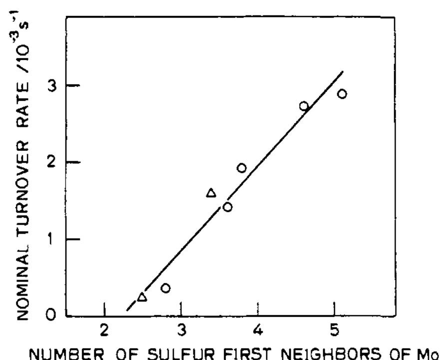

Figure 2. Correlation between NTR and N_S in CoMo/γ-Al_2O_3 samples prepared by (O) incipient wetness impregnation and (Δ) bulk impregnation.

of the peaks in the RDF. Effective phase shifts and amplitudes were estimated from the RDF of MoS_2.

Curve B in Figure 1 shows the dependence of N_S on the atomic Co/(Co + Mo) ratio. A "volcano" type curve similar to the NTR curve was also observed. Moreover, a linear correlation between NTR and N_S with a correlation factor of least-square fit equal to 0.98 is shown in Figure 2. This figure shows data for both series of catalysts. For example, there are two samples with $\alpha = 0.33$. The sample prepared by bulk impregnation has both lower activity and N_S values compared to the sample prepared by incipient wetness impregnation.

The number of nearest Mo neighbors of molybdenum in these samples was smaller compared to that of MoS_2 ($N_{Mo} = 6$). The value of N_{Mo} varied between 1.2 and 1.3 for both Mo/γ-Al_2O_3 samples and between 1.8 and 2.8 for the CoMo/γ-Al_2O_3 samples. This is in agreement with a very dispersed MoS_2-like phase.[8,10,11]

The dependence of N_S on Co loading can be understood in the following way: at $\alpha \leq 0.33$, Co interacts with the MoS_2-like phase, stabilizing this phase and thus increasing N_S. A "CoMoS" phase has been proposed by Topsøe et al.[12] to take into account this interaction. At large values of α, most of Co forms Co_9S_8. Thus, the stabilization role of Co is lost by the depletion of Co from the "CoMoS" phase.

A more detailed description of the structure and the effect of Co on the HDS activity of these sulfided CoMo/γ-Al_2O_3 will be published elsewhere.[13] It seems reasonable that as α increases, the sulfur binding energy of Mo increases until the maximum value of N_S is reached and then decreases as α is further increased. In their extensive work on the HDS activity of transition-metal sulfides, Pecoraro and Chianelli[14] recognize that there is a sulfur binding energy corresponding to a maximum HDS activity. Their result is expressed in a different way by the correlation between N_S and HDS activity proposed in this communication.

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Registry No. Thiophene, 110-02-1; cobalt, 7440-48-4; molybdenum, 7439-98-7; sulfur, 7704-34-9.

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Perfect Enzymes: Is the Equilibrium Constant between the Enzyme's Bound Species Unity?

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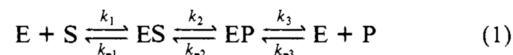
In an important study, Knowles and Albery[2,3] proposed an efficiency function to describe the effectiveness of a catalyst in accelerating a chemical reaction. The evolutionary improvement in the catalytic efficiency of enzymes can be separated into three broad stages in order of increasing difficulty: (1) "uniform binding", (2) "differential binding", and (3) "catalysis of an elementary step". The kinetics of reactions catalyzed by enzymes that have reached perfection with respect to one or more of the above three changes can be calculated by maximizing the efficiency function with respect to the same changes. One of the most interesting predictions from this calculation was that if an enzyme has reached perfection with respect to the first two changes above, the equilibrium constant between the enzyme's bound species is close to unity. This prediction has generated much interest and has been tested experimentally by Knowles and Albery[4-6] as well as by Benner.[7,8] However, the equation (eq 11 in this paper) that led to the above prediction is not general. The internal equilibrium constant can be a function of the external equilibrium constant and the intrinsic barrier of the catalytic step. The system that Knowles and Albery described is examined below.[9] Although the beginning part of the argument presented below overlaps with that given in the original study, a detailed description is given here for continuity and clarity.

The System. For the simple enzyme-catalyzed process shown



$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} EP \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} E + P \quad (1)$$

the rate of the reaction, ν, is given by

$$\nu = k[E]_T \quad (2)$$

where $[E]_T$ is the total enzyme concentration and k is the overall rate constant. Assuming steady-state concentrations for E, S, ES, and EP and assuming P is consumed rapidly in a subsequent reaction, so that there is no significant back reaction, the observed rate constant, k, is given by

$$k = 1/\{1/k_1^s + 1/k_2 + 1/k_3 + 1/(K_1^s k_2) + 1/(K_2 k_3) + 1/(K_1^s K_2 k_3)\} \quad (3)$$

where $k_1^s = k_1[S]_0$, $K_1^s = K_1[S]_0$, $K_1 = k_1/k_{-1}$ and $[S]_0$ is some constant physiological concentration of the substrate.

Uniform Binding. In uniform binding, the positions of all the internal states are shifted energetically up or down by the same amount relative to the external framework. A mathematical equation that expresses the condition for optimal k attainable by uniform binding is derived below.[10]

From thermodynamic considerations:

$$K_e = K_1 K_2 K_3 \quad (4)$$

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(10) The efficiency function (E_f) is equal to k multiplied by some constant that is independent of enzyme evolution.[2] Therefore the condition for maximum k is equivalent to the condition for maximum E_f.

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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]

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

(12) Equation iii in the Appendix of ref 2 and eq 7 of this paper are for irreversible processes. Equation 12 of ref 2 reduces to eq iii for irreversible processes.

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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.

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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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