it gives a very easy method of preparing the hitherto almost inaccessible benzenepentacarboxylic acid. It also serves for the preparation of other benzene polycarboxylic acids. Bamberger and Hooker's diphenyleneketonedicarboxylic acid from retene can be oxidized in a few hours to two isomeric *benzenetricarboxylic* acids, thus showing that the constitution given for retene and all its derivatives is incorrect.

The above work dealing with the action of acetic anhydride led to the supposition that anhydrides[1] might be prepared from *meta*- and *para*-phthalic acids and their substitution products. On trying the experiment it was found that such anhydrides could be obtained quantitatively by heating a solution of the acid in acetic anhydride to 200° until the excess of reagent was distilled off. These products apparently have a very high molecular weight. A preliminary determination, in nitrobenzene by the boiling point method, for the anhydride from chloroterephthalic acid, $[C_6H_3Cl(CO)_2O]_x$, indicates that it may be as high as 1500 or 2000.

A part of this work has been carried on with the aid of my students and I wish especially to acknowledge the valuable assistance of G. F. Parmenter, N. A. Dubois, V. S. Babasinian, M. L. Dolt, W. C. Slade and F. Keyes.

The more important results of this work thus far are as follows:

1. Satisfactory methods for the preparation of a number of aromatic propiolic acids.
2. The polymerization of these acids to derivatives of 1-phenyl-2,3-naphthalenedicarboxylic acids—giving a quantitative method of synthesis.
3. Syntheses of acids of the diphenyl, fluorene and diphenyleneketone series and a study of their characteristic reactions.
4. Syntheses of benzenepentacarboxylic acid and other benzene-polycarboxylic acids.
5. The determination of the constitution of retene and its derivatives.
6. The preparation of anhydrides from meta- and para-phthalic acids and their substitution products.

BROWN UNIVERSITY, PROVIDENCE, R. I.

CATALYSIS ON THE BASIS OF WORK WITH IMIDO ESTERS.[2]

BY JULIUS STIEGLITZ.

Received December 2, 1909.

I shall not attempt to discuss to-day the general subject of catalysis but shall use the short time rather to present briefly some results[3] in certain lines of our work which seem to shed some light on three fundamental points of interest in catalysis, namely, on the questions how in

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[1] THIS JOURNAL, 30, 1263 (1908) and 31, 1319 (1909).

[2] Presented at the Second Decennial Celebration of Clark University, Worcester, Mass., September 15, 1909.

[3] Certain parts of the work are still being carried out—as indicated below—and for such parts this report is preliminary to a final one. Complete discussion of the several parts lay outside the limits of this paper and will be brought in later special reports.

certain cases a catalytic agent does its work, why it does it, and what limitations there are to its action.

It may be recalled that an imido ester, such as methyl imido benzoate, is very slowly decomposed by pure water. One of the decompositions it undergoes under these conditions is into ammonia and methyl benzoate[1] as expressed in the equation

$$C_6H_5C(: NH)OCH_3 + H_2O \longrightarrow C_6H_5CO_2CH_3 + NH_3. \qquad (1)$$

The addition of an acid, say hydrochloric acid, enormously accelerates this otherwise extremely slow action and we were able to show that the acceleration is due to the fact that the reacting component in this decomposition is the positive ion of the ester,[2] as expressed in the equation.

$$C_6H_5(: NH_2^+)OCH_3 + H_2O \longrightarrow C_6H_5CO_2CH_3 + NH_4^+. \qquad (2)$$

In arriving at this conclusion, account had to be taken of the so-called "salt-effect" or "salt-acceleration" produced by the presence of electrolytes, entirely analogous to the "salt-effect" in other decompositions in which water is a reacting component, as in the catalysis of esters by acids. This salt-effect being allowed for, the velocity of decomposition of an imido ester by water in the presence of acids is given in the equation[3]

$$dx/dt = K_{v(ion)} \times C_{pos.\ est.\ ion} \times [C_H \times C_{OH}]. \qquad (3)$$

I have not time more than to mention the fact that it was shown that the same fundamental equation may be applied to the saponification of ordinary esters under the influence of acids, the main difference being that for such exceedingly weak oxonium bases as esters are the concentration of the positive ester ion is practically proportional to the concentrations of the ester and the hydrogen ion present at any moment, so that we may transform (3) into[4]

$$dx/dt = K_v \times C_{ester} \times C_H \times [C_H \times C_{OH}] \qquad (4)$$

which is also the equation based on experience.

The work on which the above conclusions were based was carried out wholly with the hydrochlorides of the imido esters. More recently we have also carried out measurements with the hydrobromides and nitrates, and begun work also with sulphates; if the positive *ion* is the reacting component, then, determining rigorously the degree of ionization and making rigorous allowance for the salt-effect, we should find that the velocity constant for the decomposition of the positive ion in the chloride solution should also satisfy the observed rates of decomposition of these other salts. For the rigorous treatment, the "salt-effect" produced by the chlorides, bromides, nitrates, etc., has to be determined experimentally and this has been carried out[5] with the chlorides and bromides,[6] mixtures with varying amounts of the potassium and sodium salts being examined, the degrees of ionization of each salt in the mixture being

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[1] Stieglitz, *Report International Congress of Arts and Science*, St. Louis, 4, 276 (1904), and *Am. Chem. J.*, 39, 29 (1908).

[2] Stieglitz with Derby, McCracken, Schlesinger, *Am. Chem. J.*, 39, 29, 166, 402, 437, 586, 719.

[3] $C_{pos.\ est.\ ion}$ is a function of x.

[4] C_{ester} is a function of x.

[5] W. W. Hickman, Dissertation, 1909.

[6] Mr. Weatherby is completing the work begun by Mr. Hickman on the nitrates and sulphates.

determined with the aid of the principle of isohydric solutions, which was proved to apply to such mixtures.[1] The salt-effect is, except for minute quantities of salt, proportional to its concentration or rather, more probably, only to the concentration of the ionized part of the salt. The salt-effect is an acceleration and if we call $K_{v(ion)o}$ the velocity of decomposition of the imido ester ion in the absence of any salt at all, this velocity will be increased proportionally to some specific acceleration factor A, and to the concentration $m\alpha$ of the ionized part of A salt. So we have

$$K_{v(ion)obs.} = K_{v(ion)o} (1 + A\, m\, \alpha). \tag{5}$$

$K_{v(ion)obs.}$ is the constant calculated according to equation (3) from the observations without any allowance for a salt-effect.

$K_{v(ion)o}$, the velocity constant when the salt effect is eliminated, is easily found by extrapolation from the observations when imido ester salts are present without added salts, A from the results obtained when salts have been added. We arrived thus empirically at the rather unexpected result that the accelerating factor A is approximately the same for sodium, potassium and lithium chlorides and for the bromides as well as for the chlorides, *viz.*, about 185 per cent. per gram molecule of fully ionized salt. Table I illustrates this fact for potassium chloride and potassium bromide. K_v is the velocity coefficient calculated without regard to the degree of ionization of the imido ester salt, α is the degree of ionization of the salt calculated with the aid of the principle of isohydric solutions. In the columns headed "found" are given the values obtained for $K_{v/\alpha}$ by experiment; in the columns headed "calculated" are the values obtained according to equation (5), in which the velocity coefficient $K_{v(ion)o}$ in the absence of any salts at all is taken as 164 and the salt acceleration factor A is taken as 185 per cent. for both series.

TABLE I.[2]

K Hal.	KCl. 43430 $K_{v/\alpha}$.		KBr. 43430$K_{v/\alpha}$.	
m.	Found.	Calculated.	Found.	Calculated.
0	176	176	176	177
0.1	191	190	191	190
0.2	213	214	209	215
0.25	227	226	230	227
0.333	247	245	(268)	247

I wish to emphasize this result because the work of others, notably of Arrhenius and Euler, with cane-sugar and esters, shows varying specific accelerating factors for these salts. I believe our work has the advantage of our knowing from conductivity measurements the degrees of ionization of the imido ester salts as well as of the added electrolyte so that there seems to be no unknown factor left in our estimations. But we are simply presenting these results for the time being as an empirical contribution to the whole question of catalysis and we do not consider the very complex question of "salt catalysis" as at all settled.[3]

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[1] Edith E. Barnard, Dissertation, 1907.

[2] Taken from W. W. Hickman's dissertation.

[3] Work on "salt catalysis" is being continued by L. S. Weatherby, preliminary results by Mr. Hickman on the effect of sulphates indicated an abnormally high effect.

With the aid of the determination of the salt factor for chlorides and bromides we have been able to show that the positive ester ion shows indeed the same rate of decomposition irrespective of its origin from either of these salts and very probably also for the nitrate[1] (see the values for $K_{v/\alpha}$ for the three salts in equi-molar concentrations as given in Table II). This is exactly what our theory would require, namely, that the simple reason why the addition of an acid accelerates this decomposition is that it forms a salt whose positive ion is the reacting component and that the concentration of the ion is enormously increased when the catalyzing acid is added to the free ester, which is a very weak and therefore little ionized base.

TABLE II.[2]—ETHYL IMIDO BENZOATE.

Hydrochloride.				Hydrobromide.			Nitrate.		
m.	α.[3]	Kv.[4]	Kv/α.	α.[2]	Kv.[2]	Kv/α.	α.[2]	Kv.[2]	Kv/α.
0.05	77.8	136	175	75.9	133	176	75.1	133	177
0.1	71.8	132	185	69.4	128	184	68.3	127	186
0.2	64.5	121	188	61.7	119	193	60.4	118	195
0.33	57.7	114	198	54.7	108	198	52.7	107	201

It was suggested by Arrhenius and emphasized by Euler that the salt acceleration is probably largely due to the increased ionization of water in the presence of electrolytes, but quantitative evidence in support of such a conclusion has not been brought, as far as I am aware. In view of the increase observed by Arrhenius and others[5] in the strength of other acids in the presence of added foreign salts, *e. g.*, of acetic, formic and carbonic acids in the presence of sodium chloride, it seems a sufficiently rational assumption that water should show a similar increased ionization.[6] The imido esters, enabling us to measure the actual concentration of the reacting imido ester ion, gave us an opportunity to bring experimental evidence strongly supporting this view. From equation (3) it is obvious that if the salt acceleration is due to the increased ionization of water, *viz.*, an increase in the value of the third factor, $(C_H \times C_{OH})$ then, $C_{pos.\ est.\ ion}$ being known by experiment, the velocity constant $K_{v(ion)}$ calculated *without* taking any increased value of $[C_H \times C_{OH}]$ into account, should increase in the same proportion for all the imido esters for the same concentration of added salt ions, irrespective of the fact that, according to the ester used, the decomposition may be a comparatively slow or a very fast one. We have found this to be true[7]—all the esters used show the same acceleration per gram molecule ionized salt—*i. e.*, close to 185 per cent. per gram molecule ionized potassium chloride, etc.[8]

Having found that the reacting component in these and a number of other actions under the influence of acids is the positive ion of a salt formed with the acid, we were naturally most interested in the question

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[1] The salt effect for nitrates is now being determined.

[2] Taken from W. W. Hickman's dissertation.

[3] Taken from Edith E. Barnard's dissertation.

[4] Taken from Schlesinger's results, *Loc. cit.*

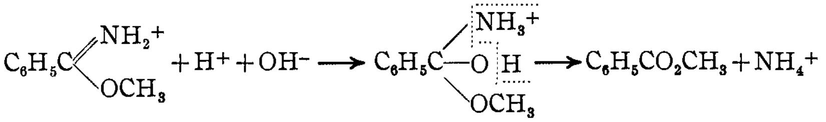
[5] E. J. Szyszkowski, *Z. physik. Chem.*, 58, 419.

[6] See a discussion of the other side of this question by Acree, *Am. Chem. J.*, 41, 474.

[7] Dissertation of Edith E. Barnard and W. W. Hickman.

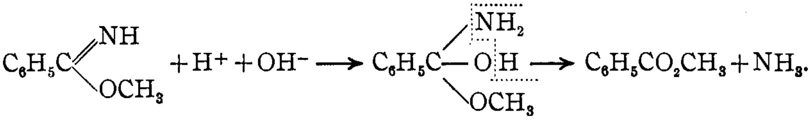
[8] The investigation of the ionization of water in salt solutions is being continued with other substances and by other methods.

why the *ion* should be so reactive, why it should be so important a component. We can hardly consider the decompositions to be *purely* ionic reactions,[1] comparable with the hydrolysis of salts in aqueous solutions, as was mistakenly assumed, for instance, by Euler and by Kastle. Such assumptions run counter to the law of mass action applied rigorously in the analysis of the conditions.[1] The law is, however, in agreement with the assumption[2] based on experience gained in organic chemistry that the following are the stages for the action:



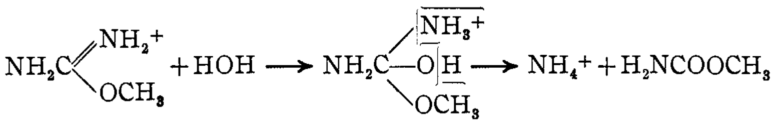
$$C_6H_5C\begin{matrix}\diagup NH_2^+\\ \diagdown OCH_3\end{matrix} + H^+ + OH^- \longrightarrow C_6H_5C\begin{matrix}\diagup NH_3^+\\ —O\;H\\ \diagdown OCH_3\end{matrix} \longrightarrow C_6H_5CO_2CH_3 + NH_4^+ \qquad (6)$$

Now, we may well ask why this should be an enormously faster action than the entirely analogous possible action of water on the non-ionized free ester, which, it is clear, could proceed in a very similar series of stages as expressed in the equations:



$$C_6H_5C\begin{matrix}\diagup NH\\ \diagdown OCH_3\end{matrix} + H^+ + OH^- \longrightarrow C_6H_5C\begin{matrix}\diagup NH_2\\ —O\;H\\ \diagdown OCH_3\end{matrix} \longrightarrow C_6H_5CO_2CH_3 + NH_3. \qquad (6')$$

For me, one of the most interesting and important features of our work is found in the unmistakable way in which the fact is brought out more and more clearly that the accelerating or catalytic effect of the acid is most intimately associated with the transformation, in acid solution, of the positive ion of a weaker base into that of a stronger one—the results no doubt of the principle of the loss of a maximum amount of free energy.[3] This is shown most strikingly in the following illustration: whereas the above imido esters are very rapidly decomposed by water in the presence of acid, this is not the case for the closely related compounds, the urea ester salts, which, *structurally considered,* could react quite as easily with water but are as a matter of fact quite stable in acid solution. The transformation



$$NH_2C\begin{matrix}\diagup NH_2^+\\ \diagdown OCH_3\end{matrix} + HOH \longrightarrow NH_2C\begin{matrix}\diagup NH_3^+\\ —O\,|\,H\\ \diagdown OCH_3\end{matrix} \longrightarrow NH_4^+ + H_2NCOOCH_3 \qquad (7)$$

only takes place to a very slight extent at 100°, and at ordinary temperatures, where imido ester salts are completely decomposed in one to ten hours, the urea ester salts have not been observed to decompose at all.[4] In this case we have the notable fact that such a transformation would involve the change of a salt of a stronger base into that of a much weaker one—an ammonium salt—and this does not take place. To test the legitimacy of our reasoning we recently examined the behavior of benzoyl urea ester salts: the benzoyl urea esters form very much weaker

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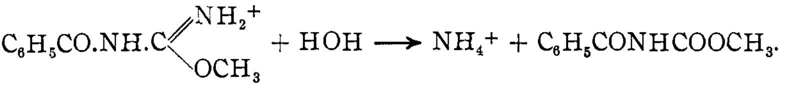
[1] See a more complete discussion by Stieglitz, *Am. Chem. J.*, 39, 402.

[2] Stieglitz, *Loc. cit.*

[3] *Ibid.*

[4] The degree of stability is being examined *quantitatively.*

bases than ammonia and our reasoning would lead us to expect that they, in turn, ought to be decomposed quite as smoothly in acid solution as the imido esters. Such is, in fact, the case;[1] urethanes and ammonium salts readily result according to the equation



$$C_6H_5CO.NH.C\begin{matrix}\diagup NH_2^+ \\ \diagdown OCH_3\end{matrix} + HOH \longrightarrow NH_4^+ + C_6H_5CONHCOOCH_3. \quad (8)$$

We find then that perfect analogy in structure is of far less importance in determining the result of the action of water than a definite physico-chemical relation subject to quantitative measurement.

This is again brought out beautifully by the behavior of the urea esters towards ammonia. The imido esters give with ammonia amidines and again the action is accelerated by the addition of an acid or an ammonium salt and, as we shall see presently, this is due to the fact that again it is the positive ester ion that reacts with ammonia, an amidine resulting according to the equation

$$C_6H_5C(:NH_2^+)OCH_3 + NH_3 \longrightarrow C_6H_5C(:NH_2^+)NH_2 + HOCH_3 \quad (9).$$

Now, urea esters which, as explained above, would not react with *water* in acid solution because the salt of a stronger base would be converted into the salt of a weaker one if they did react, would give with *ammonia* guanidines which are still stronger bases than they are themselves. They should, therefore, according to this theory, react with ammonia in the presence of an acid; as a matter of fact they do, producing guanidines very readily, and we were able to prove again that the velocity of the formation is proportional to the concentration of the positive ester ion;[1] in fact, until our theory led us to recognize the importance of having a salt-forming acid present, all our efforts to prepare guanidines from urea esters—by using ammonia alone—had proved futile; so that this theory seems to agree equally well with the reactions of a given compound which *do occur* as with those which do not take place.

We have found too that in series of structurally closely related esters where what might be called the structural and stereochemical resistances to the action are perhaps approximately the same, the transformation of the positive ion of a weaker base in the presence of acids into that of a given stronger base, say into the ammonium ion, *proceeds with the greater velocity at a given temperature the weaker the original base is.*[3] This brings, as far as I am aware, the first complete experimental proof of a theory which others, notably van't Hoff and Euler suspected to be true,[4] although there appeared so many marked contradictions to the assumption that the theory appeared at best a very uncertain one. For instance, Hemptinne[5] and Lowenherz,[6] working on this problem at van't Hoff's suggestion, obtained the following results for the saponification of esters by acids:

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[1] J. C. Moore's dissertation, 1909.

[2] R. A. Hall's dissertation (1907).

[3] Cf. Stieglitz, *Loc. cit.*, and McCracken, *Loc. cit.*

[4] See the discussion by Euler, *Z. physik. Chem.*, 36, 410.

[5] *Ibid.*, 13, 561.

[6] *Ibid.*, 15, 395.

Table III.[1]

Ester.	Velocity constant.	Ioniz. const. of the acid.
$HCOOC_2H_5$	0.11	21×10^{-5}
$CH_3COOC_2H_5$	0.0057	1.8×10^{-5}
$ClCH_2COOC_2H_5$	0.0033	155×10^{-5}
$Cl_2CHCOOC_2H_5$	0.0053	5100×10^{-5}
$CH_3CH_2COOC_2H_5$	0.0061	1.3×10^{-5}

Assuming, as Euler did, that the strongest acids produce the weakest bases in their esters, one might expect the positive ions of the chloroacetic acid esters to be saponified most rapidly to give the positive ion of a *given* stronger base, the oxonium base of ethyl alcohol. As a matter of fact the velocity constants in the above table do not tell us anything at all as to whether that is so or not and that is why the theory, heretofore, has appeared as an unproved one; obviously it does not follow from the data in Table III, where the *weakest* bases, dichloroacetic ester and chloroacetic ester, have the *smallest*, not the largest, velocity constants of decomposition. But the fact that, for instance, the velocity coefficient for the saponification of dichloroacetic ester is even smaller than that for ethyl acetate *does not mean anything at all* in regard to the real *relative rates of transformation of their positive ions*: there is a second factor involved, namely, the concentrations of the positive ions of the esters are dependent on the strength of the esters as oxonium bases, as expressed in our fundamental equations for the catalysis of an ester by an acid.[2] In our fundamental equation

$$dx/dt = K_{v(ion)} \times C_{pos.\ est.\ ion} \times [C_H \times C_{OH}] \qquad (10)$$ [3]

we may substitute for $C_{pos.\ est.\ ion}$ the relation expressed in:

$$C_{pos.\ est.\ ion} = k_{aff.}/k' \times C_{ester} \times C_H \qquad (11)$$ [4]

and have

$$dx/dt = K_{v(ion)} \times k_{aff.}/k' \times C_{ester} \times C_H \times [C_H \times C_{OH}] \qquad (12)$$

$$= K_v \times C_{ester} \times C_H \times C_H \times C_{OH} \qquad (13)$$

which is the ordinary equation representing the velocity of decomposition of esters by acids. What we determine with esters, for instance in Hemptinne's and Lowenherz's work as expressed in Table III is K_v and not the *more fundamental constant* $K_{v(ion)}$. Now

$$K_v = K_{v(ion)} \times k_{aff.}/k' \qquad (14)$$

and it is obvious that if the basic strength of the ester as expressed in $k_{aff.}$ grows very much smaller, as it undoubtedly does when we go from ethyl acetate to ethyl chloroacetate, $K_{v(ion)}$ *could easily grow very much larger* and *yet* K_v *need not change appreciably or it might even grow smaller*, without the result being in any disagreement whatever with the theory expressed. This means, of course, that determinations simply of the velocity constants K_v of decomposition of such esters do not prove any-

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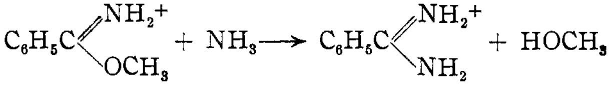
[1] The table is taken from Euler, *Loc. cit.*, p. 412.

[2] Stieglitz, *International Congress of Arts and Science*, St. Louis, 1904, 4, 276 of the report, and *Am. Chem. J.*, 39, 47 (1908).

[3] $C_{pos.\ est.\ ion}$ is a function of x.

[4] k' is the stability constant of the oxonium hydroxide. $k_{aff.}/k'$ may be considered the stability constant of the complex ester ion. Cf. Bredig, *Z. Elektrochem.*, 9, 118 (foot-note).

thing as to the principle at issue. A somewhat stronger base might well give a higher rate of change than a weaker one by virtue of the fact that a larger proportion of the base is present in its active form, the ion, and the real rate of decomposition of the ion may be much smaller than that of an ester giving a smaller velocity constant K_v. The imido esters have the advantage that their affinity constants are easily ascertained and we do not deal with any such unknown quantity at all, and thus we were able to bring what I believe is the first experimental proof of the soundness of the theory. An apt illustration of the correctness of our argument concerning the lack of data for a correct analysis of results like those given in Table III is found in the following facts: the formation of amidines from imido esters, as was stated, is greatly accelerated by the addition of acids or of an ammonium salt and we were able to show that the amidine formation may be considered essentially a function of the concentration of the positive ester ion, proceeding according to

 (9)

$$C_6H_5C\begin{cases}NH_2^+\\OCH_3\end{cases} + NH_3 \longrightarrow C_6H_5C\begin{cases}NH_2^+\\NH_2\end{cases} + HOCH_3 \qquad (9)$$

and

$$dx/dt = K_v \times C_{pos.\ est.\ ion} \times C_{NH_3} \qquad (15)^1$$

Now, if we develop the expression for the concentration of the positive ion of a very weak base like an imido ester in the presence of a much stronger one like ammonium hydroxide we find that:

$$C_{pos.\ est.\ ion} = \frac{C_{ester} \times C_{NH_4^+}}{C_{NH_3}} \times \frac{k_{aff.\ est.}}{k_{aff.\ amm.}} \qquad (16)$$

and by substitution we get:

$$dx/dt = K_{v(ion)} \times \frac{k_{aff.\ est.}}{k_{aff.\ amm.}} \times \frac{C_{ester} \times C_{NH_4^+}}{C_{NH_3}} \times C_{NH_3} \qquad (17)$$

$$= K_{v(ion)} \times \frac{k_{aff.\ est.}}{k_{aff.\ amm.}} \times C_{ester} \times C_{NH_4^+}. \qquad (18)^2$$

Now, imido *ethyl* benzoate forms benzamidine considerably faster than does the *methyl* ester: in both cases the change is from the salt of the positive ion of a weaker base to that of a much stronger one, the amidine, but the *ethyl* ester is the stronger base and yet it reacts the faster and apparently contradicts our theory. A knowledge of the affinity constants shows, however, that it reacts the faster only because by virtue of its being a stronger base it takes a larger proportion of the catalytic agent, the acid, from the ammonium chloride, and forms a proportionally larger concentration of the active component, the ester ion, than does the methyl ester under the same conditions. Calculating with the aid

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[1] $C_{pos.\ est.\ ion}$ is a function of x.

[2] In passing, it may be remarked that this last form shows that the action may be considered one of the ion ammonium acting on the ester, but we believe our original assumption to be the right one for reasons found in the behavior of organic compounds which cannot be elaborated here; it may be said, for instance, that we have found NH_3 and not NH_4^+ to react with ordinary esters to form amides and are carrying out other more crucial experiments on this point. *Vide* Acree, *Am. Chem. J.*, 38, 308. Fitzgerald and Lapworth, *J. Chem. Soc.*, 93, 2163.

of the affinity constants the true *velocities of transformation of the positive ions*, we find the true relation: $K_{v(ion)}$ for the methyl ester is 140/0.434 and for the ethyl ester only 69/0.434.[1] So the true relations resulting from an exact knowledge of all the quantitative constants involved agree perfectly with the fundamental principle given.

This reaction shows other points of great interest: for instance, the fact that the concentration of ammonia cancels out of the mathematical equation leads to the conclusion that the velocity of decomposition is independent of the concentration of ammonia, one of the reacting components.

This peculiar conclusion has been fully verified by experience; the velocity constant is as a matter of experiment almost, although not absolutely, independent of the concentration of ammonia; in the case of the above methyl ester, the constant grows only about 10 per cent. with an increase of 400 per cent. in the concentration of the ammonia. This apparent contradiction with the law of mass action is readily understood if we remember that the concentration of ammonia has two effects which oppose each other; ammonia does accelerate the action in proportion to its mass as required by the law, but it also to the same degree retards the action by depriving the weaker base of the ionizing and therefore catalyzing acid. Within a year Lapworth[2] has made the extremely important discovery that water stands in exactly the same relation to the esters in the catalysis by acids—only then the two bases competing for the acid are two oxonium bases, the ester and water.

And now in conclusion I wish to call attention to one more result with these imido esters which has impressed us very much and which seems to me to throw a very clear light on the whole question of catalysis or acceleration by showing certain limitations to catalytic effects. It was mentioned a moment ago that the velocity of formation of benzamidine from methyl imido benzoate may be expressed as a function of the positive imido ester ion and that it is almost independent of the concentration of the ammonia; but it is not absolutely independent, there is a slight but steady rise in the value of the constants with increasing concentrations of ammonia. All other secondary reactions having been excluded (*e. g.*, for fourfold increase of NH_3, the constants rise gradually from 139/0.434 to 154/0.434) as the cause of this increase by a knowledge of their velocity constants, we suspected that besides the main action of ammonia on the positive ester ion, there is a much slower action of ammonia also on the non-ionized free ester, namely, that we have two simultaneous actions:

$$C_6H_5C(:NH_2^+)OCH_3 + NH_3 \longrightarrow C_6H_5C(:NH_2^+)NH_2 + HOCH_3 \quad (18)$$

and

$$C_6H_5C(:NH)OCH_3 + NH_3 \longrightarrow C_6H_5C(:NH)NH_2 + HOCH_3 \quad (19)$$

We had the more reason to suspect this as we had already found that water, besides decomposing the positive ion of an imido ester at a very high speed, also undoubtedly decomposes the non-ionized ester at a very slow rate.[3] It was found that the experimental results agree very well with this conception of two simultaneous actions in the formation of

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[1] Miss Katharine Blunt's dissertation (1907).

[2] *Loc. cit.*

[3] In this case the products are different. *Vide* Stieglitz, Derby and Schlesinger, *Loc. cit.*

benzamidine and that the velocity constant for the action of ammonia on the positive ester methyl ion at 25° is 325, while that on the ester molecule is only 0.0069.[1] That is, the positive ion is almost 50,000 times as reactive as the non-ionized molecule. It may appear somewhat surprising that such a small constant could still be detected side by side with such an enormous one, the whole action being completed in one to two hours. But we must remember that for the ion action with the enormously high rate of change we have at any moment only minute quantities of the reacting component, *e. g.*, 0.000,005 gram ion at the beginning of a velocity measurement, which is used up at an enormous speed but always formed again instantly by the purely ionic action of imido ester on the ammonium chloride. On the other hand the transformation of the non-ionized molecule has the advantage of relatively high concentrations of each of the reacting components, say 0.05 both for the ammonia and for the free ester at the beginning of an action. With a concentration many thousand times in its favor it is then not surprising to find this very slow action becoming perceptible in careful quantitative work. Now, if we should use a much weaker base still, we might easily find the action with the non-ionized ester taking a *more and more prominent part* in the total change, even if the actual rate of change of the positive ester ion should still be very much the greater. We have recently found such to be the case for the action of ammonia and ammonium chloride on benzoyl urea ester:[2] the velocity constants are so nicely balanced against the affinity constants that the observed changes did not agree even approximately with either conception used alone, *viz.*, that the guanidine formation was due to the action of ammonia on the positive ester ion alone, or on the non-ionized ester alone. But they did agree well with the view that both actions occur simultaneously, the velocity coefficient for the action on the ion being 34.5 and the coefficient for the action on the non-ionized ester being 0.0015, a ratio of 23000 to 1 again. We were exceedingly pleased to find this case because it forms the connecting link with what we have found to be true for the formation of ordinary acid amides from acid esters in the presence of ammonia and ammonium salts:

$$CH_3COOCH_3 + NH_3 \longrightarrow CH_3CONH_2 + HOCH_3 \qquad (20).$$

This action seems to be essentially a function of the ester and ammonia and it is an extremely slow reaction.[3] We can easily understand this case now; the esters as extremely weak oxonium bases must be able to take only the faintest traces of acid from the ammonium chloride in the presence of ammonia and therefore the slow molecular transformation comes to the front as enormously favored by the concentrations of the reacting components. In the case of the actions of acids on esters and water, the esters compete only with an oxonium base of the same order of strength as they are themselves and rather weaker,[4] the oxonium base of water and here the reaction with the ion is again predominant.

These studies then show us a whole range of organic compounds, obviously of the *same type* and *family* but giving reactions which proceed quite

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[1] Mr. Norton is collecting more data on these relations.

[2] J. C. Moore's dissertation (1909).

[3] Unpublished work by J. Stieglitz and Dr. Barnard.

[4] Lapworth, *Loc. cit.*

differently with the imido esters the action of ammonia on the *positive ion* is the essential action and the use of a catalytic agent,[1] an acid is advisable, in fact, necessary; with ordinary esters the action on the ion becomes negligible because the ion simply cannot be produced in sufficient quantity under these conditions and the action *of ammonia on the non-ionized ester becomes the essential action.* The addition of acid as a catalytic agent is *practically ineffective* and therefore inadvisable. But these apparently disconnected results are now easily understood as being perfectly consistent and logical—the one case representing an almost but not quite pure type of one of the *two natural simultaneous reactions*—the enormously rapid action of the ammonia on the *imido ester ion*—and the other case representing the almost pure type of the other simultaneous action, the extremely slow action of ammonia on the non-ionized ester molecule. And the connecting link is found when the adjustment of the affinity and the velocity constants involved bring *both actions out prominently at the same time.* Of course one must then expect every possible class of reactions lying between these extremes. The results show plainly then, I believe, why a catalytic agent will work smoothly in a number of cases, and why it will fail utterly in accelerating actions apparently of exactly the same organic type, *differing only in the numerical value of the physico-chemical constants included in the final expression governing the action of a catalytic agent.* We have been using the imido esters *simply as a kind of magnifying glass* to *measure* all these constants and thus to enable us to recognize some of the general underlying principles which govern catalysis by such chemical agents, as acids, bases and salts.

ON THE BIOCHEMISTRY OF NUCLEIC ACIDS.[2]

BY P. A. LEVENE.

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Life is the most complex phenomenon in nature and its manifestations are innumerable. They all mysteriously arise in the living organism and are all harmoniously centered in it. This, even in its simplest form is the most perfect laboratory, the seat of an infinite number of chemical reactions, none of them interfering with the equilibrium of the others. The substances produced by the most primitive of the living organisms are as large in number as they are varied in their properties. The discoveries of new substances manufactured by the plant or animal cell are not yet exhausted and for ages the chemist dreamed of no better reward for his labors than the finding in tissue juices of a new body with properties hitherto unknown. The living organism was the only retort, vital force the only reaction in his possession that could furnish him with carbon-containing substances. In that sense every chemist in those days was a biological chemist.

In the year 1828 a startling discovery was announced. Wöhler wrote to Berzelius: "I must tell you that I can make urea without the aid of the kidney, or generally without the living organism whether of man or dog," and four years later the divorce of biological and organic

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[1] *Loc. cit.*

[2] Presented at the Second Decennial Celebration of Clark University, Worcester, Mass., September 15, 1909.