) value of E of OAD (10-1) face confirmed the presence of (10-1) as the slip plane.

# 5. Challenges faced and a general outlook

Given the volume of literature, the field of mechanically flexible crystals still has a lot of scope for development, specifically in terms of understanding the mechanism of deformation with respect to the topology and energetics of intermolecular interactions involved in the crystalline assembly. The exclusivity in idea of plastically bendable crystals exhibiting irreversible deformation is being evolved *via* studies where plastically bendable crystals can be restored on application of appropriate stimuli (heat/light/ pressure).<sup>44,45,57</sup>

The basis of classifying elastically and plastically bendable crystals on isotropic and anisotropic intermolecular interactions, respectively, have seemed to fit a large number of systems in the past; however, an alteration in this approach via a systematic analysis of intermolecular interactions, for cases that do not follow the abovementioned criteria, could prove to be beneficial. With respect to this dissection, a detailed investigation of the systems with elastic-plastic characteristics (as discussed in section 3.3) requires additional support from computational tools to support the suggested mechanical model. Exceptional cases where plastic deformation is observed in some molecular crystals with nearly isotropic intermolecular interactions<sup>29</sup> and elastic deformation is found in molecular crystals with anisotropic intermolecular interactions<sup>22</sup> can assist in discerning a more universal model.

A common packing feature, predominantly containing orthogonally arranged  $\pi$ /molecular stacks with twodimensional layers, displays mechanical flexibility, which have been generalized primarily for the above-mentioned class of molecules and alike. It is sufficient to justify the flexibility shown in molecules with 2D layered packing but are inadequate in explaining the flexible characteristics of a crystal with three-dimensional packing. Herein, the investigation of the mechanical flexibility of coordination polymer becomes noteworthy as the crystal packing propagates diversely in all the three dimensions, which help in better understanding the observed topology and the associated energetics. In addition, a systematic exploration of the flexible behavior by organic crystals with 3D packing will also be extremely insightful, especially in manifesting the role of intrinsic flexible torsions present in the molecule, which could be responsible for facilitating flexibility to the crystal. With only a few examples including the synergism of interaction energies amongst the molecules44,61,62,64,66 and even fewer cases acknowledging the distortion within the long-range ordering of crystals, on introducing mechanical stimuli,<sup>22,34,45,67</sup> the understanding of dynamic solid-state mechanical deformation processes, either plastic or elastic, is meagre.

The inclusion of solvent molecules in the crystal lattice have been primarily known to modify the softness of the crystal and thereby alter the mechanical properties.<sup>76</sup> In

section 3.1., the solvate of the compound under investigation is known to be brittle, in contrast to its anhydrous form, which is observed to bend elastically on applying force.<sup>28</sup> Another intriguing work in section 3.2., contradicting the earlier approach of weaker interactions (slip planes) responsible for mechanical deformation, has shown that the strong hydrogen bonds between the drug and H<sub>2</sub>O molecule is deformed on applying mechanical force.<sup>50,51</sup> These studies stress on the need for a greater number of structured and systematic explorations involving solvates/hydrates of crystals as well.

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Most of the systems discussed above hold true in terms of exhibiting flexible behavior at room temperature. With limited systems at disposal, showing mechanical flexibility either at temperature above or below room temperature, more experimental studies could help in exploring this area of research. One of the previous examples includes the comparison of the mechanical properties of C<sub>6</sub>Cl<sub>6</sub> with C<sub>6</sub>Br<sub>6</sub> by Desiraju and group, where the former shows bending at 300 K but the latter exhibits plastic deformation at 403 K.8 Recently, Zhang and group have investigated two separate systems where one ((Z)-2-(4-(((E)-2-hydroxy-5methylbenzylidene)amino)phenyl)-3-phenylacrylonitrile) shows elasticity at ultra-low temperature (77 K) and heatsetting ability at temperatures above 423 K, while the other system (9,10-bis(phenylethynyl)anthracene) shows plastic bending at higher temperatures (393 K), resembling thermoplasticity in polymers. Such systems, specifically the ones wherein flexibility or heat-setting ability in the crystal is attained on varying the temperature, help in co-relating and understanding the softening of intermolecular interactions in molecular crystals to thermoplasticity in polymers.77,78

On the computational front, it has been observed that the results given by one computational tool may not corroborate with those obtained from others. Hence, the exclusive utilization of any one computational tool is not sufficient for predicting or justifying the mechanical responses in crystals. In fact, there is a dire necessity to amalgamate other complementing computational tools with experimental data collected for the quantification of mechanical properties through nanoindentation to validate the predictions.

# 6. Potential of mechanically deformed crystals

With the surge in the discovery of materials, harnessing the long-range order of crystals with the softness of polymers, molecular crystals, specifically organic crystals, are now known to be sufficient criteria for flexible crystals and can thereby be utilized in diverse fields.<sup>79–81</sup> The discovery of reversibly flexible crystals with negligible fatigue opens up possibilities for the practical applications of these highly-ordered materials in smart bio-imaging devices, nano/micro machineries, electronic, and opto-electronic devices.<sup>27,81–84</sup>

Understanding the mechanical behavior of the active pharmaceutical ingredient (API) crystal is of significance as the tableting property of the API largely depends upon its mechanical properties.<sup>85</sup> The extent of hardness, strain rate, granularity, and flowability of the drug are crucial for the tabletability and formulation and the extent of deformation decides the quality of tabletability and powder compaction for the drug.<sup>85-87</sup> A few reports on the existence of "brittle" active pharmaceutical ingredient, which have been engineered to tune the mechanical property, have been utilized to harness better tabletability.<sup>66,88</sup>

Mechano-pharmaceutical applications of mechanically compliant therapeutic drugs could be a promising research venture as fluorescent and flexible crystals of drug molecules could be useful for medical and diagnostic imaging in biomedical applications.<sup>89</sup> Elastic bending can also be induced in intracellularly grown biogenic crystals, which can serve as templates to construct functional microdevices for biomedical applications.<sup>90</sup>

In addition, the application of molecular crystals holds tremendous potential as a light transducer, which have been identified, investigated, and exploited in recent times.91-93 Improved transduction through these light, organic, small molecule constituting optical waveguides with minimized optical losses are of paramount importance towards the design of next-generation smart materials.94,95 With fastpaced progress in the field, several difficulties in the reshaping and positioning of small crystals have also been encountered. These have been effectively overcome with precise manipulation (downsizing) of micro-sized organic crystals (with controllable aspect ratio) via atomic force microscopy (AFM) cantilever tip, which can be used to deform, cut, and slice, while maintaining their waveguiding properties (by avoiding optical losses via scattering at the defect sites). This method can be used to fabricate organic waveguides of desired shape from mechanically compliant crystals.96,97

The potential of organic flexible materials in laser applications is slowly gaining momentum. Notably, Zhang and coworkers have investigated systems (discussed above) how emissive properties as well as mechanical compliance can be tuned. The detailed work lays guidelines to engineer mechanical properties along with optical properties, which highlights the utility of crystal flexibility in optical transducing as well as light amplification.<sup>26,63</sup>

# 7. Summary

The mechanical properties of organic crystalline materials are of immense interest as this class of materials maintains long-range ordering and is known to exhibit softness akin to that in polymer and abiogenic materials. The investigation of the structure-mechanical property *via* experimental and computational tools has shown to be helpful in building an improved understanding but still there exists ample scope for further exploration and development. This is keeping in mind that these molecular crystals are now known to exhibit multi-functional properties such as flexible drug and compliant optical waveguide, to name a few. With the advancement in instrumentation, such as micro-Raman, micro-IR, and micro-SCXRD techniques, this interdisciplinary field has gradually been able to obtain new insights into this dynamic phenomenon. In spite of the challenges faced, it is striking to note the role played by intermolecular interactions in understanding the mechanical behavior and could lead to universal design strategy for mechanically flexible molecular crystals in the immediate future and years to come.

### Conflicts of interest

There are no conflicts of interest to declare.

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