Azithromycin is the most important macrolide of *azalide* class (derived from erythromycin A by insertion of an N-methyl group in the lactone ring), and shows higher antibiotic effect than the parent compound, particularly against Gram-negative bacteria. Its synthesis is based on the Beckmann rearrangement of eryrhromycin A oxime to yield the imino ether, and several ways have been reported to reduce the imino ether and finally achieve the azithromycin. One of these routes involve the synthesis of a precursor of the azithromycin, the azithromycin 11,12-hydrogen borate [1], whose acid hidrolysis affords azithromycin.

This structure was studied in solution state through NMR spectroscopy [2], but no study was done so far in solid state, to know the accurate structure and the molecular conformation

In the present communication, we show the results of the analysis by x-ray diffraction of the crystals obtained in different conditions of crystallization: solving the borate in hot acetone and slowly cooling, or solving the borate in acetone and changing the polarity by adding water.

Both solids are crystalline, as is shown on their powder patterns, with different structural parameters, and including the second sample a percentage of amorphous material.

Controling the conditions of crystallization, we can decide what crystal obtain. The knowledge of its crystal structure and composition can give us information about the role of the solvent in controling the final crystal form.

[1] Bayod-Jasanada M, Carbajo R.J., López-Ortiz F., *J. Org. Chem*., 1997, **62**, 7479-7481. [2] Bayod-Jasanada M, Carbajo R.J., López-Ortiz F., *Magn. Reson. Chem*., 1998, **36**, 217- 225.

Keywords: crystallization, azithromycin, hydrogenborate

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Modelling Disorder in 3,3'-dimethoxybenzil, $C_{16}H_{14}O_4$

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This work is part of an extended study of benzil ($C_{14}H_{10}O_2$) and derivatives which aims to understand the role that molecular flexibility plays in determining crystal packing and polymorphism [1,2]. In this study diffuse X-ray scattering is used to probe both the inter- and intra-molecular correlated motions of a series of similar compounds in order to gain insight into how molecular motion influences crystal packing. In future studies it is hoped to apply the methodology to compounds of pharmaceutical interest which display polymorphism. In the present paper we present results for the compound 3,3'-dimethoxybenzil, $C_{16}H_{14}O_4$, 33'DMOB. For this molecule the molecular flexibility is afforded by rotations about three C–C and two C–O single bonds, defined by the dihedral angles, ϕ_1–ϕ_5. Other molecular groups are considered rigid. Diffuse scattering arises from differences between the local structure of a crystal and the underlying *average* structure. Such differences (termed disorder) may be either static or dynamic in origin. The disorder in 33'DMOB is purely thermal, and conventional crystal structure determination using Bragg scattering yields a perfectly normal average structure with no anomalous atomic displacement patterns. Nevertheless all studies have observed strong and highly structured thermal diffuse scattering.

[1] Welberry T. R., Goossens D. J., Edwards A. J., David W. I. F., *Acta Cryst.*, 2001, **A57**, 101–109. [2] Welberry T. R., Heerdegen A. P., *Acta Cryst.*, 2003, **B59**, 760–769.

Keywords: diffuse scattering, molecular flexibility, monte carlo simulation

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Serendipitous Rediscovery of Three Polymorphs of Benzidine

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The search for a co-crystal of benzidine (4, 4'-biphenyldiamine) as a donor with potential acceptors has revealed three polymorphs of the source material benzidine for which, somewhat surprisingly, no structure has been reported according to a CSD search Nov. 2003.

For about 130 years, benzidine and its derivatives had very wide industrial use, mainly as dyes and pigments in a variety of applications. By the middle 1970's the use of benzidine totaled 0.5-1 million kg. At that time the compound itself was found to be carcinogenic, and its commercial use has essentially been abandoned, apparently along with interest in its structure and properties.

The biphenyls attracted the attention of many crystallographers [1 and references therein]. One of the principle reasons for interest in this compound was the fact that in the gas phase the molecule had been shown to be non-planar, while in the crystal the molecule's presence on a crystallographic inversion center requires it to be planar.

The three reported structures are characterized by the molecules packing of Z'>1 (1.5, 3 and 4.5), which according to the CSD are found in only 0.25%, 0.4% and 0.002% of the total structures.

The three forms were grown from two component solutions (one is benzidine) as well as from solutions of benzidine only. In some crystallization experiments the polymorphs grew concomitantly [2].

[1] a) Brock C. P., Minton R. P., *J. Am. Chem. Soc.*, 1989, **111**, 4586-4593; b) Brock C. P., *J. Res. Natl. Inst. Stand. Technol*., 1996, **101**, 321-325. [2] Bernstein J., Davey R. J., Henck J. -O., *Angew. Chem. Int. Ed.*, 1999, **38**, 3440-61.

Keywords: polymorph, co-crystal, concomitant crystallization

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Structures of Some Hydroxynaphthaldehyde Schiff Bases

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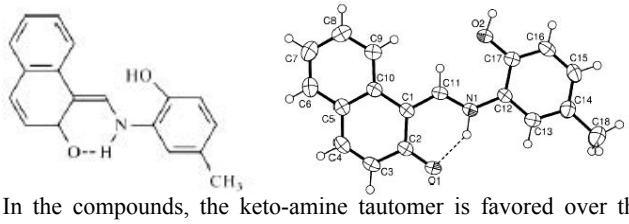
The molecules of compound, $C_{18}H_{15}N_1O_2$ (I) and $C_{17}H_{12}N_1O_2Cl_1$ (II) are not exactly planar, and adopts the keto-amine tautomeric form with an N---H…O and intermolecular O---H…O hydrogen bonds.



In the compounds, the keto-amine tautomer is favored over the phenol-imine form. The rather short C2-O1 and C1-C11 bonds can be considered as C=O and C=C double bonds, respectively. This fact, together with the very short C3-C4 bond, suggests the presence of a significant quinoidal effect. A similar quinoidal effect was observed in our previous work [1].

[1] Odabaşoğlu M., Albayrak C., Büyükgüngör O., *Acta Cryst*., 2004, **E60**, o142-o144.

Keywords: tautomerism, hydrogen bonds, diffraction structure analysis

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Two Polymorphs – Which One is Stable at Ambient Conditions?

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NN414 (6-chloro-3-(1-methylcyclopropyl)-amino-4*H*-thieno[3,2-*e*]-1,2,4-thiadiazine 1,1-dioxide) is an opener of ATP sensitive potassium channels, which attenuates hyperinsulinemia. The compound prevents diabetes and improves glucose tolerance without affecting body weight or body composition in preclinical studies. Apart from its therapeutic effects it is also interesting because of its