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Diiminoisoindoline: tautomerism, conformations, and polymorphism

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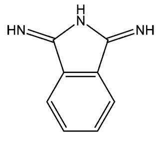
Two polymorphs of the industrially important compound diiminoisoindoline occur in the amino tautomeric form as a conformational isomorph with a 1 : 1 mixture of the *syn*- and *anti*-isomers, and a conformational polymorph containing only the *syn*-isomer.

Diiminoisoindoline (**1**) is an important commercially available intermediate for the manufacture of isoindoline pigments and phthalocyanines as well as the synthesis of other compounds such as porphyrazines.[1] In the course of our studies[2] of the solid-state reactivity of the monophenyl derivative of **1** and of polymorphism in the bis-phenyl derivatives of **1**,[3] we had occasion to grow crystals of **1**. We found that, in the solid state, **1** exists as the amino tautomeric form **2**. In one of these structures, **1** is found in two different molecular conformations in the same unit cell. While *trans*-1,4-diethynylcyclohexane-1,4-diol is reported[4] to have two different conformations in the same unit cell, our observations for the case of **1** show that this phenomenon is more widespread. We note also that **1**, in unspecified form, is manufactured on a large commercial scale while the previous known examples[3,4] are research specimens.



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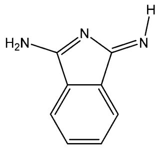
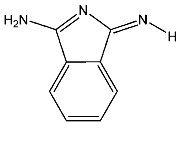


2a



2b

Crystals of the first polymorph, form **A**, obtained from dichloromethane solution, are monoclinic, space group $P2_1/c$, with $Z = 8$ (two molecules in the asymmetric unit).† Inspection of the packing diagram (Fig. 1) shows that, while both molecules are in the amino tautomeric form, they differ in stereochemistry at the imino nitrogen atom. The crystal structure consists of alternate layers of molecules, first with the N–H moiety *anti* to the aromatic ring (**2a**) and the next with the N–H *syn* to the ring (**2b**). Fig. 1 shows vertical layers of *anti*, *syn* and *anti* molecules, respectively. In each layer, pairs of molecules are involved in $R_2^2(8)$ hydrogen bonds[5] around centers of symmetry. These *anti* and *syn* dimer pairs form an infinite C(12) chain of hydrogen bonds. The dimer pairs both involve one amino hydrogen atom donor and an isoindoline ring N atom acceptor, while the chains contain the other amino hydrogen atom donor, and an imino nitrogen atom acceptor. The *syn* and *anti* hydrogen atoms attached to the imino nitrogen atoms do not participate in hydrogen bonding.

Crystals of a second polymorph, form **B,** were obtained from hot benzene solution, to which a minimum amount of methanol had been added to effect solubility. Form **B** (Fig. 2) is monoclinic, space group $P2_1/c$, with $Z = 4$. Polymorph **B** again consists of the amino tautomeric form, but only with molecules having the N–H moiety *syn* to the phenyl ring (structure **2b**). Bond lengths and angles lie in normal ranges, in excellent agreement, *e.g.*, with analogous parameters in 1-amino-3-phenylimino-isoindoline.[2] The packing of molecules is similar, but simpler than that in form **A**, with layers of dimer pairs ($R_2^2(8)$ graph set), and a C(6) infinite chain, with half the atomic repeat, owing to the presence of only one imino hydrogen atom conformation in this polymorph. In this polymorph, the hydrogen atoms attached to the imino nitrogen atoms do not

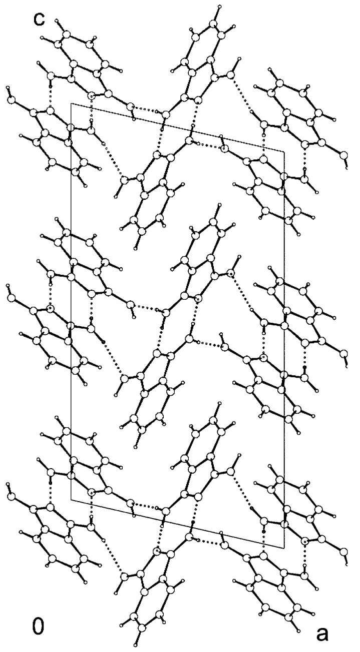


Fig. 1 Crystal structure of form **A** viewed down the *b* axis. The amino and imino C–N distance pairs are (1.317(2), 1.320(2) Å) and (1.280(2), 1.281(2) Å), respectively. The $R_2^2(8)$ hydrogen bond parameters (N···N, N–H···N) are 2.94 Å, 174° for the *anti* dimer pair and 2.94 Å, 166° for the *syn* pair. The analogous parameters for the C(12) chains are (3.02 Å, 171°) and (2.98 Å, 161°) for the *syn* and *anti* donors, respectively.

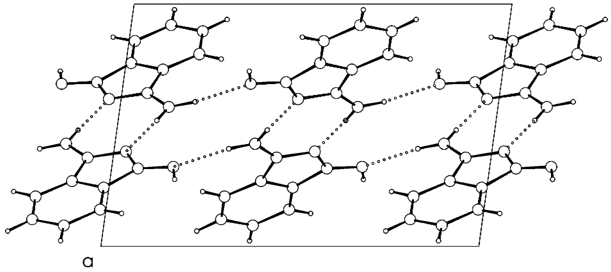


Fig. 2 Crystal structure of form **B** viewed down the *b* axis. The amino and imino C–N distances are 1.311(2) and 1.278(2) Å, respectively. The $R_2^2(8)$ hydrogen bond parameters (N···N, N–H···N) are 2.95 Å, 176°, while the analogous parameters for the C(6) chains are 2.95 Å, 169°.

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participate in hydrogen bonding. The density and molecular volume for **B**, 1.384 g cm^{-3} and 174.2 Å^3, indicate a much higher packing efficiency ($\approx 5.5\%$) compared to that for **A** ($\rho_{calc} = 1.312$ g cm^{-3}; $V_{mol} = 183.7$ Å^3). The lower density of form **A**, along with its apparent predominance, is a likely consequence of a more energetically favourable hydrogen-bond packing arrangement for this phase.[6a]

Recrystallization of **1** from methanol gave a third form as monoclinic crystals, space group $P2_1/c$, with $a = 21.535(3)$; $b = 7.303(1)$; $c = 15.977(1)$ Å; $\beta = 106.86(1)°$; $U = 2405.0(5)$ Å^3. The third form contains methanol molecules, and is thus not a polymorph, but formally a solvate.[6b] The crystals are of very poor quality, and consequently only a partial solution of the structure has thus far been obtained. The asymmetric unit contains three molecules of **1** (without distinction as to whether structures **1** or **2a,b** are present) and two molecules of methanol.

As observed for *trans*-1,4-diethynylcyclohexane-1,4-diol[4] and bis-phenyliminoisoindoline,[3] polymorphs **A** and **B** represent an additional rare example, for a compound of key industrial importance, in which the phenomena of *conformational polymorphism* (presence of different conformers in different polymorphs) and *conformational isomorphism* (presence of different conformers in the same crystal) occur for the same substance.[7]

Compound **1**, crystallized from dichloromethane, appears by visual inspection to consist largely of needles of form **A**; X-ray powder diffraction studies indicate that there is a small amount of another material in this preparation. However, the X-ray powder pattern of **1** recrystallized from ethyl acetate indicates it to be pure form **A**. When crystallization is attempted by suspending **1** in hot benzene and adding methanol until solution occurs ($\approx 5\%$ MeOH), forms **A** and **B** appear as concomitant polymorphs,[8] and X-ray diffraction patterns are consistent with the presence of forms **A**, **B**, and the methanol solvate. The concomitantly obtained needles and plates are shown in Fig. 3. Both phases begin to decompose at 140–150 °C at 5 °C min^{-1}, as evidenced by DSC studies and color changes; no evidence for a polymorphic transformation is observed.

While the crystal structures illustrated in Figs. 1 and 2 show the amino tautomeric form **2**, ^{1}H and ^{13}C NMR studies in solution reveal the diimino tautomer **1**. The ^{13}C spectrum in DMSO-d$_6$ exhibits resonances at $\delta = 169.9$, 136.7, 130.5, and 121.0 ppm, consistent with the diimino tautomer. We note that the ^{13}C solution NMR spectra of several 4,5-disubstituted derivatives[9,10] of **1** also indicate the presence of the diimino tautomer.

There are at least two quantum chemical treatments of tautomerism in **1** and **2**, semiempirical AM1 calculations[11,12] and *ab initio* 6-31G* calculations.[12] Both place tautomer **2** higher in energy than **1** in the gas phase. Further, both calculations[11,12] place isomer **2a** lower in energy than **2b** in the gas phase. While these calculations are relevant to a gas phase species at 0 K, the observation of the amino tautomer in the solid state at ambient temperatures may imply that the amino tautomer is stabilized in the crystal by intermolecular hydrogen bonds.

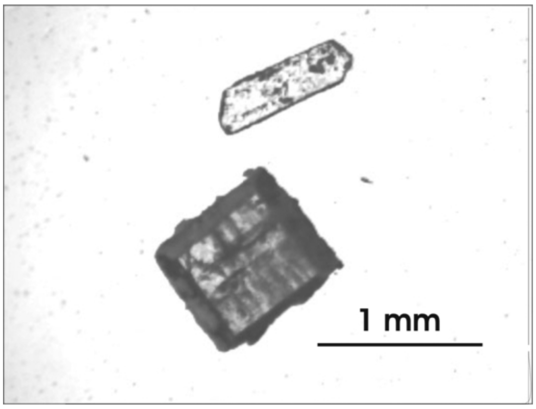

Fig. 3 Concomitant polymorphism observed for **1** as crystallized from hot benzene–methanol solution as described in the text. Upper crystal, form **A**; lower crystal, form **B**.

The diiminoisoindoline system, as well as its substituted analogues,[3] present important opportunities for the generation of conformational polymorphs and isomorphs, and suggest that the simultaneous appearance of these two phenomena for a single compound will be much more likely for molecules which can undergo dynamic isomerism.[6b] Given the observation that isomer **1** predominates in solution, isomers **2a** and **2b** must form rapidly upon crystallization.

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Notes and references

† Crystal data:[13,14] form **A**, $C_8H_7N_3$, $M = 145.16$, monoclinic, space group: $P2_1/c$; $a = 10.8323(16)$; $b = 7.0661(7)$; $c = 19.696(3)$ Å; $\beta = 102.916(11)°$; $U = 1469.4(3)$ Å^3; $Z = 8$; $\rho_{calc} = 1.312$ g cm^{-3}; $\rho_{obs} = 1.30(1)$ g cm^{-3}, $T = 294$ K, μ(CuKα) = 0.68 mm^{-1}, acicular habit, 0.14 × 0.29 × 0.54 mm. Data collected on an Enraf-Nonius CAD-4U diffractometer, 3092 unique data, 2319 [$I > 1.96\sigma(I)$], 224 parameters; $R = 0.0376$, $Rw = 0.0463$. For form **B**, $C_8H_7N_3$, $M = 145.16$, monoclinic, space group: $P2_1/c$; $a = 8.3777(4)$; $b = 6.4807(2)$; $c = 12.9513(5)$ Å; $\beta = 97.793(4)°$; $U = 696.68(5)$ Å^3; $Z = 4$; $\rho_{calc} = 1.384$ g cm^{-3}; $\rho_{obs} = 1.38(1)$ g cm^{-3}; $T = 294$ K, μ(MoKα) = 0.089 mm^{-1}, platelike habit, 0.22 × 0.58 × 0.72 mm. Data collected on an Enraf-Nonius CAD-4 Turbo diffractometer, 1406 unique data, 1196 [$I > 1.96\sigma(I)$], 113 parameters; $R = 0.0344$, $Rw = 0.0462$. CCDC 228419 and 228420. See http://www.rsc.org/suppdata/cc/b4/b400111g/ for crystallographic data in .cif or other electronic format

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