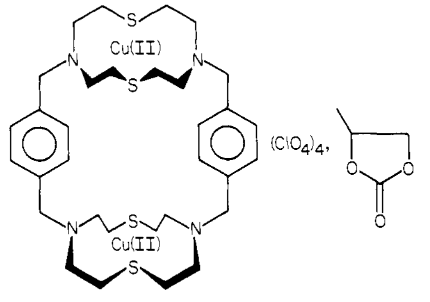
From a quantitative point of view, between 300 and 55 K, the magnetic susceptibility very closely follows eq 1 with $J = -56.7$ cm^{-1}, $g = 2.071$, and ρ negligible (see Figure 2).[11] Below 55 K, the experimental data drastically deviate from eq 1 when J is assumed to be constant in the whole temperature range. By determining the g and ρ values at high temperatures and allowing J to vary, one obtains the temperature dependence of J plotted in Figure 3. The singlet-triplet energy gap is essentially constant down to 55 K, then decreases more and more quickly as the temperature drops below 55 K.[12] The temperature dependence of the intensity of the $\Delta M_S = \pm 1$ ESR transition in the range 10-300 K nicely confirms this result.

The same phenomenon of exchange elasticity seems to occur, but in a less spectacular manner, in compound II, $[\mathrm{Cu^{II}}_{27} \subset (\mathrm{C_{32}H_{48}N_4S_4})](\mathrm{ClO_4})_4(\mathrm{C_4H_6O_3})$, the exact molecular structure of which has not yet been determined.[13] Down to 14K, the magnetic susceptibility fits eq 1 for $J = -8.39$ cm^{-1}, $g = 2.184$, and $\rho = 0.0258$.[14] Below 14 K, the magnetic data very strongly suggest a gradual decrease of $|J|$, down to a value of about 4.8 cm^{-1} at 4 K.



II

The mechanism of the exchange in complex I is in itself an interesting problem. Each Cu(II) ion is surrounded by a strongly distorted tetragonal pyramid in which the metal lies 0.34 Å above the $\mathrm{N_2S_2}$ basal plane toward the axial oxygen atom. This large displacement of the Cu(II) ion out of the $\mathrm{N_2S_2}$ plane indicates that the axial Cu-O interaction is much more important than in most of the Cu(II) complexes with a 4 + 1 coordination.[15] Consequently, the metallic contribution to the magnetic orbital around each Cu(II) ion may not be reduced to $d_{x^2-y^2}$ pointing toward the sulfur and nitrogen atoms but has a d_{z^2} axial component so that the spin density on the oxygen atom is nonnegligible. The exchange interaction between the two chromophores $\mathrm{CuS_2N_2O}$ in the cavity has three preferential pathways: once Cu-O···O-Cu and twice Cu-N-CH$_2$-CH$_2$-O-Cu. The efficiency of each of these pathways is related to the spin density on the oxygen atoms in the chromophores $\mathrm{CuN_2S_2O}$. One conceives that a slight displacement of the copper toward the basal plane at low temperature or an increase of the angle between the Cu-O bond and the z axis perpendicular to the basal plane might lead to a very sensitive lessening of the spin density on the oxygen atoms, hence to a weakening of the antiferromagnetic interaction inside the cavity. This phenomenon of exchange elasticity could also be of the same nature as the exchange striction introduced by the solid-state physicists,[17] but largely enhanced here owing to the quite specific nonrigidity of the cryptate cavity.

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(10) R. Weiss, private communication.

(11) The agreement factor R defined as $\sum(\chi_M{}^{\mathrm{obsd}} - \chi_M{}^{\mathrm{cald}})^2/\sum(\chi_M{}^{\mathrm{obsd}})^2$ is then equal to 0.35×10^{-4}.

(12) The $g_\parallel$ and $g_\perp$ factors deduced from the ESR spectra are essentially independent of the temperature in the range 10-300 K. If a small proportion, ρ, of paramagnetic impurity which would not have been detected from the experimental data in the 55-300 K range was present, the actual slope of the $|J|$ vs. T plot would be slightly weaker than it is shown in Figure 3.

(13) The ligand has been synthetized by Dr. J. Rimmer; unpublished results.

(14) The agreement fractor R is 0.52×10^{-4}.

(15) See, for example: B. J. Hathaway, *Struct. Bonding (Berlin)*, **14**, 49 (1973).

(16) On the concept of magnetic orbitals, see ref 3 and 4.

(17) M. E. Lines, *Solid State Commun.*, **11**, 1615 (1972), and references therein; J. Katriel and O. Kahn, Phys. Lett. *A*, **55A** 439 (1976).

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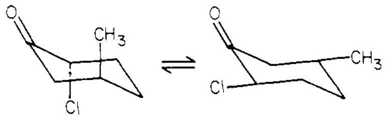
Water Penetration into Micelles as Determined by Optical Rotary Dispersion

Sir:

We have recently questioned the classical Hartley model[1] which portrays micelles as "oil droplets" encased by ionic shells.[2] In particular, we have supplied evidence that water penetrates deeply into the aggregates and that the so-called Stern layer is rough and poorly defined.[3-5] Our "porous-cluster" description has not achieved universal acceptance, however, as shown by a recent editorial in opposition to it.[6] The venerable Hartley model is obviously difficult to abandon because, for one thing, its deceptive simplicity facilitates theoretical calculations. Moreover, experiments designed to define the structure of transient aggregates in solution necessarily entail assumptions and limitations that preclude "proof" in the usual sense of the word. Presented below are optical rotary dispersion data which strongly support the presence of water inside micelles. To our knowledge, this is the first time that ORD has been applied to micellar structure.

Transferring (+)-*trans*-2-chloro-5-methylcyclohexanone from heptane to water induces a remarkable change in the sign of the Cotton effect (Figure 1, A and B).[7] This can be ascribed to a diaxial-diequatorial equilibrium which lies further to the right in water than in heptane.[8] The conformationally mobile ketone thus responds to the nature of the medium and can be used as a sensitive probe of micellar environments. The RD curves of 6.8×10^{-3} M probe in aqueous surfactant solutions composed of 0.10 M hexadecyltrimethylammonium bromide (HTAB) or 0.10 M sodium dodecyl sulfate (NaDodSO$_4$) are shown in Figure 2, A and B, respectively. It is seen that (+)-*trans*-2-chloro-5-methylcyclohexanone in the micellar solutions gives a Cotton effect similar to that in pure water. The following observations leave no doubt that the probe does in fact adsorb into or onto the micelles: (1) One can readily dissolve 0.005 M ketone in 0.20 M NaDodSO$_4$ with brief shaking whereas dissolution in pure water requires sonication. (2) The partition coefficient of the probe between heptane and water ($K_{H/W}$) equals 5.5. Adding 0.10 M NaDodSO$_4$ to the water decreases $K_{H/W}$ to 1.5, thereby proving



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(1) D. Stigter, *J. Phys. Chem.*, **78**, 2480 (1974).

(2) P. Mukerjee and J. R. Cardinal, *J. Phys. Chem.*, **82**, 1620 (1978).

(3) F. M. Menger, *Acc. Chem. Res.*, **12**, 111 (1979).

(4) F. M. Menger, J. M. Jerkunica, and J. C. Johnston, *J. Am. Chem. Soc.*, **100**, 4676 (1978).

(5) F. M. Menger, *J. Phys. Chem.*, **83**, 893 (1979).

(6) H. Wennerström and B. Lindman, *J. Phys. Chem.*, **83**, 2931 (1979).

(7) All spectra were secured with the aid of a Perkin-Elmer 241 MC polarimeter and 10-cm quartz ORD cells thermostated at 25.0 °C.

(8) C. Djerassi, L. E. Geller, and E. J. Eisenbraun, *J. Org. Chem.*, **25**, 1 (1960).

(9) This increase in rotation implies that the micelle environment, although aqueous, is different from that of bulk water (as would be expected from a micelle bearing aqueous pockets). Note that Na$_2$SO$_4$ (1.0 M) does *not* induce a similar rotation increase with the aqueous probe. Ketone (0.005 M) will not dissolve in 2.0 M Na$_2$SO$_4$ at 25 °C.

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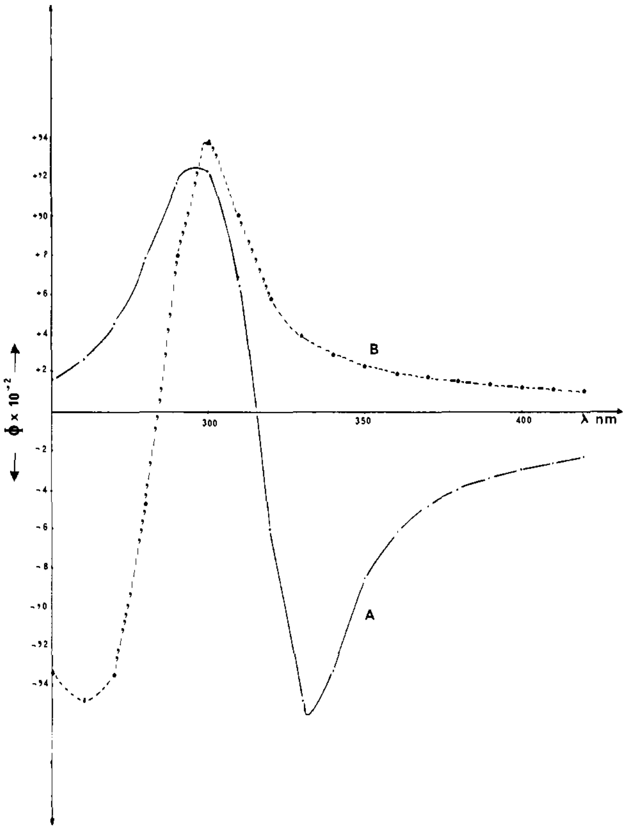


Figure 1. Plot of molecular rotation vs. wavelength for 6.8 × 10^{-3} M (+)-*trans*-2-chloro-5-methylcyclohexanone in (A) heptane and (B) water.

that the micelles solubilize the ketone in water. (3) The presence of $NaDodSO_4$ below its critical micelle concentration has no effect on the optical rotation at 320 nm of 0.005 M probe in water. However, a plot of molecular rotation vs. [SDS] *above* the cmc initially increases with $NaDodSO_4$ and then becomes level at >0.10 M $NaDodSO_4$; this horizontal region corresponds to probe which is totally micelle bound. The spectra in Figure 2, A and B, were traced by using such saturation conditions. Clearly, (+)-*trans*-2-chloro-5-methylcyclohexanone binds to both cationic and anionic micelles but fails to assume therein a diaxial conformation characteristic of nonpolar surroundings.

It is important to emphasize that the affinity of the probe for hydrocarbon solvents greatly exceeds that for water. The partition coefficient favoring heptane has already been mentioned. An even more pointed illustration is given by the behavior of the probe in reversed micelles composed of heptane, water, and sodium dioctylsulfosuccinate (AOT). The AOT surfactant encases large water clusters in the heptane to produce optically clear solutions.[10] When (+)-*trans*-2-chloro-5-methylcyclohexanone is dissolved in such "water-pool" systems, it manifests a diaxial conformation (Figure 2C) in contrast to the situation with "normal" micelles. Neither the aqueous interior not the enormous sulfonate-rich surface of the water pools attracts the probe from the surrounding heptane to induce a conformational change. Yet, despite this preference for organic media, the probe resides in water-containing regions of the HTAB and $NaDodSO_4$ micelles. If the Hartley model were correct, then one would have to wonder why the probe prefers the Stern layer (an aqueous region of high ionic strength) over the "oil-droplet" portion of the micelle. It should be mentioned in this regard that the partition coefficient between heptane and water, $K_{H/W}$, is increased about sixfold when 4 M NaCl is added to the water; the NaCl thus effectively *salts out* the probe from water. Recent statements not to the contrary,[6] micelles are best pictured as having grooves where guest molecules bind hydrophobically in a mixed medium of water and hydrocarbon. The aqueous pockets undoubtedly form and disappear rapidly within transient and fluctuating molecular assemblages.

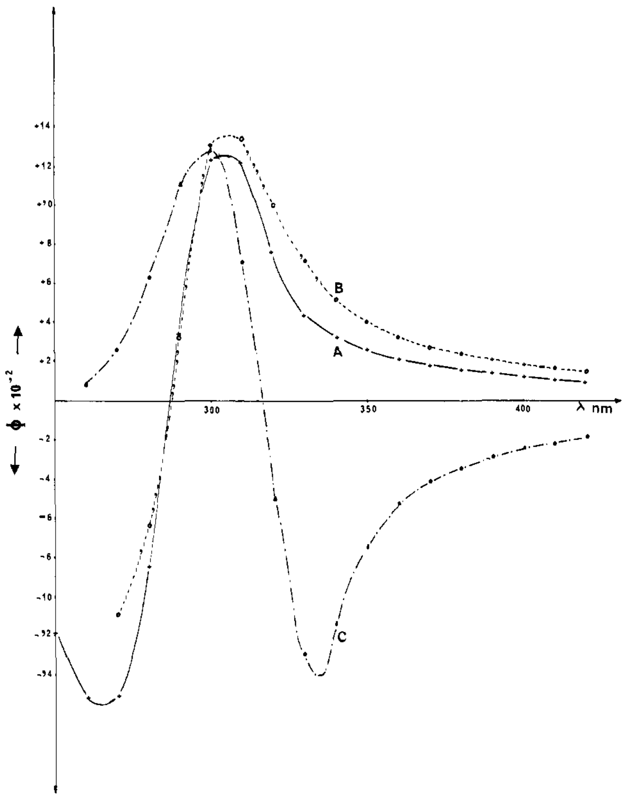
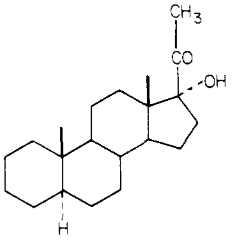


Figure 2. Plot of molecular rotation vs. wavelength for 6.8 × 10^{-3} M (+)-*trans*-2-chloro-5-methylcyclohexanone in (A) 0.10 M aqueous HTAB, (B) 0.10 M aqueous $NaDodSO_4DS$, and (C) heptane containing 0.10 M AOT and 4.0 M water.

No study of probe behavior is complete without considering how the probe might perturb the environment in which it is embedded. In this regard, the optically active probe does *not* appear to "drag" water into a normally nonaqueous micelle interior and thus enhance the diequatorial population. The following results support this assertion: (1) (+)-*trans*-2-Chloro-5-methylcyclohexanone displays the same negative Cotton effect in heptane saturated with water as it does in dry heptane. (2) Shaking a heptane solution of the probe with a small amount of water does not alter the RD curve from that found with dry heptane. (3) The probe in heptane/water/AOT has an RD curve similar to that in heptane although water is abundantly available for associating with the ketone were it prone to do so. We conclude that the diequatorial conformation within micelles arises from hydrophobic adsorption of the probe among hydrated surfactant tails.

Our conclusions are supported by peripheral experiments with a highly water-insoluble probe, 17α-hydroxy-5α-pregnan-20-one,



whose Cotton effect also displays a remarkable solvent sensitivity ($\phi_{328} = +5752$ in methanol and $\phi_{300} = -3180$ in heptane).[11] When this steroid was solubilized into HTAB and $NaDodSO_4$ micelles, it gave $\phi_{320} = +4012$ and $\phi_{320} = +3425$, respectively, which is incompatible with a hydrocarbon-like environment.

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[10] F. M. Menger, J. A. Donohue, and R. F. Williams, *J. Am. Chem. Soc.*, **95**, 286 (1973).

[11] The large difference in molecular rotation is related to the presence or absence of intramolecular hydrogen bonding. See: J. C. Danilewicz and W. Klyne, *J. Chem. Soc.*, 1306 (1965).

Since neither the ORD results nor the previous ^{13}C NMR data[4] nor the molecular model studies[3] support the Hartley concept, the time has arrived to consider favorably an alternative micelle model.[12]

Acknowledgments. This work was supported by the National Science Foundation, the National Institutes of Health, and the donors of the Petroleum Research Fund, administered by the American Chemical Society.

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(12) Not only do we not take literally the "asterick" micelle attributed to Hartley, neither did Hartley. He states, "It has no physical basis and is drawn for no other reason than that the human mind is an organizing instrument and finds unorganized processes uncongenial." G. S. Hartley, "Aqueous Solutions of Paraffin-chain Salts: A Study in Micelle Formation", Paris, Hermann and Co., London, 1936, p 44.

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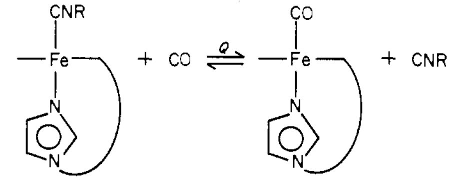
Isocyanide Binding to Chelated Protoheme. Kinetic Criteria for Distal Steric[1] Effects in Hemoproteins

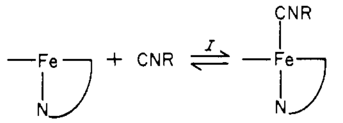
Sir:

In previous studies, chelated hemes such as protoheme monomethyl ester mono-3-imidazolylpropylamide (**1**) were shown to model the CO and O_2 binding to the R state of hemoglobin.[1-3] Herein, we describe studies of isocyanide binding to **1** which quantify the large distal steric effects in hemoglobin (Hb) and myoglobin (Mb), first recognized in the classic work of St. George and Pauling.[4] In the accompanying communication, we report isocyanide binding to a cyclophane heme, designed to model these distal steric effects in hemoproteins.

Early work of Pauling and others[5,6] on simple hemes is complicated by formation of both mono- and diisocyanide complexes. The binding of isocyanides to the five-coordinated chelated heme **1** is more directly comparable to Hb and Mb.[7] The CO/CNR competition (eq 1) was followed spectrometrically in benzene (see Figure 1). Equilibrium constants for the direct binding (eq 2) were then calculated from the known CO binding constant for **1** in benzene (Table I).



(1)



(2)

Steric effects are unimportant in binding to **1**. The affinities of the isocyanides correlate with the electron-withdrawing properties of R, the electron-withdrawing tosylmethyl group enhancing the π-acceptor properties of the isocyanide and thus binding more strongly. Solvent effects on isocyanide binding are as small as those on CO binding.[2] The value of Q is two times smaller in aqueous cetyltrimethylammonium bromide suspension than it is in benzene.

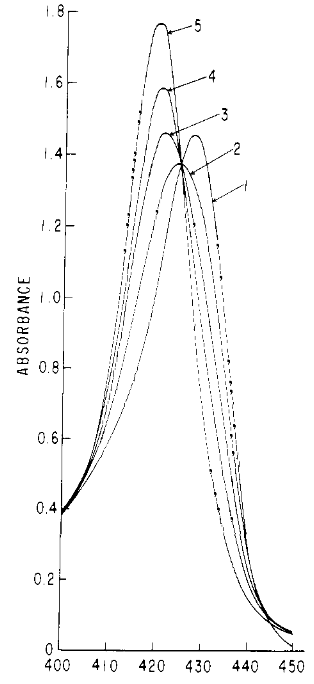


Figure 1. Spectral changes accompanying addition of carbon monoxide to 1-*t*-BuNC in benzene. [*t*-BuNC] = 3 × 10^{-3} M. [CO] × 10^4 = 0, 5.86, 11.7, 23.4, and 65 M in 1 → 5.

Table I. Isocyanide Binding to 1 in Benzene

	Q^a	$I,^b$ M^{-1}
n-BuNC	0.9	4.4×10^8
t-BuNC	2.4	1.7×10^8
TMIC	0.06	7×10^9

[a] Equation 1. Symbols are those in common usage.[7] [b] Equation 2, calculated from Q by using CO binding constant of 4×10^8 M^{-1} for 1.[2]

Comparison with isocyanide binding to proteins shows ~10^4 times poorer binding of *n*-BuNC to Mb compared to **1** and over 10^5 times for *t*-BuNC or *p*-toluenesulfonylmethyl isocyanide (TMIC). These large differences are due to distal steric effects present in the restricted pocket of Mb which are not present in **1**.

The kinetic studies on **1** were carried out to determine the dynamic differences between **1** and Mb. Flash photolysis studies of **1**-CNR are complicated by the much smaller quantum yield for **1**-CNR compared to **1**-CO and the smaller spectral differences between **1** and **1**-CNR, λ_{max} = 428 nm. The rate of BuNC association with **1** can be obtained from flash photolysis of **1**-CO in the presence of BuNC in a technique exactly analogous to that used for determining O_2 kinetic data for Hb, Mb,[7] or **1**.[1,3] Photolysis of benzene solutions containing primarily **1**-CO ([Hm] = 5×10^{-6} M, [CO] = 6×10^{-5} M, [BuNC] = 1×10^{-5} to 5×10^{-5} M) results in most of the intermediate, **1**, being trapped as the **1**-BuNC even when [CO] is in large excess over [BuNC]. This can only occur if the rate constant for BuNC association with **1** is larger than that for CO.

Absorbance changes at 440 nm proved most convenient for following the rate of isocyanide association. Under conditions where BuNC adds 10 times faster than CO, clean pseudo-first-order kinetics are followed, giving an association rate constant of 2.2×10^8 M^{-1} s^{-1} for *n*-BuNC.

Attempts to obtain the dissociation rate for **1**-BuNC by following the rate of the slow reaction after photolysis in CO-saturated benzene (eq 3) containing varying [BuNC] (3×10^{-5} to 3

$$\textbf{1}\text{-BuNC} + \text{CO} \rightarrow \textbf{1}\text{-CO} + \text{BuNC} \qquad (3)$$

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(1) Traylor, T. G.; Chang, C. K.; Geibel, J.; Berzinis, A.; Mincey, T.; Cannon, J. *J. Am. Chem. Soc.* **1979**, *101*, 6716.

(2) White, D. K.; Cannon, J. B.; Traylor, T. G. *J. Am. Chem. Soc.* **1979**, *101*, 2443.

(3) Geibel, J.; Cannon, J.; Campbell, D.; Traylor, T. G. *J. Am. Chem. Soc.* **1978**, *100*, 3575.

(4) St. George, R. C. C.; Pauling, L. *Science* **1951**, *114*, 629.

(5) Keilin, J. *Biochem. J.* **1949**, *45*, 440.

(6) Imai, Y.; Sato, R. *J. Biochem.* (*Tokyo*) **1968**, *64*, 147.

(7) Antonini, E.; Brunori, M. "Hemoglobin and Myoglobin in Their Reactions with Ligands", North-Holland Publishing Co.: Amsterdam, 1971; p 259.

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