

**MS11.08.03 CHIRALITY IN DRUG DISCOVERY RESEARCH.** Uli Hacksell, Preclinical R&D, Astra Draco AB, S-221 00 Lund, Sweden.

Regulatory requirements regarding documentation of chiral drugs have been increased during recent years. Today, a new drug application of a chiral drug normally contains pharmacodynamic, pharmacokinetic and toxicological documentation on the individual enantiomers even if it is the racemate that is considered for therapeutic use. This additional documentation is time consuming and increases the cost for drug development. It might, therefore, be advantageous to aim for the development of achiral drugs. However, in drug discovery research, chiral drugs may offer certain advantages; provided that enantiopure compounds are studied, chiral molecules will provide much more information about receptor/enzyme - ligand/substrate interactions than achiral analogues. In addition, recently developed synthetic methods affording enantiopure compounds and analytical methods for quantifying enantiopurity are available. Several examples will be given demonstrating that enantiopure ligands have provided essential information on the molecular basis for activation of G-protein coupled receptors. It is of particular interest that the chirality of a receptor ligand may be used to fine-tune the pharmacological profile.

**MS11.08.04 SECOND-HARMONIC GENERATION STUDIES OF CHIRAL ORGANIC SALTS.** Brian O. Patrick, Bozena Borecka-Bednarz, John R. Scheffer, James Trotter & Alan Bree. Department of Chemistry, University of British Columbia, Vancouver, B.C., Canada, V6T 1Z1.

Nonlinear optical (NLO) materials designed for second-harmonic generation (SHG) are governed by two symmetry related requirements. They are: (i) the molecule must not possess a center of symmetry; and (ii) the crystalline packing arrangement must be non-centrosymmetric. If either condition is not met the material becomes SHG-inactive. As well, electrostatic forces between adjacent, highly polar molecules often causes them to pack in an anti-parallel (head-to-tail) fashion, decreasing the bulk nonlinearity. The introduction of chirality satisfies both symmetry conditions; however this does not ensure that the NLO chromophores will orient themselves inside the unit cell so as to produce SHG efficiently. Derivatives of p-nitroaniline and 2,4-dinitroaniline (NLO materials that are SHG-inactive) with the amino acid glycine have been coupled with derivatives of L-proline and with (1S,2S)-pseudoephedrine to form chiral salts. In both series of materials the uncoupled NLO acid is SHG-inactive, while a majority of the salts have become significantly SHG-active. X-ray crystal structures of both acids and ten of the twelve salts reveal that hydrogen bonding and shielding from the counterion play important roles in discouraging the NLO chromophores from packing in the inefficient head-to-tail fashion described above.

**MS11.08.05 FERROELECTRIC SWITCHING, ATOMIC DISPLACEMENTS AND PIEZOELECTRIC MODULI IN CTA (CsTiOAsO<sub>4</sub>) AND KTP (K<sub>2</sub>HfOPO<sub>4</sub>).** Jörgen Albertsson,<sup>a</sup> Kenny Ståhl,<sup>b</sup> Jonathan C. Hanson,<sup>c</sup> Göran Svensson<sup>a</sup>, Rindert Bolt.<sup>a</sup> <sup>a</sup>Inorganic Chemistry, CTH, S-412 96 Göteborg, Sweden; <sup>b</sup>Chemistry Dept. B, DTU, DK-2800 Lyngby, Denmark; <sup>c</sup>Chemistry, BNL, Upton, NY 11973, USA

Peak shifts in selected reflections of extended face crystals of CTA and KTP under a square-wave electric field, have been measured aiming at a determination of (i) the field strengths necessary to switch the ferroelectric domain and (ii) the values of the piezoelectric coefficients. The difference in intensity between the two parts of a split peak of CTA was measured by repeated  $\omega$  scans for 20  $\lambda$  values, 0.05° apart. While the peak shifts are caused by

the variation in elastic strain with the electric field, differences in intensity correspond to the atomic displacements induced by the field.

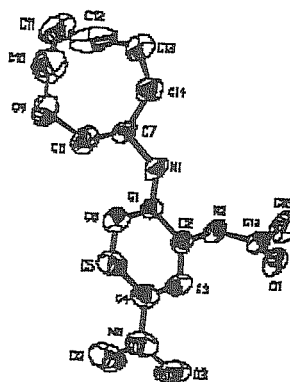
Single crystals of CTA and KTP were grown from self fluxes by the top seeded solution growth technique. They were cut and polished to {001} plates with a thickness between 300 and 450  $\mu$ m. Layers of ca. 200 Å of Au or Al was evaporated onto the {001} faces. The crystals were mounted on the diffractometer at beam line X7B at the National Synchrotron Light Source at Brookhaven National Laboratory (USA), with electric leads connecting the metal layers to a power supply and a generator producing a square-wave variable voltage up to 1500 V. The tension was alternatingly applied to each side of the crystal at a frequency of 20 Hz. A scaler and a clock were gated to each of the two square-waves thus allowing the detection of a possible shift in position and intensity of a reflection between the two field directions. Experiments at low temperature were made with the crystal mounted on the cold finger of a Displex® closed-cycle refrigerator within an evacuated Be can.

Both CTA and KTP crystallizes in space group  $Pna2_1$  with  $Z = 8$ . The unit cell dimensions are  $a = 13.486(2)$ ,  $b = 6.8616(7)$ ,  $c = 10.688(1)$  Å (CTA) and  $a = 12.819(3)$ ,  $b = 6.399(1)$ ,  $c = 10.584(2)$  Å (KTP).

**PS11.08.06 CRYSTAL GROWTH AND STRUCTURE OF 3-ACETAMIDO-4-N-CYCLOOCTYLAMINO-NITROBENZENE, A NEW ORGANIC MATERIAL FOR NONLINEAR OPTICS.** <sup>a</sup>Ruiz-Perez C., González-Platas, J., Yanes, A.C., Torres, M.E. (Dpto. Física Fundamental y Experimental, Universidad de La Laguna, Spain) <sup>b</sup>Solans, X. (Dpto. Cristalografía, Mineralogía y Depositos Minerales Universitat de Barcelona, Spain).

Nonlinear optical crystals appear very attractive for applications in image processing and optical communication. In recent years the interest in using organic crystals with charge correlated and highly delocalized  $\pi$ -electron states (e.g., nitroanilines with donor and acceptor substitution at parapositions) has increased considerably, since very large nonlinear optical susceptibilities have been measured in some of the materials which make them attractive for future *cw*-laser applications.

The title compound is a donor-acceptor (DA) substituted benzene derivative, with a charge-transfer (CT) interaction between the *para*-disposed cyclooctylamino donor and the nitro acceptor groups.



The compound crystallized in the orthorhombic system (Pcmb) with two both molecules in the conformation of the cyclooctyl. The T have structural similarity to NPP, PNP and COANP, in all compounds the aromatic ring is essentially planar. An analysis of seminormal probability indicate that the big difference between monomeric molecules in the asymmetric unit.

#### References:

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D.J. Williams, Angew. Chem.Int. De. Engl. 23, 690 (1984)