Ethyl *o*-ethyl-β-cyano-α-hydroxycinnamate (0.020 mole) was reacted with bromine (0.021 mole) and water (0.020 mole) in 16 cc. of chloroform at 50° for six hours and then allowed to stand at room temperature for two days. No precipitate separated. Concentration of the solution gave 3.7 g. of yellow crystals, m.p. 149–153°. After crystallization from chloroform this unbrominated compound melted at 155–156°. When the same amounts of reagents were dissolved in the minimum amount of chloroform the reaction product soon separated as a solid. The minimum amount of hot chloroform now needed to dissolve this product after standing two days was 50 cc. Fractional crystallization gave 2.8 g. (47%) of very insoluble 4-(4-bromo-2-ethylphenyl)-pyrrolidinetrione and 1.3 g. (29%) of very soluble 4-(2-ethylphenyl)-pyrrolidinetrione.

Ethyl *o*-isopropyl-β-cyano-α-hydroxycinnamate (0.020 mole) in 16 cc. of chloroform by similar treatment gave no solid precipitate. The viscous residue after removal of the chloroform under diminished pressure could then be crystallized from chloroform to give 4.5 g. of crude lemon-yellow product melting at 171–174° with some decomposition. After several crystallizations the 4-(2-isopropylphenyl)-pyrrolidinetrione melted at 186–187°. When the experiment was repeated using the minimum amount of solvent (6 cc.) crystals separated much more slowly (one day) and in smaller amount (1.0 g.) than in the case of the *o*-ethyl derivative. This product contained bromine. After repeated crystallization from chloroform the amount diminished to 0.1 g., and the melting point of the lemon-yellow crystals was still rising at 194–196°. This is probably the brominated pyrrolidinetrione but it was not further investigated on account of insufficient material.

Characterization of Pyrrolidinetriones.—4-(4-Ethylphenyl)-pyrrolidinetrione (6.51 g.) was dissolved in a mixture of 1.84 g. of potassium hydroxide and 20 cc. of water, heated to boiling and then allowed to cool. The weight of 4-ethylphenylacetamide was 2.4 g. By reheating the filtrate twice the yield of crude product was increased to 4.9 g. The pure product was obtained by recrystallization from boiling alcohol, m.p. 199–200°. It was identified by alkaline hydrolysis to 4-ethylphenylacetic acid which was crystallized from hot alcohol, m.p. 89–90°. Similarly, amides from other pyrrolidinetriones (Table IV) were identified in the case of known acids.

4-Bromo-2-ethylphenylacetamide (0.5 g.) was refluxed three hours with 0.16 g. of sodium hydroxide in 10 cc. of alcohol to give 4-bromo-2-ethylphenylacetic acid, m.p. 87–88° (from ligroin). This gave 4-bromo-*o*-phthalic acid,[16] m.p. 176–178°, by oxidation with alkaline permanganate.

o-Isopropylphenylacetamide (0.5 g.) was incompletely (50–60%) hydrolyzed, under the above conditions after refluxing five hours, to the acid, m.p. 58–59° (from ligroin). Calcd. for $C_{11}H_{14}O_2$: neut. equiv., 178. Found: neut. equiv., 170. This acid by oxidation with alkaline permanganate gave *o*-phthalic acid, m.p. 208–210°, which was isolated and purified as previously described.[16]

NEWARK, DEL. RECEIVED NOVEMBER 14, 1950

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Thermal Decomposition of Iminoester Salts and the Cleavage of Orthoesters by These Salts

BY S. M. MCELVAIN AND BRYCE E. TATE*

The thermal decomposition of iminoester hydrohalides (I) into the corresponding amide (III) and alkyl halide in chloroform or *t*-butyl alcohol solution follows first order kinetics as determined by the rate of disappearance of the chloride ion. The rate data are shown to be consistent with either a first order intramolecular decomposition of the un-ionized salt (reaction (1)) or an ionic mechanism (reactions (2) and (3)) involving a bimolecular, rate determining step. The relative rates of cleavage of orthoesters to the corresponding normal esters and an alkyl halide (reaction (6)) by iminoester hydrohalides have been determined in chloroform solution. Some relationships between the structures of the reactants and the rates of cleavage are discussed and a mechanism for the cleavage reaction (reactions (6) and (7)) is proposed. An alternative reaction, which would yield the normal ester and ether in an alcohol solution (reaction (8)), is shown to be insignificant.

The alcoholysis of iminoester hydrochlorides (I) derived from straight chain carboxylic acids gives the corresponding orthoesters (I) in yields of 60–80%.[1] The presence of a single negative α-substituent such as chloro,[1] ethoxyl,[2] phenyl,[3] carbethoxyl[4] or cyano[4] in the iminoester hydrochloride usually does not appreciably change these yields. However, the presence of two α- or β-substituents in the iminoester hydrochlorides usually lowers the yield of the orthoester to 20–30% or less.[1,5]

$$\underset{\text{I}}{RC(OC_2H_5)=NH_2Cl} + 2C_2H_5OH \longrightarrow \underset{\text{II}}{RC(OC_2H_5)_3} + NH_4Cl$$

While alcoholysis of each of the three types of iminoester hydrochlorides gives some amide (III) as a side product, amide formation becomes quite important in the alcoholysis of disubstituted compounds where the yields of this side product may approach 50%.[5a] The normal ester and the nitrile from which the iminoester hydrochloride is derived have also been found to be products of the alcoholysis.[5a] Normal ester and nitrile formation have not been observed in the straight chain series, but some normal ester is formed when the single α-substituent is phenyl,[6] and much larger amounts of normal ester are formed when the iminoester has two α- or β-substituents.[1,5]

This paper reports the results of work initiated for the purpose of determining the mechanisms of the reactions by which amides and normal esters are formed during the alcoholysis of iminoester hydrochlorides. The conclusions which have been drawn are based on the relationships of structure to the rates of thermal decomposition of iminoester salts in solution and the cleavage of orthoesters by these salts.

The Thermal Decomposition of Iminoester Salts.—Although the decomposition of an iminoester hydrochloride (I) to an amide (III) and alkyl chloride was first observed many years ago,[7] no

(*) E. I. du Pont de Nemours and Company Research Assistant, 1949–1950.

(1) S. M. McElvain and W. Nelson, THIS JOURNAL, **64**, 1825 (1942).

(2) S. M. McElvain and P. M. Walters, *ibid.*, **64**, 1963 (1942).

(3) S. M. McElvain and C. L. Stevens, *ibid.*, **68**, 1917 (1946).

(4) S. M. McElvain and J. P. Schroeder, *ibid.*, **71**, 40 (1949).

(5) S. M. McElvain and (a) R. L. Clarke, *ibid.*, **69**, 2661 (1947); (b) C. L. Stevens, *ibid.*, **69**, 2663 (1947).

(6) S. M. McElvain and J. T. Venerable, *ibid.*, **72**, 1664 (1950).

(7) A. Pinner and F. Klein, *Ber.*, **10**, 1892 (1877).

investigation of the relationship of the structures of these salts to their rates of decomposition appears to have been made. The mean temperatures of decomposition of various *crystalline* iminoester hydrochlorides, as determined by Hartigan and Cloke,[8] fall within a narrow range and are of little value in determining the relative stabilities of these salts in solution.

In the present work the rates of decomposition of a number of iminoester hydrohalides in both chloroform and *t*-butyl alcohol have been determined by measuring the rate of disappearance of halide ion. These solvents are well suited for such determinations because each readily dissolves these salts without reacting with them. The decompositions proceeded more rapidly, but still at a conveniently measured rate, in *t*-butyl alcohol than in chloroform (see Fig. 1), and for this reason most of the determinations were carried out in this alcohol at 60°; for comparison one determination (note, Table I) at 35° was made. Also, it seemed likely that *t*-butyl alcohol would more nearly simulate the ionizing conditions existing during the alcoholysis of an iminoester salt in methyl or ethyl alcohol solution.

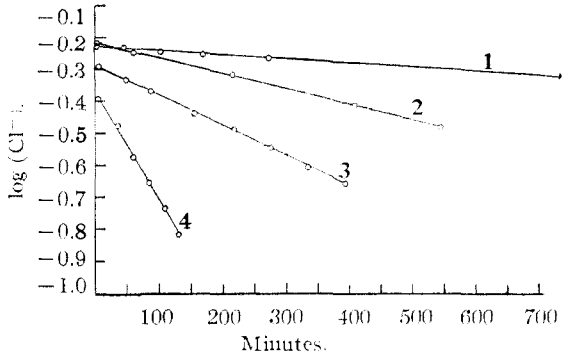


Fig. 1.—Thermal decomposition of ethyl iminoacetate hydrohalides at 60°: 1, hydrochloride in chloroform; 3, hydrochloride in *t*-butyl alcohol; 2, hydrobromide in chloroform; 4, hydrobromide in *t*-butyl alcohol.

In all cases the thermal decomposition of iminoester salts in solution followed first order kinetics with respect to the disappearance of chloride ion. The data were plotted as log [Cl⁻] *vs.* time; representative examples of these plots are shown in Fig. 1. Plots of $1/[Cl^-]$ *vs.* time in all cases gave curves rather than the straight lines shown in Fig. 1. The slope of each plot was multiplied by 2.303 to obtain the value of the rate constant, k_2K (equation (4)), which was converted to the half-life period from formula: $t_{1/2} = 0.693/k_2K$. The pertinent data for the decomposition of the various iminoester hydrohalides studied are listed in Table I.

TABLE I

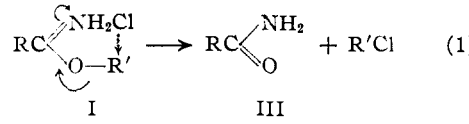
THERMAL DECOMPOSITION OF IMINOESTER SALTS, RC(OR′)=NH₂X, AT 60–62°

Run	R is	R′ is	X is	Solvent	Time followed, min.	$t_{1/2}$, min.
1	CH_3	CH_3	Cl	*t*-BuOH	61[a]	19
2	CH_3	C_2H_5	Cl	$CHCl_3$	1564	1770
3	CH_3	C_2H_5	Cl	*t*-BuOH	395	317
4	CH_3	C_2H_5	Br	$CHCl_3$	546	607
5	CH_3	C_2H_5	Br	*t*-BuOH	133	87
6	CH_3	$(CH_3)_2CH$	Cl	*t*-BuOH	1395	1000
7	$(CH_3)_2CH$	C_2H_5	Cl	*t*-BuOH	311	200
8	$C_6H_5CH_2$	C_2H_5	Cl	*t*-BuOH	181	118
9	$C_2H_5OOCCH_2$	C_2H_5	Cl	*t*-BuOH	75	34

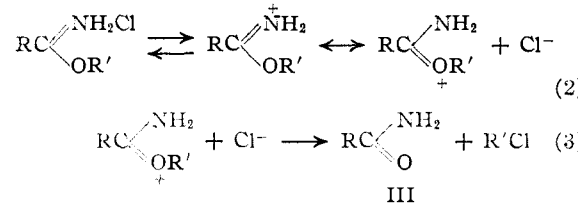
[a] The observed values of [Cl⁻] in moles/l. after various times (minutes) in this experiment, which has run for approximately three half-lives of the salt, are: 0.231 (0), 0.132 (16), 0.076 (31), 0.043 (46), 0.025 (61). A plot of log [Cl⁻] *vs.* time gives a straight line similar to those in Fig. 1. The same reactants at 35° for a total time of 352 min. gave $t_{1/2}$ of 328 min.

(8) R. H. Hartigan and J. B. Cloke, THIS JOURNAL, **67**, 709 (1945).

The first order kinetics followed in the thermal decomposition of these salts could indicate a first order reaction involving an intramolecular attack of the halogen of an undissociated ion pair (I) on the carbon of the alkoxyl group (reaction (1)).



However, the rate data, which follow the rate law (equation (4)), are also consistent with a two step mechanism (reactions (2) and (3)).



Although reaction (3) is bimolecular, first order kinetics would be observed if the ionization of the salt (I) is slight and the equilibrium of reaction (2) is so far to the left that the total chloride, as determined by the Volhard titration, is almost identical with the undissociated iminoester hydrochloride. This follows from the equations

$$-d[BHCl]/dt = k_2[BH^+][Cl^-];\quad BH^+ = RC(OR')NH_2^+$$
$$[BH^+][Cl^-] = K[BHCl]$$
$$-d[BHCl]/dt = k_2K[BHCl] \qquad (4)$$

The bimolecular mechanism[8a] postulated in reaction 3 is supported by the rates of decomposition of the hydrochlorides of methyl, ethyl and isopropyl iminoacetates in *t*-butyl alcohol (runs 1, 3 and 6, Table I). These follow the order for nucleophilic displacements on carbon; indeed the relative rates of these decompositions are of the same order as those of other well established S_N2 reactions. For example, the relative rates of conversion of RI to $ROCH_2C_6H_5$ by $C_6H_5CH_2O^-$ are: CH_3, 1.00; C_2H_5, 0.091; $(CH_3)_2CH$, 0.021,[9] while the relative rates for the alkyl iminoacetate hydrochloride decompositions, as calculated from the half-lives in Table I, are: CH_3, 1.00; C_2H_5, 0.060; $(CH_3)_2CH$, 0.019. The conformity of these relative rates to the usual S_N2 order indicates that K in equation (4) for each of these salts is of about

(8a) An alternative mechanism involving the prior dissociation of BHCl into B and HCl and the reaction of these products to form III has been suggested by a referee. This mechanism is not distinguishable from that postulated in reactions (2) and (3) by the kinetic data presented in Table I.

(9) P. C. Haywood, *J. Chem. Soc.*, **121**, 1904 (1922).

the same value in *t*-butyl alcohol. The higher rate of decomposition of the hydrobromide salts as compared to the corresponding hydrochlorides (Fig. 1 and runs 2, 3, 4 and 5, Table I) are also in accord with the known order of reactivities of these halide anions in the type of bimolecular replacement reaction shown in (3).

The effect of α-substituents on the rates of decomposition of iminoester hydrochlorides is shown in runs 3, 7, 8 and 9 of Table I. The relative rates of decomposition of these iminoester salts are: acetate, 1.00; isobutyrate, 1.58; phenylacetate, 2.68; carbethoxyacetate, 9.32. The first, third and fourth of these are in the expected order, as it would seem likely that electron-attracting α-substituents would enhance the positive character of the carbon at which displacement occurs (equation (3)) and hence increase the rate of decomposition. Similar considerations would indicate that the isobutyrate should decompose at a lower rate than the acetate, which is contrary to fact. However, the observed rates for the decomposition of the acetate and isobutyrate are in the same order as the relative amounts of corresponding amides produced in the alcoholysis of these iminoester salts to the orthoesters.

The temperature dependence of the decomposition of methyl iminoacetate hydrochloride in *t*-butyl alcohol is shown in run 1 and footnote *a*. The rather short half-life (5.5 hr.) of this salt in *t*-butyl alcohol at 35° is at least equivalent to, and probably greater than, its half-life in methyl or ethyl alcohol. This would indicate that alcoholyses of such iminoester salts to orthoesters in either of these alcohols occur quite rapidly, as yields of orthoester much greater than 50% generally are obtained.[1,3]

The alcoholysis of certain iminoester salts to orthoesters has been found to give maximum yields when carried out in refluxing diethyl ether.[1] This hitherto unexplained observation is consistent with the mechanism postulated in reactions (2) and (3). This non-polar solvent probably represses amide formation by decreasing the dissociation of the ion pairs (equation (2)) to give a lower value of K (equation 4).

The Cleavage of Orthoesters by Iminoester Salts.—The demonstration that diethyl diiminomalonate dihydrochloride was capable of cleaving the orthoester produced from it during alcoholysis[4] led to a more extensive investigation of this reaction as a possible source of the normal esters which are obtained occasionally as side products in the preparation of orthoesters.

The rates of interaction of a number of iminoester salt-orthoester pairs in chloroform solution at 25° have been determined by measuring the rates of disappearance of the halide ion resulting from reaction (5)

$$R'C(OR)_3 + R''C(OR''')=NH_2Cl \longrightarrow R'COOR + R''C(OR''')=NH + RCl + ROH \quad (5)$$

In this solvent at 25° the extents of the competing decomposition of the ethyl iminoester salts into the corresponding amide and ethyl halide after seventy hours were quite low, as may be seen from the values obtained with the following representative salts: ethyl iminoacetate hydrobromide (1.5%), ethyl iminoisobutyrate hydrochloride (1.2%), ethyl phenyliminoacetate hydrochloride (1.5%), ethylcarbethoxyiminoacetate hydrochloride (8.5%), and methyl phenyliminoacetate hydrochloride (25%). The relatively high value for the latter salt reiterates the greater sensitivity of a methyl group to nucleophilic attack that was noted in the previous section.

In comparing the rates of cleavage of orthoesters in chloroform as measured by the rate of disappearance of halide ion, it has been necessary to assume that the presence of the orthoester, normal ester, and more particularly the alcohol formed in reaction (5) does not change appreciably the rate of decomposition of the iminoester hydrohalide into the amide (reaction (1)). As this latter reaction is more rapid in *t*-butyl alcohol than in chloroform (see Fig. (1)), an acceleration of the rate of disappearance of halide ion by the alcohol formed during the cleavage would be expected. This alcohol is removed in part by alcoholysis of the iminoester salt, as a small amount of the insoluble ammonium halide was noticeable in some of the cleavage runs, particularly those involving methyl orthoesters.

Usually the ammonium halide settled to the bottom of the reaction vessel and was not measured in the halide analysis. This method of withdrawing samples has the effect of making these cleavages appear somewhat more rapid than they really are. Because of these competing reactions, the data obtained are of value only for a comparison of the effect of structure on the relative rates of cleavage.

The rates of cleavage of certain orthoesters by equimolar quantities of iminoester salts are shown graphically in Figs. 2–5 as plots of $[Cl^-]$ in moles/l. *vs.* time. Figure 2 shows that the α-substituent of the orthoester has no significant effect on the rate of its cleavage by two representative iminoester salts, ethyl iminoacetate hydrochloride and ethyl phenyliminoacetate hydrochloride. Ethyl orthoacetate and ethyl orthophenylacetate are cleaved by either of these salts at essentially the same rate.

The effect of the acidity of the iminoester salt on the rate of cleavage of ethyl orthoacetate is shown in Fig. 3. It is seen that the salts of the less basic iminoesters,[10] ethyl carbethoxyiminoacetate and the phenyliminoacetic esters, show the highest rates of cleavage. The data shown in Figs. 2 and 3 indicate that this reaction is acid catalyzed and that the rate is dependent upon the acidity of the iminoester salt.

In Fig. 4 the relative rates of cleavage of methyl and ethyl orthoesters are shown. Both methyl and ethyl phenyliminoacetate hydrochloride cleave the methyl orthoester more rapidly than they cleave the ethyl orthoester, although the differ-

(10) The order of basicities of the ethyl iminoesters of the salts shown in Fig. 3 is: iminoacetate ~ iminoisobutyrate > phenyliminoacetate > carbethoxyiminoacetate. The determinations were carried out by J. F. Jones in this Laboratory by measuring the *p*H of a freshly prepared solution of the iminoester in an alcohol–water mixture. Hartigan and Cloke (ref. 8) have shown that methyl iminoesters are less basic than the corresponding ethyl esters.

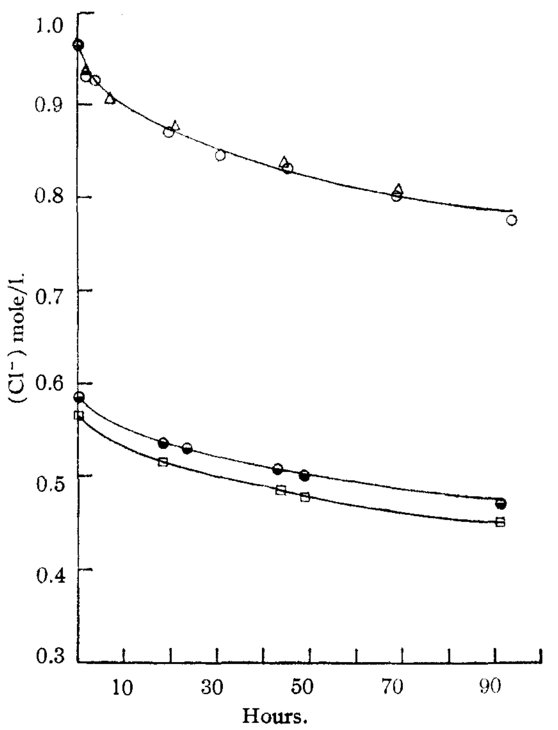


Fig. 2.—Cleavage of orthoesters by iminoester hydrochlorides in chloroform at 25°. Effect of α-substituents of the orthoester: △, ethyl phenyliminoacetate hydrochloride + ethyl orthophenylacetate; ○, ethyl phenyliminoacetate hydrochloride + ethyl orthoacetate; ⊖, ethyl iminoacetate hydrochloride + ethyl orthoacetate; □, ethyl iminoacetate hydrochloride + ethyl orthophenylacetate.

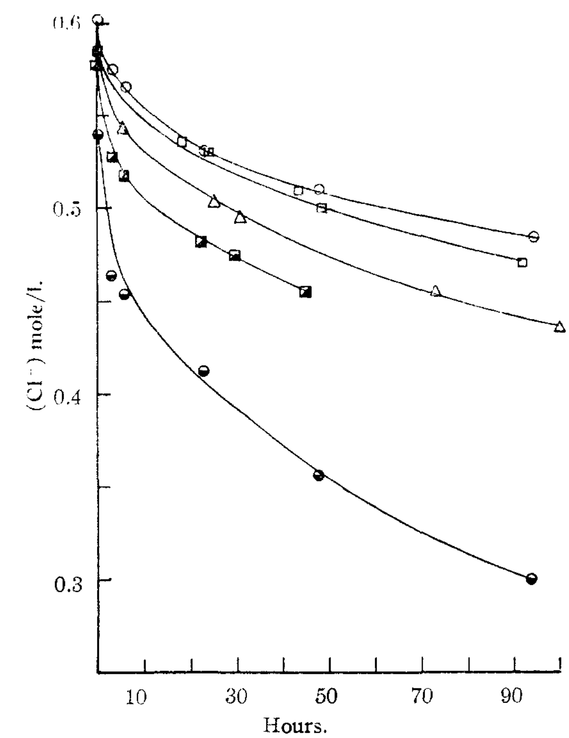


Fig. 3.—Cleavage of orthoesters by iminoester hydrochlorides in chloroform at 25°. Effect of acidity of iminoester hydrochloride: ○, ethyl imino isobutyrate hydrochloride + ethyl orthoacetate; □, ethyl iminoacetate hydrochloride + ethyl orthoacetate: △, ethyl phenyliminoacetate hydrochloride + ethyl orthophenylacetate; ◪, methyl phenyliminoacetate hydrochloride + ethyl orthoacetate; ⊖, ethyl carbethoxyiminoacetate hydrochloride + ethyl orthoacetate.

ences in the rates of reaction of the two salts are in the same order as shown in Fig. 3. The more rapid cleavage of the methyl orthoesters as compared to the corresponding ethyl orthoesters conforms to the same order as was noted for the thermal decomposition of the methyl and ethyl iminoester salts in the previous section (runs 1 and 3, Table I).

The effect of the anion on the rate of cleavage of ethyl orthoacetate is shown in Fig. 5. The more rapid cleavage of this orthoester by the hydrobromide salt indicates that this reaction involves a similar type of S_N2 attack of the halide anion on the alkyl group of the orthoester as is shown for the decomposition of the iminoester cation in reaction (3).

The relative rates of cleavage of orthoesters by iminoester salts illustrated in Figs. 2–5 suggest a reaction mechanism involving a reversible proton transfer from the acidic salt to the orthoester (reaction (6)) followed by the slower, irreversible, rate-determining interaction of the resulting oxonium cation and the halide anion (reaction (7)).

$$R'C(OR)_3 + R''C(OR'''){=}NH_2X \rightleftharpoons R''C(OR'''){=}NH + R'C(OR)_2\overset{+}{O}(H)R + X^- \quad (6)$$

$$R'C(OR_2)\overset{+}{O}(H)R + X^- \longrightarrow R'COOR + RX + ROH \quad (7)$$

Inasmuch as all of the cleavages of orthoesters discussed above were carried out in chloroform solution, they are not strictly comparable to those that occur in alcohol solution during the preparation of an orthoester. In such preparations the alcoholysis reaction usually is the most rapid as evidenced by the good yields of orthoesters that are obtained, particularly from the straight chain aliphatic iminoester salts. In other cases, such as ethyl phenyliminoacetate and ethyl carbethoxyiminoacetate hydrochlorides, the cleavage of the orthoester to the normal ester may become of some importance. With such branched chain iminoester salts as the isobutyrate or the isovalerate, the alcoholysis rate is lower and the cleavage reaction and amide formation become correspondingly more important.[11] Also, in alcohol the dissociation of the salt into its ions is greater and this would tend to increase the rates of both amide formation from the iminoester salt (*via* reactions (2) and (3)) and the cleavage of the orthoester after it had formed.

In alcohol solution the possibility of ether formation should be considered, as it would not be unreasonable to expect that the alcohol could attack the oxonium ion postulated in reaction (6) in the manner shown in reaction (8). Indeed, small amounts of ether have been isolated from certain alcoholyses.[5]

(11) *Cf.* Table I of ref. 1, p. 1826.

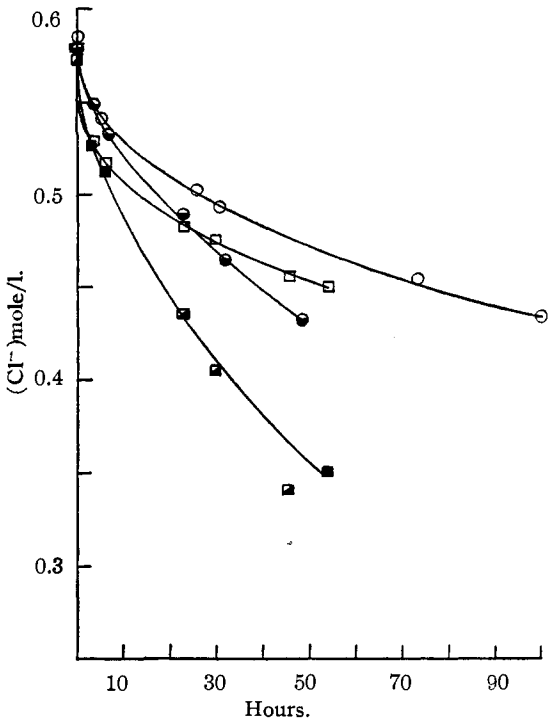


Fig. 4.—Cleavage of orthoesters by iminoester hydrochlorides in chloroform at 25°. Effect of alkyl groups of orthoester: O, ethyl phenyliminoacetate hydrochloride + ethyl orthophenylacetate; ◒, ethyl phenyliminoacetate hydrochloride + methyl orthoacetate; □, methyl phenyliminoacetate hydrochloride + ethyl orthoacetate; ◪, methyl phenyliminoacetate hydrochloride + methyl orthoacetate; ■, mixture agitated and suspended ammonium chloride included in aliquot.

$$R'C(OR)_2\overset{+}{O}R + EtOH \longrightarrow \underset{H}{\overset{|}{}}$$

$$R'COOR + ROEt + ROH + H^+ \quad (8)$$

To discover if reaction (8) occurs to any appreciable extent, diethyl diiminomalonate dihydrochloride,[4] $EtOC(=NH_2Cl)CH_2C(=NH_2Cl)OEt$, was allowed to react with ethyl orthophenylacetate in alcohol solution. As this salt is rather insoluble in alcohol and undergoes alcoholysis quite slowly, the cleavage of the orthoester is the predominating reaction. After twenty-four hours at room temperature, a 75% yield of ethyl phenylacetate and a 77% yield of diethyl diiminomalonate monohydrochloride were recovered from the reaction mixture. No diethyl ether was found, but an 85% yield of ethyl chloride was obtained. It would seem, therefore, that reaction (8) is not a significant side reaction in the alcoholysis of an iminoester salt and that the principal source of the normal ester is *via* reaction (5).

The nitrile, which has been observed as a side product in the preparation of orthoesters, doubtless is formed by the loss of alcohol from the free iminoester produced in reaction (6).

Acknowledgment.—The authors gratefully acknowledge the assistance of Professor E. L. King of the Department of Chemistry, University of Wisconsin, during the course of the work and in the preparation of this manuscript.

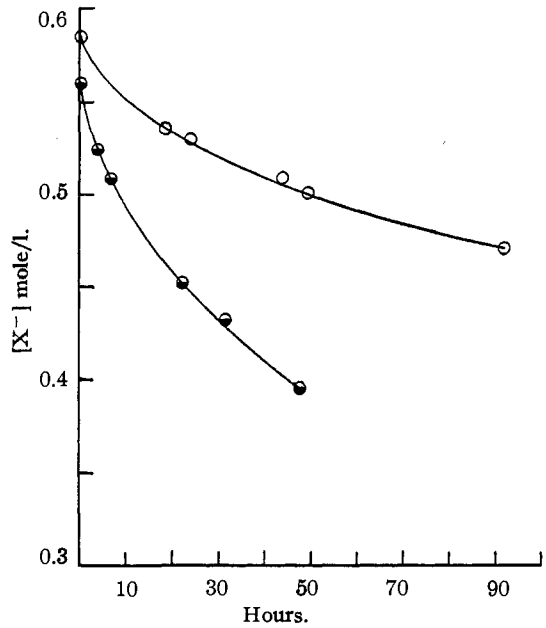


Fig. 5.—Cleavage of orthoesters by iminoester hydrohalides in chloroform at 25°. Effect of halide ion: O, ethyl iminoacetate hydrochloride + ethyl orthoacetate; ◒, ethyl iminoacetate hydrobromide + ethyl orthoacetate.

Experimental

Procedures for Measuring Rates.—For the determination of the rates of decomposition of iminoester hydrohalides in *t*-butyl alcohol at approximately 60° an electrically heated oil-bath was used, and major fluctuations in temperature (more than 2–3°) were avoided by manual control of a variable resistance in the circuit. The temperature could be maintained constant to within 2–3° when the operator was present, but in overnight runs the temperature varied somewhat more and consequently, the runs of longer than 12 hours did not yield data as precise as those of less than 12 hours.

When a kinetic run was to be made, approximately 70–80 ml. of dry *t*-butyl alcohol (dried by refluxing with sodium and distillation from the sodium hydroxide and butoxide) was pipetted into a 100-ml., 3-necked, round-bottomed flask equipped with a condenser protected with a Drierite tube, a mercury seal glass stirrer, and a thermometer. The oil-bath was raised and the temperature of the *t*-butyl alcohol was brought to approximately 60° while the stirrer was running. After the temperature had become constant the aminoester hydrohalide was introduced. After solution was complete, the stopper carrying the thermometer was removed and an aliquot was taken with a pipet inserted through the side arm. The contents of the pipet were drained into a 250-ml. flask and diluted with distilled water. The halogen was determined by the Volhard method. During removal of the samples no attempt was made to keep air or atmospheric moisture from the system. Duplicate runs using this method gave values of the half-life and k_2K which agreed within 10%. The largest single source of error is probably the difficulty of making different runs at the same temperature.

The determinations of these rates in chloroform at 60° were made in the following way. The proper amount of the iminoester hydrohalide was dissolved in dry alcohol-free chloroform in a flask equipped with a side arm and a condenser attached by a ground glass joint. The condenser was equipped with a calcium chloride tube to exclude atmospheric moisture during the course of the run. The chloroform was heated to boiling with a preheated oil-bath. When solution was complete, the bath was lowered for two minutes and a pipet was inserted through the side arm to withdraw the sample for analysis. The oil-bath was immediately raised, and the chloroform was refluxed. The bath was lowered for two minutes before each sample was withdrawn.

The rate studies of the decomposition of the salts in chloroform at 25° and the orthoester cleavage runs were made in volumetric flasks kept in a thermostat held at 25 ± 0.05°.

In determining the rates of cleavage of orthoesters by iminoester hydrohalides, the proper amount of the iminoester hydrohalide was placed in a volumetric flask, alcohol-free chloroform was pipetted in until the flask was about two-thirds full. Orthoester equivalent to the iminoester salt was then added and the mixture made up to volume with chloroform. Some warming occurred on mixing the orthoester and iminoester salt solution, and the flask was cooled to room temperature as rapidly as possible. Samples were withdrawn by pipet with no precautions being taken during this time to exclude air and atmospheric moisture.

Iminoester Hydrohalides.—The iminoester hydrohalides were prepared by the method of McElvain and Nelson.[1] After the hydrohalide crystallized from the reaction mixture in the refrigerator, the solvent was decanted, fresh ether added, and the hydrohalide triturated in the flask. This was done twice more before the product was collected on a Buchner funnel, pressed dry and transferred to a vacuum desiccator containing potassium hydroxide and sulfuric acid. After at least several hours in the vacuum desiccator, the crystalline salt was transferred to a mortar and again ground under dry ether, filtered and placed in a vacuum desiccator overnight.

Ethyl iminoacetate hydrobromide, which was prepared in yields greater than 90%, melted at 112–113° (dec.).

Anal. Calcd. for $C_4H_{10}BrNO$: Br, 47.6; N, 8.34. Found: Br, 47.6; N, 8.34.

Isopropyl iminoacetate hydrochloride was prepared in 38% yield and melted at 88–91°.

Anal. Calcd. for $C_5H_{12}ClNO$: Cl, 25.8; N, 10.17. Found: Cl, 25.9; N, 10.23.

Orthoesters.—Ethyl orthophenylacetate was prepared by the method of McElvain and Stevens,[3] except that after filtration of the ammonium chloride the filtrate was neutralized to phenolphthalein with alcoholic sodium ethoxide. The orthoester prepared in this way was dissolved in petroleum ether (b.p. 60–68°) and the mixture refluxed with sodium hydride in order to remove traces of nitrile, normal ester and amide. After distillation, the orthoester so treated boiled at 120–121° (10 mm.), $n^{25}D$ 1.4754. The other orthoesters used in the cleavage reactions were prepared by the method of McElvain and Nelson.[1]

Products of Thermal Decomposition of Iminoester Hydrohalides.—In every decomposition carried out the amide which was produced was isolated and identified. No attempt was made to isolate the alkyl halide in every case, but it was found whenever an attempt was made to isolate it. No *t*-butyl ether was found in any pyrolysis carried out in *t*-butyl alcohol. A typical example is the decomposition of isopropyl iminoacetate.

To 45.6 g. (0.33 mole) of isopropyl iminoacetate hydrochloride was added 400 ml. of dry *t*-butyl alcohol. The solution was heated under a reflux condenser protected with a Drierite tube for 48 hours. Upon distillation of the mixture through a 7-inch Vigreux column, isopropyl chloride and *t*-butyl alcohol distilled at 45–70°. Upon refractionation of this mixture 10.41 g. (40%) of isopropyl chloride, b.p. 32–35°, $n^{25}D$ 1.3733 was obtained. After completely removing the *t*-butyl alcohol, a small amount of ammonium chloride contaminated the acetamide which remained. After recrystallization from an ethyl acetate–benzene mixture, the acetamide melted at 76–79°.

Products of Cleavage of Ethyl Orthophenylacetate by Ethyl Phenyliminoacetate Hydrochloride in Chloroform at Room Temperature.—To a solution of 50.5 g. (0.252 mole) of ethyl phenyliminoacetate hydrochloride in 250 ml. of dry alcohol-free chloroform was added 60 g. (0.252 mole) of ethyl orthophenylacetate. After standing at room temperature for 23 days the mixture was filtered to remove a small amount of ammonium chloride. The chloroform was removed from the filtrate by distillation under reduced pressure. The ethyl chloride formed in the reaction was not isolated. After removal of the low-boiling materials 29.0 g. (70%) of ethyl phenylacetate, b.p. 68–75° (0.6 mm.), $n^{25}D$ 1.4955, was collected. A nitrogen determination on this material showed no nitrile or iminoester was present. About 7.4 g. of material distilled at 75–180° (0.6 mm.) and the remainder (19.4 g.) did not distil. The rather large amount of high boiling or non-distillable product indicates that the free iminoester polymerized during the long period of standing.

Cleavage of Ethyl Orthophenylacetate by Diethyl Diiminomalonate Dihydrochloride in Alcohol.—To 86.2 g. (0.373 mole) of this salt[4] was added 88.8 g. (0.373 mole) of the orthoester and 600 ml. of anhydrous ethanol. The resulting mixture was stirred for 24 hours with precautions taken to exclude atmospheric moisture. After this time, the suspended salt was collected on a filter and washed several times with 40–50-ml. portions of anhydrous ethanol. In this way 12.86 g. (20%) of material which was indicated by analysis to be malondiamidine dihydrochloride[12] contaminated with some ammonium chloride was collected.

The solvent was removed under reduced pressure at room temperature and the hard white cake remaining was broken up under 180–200 ml. of anhydrous ether. After the mixture was triturated under the ether, it was filtered and the salt was rapidly transferred to a beaker and washed well with several hundred ml. of anhydrous ether. The salt was collected on a Buchner funnel, pressed dry with a cork and rapidly transferred to a vacuum desiccator which contained sulfuric acid and potassium hydroxide. Since this hydrochloride is quite deliquescent, it was necessary to filter and wash it rapidly. After drying, the diethyl diiminomalonate monohydrochloride amounted to 55.4 g. (76.4%), m.p. 102–104°.

Anal. Calcd. for $C_7H_{15}ClN_2O_2$: Cl, 18.2. Found: Cl, 18.1.

The ether solution obtained from washing the monohydrochloride, upon distillation, gave 43.18 g. of ethyl phenylacetate, b.p. 104–107° (10 mm.), $n^{25}D$ 1.4937. Ammonolysis of the forerun of this fraction with aqueous ammonia gave 2.14 g. of phenylacetamide, corresponding to 2.6 g. of ester in the forerun, and making a total of 45.78 g. (74.8%) of normal ester.

In a similar run, the alcoholysis mixture was distilled at atmospheric pressure until about 200 ml. of distillate had collected (Dry Ice trap in system). The material in the Dry Ice trap was combined with this distillate and distilled through a Fenske column attached to a Dry Ice trap. In this way 85% of the theoretical amount of ethyl chloride was collected. There was no evidence of the presence of diethyl ether after this material had distilled. The ethyl chloride was converted by means of the Grignard reaction and α-naphthyl isocyanate to N-(α-naphthyl)-propionamide, m.p. 115–116°. A mixed melting point with authentic material showed no depression.

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(12) This salt rather than ammonium chloride is produced in the alcoholysis of diethyl diiminomalonate monohydrochloride. The details of this alcoholysis are the subject of a future communication from this Laboratory.