Table X. Per Cent Thallic Acetate as a Function of Per Cent Water at 60°

Reaction time, hr	H_2O added, %	Yield of $Tl(OAc)_3$, %
5.5	2	95
4	4	95
2	8	95
1.7	10	95

filtration. Most of the acetic acid was removed under reduced pressure. The solid was dissolved in a minimum amount of acetic acid at 75° and the thallic acetate crystallized upon cooling. The solid was suction filtered and dried under a continuous vacuum. A 73.7% yield of 12.3 g (0.032 mol) of thallic acetate was obtained and the dry solid stored in a desiccator. The thallium triacetate was found to be 98% pure by the previously described iodide–thiosulfate analytical procedure.

In another preparation a mixture of 15 g (0.033 mol) of thallic oxide in 100 ml of acetic acid and 15 ml of water was stirred for 21 hr at 55°. A yield of 65% of 99% pure thallic acetate was obtained.

Thallium triacetate exhibits no sharp decomposition or melting point to 200° but it does begin slow decomposition at *ca.* 75–80°.

Table XI. Apparent One-Third-Order Rate Constants for the Decomposition of Thallium Triacetate

$Tl(OAc)_3$, mol/l.	Temp, °C	$k \times 10^4$, $mol^{2/3}/l.^{2/3}$ min
0.0300	75.3	0.34
0.0305	99.3	3.9
0.0210	99.3	3.6
0.0156	99.4	3.6
0.0107	99.3	3.8

Preparation of Thallous–Thallic Acetate Double Salt. A solution of 0.527 g (0.0020 mol) of thallous acetate and 0.763 g (0.0020 mol) of thallic acetate in 15 ml of anhydrous acetic acid was concentrated under reduced pressure. The remaining white solid exhibits a sharp decomposition at 178–180° with no prior discoloration or melting.

Kinetics of Decomposition of Thallic Acetate. Solutions for kinetic analysis were prepared by dissolving the desired amount of thallic acetate in a volumetrically measured quantity of anhydrous acetic acid. Aliquots were sealed in test tubes and the iodide–thiosulfate procedure was used to analyze the aliquots. The rate constants for a one-third-order reaction are listed in Table XI.

Concerning the Mechanism of Hydrolysis of N-Methylacetimidate Esters[1]

T. C. Pletcher,[2] S. Koehler, and E. H. Cordes[3]

Contribution No. 1621 from the Department of Chemistry, Indiana University, Bloomington, Indiana 47401. *Received August 5, 1968*

Abstract: The rates of hydrolysis of 2,2,2-trifluoroethyl-, 2-methoxyethyl-, and ethyl N-methylacetimidate in aqueous solution have been investigated in the pH range 1–10 at 25°. At values of pH below 4, first-order rate constants for hydrolysis are independent of pH and increase markedly as the electron-withdrawing power of the alkoxy group increases: $\rho^* = 2.1$. Above pH 4, first-order rate constants for the ethyl and 2-methoxyethyl derivatives increase with increasing pH while those for the 2,2,2-trifluoroethyl substrate decrease with increasing pH. At values of pH above 8, the rate constants again are independent of pH and decrease slightly as the electron-withdrawing power of the alkoxy group increases: $\rho^* = -0.7$. Values of pK_a for the conjugate acids of the acetimidates determined titrimetrically and from the breaks in the pH–rate profiles are in good agreement: ethyl, 7.5; 2-methoxyethyl, 7.0; and 2,2,2-trifluoroethyl, 5.5. These results suggest that attack of water on the conjugate acids of the substrates is rate determining under acidic conditions and that attack of hydroxide ion on these species is rate determining under basic conditions. Under acidic conditions, each of the acetimidates decomposes to yield the corresponding esters quantitatively. As the pH is increased, the product distribution gradually changes until the corresponding amides are produced in near-quantitative yields above pH 10. The change in product distribution does not parallel the break in the pH–rate profile. The independence of the rate-determining and product-determining steps provides strong evidence for the existence of a tetrahedral intermediate in these reactions. Investigation of the effects of lithium chloride concentration on the kinetics of hydrolysis of phenyl N-methylacetimidate under acidic conditions reveals that the previously observed break in the pH–rate profile for this reaction near pH 2 is a consequence of a change in the activity of water and not of a transition in rate-determining step.

The elegant work of Schmir and his associates has provided strong evidence that hydrolysis of both cyclic and acyclic imidates proceeds through the formation of tetrahedral intermediates: (i) rate constants and product distributions are independent functions of pH,[4,5] and (ii) rate constants and product distributions are independent functions of buffer concentration.[4,6] Thus, the hydrolysis of imidates must be included in the group of nucleophilic reactions at acyl and carbonyl carbon for which reasonably strong evidence has been provided to support the concept of tetrahedral intermediates.[7,8]

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[1] Supported by Grant No. AM 08232-04 from the National Institutes of Health.

[2] National Defense Educational Act Predoctoral Fellow.

[3] Career Development Awardee of the National Institutes of Health (K3 GM 10-248-02). Fellow of the Alfred P. Sloan Research Foundation.

[4] G. L. Schmir and B. A. Cunningham, *J. Amer. Chem. Soc.*, **87**, 5692 (1965).

[5] R. K. Chaturvedi and G. L. Schmir, *ibid.*, **90**, 4413 (1968).

[6] B. A. Cunningham and G. L. Schmir, *ibid.*, **88**, 551 (1966).

[7] (a) M. L. Bender, *Chem. Rev.*, **60**, 53 (1960); (b) T. C. Bruice

In addition to the importance of reactions of imidates with regard to the matter of tetrahedral intermediates, studies of the behavior of these substrates provides important information relevant to ester aminolysis. This follows since, if tetrahedral intermediates are formed in these reactions, that formed from the addition of water to an imidate and that formed from the addition of an amine to an ester must be the same. Therefore, provided that proton transfer reactions are not rate determining in these reactions, the nature of the product formed in the imidate hydrolysis reaction will suffice to establish the nature of the rate-determining step for ester aminolysis. Thus, the observation that the hydrolysis of phenyl N-methylacetimidate yields principally amide and phenol has been interpreted to mean that the aminolysis of phenyl acetates involving strongly basic amines must proceed with rate-determining attack of the nucleophilic reagent.[9]

In view of the above considerations, we have pursued kinetic studies of imidate hydrolysis involving novel substrates in which the nature of the resident alkoxide group has been varied in a systematic fashion. Results of these studies are presented herein.

Experimental Section

Materials. 2,2,2-Trifluoroethyl N-methylacetimidate (bp 95.5–96.0° (760 mm)), 2-methoxyethyl N-methylacetimidate (bp 45.5–46.0° (5 mm)), ethyl N-methylacetimidate[10] (bp 98.0–98.5° (760 mm), lit.[10] bp 99.0° (760 mm)), and phenyl N-methylacetimidate[11] (bp 79.0° (5 mm), lit.[11] bp 65.0° (1.2 mm)) were prepared by refluxing the corresponding alcohol and acetoxime benzene sulfonate in dried toluene, according to the precedure of Oxley and Short.[11] Acetoxime benzene sulfonate (mp 53.0°, lit.[12] mp 53.0°) was prepared according to the procedure of Kenner, Todd, and Webb.[12] The corresponding esters were obtained by the Schotten–Baumann technique.[13] Elemental analysis and positions of the imine stretching frequencies are listed according to alkoxyl function for each acetimidate used in this study: $-OCH_2CF_3$: C, 38.71 (39.39), H, 5.16 (5.30), N, 9.04 (9.12), 5.87 μ; $-OC_6H_5$: 5.88 μ;[9] $-OCH_2CH_2OCH_3$: C, 54.92 (54.44), H, 9.95 (10.05), N, 10.69 (10.83), O, 24.44 (24.39), 5.89 μ; $-OCH_2CH_3$: 5.90 μ.[10] After distillation on a Nester–Faust spinning-band column, proton magnetic resonance spectra verified the presence of the correct number and combinations of the protons for each compound. Gas–liquid partition chromatography confirmed the presence of only one component in each preparation.

Purified (sublimed) anhydrous ferric chloride was used to prepare a 10% $FeCl_3$ solution in 0.7 *N* hydrochloric acid. Commercially obtained hydroxylamine hydrochloride was recrystallized from ethanol–water and 4 *M* solutions of this compound were made up just prior to use. Buffers were prepared from reagent grade chemicals with the exception of imidazole which was first recrystallized from benzene solutions. Other reagent grade inorganic salts were used without further preparation. Glass-distilled water was used throughout.

Kinetics. The kinetics of the hydrolysis of the above acetimidates were obtained by following the appearance of ester products by the hydroxylamine–ferric chloride method of Lipmann and Tuttle.[14] Aliquots (1 ml) of a known concentration of substrate ($\simeq 3 \times 10^{-4}$ *M*) in a buffered solution at constant ionic strength (0.5 *M* maintained with KCl) were transferred at definite time intervals to 0.75 ml of a solution prepared by mixing one volume of 4 *M* $H_2NOH \cdot HCl$ and two volumes of 3.5 *M* NaOH with an automatic syringe or pipet. Ten minutes later, 4.0 ml of the ferric chloride solution was added; the solution was read at 540 mμ employing a Zeiss PMQII spectrophotometer. The temperature was maintained at 25° by a thermostated water bath. In all kinetic runs hydrochloric acid, formate, acetate, phosphate, imidazole, or borate buffers were utilized in the appropriate pH ranges for the maintenance of constant pH. Values of pH were determined with a glass electrode and a Radiometer PHM4c pH meter. All reactions were carried out in glass-distilled water. In order to ensure that neither substrate nor product was lost from the reaction mixtures through evaporation in the course of the kinetic runs, two sets of control experiments were carried out under the conditions of the kinetic measurements. In one set of these, the reaction tubes were deliberately left open for substantial periods of time and in the other the tubes were not opened at all until the reaction was complete. Yields of ester in both sets of controls were in excellent agreement with those obtained at the conclusion of the kinetic runs. Furthermore, the yields of ester at the conclusion of kinetic runs under acidic conditions were found to be equal to the amounts of acetimidate substrate added initially as judged from standard curves of optical density against ester concentration constructed from experiments involving the esters prepared independently.

The kinetics of phenyl N-methylacetimidate hydrolysis were followed spectrophotometrically employing the Zeiss PMQII spectrophotometer by following the appearance of phenol at 270 mμ. Circulation of water from a thermostated bath maintained a constant temperature of 25° in the cell compartment. Ionic strength was maintained at 0.5, 1.0, and 1.5 by the addition of lithium chloride. All runs were carried out in glass-distilled water.

Infinite time values were obtained by checking all reactions at an estimated ten half-times and at appropriate intervals thereafter until the optical densities remained constant.

For each acetimidate studied, first-order rate constants were determined from the slopes of the difference in optical density at infinite time and at time *t* *vs.* time *t*.

Values of pK_a for the alkoxy N-methylacetimidates employed in this study were measured in water at an ionic strength of 0.5 from measurements of values of pH of the purified acetimidates carefully titrated to various degrees of protonation with standard hydrochloric acid and the Henderson–Hasselbach equation ($pH = pK_a + \log(\text{acid/base})$). Care was taken to ensure against hydrolysis of substrate during these titrations by conducting each one as rapidly as possible and repeating each one several times to verify the accuracy of the measurement.

Product Analysis. Analysis of the products of hydrolysis of each of the acetimidates was accomplished in the following manner. A weighed sample of the acetimidate was transferred to a glass-stoppered flask of a solution buffered at a particular pH preincubated at 25°. Samples of 1.0 ml were withdrawn and assayed for ester by the hydroxamic acid method indicated above after the reaction was complete as judged from results of the kinetic studies.

Standard curves for each of the corresponding esters were prepared by determining the optical density obtained by treating a known concentration of ester with hydroxylamine hydrochloride and then with ferric chloride as above. Aided with these standard curves it was possible to calculate the percentage of ester production for a given reaction.

Results and Discussion

The mechanism originally proposed by Schmir and Cunningham to account for the experimental facts relevant to the hydrolysis of N-phenyliminotetrahydrofuran[4] has been shown to suffice for the hydrolysis of certain acyclic imidates as well.[5] Inasmuch as it also provides a complete description for the hydrolysis

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and S. J. Benkovic, "Bioorganic Mechanisms," Vol. I. W. A. Benjamin, Inc., New York, N. Y., 1966, Chapter I.

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[12] G. W. Kenner, A. R. Todd, and R. F. Webb, *ibid.*, 1231 (1956).

[13] R. T. Morrison and R. N. Boyd, "Organic Chemistry," Allyn and Bacon Inc., Boston, Mass., 1962, p 476.

[14] F. Lipmann and L. C. Tuttle, *J. Biol. Chem.*, **159**, 21 (1945).

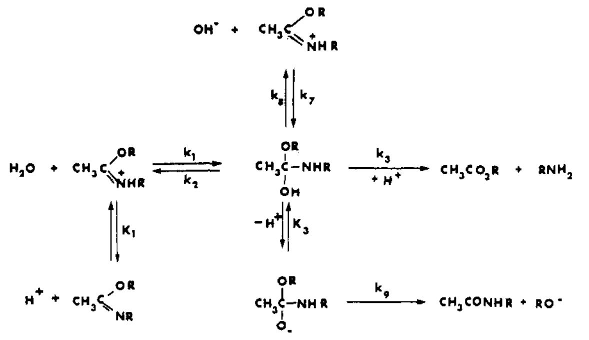


Figure 1. The mechanism of hydrolysis of imidates.

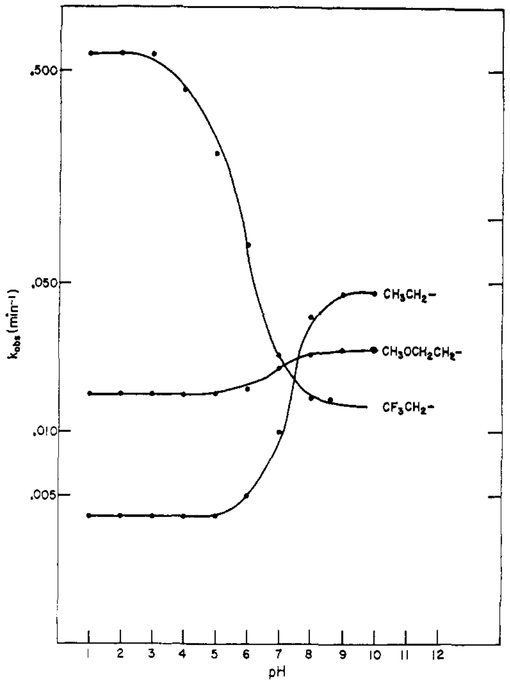


Figure 2. Logarithms of the first-order rate constants for the hydrolysis of a series of N-methylacetimidates in aqueous solution at 25° plotted as a function of pH.

of the substrates studied in this work, it is reproduced in Figure 1.

In Figure 2, the first-order rate constants for hydrolysis of 2,2,2-trifluoroethyl-, 2-methoxyethyl-, and ethyl N-methylacetimidate in aqueous solution at 25° are plotted as a function of pH. In the reactions of 2,2,2-trifluoroethyl N-methylacetimidate in which phosphate buffers were employed, first-order rate constants increase by about 50% as the buffer concentration is increased from 0.03 to 0.08 *M* at pH 6. Rate constants were measured at four concentrations of phosphate buffer and the values were extrapolated to zero concentration prior to inclusion in Figure 2. General base catalysis by phosphate buffers for imidate hydrolysis has previously been observed.[4,5,9] Over the same concentration range, phosphate catalysis was not observed for hydrolysis of the other imidates. Buffer solutions from 0.02 to 0.06 *M* formate, acetate, imidazole, and borate were found not to catalyze the hydrolysis of any of the three imidates. On the whole, the pH–rate profiles for hydrolysis of the three imidates of interest here are strongly reminiscent of those for hydrolysis of ethyl N-phenylacetimidate and methyl N-α-methylphenethylamineacetimidate.[5] Under acidic conditions, first-order rate constants for imidate hydrolysis are independent of pH. Since, as is developed below, the attack of solvent species on the substrates is rate determining over the whole pH–rate profile, the reaction under acidic conditions, in which the imidates are fully converted to the corresponding conjugate acids, reflects the rate-determining attack of water on the protonated imidates (Figure 1). Values of k_1 for these reactions are collected in Table I. These values increase by almost two orders of magnitude as the leaving group is changed from 2,2,2-trifluoroethyl to ethyl reflecting the greater destabilization of substrate relative to transition state by the more electron-withdrawing trifluoroethyl group. The rate constants are reasonably well correlated by the σ^* substituent constants with a value of ρ^* near 2.1.

Under more basic conditions, the rate constants for hydrolysis of 2-methoxyethyl and ethyl N-methylacetimidate increase with increasing pH while those for 2,2,2-trifluoroethyl N-methylacetimidate decrease with increasing pH. The breaks in the pH–rate profile are associated with conversion of the protonated imidates to the free bases since values of pK_a determined from the midpoint of these breaks agree with those determined titrimetrically within 0.05 pH unit. These values are collected in Table I and exhibit the expected increase with increasing electron withdrawal in the alkoxy moiety.

Under still more basic conditions, the first-order rate constants again become independent of pH: the ethyl compound is most reactive and the trifluoroethyl derivative is least reactive under these conditions ($\rho^* = -0.7$). This situation is very strongly reminiscent of the hydrolysis of benzylidene-1,1-dimethylethylamines[15] and reflects the opposing effects of polar substituents on substrate protonation and attack of the nucleophilic reagent in a reaction which must be interpreted as the attack of hydroxide ion on the protonated substrate (Figure 1) and not the attack of water on the free base form of the substrate. Values of the first-order rate constants under basic conditions together with calculated second-order rate constants for the attack of hydroxide on the protonated species, k_7, are collected in Table I. As pointed out by Chaturvedi and Schmir, substrates having high values of k_7/k_1 and pK_a will tend to exhibit pH–rate profiles such as that for ethyl N-methylacetimidate and those having low values of these parameter profiles such as that for the trifluoro derivative.[5] Put another way, the shape of the pH–rate profiles will vary with substrate reactivity since values of ρ^* for the reaction with hydroxide ion are generally smaller than those for reaction with water.[15] The values of the ratio k_7/k_1 for the substrates employed in this study (Table I) are similar to those for related reactions.[5]

In Table II, the effects of pH on the yield of ester obtained from the hydrolysis of each of the three imidates are collected. The yield of ester produced from imidate hydrolysis in each of the three cases is independent of the concentration of formate, acetate, phosphate, imidazole, and borate buffers over the

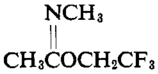
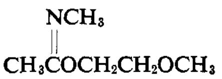
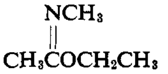
[15] E. H. Cordes and W. P. Jencks, *J. Amer. Chem. Soc.*, **85**, 2843 (1963).

Table I. Basicities of a Series of N-Methylacetimidates and Rate Constants for Their Hydrolysis in Aqueous Solution at 25° and Ionic Strength 0.5

Imidate	pK_a[a]	k_1,[b] min^{-1}	k_{obsd},[c] min^{-1}	k_7,[d] M^{-1} min^{-1}	k_7/k_1 M^{-1}
2,2,2-Trifluoroethyl	5.50	0.6	0.013	4.0×10^6	6.7×10^6
2-Methoxyethyl	7.00	0.015	0.025	2.5×10^5	1.7×10^7
Ethyl	7.50	0.004	0.045	1.4×10^5	3.7×10^7
Phenyl	6.20	0.065	0.012	6.9×10^5	1.1×10^7

[a] Of the conjugate acids. Values derived from kinetic data and titrimetric data are in substantial agreement. [b] Observed first-order rate constants for the pH-independent reactions under acidic conditions. [c] First-order rate constants for the pH-independent reactions under basic conditions. [d] Calculated second-order rate constants for the attack of hydroxide ion on the conjugate acids of the substrates.

Table II. The Effect of pH on the Yield of Ester from the Hydrolysis of a Series of N-Methylacetimidates[a]

Substrate	pH	Ester produced, %
 $CH_3C(=NCH_3)OCH_2CF_3$	1.0	100
	2.0	100
	3.0	100
	4.0	88
	5.0	75
	6.0	57
	7.0	21
	8.0	5
 $CH_3C(=NCH_3)OCH_2CH_2OCH_3$	1.0	100
	2.0	100
	3.0	100
	4.0	100
	5.0	100
	6.0	100
	7.0	100
	8.0	92
	9.0	65
	10.0	21
 $CH_3C(=NCH_3)OCH_2CH_3$	1.0	100
	2.0	100
	3.0	100
	4.0	100
	5.0	100
	6.0	100
	7.0	100
	8.0	93
	9.0	77
	10.0	38

[a] All reactions carried out at 25° and ionic strength 0.50.

concentration range 0.03 to 0.08 M with the single exception of the 2,2,2-trifluoroethyl N-methylacetimidate reaction in the presence of phosphate buffer at pH 6. For this case, the yield of the ester increases from 69 to 89% as the phosphate buffer increases from 0.03 to 0.08 M. The value included in the table has been extrapolated to zero buffer concentration. Buffer effects on the partitioning of the tetrahedral intermediates formed in imidate hydrolysis have previously been observed and are believed to be bifunctional in nature.[4-6] In each case, ester is produced in quantitative or near-quantitative yield under sufficiently acidic conditions. As the pH is increased, the yield of ester begins to decrease and eventually seems to approach zero. These results accord well with those previously obtained from related reactions[4,5] and reflect the tendency of the neutral (or zwitterionic) tetrahedral intermediate to decompose with expulsion of amine and of the anionic tetrahedral intermediate to expel alcohol (Figure 1). Clearly, the nature of the products depends both on the relative rate constants for decomposition of the two species of tetrahedral intermediate, k_8 and k_9 of Figure 1, and on the equilibrium constant, K_3, for their interconversion. Although these cannot be sorted out at the moment, it is possible to define a value of pK' to represent the midpoint of the product transition.[4,5] Approximate values of pK' for the substrates employed here are: trifluoroethyl, 6.5; methoxyethyl, 9.4; ethyl, 9.8. These values are similar to those for related systems.[5] It is important to note that the pH–product transition is quite different from the pH–rate transition for each imidate. This fact provides strong evidence for the existence of tetrahedral intermediates in these reactions and for the formulation involving rate-determining formation of the tetrahedral intermediate over the entire pH range.

Provided that the aminolysis of esters proceeds through the formation of tetrahedral intermediates[16] and assuming that the various forms of these intermediates are in rapid protolytic equilibrium, Schmir has shown that the value of pK' describing the change in product composition for imidate hydrolysis corresponds to the pH at which a transition in rate-determining step must occur for the corresponding ester aminolysis reaction[9b] (see Figure 1). Examples of precisely this behavior have been provided by Blackburn and Jencks for the aminolysis of methyl formate.[9b] Results provided herein indicate that the pH at which the transition from rate-determining nucleophile attack to rate-determining tetrahedral intermediate decomposition for the reaction between methylamine and alkyl acetates becomes increasingly acidic as the acidity of the leaving alcohol increases. This is certainly the expected behavior.

Kandel and Cordes have reported that the hydrolysis of phenyl N-methylacetimidate in aqueous solution, ionic strength 0.5 maintained with KCl, proceeds quantitatively with the expulsion of phenol at values of pH greater than 4.[9a] Furthermore, it was observed that the first-order rate constants for this reaction decrease somewhat with increasing acidity below pH 2, a result suggestive of a transition in rate-determining step. More recently, Jencks and Gilchrist[16] have reported that the hydrolysis of this substrate in solutions of low ionic strength proceeds quantitatively with phenol expulsion at values of pH greater than 5 but with the production of approximately 10% phenyl acetate between pH 3 and 5 and with production of at least 40% phenyl acetate under still more acidic conditions. These results are most readily interpreted in terms of the breakdown of an anionic tetrahedral intermediate with expulsion of phenol, of a neutral intermediate with the predominant expulsion of phenol, and of a cationic intermediate with expulsion of phenol

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(16) W. P. Jencks and M. Gilchrist, *J. Amer. Chem. Soc.*, **90**, 2622 (1968).

Table III. First-Order Rate Constants and Product Distribution for the Hydrolysis of Phenyl N-Methylacetimidate at 25° and Ionic Strength 0.50[a]

pH	k_{obsd}, min^{-1}	Ester produced, %
0.35	0.055	50
0.53	0.053	53
0.67	0.055	55
0.75	0.055	55
1.0	0.052	54
1.22	0.050	50
1.7	0.053	35
2.0	0.052	28
2.5	0.052	24
3.0	0.053	20
3.5	0.052	20
4.0	0.053	20
4.5	0.053	18
5.0	0.052	17

[a] Ionic strength maintained with lithium chloride.

and methylamine in about equal amounts.[16] This interpretation requires that the break in the pH–rate profile previously observed must be the consequence of changes in activity coefficients with increasing acidity rather than a transition in rate-determining step. In view of these considerations, we have extended our previous investigations both to include product analysis under more acidic conditions and to study the reaction kinetics in solutions in which the ionic strength is maintained constant with lithium chloride.[9b] The results of these studies are collected in Table III. In the first place, our product analyses are clearly in substantial agreement with those of Jencks and Gilchrist although the higher ionic strength employed here tends to increase somewhat the tendency of the neutral and cationic tetrahedral intermediates to expel methylamine rather than phenol. It is important to note that the yields of ester below pH 2 are minimum yields since it is probable that phenyl acetate hydrolyzes to some extent as it is being formed. Jencks and Gilchrist did observe that the yield of ester in this reaction was time dependent under these conditions suggesting that such hydrolysis does occur.[16] In the second place, the rate constants measured in the presence of lithium chloride do not exhibit the break in the pH–rate profile observed for this reaction in the presence of potassium chloride. Clearly, then, the break is a consequence of a change in activity coefficients and not a consequence of a change in the rate-determining step.

Acknowledgment. We are indebted to Dr. Gaston Schmir for communicating pertinent results to us prior to publication and to Drs. Schmir and Jencks for helpful comments.

Reactions of Cyclic 1,3-Diketones with Hydrazine. The Mechanism of Cinnolino[5,4,3-*cde*]cinnoline Formation. An Unusual Oxidation as a Result of Steric Crowding[1]

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Abstract: The condensation of 5,5-dimethyl-1,3-cyclohexanedione with hydrazine to afford 2,2,7,7-tetramethyl-1,2,3,6,7,8-hexahydrocinnolino[5,4,3-*cde*]cinnoline was shown to proceed through an unstable diazine intermediate, 6,6,13,13-tetramethyl-2,3,9,10-tetraazatricyclo[9.3.1.1^{4,8}]hexadeca-1,3,8,10-tetracene. The mechanism of this reaction was investigated with respect to the conditions and steric requirements for the unusual oxidation reaction of the diazine intermediate. This oxidation occurs with atmospheric oxygen relatively easily, probably due to the steric crowding on the internal methylene groups of the intermediate. This method of cinnolinocinnoline formation was studied utilizing other six-membered cyclic β-diketones, as well as five- and seven-membered cyclic β-diketones. The five-membered compounds do not form the pyridazino[4,5-*d*]pyridazine derivatives with hydrazine; instead only hydrazone formation was observed. However, the condensation of 2,2′-biindan-1,1′3,3′-tetrone with hydrazine gave diindeno[1,2-*c*:2′,1′-*e*]pyridazine-11,12-dihydrazone. The seven-membered compounds did not form pyridazino[4,5-*d*]pyridazine derivatives with hydrazine and no identifiable products were isolated.

The reactions of 1,3-cyclohexanedione (**1**) and 5,5-dimethyl-1,3-cyclohexanedione (**2**) with hydrazine hydrate have been shown to afford 1,2,3,6,7,8-hexahydrocinnolino[5,4,3-*cde*]cinnoline (**3**) and 2,2,7,7-tetramethyl-1,2,3,6,7,8-hexahydrocinnolino[5,4,3-*cde*]cinnoline (**4**), respectively.[2] The formation of **3** and **4** was proposed to proceed through the unstable intermediates, 2,3,9,10-tetraazatricyclo[9.3.1.1^{4,8}]hexadeca-1,3,8,10-tetracene (**5a**) and 6,6,13,13-tetramethyl-2,3,9,10-tetraazatricyclo[9.3.1.1^{4,8}]hexadeca-1,3,8,10-tetracene (**5b**), respectively, which then oxidized in the presence of air to the aromatic products. An oxidation of this nature occurs in several [2.2]metacyclophane derivatives, affording products containing the pyrene nucleus.[3–8] The observation of the inter-

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[2] J. K. Stille and R. Ertz, *J. Amer. Chem. Soc.*, **86**, 661 (1964).

[3] B. H. Smith, "Bridged Aromatic Compounds," Academic Press, New York, N. Y., 1964, p 259.