## Plenary Lectures

### Solute–Solvent Interactions in Bioinorganic Chemistry

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The role of solvation in the electron transfer reactions of metalloproteins has been examined. Measurements of the rates of electron transfer reactions between metalloproteins and various inorganic complexes at different temperatures show that the mechanisms employed by hydrophobic and hydrophilic substrates vary significantly. Reactions of blue copper proteins and cytochromes with oxidants such as $Co(dipic)_2^-$ (dipic = dipicolinate) and $Co(phen)_3^{3+}$ (phen = 1,10-phenanthroline) exhibit large positive activation enthalpies and small (in some cases positive) activation entropies. One interpretation of these results is that substantial solvation changes accompany the interaction of the protein with the substrate in the activated complex. Specifically, penetration of hydrophobic substrates into hydrophobic protein interiors is thought to lead to displacement of ordered solvent molecules, thereby increasing entropy. This effect is apparently even larger in electron transfer reactions involving proteins that are believed to be physiological partners.

Solvation of metalloproteins is believed to play a critical role in preventing close approach of reagents with hydrophilic electron transfer surfaces to the protein redox centers. In several cases electron tunneling between redox centers occurs over distances that are determined by the primary solvation shells. These distances have been calculated from electron transfer rate constants determined for several proteins.

Measurements of the redox potentials and the standard enthalpies and entropies for several electron transfer reactions of cytochromes, iron–sulfur proteins, and blue copper proteins have been made. The determination of thermodynamic parameters for protein redox couples was accomplished by measuring the temperature dependence of the electrode potential of suitably designed electrochemical cells. If the electrochemical cell is in a nonisothermal configuration, the experimental temperature dependence, $dE^\circ/dT$, of the electrode potential can be separated into the following components:

$$dE^\circ/dT = d\phi_{tlj}/dT + d\phi_{tc}/dT + d\phi_f^m/dT$$

$\phi_{tlj}$ is the Galvani potential difference across the thermal liquid junction within the KCl salt bridge, $\phi_{tc}$ is the 'thermocouple' potential difference between the hot and cold regions of the working electrode, and $\phi_f^m$ is the Galvani metal–solution potential difference at the working electrode. Since

$$S^\circ_{red} - S^\circ_{ox} = F\cdot(d\phi_f^m/dT)$$

where $F$ is the Faraday, if $d\phi_{tc}/dT$ and $d\phi_{tlj}/dT$ are constant or can be neglected, partial molal entropy differences for the redox couples of interest can be obtained *directly* from measurements of $dE^\circ/dT$. It has been proposed that in the nonisothermal electrochemical cell configurations under consideration $d\phi_{tc}/dT < 14\ \mu V/deg$ and $d\phi_{tlj}/dT < 20\mu V/deg$. Since these values are well below the experimental precision of the $dE^\circ/dT$ measurements, we neglect $d\phi_{tc}/dT$ and $d\phi_{tlj}/dT$ in nonisothermal experiments. Furthermore, since $d\phi_{tc}/dT$ and $d\phi_{tlj}/dT$ are constant for a given experimental arrangement, the relative values of $dE^\circ/dT$ for various systems will be unaffected even if these two sources of the observed temperature dependences are not negligible.

We have determined the enthalpy and entropy differences for oxidation state changes in metalloproteins using an optically transparent thin-layer electrode (OTTLE) in a nonisothermal electrochemical cell configuration. The most striking result is that large negative values of $\Delta S^\circ$ are obtained for proteins with buried copper or iron sites. Possible interpretations of these $\Delta S^\circ$ values include conformational effects as well as solvation changes in the oxidized and reduced states.

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### Solvent Effects on Molecular Properties

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When molecules collide there may be changes in electronic structure that vary from a minor perturbation to a chemical reaction. The lecture will survey the effects of the environment of a molecule on its structure and properties.

Some properties, including frequencies and intensities of spectral transitions, may suffer profound changes on a change of solvent, thereby providing a means of adapting the property to various needs. And some properties result entirely from the interaction of the molecules – for example, the dipole moment of a pair of unlike inert-gas atoms, or the circular dichroism of an achiral compound in the presence of a chiral species –.

In the general theory of the effects of long-range intermolecular forces on molecular properties, the change in the property with distance between two molecules is expressed in terms of properties of the free molecules. The limitations of such a description will be discussed, and the role of short-range forces considered.

Progress in understanding intermolecular forces, and solvent effects, will depend upon a combination of experiment and *ab initio* computation.

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## The Nature of 'Solvent Effects'

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The coordination model for nonaqueous solvent chemistry was the first attempt to offer a unified presentation of those interactions essential to the understanding of the behavior of solutes in nonaqueous solvents. The model focused on two distinct aspects of the problem; specific interactions of the Lewis acid base type and non-specific interactions in which coordinate bond formation is not involved. As in any classification, there are gray areas in which it is difficult to assign the interaction to one category or another. However, in many instances the assessment is straightforward. Though the original publication of this work met with considerable resistance, it is now quite generally accepted that the Coordination model accurately represents the behavior of solutes in a wide variety of solvents including many of the oxyhalides.

In recent years the problem has become one of ascertaining coordination strengths and solvation energies. With the wide publicity given to the class A and B concept, HSAB theory and the E and C model, it should be obvious to all that there is no single scale of donor strength that permits an estimate of solvent coordinating abilities. However, one still finds in the literature attempts to correlate all sorts of phenomena with single scale models; for example, $pK_B$ data or donor numbers. In this talk the pitfalls associated with such procedures will be discussed. In their place an approach will be described that enables one to determine if observed phenomena are being dominated by sigma bond, donor strengths. A set of experiments will also be discussed which permits one to detect when coordination involves contributions other than a normal sigma bond type of interaction. Procedures for ascertaining the source of these additional effects will be discussed.

A second and independent contribution to reactions in non-aqueous solvents involves the solvating ability of the solvent. This was demonstrated earlier by showing that solvents with similar donor properties behaved quite differently toward the solute iron(III) chloride in terms of chloride ion dissociation. Models have been developed which enable one to work in polar solvents and correct the enthalpies obtained back to the solvent minimized type of data that one measures in carbon tetrachloride or in alkanes. These studies provide insight regarding some subtle solute–solvent interactions and permit one to obtain data that can be interpreted in terms of bond strength considerations for systems in which it is necessary to work in more polar solvents because of solubility limitations.

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## Cycloaddition Mechanism and the Solvent Dependence of Rate

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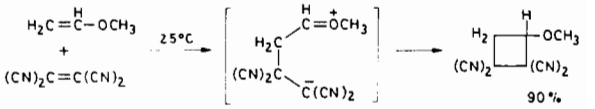
The dependence of the rate constant on solvent polarity is an important mechanistic criterion which should always be used in conjunction with other diagnostic tools. The slow step of 2 + 2 cycloaddi-




tions of tetracyanoethylene (TCNE) with enol ethers [1], thioenol ethers [2] and *trans*-fixed 1,3-dienes [3] is the formation of a zwitterionic intermediate. The log $k_2$ values are linear functions of the Dimroth–Reichardt parameter $E_T$. The rate accelerations of TCNE cycloadditions in going from cyclohexane to acetonitrile amount to 29,000 for anethole, 10,800 for 1-ethoxyisobutene, 2,600 for butyl vinyl ether, 17,000 for ethyl 1-propenyl sulfide and 54,000 for verbenene. The violation of stereospecificity becomes greater with increasing solvent polarity.