term may be accounted for in terms of transition state I provided one assumes either that, in the transition state, the proton transferred between the imidazole molecules is quite asymmetrically placed[10] or that the position of the proton transferred from water to imidazole in the transition state is altered by the presence of the second imidazole molecule. The strongest evidence in favor of transition state I is the failure to observe a second-order term in the rate law for catalysis by N-methylimidazole. N-Methylimidazole is similar to imidazole in terms of structure and base strength but cannot lose a proton from one nitrogen atom concurrent with the attack of the other. Although other kinetically indistinguishable mechanisms for the reaction involving two imidazole molecules cannot be rigorously excluded, the present evidence strongly suggests that transition state I is correct for this reaction. The imidazole-catalyzed hydration of *sym*-dichloroacetone appears to be the only known case of general base catalysis for general base catalysis.

The fact that reported kinetic runs were carried out in unbuffered solutions raises the possibility of a contribution to the observed rates from a reaction involving hydroxide ion or the imidazole anion, particularly at high imidazole concentrations. The imidazole catalysis data cannot be explained on the basis of concurrent reactions of imidazole and hydroxide ion since no hydroxide ion reaction was observed in the presence of N-methylimidazole, an equally strong base. General base catalysis of imidazole catalysis by either hydroxide ion or the imidazole anion cannot be rigorously excluded although such reactions, in the absence of detectable direct attack of hydroxide ion on the substrate, seem quire unlikely. Furthermore, such reactions should not depend on the square of the imidazole concentration since the concentration of hydroxide ion or the imidazole anion depends, approximately, on the square root of imidazole concentration. Thus the rate law would have contained terms proportional to the first and to the three-halves powers of imidazole concentration. At any event, such reactions would be mechanistically similar to that proposed in I. A second-order term in imidazole concentration is observed in buffered reaction mixtures containing 90% of the imidazole as the free base and 10% as the hydrochloride. This second-order term may, of course, be due to a reaction involving an imidazole–imidazolium ion or its kinetic equivalent. Many such reactions have been observed for the hydration of *sym*-dichloroacetone catalyzed by a variety of acid–base pairs.

Imidazole, in contrast to N-substituted imidazoles, is known to be associated, presumably through hydrogen-bonded structures, in nonpolar media such as benzene, naphthalene, and carbon tetrachloride.[11] This observation raises a question as to the extent of imidazole self-association in 95% aqueous dioxane. Although experimental data concerning this point are not available, the observed rate laws suggest that imidazole is probably not largely associated in this solvent, since, if dimer formation were to approach completion, one would obtain only first-order rate dependence on imidazole concentration. Regardless of the extent of imidazole association, the observation that the first-order rate constants increase more rapidly than imidazole concentration indicates that the imidazole dimer is a more effective catalyst than the monomeric species for this reaction.

Experimental

Materials.—Imidazole was recrystallized twice from benzene, and N-methylimidazole and *sym*-dichloroacetone were redistilled before use. Dioxane was purified according to the method given by Wiberg.[12] Distilled water was employed throughout. "95% aqueous dioxane solutions" were prepared by diluting 5 volumes of water to 100 volumes with dioxane.

Kinetic measurements were carried out spectrophotometrically with a Zeiss PMQ II spectrophotometer equipped with a thermostated cell compartment as previously described.[13] All reactions were carried out at 25°. Rate laws for reactions exhibiting both first- and second-order terms in catalyst concentration were derived from plots of k_{obs}/[catalyst] against [catalyst]. The rate coefficient for the first-order term was evaluated from the intercept of such plots at zero catalyst concentration, and the second-order rate coefficients were evaluated from the slopes of these plots.

Acknowledgment.—We are indebted to Dr. William P. Jencks, Brandeis University, for communicating his findings concerning base catalysis for imidazole-catalyzed reactions prior to publication.

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The Mechanism of Acid-Catalyzed Methyl Orthobenzoate Hydrolysis[1,2]

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Results of determinations of entropies of activation, volumes of activation, Bunnett's *w* values, and correlation of hydrolysis rates with the Hammett H_0 acidity function, strongly suggest that the acid-catalyzed hydrolysis of formals,[3-6] acetals,[3-7] ketals,[4] and ethyl orthoformate[4,5] does not involve solvent as a nucleophilic reagent in the transition state (A-1). In contrast, Kwart and Price have suggested, principally on the basis of correlation of the rate of hydrolysis of methyl ortho-*p*-nitrobenzoate with a solvent composition–acidity function,[8] that the acid-catalyzed hydrolysis of methyl orthobenzoates, a reaction related to those indicated above, does involve solvent as a nucelophilic reagent in the transition state (A-2).[9] More re-

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cently, DeWolfe and Jensen have pointed out that the observations of Kwart and Price may be interpreted in a fashion consistent with an A-1 mechanism for this reaction and, on the basis of the magnitude of the entropy of activation and deuterium solvent isotope effect, have suggested that the correct mechanism is, in fact, A-1.[10] We have further investigated the mechanism of the acid-catalyzed hydrolysis of methyl orthobenzoate employing a technique closely related to the rate–product criterion originally used by Ingold and coworkers for the identification of unimolecular solvolysis reactions.[11] Results of this investigation strongly support the conclusion of DeWolfe and Jensen that this reaction proceeds by an A-1 mechanism.

In Table I, first-order rate constants for the decomposition of methyl orthobenzoate at pH 5.45 in aqueous solutions of hydroxylamine are listed. The first-order rate constants are independent of the total hydroxylamine concentration over the concentration range 0 to 0.9 M. Over this concentration range, the fraction of methyl orthobenzoate yielding the hydrolysis product, methyl benzoate, decreases from 1.0 to 0.15 (Table I). Thus, at the highest concentration of hydroxylamine employed, approximately 85% of the orthobenzoate yields a hydroxylamine addition product, probably N-hydroxymethyl benzimidate.[12] Methyl benzoate does not react with hydroxylamine at a detectable rate under these experimental conditions. The fraction of methyl orthobenzoate yielding methyl benzoate as product may be accurately calculated assuming that the ortho ester, as the conjugate acid, undergoes a rate-determining unimolecular decomposition yielding an intermediate carboxonium ion which is then rapidly partitioned between water, yielding methyl benzoate, and hydroxylamine, yielding a hydroxylamine addition product. The calculated fractions of ortho ester yielding methyl benzoate (Table I) were obtained by assuming that the free base of hydroxylamine is 2000-fold more reactive than water toward the carboxonium ion. Quite similar results also were obtained at pH 4.25 employing semicarbazide as the nucleophilic reagent (Table I). The first-order rate constants for methyl orthobenzoate disappearance are independent of semicarbazide concentration up to at least 1.2 M, and the observed product composition may be quantitatively accounted for by assuming that the free base of semicarbazide is 275-fold more reactive than water toward the carboxonium ion. Employing the reasonable assumption that the amine addition products do not arise from an S$_N$2 attack of amine on a tetrahedral intermediate formed from the attack of water on the ortho ester, these results strongly suggest that solvent does not participate as a nucleophilic reagent in the rate-determining step of acid-catalyzed methyl orthobenzoate hydrolysis.

TABLE I

FIRST-ORDER RATE CONSTANTS AND PRODUCT COMPOSITION FOR THE ACID-CATALYZED DECOMPOSITION OF METHYL ORTHOBENZOATE IN AQUEOUS SOLUTIONS OF HYDROXYLAMINE AND SEMICARBAZIDE AT 25°

[Hydroxylamine]$_{total}$, M	[Semicarbazide]$_{total}$, M	pH	k_{obs}, sec.$^{-1}$	f_{obs}[a]	f_{calcd}[b]
0.00		5.45	0.00035	1.00	1.00
.10			.00030	0.57	0.58
.20			.00033	.41	.41
.30			.00033	.31	.31
.40			.00032	.26	.25
.50			.00038	.21	.20
.60			.00028	.18	.18
.70			.00028	.16	.16
.90			.00038	.15	.13
	0.00	4.25	.0058	1.00	1.00
	.16		.0071	0.55	0.61
	.40		.0053	.38	.38
	.80		.0053	.26	.24
	1.20		.0052	.18	.17

[a] Fraction of methyl orthobenzoate yielding methyl benzoate as product. [b] Calculated fraction of methyl orthobenzoate yielding methyl benzoate as product assuming that the free base of hydroxylamine is 2000-fold more reactive and that the free base of semicarbazide is 275-fold more reactive than water toward a unimolecular decomposition product of methyl orthobenzoate (see text).

The above conclusion is supported by the finding of a positive entropy of activation for this reaction. First-order rate constants for the hydrolysis of methyl orthobenzoate at several temperatures and pH 4.65 and 4.97 are listed in Table II together with the calculated activation energies. From this data the entropy of activation at 25° has been calculated as +8.2 e.u. at pH 4.97 and +8.6 e.u. at pH 4.65.[13] These values are somewhat more positive than those obtained by DeWolfe and Jensen[10] for the hydrolysis of ethyl orthobenzoate, but both sets of data fall within the range for acid-catalyzed reactions thought to occur without the participation of solvent as nucleophilic reagent.[5]

TABLE II

RATE CONSTANTS AND ACTIVATION PARAMETERS FOR THE HYDROLYSIS OF METHYL ORTHOBENZOATE AT pH 4.65 AND 4.97 AT SEVERAL TEMPERATURES

pH	Temperature, °K.	k_{obs}, sec.$^{-1}$	E_a, cal./mole	ΔS^*, e.u.
4.97	297.7	0.00096	17,800	8.2
	300.6	.00138		
	303.5	.00149		
	306.4	.00248		
	309.7	.00308		
	312.2	.00400		
4.65	297.6	.00197	17,600	8.6
	300.8	.00277		
	303.8	.00354		
	306.8	.00510		
	310.6	.00630		

The first-order rate constants for the hydrolysis of methyl orthobenzoate in water and deuterium oxide were found to increase linearly with the hydrogen ion concentration over the pH range 3.60 to 4.97 and over the pD range 4.47 to 5.54. From the slopes of plots of the first-order rate constants against hydrogen ion concentration, the second-order rate constant for this reaction was calculated as 113 mole^{-1} sec.$^{-1}$ in water and 250 mole^{-1} sec.$^{-1}$ in deuterium oxide. The solvent

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(13) Owing to an error in calculation, the value of the entropy of activation given in ref. 2 is incorrect.

deuterium isotope effect, k_{H_2O}/k_{D_2O}, is, therefore, 0.45, a value similar to those found for related reactions[14] and nearly identical with the value found by DeWolfe and Jensen for the hydrolysis of ethyl orthobenzoate.[10] This solvent deuterium isotope effect is consistent with either pre-equilibrium substrate protonation or with general acid catalysis by the hydrated proton, provided that, in the transition state, the proton is largely transferred to the substrate.[15] This condition appears to be met in the present case since Kwart and Price have observed a Brønsted α value of 0.74 for general acid catalysis of methyl orthobenzoate hydrolysis.[9] The observation that methyl orthobenzoate hydrolysis is subject to general acid catalysis[9,10] suggests, but does not prove, that the specific acid-catalyzed reaction is, in fact, general acid catalysis by the hydrated proton.

Experimental

Materials.—Methyl orthobenzoate was prepared from benzotrichloride as previously described.[16] Other reagents were recrystallized or redistilled before use. Distilled water was employed throughout.

Kinetic measurements were carried out spectrophotometrically with a Zeiss PMQ II spectrophotometer equipped with a thermostated cell holder as previously described.[17,18] At the conclusion of several runs involving the hydrolysis of methyl orthobenzoate in the presence of hydroxylamine or semicarbazide, the amount of methyl benzoate produced was determined by the ferric chloride–hydroxylamine method of Lipmann and Tuttle.[19] Ionic strength was adjusted to 0.50 with potassium chloride in all kinetic runs.

Measurements of pH were made with the glass electrode and a Radiometer Model PHM 4c pH meter. Values of pD were obtained from measured pH values and the relationship pD = pH + 0.40.[20] This relationship was verified for our pH meter using carefully neutralized acetate buffers.

Activation parameters were obtained from second-order rate constants measured at several temperatures and the Eyring equation, $\ln k = \ln ekT/h + \Delta S^*/R - E_a/RT$.[21]

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The Reaction of Guanazole and Diformylhydrazine[1]

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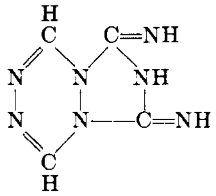
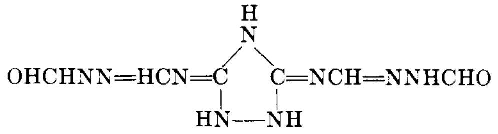
Papini and Checchi[2] treated equimolar quantities of guanazole (3,5-diamino-1,2,4-triazole) and diformylhydrazine and obtained a compound, $C_4H_5N_7$, to which they assigned the structure 7,8-dihydro-6,8-diimino-6*H*-*s*-triazolo[1,2-*a*]-*s*-tetrazine (I). Wiley and Hart[3] treated 1 mole of guanazole with 2 moles of diformylhydrazine and obtained a product to which they tentatively assigned the empirical formula $C_6H_9N_9O_2$[4] and the structure 3,5-bis{[(2-formylhydrazono)methyl]-imino}-1,2,4-triazolidine (II).

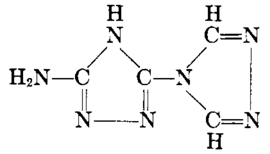


I



II

In the present work, we have found that the material obtained by Wiley and Hart is not $C_6H_9N_9O_2$ but a tetarto hydrate, $C_4H_5N_7 \cdot 1/4H_2O$,[5] of the material obtained by Papini and Checchi. Further, the product of the equimolar reaction, postulated as I, is in fact the isomeric 5-amino-3,4′-bi-1,2,4-triazole (III).



III

The reaction of 2 moles of diformylhydrazine and 1 mole of guanazole by the procedure of Wiley and Hart[3] gave two distinct products. The first of these (A-1) was obtained on rapid cooling of the water used to extract the reaction melt. The elementary analysis of A-1 fitted the empirical formula $C_4H_5N_7$. On standing, the aqueous extract deposited a second solid (A-2) whose carbon–hydrogen analysis was substantially the same as that given by Wiley and Hart. However, the nitrogen analysis of A-2 did not fit the empirical formula $C_6H_9N_9O_2$.

The formula $C_6H_9N_9O_2$ had been assigned on the basis of carbon–hydrogen analysis and the fact that the material did not appear to lose water on drying. When a sample of A-2 was dried for 24 hr. at 60° (1 mm.), there was no detectable weight loss and no change in microanalysis. When the same sample was dried for 24 hr. at 150° (1 mm.) water was given off and the resulting material was identical with A-1. In addition, A-2 could be converted to A-1 by solution in the minimum amount of boiling water, followed by quick cooling.

This unusual dehydration was repeatedly confirmed and, in fact, samples of A-1 prepared from A-2 in this manner could be air-dried without retaining or regaining water. Similarly, A-1 gave A-2 on solution in excess boiling water and very slow cooling.

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(1) This research was supported by the Advanced Research Projects Agency, Propellant Chemistry Office, and was monitored by the Bureau of Naval Weapons, RMMP, under Contract NOrd 18728. Presented at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963.

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(4) Based on the remainder of their paper, it is assumed that the formula $C_6H_9N_4O_2$ in the Experimental section of the paper by Wiley and Hart is a typographical error.

(5) Based on X-ray powder patterns this material may be $2(C_4H_5N_7) \cdot 1/2H_2O$ or $4(C_4H_5N_7) \cdot H_2O$, but the evidence is not conclusive.