s9.m2.p3 **Crystallographic and Thermodynamic Aspects of Cephalosporin Complexation.** R. de Gelder, G.J. Kemperman, F.J. Dommerholt, A.J.H. Klunder, and B. Zwanenburg, *NSR Center for Molecular Structure, Design and Synthesis, University of Nijmegen, Toernooiveld 1, 6525 ED Nijmegen, The Netherlands.*
Keywords: cephalosporin, crystal chemistry, host-guest complexes

Cephalosporins are life saving antibiotics which have been in medical use for many years all over the world. Cephalosporins can be isolated and purified from aqueous reaction mixtures by selective complexation using an additive, e.g. beta-naphthol.[1] Fundamental insight into the complexation process is highly relevant from an industrial point of view, since the overall yield of antibiotic product after isolation and purification strongly depends on the complexing agent used.

The aim of our research is to understand all relevant aspects of efficient complexation and to translate fundamental insight into optimal complexing agents for the cephalosporin antibiotics. X-ray diffraction studies revealed that all cephalosporin complexes found thus far are inclusion compounds in which the antibiotics form the hosting framework and the complexing agents act as guest molecules. It is shown that the nature of the hosting framework can be controlled by the complexing agent used[2] and that, dependent on the guest molecule, frameworks containing layers, channels or cavities can be obtained.[3] It appears that, although the hosting frameworks can be significantly altered, a number of remarkable structural features remain unaffected.

The complexation efficiency, which expresses to which extent the cephalosporins can be withdrawn from solution, is explained in terms of the thermodynamics of the complexation reaction. This is used to determine the subtle relationship between the molecular structures of a number of naphthalene derivatives and the relative stabilities of the complexes they form with Cephradine, one of the cephalosporin antibiotics of interest.

The main conclusion reached is that a structural modification of the guest molecule which significantly stabilizes the cephalosporin complex not necessarily results in a more efficient complexation. This is demonstrated for a number of cases. The accompanied, uncorrelated change in the solvation energy of the guest molecule plays, for these systems, a major role and should in principle be known to predict reliably the overall effect of the modification of the guest molecule on the resulting change of the complexation efficiency.

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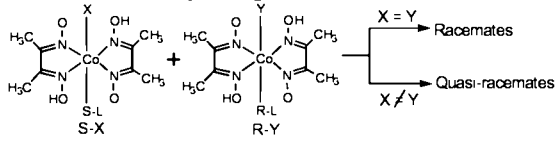
s9.m2.p4 **Quasi-racemates, Racemates and Enantiomers of Cobaloximes.** C. Hu, R. Härter, I. Kalf, U. Englert, *Institut für Anorganische Chemie der RWTH, Professor-Pirlet-Straße 1, D-52056 Aachen, Germany.*
Keywords: chiral Cobaloxime, quasi-racemate, lattice energy calculation.

Cocrystallizing $[Co(dmgH)_2(NCO)(S\text{-}L)]$ and its closely related compound of opposite chirality $[Co(dmgH)_2(NCS)(R\text{-}L)]$ (L is α-phenylethylamine), we obtained a 'strange' quasi-racemate [1]. In a unit cell three S-NCO and one R-NCS molecules are found. Compared to their enantiomers and true racemates, the cocrystal has the similar molecular packing and hydrogen-bond pattern with the latter. After checking all related compounds, a conclusion can be drawn that H-bonds play a decisive role in such molecular packings.



(X, Y are adjustable anionic ligands, L is a chiral substituent)

Scheme I. The process to form racemates and quasi-racemates from enantiomers

Because of the presence of the complex H-bonds, it is more difficult to calculate this interesting cocrystal's lattice energy than our first quasi-racemate's [2], which can be seen as a simple van der Waals crystal from S-CN and R-NO_2 with a normal 1:1 molecular ratio and a pseudo center of inversion as expected [3]. How to eliminate H-bonds' effect and carry out lattice energy calculations in a more reliable way [4]? Two principle approaches can be considered and involve either H donor or acceptor capabilities of our compounds. As for the former we want to change α-phenylethylamine into the chiral pyridine derivatives [5] which have no hydrogen atoms as donors. As for the latter, we can keep the old chiral ligand and find the suitable X or Y anions with no ability to accept hydrogens, for example, alkyl groups [6]. Surely, these new cobaloximes should be stable in air and solution and soluble in the common solvents like in the old system.

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