

## MS34.P22

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## A Charge Density Study of Arylacetylene Substituted Cytochrome P450 Inhibitors

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Cytochrome P450 enzymes belong to the super family of proteins containing the heme cofactor, and are involved in the metabolism of endogenous and exogenous compounds including drugs, sterols, fatty acids, carcinogens, vitamins and steroids. It has been shown that arylacetylenes can function as mechanism-based inhibitors of P450 enzymes involved in carcinogenesis and possibly prevent the initiation of cancer. Previous studies of the docked inhibitor-protein complexes revealed a direct relationship between the inhibition potency and the proximity of the inhibitor's triple bond to the prosthetic heme Fe of the enzyme. 7-(4-trifluoromethyl)coumarin propargyl ether,  $\alpha$ -naphthoflavone 2'-propargyl ether, and 2-phenylflavone-7-propargyl ether were synthesized as potential therapeutics for inhibiting P450 metabolism because each docks in the heme active site and is substituted with an arylacetylene group. Extensive high resolution data sets were collected on a Bruker Kappa APEX II CCD X-ray diffractometer at 150(2) K. Conventional, radial, and multipole refinements were performed on the data using the Shelx and the XD software packages. Deformation density maps of the propargyl ether groups show a buildup of density in the triple bonds. Electrostatic potential maps have been calculated and show negative potential associated with regions of reactivity near the trifluoromethyl substituent and the ketone groups. Net atomic charges calculated in the radial refinement allow differentiation of the acetylene carbon atoms. Critical points show the presence of C-H...F and C-H...O hydrogen bonds. NIH/MBRS-CORE (SC1GM084722) and NIH/RCMI (1G12RR026260) support is gratefully acknowledged.

**Keywords:** charge density, P450 inhibitor

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## Conformation of half-sandwich Mn(I) O-alkyl and O-aryl Fischer carbene complexes: a joined experimental-theoretical study

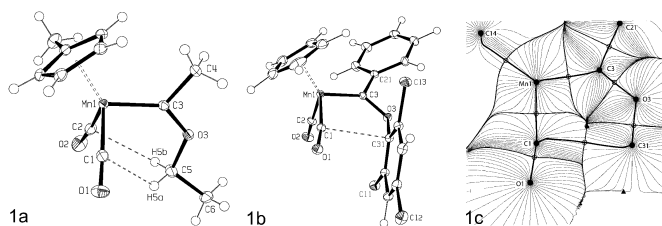
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Seminal MO calculations by Hoffman *et al.*<sup>[1]</sup> predicted that carbene ligands in half-sandwich complexes of the type Cp(CO)<sub>2</sub>M=C(R)R' should adopt a so-called 'vertical coordination mode',<sup>[2]</sup> whereby the carbene plane sits in the symmetry plane of the Cp(CO)<sub>2</sub>M unit (see Fig. 1a for an example). Such a coordination mode gives rise to two different rotamers, differing in the orientation of the R/R' groups relative to the Cp ligand. Early theoretical<sup>[3]</sup> and structural<sup>[4]</sup> studies of the half-sandwich Mn(I) O-alkyl carbene complexes Cp(CO)<sub>2</sub>Mn=C(OR)Ph (R = Me, Et) have nevertheless revealed some discrepancies between their predicted and observed conformation.

For our part, we have investigated the structure and conformation of a series of half sandwich Mn(I) O-alkyl- and O-aryl Fischer carbene complexes by mean of a joined experimental-theoretical study based on

the experimental X-ray charge density analysis of two representative examples of such complexes, namely Cp'(CO)<sub>2</sub>Mn=C(Me)OEt (Fig. 1a) and Cp(CO)<sub>2</sub>Mn=C(Ph)O(2,4,6-C<sub>6</sub>H<sub>2</sub>Cl<sub>3</sub>) (Fig. 1b) (*S* < 1.1 Å<sup>-1</sup> (MoK $\alpha$ ), 100K), and DFT calculations.

Both the topological analysis of the experimental electron density within Bader's AIM theory, and the DFT calculations, through the Second-Order Perturbation Theory (SOPT) of the NBO method, clearly revealed that hitherto unsuspected weak intramolecular interligand interactions including C...H interactions between the O-alkyl group and the carbonyl ligands (Fig. 1a)<sup>[5]</sup> or C...C interactions between the O-aryl group and the carbonyl ligands (Fig. 1b and 1c)<sup>[6]</sup> play a key role regarding the conformation of those complexes.



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**Keywords:** charge density analysis, AIM, DFT

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## Electronic structure of Bis{bis(methoxycarbimido)aminato}-copper(II) complex

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The bonding properties of transition metals in coordination compounds are of great importance for inorganic as well as bio-inorganic chemistry. Recently, we have found that in tetrakis( $\mu_2$ -Acetato)-diaqua-di-copper(II) complex (I) for Cu central atom only Cu-O bonds in the equatorial plane are actual the coordination bonds [1,2]. Contrary to very small apical Cu-O bond distance of 2.1443(1) Å, this interaction is not a coordination bond. The lone electron pair of water oxygen atom is faced directly to the fully populated Cu  $d_z^2$  orbital. To compare the distribution of electrons in 3d-orbitals in different geometries we have chosen the compound Bis{bis(methoxycarbimido)aminato}-copper(II) complex (II) [3,4]. Central atom in this complex is square-planar coordinated with Cu atom in the centre of symmetry. In axial direction the closest interaction is on the distance of 3.7 Å. The aim of this study is to compare the bonding properties of Cu central atom in the compounds (I) and (II).

The GEMINI R diffraction data at 100K will be used for electronic structure study. To guarantee a high redundancy the whole diffraction sphere was measured also for a monoclinic space group (P 2<sub>1</sub>/n) up to resolution of 0.39 Å. In 63 omega runs 120163 diffractions were collected with the average redundancy of 10.3. The multipole refinement and the results of both experimental and theoretical topological analysis for both coordination polyhedra will be discussed.

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**Keywords:** Cu-complex, electronic structure, d-orbitals

## MS34.P25

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### First principle calculation of perovskite type oxide $\text{LaMO}_3$ ( $M = \text{Cr, Mn, Fe, Co, Ni, Cu}$ ): Correlation of electron density at the $M\text{-O}$ bond with structure

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Perovskite-type oxide  $\text{LaMO}_3$  ( $M = \text{Cr, Mn, Fe, Co, Ni, Cu}$ )-based materials are utilized in a wide variety of applications such as solid-oxide fuel cells, catalysts, and gas sensors. Electronic structure and chemical bonding are important, because almost all the properties are governed by them. The covalency at the  $M\text{-O}$  bond may influence on the material properties. But, the covalency of  $M\text{-O}$  bond has not been investigated in the literature. The covalency at the  $M\text{-O}$  bond can be studied by the minimum electron density (MED). In the present work, the MED at the  $M\text{-O}$  bond in was studied through the density functional theory (DFT).

The *ab initio* total energy program VASP (Vienna *Ab initio* Simulation Package) [1] was employed to calculate the valence electron-density distribution of  $\text{LaMO}_3$  ( $M = \text{Cr, Mn, Fe, Co, Ni, Cu}$ ). Unit-cell parameters and atomic coordinates of  $\text{LaMO}_3$  were optimized with the convergence condition of 0.02 eV/Å. Projector augmented-wave (PAW) potentials were used for  $M$ , O, and La atoms [2]. A plane-wave basis set with a cutoff of 500 eV was used. The Perdew-Burke-Ernzerhof (GGA) was employed for the exchange and correlation functional. Sums over occupied electronic state were performed using the Monkhorst-Pack scheme [3] on  $5 \times 5 \times 5$ ,  $5 \times 5 \times 5$  and  $7 \times 7 \times 7$  sets of  $k$ -point meshes for  $M = \text{Cr, Mn, Fe, Co, Ni, Cu}$ , respectively. Optimized crystal structure and valence electron density distribution were drawn with a computer program VESTA [4].

Calculated valence electron density distributions clearly indicate that the  $M\text{-O}$  bond is covalent, while the La atom is more ionic. The MED of Cu-O bond in  $\text{LaCuO}_3$  ( $0.61 \text{ \AA}^{-3}$ ) is higher than that of Mn-O bond in  $\text{LaMnO}_3$  ( $0.50 \text{ \AA}^{-3}$ ), which is ascribed to the shorter Cu-O bond (1.938 Å) compared to the Mn-O one (1.9904 Å). The MED of  $M\text{-O}$  bond in  $\text{LaMO}_3$  ( $M = \text{Cr, Mn, Fe, Co, Ni, Cu}$ ) decreases with an increase of  $M\text{-O}$  bond length.

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**Keywords:** first principles calculation, perovskite-type oxide, electron density, density functional theory (DFT)

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### Evaluating electron delocalization: the need for aromaticity descriptors

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Our aim is to derive chemical properties such as reactivity, coordination behaviour and bond strengths from experimental charge density analysis. Currently, our research is focused on the understanding of catalytically active compounds. In the rapidly progressing field of homogenous organometallic catalysis, the large group of phosphanes can be considered to be one of the most important variables in catalyst design.

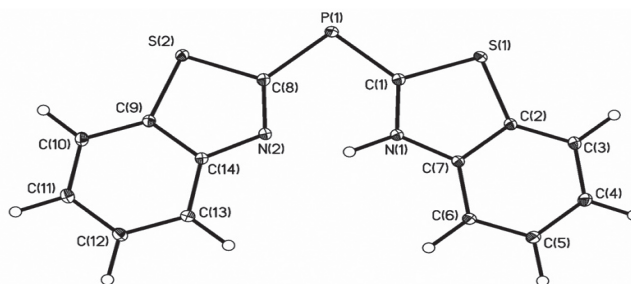
The secondary phosphane  $\text{P}[\text{Hbth}][\text{bth}]$  ( $[\text{bth}] = \text{benzothiazol-2-yl}$ ) with phosphorus, sulfur, and nitrogen donor sites provides coordination site selectivity in heterobimetallic complexes.[1,2] Its unusual structure can be explained by tautomerism.

After multipole structure refinement on a high-resolution dataset of the compound obtained at a temperature of 15 K, we showed that two Lewis lone pairs are located at each of the phosphorus and the sulfur atoms, giving them approximately tetrahedral environments according to VSEPR theory.

This conflicts with common textbook concepts employed to describe aromaticity since one of the two sulfur lone pairs is believed to be delocalized in the case of sulfur-containing heteroaromatic rings, which would lead to trigonal-planar symmetry.

There is no direct method to measure the amount of aromaticity and no unambiguous aromaticity descriptors are applicable to results from multipole refinements.

We are combining results from approved methods derived from Bader's Quantum Theory of Atoms in Molecules [3] with new approaches including the Source Function [4] to explain the observed ambiguity. Our results lead to the conclusion that the established rules for delocalization that strictly apply to elements of the second period may not be as compelling to the heavier elements.



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**Keywords:** aromaticity, catalysis, high resolution data.