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A new polymorph of 2-methyl-6-nitroaniline

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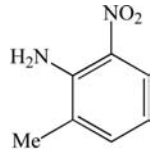
A new crystal form of 2-methyl-6-nitroaniline, $C_7H_8N_2O_2$, crystallizing with $Z' = 2$ in the space group $P2_1/c$, has been identified during screening for salts and cocrystals. The different N—H···O hydrogen-bonding synthons result in linear V-shaped chains in the new polymorph, rather than the helical chain arrangement seen in the known form where $Z' = 1$. The presence of a second component during crystallization appears to have determined the resultant crystal form of 2-methyl-6-nitroaniline.

Comment

The formation of polymorphs by solution crystallization is influenced by thermodynamic and kinetic factors which control the processes of nucleation and crystal growth. The mechanisms and rate by which crystallization occurs depend on a number of factors including solubility, supersaturation and impurities. If a solution crystallization is performed, the solvent used can be a major factor in determining the polymorph formed (Buckley, 1951), as can be the concentration and temperature (Threlfall, 2000; Lahav & Leiserowitz, 2001; Rohani *et al.*, 2005). The cooling rate can also affect polymorph selection; for example, flash cooling a melt often produces the metastable form (Kuhnert-Brandstätter, 1971). The presence of additives or impurities can also affect the polymorphic outcome through inhibiting the growth of one form, or accelerating the growth of nuclei of another (Blagden, 2004). As a consequence of these many possible contributions, the investigation of the effects of various crystallization parameters and the role of structure in determining the properties of compounds still depends extensively on experimental screening methods. Temperature and solvent are usually the first factors to be assessed. We are currently engaged in a systematic study of solid forms, including polymorphs, cocrystals and salts, produced by simple organic molecules with weakly interacting functional groups. In this paper, a crystal form of pure 2-methyl-6-nitroaniline, 2M6NA, produced unexpectedly during cocrystal screening, is reported. It should be noted that the other isomers of 2-methylnitroaniline (*viz.* 2-methyl-3-nitroaniline, 2-methyl-4-nitroaniline and 2-methyl-5-nitroaniline) so far only have one characterized crystal form.



(I)/(II)

The crystallization of two binary systems each containing 2M6NA resulted in two polymorphs of 2M6NA being formed. One polymorph, (I), produced by crystallization with imidazolidine-2-thione, was found to be the same form as that characterized by Jing *et al.* (2006). Further studies have found that (I) crystallizes from methanol, ethanol, propan-2-ol, butan-1-ol, acetone, acetonitrile and dimethylformamide. A second polymorph, (II), only formed on crystallization in the presence of benzenesulfonic acid. The crystallographic data for each structure are summarized in Tables 1 and 2.

Although the room-temperature structure of the most common polymorph of 2M6NA, (I), has already been published, a structure description has not been given which is

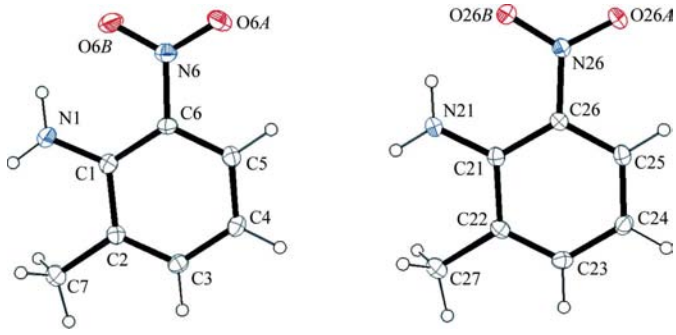


Figure 1
The molecular structures of molecules *A* (left) and *B* (right) of (I), showing the atom-numbering schemes. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

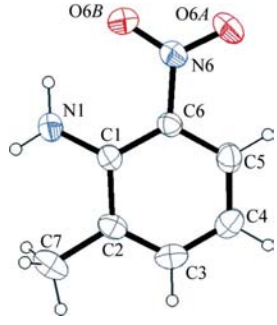


Figure 2
The molecular structure of (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

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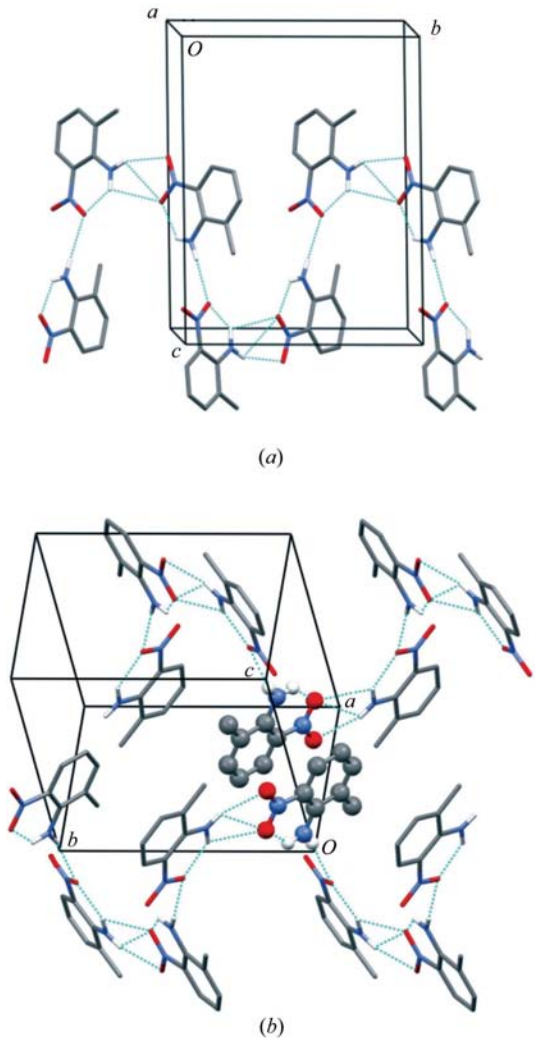

Figure 3
(*a*) Hydrogen-bond interactions (dotted lines) between the molecules of (I). Molecules *A* and *B* form different hydrogen-bond synthons, resulting in a helical chain arrangement. (*b*) Possible π–π interactions between the pair of highlighted *B* molecules, one from the chain at the top and one from the chain at the bottom.

pertinent for the comparison of the two polymorphs. In (I), where $Z' = 2$, the two independent molecules form a dimer connected by a single and a bifurcated hydrogen bond between the amine and nitro groups (Fig. 3*a*). Although single and bifurcated N—H···O hydrogen bonds between amine and nitro groups are more commonly found separately in the Cambridge Structural Database (CSD, Version 5.30; Allen 2002), this synthon is seen in a number of structures with similar distances between the amine and O atoms. The nitro group of molecule *A* then forms a single hydrogen bond with the amine group of a crystallographically different molecule *B*. This results in a helical chain arrangement, due to the orientation of the molecules [83.52 (4)° between the planes of the molecules]. The chains then fit together with weak C—H···O hydrogen bonds to the remaining O atom of the nitro group of molecule *A* that is not involved in any N—H···O hydrogen bonding. This results in molecules *B* being arranged in pairs in

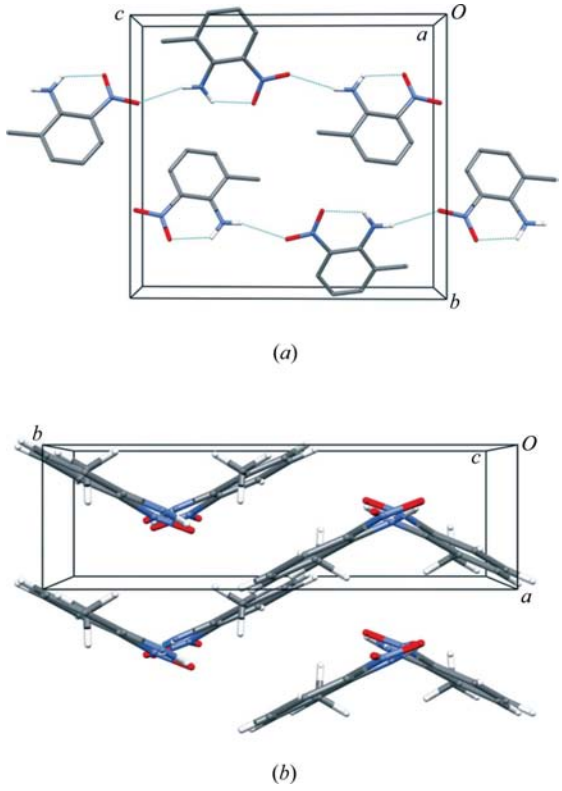

Figure 4
(*a*) The hydrogen-bonded (dotted lines) chain in (II). (*b*) The arrangement of the hydrogen-bonded chains in (II) into stacks (chains are viewed end-on), with no hydrogen-bonding interactions between adjacent stacks of chains.

an offset manner where the perpendicular distance between the molecules in a pair is about 3.38 Å, which is suggestive of π–π interactions (Fig. 3*b*). The nitro groups are nearly coplanar with the aromatic ring, due to an intramolecular hydrogen bond in both molecules between the amine and nitro groups. The angles between the planes of the ring and the nitro group are 1.8 (1) and 6.0 (3)° for molecules *A* and *B*, respectively.

The new form of 2M6NA, (II), consists of chains of N—H···O hydrogen-bonded molecules. However, the hydrogen bonds do not form rings as seen in (I). The molecules form linear V-shaped chains, with an angle of 127.8 (2)° between the planes of adjacent molecules (Fig. 4). The chains are stacked on top of each other in an offset manner, with a perpendicular distance of about 3.51 Å between the molecules. Similar to (I), the nitro group is approximately coplanar with the aromatic ring [angle between the planes of the ring and nitro group = 5.2 (2)°], due to the intramolecular hydrogen bond between the amine and nitro group.

Although not immediately noticeable by eye, the program *XPac* (Gelbrich, 2002) identifies a zero-dimensional construct that is common to both structures (Fig. 5). This consists of two molecules arranged about an inversion centre, with O6*A*···H4^{iii} and H5···H5^{iii} distances of 3.09 and 2.58 Å, respectively, in (I), and O6*A*···H4^{iv} and H5···H5^{iv} distances of 2.93 and 2.50 Å, respectively, in (II) [symmetry codes: (iii) $-x+2, -y+1, -z+1$; (iv) $-x+1, -y+2, -z+1$].

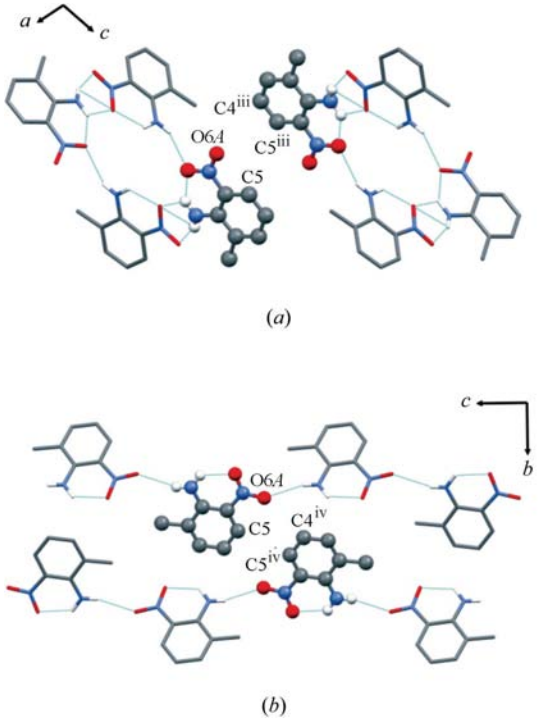

Figure 5
The zero-dimensional construct identified by *XPac* as being common to both polymorphs is highlighted in (*a*) for (I) and (*b*) for (II). In (I), the helical chain arrangement can be seen. In both structures, the construct involves molecules from adjacent hydrogen-bonded chains. [Symmetry codes: (iii) $-x+2, -y+1, -z+1$; (iv) $-x+1, -y+2, -z+1$.]

It was noted by Rafilovich & Bernstein (2006) that a number of attempts to prepare cocrystals have led to new polymorphic forms of the intended cocrystal components due to the creation of new 'crystallization media'. In the present work, the occurrence of the second polymorph of 2M6NA may be due to the more acidic conditions instigated by the benzenesulfonic acid in the methanol solution, or the benzenesulfonic acid may have acted as an impurity, thus enabling a different polymorph to form. Both of these scenarios are evidenced in the literature; of particular note is a study by Towler *et al.* (2004) concerning the role of pH and additives in the polymorphic selection of γ-glycine. They attribute the appearance of the more stable but less kinetically favourable γ form to an 'impurity' effect, where the glycine ions selectively inhibit the nucleation and crystal growth of α-glycine which is kinetically more favourable. Indeed, further work by Poornachary *et al.* (2008) regarding the glycine polymorphs highlighted the controlling effect of pH over the charged impurities. There are a number of other studies in the literature where impurities or additives that are structurally similar to the target compound have been shown to inhibit the development of one polymorphic form or to stabilize one kinetic form over another (Gu *et al.*, 2002; Lancaster *et al.*, 2007; Davey *et al.*, 1997; Mukuta *et al.*, 2005). Other work involving structurally different impurities affecting polymorph formation attributes the selection to a change in solubility or the impeding of mass transport (Mohan *et al.*, 2001), or inclusion of the impurity in the fastest growing faces (Blagden *et al.*, 1998). Due to the small molecules used here, the mass transport theory will not be applicable, whereas hydrogen bonding between the crystallization components is a possibility. Review of the literature and the unique occurrence of the second 2M6NA polymorph suggest that benzenesulfonic acid most likely acts as an impurity during the crystallization, but further work is required to substantiate this concept.

Experimental

All chemicals were purchased from Sigma–Aldrich and were used without further purification. Crystals of polymorphs (I) and (II) were obtained by mixing equimolar amounts of 0.1 *M* methanol solutions of 2M6NA with imidazolidine-2-thione and benzenesulfonic acid hydrate, respectively. The mixtures were then left to evaporate slowly at room temperature. Solution crystallizations of 2M6NA were also prepared with methanol, ethanol, propan-2-ol, butan-1-ol, acetone, acetonitrile and dimethylformamide, and left to evaporate slowly at room temperature. These all yielded polymorph (I).

Polymorph (I)

Crystal data

$C_7H_8N_2O_2$
$M_r = 152.15$
Monoclinic, $P2_1/c$
$a = 8.9267$ (5) Å
$b = 11.1863$ (6) Å
$c = 14.6796$ (4) Å
$\beta = 104.788$ (3)°
$V = 1417.30$ (12) Å^3
$Z = 8$
Mo $K\alpha$ radiation
$\mu = 0.11$ mm^{-1}
$T = 120$ K
0.10 × 0.08 × 0.04 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.989$, $T_{max} = 0.996$
18662 measured reflections
3252 independent reflections
2369 reflections with $I > 2\sigma(I)$
$R_{int} = 0.065$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.049$
$wR(F^2) = 0.117$
$S = 1.05$
3252 reflections
213 parameters
4 restraints
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max} = 0.21$ e Å^{-3}
$\Delta\rho_{min} = -0.28$ e Å^{-3}

Polymorph (II)

Crystal data

$C_7H_8N_2O_2$
$M_r = 152.15$
Monoclinic, $P2_1/c$
$a = 3.9248$ (2) Å
$b = 12.8496$ (8) Å
$c = 14.2746$ (9) Å
$\beta = 91.464$ (4)°
$V = 719.66$ (7) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.11$ mm^{-1}
$T = 120$ K
0.50 × 0.08 × 0.05 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.949$, $T_{max} = 0.995$
8872 measured reflections
1631 independent reflections
1089 reflections with $I > 2\sigma(I)$
$R_{int} = 0.034$

Table 1
Hydrogen-bond geometry (Å, °) for polymorph (I).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1A···O6B	0.894 (15)	1.97 (2)	2.628 (2)	129.7 (19)
N1—H1A···O26B^{i}	0.894 (15)	2.68 (2)	2.980 (2)	100.4 (15)
N1—H1B···O26A^{i}	0.873 (16)	2.276 (17)	3.091 (2)	156 (2)
N1—H1B···O26B^{i}	0.873 (16)	2.65 (2)	2.980 (2)	104.0 (16)
N21—H21A···O26B	0.890 (16)	1.962 (19)	2.616 (2)	129.2 (18)
N21—H21B···O6B	0.883 (15)	2.262 (16)	3.0891 (19)	155.9 (18)

Symmetry code: (i) $-x+1, y+\frac{1}{2}, -z+\frac{3}{2}$.

Table 2
Hydrogen-bond geometry (Å, °) for polymorph (II).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1A···O6A^{ii}	0.868 (15)	2.322 (16)	3.160 (2)	162.4 (17)
N1—H1B···O6B	0.904 (15)	1.98 (2)	2.625 (2)	127.5 (17)

Symmetry code: (ii) $x, -y+\frac{3}{2}, z-\frac{1}{2}$.

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.045$
$wR(F^2) = 0.125$
$S = 1.04$
1631 reflections
110 parameters
2 restraints
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max} = 0.17$ e Å^{-3}
$\Delta\rho_{min} = -0.13$ e Å^{-3}

H atoms were located in difference maps. Those bonded to C atoms were treated as riding atoms in geometrically idealized positions, with C—H = 0.95 (aromatic) or 0.98 Å (methyl), and with U_{iso}(H) = kU_{eq}(C), where k = 1.5 for the methyl groups, which were permitted to rotate but not to tilt, and 1.2 for the remainder. The coordinates of the H atoms bonded to N atoms were refined subject to an N—H distance restraint of 0.89 (2) Å. For (I), the U_{iso}(H) values were set at 1.4U_{eq}(N), while U_{iso}(H) values were refined in (II).

For both polymorphs, data collection: *COLLECT* (Nonius, 1998); cell refinement: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *publCIF* (Westrip, 2009).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD3303). Services for accessing these data are described at the back of the journal.

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