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Biomimetic Interaction of Dioxygen with Transition-Metal Complexes

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Abstract. Our research focuses on two rather different, but nevertheless interdependent areas: redox activity of transition-metal complexes and numerical analysis of multivariate data. Kinetics and activation parameters of biomimetic oxygenations and oxidations are studied by low-temperature diode-array stopped-flow spectrometry. Intensive international collaboration with more synthetically oriented groups, especially *K.D. Karlin* (The *Johns Hopkins* University, Baltimore) and *W.B. Tolman* (University of Minnesota), has become fruitful and of paramount importance to our research.

Andreas Zuberbühler was born in Basel and studied chemistry at the University of Basel. He received his Ph.D. in 1965 under the guidance of *S. Fallab*. He completed his habilitation in Basel in 1969 after a period as a research associate working with *H.S. Mason* at the University of Oregon Medical School. He was appointed to his present position as a Professor in Basel in 1978. He is president of the Energy Commission of the Swiss Academy of Engineering Sciences and member of the Federal Commission for the Safety of Nuclear Power Plants.

1. Oxygenation and Oxidation of Transition-Metal Complexes

Starting from studies of equilibria, autoxidation, and catalytic activity of relatively simple transition-metal complexes, we have, in the past years, concentrated on the properties of quasi-reversible biomimetic dioxygen adducts, particularly with copper centers. Besides functioning as dioxygen carriers, such species play a key role in redox enzymes catalyzing oxidation and oxygenation of organic substrates. While dioxygen adducts (or peroxo complexes) of cobalt have been known and studied for several decades, analogous species with the biologically more relevant Cu(I) have long escaped direct observation. Low-temperature diode-array stopped-flow spectrometry in organic solvents has afforded activation parameters for the individual kinetic steps along with spectra of otherwise elusive intermediates. By optimizing ligand design and solvent, significant stability of such species has recently been obtained even at room temperature.

With binucleating complexes of type **1**, a complete set of activation parameters for the formation and decay of adduct **2** as well as subsequent arene hydroxylation to **3** was obtained for the first time in a partial mimic of tyrosinase [1]. The reaction enthalpies for dioxygen binding are comparable to those of biological dioxygen carriers, but stability at room temperature is precluded by strongly unfavorable reaction entropies.

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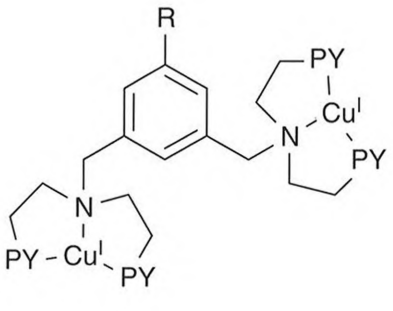

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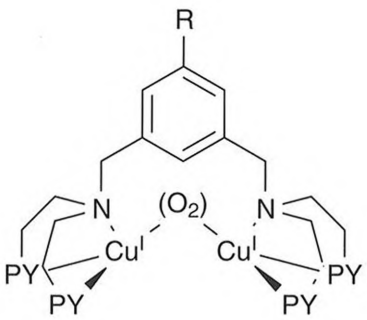

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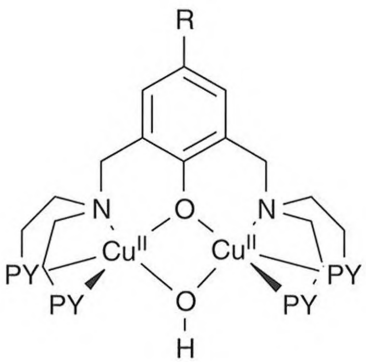

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With complexes of type **4** and **5**, the stepwise formation of superoxo and peroxo complexes could be observed and again the activation parameters of the individual kinetic steps elucidated. By optimizing the length of the tethering chain and switching from propionitrile to less coordinating acetone or THF, practically complete formation of dioxygen adducts could be achieved even at room temperature [2].

Fundamental insight into the making and breaking of the O–O bond of dioxygen, mediated by metal ions, has been obtained with complexes of a substituted triaza macrocycle. The corresponding μ-η^2:η^2-peroxo complex **6** is in a rapid equilibrium with the corresponding bis μ-oxo species **7** that depends on solvent, temperature, and ligand substitution. The adduct oxidatively cleaves the isopropyl groups even at low temperature, but its stability can be substantially increased by perdeuteration and by tethering of two macrocycles producing a binucleating complex [3][4].

Recently, we have started looking into models of cytochrome-*c* oxidase, containing heterobinuclear iron(II)-porphyrin/Cu(I) centers. While kinetic data on actual heterobinuclear systems have yet to be published, analysis of one of the tested Cu(I) subsystems has yielded a remarkably high binding enthalpy and exogenous hydrocarbon-substrate oxidation [5]. A summary of the kinetic data related to the systems discussed above has been published [6].

2. Numerical Analysis of Multivariate Data

Diode-array and other multiwavelength data need highly efficient algorithms and corresponding computer code for reasonable analysis. We have long been engaged in this field of research and again fruitful international collaboration has resulted with *R. Binstead* (Chapel Hill) and *M. Maeder* (Newcastle, Australia):

- The program *Specfit*, originally developed in Basel and now expanded and commercialized with *Binstead*, is used worldwide for the analysis of kinetics and equilibria based on multivariate spectrometric data [7]. A completely *Windows*-based version is soon to be completed.
- Evolving-factor analysis (EFA), developed together with *M. Maeder*, has become a powerful tool in chemometrics. Absorption spectra and concentration profiles are obtained directly without the need of an underlying chemical model [8].
- Second-order global analysis is carrying the idea of global analysis (simultaneous analysis of multivariate data from different wavelengths, preferably in the corresponding eigenvector space) one step further. Data from completely independent experiments (*e.g.*, at different temperatures or pressures, or with different concentrations) are analyzed simultaneously yielding optimized nonlinear parameters (equilibrium constants, activation or thermodynamic parameters) in one single analysis of the complete data set [9].

The work of all dedicated coworkers and collaborators is gratefully acknowledged. I wish to thank the *Swiss National Science Foundation* for continuous financial support.

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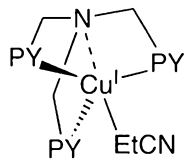

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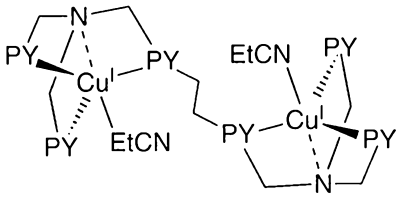

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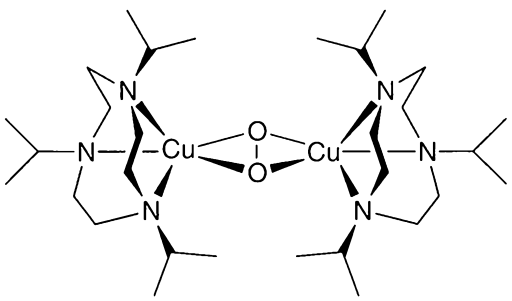

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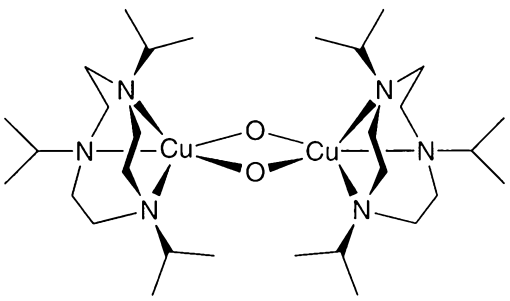

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