Activator Effects on Urease Kinetics

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An experimental study of the effects of amino acid additives on the rates of urease kinetics showed that the degree of enhancement is sensitive to the relative levels of additives and substrate, and that enhancement can turn to inhibition at especially low concentrations of either arginine, DL-alanine, or glycine. Kinetic models developed to interpret these and prior literature data showed that all the data are consistent in the framework of the steady state model proposed but contradict the expectations that would follow from an equilibrium based treatment.

SCOPE

A fixed-bed differential reactor was used to evaluate experimentally the steady state kinetics of the urea hydrolysis reaction catalyzed by urease immobilized on nonporous glass beads. In particular, data were sought that would make possible distinctions between the equilibrium and steady state models, both of which attempt to explain and predict the effects of amino acid additives. A model was needed that would be consistent in at least qualitative trends with both the measurements of this study and the earlier data reported in the literature, to the effect that rate enhancement occurred for some concentration ranges of additive amino acids and substrate urea. Specific tests were run at room temperature, neutral *p*H, and with additives arginine, DL-alanine, and glycine, respectively. The results would have special relevance to the use of immobilized enzymes as selective reusable catalysts but may also shed light on the more general questions associated with catalysts sensitive to small traces of reactant additives, whether intentionally present or not.

CONCLUSIONS AND SIGNIFICANCE

Experimental measurements show that amino acid additives can either enhance or retard the rate of urea hydrolysis catalyzed by immobilized urease, the specific sensitivity depending on the relative concentrations of the additive and the substrate. In general, the rate is increased at higher substrate levels and reduced in very dilute substrate to the extent that sharp minimum rates are detectable for some amino acid systems. A steady state model accounts very satisfactorily for these observations, and a previously used equilibrium viewpoint is shown to be inadequate to this purpose. Earlier literature reports are also reconciled by the new model. These results have primary significance for data explanation, correlation, and prediction in enzyme activator engineering systems, but they may also raise considerations of major importance in cell physiology, where interaction between competing enzymatic chemical species are critical in enhancement and retardation effects.

In 1953 Wall and Laidler showed by experiments in two different buffer systems on the well-known urease catalyzed hydrolysis

$$(NH_2)_2CO + 3H_2O \rightarrow CO_2 + 2NH_4OH$$

that the system was substrate inhibited by urea in concentrations over about 0.25 M, and that the reaction rate was increased by small additions of any one of the amino acids glycine, DL-alanine, or L-tyrosine, when the urea level was also in its inhibiting range of concentrations. They demonstrated further that the rate enhancement is independent of the urea substrate concentration below a critical level, which appeared to be at the reaction rate maximum. The enhancement was found to be increased above the critical substrate level, and they attributed this finding to the competition between activator and substrate for the substrate inhibitory sites. More recently, Ramachandran and Perlmutter (1976) reported from their work on urease that had been immobilized by diazo-coupling to nonporous glass that the enhancement effect of the amino acids is dependent on substrate concentration even at levels well below the range that produces substrate inhibition. They noted that this result appeared to be inconsistent with the earlier finding but were not able to adequately explain the discrepancy.

It is the purpose of this paper to offer a kinetic model, new supporting data, and an interpretation of all sets of data that shows them to be consistent in the new framework. It is not necessary to resort to explanations that invoke the differences in buffers or in the nature of immobilized enzymes, except to the extent that these affect the relative magnitudes of pertinent kinetic or equilibrium constants.

KINETIC MODEL

Following Wall and Laidler (1953) and Ramachandran and Perlmutter (1976), assume that the enzyme E is partially converted to the more active form E^* by the action of the amino acid and that both E and E^* combine with the substrate S to produce intermediate complexes ES and E^*S. These subsequently decompose to regenerate enzyme and produce product P according to the reactions

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E + P \qquad (1)$$

$$E + A \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} E^* \tag{2}$$

$$E^* + S \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} E^*S \xrightarrow{k_6} E^* + P \tag{3}$$

By assuming in the usual way that both product forming reactions are first-order batch decompositions, the rate is

$$\frac{dP}{dt} = k_6 E^*S + k_2 ES \tag{4}$$

Further development depends on the model and the associated algebraic technique used to eliminate the unknown intermediate concentrations in favor of measureable substrate, activator, and enzyme amounts. The total quantity of enzyme E_T is partitioned by this system of reactions among four possible forms: free enzyme E, the substrate complex ES, the activator complex E^*, and the substrate-activator complex E^*S.

Equilibrium Treatment

If one considers that except for the two controlling product forming steps all the reactions in the set (1) to (3) are at equilibrium, repeated substitutions in Equation (4) yield the rate equation

$$\frac{dP}{dt} = \frac{k_2 K_1 E_T S}{1 + K_1 S + K_3 (1 + K_4 S) A} \left[1 + \frac{k_6}{k_2} \frac{K_3 K_4}{K_1} A \right] \tag{5}$$

where, as usual, the equilibrium constants are defined in terms of forward and backward rate constants

$$K_i = \frac{k_i}{k_{-i}} \tag{6}$$

This reduces in the absence of the activator to

$$\frac{dP}{dt} = \frac{k_2 K_1 E_T S}{1 + K_1 S} \tag{7}$$

Although their treatment of the problem was not algebraically explicit, Wall and Laidler (1953) in effect defined a rate enhancement factor by

$$R(S, A) = \frac{\left[\begin{array}{l}\text{reaction rate at substrate}\\ \text{concentration S in the presence}\\ \text{of the activator at concentration } A\end{array}\right]}{\left[\begin{array}{l}\text{reaction rate at substrate}\\ \text{concentration S in the absence}\\ \text{of the activator}\end{array}\right]} \tag{8}$$

By substituting Equations (5) and (7), one can derive

$$R(S, A) = \frac{1 + K_3 A \dfrac{k_6 K_4}{k_2 K_1}}{1 + K_3 A \dfrac{(1 + K_4 S)}{(1 + K_1 S)}} \tag{9}$$

Equation (9) can be reduced to a variety of special cases for specific purposes. By adopting the assumption that $K_1 = K_3 = K_4 = K$, one obtains the equivalent of Wall and Laidler's interpretation, and Equation (9) reduces to the substrate independent form

$$R(A) = \frac{1 + (k_6/k_2) KA}{1 + KA} \tag{10}$$

Ramachandran and Perlmutter (1976) expressed this same relationship in terms of experimentally derived parameters as

$$R(A) = 1 + \frac{KA}{1 + KA} \left[\frac{V^a_{\max}}{V_{\max}} - 1 \right] \tag{11}$$

where $V_{\max} = k_2 E_T$ and $V^a_{\max} = k_6 E_T$. Since these equations do not include any substrate dependence, they cannot in any way be used to interpret the data reported by Ramachandran and Perlmutter.

As alternative simplifications of the more general Equation (9), consider restrictions on the range of concentrations rather than arbitrary assumptions regarding the relative magnitudes of the equilibrium constants. For small substrate levels such that

$$S << \frac{1}{K_4} \tag{12}$$

and

$$S << \frac{1}{K_1} \tag{13}$$

Equation (9) reduces to

$$R(A) = \frac{1 + (k_6/k_2)(K_3 K_4/K_1) A}{1 + K_3 A} \tag{14}$$

If, in addition, high activator levels are used such that

$$A >> \frac{1}{K_3} \tag{15}$$

and

$$A >> \frac{k_2}{k_6} \frac{K_1}{K_3 K_4} \tag{16}$$

then the constant

$$R = \frac{k_6}{k_2} \frac{K_4}{K_1} \tag{17}$$

It is, on the other hand, also possible to obtain a special form of Equation (9) that is independent of substrate level if

$$S >> \frac{1}{K_4} \tag{18}$$

and

$$S >> \frac{1}{K_1} \tag{19}$$

With these restrictions, Equation (9) becomes

$$R(A) = \frac{1 + (k_6/k_2)(K_3 K_4/K_1) A}{1 + (K_3 K_4/K_1) A} \tag{20}$$

If in addition

$$A >> \frac{K_1}{K_3 K_4} \tag{21}$$

and condition (16) applies, Equation (20) reduces to the constant

$$R = \frac{k_6}{k_2} \tag{22}$$

A comparison of Equations (14) and (20) suggests that the sensitivity of R with respect to A will differ at high and low substrate levels. Furthermore, Equations (17) and (22) indicate that although R approaches a maximum value at high A regardless of S level, the limiting values will be different by a factor of the ratio of the equilibrium constants (K_4/K_1). Such trends are illustrated in Figure 1, where calculated enhancement factors are shown for particular plausible values of the system parameters. Finally, it should be noted that for

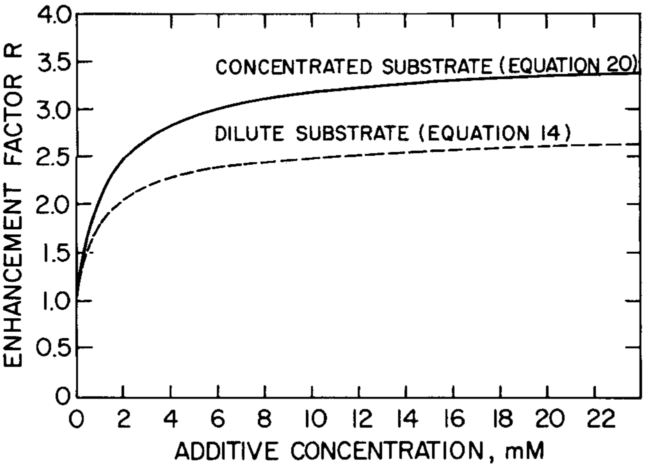

Fig. 1. Effect of additive concentration on enhancement factor at high and low substrate levels, calculated from Equations (14) and (20) for $K_3 = 1$, $(k_6/k_2) = 3.41$, and $(K_1/K_4) = 1.32$.

systems that show no rate enhancement under conditions of dilute substrate and concentrated activator, Equation (17) yields $R = (k_6K_4/k_2K_1) = 1$ and simplifies Equation (14) to $R = 1$ at any level of A. Since these findings all arise from an equilibrium model argument, it is pertinent to ask whether the same results would arise from a steady state interpretation of the kinetics. The next section undertakes to examine this question.

Steady State Treatment

Assume as before that the reaction mechanism follows the chemistry of Equations (1) to (3), but as a point of departure from this earlier treatment, consider in addition that the intermediate E^*S can also be formed by

$$ES + A \underset{k_{-5}}{\overset{k_5}{\rightleftharpoons}} E^*S \tag{23}$$

Once again the development of a single equation rate model proceeds from Equation (4) by repeated substitutions to eliminate the unmeasured intermediates. This time the needed algebraic relations are obtained by applying to the elementary reactions the pseudo steady state hypothesis (PSSH) in the manner presented in detail by Aris and his co-workers (1967, 1972). The result yields the rate of product formation as

$$\frac{dP}{dt} = \beta E_T(k_2\gamma + k_6\alpha) \tag{24}$$

where:

$\alpha = E^*S/E =$ the ratio of enzyme in the substrate activator complex to that in the free state

$\beta = E/E_T =$ the fraction of total enzyme existing in the free state

$\gamma = ES/E =$ the ratio of enzyme in the substrate complex to that in the free state

The ratios α, β, and γ can be expressed in terms of kinetic constants and the measurable substrate and activator concentrations as

$$\alpha = \frac{[k_3k_4(k_{-1} + k_2 + k_5A) + k_1k_5(k_{-3} + k_4S)]SA}{k_{-3}(k_{-4} + k_6)(k_{-1} + k_2 + k_5A) + k_{-5}(k_{-1} + k_2)(k_{-3} + k_4S)} \tag{25}$$

$$\beta = \left[1 + \alpha + \frac{k_1S + k_{-5}\alpha}{k_{-1} + k_2 + k_5A} + \frac{k_3A + (k_{-4} + k_6)\alpha}{k_{-3} + k_4S}\right]^{-1} \tag{26}$$

$$\gamma = \frac{k_1S + k_{-5}\alpha}{k_{-1} + k_2 + k_5A} \tag{27}$$

Since it is the purpose of this study to provide a framework for data interpretation, it is advantageous to examine reduced forms of Equation (24) in specific ranges of substrate and activator concentrations.

Dilute Substrate. As the substrate concentration is reduced to the level of

$$S << (k_{-3}/k_4) \tag{28}$$

Equations (25) and (26) become

$$\alpha = \delta S \tag{29}$$

$$\beta = \left[1 + \delta S + \frac{k_1S + k_{-5}\delta S}{k_{-1} + k_2 + k_5A} + K_3A + \frac{K_{MA}k_4}{k_{-3}}\delta S\right]^{-1} \tag{30}$$

and Equation (24) simplifies to

$$\frac{dP}{dt} = \beta E_TS\left[k_6\delta + \frac{k_2(k_1 + k_{-5}\delta)}{k_{-1} + k_2 + k_5A}\right] \tag{31}$$

where

$$\delta = \frac{[k_3k_4(k_{-1} + k_2 + k_5A) + k_1k_{-3}k_5]A}{k_{-3}(k_{-4} + k_6)(k_{-1} + k_2 + k_5A) + k_{-3}k_{-5}(k_{-1} + k_2)} \tag{32}$$

Applying the defining Equation (8), one gets

$$R(S, A) = \beta\left[\frac{k_{-1} + k_2}{k_1} + S\right]\left[\frac{k_6}{k_2}\delta + \frac{k_1 + k_{-5}\delta}{k_{-1} + k_2 + k_5A}\right] \tag{33}$$

with β as given by Equation (30). If the substrate level is further restricted to the range

$$S << \frac{1 + K_3A}{\delta + \dfrac{1 + (k_{-5}\delta/k_1)}{K_M + (k_5A/k_1)} + K_{MA}\dfrac{k_4}{k_{-3}}} \tag{34}$$

the enhancement factor becomes

$$R(A) = \frac{K_M}{1 + K_3A}\left[\frac{k_6}{k_2}\delta + \frac{1 + (k_{-5}\delta/k_1)}{K_M + (k_5A/k_1)}\right] \tag{35}$$

Dilute Substrate and Concentrated Activator. When the substrate concentration is reduced to the level of

$$S << \frac{K_{MA}}{1 + (k_4K_{MA}/k_{-3})} \tag{36}$$

and condition (28) applies, while activator is present at high concentrations defined by

$$A >> \frac{1}{K_3} \tag{37}$$

$$A >> \frac{k_1}{k_4K_3} \tag{38}$$

$$A >> \frac{k_{-1} + k_2}{k_5} \tag{39}$$

$$A >> \frac{1}{K_5\left[1 + \dfrac{K_{MA}k_4}{k_{-3}}\right]} \tag{40}$$

and

$$A >> \frac{k_1}{k_4}\frac{K_M}{K_{MA}}\frac{1}{K_5} \tag{41}$$

then the rate enhancement factor becomes

$$R = \frac{k_6}{k_2}\frac{k_4}{(k_{-4}+k_6)}\frac{(k_{-1}+k_2)}{k_1} = \frac{k_6}{k_2}\frac{K_M}{K_{MA}} = \frac{V^a_{\max}}{V_{\max}}\frac{K_M}{K_{MA}} \tag{42}$$

Concentrated Substrate and Concentrated Activator. As substrate concentration increases sufficiently to the level that

$$S >> (k_{-3}/k_4) \tag{43}$$

and

$$S >> (k_3A/k_1) \tag{44}$$

Equation (24) reduces to

$$\frac{dP}{dt} = \frac{k_2E_T}{1+K_5A}\left[1 + (k_6K_5A/k_2)\right] \tag{45}$$

and the enhancement factor can be obtained as

$$R(A) = \frac{1 + (k_6K_5A/k_2)}{1+K_5A} \tag{46}$$

At high enough levels of activator, Equation (46) becomes

$$R = k_6/k_2 \tag{47}$$

Comparison of Equations (42) with (47) shows the same effect of substrate level on the sensitivity of R with respect to A as was noted earlier in comparing Equations (17) and (22). In this respect the equilibrium and steady state models lead to the same conclusion in the limit of concentrated activator; other characteristics of the more general forms of the equations may be used, however, to distinguish between the two models. To focus on these points, it is convenient to examine Figure 2 which shows values of the enhancement factor calculated from Equations (35) and (46) at the selected parameter settings indicated and the same information reproduced on the expanded log scale as Figure 3. In contrast to the lack of such sensitivity exhibited in Figure 1 for the equilibrium model, the curves in Figures 2 and 3 show very different dependence on activator addition at high and low substrate levels. In the particular case chosen for the example of Figures 2 and 3, the difference is so marked as to produce a sharp minimum in the enhancement curve as well as fractional values of R over part of the range of activator. Values of $R < 1$ imply, of course, that the activator has in fact become an inhibitor. The location of the minimum in R will shift with changes in the system parameters, disappearing entirely for some ranges of activator concentrations.

EXPERIMENTAL RESULTS

Since the alternative models developed for the urease-activator systems lead to sharply divergent predictions, a series of experiments were run that tested the expectations at amino acid levels well below those previously reported (Wall and Laidler, 1953; Ramachandran and Perlmutter, 1976). In all other respects the apparatus and materials used were the same as those described by Ramachandran and Perlmutter (1976). It should be noted, however, that the immobilized enzyme differs from batch to batch, sometimes considerably even under conditions believed to be identical. In the constant flow differential fixed-bed reactor used in this study, the concentrations of all enzyme species remain invariant with time.

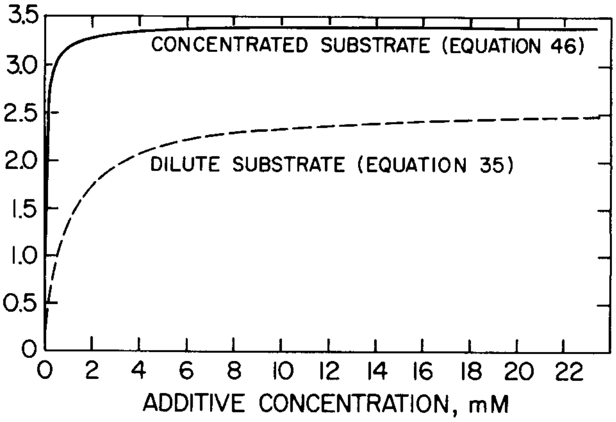

Fig. 2. Effect of additive concentration on enhancement factor at high and low substrate levels, calculated from Equations (46) and (35) for $(k_{-1}/k_1) = 100$, $(k_{-5}/k_4) = 0.001$, $K_5 = 10$, $K_3 = 1$, $K_M = 3.1$, $K_{MA} = 4.1$, $(k_6/k_2) = 3.41$.

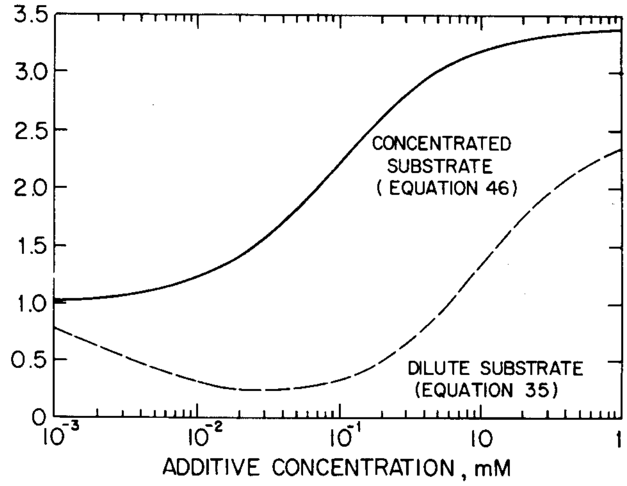

Fig. 3. The calculated curves of Figure 2 on an expanded scale.

Experiments were run on three different enzyme-bead batches with three different amino acid additives at three levels of urea substrate concentration, as itemized in Table 1. These results are presented as Figures 4 to 6 covering a total range of activator concentrations of about 10^5. Flow rates, particle dimensions, and catalyst activities were for all runs in the ranges previously demonstrated (Ramachandran and Perlmutter, 1976) to be beyond any significant diffusional interference.

TABLE 1. ADDITIVES AND CONCENTRATIONS USED IN EXPERIMENTAL SERIES

Amino acid	Additive concentration range, M	Urea substrate concentration, M	Enzyme batch
DL-alanine	4×10^{-6} to 2×10^{-2}	0.002	I
Arginine	2×10^{-5} to 5×10^{-2}	0.002	II
DL-alanine	2×10^{-4} to 2×10^{-2}	0.01	I
Arginine	9×10^{-6} to 1×10^{-3}	0.01	II
Arginine	1×10^{-3} to 1×10^{-1}	0.01	III
DL-alanine	2×10^{-3} to 1×10^{-1}	0.10	II
Glycine	6×10^{-4} to 2×10^{-2}	0.10	II

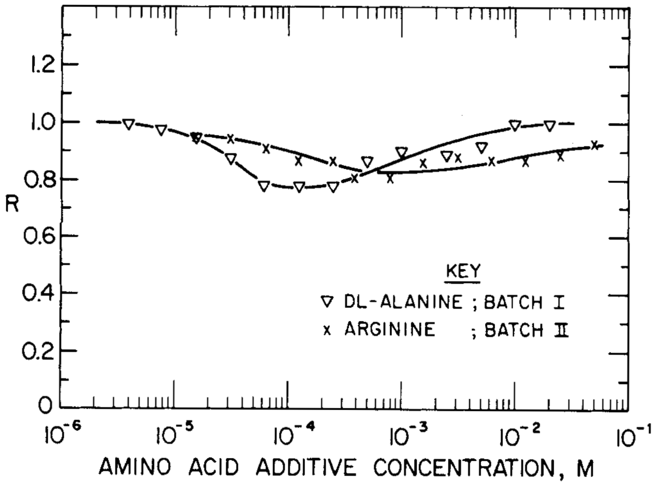

Fig. 4. Effect of additive concentration on enhancement factor at urea level = 2 mM.

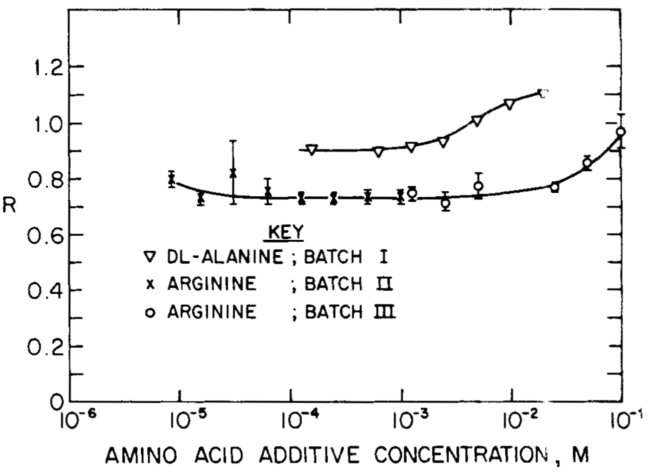

Fig. 5. Effect of additive concentration on enhancement factor at urea level = 10 mM.

DATA INTERPRETATION AND DISCUSSION

An assessment of the relative merits of the models developed here can be based on comparisons of the experimental trends with those predicted by the equations, or comparisons of the numerically estimated parameters derived by alternative arguments from the equations. Both approaches are explored in this section.

A common method for estimation of Michaelis constants utilizes measured reaction rates at a series of substrate concentrations to extract the appropriate constants by simply determining the substrate levels corresponding to rates that are half their maximum values. For this purpose, supplementary data are needed on reaction rates in the complete absence of amino acid and at relatively high activator levels. Such measurements are available for the immobilized enzyme systems of interest (Ramachandran and Perlmutter, 1976) and are presented as Figure 7. Application of the half maximum procedure to these data yields the same results for both glycine and DL-alanine:

$$K_M = 3.1 \text{ mM}$$

$$K_{MA} = 4.1 \text{ mM}$$

$$(K_{MA}/K_M) = 1.33$$

The relationships expressed as Equations (42) and (47) for the steady state model suggest that there is another independent way of using experimental data to estimate the (K_M/K_{MA}) ratio. This alternative is based on the expectation arising from the ratio of Equations (42) and (47) to the effect that the enhancement factor R approaches limits at concentrated A that differ by the ratio (K_{MA}/K_M). Thus, a comparison of R values from experiments in concentrated A for dilute and concentrated S yields

$$\frac{R(\text{concentrated } A, \text{ concentrated } S)}{R(\text{concentrated } A, \text{ dilute } S)} = \frac{K_{MA}}{K_M}$$

Choosing values for glycine from Table II of Ramachandran and Perlmutter (1976), we get

$$\frac{R(\text{concentrated } A, S = 250 \text{ mM})}{R(\text{concentrated } A, S = 2 \text{ mM})} = \frac{3.41}{2.57}$$

and

$$(K_{MA}/K_M) = 1.32$$

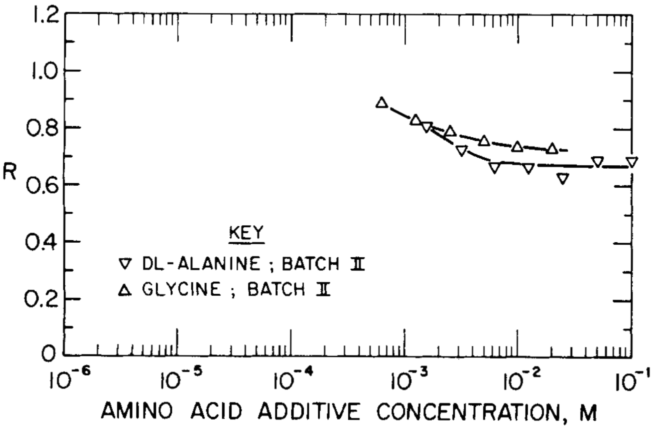

Fig. 6. Effect of additive concentration on enhancement factor at urea level = 100 mM.

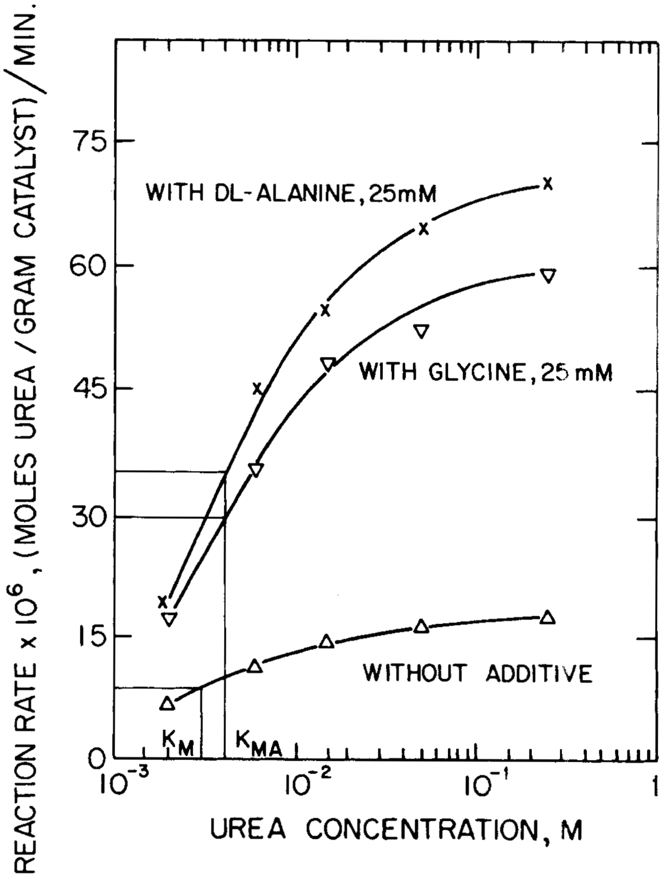

Fig. 7. Experimental reaction rates at various substrate levels with and without additives.

a result virtually identical to the value obtained above. The analogous figures for DL-alanine are

$$\frac{R(\text{concentrated } A,\, S = 250\,\text{mM})}{R(\text{concentrated } A,\, S = 2\,\text{mM})} = \frac{4.03}{2.83}$$

and

$$(K_{MA}/K_M) = 1.42$$

This result and the prior figure differ by about 7%, but this difference is within the range of experimental error and offers no substantive basis for any distinction.

A related but different data interpretation may be extracted by referring to the equilibrium model. In this case, comparison between Equations (17) and (22) shows that the limiting R values are related by

$$\frac{R(\text{concentrated } A,\, \text{concentrated } S)}{R(\text{concentrated } A,\, \text{dilute } S)} = \frac{K_4}{K_1}$$

Using the same experimental data as previously, one gets

$$\frac{K_4}{K_1} = 1.32 \quad \text{for glycine}$$

and

$$\frac{K_4}{K_1} = 1.42 \quad \text{for DL-alanine}$$

Evidently, these numerical results cannot distinguish between the steady state and equilibrium models at high substrate levels but can only be used to estimate ratios of appropriate rate or equilibrium constants, respectively. They were used for this purpose in the calculations shown in Figures 1, 2, and 3.

To emphasize the qualitative trends implied in each model, it is useful to compare the data of Figures 4 to 6 with the computed Figures 1 to 3. The expanded log scale of Figure 3 focuses especially on the dilute ranges of additive concentrations that correspond to the data. It is evident that the data trends conform qualitatively to the expectations of the steady state model and not to the predictions of the equilibrium model. This generalization accounts for the enhancement values less than unity, for the minimum with respect to additive concentration, and for the very dilute range of amino acids in which these phenomena show up. In addition, the data suggest a move to enhancement factors greater than unity as additive concentrations increase toward the ranges of previous tests. The markers on Figure 5 report the spread between duplicate runs for which the points are averages.

Further support for the steady state model may be obtained from the literature reports. At low substrate levels the results in Ramachandran and Perlmutter's (1976) Table 2 show a dependence on glycine concentration that disappears at higher substrate concentrations. This trend in sensitivity is consistent with the expectations arising from Equations (35) and (46) but is not predicted by the equilibrium model. The curves of Figures 2 and 3 based on the steady state model show the same pattern as the glycine data in that sensitivity depends sharply on substrate level. The Figure 1 curves are based on the equilibrium model and show no marked effect of this sort.

The details of enhancement behavior will, of course, depend on the parameters applicable to a specific set of experiments. Accordingly, the differences observed by Ramachandran and Perlmutter (1976) between the activating effects of glycine and DL-alanine are probably to be attributed to the differences in rate and equilibrium constants, rather than to a necessary change in mechanisms. Similarly, there is no need to postulate any supplemental mechanistic steps in interpreting the earlier Wall and Laidler (1953) results on homogeneous urease activators. The findings reproduced as Table 2 are entirely consistent with the models described here for appropriate choices of the relevant constants. In the range of urea substrate concentrations between $U = 0.005$ and $U = 0.15$ M, the enhancement factor is independent of substrate level, increasing only at the higher level of $U = 0.83$ M, a result that would be expected from Equations (42) and (47) if $K_{MA} \approx K_M$ in the two buffers, respectively, and provided that the higher values of R at $U = 0.83$ M correspond to a change from the simple Michaelis-Menton rate form to a substrate inhibition.

TABLE 2. DATA REPORTED BY WALL AND LAIDLER (1953) ON APPROXIMATE R VALUES AT VARIOUS UREA CONCENTRATIONS

	R	
Urea concentration, M	Phosphate buffer (pH = 6.6)	THMAM-H_2SO_4 buffer (pH = 7.13)
0.005	1.4	1.4
0.025	1.4	1.4
0.15	1.4	1.4
0.83	2.5	2.0

The experimental findings, new and old, give support to the prediction of the steady state model that a given additive can have either positive or negative effects on reaction rate at different concentrations, and depending on the related substrate level. Since this reversal arises from the interaction between competing active species, it would appear to be a consideration of major importance in enzymatic behavior related to cell physiology or mass transport. In particular, there may be applications to membrane processes such as occur in artificial kidney devices which handle urea.

ACKNOWLEDGMENT

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NOTATION

A = concentration of activator
E = concentration of enzyme in free state
ES = concentration of enzyme substrate complex
E^* = concentration of enzyme activator complex
E_T = total enzyme concentration
k_i = rate constants of the elementary steps in Equations (1) to (4)
$K_i = k_i/k_{-i}$
$K_M = \dfrac{(k_{-1} + k_2)}{k_1} = \dfrac{1 + (k_2/k_{-1})}{K_1}$
$K_{MA} = \dfrac{(k_{-4} + k_6)}{k_4} = \dfrac{1 + (k_6/k_{-4})}{K_4}$
P = concentration of product
R = the enhancement factor defined by Equation (5)
S = concentration of substrate
$V^a{}_{\max} = k_6 E_T$
$V_{\max} = k_2 E_T$
α, β, γ = ratios defined by Equations (20), (21), and (22)
δ = constant defined by Equation (23)

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Hydrogenolysis Kinetics of Ethane and *n*-Pentane Over Unsupported Copper/Nickel and Platinum Catalysts

Two kinetic models of hydrocarbon hydrogenolysis over monometallic surfaces, based respectively on *catalytically uniform* or *nonuniform* surfaces, are applied to ethane and *n*-pentane hydrogenolysis results over copper-nickel alloy catalysts as well as the monometallic catalysts platinum and nickel. If no direct hydrogen desorption appears in any postulated irreversible step, both models predict the same composition for the important surface intermediates C_nH_x (n = 1, s), where x depends upon the catalyst.

This analysis predicts that for essentially all alloy catalysts to which the postulated sequences may apply, the hydrogenolytic surface intermediate C_nX_x contains one more hydrogen atom than that calculated for a nickel catalyst: specifically, C_2H_3 (alloy) vs. C_2H_2 (nickel) for ethane and C_5H_6 (alloy) vs. C_5H_7 (nickel) for *n*-pentane.

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SCOPE

The hydrogenolysis of ethane is by now a classical reaction in heterogeneous catalysis, having been characterized kinetically by studies over iron, cobalt and nickel catalysts (Cimino et al., 1954), other group VIII metals (Sinfelt and Taylor, 1968), and copper-nickel alloys (Sinfelt et al., 1972; Sinfelt, 1973). An obvious industrial interest has existed for some time in finding base metal alloy catalysts which might be used as a substitute for such noble metals as platinum and palladium. In the petroleum refining industry, reactions of C_5, C_6, and C_7 hydrocarbons are important; in particular, the selectivity for hydrogenolysis vs. nondestructive rearrangements [(de)hydrocyclization, skeletal isomerization, dehydrogenation] is of prime concern.

It has been appreciated previously that copper-nickel catalysts, in the presence or absence of solid acid catalysts, exhibit lower hydrogenolytic activity than nickel toward both ethane (Sinfelt et al., 1972) and C_5-C_7 hydrocarbons (Reman et al., 1971; Ponec and Sachtler, 1972). A kinetic scheme involving equilibrated hydrocarbon adsorption on a catalytically uniform surface has been proposed by Cimino et al. (1954) and subsequently modified by Sinfelt (1972) to rationalize reaction orders in ethane and hydrogen at temperatures where hydrogenolysis rates first become appreciable. An alternate proposal set forth by Boudart (1972) considers this reaction as a two-step irreversible sequence occurring on a catalytically nonuniform surface for several *monometallic* nickel or iron catalysts.

The purpose of the present paper is to establish that either scheme provides a reasonable description of hydrogenolysis reaction orders over copper-nickel alloy surfaces, in particular, for the alkanes, ethane (Sinfelt et al., 1972), and *n*-pentane (Taheri, 1975; Taheri and Ollis 1975). Further, the results provide a quantitative connection between hydrogenolysis kinetics of alkanes over copper-nickel alloys vs. the well-studied examples of monometallic nickel or platinum catalysts.

The implications of these results are twofold. First, the utility of ethane hydrogenolysis models in developing fruitful approaches to hydrogenolysis of ethane and considerably larger molecules over metal alloy catalysts encourages application of other classical kinetic laws to reactions catalyzed on alloy surfaces. Also important, the present paper provides a quantitative experimental example of the nearly identical kinetic features resulting from considering catalytic surfaces as either uniform or nonuniform.