A Charge Density Study of Arylacetylene Substituted Cytochrome P450 Inhibitors
Cheryl Stevens,* Najie Zhang,† Edwin Stevens,* ‡Xavier University of Louisiana, †University of New Orleans New Orleans (USA), E-mail cklein@xula.edu

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, steroids, 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, α-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-SORE (SC1GM084722) and NIH/RCMI (1G12RR026260) support is gratefully acknowledged.

Keywords: charge density, P450 inhibitor

Conformation of half-sandwich Mn(I) O-alkyl and O-aryl Fischer carbene complexes: a joined experimental-theoretical study
Noel Lujan, Israel Fernandez, Dmitry A. Valyaev,* Rémy Brousses,* Miguel A. Sierra, Nikolai A. Ustynyuk. "Laboratoire de Chimie de Coordination du CNRS, 205 route de Narbonne, 31077 Toulouse Cedex 4 (France), 2Departmento de Quimica Organica, Facultad de Quimica, Universidad Complutense de Madrid, 28040 Madrid (Spain), 3A.N. Nesmeyanov Institute of Organoelement Compounds, RAS, 28 Vavilov str., 119991 Moscow (Russia). E-mail: noel.lujan@icc-toulouse.fr

Seminal MO calculations by Hoffinan et al.[1] predicted that carbene ligands in half-sandwich complexes of the type Cp(II)M=C(R)R should adopt a so-called ‘vertical coordination mode’ [2] whereby the carbene plane sits in the symmetry plane of the Cp(II)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[3] and structural[4] studies of the half-sandwich Mn(I) O-alkyl and O-aryl Fischer carbene complexes suggest[5] that carbene ligands in half-sandwich complexes of the type Cp(II)M=C(R)R ‘vertically’ bind to the metal. These calculations have been 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-SORE (SC1GM084722) and NIH/RCMI (1G12RR026260) support is gratefully acknowledged.

Keywords: charge density, AIM, DFT

Electronic structure of Bis{bis(methoxycarbimido)aminato}-copper(II) complex
Marek Fronec, Peter Herich, Jozef Kožišek, Department of Physical Chemistry, Slovak University of Technology, Radlinského 9, SK-812 37 Bratislava, (Slovak Republic). E-mail: marek.fronec@stuba.sk

The bonding properties of transition metals in coordination compounds are of great importance for inorganic as well as bioinorganic chemistry. Recently, we have found that in tetrakis(pyrazolato)-diazqua-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 2.144(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 d3 orbital. To compare the distribution of electrons in 3d-orbitals in different geometries we have choosen 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 the 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 21/m) 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.

Keywords: charge density analysis, AIM, DFT

Poster Sessions

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