culated $R_{C_6H_{12}O_2}$ from the equation

$$R_{C_6H_{12}O_2} = \frac{k_2^{1/2}k_{18b}}{k_{11}^{1/2}k_{18a}} \frac{R_{C_2H_6}^{1/2}{}_{(11)}}{R_{C_4H_{10}}^{1/2}} R_{C_7H_{14}O_2}$$

assuming $k_2^{1/2}k_{18b}/k_{11}^{1/2}k_{18a} = 1$. Data obtained for $R_{C_6H_{12}O_2}$ by this calculation are admittedly extremely rough. The final result for R_{CH_3} will, however, be considerably more accurate since $R_{C_6H_{12}O_2}$ does not contribute more than 20% of the total value of R_{CH_3}.

Data obtained *via* equation VI indicate $k_9k_2^{1/2}/k_4 = 25 \pm 4 \times 10^5$ molec.$^{1/2}$/(sec.$^{1/2}$ cc.$^{1/2}$) at 29°. Data calculated for k_{16}/k_9 are given in Table III. In Fig. 6 log k_{16}/k_9 is plotted against $1/T$. Although the data in this plot show considerable scatter, they leave little doubt that $E_9 - E_{16} = 7.5 \pm 1$ kcal. Accepting, as determined earlier, $E_{16} = 5.5$ kcal., an activation energy of about 13 kcal. is obtained for the thermal decomposition reaction of the ethoxy radical into methyl radicals and formaldehyde.

It is interesting to compare the activation energy of reaction 9 with the value obtained for reaction 23.

$$(CH_3)_3CO \longrightarrow CH_3COCH_3 + CH_3 \qquad (23)$$

Recent data for the activation energy of reaction 23 are $E_{23} = 11 \pm 2$ kcal.,[13,14] $E_{23} = 9 \pm 2$ kcal.[15] and $E_{23} = 13.2 \pm 2.4$ kcal.[16]

Values for the dissociation energy of the C_2H_5O radical into CH_3 and CH_2O and of the *t*-butoxy radical into CH_3 and CH_3COCH_3 have been calculated by Luft[17] as 7.5 and 6.6 kcal., respectively. From these values it might be expected that E_9 and E_{16} would not differ to any appreciable extent. Our value of about 13 kcal. for E_9 is thus in good agreement with data obtained for the activation energy of reaction 23.

Acknowledgment.—The author wishes to express his sincere thanks to Mr. J. A. Guercione for carrying out the experiments described in this paper.

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(15) G. R. McMillan and M. H. J. Wijnen, *Can. J. Chem.*, **36**, 1227 (1958).

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(17) N. W. Luft, *Z. Elektrochem.*, **60**, 94 (1956).

[CONTRIBUTION FROM THE CENTRAL RESEARCH LABORATORIES, TOYO RAYON CO., LTD., OTSU, SHIGA-KEN, JAPAN]

CH_2 Rocking Frequencies of Ethylene Glycol and Its Derivatives in Relation to the Configuration of Polyethylene Glycol

BY AKIHISA MIYAKE

RECEIVED OCTOBER 29, 1959

Ethylene glycol, its esters and its ethers always show two absorption bands about 20 cm.$^{-1}$ apart in the range 950–850 cm.$^{-1}$. These two bands are assigned to the CH_2 rocking vibrations of a *gauche* OCH_2CH_2O group. The CH_2 rocking vibration of a *trans* OCH_2CH_2O group appears in the range 850–800 cm.$^{-1}$. From these assignments, it has been concluded that the OCH_2CH_2O groups in polyethylene glycol exist in two forms, *trans* and *gauche*.

A complete X-ray analysis of the structure of polyethylene glycol has not yet been reported. The dimensions of the unit cell[1,2] show that the chain has a crooked configuration. From infrared absorption studies, Davison[3] has proposed a helical structure in which OCH_2CH_2O groups exist only in the *gauche* configuration. His conclusion is primarily based on the analogies between the spectra of the polymer and *gauche* 1,2-dichloroethane. The positions of two CH_2 rocking vibrations of polyethylene glycol, 960 (doublet) and 844 cm.$^{-1}$, were in better agreement with those of the *gauche* dichloroethane than those of the *trans*.

In several esters of ethylene glycol, however, CH_2 rocking frequencies are different from those of dichloroethane. Table I lists the frequencies in some of the esters previously investigated.[4,5] In these esters, the CH_2 rocking frequency of a *trans* OCH_2CH_2O group has been assigned to bands at about 850 cm.$^{-1}$. This is supported by the fact that a similar band in polyethylene terephthalate (848 cm.$^{-1}$) intensifies as the polymer crystallizes. It has been shown by X-ray diffraction studies[6] that the OCH_2CH_2O group in the crystalline part of this polyester exists in a *trans* configuration. Two bands at about 900 cm.$^{-1}$ assigned to the *gauche* CH_2 rocking frequencies (A and B), weaken as the band mentioned above intensifies, indicating that these two arise from a different isomeric configuration.[4]

TABLE I[a]

CH_2 ROCKING FREQUENCIES IN CM.$^{-1}$ OF ETHYLENE GLYCOL ESTERS

Compound	B_g	A	B	A_u	Ref.
$C_6H_5COOCH_2CH_2$-$OOCC_6H_5$ (soln.)		900	884	847	4
$CH_3C_6H_4COOCH_2CH_2$-$OOCC_6H_4CH_3$ (cryst.)		899	884	853	4
$[OCC_6H_4COOCH_2$-$CH_2O]_3$ (cryst.)		904	891		4
$HOCH_2CH_2OOCC_6H_4$-$COOCH_2CH_2OH$ (α-form)	909	897	870	861	5

[a] Symmetry species are those for point groups C_{2h} (B_g and A_u: *trans*) and C_2 (A and B: *gauche*).

Thus the assignments given in Table I are believed to be well established. In comparing these frequencies with the known CH_2 rocking frequencies of other 1,2-disubstituted ethanes (Table II), at least two important differences are apparent. The first is that the A_u type vibration occurs near

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(1) E. Sauter, *Z. physik. Chem.*, **B21**, 161 (1933).

(2) E. R. Walter and F. P. Reding, Abstracts of the 133rd Meeting of the American Chemical Society, San Francisco, April, 1958.

(3) W. H. T. Davison, *J. Chem. Soc.*, 3270 (1955).

(4) A. Miyake, *J. Polymer Sci.*, **38**, 479 (1959).

(5) A. Miyake, *Bull. Chem. Soc. Japan*, **30**, 361 (1957).

(6) R. Daubney, C. Bunn and C. Brown, *Proc. Roy. Soc.* (*London*), **A226**, 531 (1954).

TABLE II

CH_2 ROCKING FREQUENCIES IN CM.$^{-1}$ OF 1,2-DISUBSTITUTED ETHANES

Compound	B_g	A	B	A_u
$CH_3CH_2CH_2CH_3$[a]	820	788	747	732
$CH_3CH_2CH_2Cl$[a]	860	855	788	748
$CH_3CH_2CH_2Br$[a]	850	839	778	740
$CH_3CH_2CH_2I$[a]	827	816	763	715
$ClCH_2CH_2Cl$[b]	989	943	881	768
$ClCH_2CH_2Br$[c]	961	923	856	763
$BrCH_2CH_2Br$[d]	932	898	836	753
$CH_3SCH_2CH_2SCH_3$[e]		900	840	736
$NCSCH_2CH_2SCN$[f]		918	845	749

[a] J. K. Brown and N. Sheppard, *Trans. Faraday Soc.*, **50**, 1164 (1954). [b] I. Nakagawa and S. Mizushima, *J. Chem. Phys.*, **21**, 2195 (1953). [c] J. K. Brown and N. Sheppard, *Trans. Faraday Soc.*, **48**, 128 (1952). [d] J. T. New and W. D. Gwinn, *J. Chem. Phys.*, **18**, 1642 (1950). [e] D. M. Sweeny, S. Mizushima and J. V. Quagliano, THIS JOURNAL, **77**, 6521 (1955). [f] S. Mizushima, I. Ichishima, I. Nakagawa and J. V. Quagliano, *J. Phys. Chem.*, **59**, 293 (1955).

850 cm.$^{-1}$ in ethylene glycol esters. This is about 100 cm.$^{-1}$ higher than those of the compounds listed in Table II. The second is that the spacing between two *gauche* vibrations, A and B, is only about 20 cm.$^{-1}$ in the esters. In all the other disubstituted ethanes, this spacing amounts to about 60 cm.$^{-1}$.

Now, if the above assignments for ethylene glycol esters, instead those for dichloroethane, are carried over to polyethylene glycol, the doublet at 960 and 947 cm.$^{-1}$ must be considered to arise from a *gauche* OCH_2CH_2O group, whereas the band at 844 cm.$^{-1}$ must be from a *trans* one. This interpretation is in contradiction with that of Davison. In order to settle this point, it was intended to identify the corresponding frequencies in some simple ethers of ethylene glycol.

Infrared spectra of 2-methoxyethanol, 2-phenoxyethanol, 1,2-dimethoxyethane and 1,2-diphenoxyethane are shown in Fig. 1. The CH_2 rocking frequencies for the methyl ethers readily can be identified because no other fundamental frequencies are expected in the range 950–750 cm.$^{-1}$. For the phenyl ethers, the doublets at about 940–900 cm.$^{-1}$ are assigned to the CH_2 rocking vibration. All the other bands below these doublets do not arise from CH_2CH_2 groups because similar bands at similar positions (882, 818, 783 and 752 cm.$^{-1}$) are found in anisole. The CH_2 rocking frequencies thus found in these ethers are listed in Table III together with those of ethylene glycol.[7] Since it has been shown by experimental results (Table II) as well as by theoretical calculations[8] that the CH_2 rocking frequencies of disubstituted ethanes increase in the order A_u(*trans*) < B(*gauche*) < A (*gauche*) < B_g(*trans*), the lowest frequency is assigned to A_u, the next to B, and the highest to A type mode. The B_g mode is not identified.

In Table III, again, the A_u type vibration occurs at about 850 cm.$^{-1}$. The frequencies assigned to A and B type vibrations become higher as the hydrogen of the hydroxyl group is replaced by an alkyl or aryl group, but the frequency differences between these two are always about 20 cm.$^{-1}$.

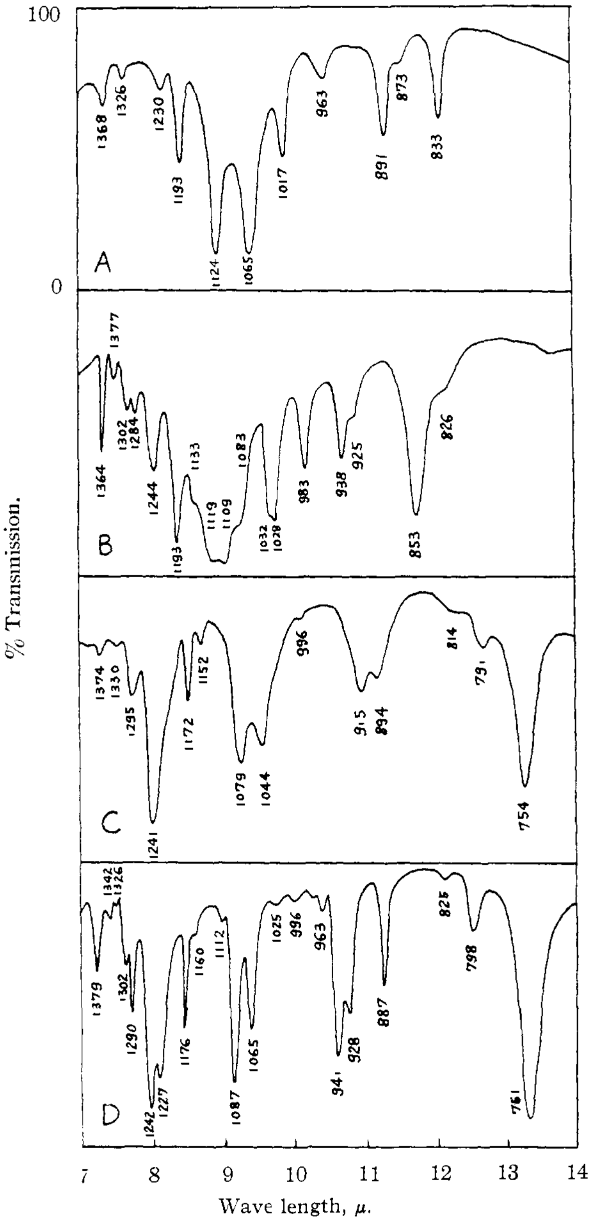

Fig. 1.—Infrared spectra of 2-methoxyethanol (A), 1,2-dimethoxyethane (B), 2-phenoxyethanol (C) and 1,2-diphenoxyethane (D).

The general feature of CH_2 rocking frequencies is therefore substantially the same in the ethers as in the esters.

Davison has attributed both the bands at 960 and at 844 cm.$^{-1}$ of polyethylene glycol to the *gauche* form. Splitting of the former into 960 and 947 cm.$^{-1}$ has been explained as a result of coupling between vibrations in the crystalline state. However, even if the assignments given in Table III are not correct, his interpretations encounter several difficulties. First, doublets similar to that in polyethylene glycol are also found in liquid ethers in which no coupling is expected. Second, the separation of the two bands, 960 and 844 cm.$^{-1}$, amounts to more than 100 cm.$^{-1}$ None of the compounds listed in Tables I–III exhibits such a large separation for the *gauche* form. Third, if the two

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(7) A. Miyake, *Bull. Chem. Soc. Japan*, **32**, 1381 (1959).

(8) I. Nakagawa and S. Mizushima, *ibid.*, **28**, 589 (1955).

TABLE III

CH_2 ROCKING FREQUENCIES IN CM.$^{-1}$ OF ETHYLENE GLYCOL AND ITS ETHERS

Compound	A	B	A_u
$HOCH_2CH_2OH$ (liq.)	881	861	
$HOCH_2CH_2OH$ (cobalt complex I)[a]	887	856	
$HOCH_2CH_2OH$ (cobalt complex II)[a]	892	881	
$CH_3OCH_2CH_2OH$ (liq.)	891	873	833
$C_6H_5OCH_2CH_2OH$ (liq.)	915	894	
$CH_3OCH_2CH_2OCH_3$ (liq.)	938	925	853
$C_6H_5OCH_2CH_2OC_6H_5$ (cryst.)	941	928	

[a] These complexes are bis-(ethylene glycol)-cobalt(II) chloride; complex I is probably the dihydrate and complex II the monohydrate (ref. 7).

bands arise from the same configuration, why has the band at 844 cm.$^{-1}$ no counterpart in the spectra of phenyl ethers?

All these difficulties can be removed easily by an alteration of the assignments, that is, by assigning the doublet to *gauche* vibrations and the 844 cm.$^{-1}$ band to *trans* vibration. 1,2-Dimethoxyethane provides strong evidence for this alteration. This compound is absorbed by dehydrated cobalt(II) chloride (light blue in color) giving a blue product. The absorbed 1,2-dimethoxyethane exhibits a spectrum completely different from that of the liquid state and is not removed by washing with heptane. This indicates that the compound is coördinated to cobalt(II) chloride. The infrared spectrum of the blue product (see Experimental) is shown in Fig. 2. All the bands shown in Fig. 2 can be attributed to the coördinated 1,2-dimethoxyethane since neither cobalt(II) chloride nor the coexisting water of hydration shows appreciable absorption bands in the range 7–15μ. Now, the doublet, 938 and 925 cm.$^{-1}$, observed in the liquid state disappears completely in the coördinated state. On the other hand, the band 853 cm.$^{-1}$ observed in the liquid state persists at practically the same frequency. This is explained readily by assuming that there exist two isomeric configurations in the liquid state but only one in the coördinated state. The existence of only one CH_2 rocking band at 862 cm.$^{-1}$ together with the general simplification of the spectrum indicates that the coördinated molecule is present in the *trans* form.

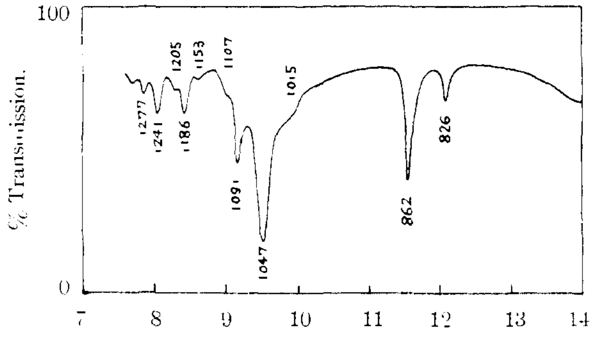

Fig. 2.—Infrared spectrum of 1,2-dimethoxyethane coördinated to cobalt(II) chloride.

Polyethylene formal $(-OCH_2CH_2OCH_2-)_n$ provides additional evidence. This polymer shows also a doublet at about 850 cm.$^{-1}$ corresponding to that at 960 cm.$^{-1}$ of polyethylene glycol (Fig. 3). However, there is no band corresponding to the lower CH_2 rocking vibration at 844 cm.$^{-1}$ of polyethylene glycol. This indicates that OCH_2CH_2O groups in polyethylene formal exist in only the *gauche* form.

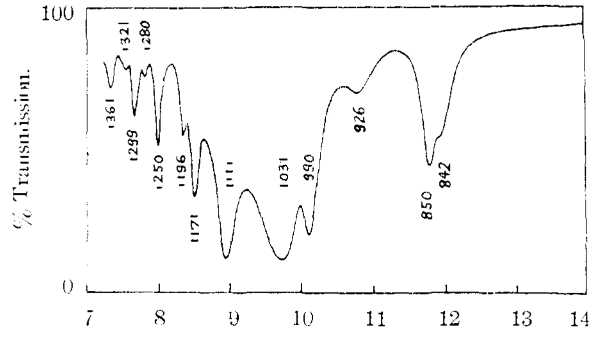

Fig 3.—Infrared spectrum of polyethylene formal.

Thus, it can be concluded with fair certainty that OCH_2CH_2O groups in polyethylene glycol exist in two configurations, *gauche* and *trans*. Several experimental facts observed in polyethylene glycol are consistent with the above conclusion. For example, opposite dichroisms found in two components[3] of the doublet at 960 cm.$^{-1}$ are consistent with their assignments to A and B modes. The doublet referred to above increases in intensity relative to that of the band at 844 cm.$^{-1}$ in the order of annealed, quenched and molten states.[9] This indicates that the *gauche* OCH_2CH_2O group becomes more abundant in the melt.

In relation to this, mention should be made of reports by Kuroda and Kubo.[10] They have assigned bands at about 880 cm.$^{-1}$ in lower members of polyethylene glycol to the *trans* form, confirming their result of dipole moment measurements that both *gauche* and *trans* forms are present. These bands decrease in intensity with increasing molecular weight, indicating that they arise from end groups presumably in the *gauche* form. As is seen in Table III, the CH_2 rocking frequencies of an OCH_2CH_2OH group are lower than those of a fully substituted OCH_2CH_2O group.

Experimental

Materials.—2-Methoxyethanol was prepared from methanol and ethylene oxide, b.p. 123°. 1,2-Dimethoxyethane was the commercial product redistilled at 83°. 2-Phenoxyethanol was prepared from phenol and 2-chloroethanol, b.p. 110.5° (6 mm.). 1,2-Diphenoxyethane was prepared from phenol and 1,2-dibromoethane, m.p. 98°. Polyethylene formal was obtained from 1,3-dioxolane (b.p. 75°) in the presence of a small amount of boron trifluoride–ether complex at room temperature. It was a white waxy solid, m.p. *ca.* 60°.

Coördination of 1,2-dimethoxyethane to cobalt(II) chloride dehydrated *in vacuo* at 160° was carried out by three procedures. Procedure A: To a suspension of 5 g. of finely pulverized cobalt(II) chloride in 50 ml. of hexane was added with agitation 35 g. of 1,2-dimethoxyethane. After standing overnight, the blue crystals were collected by filtration, washed with heptane and dried at reduced pressure (Product A). Pro-

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(9) F. P. Reding, H. F. White and C. M. Lovell, private communication.

(10) Y. Kuroda and M. Kubo, *J. Polymer Sci.*, **26**, 323 (1957); **36**, 453 (1959).

cedure B: Pure 1,2-dimethoxyethane (8 g.) was added to 5 g. of finely pulverized cobalt(II) chloride with vigorous shaking. The mixture was allowed to stand overnight and then the blue crystals were collected by filtration. They were thoroughly washed with heptane and dried at reduced pressure (Product B). Procedure C: A mixture of 6 g. of cobalt(II) chloride and 100 g. of 1,2-dimethoxyethane was refluxed for an hour. A dark blue liquid which appeared as the lower layer was separated. This liquid gave a blue solid (Product C) on standing 10 hr. in a vacuum desiccator. All the products were very hygroscopic and turned pink in color in the air. All the handlings described above were made in a desiccated chamber or under nitrogen atmosphere but complete exclusion of moisture was not possible.

None of the products A, B and C is a pure compound. Their typical analytical values (Table IV) indicate that they are mixtures of $Co(C_4H_{10}O_2)_x(H_2O)_yCl_2$ differing in x and y. However, infrared spectra of these products in the range 7–15 μ showed no significant differences. Several products not listed in Table IV obtained by any of the three procedures and differing in carbon content (6–17%) also gave substantially the same spectrum. This means that the ligand, 1,2-dimethoxyethane, assumes the same configuration in all these products. It is possible that the ligand acts as a bidentate group and links two cobalt atoms, because two products whose approximate compositions were, respectively, $Co(C_4H_{10}O_2)_{0.5}Cl_2$ and $Co(C_4H_{10}O_2)Cl_2$ showed the same spectrum.

TABLE IV

ANALYTICAL VALUES FOR THE PRODUCTS

Product	C	H	Co
A	9.65	3.63	29.75
B	16.07	3.73	28.05
C	15.68	4.55	24.33
Calcd. for $CoCl_2 \cdot H_2O$	0	1.36	39.86
$Co(C_4H_{10}O_2)_{0.5}Cl_2$	13.73	2.88	33.70
$Co(C_4H_{10}O_2)_{0.5}Cl_2 \cdot H_2O$	12.45	3.66	30.55
$Co(C_4H_{10}O_2)Cl_2$	21.84	4.58	26.79
$Co(C_4H_{10}O_2)Cl_2 \cdot H_2O$	20.18	5.08	24.77

The infrared spectrum of the liquid intermediate (*Anal.* C, 22.5; H, 6.5; Co, 16.0) obtained in the procedure C had also a strong band at about 850 cm.$^{-1}$ but no band in the range 960–890 cm.$^{-1}$. However, it was somewhat different from that of the solid products especially in the region 1100–970 cm.$^{-1}$. The ligand in this liquid seems still to exist in the *trans* form, but in this case it may act as a unidentate group.

The products were very labile and attempts to purify them by recrystallization failed to give purer products.

Infrared Spectra.—The infrared spectra were obtained with a Perkin-Elmer model 21 spectrophotometer equipped with a sodium chloride prism. Liquid samples were examined as capillary films supported between rock salt plates. Solid samples were examined as Nujol mulls.

[CONTRIBUTION FROM THE NAVAL MEDICAL RESEARCH INSTITUTE, BETHESDA, MARYLAND]

Kinetics of the System α-Chymotrypsin Methyl Hippurate Water Hydroxylamine: the Role of Water in Enzymatic Hydrolysis[1]

BY SIDNEY A. BERNHARD,[2] WILLIAM C. COLES AND JOHN F. NOWELL

RECEIVED JUNE 15, 1959

In view of the characteristic formation of measurable intermediate complexes between enzyme and substrate, it has been of interest to ascertain whether such reactants and complexes equilibrate during the reaction process. Dissociation constants (K_M) can be determined for these complexes. These constants pertain to either a stationary state or a state of quasi-equilibrium. A method has been devised for distinguishing these two possibilities which involves the competition of two reagents for alternate reaction paths. The kinetics of α-chymotrypsin catalyzed hydrolysis and hydroxylaminolysis of methyl hippurate as a function of substrate, hydroxylamine and hydronium ion concentration has been investigated. In the presence of α-chymotrypsin in aqueous solution at the order of tenth-molar hydroxylamine, both hippurate ion and hippuryl hydroxamic acid are formed. The formation of hippuryl hydroxamic acid is accompanied by a diminution in the rate of hippurate formation, although the total rate of disappearance of methyl hippurate is always larger in the presence of hydroxylamine than in its absence. The dissociation constant for methyl hippurate–enzyme complex is independent both of the concentration of hydroxylamine and of the particular reaction path employed in its determination. According to the theory of the above mentioned method, this latter fact constitutes a proof that this dissociation constant is an equilibrium constant, whereas the independence of binding constant on hydroxylamine concentration constitutes a proof that the binding of hydroxylamine (and water by analogy) is independent of the binding of substrate (according to a corollary of the theory). The enzyme-catalyzed hydroxylaminolysis reaction, by its *p*H dependence, must involve the free base NH_2OH as the principal reactant species in correspondence with the hydrolysis reaction, which involves molecular water. As with all other neutral substrates for this enzyme, the activity depends on the dissociation of a proton (*pK* ~7) from the enzyme. This dissociation is independent of the nature of the reagent and of both the dissociation of substrate and reagent from the enzyme.

Introduction

Nearly all enzymatic processes involve the interaction of three or more molecules, namely, two or more substrates and an enzyme. In the present paper, we shall consider evidence bearing on the simplification of the complex model which follows from the complete steady-state treatment of a process involving the interaction of three molecular participants for finite times. In another communication[3] the kinetic consequences of the association of these participants for finite times is considered. Often, the chemical kinetics of enzymatic processes have been simplified by neglecting the concentration dependence of one of the substrates, as for example water in hydrolysis reactions. Such omissions, although mathematically valid when the substrate omitted is present in large excess,[4] limit to a large extent the mechanistic

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[1] The opinions expressed herein are those of the authors and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

[2] National Institute of Mental Health, Bethesda, Md.

[3] S. A. Bernhard, THIS JOURNAL, in preparation.

[4] More precisely, the omission is valid for either of the following two cases only: (1) All sites for this substrate (W) are occupied. (2) The pathway of complex formation is such that only the terminal complex contains this substrate W, and the terminal complex concentration is infinitesimally small due to extremely rapid reaction (*i.e.*, EW does not exist in appreciable quantities and the formation of ES is rate controlling).

$$W + E + S \rightleftharpoons ES + W \rightleftharpoons ESW \xrightarrow{\text{Very rapid}} E + \text{Products}$$

(S. A. Bernhard, *Discussions Faraday Soc.*, **20**, 267 (1956).)