Crystal Growth

Polymorphism of 1,3,5-Trinitrobenzene Induced by a Trisindane Additive**

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Additive-induced polymorphism has always interested the solid-state chemist for fundamental and practical reasons.[1] Polymorphism is, in itself, an enigmatic phenomenon and the reasons for its occurrence are only now beginning to be unraveled.[2] The role of tailor-made additives (auxiliaries) in the control of various aspects of crystallization (nucleation,

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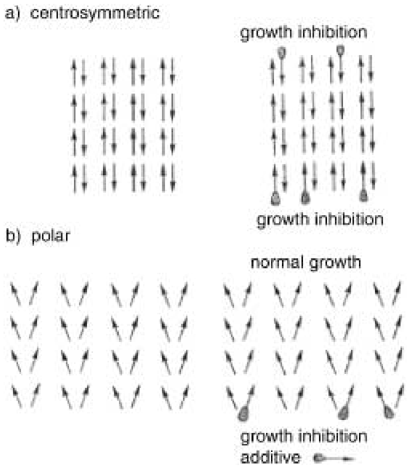
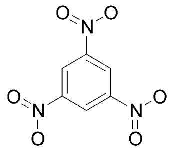
growth, morphology, dissolution, structure) has been described.[3] Polymorphism is one of the least controllable aspects of crystallization. Therefore it would be extremely useful if there were a reliable and general way of engineering additive-induced polymorphism. These ideas are also relevant in crystal-structure prediction.[4] Three questions are pertinent: 1) Does the presence of an additive change the polymorph that is obtained? 2) If so, can the structure of the polymorph so obtained be correlated with the structure of the additive? 3) What is the mechanism of enhancement/inhibition of a polymorph? Despite the importance of these questions, the number of well-documented examples of additive-induced polymorphism is very limited.

Leiserowitz, Lahav, and co-workers[1f,g] have provided a basic model for additive-induced polymorphism (Scheme 1). The additive is structurally similar to the molecule of interest (host) and it may be selectively adsorbed on its crystal faces. Depending on the degree of similarity between the host and the additive, the latter may selectively inhibit the growth of a few faces of the embryonic crystal of the host. These ideas find a practical application in the preferred crystallization of a noncentrosymmetric polymorph (Scheme 1 b, left) at the expense of a centrosymmetric one (Scheme 1 a, left). An appropriate tailor-made additive will inhibit growth of the centrosymmetric form at two opposite ends thereby precluding it (Scheme 1 a, right), but it will inhibit growth of the polar form at only one end of the crystal (Scheme 1 b, right) so that it survives. This concept was demonstrated for *N*-(2-acetamido-4-nitrophenyl)pyrrolidine (PAN) with the 2-nitro and 2-amino derivatives as additives, and for the γ-form of glycine in aqueous solution with racemic hexafluorovaline as an additive. [1f,g] Another clear example is provided by Davey and co-workers[5] who selected trimesic acid and *trans*-glutaconic acid as inhibitors of the stable β-polymorph of L-glutamic acid leading to the metastable α-polymorph. He, Stowell, and co-workers[6] designed isomorphous additives that induced crystallization of a metastable form of 4-methyl-2-nitroacetanilide. The phenomenon has been reviewed.[7,8]

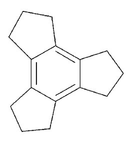


Scheme 1. Basic model for additive-induced polymorphism, see text for details.

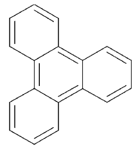
Herein we report on the polymorphism of 1,3,5-trinitrobenzene (TNB) induced by the additive trisindane (TI). TNB has been known for 120 years as an explosive and in the formation of crystalline π–π donor–acceptor complexes.[9] However, and in contrast to the related molecule 2,4,6-trinitrotoluene (TNT),[2a,10] there has been no report of its polymorphism.[11] The only known crystal structure of TNB is that of the centrosymmetric orthorhombic form (space group *Pbca*, $Z' = 2$), which we shall call Form **I**.[12] More recently, TNB has been used as a component of C−H···O hydrogen-bonded molecular complexes for applications in nonlinear optics (NLO). For example, we co-crystallized an equimolar mixture of TNB and triphenylene (TP) to obtain a 1:1 molecular complex, which we studied in detail.[13] Continuing this strategy, we attempted to co-crystallize 1:1 and 2:1 mixtures of TNB and the closely related TI from CCl_4.[14] There was distinct evidence of complex formation in solution in that the solution changed from pale yellow to dark red. However, instead of obtaining the desired 1:1 or 2:1 molecular complexes, we obtained (from a 2:1 experiment in CCl_4) a new polymorph of TNB, henceforth, Form **II**.



TNB



TI



TP

Figure 1 shows the crystal structure of the new and unexpected noncentrosymmetric polymorph, in the orthorhombic space group $Pca2_1$, also with $Z' = 2$.[15] Close inspection of this intricate structure shows two patterns generated, respectively, from the two independent molecules in the asymmetric unit. These patterns are shown in green and yellow in Figure 1. The green colored molecules form a V-shaped trough while the yellow colored molecules form a zigzag arrangement. The V-shaped trough and the zigzag chains are linked with weak C−H···O, C−H···N, and NO_2···NO_2 contacts.[16]

We next redetermined the structure of Form **I** because we wished to verify the Lahav–Leiserowitz model for additive induced polymorphism.[15] Figure 2 shows that the *Pbca* structure of Form **I** is closely related to the $Pca2_1$ structure of Form **II**. In both forms, there are V-shaped troughs made up of one of the two symmetry independent molecules in the crystal (green). The major distinction is that the V-shaped troughs point in opposite directions in the centrosymmetric Form **I** crystal and only in one direction in the polar Form **II** crystal. The *Pbca* structure is in effect a doubled version of the $Pca2_1$ structure across an inversion center[18] so that the mechanism in Scheme 1 broadly applies leading to Form **II** crystals. The unit cell parameters (Form **I**, $a = 12.587$, $b = 9.684$, $c = 26.86$; Form **II**, $a = 9.297$, $b = 18.730$, $c = 9.633$) show some relationship in that $b_{\mathbf{I}} \cong c_{\mathbf{II}}$ and that $(a_{\mathbf{I}} c_{\mathbf{I}}) \cong 2\,(a_{\mathbf{II}} b_{\mathbf{II}})$. While the V-shaped troughs point along [010] and [0−10] in Form **I** they point only along [001] in Form **II**.

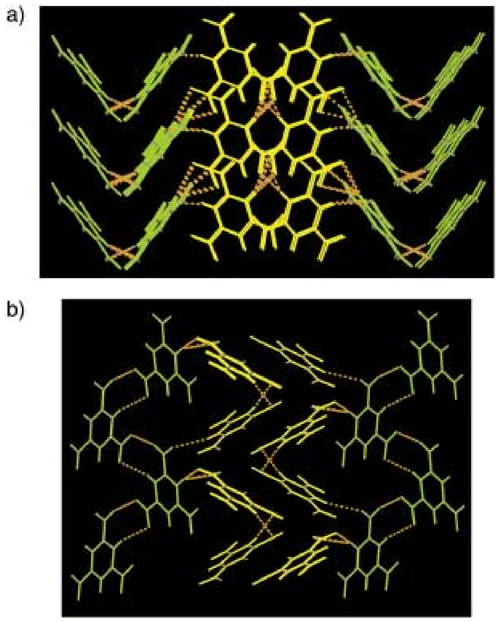


Figure 1. Noncentrosymmetric Form **II** crystal of TNB. The two symmetry-independent molecules are shown in green and yellow. a) View down the *a* axis showing alternate V-shaped troughs and zigzag chains. b) View down the *c* axis showing TNB tape based on C−H⋯O and $NO_2 \cdots NO_2$ interactions along the *a* axis (green), and zigzag chains (yellow). For clarity C−H⋯N and ON−O⋯NO_2 interactions are removed between the green TNB molecules. Molecular graphics were generated using X-seed and POV-Ray.[17]

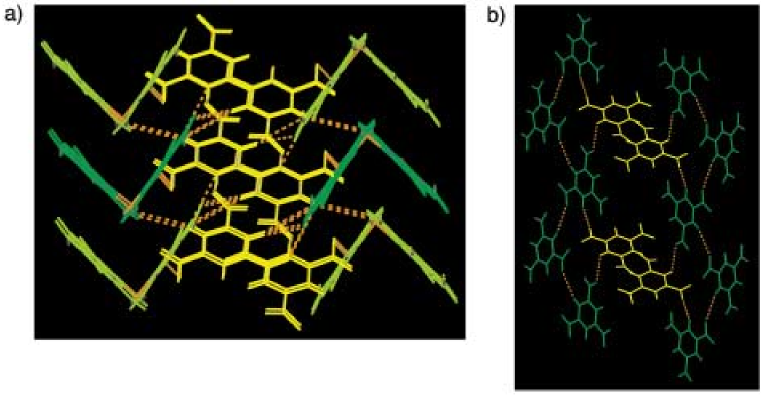


Figure 2. Centrosymmetric Form **I** crystal structure of TNB (*Pbca*). a) View down the *a* axis. b) View down the *b* axis.

The experimental morphology of the Form **I** crystals was determined. Figure 3 shows the crystal faces in a well-grown specimen. The main faces are (010) and (001) and their centrosymmetrically related equivalents. From the direction of the V-shaped troughs in the two forms, it may be assumed that binding of TI on the (010) faces is likely. If the binding is slightly different on (010) and (0−10) there will be a symmetry reduction from *Pbca* to $Pb2_1a$. A permutation of the *b* and *c* axes ($b_{\mathrm{I}} \cong c_{\mathrm{II}}$) leads to space group $Pca2_1$ for Form **II**. According to this model it is not mandatory that $a_{\mathrm{I}} \cong a_{\mathrm{II}}$ with $c_{\mathrm{I}} \cong 2\,(b_{\mathrm{II}})$. It is sufficient if $(a_{\mathrm{I}}\,c_{\mathrm{I}}) \cong 2\,(a_{\mathrm{II}}\,b_{\mathrm{II}})$ and this condition is achieved by a slight shearing of molecules in the

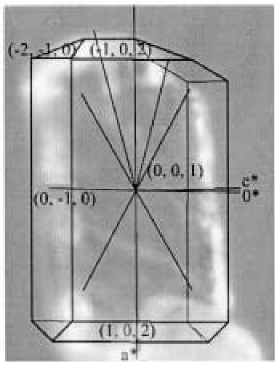


Figure 3. Experimental morphology of Form **I** crystal of TNB. Note the (010) and (0−10) faces.

(010) planes of the Form **I** crystal. Indeed such shearing is unsurprising. It would have been more exceptional if the preferential growth along +b or −b were accompanied by no change whatsoever in the (010) planes, in effect along the *a* and *c* directions. These results also demonstrate that it is the adsorption of TI additive on (010) and (0−10) that is critical to the formation of the new polymorph because it is the *b* axis of Form **I** that is unchanged in length in going to Form **II** (where it is termed the *c* axis), while the *a* and *c* axes of Form **I** (renamed as the *a* and *b* axes in Form **II**) change in length. The experimental morphology shows that (010) and (001) are major faces, with (001) being more prominent. Yet, only adsorption of TI on (010) is critical to the growth of Form **II** with any possible adsorption on (001) being innocuous.

In considering the growth of Form **II** crystals from a CCl_4 solution of TNB that contains TI additive, an important assumption that is implicit in the Lahav–Leiserowitz model needs to be mentioned,[3a] namely that any solution contains a variety of molecular aggregates, some of which have structures akin to those of the macroscopic crystalline forms. This assumption is a triviality when polymorphs appear concomitantly. However, if say solution *A* normally results in polymorph *A* and one wishes to design an additive that will yield polymorph *B* from this solution, then this assumption must be taken into account. This is pertinent in the present case because both Forms **I** and **II** were obtained from CCl_4 solution.

Another consideration that has been utilized in certain layered structures wherein layer stabilities and bulk stabilities are inverted in two polymorphs is to induce nucleation layer by layer so as to obtain the less stable polymorph.[3a] But this is not applicable in the present case because the structures of Forms **I** and **II** are not layered and Form **II** is more stable than Form **I** (see below).

In attempting to reproduce these results we set up a series of crystallization experiments from various solvents (in Essen) with varying mole proportions of TNB and TI.[19] However, we never again were able to obtain the noncentrosymmetric Form **II** (which had appeared originally in Hyderabad), even after nearly 100 crystallization attempts spread over a six-month period. However, during these experiments, we isolated another polymorph, Form **III**, when TNB (80 %) and TI (20 %) were taken in EtOAc. This form of TNB crystallizes in the centrosymmetric space group $P2_1/c$ with $Z' = 1$ (Figure 4). Unlike Form **II**, we were able to obtain crystals of Form **III** a second time but only after several attempts. Close inspection of this new(est) structure of TNB shows that it is not obviously related to Form **I** and Form **II**. There are no V-shaped troughs or zigzag chains. The structure is "normal" and emphasizes Kitaigorodskii-type close packing.[20] The TNB tape building block shown in Figure 4b is common in TNB molecular complexes[21] but is not seen in Forms **I** and **II** (see Supporting Information).

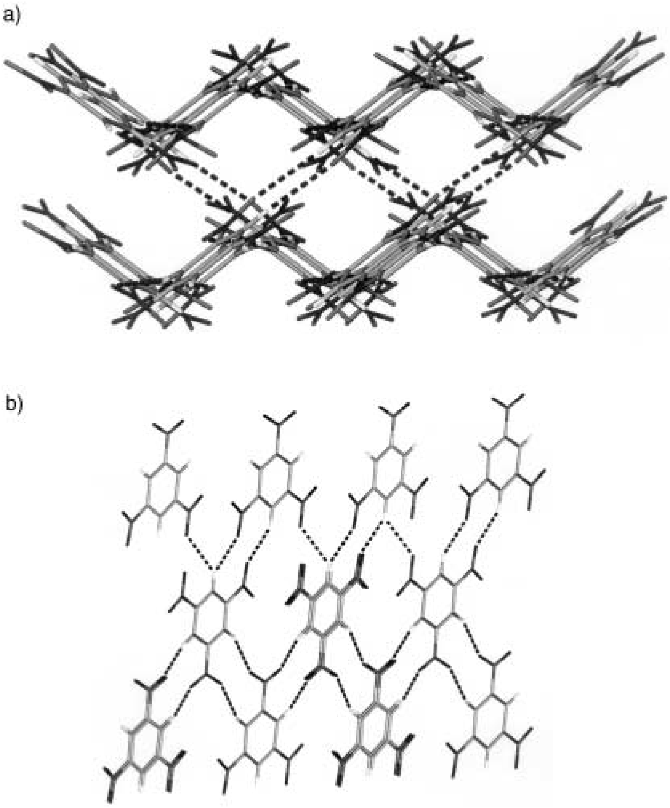


Figure 4. Centrosymmetric Form **III** crystal of TNB. a) View down the *a* axis. b) View down the *b* axis showing the TNB tape.

These results, unanticipated as they were, open up several lines of discussion. What is the role of TI in inducing the appearance of Form **III** crystals? First, although many crystallization experiments were carried out,[22] Forms **II** and **III** were only obtained when TI was present. An additional indication that TI is indispensable for the production of polymorphic structures is that there is no evidence of any phase transformation of Form **I** crystals, at least as evidenced from differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), and variable-temperature powder diffraction traces. Second, we note that TNB gives stoichiometric molecular complexes with a very large number of planar π donors.[23,24] Thus, TNB readily gives a 1:1 molecular complex with the planar TP. It is possible that the difficulty of formation of a molecular complex between TNB and TI arises from the nonplanarity of the TI molecule. In any event, we observed the formation of small amounts of red microcrystalline material coating the crystals of TNB (shown in a photograph in the Supporting Information) in most of the cocrystallization experiments (regardless of the crystalline form of TNB obtained). We made several attempts to isolate a single crystal from this microcrystalline mass but were unsuccessful. We infer that this material corresponds largely to a TNB–TI molecular complex of unknown structure. Whilst formation of a stoichiometric molecular complex between TNB and TI may be difficult as explained above, there is a close degree of molecular similarity as is revealed in the overlap diagram in Figure 5. This situation leads to the possibility of nonstoichiometric solid–solution formation at the surface. As very little of this red material was obtained (we estimate less than 5 % according to powder X-ray diffractometry) we conclude that the degree of molecular similarity is not high enough.[25,26] In summary, it is this serendipitous duality of events that appears to favor the formation of Form **III**. The nonplanar TI cannot form a stoichiometric molecular complex readily with TNB, for if this were so there would be no other result in the cocrystallization experiments,[9a] and the degree of molecular similarity between TI and TNB is not so high as to lead to the formation of nonstoichiometric solid–solutions. Yet the interaction between TNB and TI is sufficiently good to promote some sort of association. What appears plausible, is an ill-defined outcome with an indiscriminate adsorption of TI molecules over all the faces of the growing TNB crystals.

Figure 5. Overlay of TNB and TI molecules.

Such nonselective adsorption of TI on the TNB faces may be rationalized by considerations of molecular and crystal symmetry. It is not straightforward to establish at which faces of the centrosymmetric Form **I** crystal the additive is adsorbed, since TI has molecular threefold symmetry, as does TNB. This issue is resolved for adsorption leading to Form **II**, because it is noncentrosymmetric, but Form **III** is centrosymmetric. How does the additive work in this case? The clue lies in the actual point groups of Forms **I** and **III** which are *2/m 2/m 2/m* and *2/m*, respectively. The idea here is that the higher the crystal point symmetry, the more different orientations in the lattice the constituent molecules may occupy, making the inhibition process less selective, or in other words, more indiscriminate. This principle was enunciated by Weissbuch et al.[3b] but no examples have been found to support this conjecture until the present case. Here, we may suggest that the threefold symmetric additive molecule may substitute for the threefold symmetric host molecule, of roughly the same size and shape, at several locations because many of the orientations that the host molecule presents in the growing crystal are equivalent.

Finally, let us consider the energetics of the three polymorphs of TNB. To compare the relative stability of the three polymorphs one should consider their lattice energies,[27] melting points, densities, and packing coefficients (see Supporting Information). The crystallographic and physical details are given in Table 1. The data in Table 2 shows that Form **III** is the most stable polymorph being more stable than Form **II** by 0.33 kcal mol^{-1} and more stable than Form **I** by as much as 5.80 kcal mol^{-1}.[28] The observed melting points of Forms **I** and **III** support these calculations. Surprisingly, the least stable polymorph (Form **I**) is also the densest. This is not unprecedented but it is uncommon.[29] That a crystal form that is of such high relative energy has been reported after more than a century of experimental work on TNB is noteworthy, and suggests that Form **I** is distinctly favored kinetically.[30] The adsorption of TI on the faces of the kinetic Form **I** crystal leads (in an orderly fashion according to Scheme 1) to Form **II** and the adsorption is selective. If the adsorption is indiscriminate, the growth of all faces of all possible kinetic forms may be affected,[31] and what crystallizes out might be the most stable (thermodynamically favored) Form **III**. The fact that the highest melting Form **III** has a "normal"[20] packing ($P2_1/c$, $Z'=1$) also corroborates that it is the thermodynamic form, or at any rate close to the thermodynamic form, which may still remain to be isolated. Whether Form **II** is a disappearing form[32] or not is an open question, and we reserve comment at present.[33]

Table 1: Crystallographic data for the compounds studied

Parameter	I	II	III
crystal system	orthorhombic	orthorhombic	monoclinic
space group	*Pbca*	$Pca2_1$	$P2_1/c$
Z	16	8	4
Z'	2	2	1
ρ_{calcd} [g cm^{-3}]	1.729	1.688	1.717
C_{k*}	72.5	71.0	72.5
m.p. [°C]	121.8	119.2	122.7

Table 2: Lattice energy calculations on the polymorphs of TNB

Energy	Form **I** [Kcal mol^{-1}]	per molecule	Form **II** [Kcal mol^{-1}]	per molecule	Form **III** [Kcal mol^{-1}]	per molecule
Van der Waals	−267.830	−16.739	−124.327	−15.541	−65.817	−16.454
electrostatic	−261.686	−16.355	−176.639	−22.079	−82.907	−20.727
hydrogen bond	−43.158	−2.697	−29.152	−3.644	−17.655	−4.414
total energy	−572.67	−35.792	−330.118	−41.265	−166.38	−41.595

In conclusion, it may be said that the isolation and detection of new polymorphs is still unpredictable. A combination of serendipity and subsequent rigorous observation could well lead to novel and unanticipated polymorphs. For instance, in this work, crystal forms have been found that were hitherto unreported. In general, it would appear that McCrone's dictum[34] is correct but again, perhaps only for some categories of molecules.[35] In the present instance, the fact that molecules of TI can interact with those of TNB, but not too well, seems to be the critical factor that determines the appearance of new polymorphs. But why is so much of additive required? And why is it that while additives change crystal morphology easily,[3] they do not seem to be able to change the polymorph that is obtained so readily? It appears that if the additive completely surrounds the embryonic crystal of the kinetic forms (through an indiscriminate adsorption on all the crystal faces), then only the most stable crystal form is able to survive.[31] Normally, thermodynamic forms are obtained under conditions when nucleation is inhibited (dilute solutions, annealing, supercritical fluids, hydrothermal methods, gel crystallization, high pressure). The present study shows that there may be another way of inhibiting nucleation, namely through the use of additives that bind nonselectively to all crystal faces of all kinetic forms.[36] However, this does not mean that such an additive may be designed, in advance, with our present understanding of the crystallization event although the appearance of Form **II** may be rationalized on the basis of an accepted model. Could one have computed the structure of the stable Form **III**? What would happen if TNB was given as a candidate molecule in a blind test for crystal structure prediction (CSP)?[4] Why is it that the presence of TI in the crystallization vessel does not invariably lead to the formation of Forms **II** or **III**? In other words, why is the formation of these more stable forms much less frequent? We are not particularly disappointed that we obtained Form **II** only once and Form **III** only twice. It is possible that if the crystallization is carried out with TI and also employing some other condition that inhibits nucleation (such as those listed above), the appearance of more stable crystal forms might become much more frequent. We are pursuing these and other related experiments currently. On a more speculative note, is the occurrence of multiple molecules in the crystallographic asymmetric unit for nonpseudosymmetric structures correlated with the appearance of kinetic forms? Perhaps some of the questions posed in this paragraph might appear to be rhetorical, or even fanciful. However, they do show that the phenomenon of polymorphism is one of the most difficult frontiers in the chemistry of the molecular solid state today.

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[8] It is possible that additive-induced polymorphism is far more widespread than has been actually documented. In industrial crystallization, it is known, for example, that the crystal form of a substance obtained from the reaction mixture is sometimes different from the forms obtained upon subsequent crystallization of purified material. Considering that the synthetic precursor of a particular molecule of interest is likely to have a related chemical structure, it may well be able to behave as an unintended crystallization auxiliary. For a general reference on industrial crystallization, see *Crystal Growth of Organic Materials* (Eds.: A. S. Myerson, D. A. Green, P. Meenan), ACS Conference Proceedings Series, American Chemical Society, Washington DC, **1996**.

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[11] There is solitary report in the patent literature, [G. B. Ravich, O. F. Bogush, *Dokl. Akad. Nauk. SSSR* **1962**, *142*, 831–834] but the forms reported there do not bear a resemblance to the new crystal forms in the present work.

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[14] TI was synthesized by using a literature procedure (S. Kotha, K. Chakraborty, E. Brahmachary, *Synlett* **1999**, 1621–1623). TNB was either synthesized by using a literature procedure (P. Segura, J. F. Bunnett, L. Villanova, *J. Org. Chem.* **1985**, *50*, 1041–1049) or obtained from Dynamit Nobel AG. We attempted to cocrystallize TNB and TI in 1:1 and 2:1 proportions from chloroform, dichloromethane, ethyl acetate, acetonitrile, acetone, dioxane, nitromethane, and from solvent combinations but in none of these cases could we isolate any diffraction-quality crystals of any molecular complexes.

[15] Crystal data for TNB Form **I**: orthorhombic, *Pbca*, $a = 12.587(11)$, $b = 9.684(9)$, $c = 26.86(2)$ Å, $V = 3274(5)$ Å^3, $Z = 16$, $\rho_{\text{calcd}} = 1.729\ \text{g cm}^{-3}$, $T = 183$ K, $\mu = 0.159\ \text{mm}^{-1}$, $2\theta_{\max} = 57.5°$, 36564 measured, 4188 independent, 1396 observed ($I > 2\sigma_1$) reflections, 271 parameters, $R1 = 0.0450$, $wR2 = 0.0985$ (for $I > 2\sigma_1$), residual electron density $+0.188/-0.191\ \text{e Å}^{-3}$ (CCDC-213310); Crystal data for TNB Form **II**: orthorhombic, *Pca*2_1, $a = 9.2970(19)$, $b = 18.730(4)$, $c = 9.6330(19)$ Å, $V = 1677.4(6)$ Å^3, $Z = 8$, $\rho_{\text{calcd}} = 1.688\ \text{g cm}^{-3}$, $T = 120$ K, $\mu = 0.155\ \text{mm}^{-1}$, $2\theta_{\max} = 55.8°$, 2117 measured, 2117 independent, 1924 observed ($I > 2\sigma_1$) reflections, 271 parameters, $R1 = 0.0397$, $wR2 = 0.0985$ (for $I > 2\sigma_1$), residual electron density $+0.240/-0.317\ \text{e Å}^{-3}$ (CCDC-213311); Crystal data for TNB Form **III**: monoclinic, $P2_1/c$, $a = 12.896(5)$, $b = 5.723(2)$, $c = 11.287(5)$ Å, $\beta = 98.190(8)°$, $V = 824.5(6)$ Å^3, $Z = 4$, $\rho_{\text{calcd}} = 1.717\ \text{g cm}^{-3}$, $T = 183$ K, $\mu = 0.158\ \text{mm}^{-1}$, $2\theta_{\max} = 56.60°$, 4936 measured, 2008 independent, 1221 observed ($I > 2\sigma_1$) reflections, 136 parameters, $R1 = 0.0609$, $wR2 = 0.1462$ (for $I > 2\sigma_1$), residual electron density $+0.419/-0.231\ \text{e Å}^{-3}$ (CCDC-213312); Crystal data for TI: monoclinic, $P2_1/c$, $a = 11.920(3)$, $b = 6.0733(13)$, $c = 16.584(4)$ Å, $\beta = 110.670(4)°$, $V = 1123.4(4)$ Å^3, $Z = 4$, $\rho_{\text{calcd}} = 1.172\ \text{g cm}^{-3}$, $T = 203$ K, $\mu = 0.065\ \text{mm}^{-1}$, $2\theta_{\max} = 54°$, 12490 measured, 2443 independent, 1428 observed ($I > 2\sigma_1$) reflections, 136 parameters, $R1 = 0.0559$, $wR2 = 0.1260$ (for $I > 2\sigma_1$), residual electron density $+0.208/-0.139\ \text{e Å}^{-3}$ (CCDC-213313). The data for Form **I**, **III**, and TI were collected on a SMART diffractometer using $\text{Mo}_{\text{K}\alpha}$ radiation. For Form **II** the instrument used was Nonius FAST area detector. Structure solution by direct methods and refinements on F^2 with SHELXTL (Version 6.10 and 6.12). Non-hydrogen atoms were refined anisotropically and the H atoms of the phenyl groups were generated at idealized geometries and refined isotropically using a riding model. CCDC 213310–213312 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

[16] a) G. R. Desiraju, T. Steiner, *The Weak Hydrogen Bond in Structural Chemistry and Biology*, Oxford University Press, Oxford, **1999**; b) M. Mascal, *Chem. Commun.* **1998**, 303–304; c) K. Wozniak, H. He, J. Klinowski, W. Jones, E. Grech, *J. Phys. Chem.* **1994**, *98*, 13755–13765; d) R. K. R. Jetti, P. K. Thallapally, A. Nangia, C.-K. Lam, T. C. W. Mak, *Chem. Commun.* **2002**, 952–953.

[17] a) L. J. Barbour, *J. Supramol. Chem.* **2001**, *1*, 189–191; b) J. L. Atwood, L. J. Barbour, *Cryst. Growth Des.* **2003**, *3*, 3–8.

[18] See Supporting Information for details of the calculated crystal morphology.

[19] Cocrystallization of TNB with TI in these exhaustive trials was attempted with mole percentages of TI from 10% to 50%. Recrystallization was carried out separately for both TNB and TI and as well as for mixtures from a variety of solvents, such as EtOAc, MeOH, EtOH, CH_2Cl_2, $CHCl_3$, CCl_4, benzene, toluene, *m*-xylene, *p*-xylene, mesitylene, acetone, MeCN, *n*BuOH, *n*PrOH, *i*PrOH, $MeNO_2$, THF, dioxane, Et_2O, DMF, and DMSO. Solvent combinations, such as MeOH–MeCN, benzene–CCl_4, benzene–hexane, EtOAc–hexane, and benzene–MeCN, were also tried. Invariably, we obtained crystals of Form **I** or TI. In all, approximately 100 single crystals from different crystallization experiments were selected for cell measurements. While the crystals very often had different morphologies, all of them turned out to be those of either Form **I** or TI.

[20] A. I. Kitaigorodskii, *Molecular Crystals and Molecules*, Academic Press, New York, **1973**. By "normal" is meant a three-dimensionally close-packed structure without any easily identifiable substructural motifs, such as V-shaped troughs, molecular tapes.

[21] a) P. K. Thallapally, A. K. Katz, H. L. Carrell, G. R. Desiraju, *CrystEngComm* **2003**, *5*, 87–92; b) P. K. Thallapally, K. Chakraborty, H. L. Carrell, S. Kotha, G. R. Desiraju, *Tetrahedron* **2000**, *56*, 6721–6728.

[22] We carried out around 150 crystallization experiments with TNB. In roughly 50 of these trials, we did not use any TI. In these cases, there were two outcomes. For non-aromatic solvents, only Form **I** was obtained. With some aromatic solvents (benzene, toluene, chlorobenzene, *m*-xylene, *p*-xylene, mesitylene) we obtained solvates with a greater or lesser degree of difficulty.[23] With other aromatic solvents (nitrobenzene, bromobenzene, triflurotoluene, pyridine, collidine, picolines), only Form **I** was obtained.

[23] R. K. R. Jetti, P. K. Thallapally, R. Boese, G. R. Desiraju, *Cryst. Growth Des.* **2003**, *3*, 1033–1040.

[24] The current version of the CSD contains 61 (CSD version 5.23, April **2002**) of these molecular complexes; F. H. Allen, O. Kennard, *Chem. Des. Autom. News* **1993**, 8, 1–57.

[25] A. I. Kitaigorodskii, *Mixed Crystals*, Springer, Berlin, **1984** (Springer Series in Solid-State Science 33).

[26] We redetermined the crystal structure of pure TI (the earlier CSD known crystal structure is of limited precision with no hydrogen-atom positions reported; E. R. Boyko, P. O. Vaughan, *Acta Crystallogr.* **1964**, *17*, 152–154; see ref. [15]) but this is quite different from any of the forms of TNB. If the structures were isomorphous, solid–solution formation would be more likely.

[27] The lattice energies were carried out using "Smart Minimizer" option of the Cerius2 package. All molecules in the crystal were treated as rigid entries. Atom–atom potentials were estimated using Dreiding 2.21 force field and atomic charges were estimated using the charge equilibration method. Cerius2, Accelrys, Cambridge (UK). See www.accelrys.com.

[28] These energy values include the small variations in energy owing to the conformational differences between the nitro groups in the three forms.

[29] a) J. M. Robertson, *Proc. R. Soc. London Ser. A* **1936**, *157*, 79–83; b) J. M. Robertson, A. R. Ubbelohde, *Proc. R. Soc. London Ser. A* **1938**, *167*, 122–125.

[30] The relationship between the kinetic accessibility, higher relative energy, and high density of the most common Form **I** and the explosive character of TNB is an aspect that might need to be investigated in the future.

[31] We estimate that at a 20% loading of the additive, the embryonic TNB crystal contains 24580 molecules (crystal radius 107 Å) if the additive coats the crystal at monomolecular thickness, this is reasonable for a crystal in the very early stages of growth. Both TNB and TI are assumed to be spherical and the embryonic crystal is also assumed to be spherical. We thank Mr. T. Omlor for these calculations.

[32] J. D. Dunitz, J. Bernstein, *Acc. Chem. Res.* **1995**, *28*, 193–200.

[33] We do not rule out the possibility that Form **II** may be isolated in another laboratory at a future date, see for example the work on tetraacetyl ribofuransose by P. Bombicz, M. Czugler, R. Tellgren, A. Kálmán, *Angew. Chem.* **2003**, *115*, 2001–2004; *Angew. Chem. Int. Ed.* **2003**, *42*, 1957–1960.

[34] W. C. McCrone, *Polymorphism in Physics and Chemistry of the Organic Solid-State* (Eds.: D. Fox, M. M. Labes, A. Weissberger), Interscience, New York, **1965**.

[35] One of us (GRD) has pointed out on several occasions that despite rigorous experimentation, compounds such as benzoic acid, anthracene, and D-glucose do not yield normal pressure polymorphs.

[36] Leiserowitz et al. made a similar observation with PAN (see refs. [1f, 1g]).