

## Poster Sessions

depend on alloy microstructure and is determined by intersection with forest dislocations. As the deformation temperature increases in the range 150-200 K, the strain rate sensitivity rises owing to activation of dynamic recovery and contribution of diffusion processes under plastic deformation of fine-grained materials.

**Keywords:** magnesium alloy, structure, low temperature.

### MS31.P01

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#### Coordinated productive and unproductive substrate binding in the COX-2 homodimer

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The cyclooxygenases (COX-1 and COX-2) are membrane-associated heme-containing homodimers that generate prostaglandin H<sub>2</sub> from arachidonic acid (AA) in the committed step of prostaglandin and thromboxane biogenesis and are the targets for nonsteroidal anti-inflammatory drugs. Both isoforms behave as heterodimers during catalysis, exhibiting half-of-sites reactivity. Although AA is the preferred substrate for both COX isoforms, these enzymes, with varying efficiencies, oxygenate other fatty acid and endocannabinoid substrates. To elucidate the atomic level interactions that are involved with binding and conformational positioning of substrates for catalysis, we determined the X-ray crystal structures of AA, eicosapentaenoic acid (EPA), and 1-arachidonoylglycerol (1-AG) bound to murine COX-2 to 2.10, 2.40, and 2.20 Å, respectively. AA, EPA, and 1-AG bind in different conformations in each monomer constituting the homodimer in their respective structures, such that one monomer exhibits productive binding and the other unproductive binding of the substrate in the cyclooxygenase channel. Comparison of the COX-2: substrate crystal structures revealed an alternate rotamer conformation of Leu-531 that allowed for these novel substrate conformations; but interestingly, mutagenesis of Leu-531 in COX-2 did not result in a significant decrease in  $V_{max}$  or  $K_m$ , in contrast to similar studies with COX-1. We conclude that the mobility of Leu-531 increases the accessible volume at the opening of the cyclooxygenase channel, and contributes to the observed ability of COX-2 to oxygenate a broader spectrum of substrates compared to COX-1. Furthermore, the alternate conformations of substrates bound to the COX-2 homodimer may be mechanistically associated with the observed half-of-sites reactivity.

**Keywords:** substrate\_complex, bioactive\_lipid, enzyme\_allostery

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#### The role of crystallography in chemical kinetics and industrial processes

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Single crystal crystallography plays a very important part in understanding the mechanisms of chemical reactions, including catalytic reactions. The isolation and identification of intermediates and products provide the researcher with a clearer understanding of reaction routes and the effects of steric bulkiness and/or electronic effects of coordination compounds.

Transition metal-catalyzed ethylene oligomerisation typically produces a broad range of  $\alpha$ -olefins. The development of alpha-olefins is an ongoing process [1] and recently the selective tetramerisation of ethylene to 1-octene was reported [2]. The evaluation of a large number of diphosphinoamine (PNP) ligands with various substituents on both N and P ligands reported that the predominant factor in the catalytic selectivity is the steric bulk on the central nitrogen atom compared to the basicity of the phosphine [3-7].

This study reports the synthesis of a range of PNP ligands with varying catalytic activity and selectivity and with a systematic variation of electro-steric properties of the N-substituents. A range of crystal studies were completed to further evaluate any correlations [8-9]. A comparison of the crystallographic data of these PNP ligands with the catalytic behaviour was made in an attempt to further understand this process, but also to provide more information for further catalyst design [10].

[1] J.T. Dixon *et al.*, *J. Organomet. Chem.* **2004**, 689, 3641. [2] A. Bollman *et al. J. A.C.S.*, **2007**, 126, 14712-14723. [3] K. Blann *et al. J. Catal.*, **2007**, 249, 244. [4] M.J. Overett *et al. Chem. Comm.* **2005**, 622. [5] K. Blann *et al. Chem. Comm.*, **2005**, 620. [6] S. Kuhlmann *et al. J. Catal.*, **2007** 245, 277. [7] E. Killian *et al. J. Mol. Catal. Chem.* **2007**, 270, 214. [8] N. Cloete *et al. Acta Cryst.* **2008**, E64, o480. [9] N. Cloete *et al. Acta Cryst.* **2009**, E65, o3081. [10] N. Cloete *et al. Angewandte*, submitted for publication February **2011**.

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#### Structural properties of various Copper(II) catalysts for oxidation catalysis

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The aerobic oxidation of substituted phenols as a research topic plays an important role in synthesis and biological systems. The demand for value added derivatives of phenolic compounds is steadily growing in the world market, with benzoquinone derivatives constituting a key intermediate in the industrial production of Vitamin E<sup>1</sup>. The use of dioxygen as oxidant is environmentally friendly and available in bulk from the atmosphere. Dioxygen can be catalytically activated by first row transition metal complexes (Cu(II), Co(II) and Mn(IV))<sup>2</sup>. The addition of co-catalysts (LiCl or MgCl<sub>2</sub>) can significantly increase the reactivity of these catalysts during the oxidation cycle<sup>3</sup>.

In the current study, model catalyst precursors containing O,O bidentate ligand systems such as troplone and 2-methyl-3-hydroxy-4-pyrone derivatives, which form five-membered chelates, have been synthesized and structurally characterized, and will be discussed. Different aspects of the dioxygen oxidation of selected organic substrates by these copper(II) catalysts, as well as a proposed mechanism for the process, will also be presented.

[1] H. Sun, K. Harms, J. Sundermeyer, *J. Am. Chem. Soc.*, **2004**, 126, 9550. [2] L.I. Simandi, *Catalytic Activation of Dioxygen by Metal Complexes, Catalysis by Metal Complexes*, **1992**, 13, 10. [3] W. Brenner, *German Patent Hoffman-La Roche*, **1972**, 2(221), 624

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