where K_e is the equilibrium constant between S and P. The value of k_1^s is at a maximum when

$$k_1 = k_d \quad (5)$$

where k_d is the bimolecular rate constant for a diffusion-controlled process. The value of k_3 is at a maximum for a given value of K_3 when $k_3 = k_d$. It follows that

$$k_3 = (k_{-1}K_e)/K_2 \quad (6)$$

Substituting eq 6[11] and 5 into eq 3 and maximizing k (equivalent to minimizing $1/k$) with respect to k_{-1} at fixed[10] k_2 and k_{-2} gives

$$\partial k/\partial k_{-1} = 0$$

$$1/K_1^s k_2 = (1 + 1/K_2)(1/k_3) \quad (7)$$

As pointed out by Knowles and Albery, eq 7 is a result of maximizing the efficiency function under the constraint of uniform binding.[12]

Differential Binding. Differential binding involves changes in the relative stabilities of the internal intermediates and the consequential effects on the internal transition states. A mathematical equation that describes the condition for optimal k attainable by uniform binding and differential binding is derived below.

Solving eq 6 for k_{-1} and substituting this into eq 7 after converting K_1^s into k_1^s/k_{-1} gives

$$k_3 = \left(\frac{K_e}{K_2}k_1^s k_2\left(\frac{K_2 + 1}{K_e}\right)\right)^{1/2} \quad (8)$$

Assuming that a linear free energy relationship[13] holds for the elementary catalytic step (k_2),

$$k_2 = CK_2^{\beta} \quad (9)$$

where C is a constant and β is the **Brønsted** coefficient. Using eq 5, 8, and 9, the terms k_1^s, k_3, k_2, and k_2 in eq 3 can be replaced, and k can be written in terms of $k_d[S]_0$, K_e, K_2, C, and β. Maximizing k with respect to K_2 gives

$$\partial k/\partial K_2 = 0$$

$$\left(\frac{K_2^{\beta}}{K_2 + 1}\right)^{1/2}(K_2/\beta - (K_2 + 1)) = \left(\frac{k_d^s K_e}{C}\right)^{1/2} \quad (10)$$

where $k_d^s = k_d[S]_0$. Equation 10 is the result of maximizing k (or minimizing $1/k$) with respect to k_{-1} and K_2 (corresponding to maximizing k by uniform binding and differential binding). In the original paper by Knowles and Albery[2] it is suggested that after minimizing $1/k$ with respect to k_{-1}, minimizing $1/k$ with respect to K_2 is equivalent to minimizing $1/K_1^s k_2$ with respect to K_2. They arrived at this conclusion from inspection of their energy diagram. At a first glance, this appears reasonable since minimizing $1/K_1^s k_2$ also minimizes $1/k_3 + 1/(K_2 k_3)$ (by eq 7). The terms $1/k_1^s$ and $1/(K_1^s K_2 k_3)$ are constants since they are equivalent to $1/k_d^s$ and $1/(k_d^s K_e)$, respectively. However, it is clear from eq 3 that the therm $1/k_2$ has to be accounted for. Maximizing k with respect to k_{-1} and maximizing $K_1^s k_2$ with respect to K_2 leads to eq 11, in agreement with Knowles and Albery:

$$K_2 = \beta/(1 - \beta) \quad (11)$$

Clearly, eq 10 is inconsistent with eq 11 since the left side of eq 10 is zero if eq 11 holds, whereas the right side of eq 10 is a constant. Knowles and Albery applied eq 11 to conclude that the equilibrium constant between the enzyme's bound species is unity.

The right side of eq 10 approaches zero when the external equilibrium constant (K_e) approaches zero or when C is large, which corresponds to a small intrinsic barrier.[14]

Equation 3 was derived for the case that the product is consumed rapidly in a subsequent reaction, so that there is no significant back reaction (irreversible case). If the product concentration is allowed to accumulate to its equilibrium value (reversible case), the observed rate constant is given by a different equation. It had been unclear[7,12] whether the internal equilibrium constant should be unity for the irreversible case, the reversible case, or both. Equation 11 is obtained by solving the equilibrium equation[9] in a manner analogous to that shown in this paper for solving the steady-state equation. Therefore, the internal equilibrium constant should be unity if the enzyme is under evolutionary pressure when the product concentration is at its equilibrium value.

In conclusion, the previous theoretical prediction that the equilibrium constant between the enzyme's bound species is close to unity is not general. This prediction is a result of optimizing only a part ($K_1^s k_2$) of the overall rate constant (k) involved in the enzyme-catalyzed process. The "internal" equilibrium constant is a function of the "external" equilibrium constant and the intrinsic barrier of the catalytic step when the reaction is catalyzed irreversibly. Knowles and Albery's perfect-enzyme theory is a powerful theory in that it can predict the values of all of the rate constants involved in a given reaction mechanism provided that the mechanism involves catalysis by a perfect enzyme. The precision of the prediction may be qualitative or quantitative depending on the validity of the assumptions inherent in the theory. As experimental techniques improve, allowing more and more accurate measurements of kinetic and thermodynamic parameters, the perfect-enzyme theory may be tested[15] more precisely and improved upon as it becomes necessary.

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Supplementary Material Available: Derivations of eq 3, 7, 10, and 11 (6 pages). Ordering information is given on any current masthead page.

(11) Inherent in substituting eq 6 into eq 3 is the assumption that it is easier to improve k_3 relative to K_2.

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Solubilization in Detergent Micelles: "Interactive" Nature of the Solubilization Process As Indicated by a Study of Intermolecular Charge-Transfer Complexes[1]

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The question of solubilization sites provided by micelles, vesicles, and microemulsions is one of considerable interest and investigation. Although many early and even some recent studies suggest that organic reagents are solubilized in an oil-like interior for both micelles and vesicles,[2-5] much recent evidence suggests that a wide variety of solutes are solubilized in what appear to be moderately

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Table I. HC–MV^{2+} Charge-Transfer Complex Maxima Correlated with the "Py" (I_1/I_3 Fluorescence) Solvent Parameter

HC	slope of "Py" vs. $h\nu_{CT}$[a]	"Py"$_{SDS}$	"Py"$_{SDeS}$
trans-stilbene	2.51×10^{-4}	1.25	
trans-4-methoxystilbene	2.60×10^{-4}	1.29	1.46
trans-4-hydroxystilbene	2.27×10^{-4}	1.37	
trans-4,4'-dimethoxystilbene	2.56×10^{-4}	1.48	
trans,trans-1,4-diphenyl-1,3-butadiene	2.66×10^{-4}	1.29	
trans,trans-1-(*p*-methoxyphenyl)-4-phenyl-1,3-butadiene	2.77×10^{-4}	1.35	1.64

[a] All spectra recorded at 25 °C.

polar and, most likely, interfacial sites, especially in simple detergent micelles.[6-10] With regard to the latter, a major question is how much the solute "perturbs" the micelle. Since micelles are highly dynamic it is not unreasonable to expect that different solutes may modify the micelle such that the solubilization process is highly interactive.

In the present paper we report results of a study of intermolecular charge-transfer complex formation between a variety of hydrocarbons (HC) and methyl viologen (MV^{2+}) in homogeneous solution and in aqueous anionic micelles. The results of this study suggest that even in a "family" of similar complexes rather different solubilization sites are occupied. Although the results do not provide a distinction between the two "limiting" views of a micelle—the one a more-or-less static picture in which the micelle provides a rich variety of solvent environments (and/or interface sites), which are occupied differently by different solutes, with the other an interactive one in which a fluid detergent aggregate, water, and solute interact to provide perhaps a unique environment or range of environments for a given solute—they emphasize the complexity of the solubilization process and underline the difficulty of making generalizations regarding the "solvent" properties of microheterogeneous media.

We previously reported that hydrocarbons such as *trans*-stilbene, some surfactant stilbenes, and 1,4-diphenyl-1,3-butadiene form ground-state complexes with organic cations such as MV^{2+}.[10,11] Other studies[12-14] have shown that similar complexes are formed between the same cations and nicotinamide derivatives and other hydrocarbons such as pyrene. Complex formation is readily detectable by fluorescence quenching, as well as by a broadening of the long-wavelength π,π^* transition of the hydrocarbon. We also observed that at high concentrations of HC and MV^{2+} a weak, unstructured band appears in the visible spectrum. This band is evidently a classical intermolecular charge-transfer (CT) transition since its position is strongly solvent dependent. The blue shift in the spectrum with increasing solvent polarity (e.g., from 492 nm in ethanol to 445 nm in acetonitrile for *trans*-4-hydroxystilbene and MV^{2+}) and the little-modified HC π,π^* band are consistent with a complex according to the Mulliken formulation[15] in which there is little CT in the ground state but extensive electron displacement from donor to acceptor during excitation (eq 1).

$$HC,MV^{2+} \xrightarrow{h\nu_{CT}} (HC^+,MV^+)^* \qquad (1)$$

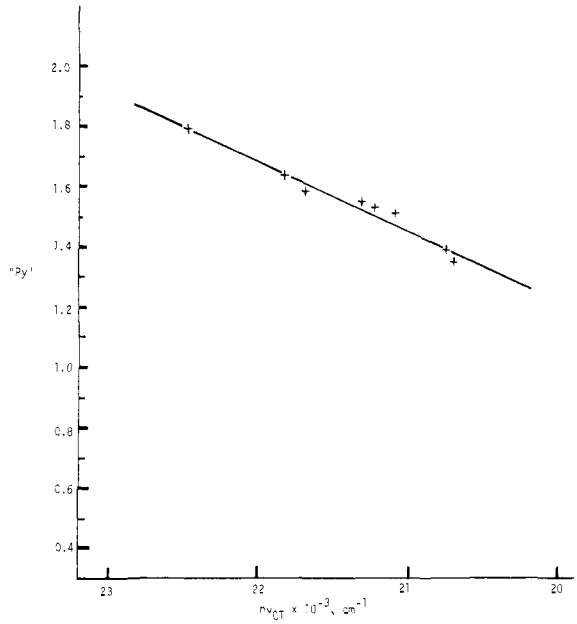

Figure 1. Plot of "Py" Vs. absorption maxima (cm^{-1}) for the *trans*-4-hydroxystilbene/methyl viologen CT complex.

Efforts to correlate $h\nu_{CT}$ with various single-parameter measures of solvent polarity have met with mixed success. For example, neither the Kosower "*Z*"[16] or Reichardt–Dimroth E_T[17] values give good linear plots for a range of moderately polar protic and aprotic solvents; this can be attributed to the sensitivity of these parameters to H-bonding effects. In contrast a good linear relationship exists for $h\nu_{CT}$ for each of the HC–MV^{2+} systems examined and the empirical I_1/I_3 values for pyrene fluorescence (Py) developed by Thomas,[18] Nakajima,[19] and Dong and Winnik.[20] The latter has been suggested as a good single-parameter indicator of solvent polarity that is insensitive to H-bonding or aprotic–protic effects.[19,20] A typical plot is shown in Figure 1, and slopes obtained for several HC–MV^{2+} complexes are given in Table I.

The readily observed CT complex between the different HC's and MV^{2+} in anionic micelles suggests that the measured $h\nu_{CT}$ values could be used to provide an estimate of apparent polarity or "Py_{eff}" in the micelle solubilization sites. In fact, pyrene in aqueous sodium dodecyl sulfate (SDS) gives an I_1/I_3 ratio of 1.21, which is slightly higher than that for ethanol.[21] As entries in Table I indicate, a rather wide range of values is obtained for the two surfactants, SDS and sodium decyl sulfate (SDeS), for the several systems; values extracted from the plots range from 1.25 to 1.64, according to "Py" values spanning the range from chloroform to ethylene glycol.[20] The deviation for the different micelles are clearly significant since the average deviation of individual points is in the range ±0.02 ("Py" values). Furthermore, an independent estimate of "Py" for nitromethane from $h\nu_{CT}$ values ("Py" cannot be measured in this solvent) gives 1.47 ± 0.03 with no systematic variation.

There appears to be a systematic variation in the "Py" values abstracted for the different HC–MV^{2+} complexes in the two surfactant solutions. In SDS there is a general increase in "Py" with the substitution of polar, electron-donating groups (OH and OCH_3) on the hydrocarbon; the "Py" values in both surfactants tend to be higher for the 1,4-diphenyl-1,3-butadienes than for corresponding stilbene derivatives, and there is a marked increase

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in Py on going from SDS to the smaller SDeS. These trends are explainable: the more polar HC derivatives and their corresponding CT complexes with MV^{2+} should prefer more polar solubilization sites. The SDS/SDeS and butadiene/stilbene differences can both be attributed to size effects. A reasonable estimate of the "length" of stilbene in terms of effective CH_2 groups is ca. 10,[22] and *trans,trans*-1,4-diphenyl-1,3-butadiene is certainly "longer" such that the two rigid molecules are comparable in length to the micelle radius in any reasonable model for the surfactant aggregate; clearly then the HC–MV^{2+} complexes are of significant size or volume compared to the SDS or SDeS aggregates that solubilize them. Obviously the probability of the hydrocarbon portion of the aggregate completely "swallowing" the CT complexes decreases as the size of the complex increases, or the length of the detergent chain decreases, and it is thus more likely that greater exposure to the aqueous phase will result. It is probably not necessary or prudent to speculate further on the nature of the various solubilization sites other than to suggest that they are probably moderately polar and, hence, "interfacial". What is noteworthy about the results obtained is the pronounced difference in solubilization sites for such small variations in complex and detergent structure. This underlines the danger of ascribing a single "character" to the solvent environment provided by detergent micelles and helps to reconcile apparent contradictions raised by different studies employing different techniques or probes to assess the solvent properties of aqueous surfactants.

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EPR Spectra of Some α-Tocopherol Model Compounds. Polar and Conformational Effects and Their Relation to Antioxidant Activities[1]

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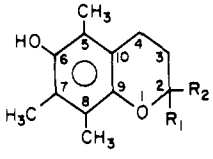
We recently reported[3,4] absolute rate constants, k_1, for the reaction of α-tocopherol (**1a**) and some related phenols (ArOH)



1a $R_1 = CH_3$, $R_2 = C_{16}H_{33}$

1b $R_1 = CH_3$, $R_2 = CH_3$

1c $R_1 = CH_3$, $R_2 = CO_2H$

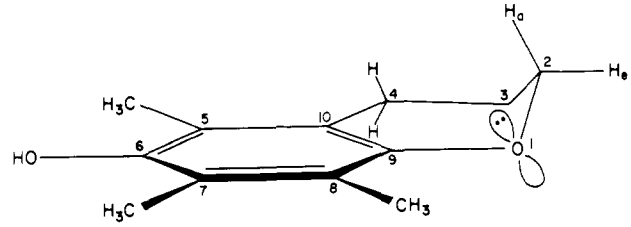
1d $R_1 = CH_3$, $R_2 = CO_2CH_3$

1e $R_1 = H$, $R_2 = H$

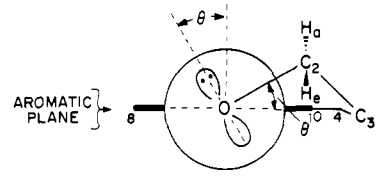
with poly(peroxystyryl)peroxyl radicals (ROO·) at 30 °C (eq 1).

$$ROO\cdot + ArOH \xrightarrow{k_1} ROOH + ArO\cdot \quad (1)$$

Compounds **1a** and **1b** were found to be more reactive toward ROO· than any other phenolic, chain-breaking antioxidants (k_1(**1a**) = 3.2 × 10^6, k_1(**1b**) = 3.8 × 10^6 M^{-1} s^{-1}).[4] This was attributed to stereoelectronic factors relating to the orientation of the p-type lone pair on the oxygen in position 1 with respect to the aromatic ring. This lone pair will stabilize the phenoxyl radical—and hence make the phenol a better antioxidant—provided its orbital can overlap with the orbital containing the unpaired electron. The extent of the stabilization is expected to follow a $\cos^2\theta$ relation, where θ is the dihedral angle between the O_1–C_2 bond and the C_8–C_9–C_{10} plane. By inference θ is also the dihedral angle between the 1-oxygen's p-type lone-pair orbital and the p-orbital of the adjacent aromatic carbon (see **2a** and **2b**).



2a



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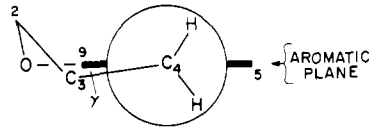
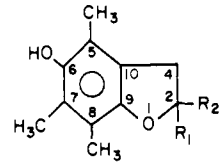


2c

Maximum stabilization will occur when $\theta = 0°$. The fused-ring system in **1a** ensures that θ will at least tend to approach this value, and indeed, an X-ray structure for **1b**[3] gives $\theta = 18.5°$ and 15.2°.[5,6] In contrast, k_1, for the ring-opened analogue, 4-methoxy-2,3,5,6-tetramethylphenol, is only 2.1 × 10^5 M^{-1} s^{-1}.[3] This compound has $\theta = 90°$ so that stabilization is minimized.

Work aimed at gaining additional understanding of the factors that control k_1 led to the discovery of a compound, **3a**, that was



3a $R_1 = CH_3$, $R_2 = H$

3b $R_1 = CH_3$, $R_2 = CO_2H$

1.66 times as reactive toward ROO· as **1a** and 1.43 times as reactive as **1b**.[4] Although some enhanced activity was anticipated because of the expected decrease in θ, the magnitude of the enhancement was surprising. That is, if in **1b** θ has the average value of 16.85°, then even if θ is 0° in **3a** the increase in the extent of stabilization would be only 1.09 (=$1/\cos^2 16.85°$). The increase

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(5) There are two different molecules in the unit cell.
(6) These angles differ slightly from those given originally,[3] which corresponded to the dihedral angle between the C_8–C_9 bond and the O_1–C_2 bond.

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