s9'.m2.p1 **Simple Structure Prediction? Use Of Crystallographic Data To Aid Design And Prediction Of Molecular Structure Using Molecular Modelling Techniques.** A. Parkin, D. Coventry, R.A. Coxall, S. Parsons, P.A. Tasker, *Department of Chemistry, University of Edinburgh, Kings Buildings, West Mains Road, Edinburgh EH9 3JJ.*
Keywords: molecular interactions, ab initio structure prediction, crystal packing.

A number of copper(I) crystal structures of the types shown in Figure 1 have been characterised locally at the University of Edinburgh, and a number of others have been mined from the Cambridge Structural Database. By the use of the structural information such as bond lengths and angles available from these compounds it is possible to use *ab-initio* calculations, or more simply some of the physical properties of the ligand, to predict whether the copper(I) will be 3- or 4-co-ordinate. It may then be possible to predict the molecular structures of these compounds using molecular modelling force-field techniques. This method not only enables structure prediction, but could aid design of specific compounds for use in industry. This is currently an area of ongoing research to determine how widely applicable this method could be.

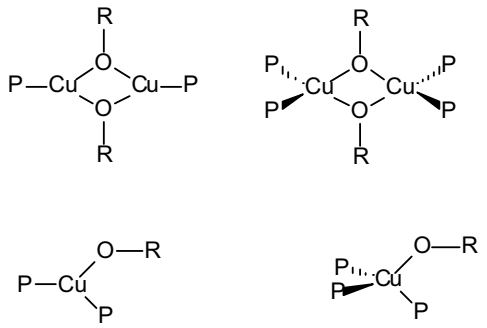

Figure 1 - Both 3- and 4-co-ordinate monomer and dimer crystal structures have been characterised from copper phosphine compounds with various alcohols, including one dimer containing both a 3- and a 4-co-ordinate metal. Can these features be predicted?

s9'.m2.p2 **Novel Chiral Local Anesthetic: Multidisciplinary Characterisation**. J. Grochowski[a], P. Serda[a], M. Pasenkiewicz-Gierula[b], P. Talik[b], R. Czarnecki[c], T. Librowski[c], S. Lochynski[d] ,[a]*Regional Laboratory, Jagiellonian University, Ingardena 3, 30-060 Kraków, Poland;* [b]*Institute of Molecular Biology, Jagiellonian University;* [c]*Department of Pharmacodynamics, CM JU, Kraków;* [d]*Institute of Organic Chemistry, Biochemistry and Biotechnology, Wroclaw University of Technology*.
Keywords: ab initio structure prediction, molecular crystals.

$C_{16}H_{30}O_2N_2 \cdot HCl$ (KP-23), a naturally originated carane derivative extracted from *Pinus sylvestris,* has potent local anesthetic properties. The duration of its anesthetic action in solution exceeds by 2-6 times the respective values for lidocaine.

Earlier X-ray crystallographic studies revealed[1] that the molecule possesses four chiral centres and appears in diastereoisomeric form in the triclinic P1 space group. Two molecules in the unit cell, joined by hydrogen bonds, form a dimer. Stereoisomers have identical RSR absolute configuration at the chiral centres in the carane moiety, and the absolute configuration at the chiral centre in the chain substituent can be opposite (diastereoisomeric form, KP-23) or identical (two possible homochiral forms, KP-23R and KP-23S).

The KP-23S structure is similar to that of KP-23 (in spite of opposite configuration at one chiral centre). Both substances crystallise in P1 space group with similar values of lattice constants. The conformation of the S isomer from KP-23 is virtually the same as conformation of one of the KP-23S isomers.

Structure optimisation revealed that the energy of both conformations in the unit cell of KP-23S crystal is practically the same and by ~3% higher than that of the R isomer from KP-23. Molecular dynamics (MD) simulation was applied to study the stability of diastereoisomeric and homochiral dimers in solution and their interactions with palmitoyloleoylphosphatidyl-choline (POPC) bilayer – a good model for a plasma membrane of eucariotic cells. Adequately to pH 5.0 value in dilute water solution of KP-23, both neutral and protonated forms of the isomers were used in simulations.

MD simulations of neutral dimers in water at 37 °C decay after 500 ps of the simulation time. Dimers of protonated forms are less stable. MD simulation of all isomers in the bilayer are in progress. So far neutral forms preferentially locate in the interfacial region of the bilayer, while the protonated forms – in the water phase.

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[1] Czarnecki, R., Czerwinska, K., Grochowska, K., Grochowski, J., Librowski, T., Serda, P., Arzneimittel-Forschung, (1992), 42, 1279-1283.