



Unexpected Polymorphism in Nitroanilines.

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Introduction

The existence of polymorphic forms provides a unique opportunity for the investigation of structure-property relationships as, by definition, differences in properties among the polymorphs must be due to differences in structure.¹ The polymorphic behaviour of a compound is a result of the crystallisation kinetic parameters which control the processes of nucleation and crystal growth. The mechanisms and rate by which crystallisation occurs depend on a number of factors including solubility, and supersaturation. Hence the solvent used is a major factor in determining the polymorph formed as the solvent influences crystallisation through solubility. Investigation into the effects of various crystallisation 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.

Experimental

We are currently engaged in a systematic study of solid forms, including polymorphs, co-crystals and salts, produced by simple organic molecules with weakly interacting functional groups. A Microvate² reaction block has been used to investigate the effects of temperature and solvent on crystallisation of polymorphs, co-crystals and salts. This allows various temperature profiles involving different rates of heating, cooling and stepped cooling to be used with a number of solvents.

Results

The crystallisation of two binary systems containing 2-methyl-6-nitroaniline resulted in two polymorphs of 2-methyl-6-nitroaniline being formed. Form 1 was initially produced by crystallisation with imidazolidinethione, and Form 2 on crystallisation with benzenesulfonic acid. Further studies have found that Form 1 is crystallised from ethanol, propan-2-ol, 1-butanol, acetone, acetonitrile and DMF, and over a range of temperatures in slurries and in solution with methanol.

A crystal form of 2-methyl-3-nitroaniline has been obtained through crystallisation with the above solvents and also over a range of temperatures in slurries and in solution with methanol.

Parameter	2-Methyl-6-Nitroaniline, Form 1	2-Methyl-6-Nitroaniline, Form 2	2-Methyl-3-Nitroaniline
Crystal System	Monoclinic	Monoclinic	Orthorhombic
Space Group	$P2_1/c$	$P2_1/c$	$P2_12_12_1$
$a/\text{\AA}$	8.927 (1)	3.925 (1)	3.804 (1)
$b/\text{\AA}$	11.186 (1)	12.850 (1)	12.987 (4)
$c/\text{\AA}$	14.680 (1)	14.275 (1)	14.401 (3)
α	90°	90°	90°
β	104.788 (3)°	91.464 (4)°	90°
γ	90°	90°	90°
Volume/ \AA^3	1417.30 (1)	719.66 (1)	711.53 (3)
Z	8	4	4

Table 1. Crystal data for the 2 polymorphs of 2-methyl-6-nitroaniline, and 2-methyl-3-nitroaniline.

2-Methyl-6-Nitroaniline, Form 1

In Form 1 two molecules are orientated so as to form a 'dimer,' through weak hydrogen bridging between the NH₂ on one molecule and the NO₂ on another. The crystal consists of a herringbone structure that is typical when π - π interactions have a significant effect on the layout of the molecules.

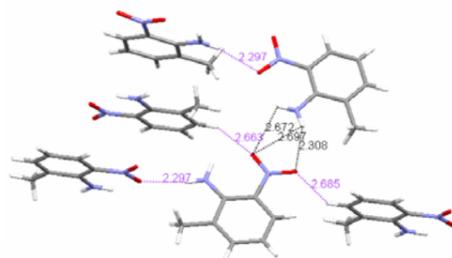


Figure 1. The interaction distances of the dimer shown in blue, other NO₂ and NH₂ interactions shown in purple.

The molecules are not stacked directly over each other and instead are offset. This may be due to steric hindrance of the functional groups together with the π - π interactions of the aromatic rings. The distance between the aromatic rings of the stacked molecules is ~3.5 Å.

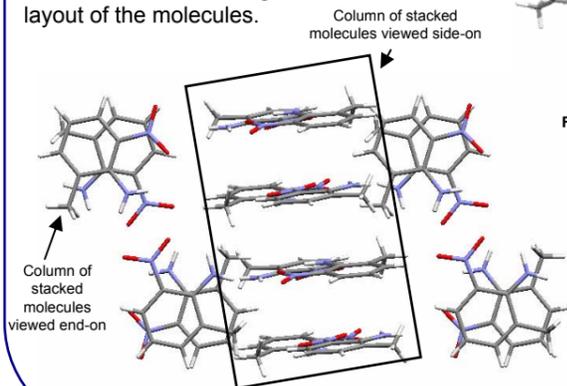


Figure 2. The herringbone structure of Form 1

2-Methyl-6-Nitroaniline, Form 2

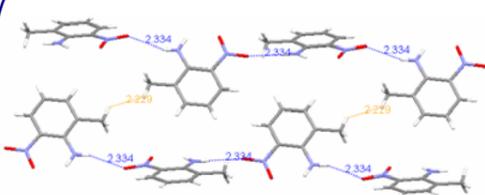


Figure 3. The distances of the intermolecular forces between the functional groups within a sheet

Form 2 was generated by crystallisation with benzenesulfonic acid and methanol.

There is again weak intermolecular hydrogen bridging between O6B...H1B-N1 (a distance of 2.333 Å) to give a chain form. The chains pack via weak CH₃-CH₃ contacts to produce sheets. The sheets are stacked on top of each other to form columns of tilted molecules.

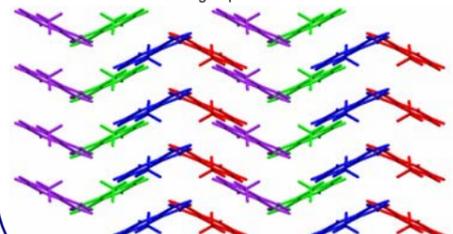


Figure 4. Zig-zag sheets are stacked on top of each other to form columns of molecules

When the molecules are positioned horizontally, it can be seen that they are staggered due to π - π interactions between the aromatic rings.

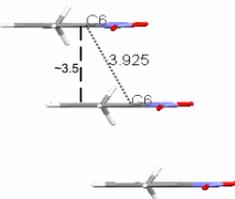


Figure 5. The alignment of the molecules due to π - π interactions

2-Methyl-3-Nitroaniline

This structure also contains weak hydrogen bridging interactions between the molecules. It forms a similar structure to that of 2-methyl-6-nitroaniline Form 2 with stacks of tilted molecules which are linked via weak interactions between the NO₂-NH₂, NO₂-CH₃, NO₂-CH₂ and NH₂-NH₂ functional groups of neighbouring molecules.

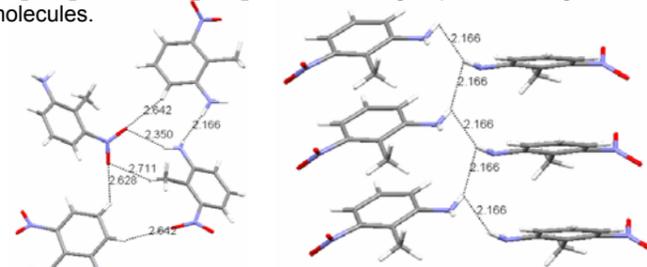


Figure 6. The intermolecular distances between the functional groups

The intermolecular interactions link the columns of molecules to form a 3-d structure. Again, π - π interactions between the aromatic rings cause the molecules to be staggered which results in the tilting appearance of the molecules in each column.

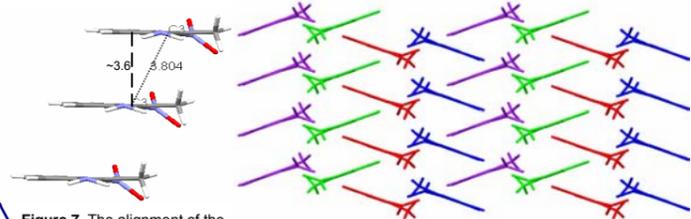


Figure 7. The alignment of the molecules due to π - π interactions

Figure 8. The arrangement of the stacks of tilted molecules

In a typical herringbone structure, as seen in 2-methyl-6-nitroaniline Form 1, the angle between the planes of the molecules in adjacent columns is 90°. In Form 2 and 2-methyl-3-nitroaniline this is not the case and the angles between the planes are much larger: 123.86° and 141.11° respectively.

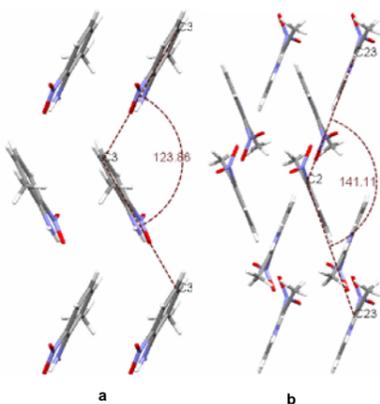


Figure 9a. Form 2 – for clarity only one layer of molecules is shown

b. 2-Methyl-3-nitroaniline

References

1. J. Bernstein, *J. Phys. D: Appl. Phys.*, 1993, **26**, (8B), B66-B76.
2. www.ReactArray.com