# Sorting of polymorphs based on mechanical properties. Trimorphs of 6-chloro-2,4-dinitroaniline†

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**Mechanical shearing of crystals of a polymorph with a layered structure may be used to separate them from harder crystals of a visually indistinguishable polymorph that resist such shearing.**

Polymorphism has emerged as a solid state property of outstanding fundamental and practical importance,[1] principally because of the extensions of pharmaceutical space provided by the identification of new, but also more useful, crystalline forms of a drug.[2] Ideally, one would like to obtain a particular polymorph with one set of experimental crystallisation conditions, and another polymorph with another set. However, this may not always be possible and polymorphs may be obtained concomitantly[3] whatever be the experimental conditions employed. In such cases, rapid identification and separation of the polymorphs is necessary. This has traditionally been carried out by visual inspection and two methods are generally employed. The polymorphs are sorted either on the basis of colour[4] or morphology. Of these two methods, the latter is vastly more common. In this communication, we report a third method, based on the mechanical properties of crystals, of separating concomitant polymorphs. This method is illustrated with respect to the three crystalline forms of the title compound, 6-chloro-2,4-dinitroaniline, **1**.

We have recently observed that crystals of 1,3,5-tribromo-2,4,6-triiodobenzene, **2**, and related compounds may be deformed to give curved and other irregular shapes when subjected to shear stress. This phenomenon, although not unprecedented,[5] is certainly unusual because crystals usually break when subjected to shear stress and do not deform in this way. It is possible that such shearing behaviour follows from layered packing—more specifically, one in which the intralayer interactions are strong and specific while the interlayer interactions, even if strong, are non-specific.[6] In compound **2**, for example, the interlayer spacing is 3.395 Å. A layered crystal structure with non-specific interlayer interactions appears to be a necessary (and perhaps even sufficient) condition for mechanical shearing. Accordingly, we began a survey of such crystalline samples in our laboratory noting that many crystals with a short axis of *ca.* 4 Å are packed as parallel stacked layers.[7]

We found, during this search, that 6-chloro-2,4-dinitroaniline, **1**, has a layered structure.[8] The short axis of the reported monoclinic form (Form I) is 7.886 Å (nearly 2 × 4 Å) and the layers are stacked in an antiparallel fashion at separations of 3.057 Å and 3.209 Å. Fig. 1 shows that these layers along $(1\ 0\ \bar{1})$ consist of strong and specific N–H···O (*d*/Å, *θ*/°: 2.30, 156.5; 2.12, 150.1; 2.14, 149.76; 2.26, 156.4), C–H···O (2.34, 175.4; 2.35, 172.3), C–H···Cl (2.82, 165.2; 2.83, 161.0) and C–Cl···O (3.15, 146.7; 3.17, 146.1) interactions. The C–H groups in **1** are unusually activated, and the formation of intralayer C–H···O and C–H···Cl interactions is favoured. The interlayer interactions are, however, of the van der Waals type and are non-specific.

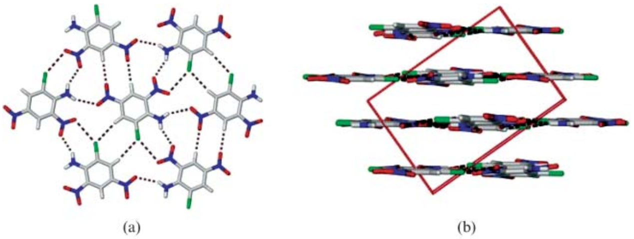

**Fig. 1** Crystal structure of Form I of 6-chloro-2,4-dinitroaniline, **1**. (a) Layer structure to show N–H···O, C–H···O, C–H···Cl and C–Cl···O interactions. (b) View down [010] to show stacking of antiparallel layers.

Crystallisation of **1** from $CH_2Cl_2$ gave both prismatic chunks and fine needles (Fig. 2). These were sorted visually, and it was found that the needles correspond to a new polymorph (Form II). The crystal structure of this polymorph‡ (Fig. 3) was determined with some difficulty,§ because the crystals were extremely thin. In keeping with the theme of this work, a couple of chunky crystals were selected and subjected to mechanical shear. As expected, they did undergo a shearing deformation (Fig. 4). We also selected a chunky crystal and determined its crystal structure.§ We found it to be identical to the already reported Form I,[8] which has a layered structure, thereby confirming our model.

At this point, we could well have stopped work on this compound but, as a routine exercise, we recorded the powder X-ray diffraction (PXRD) pattern of the chunky crystals

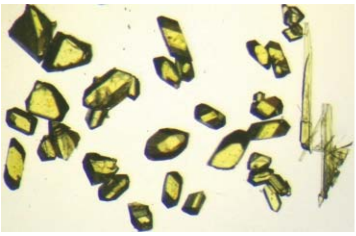

**Fig. 2** Mixture of polymorphs I, II and III of aniline **1** obtained concomitantly from $CH_2Cl_2$. Notice that the needles (Form II) are easily separated from the chunks but that the two polymorphs amongst the chunks (Forms I and III) are visually indistinguishable.

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† Electronic supplementary information (ESI) available: ORTEP diagrams, PXRD pattern and overlay coordinates. See http://www.rsc.org/suppdata/cc/b5/b500712g/

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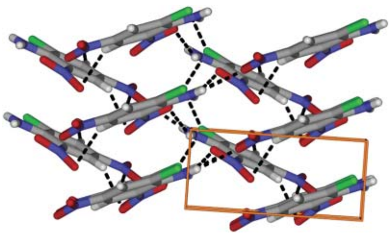
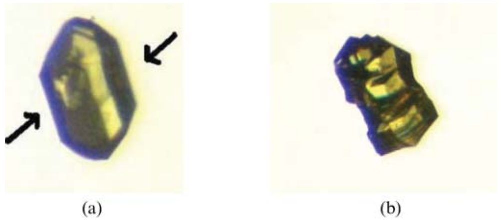


**Fig. 3** Crystal structure of Form II showing a corrugated arrangement with N–H···O, C–H···O and C–Cl···Cl interactions.



(a)

(b)

**Fig. 4** Crystal of Form I (a) before and (b) after shearing. The arrows show the direction along which the shear stress was applied.

(supplementary information†) and compared it with the PXRD pattern simulated from the crystal structure of Form I. To our surprise, there were many additional lines in the experimental powder spectrum showing the presence of at least one more polymorph among the chunky crystals. However, it was not possible to determine by visual inspection that there is more than one polymorph among these crystals (Fig. 2). All the chunky crystals look alike.

A closer inspection of the chunky crystals showed that some of them (which were generally softer) could be sheared when one end was held fixed with a forceps and the other end disturbed with a metallic needle (Fig. 4). This was done while viewing the crystal under a microscope. Other chunky crystals, however, were quite hard and resisted mechanical shear. Without much effort, it was possible to sort the chunky crystals into two sets corresponding to the soft and hard specimens. Typically, the crystals were viewed under a microscope and pressed lightly with the metallic needle; crystals that yielded to the pressure correspond to the soft specimens and those that remained robust correspond to the hard specimens. In this way, approximately 50 mg of crystalline material was sorted in about 1 h. The two sets contained approximately the same number of crystals. PXRD patterns of the two sets of sorted crystals showed immediately that the separation was successful (Fig. 5). The soft crystals, which could be sheared mechanically, correspond to Form I while the hard crystals, which resisted shearing, correspond to the third polymorph of **1** (Form III).

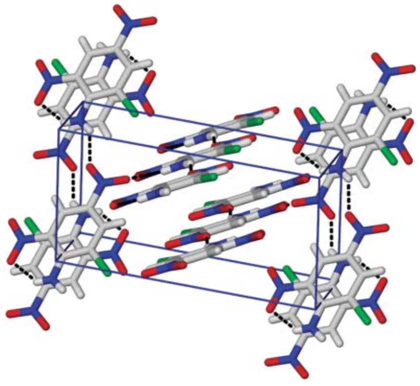


**Fig. 6** Crystal structure of Form III. Note that the packing is not layered.

The crystal structure of the triclinic Form III was determined and, as expected, it is not layered (Fig. 6). We note, however, that the short axis is *ca.* 8 Å. This shows that while crystals that can be sheared have short axes of ~4 Å or ~8 Å, the presence of such short axes is not in itself a sufficient condition for a crystal to show shearing. The crystal structure should also be layered.

In conclusion, we note that the title compound **1** exists as three polymorphs which are obtained concomitantly from a variety of solvents.¶ Separation of Form II is carried out easily by visual inspection because it is obtained as visually distinctive needles. Separation of Forms I (monoclinic) and III (triclinic), which crystallize as visually indistinguishable chunks, is accomplished by sorting them based on their ability to withstand (Form III) or collapse (Form I) on application of mechanical shear. This method of polymorph separation is useful as differences in morphology are by no means an infallible guide to the presence of polymorphs. The same polymorph may well have different morphologies. Our method may also be of general utility because layered crystal structures are common among organic solids. Significantly, Forms I and III are quite different in terms of their mechanical hardness/softness, and this is surely a property of interest in the chemical industry, because the harder form will have better granularity, filterability and flowability properties. For example, while grinding Form I we observed its waxy nature whereas Form III could be ground to a fine powder. Crystal structures that are more three-dimensional in nature, and not layered, are more likely to have

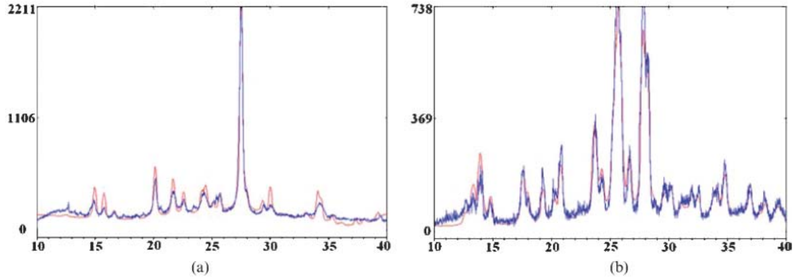


**Fig. 5** PXRD traces (blue) of polymorphs separated mechanically (a) Form I, soft crystals, (b) Form III, hard crystals. The simulated spectra from the single crystal structure determinations are also shown (red). The *x*-axis shows the diffraction angles [2$\theta$ (°)] and the *y*-axis the diffraction intensities.

these favourable properties, extending in this way the paradigm of crystal engineering.[9]

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## Notes and references

‡ It is of interest to note that crystals of Form II are non-centrosymmetric and that they readily show a distinct SHG effect with a laser at 1064 nm.

§ We redetermined the crystal structure of Form I and the hydrogen bond metrics are taken from our analysis. *Crystal Data* for Form I: ($C_6H_4N_3O_4Cl$), $M$ = 217.57, mp 434 K, Enraf-Nonius MACH3, 293(2) K, monoclinic, $a$ = 11.285(3), $b$ = 18.220(3), $c$ = 7.886(8) Å, $\beta$ = 90.44(4)°, $V$ = 1621.4(17) Å$^3$, space group $P2_1/c$, $Z$ = 8, $\mu$ (Mo-K$\alpha$) = 0.463 mm$^{-1}$, size 0.28 × 0.24 × 0.20 mm. 3079 total reflections of which 2853 were independent, 1569 observed [$I > 2\sigma(I)$]. Refinement against $F^2$ with 261 parameters, $R_1$ [$I > 2\sigma(I)$] = 0.0480. Form II: ($C_6H_4N_3O_4Cl$), $M$ = 217.57, mp 432 K, Bruker Nonius Smart Apex CCD, 100(2) K, monoclinic, $a$ = 8.1619(18), $b$ = 3.6646(8), $c$ = 13.278(3) Å, $\beta$ = 91.310(3)°, $V$ = 397.04(15) Å$^3$, space group $P2_1$, $Z$ = 2, $\mu$ (Mo-K$\alpha$) = 0.473 mm$^{-1}$, size 0.83 × 0.12 × 0.03 mm. 6858 total reflections of which 1608 were independent, 1569 observed [$I > 2\sigma(I)$]. Refinement against $F^2$ with 135 parameters, $R_1$ [$I > 2\sigma(I)$] = 0.0385. Form III: ($C_6H_4N_3O_4Cl$), $M$ = 217.57, mp 436 K, Enraf-Nonius MACH3, 293(2) K, triclinic, $a$ = 7.94651(12), $b$ = 8.917(3), $c$ = 12.980(4) Å, $\alpha$ = 89.35(3), $\beta$ = 85.575(19), $\gamma$ = 63.978(15)°, $V$ = 823.8(4) Å$^3$, space group $P\bar{1}$, $Z$ = 4, $\mu$ (Mo-K$\alpha$) = 0.456 mm$^{-1}$, size 0.30 × 0.21 × 0.20 mm. 3132 total reflections of which 2901 were independent, 2362 observed [$I > 2\sigma(I)$]. Refinement against $F^2$ with 285 parameters, $R_1$ [$I > 2\sigma(I)$] = 0.0355. CCDC 260455–260457. See http://www.rsc.org/suppdata/cc/b5/b500712g/ for crystallographic data in CIF or other electronic format.

¶ All three concomitant polymorphs of compound **1** were obtained from $CH_2Cl_2$, EtOAc, benzene, $CH_3CN$ or $CH_3NO_2$. DSC shows that these polymorphs do not interconvert upon heating.

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