

geraniol as 2(*R*), 3(*R*). We have found that the (+)-2,3-epoxygeraniol acetate produced in our system (entry 7, Table I) gives (–)-2,3-epoxygeraniol upon hydrolysis (K₂CO₃, MeOH). Thus, in the case of geraniol, the two systems selectively form opposite epoxide enantiomers.

- (18) Sizeable asymmetric inductions (ca. 50% ee) have been attained in the formation of oxaziridines by the reaction of chiral peracids with imines (see J. Bjørge, D. R. Boyd, R. M. Campbell, N. J. Thompson, and W. B. Jennings, *J. Chem. Soc., Perkin Trans. 2*, 606 (1976), and references cited therein).

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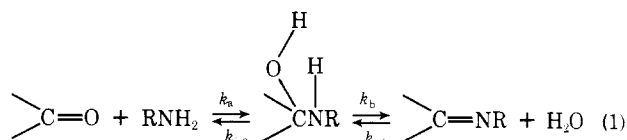
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Rate of Carbinolamine Formation between Pyridoxal 5'-Phosphate and Alanine¹

Sir:

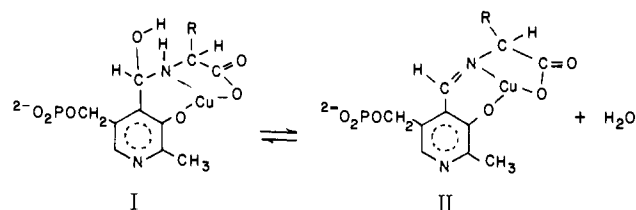
In Schiff base formation reactions between amines and carbonyl compounds a two-step mechanism involving an intermediate carbinolamine is often observed.²⁻⁴ However, in



the reactions of the physiologically important pyridoxal 5'-phosphate (PLP), 3-hydroxypyridine-4-carboxaldehyde⁵ or salicylaldehyde,⁶ carbinolamine does not form in readily detectable amounts. The same rate equation, which is first order in each of aldehyde and amine, describes both the disappearance of aldehyde and the formation of aldimine. In two limiting cases which could account for this behavior either a low pre-equilibrium concentration of carbinolamine is formed with dehydration being rate limiting, or carbinolamine formation is rate limiting with dehydration being fast. Arguments in favor of the latter mechanism have been presented.^{5,7} Alternatively, an intermediate steady state situation could exist. By trapping the carbinolamine formed during the reaction of PLP and ala with Cu(II) we have been able to determine both the stability of the Cu(II)-carbinolamine complex and the rate law for its formation. Both Cu(II) independent and dependent pathways were found. A comparison of the values of the rate constants found for the former set of reactions with those found for the formation of (*N*-pyridoxylidene 5'-phosphate)alaninate in the absence of Cu(II) shows unequivocally that carbinolamine formation in this system is considerably faster than dehydration.

Intermediates having a lower absorbance in the near-UV than either reactants or products have been observed in the hydrolysis of bis(*N*-salicylideneethylamine)copper(II) in borax

buffers at pH 8.5,⁸ and during the reaction of PLP with glutamate in the presence of Cu(II).⁹ These intermediates have been attributed to Cu(II) carbinolamine complexes. We have found that under certain conditions on mixing PLP with copper(II)-alanine solution⁵ the absorbance bands of PLP decrease in intensity owing to a reaction which is complete in 1 min or less, and, concurrently, a new absorption maximum centered at 325 nm appears. In a second reaction which requires about 1 h, the absorption spectrum of the Cu(aldimine) product slowly appears as the 325-nm band disappears. A similar 325-nm band is also observed with the Cu(II) complexes of pyridoxamine 5'-phosphate, in which the 4 position of the aromatic ring is occupied by a saturated substituent.¹⁰ Thus, it appears that this intermediate is, indeed, the carbinolamine complex, I. If too little Cu(II) is present, or if it is extensively bound as alaninate complexes, I is not observed, but PLP is converted to the aldimine complex (II) in an apparent single step reaction. Because the rate of formation of I is so much faster than its dehydration to II, the two steps may very easily be studied separately. We report here the results of a stopped flow spectrophotometric examination of the rates of formation of I as the reaction systems approached the first metastable equilibrium state. The subsequent conversion of I to II was followed using a double beam recording spectrophotometer.



Near equilibrium kinetic data provide information regarding the composition of products as well as formation rates. In this case the results of 96 determinations under a variety of conditions confirmed that I is a 1:1:1 Cu(II)-ala-PLP complex that can add one or two protons, depending on pH. The reaction conditions for a few representative experiments and their observed first-order rate constants as equilibrium was approached are given in Table I.

The data were found to conform to the rate law,

$$k_{\text{obsd}} = \left(\sum_{i=0}^4 k_{a,i} f_{\text{HiPLP}} + \sum_{i=0}^2 k_{a,i}^{\text{Cu}} f_{\text{CuHiPLP}} \right) [\text{ala}^-] \left(1 + \frac{1}{K_{\text{cond}}} \right) \quad (2)$$

where the $k_{a,i}$ are forward rate constants for the formation of I, the f_x are the fractions of PLP present in the form of species x , and K_{cond} is the conditional equilibrium constant for carbinolamine formation. K_{cond} is equal to the ratio of the sum of the equilibrium concentrations of the unprotonated and protonated forms of I to the sum of all forms of PLP not present

Table I. Some Observed and Theoretical Values of the Near Equilibrium Rate Constants for Cu(carbinolamine) Formation ($T = 25^\circ\text{C}$, $I = 0.5$)

	$10^3 (\text{Cu}_{\text{tot}})$, M	$10^2 (\text{Ala}_{\text{tot}})$, M	$10^4 (\text{PLP}_{\text{tot}})$, M	pH	k_{obsd} , s^{-1}	$k_{\text{calcd}} \text{ s}^{-1}$ (no Cu terms)	$k_{\text{calcd}} \text{ s}^{-1}$ (Cu terms)
1	5.8	5.0	1.0	5.35	0.84	0.90	0.91
2	5.8	10.0	1.0	5.14	2.2	1.7	1.7
3	1.9	2.0	1.0	6.24	3.0	3.2	3.2
4	0.49	1.0	1.0	4.20	0.22	0.17	0.18
5	5.0	1.0	5.2	6.90	0.54	0.59	0.63
6	2.0	4.4	0.8	8.83	12.8	14.5	14.6
7	4.9	1.0	1.0	4.08	0.058	0.031	0.059
8	4.9	1.0	1.0	5.11	0.082	0.044	0.076
9	5.8	0.5	1.0	5.25	0.041	0.004	0.030

Table II. Rate and Equilibrium Constants for Carbinolamine and Aldimine Formation ($T = 25^\circ\text{C}$, $I = 0.5$)

A. Reaction: $\text{H}_i\text{PLP}^{i-3} + \text{ala}^- \rightleftharpoons \text{H}_i\text{PLP}\cdot\text{ala}^{i-4}_{\text{carbinolamine/aldimine}}$			
i	Carbinolamine formation $k_{a,i}$ ($\text{M}^{-1} \text{s}^{-1} \times 10^{-5}$)	Aldimine formation $\text{Log } K_{\text{eq}}$	$k_{f,i}$ ($\text{M}^{-1} \text{s}^{-1}$)
0	2.7	0.53	4.1
1	3.3	4.19	2.8×10^1
2	4.0	4.81	1.7×10^3
3	23	6.69	1.0×10^5
4	6000	8.11	7.0×10^6

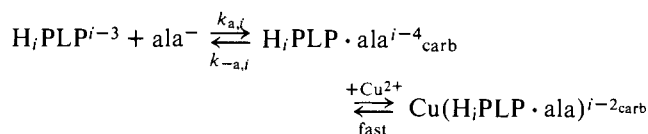
B. Reaction: $\text{Cu}(\text{H}_i\text{PLP})^{i-1} + \text{ala}^- \rightleftharpoons \text{Cu}(\text{H}_i\text{PLP}\cdot\text{ala})^{i-2}_{\text{carbinolamine/aldimine}}$			
i	$\text{Log } K_{\text{eq}}$	Carbinolamine formation $k_{a,i}\text{Cu}$ ($\text{M}^{-1} \text{s}^{-1} \times 10^{-5}$)	Aldimine formation $\text{Log } K_{\text{eq}}$
0	8.60	8.2	10.74
1	8.87	14	11.46
2	9.32	220	12.56

C. Reaction: $\text{Cu}(\text{H}_i\text{PLP}\cdot\text{ala})^{i-2}_{\text{carbinolamine}} \rightleftharpoons \text{Cu}(\text{H}_i\text{PLP}\cdot\text{ala})^{i-2}_{\text{aldimine}} + \text{H}_2\text{O}$		
i	$\text{Log } K_{\text{eq}}$	$k^i_{\text{dehydration}}$ (s^{-1})
0	2.14	0.001 7
1	2.59	0.000 553
2	3.24	0.000 334

as I. The values of the rate and equilibrium constants resolved from the data are given in Table II, along with values determined for the "direct" conversion of PLP to aldimine. Cu(II) dependent pathways were not observed for these latter reactions.

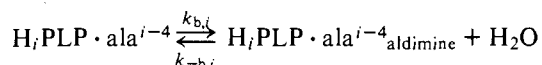
Equation 2 shows that I is formed from PLP along both Cu(II) independent and Cu(II) dependent pathways. Under the conditions that we have investigated, the former were usually found to be dominant, with the latter becoming important only under conditions where the relatively weak $\text{Cu}\text{-H}_i\text{PLP}^{i-1}$ complexes are formed in appreciable concentrations. This can be seen by comparing the two sets of theoretical first-order rate constants for carbinolamine formation which have been calculated from the results and are given in Table I. The first set has been calculated neglecting the Cu(II) pathways, and the second set included them. In experiments 1-6 of Table I, it is seen that the difference between these two sets is small being within the experimental error. Under the conditions employed in experiments 7-9, however, the Cu(II) dependent pathways become important. In all cases good agreement has been achieved between the theoretical and observed values.

In the Cu(II) independent pathways I is formed by the rate limiting reaction of protonated or unprotonated PLP with ala^- , followed by rapid reaction (trapping) of the carbinolamine with Cu(II),



Cu(II) ligand exchange reactions involved in the second step are considerably faster than those studied here,¹¹⁻¹³ as is borne out by the results. The Cu(II) dependent pathways, no doubt, involve the attack of ala^- on Cu(II) bound PLP.

In the absence of Cu(II), or other suitable trapping agent, carbinolamine rapidly dehydrates,

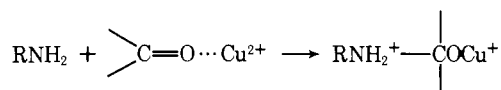


and is formed in only a low steady state concentration. In this context, the overall forward rate constant for aldimine formation along a given path is related to the microscopic rate constants by the expression,

$$k_{f,i} = \frac{k_{a,i}}{1 + k_{-a,i}/k_{b,i}} \quad (3)$$

From the measured values of $k_{f,i}$ and $k_{a,i}$ in Table II, the ratios $k_{-a,i}/k_{b,i}$ are found to be sufficiently greater than unity that eq 3 takes the form, $k_{f,i} = (k_{a,i}/k_{-a,i})k_{b,i}$; i.e., amine addition comprises a preequilibrium step to rate limiting dehydration. The rate of PLP carbinolamine formation is found here to be similar to that reported for pyridine-4-carboxaldehyde (PC)⁴ but in agreement with the postulated catalytic effect of the aromatic phenolate group,⁵ dehydration of the PLP carbinolamine is considerably faster than that of PC.^{3,4}

It is also seen in Table II that the equilibrium constant for the reaction $\text{I} \rightleftharpoons \text{II}$ lies far to the right. In spite of this, the rate of formation of I is considerably faster than its dehydration. The hydration of II is very slow. The $\text{Cu}\text{H}_i\text{PLP}^{i-1}$ complexes react significantly faster with ala^- than does uncomplexed PLP. Activation possibly arises from polarization of PLP, or from stabilization of the zwitterion that is the immediate reaction product of amine addition.¹⁴



References and Notes

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Stereospecific Synthesis of Heteroatom-Substituted Olefins from α,β -Epoxy-silanes. Preparation of Vinyl Bromides, Enol Acetates, Enol Ethers, and Enamides¹

Sir:

Considerable research effort has been devoted to the development of methods for the stereospecific synthesis of olefins in which only carbon or hydrogen atoms are directly attached to the carbon-carbon double bond.² Many methods for the stereospecific synthesis of vinyl halides have also been developed.³ However, no general methods for the stereospecific synthesis of other heteroatom-substituted olefins exist. We report here the first general stereospecific method for preparing a variety of heteroatom-substituted olefins, and show its applicability to the synthesis of vinyl bromides, enol acetates, enol