

CCLXVII.—*The Action of Nitrous Acid on Amino-compounds. Part III. Dimethylamine, n-Propylamine, and Glycine Ethyl Ester.*

By THOMAS WESTON JOHNS TAYLOR and LESLIE SLATER PRICE.

IN Part I of this series (Taylor, J., 1928, 1099) it was shown that the simplest aliphatic amine, methylamine, reacts with nitrous acid at a rate which is proportional to the product of the concentrations of the methylamine ion, the nitrite ion, and undissociated nitrous acid. This result does not, of course, give any direct information as to the actual mechanism of the reaction, but it rules out many of the hypotheses that were formerly possible, as, for example, that the reaction is the decomposition of methylamine nitrite.

The investigation has been extended to three cases which differ in various ways from the simple case of methylamine, but the results are nevertheless the same and can be summarised in the statement that with these three compounds also the reaction velocity varies as the product $[\text{RNH}_3^+][\text{NO}_2^-][\text{HNO}_2]$.

A. *Dimethylamine.*

Here the amine is secondary and the product a nitrosoamine, whereas in the simple case it is an alcohol.

Method and Materials.—The reaction was investigated at 25° and followed by estimation of the dimethylamine concentration from time to time; preliminary experiments showed this could be done by distilling the base in steam from alkaline solution into a known excess of standard acid, and that the nitrosoamine, even if present in large excess (1.38*N* with 0.084*N*-dimethylamine), has no effect on the accuracy of the titration. Renouf (*Ber.*, 1880, **13**, 2170) states that pure dimethylnitrosoamine shows an alkaline reaction, but we are unable to confirm this.

Dimethylamine hydrochloride was recrystallised twice from chloroform, and an aqueous solution of the free base prepared from this was used. Details as to the other materials and the method will be found in Part I (*loc. cit.*).

Results.—The behaviour towards nitrous acid is exactly parallel to that of methylamine.

0.05*N*-Dimethylamine + 0.05*N*-nitrous acid. There is no observable reaction in a period of two hours.

0.05*N*-Dimethylamine + 0.1*N*-nitrous acid. The mean of a large number of results is given in Table I, together with the velocity coefficient, k (min.⁻¹; normality⁻²), calculated on the assumption that the velocity varies as the product $[(\text{CH}_3)_2\text{NH}_2^+][\text{NO}_2^-][\text{HNO}_2]$;

corrections have been applied for the spontaneous decomposition of the nitrous acid (Part I, p. 1102).

TABLE I.

<i>t</i> , mins.	NHMe ₂ , <i>N</i> .	<i>k</i> .	<i>t</i> , mins.	NHMe ₂ , <i>N</i> .	<i>k</i> .
0	0.05	—	120	0.0425	0.636
30	0.0478	0.624	150	0.0410	0.644
60	0.0458	0.636	180	0.0396	0.656
90	0.0441	0.628		Mean	0.637

0.05*N*-Dimethylamine + 0.1*N*-nitrous acid + 0.05*N*-potassium chloride. The reaction proceeds more slowly in the presence of a neutral salt, as would be expected, since ions of opposite sign are involved. The mean value of *k* from a series of experiments is 0.58.

Influence of excess of nitrite ion or of dimethylamine ion. The reaction is equally accelerated by the presence of either ion at 0.05*N*-concentration. The value of *k* calculated as in Part I (p. 1103) is 0.59, which agrees satisfactorily with its foregoing value in the presence of 0.05*N*-potassium chloride.

0.05*N*-Dimethylamine + 0.15*N*-nitrous acid. The velocity coefficient should be $2 \times 0.637 = 1.274$, since the concentration of free nitrous acid is twice that in the first series of measurements; the mean value found was 1.25.

The reaction is much repressed by the addition of sulphuric acid, which is in agreement with the above conclusion.

B. *n*-Propylamine.

The reaction of nitrous acid with *n*-propylamine is remarkable in that the product consists of 42% of *n*- and 58% of *iso*-propyl alcohol (Linnemann and Siersch, *Annalen*, 1867, **144**, 140; Linnemann, *ibid.*, 1872, **161**, 44; V. Meyer and Forster, *Ber.*, 1876, **9**, 529; Henry, *Compt. rend.*, 1907, **145**, 899). Various views have been advanced in order to account for the formation of these products, but none has any definite experimental support.

Reaction-velocity measurements are capable of discovering whether the products are formed by two independent reactions of different order, since if that were the case the rate of disappearance of the amine could not be expressed by a simple one-term differential equation.

Method and Materials.—The method was exactly the same as that used in the previous cases. *n*-Propylamine hydrochloride was recrystallised several times from water, in which it is very soluble.

Results.—The reaction velocity is proportional to the product $[\text{PrNH}_3^+][\text{NO}_2^-][\text{HNO}_2]$, analogously to the previous cases. There is no sign of two simultaneous reactions of different order. This was

established by studying the reactions shown in Table II, the values of k being calculated as in Part I of this series.

TABLE II.

Reaction mixture.		k .
0.05N-C ₃ H ₇ -NH ₂	+ 0.05N-HNO ₂	No reaction.
" "	+ 0.10N- "	0.69
" "	+ " " + 0.05N-KCl	0.66
" "	+ " " + 0.05N-PrNH ₃ Cl or 0.05N-Ba(NO ₂) ₂	0.66
" "	+ 0.15N- "	1.29

In the light of this result the formation of the two alcohols can be best accounted for by saying that the reactive complex consisting of the three species can decompose in two ways, giving nitrogen, nitrous acid, and either *n*- or *iso*-propyl alcohol. The ratio of the quantities of the two alcohols formed is a measure of the probabilities of the two modes of decomposition. There is, however, no evidence upon which to base any hypothesis as to the structure of the reactive complex, if, indeed, such a complex can be said to have a structure, or as to the reasons why there are two modes of decomposition. The problem can obviously receive no satisfactory solution until the rôle played by the apparently unnecessary molecule of nitrous acid in the reactive complex is understood.

C. Glycine Ethyl Ester.

Here the product of reaction is an aliphatic diazo-compound, and not an alcohol.

Materials.—Throughout the work, glycine ethyl ester was used as its hydrochloride, which had been recrystallised many times from an ethyl-alcoholic solution of hydrogen chloride. Its purity was established by estimating the chloride content by Volhard's method, and the glycine content by the method described below. Reaction mixtures were made up from the hydrochloride and barium nitrite, and thus they all contained barium and chloride ions. It would have been more advantageous to have used the ester sulphate, since the reaction mixture would then have been free from the ions of a neutral salt, but difficulty was met in obtaining analytically pure samples of the sulphate in quantity. The influence of the neutral salt is discussed below. The other materials were the same as those used in the previous cases.

Method.—To devise an analytical scheme for following the progress of the reaction is not simple. After several attempts, the following method was found to be satisfactory. A sample of the reaction mixture containing glycine ester, diazoacetic ester and its decomposition products, and nitrous acid is run into large excess

of baryta solution, and the whole warmed at 40—50° for 20 minutes. During this time the ester present is hydrolysed to free glycine. After cooling, the glycine is estimated by the method used in Part II of this series (Taylor, J., 1928, 1897). The method is not very accurate because the dilution becomes so great during the analysis, if the initial concentration of ester is small, that the end-point of the titration is not sharp; this was overcome to a large extent by making dilute solutions of analytically pure glycine, adding neutralised formaldehyde, phenolphthalein, and the equivalent amount of standard baryta solution, and using the solutions so prepared as colour standards in the titrations.

Since esters of amino-acids are not very stable in aqueous solution, the reaction mixtures were not made from a stock solution, but by weighing the necessary quantity of pure solid. The results are not vitiated by hydrolysis of the ester during the reaction, since Curtius and Goebel (*J. pr. Chem.*, 1888, **37**, 160) have shown that hydrolysis by dilute acids is slow.

The reaction velocities were measured at 25°, and the mixtures were covered with a layer of medicinal paraffin in order to stabilise the nitrous acid.

Results.—The general behaviour can be seen from the curves in Fig. 1. There is a rapid reaction between 0.05*N*-glycine ester and 0.05*N*-nitrous acid; with twice this concentration of nitrous acid, the reaction is so rapid that measurement is difficult by the method used. The behaviour is, at first sight, quite unlike that of methylamine.

The velocity of reaction is lowered by the addition of a neutral salt (1.0*N*-potassium chloride); hence ions of opposite sign are most probably involved in the reaction. Addition of mineral acid also lowers the velocity; in the presence of 1.90*N*-sulphuric acid the reaction does not proceed at all, as the following results show.

<i>t</i> (min.)	0	3.5	16.5	31	51	106	122
Glycine ester,							
<i>N</i>	0.05	0.0502	0.0495	0.0495	0.0502	0.0501	0.0495

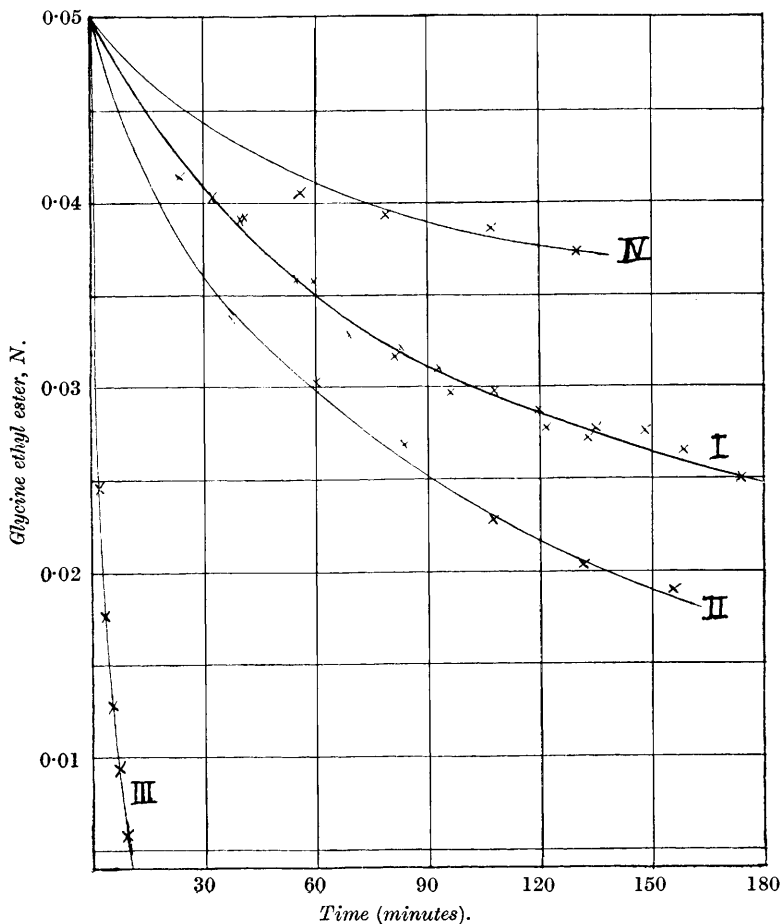
Hence the nitrite ion is one of the reacting ions, since this is the only ion of which the concentration could possibly become vanishingly small in the presence of excess of mineral acid.

Thus a possible hypothesis is that the reaction velocity varies as the product $[\text{GEH}^+][\text{NO}_2^-]$.* The results shown in Curve I of Fig. 1 should then give a bimolecular velocity coefficient; this, however, is not the case, as is seen from Table III, in which α is

* GE is used throughout as symbol for glycine ethyl ester and GEH⁺ for the kation.

the normality of glycine ester and of barium nitrite at time t (min.), k_2 is the bimolecular coefficient, and k_3 is a termolecular coefficient (see below).

FIG. 1.



Curve I. 0.05N-Glycine ethyl ester + 0.05N-barium nitrite.

„ II. „ „ + 0.10N „ „
 „ III. „ „ + 0.05N „ „ + 0.05N-nitrous acid.
 „ IV. „ „ + „ „ „ + 1.0N-KCl.

TABLE III.

t .	x .	k_2 .	k_3 .	t .	x .	k_2 .	k_3 .
0	0.05	—	—	120	0.0286	0.125	3.42
30	0.0408	0.150	3.34	150	0.0265	0.118	3.41
60	0.0350	0.143	3.47	180	0.0248	0.113	3.41
90	0.0312	0.134	3.47				

The fall in the values of k_2 cannot be attributed to spontaneous decomposition of nitrous acid, since there is hardly any such free acid in the mixture. The results, however, give a very constant coefficient for a reaction of the third order.

Now glycine ester nitrite is the salt of a weak acid and a weak base ($K_a = 4 \times 10^{-4}$, Blanchard, Landolt-Börnstein, 5th Edn.; $K_b = 9.7 \times 10^{-8}$, Veley, J., 1908, **93**, 662), and hence there is an appreciable concentration of undissociated acid in dilute solution; on the analogy of the previous cases, the most probable third molecular species involved is nitrous acid. As in those cases, only one molecule of nitrous acid disappears for each molecule of glycine ester, since in the mixture 0.05*N*-barium nitrite + 0.1*N*-glycine ester the concentration of the latter fell to the constant value 0.05*N*.

For the equimolecular mixture, if the concentration of glycine ester nitrite at time t is x , and the fraction hydrolysed to free ester and acid is f , from the above values of K_a and K_b and with $K_w = 1.27 \times 10^{-14}$ (Michaelis, "Hydrogen Ion Concentration," 1926), f is found to be 0.0178, and is independent of x . On the assumption that the reaction velocity varies as the product $[\text{GEH}^+][\text{NO}_2^-][\text{HNO}_2]$, the equation for the reaction should be

$$- dx/dt = kx^3(1 - f)^2f,$$

a simple third-order reaction, which is the behaviour found. The value of k in this equation can be obtained from the mean value of k_3 in Table III and from the value of f ; it is 1.98×10^2 (min.^{-1} ; normality⁻²).

The truth of the above assumption is supported by the results shown by the other curves.

0.05*N*-Glycine ester hydrochloride + 0.1*N*-barium nitrite. Let the concentration of glycine ester be a initially, and x at time t , and let a fraction f_2 be salt-hydrolysed. Then we have at time t ,

$$K_b = (1 - f_2)x[\text{OH}^-]/f_2x \text{ and } K_a = (a + x - f_2x)[\text{H}^+]/f_2x.$$

Multiplying, and inserting K_w for $[\text{OH}^-][\text{H}^+]$, we have

$$K_a K_b / K_w = (1 - f_2)x(a + x - f_2x) / f_2^2 x^2.$$

If, as an approximation, f_2x is neglected in comparison with $a + x$, and f_2 in comparison with unity,

$$f_2x = \sqrt{x(a + x)K_w / K_a K_b}.$$

On the above assumption,

$$- dx/dt = k[\text{GEH}^+][\text{NO}_2^-][\text{HNO}_2] = k(x \cdot \overline{a + x})^{\frac{3}{2}} (K_w / K_a K_b)^{\frac{1}{2}}.$$

Integration between times 0 and t gives

$$k = \frac{2}{a^{\frac{3}{2}}} \sqrt{\frac{K_a K_b}{K_w}} \left(\frac{1}{\sqrt{x}} - \frac{1}{\sqrt{a + x}} - \frac{1}{\sqrt{a}} + \frac{1}{\sqrt{2a}} \right).$$

Values of k calculated from this expression are :

t	0	30	60	90	100
x	0.05	0.0359	0.0298	0.0255	0.0221
$k \times 10^{-2}$	—	1.88	1.60	1.52	1.44

The agreement with the value of k in the previous series is sufficiently good; the values fall with time, but it can be shown that the approximation introduced above will have this effect. The value of $k \times 10^{-2}$ so obtained would be expected to be smaller than 1.98, since there is double the amount of barium nitrite and the salt effect of this will diminish the reaction velocity.

0.05N-Glycine ester hydrochloride + 0.05N-barium nitrite + 0.05N-nitrous acid (Curve III). The reaction proceeds extremely rapidly. If the value of k is taken as 198, the times taken for the concentration of glycine ester to fall to the observed values can be calculated on the present assumption and compared with the actual times, thus

x	0.05	0.0246	0.0176	0.0128
t (obs.)	0	2.0	3.5	5.0 mins.
t (calc.)	—	2.1	3.7	5.9 ,,

In view of the inaccuracy involved in observing the times of making the mixture and withdrawing samples, the agreement is good.

0.05N-Glycine ester hydrochloride + 0.05N-barium nitrite + 1.0N-potassium chloride. If the above assumption is correct, the salt effect on the reaction velocity will be of two kinds, the true salt effect (Brönsted's primary effect), and the effect arising from changes in the value of K_a , K_b , and K_w owing to the increased ionic strength (Brönsted's secondary effect). The magnitude of the second effect can be estimated: Harned and James (*J. Physical Chem.*, 1926, **30**, 1060) have measured the necessary value of K_w , and Sidgwick and Woodward (unpublished research) give a value for the influence of neutral salt on the dissociation of acetic acid. If it is assumed that the change in K_a and K_b is of the same magnitude as for acetic acid, the secondary effect will be to diminish the velocity coefficient by 10.9%; the observed diminution is of the order of 53%, so that there is a marked negative primary salt-effect.

Discussion.—The results indicate that in this reaction the velocity is proportional to the product of the concentrations of the glycine ester ion, the nitrite ion, and nitrous acid, and is analogous to the reaction with methylamine, except in that the velocity coefficient is about 200 times as great. There are two reasons which may underlie this difference. (a) The presence of the carboxyl group in the α -position in the ester may largely increase the probability of the formation of the reactive complex; this may arise from the formation of a co-ordinate link by the doubly-bound oxygen atom.

(b) If in the reaction with methylamine an aliphatic diazo-compound is not an intermediate, then the two reactive complexes are decomposing in entirely different ways, the energies of activation could be quite different, and no parallelism would be expected. On the other hand, the fact that the two reactions both need the same types of molecular species suggests that they are similar in mechanism.

THE DYSON PERRINS LABORATORY,
OXFORD.

[Received, July 9th, 1929.]
