our ongoing work [3] directed to manage together the diversity and flexibility within a pool of ligand candidates for bioassays, [4] we present here the results of a study concerning the replacement of CH_2 group (X in figure) in Irurre compounds, [2] with oxygen, sulfur, or with a SO_2 group. The structural properties of the resulting molecules were studied in the solid state, by single crystal X-ray diffraction, and calculated in the gas phase, by ab-initio methods. In each case the energy barrier to be overcome for the enantiomers interconversion as well as the transition state have been determined. The resulting scale of flexibility has been correlated with the chemical and structural features of the diverse library members.

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MS20 P10

Quantification of pharmaceuticals in solid dosage forms Hana Petrickova[a] [a]*Zentiva a.s., R&D Analytical department, U kabelovny 130, 10237 Prague 10 – Dolni Mecholupy, Czech Republic.*
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Keywords: quantitative XRPD, pharmaceuticals, phase identification

XRPD is nowadays a routine widespread tool for characterisation pharmaceutical solids. The qualitative phase analysis is essential for development either API itself or the final solid dosage form and a lot of applications were introduced ranging polymorphic screenings, pre-formulation, formulation, stability testing or crystallography [1]. On the other hand importance of quantitative phase analysis (QPA) of polycrystalline mixtures comes into ever-increasing attention. After identification comes, of course, question: “How much?”. Crutial for the analysis is to decide which of the quantitative information is expected, concrete number, limit test or simple positive/ negative evidence.
Examples of different approaches of QPA will be presented using the FullPat [2], the Rietveld [3] and the single peak method. Influence of the sample (amorphous/crystalline, with/ without knowledge of 3D crystal structure, crystal size and shape) will be discussed on two examples: crystalline three component mixture and almost amorphous tableting mixture.

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MS20 P11

Structural investigation of new insulin derivative at room temperature Biserka Prugovečki[a], Stjepan Prugovečki,[b] Detlef Beckers,[b] Dubravka Matković-Čalogović;[a] [a]*Department of Chemistry, University of Zagreb, Croatia.* [b]*Panalytical B.V., Almelo, The Netherlands.* E-mail: biserka@chem.pmf.hr

Keywords: insulin, protein crystallography, powder diffraction

Insulin is a hormone protein that regulates carbohydrate metabolism and it also takes part in the metabolism of fat and proteins. It is used medically in patients with Type 1 diabetes mellitus. Occasionally some patients with Type 2 diabetes mellitus also require insulin.
Owing to its crucial metabolic role and its pharmaceutical importance many structural studies on chemically and genetically modified insulins have been done.
We will present the results of our investigation on human bromo-derivative of insulin. Both single crystal and powder diffraction data were collected on laboratory instruments at room temperature. The investigated insulin derivative belongs to the $T_3R_3^f$ rhombohedral form [1] with cell parameters a = 80.96 Å and c = 37.30 Å. The unit cell parameter c at room temperature is two times smaller in comparison to the one at 100 K [2]. Coordination of zinc ions and conformation of insulin molecule will be discussed.

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MS20 P12

Structure solution and metastable zone width experiments of a tri-substituted aromatic compound. . Andrew O’Neill, Chick C. Wilson, WestCHEM, *Department of Chemistry*, *University of Glasgow*, Glasgow G12 8QQ, Alastair J. Florence, *Department of Pharmaceutical Sciences*, *University of Strathclyde*, 27 Taylor Street, Glasgow G4 0NR.

Keywords: polymorphism, crystal nucleation, metastable zone

Polymorphism in molecular crystals is the ability of a substance to exist in different crystal packing arrangements [1]. Understanding the phenomenon of polymorphism has become an increasingly important challenge, particularly in the pharmaceutical industry, where there would be considerable advantages were it possible to be able to identify which compounds will be likely to display different polymorphic forms from a knowledge of molecular structure alone. We are part of the UK Research Councils' Basic Technology CPOSS project (Control and Prediction of the Organic Solid State), which has been set up to tackle this problem.
Whilst accurate thermodynamic models are available to predict polymorphism, they do not currently accommodate kinetic factors such as nucleation and crystal growth resulting in an inclination to overestimate the tendency to polymorphism [2]. Nucleation is the initial process leading to the growth of crystals. Due to rapid onset, nucleation studies have proven to be a highly challenging area to study experimentally. However, an understanding of the process is essential as increasing numbers of important materials are found to exhibit polymorphism, even when grown under seemingly identical conditions.
This poster will describe the experimental approach to study model systems, the identification and structure solution of suitable systems and establishment of conditions that are suitable for subsequent examination by scattering techniques.
Methyl 2,5-dibromobenzoate ($C_8H_6O_2$ Br_2), a tri-substituted aromatic compound, with a previously unsolved crystal structure, has been selected for the investigations. The choice of this material is governed by

the presence of the two heavy atoms on the benzene ring, which make the compound potentially favourable for further liquid scattering studies to examine the crystal growth from the nucleation point. The physical form has been characterised at low temperature due to sublimation occurring at room temperature – this makes the full characterisation of the crystallisation conditions for this material challenging. The solubility profile, as a function of temperature, and metastable zone-width experiments, that have been studied using in situ measurements from ATR-UV spectroscopy and FBRM measurements, have been determined for this compound. We present our findings to date and comment on the suitability of this compound for further examination using scattering techniques.

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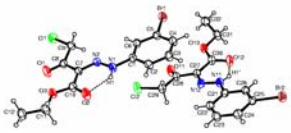
MS20 P13

(*Z*)-Ethyl 2-[2-(3-bromophenyl)hydrazono]-4-chloro-3-oxobutanoate Gökhan Alpaslan[a], Özgür Özdamar[b], Mustafa Odabaşoğlu[b], Nazan Ocak İskeleli[a], Ahmet Erdönmez[a] [a]*Ondokuz Mayıs Univ., Department of Physics, Samsun-Turkey.* [b]*Ondokuz Mayıs Univ., Department of Chemistry, Samsun-Turkey.* E-mail: gokhana@omu.edu.tr

Keywords: Single-crystal X-ray study; Keto-hydrozo tautomeric form, aliphatic chain

(*Z*)-Ethyl 2-[2-(3-bromophenyl)hydrazono]-4-chloro-3-oxobutanoate ($C_{12}H_{12}ClBrN_2O_3$) was synthesized and its crystal structure determined. It crystallizes in the monoclinic space group, $P2_1/n$, with a = 7.4266(3), b = 14.1636(7), c = 26.6760(10) Å, $R(F^2)$ = 0.032 for 5479 independent reflections.



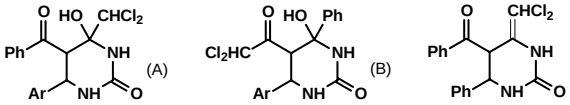
There are two crystallographically independent molecules in the asymmetric unit of the title compound, $C_{12}H_{12}ClBrN_2O_3$. The molecules adopt a keto-hydrazo tautomeric form, stabilized by an intramolecular hydrogen bond.

MS20 P14

Crystal and molecular structure of 4,5,6-trisubstituted perhydropyrimidin-2-one derivatives. Ekaterina V. Mironova, Aidar T. Gubaidullin, Igor A. Litvinov, Svetlana V. Vdovina, Vakhid A. Mamedov. *A.E. Arbuzov Institute of Organic and Physical Chemistry, Russian Academy of Sciences, Kazan, Russia.* E-mail: katy@iopc.knc.ru.

Keywords: 2(1*H*)-pyrimidones, X-ray structure, tautomerism.

2(1*H*)-Pyrimidones represent a heterocyclic system of remarkable pharmacological activity. In recent years functionalized derivatives have emerged as calcium channel modulators, α_1-adrenoreceptor selective antagonists and antiviral agents. Here we report the structures of four novel compounds of this range (**I-IV**), which were analysed in order to make the definite choice between two possible isomeric products of the reaction in the system containing urea, aromatic aldehydes and dichloromethylacetylbenzoylmethanes. The compounds **I**, **II**, **IV** crystallize in centrosymmetric space groups, **III** – in noncentrosymmetric space group (conglomerate). The molecules **I, II** form the solvates with DMSO and acetonitrile respectively. The heterocycle of molecule **I** has "envelope" conformation, and **II**, **III**, **IV** – "half-chair" conformation.



Ar = 2-IC_6H_4 (**I**); 3-IC_6H_4 (**II**); 4-$Me_2NC_6H_4$ (**III**)

The hydrogen bonds system (intra- and intermolecular ones), the packing coefficient and solvent accessible potential area in crystal were also analyzed. The authors greatly acknowledge the Russian Foundation for Basic Recearch (grant N. 04-03-32156 and 05-03-33008) and Russian Science Support Foundation for the financial support.

MS20 P15

Structural Diversity of Synthetic Estrogen Solvates Jan Smits, Carmen Guguta, Ineke Eeuwijk, René de Gelder, *Molecular Materials, Institute for Molecules and Materials, Radboud University Nijmegen, The Netherlands.*
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Keywords: single crystal structure determination, solvates, drug packing

The success rate of discovering new polymorphs by crystallization from solution may be increased if solvents with diverse properties are used during initial polymorph screening. Over the last years, several solvent classifications were made to provide guidelines for the judicious choice of solvents with diverse properties for polymorph screening. Often solvates are found instead of new polymorphs. At the moment the formation of solvates is little understood and systematic studies on the formation and crystal structure determination of solvates are important for obtaining insight into the factors that determine the formation of these multicomponent crystals [1-2]. We have been engaged in such a study, focusing on ethinyl estradiol and related estrogen analogues. Estrogens are the essential hormones for the development of primary and secondary female sex characteristics and have a common steroid ring skeleton. Steroids in general have been studied intensively with respect to their molecular and crystal structures. Thousands of crystal structures of steroids are present in the Cambridge Structural Database and for certain steroids large series of solvates are found.