KINETICS AND MECHANISM OF REACTION OF N-(2,4-DINITROPHENYL)PYRIDINIUM CHLORIDE WITH PIPERIDINE. DETERMINATION OF RATE CONSTANTS AND KINETIC EQUATIONS OF INDIVIDUAL REACTION STEPS

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Kinetic equations and rate constants have been determined for reaction of the compound *I* with piperidine giving the intermediate *V*, for the reverse reaction of the aldehyde *VII* with piperidine giving the intermediate *IV*, for the reaction of the intermediate *IV* with piperidine giving the product *VI*, and for the subsequent reaction of the compound *VI* with OH^- ion giving the aldehyde *VIII*. Reaction mechanisms have been suggested for these reactions, and the difference is discussed between the course of reactions of the compound *I* with piperidine and aromatic amines.

Previous part[1] dealt mainly with isolation and identification of the reaction products and determination of the overall reaction mechanism represented in Scheme 1. This part contains the determination of kinetic equations and rate constants of individual reaction steps and their detailed mechanism.

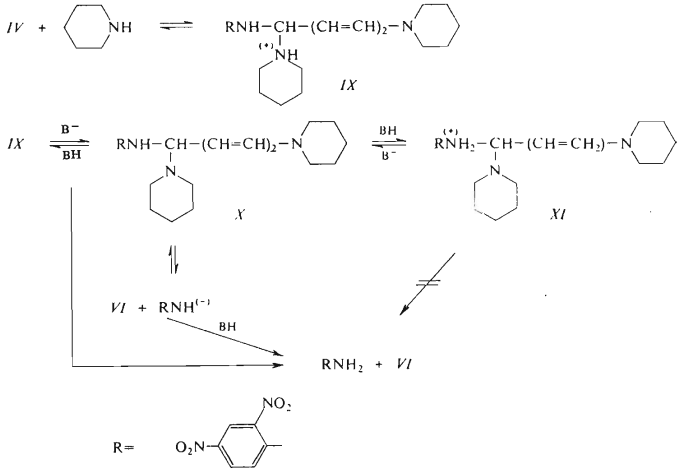
EXPERIMENTAL

Kinetics measurements were carried out with the same chemicals as those used in the previous part, the reaction conditions being: 50% by vol. aqueous ethanol, temperature 20°C, ionic strength 0·2 adjusted by addition of potassium chloride, pH range 8 to 11 adjusted by N-ethylpiperidine, triethylamine and phosphate buffers. pH of solutions was checked immediately after finishing the reaction, wherefor a pH-meter 4 (Radiometer, Copenhagen) and a glass and calomel electrodes (of the same firm) were used. The reactions having half-lives longer than 5 s were measured with the use of a Zeiss VSU-2P spectrophotometer, for faster reactions a Durrum Stopped-Flow Spectrophotometer Model D-110 was used. The reactions were followed at the wavelength 420 nm (*VI*), 550 nm (*V*) and 460 nm (*IV*). Experimental rate constants were obtained from the time dependence of log $(E_t - E_\infty)$ or log $(E_\infty - E_t)$ (the slower reactions) or from the half-life values read from the screen of the Durrum apparatus according to the relation $k = 0{\cdot}693/t_{1/2}$ (the faster reactions).

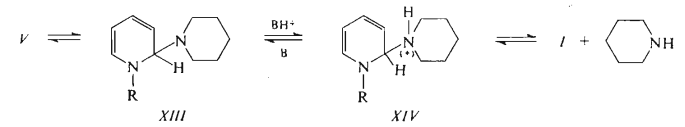
Scheme 1

RESULTS AND DISCUSSION

Study of reactions of the intermediates *IV* and *V* with piperidine leading to formation of the product *VI* and their reverse reactions have the key importance for determination of the kinetic equations and rate constants. For measurements of the reaction (*IV* and *V*) → *VI* either the compound *IV* or the compound *I* was used as the starting substance. The compound *I* was used under those conditions, where the rate of formation of the intermediates (*IV* and *V*) was much higher than that of the subsequent reaction, so that the concentration of the intermediates reached almost 100%. Under those conditions it was possible to follow both the reactions separately using the



SCHEME 2



SCHEME 3

Durrum apparatus with suitably adjusted time constants. Theoretically both compounds *IV* and *V* can react with piperidine, however, practically only the former compound reacts under these conditions, which was confirmed also by informative experiments in previous part[1]. Rate of this reaction is expressed by kinetic equation (*1*) where K_a (*IV*) equals 8·85.

$$v = k_{exp}([IV] + [V]) = k_1[IV][(CH_2)_5NH] =$$
$$= k_1[H^+][(CH_2)_5NH]([IV] + [V])/(K_a + [H^+]), \qquad (1)$$

$$k_1 = k_{01} + k_2[RO^-]. \qquad (2)$$

Dependence of k_1 on RO^- concentration is linear (Eq. (*2*)). The slope of this straight line gives the value of the rate constant $k_2 = 3{\cdot}35 \cdot 10^4\ l^2\ mol^{-2}\ s^{-1}$ of the lyate ion-catalyzed reaction. Extrapolation to $[RO^-] = 0$ gave the rate constant $k_{01} = 24{\cdot}6\ l\ mol^{-1}\ s^{-1}$ of the non-catalyzed reaction. The mechanism given in Scheme 2 can be considered for this reaction. A mechanism involving the intermediate *XI* is out of question, because the nitrogen atom of the 2,4-dinitroaniline residue (in the compound *XI*) is by about 14 orders of magnitude less basic than that of the piperidine residue, so that the rate constant of decomposition of the compound *XI* into *VI* and 2,4-dinitroaniline should have to be greater than $10^{15}\ s^{-1}$. The conversion $IV \rightarrow IX$ can be excluded as the rate determining step of the non-catalyzed reaction, as it would be difficult to explain catalytic effect of the lyate ion in such a case. The most likely pathway of the lyate ion-catalyzed reaction is that involving the rate-determining splitting of the compound *X* into *VI* and 2,4-dinitroaniline anion. Direct conversion $IX \rightarrow VI$ involving a proton-transfer form piperidine nitrogen atom to dinitroaniline nitrogen atom mediated by solvent molecules can be considered for the non-catalyzed (or solvent-catalyzed) reaction.

The reaction product *VI* is converted into the compound *VIII* at much higher lyate ion concentration. Kinetics of this reaction was followed in the lyate ion concentration range 0·001 to 0·1 mol/l. The dependence of the rate constant on RO^- ion concentration was linear up to the concentration $1{\cdot}5 \cdot 10^{-2}$ mol/l, then the value of angular coefficient gradually decreased. The rate constant calculated from the slope of the linear part has the value $k_{OH} = 0{\cdot}175\ l\ mol^{-1}\ s^{-1}$.

Mechanism of the reverse reaction $V \rightarrow I$ (Scheme 3) can be considered to be analogous to that found in the study of reaction of the compound *I* with aniline[2] (in the opposite direction). Informative experiments in the first part showed that the compound *I* is the predominant primary product, being rapidly converted into the aldehyde *VII* at higher pH values (>10). Therefore, the found kinetic data hold for the shown mechanism (Scheme 3) involving the formation of the compound *I* and not for the conversion $IV \rightarrow VII$. The reaction was followed in N-ethylpiperidine and

triethylamine buffers and in mixtures of primary and secondary phosphates. The reaction rate is given in Eq. (3).

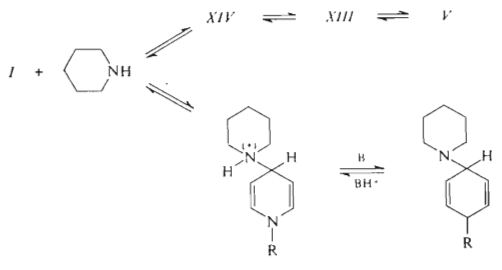
$$v = k_{exp}([IV] + [V]) = k_3[V] = k_3 K_a([IV] + [V])/(K_a + [H^+]) \qquad (3)$$

The rate constant k_3 increases linearly with increasing concentration of ethylpiperidinium or triethylammonium chloride (Eq. (4)). The values of constants were obtained

$$k_3 = k_{03} + k_4[BH^+] \qquad (4)$$

by usual way from the slope and intercept. The rate constant $k_{03} = 2{\cdot}19 \,.\, 10^{-3}\ s^{-1}$ for non-catalyzed (resp. solvent-catalyzed) reaction and $k_4 = 3{\cdot}39 \,.\, 10^{-2}$ and $1{\cdot}60 \,.\, 10^{-2}\ l\ mol^{-1}\ s^{-1}$ for N-ethylpiperidine- and triethylamine-catalyzed reactions were found, respectively. Addition of the proton to the intermediate *XIII* (Scheme 3) is the rate-determining step, triethylamonium resp. N-ethylpiperidinium ions and solvent molecules acting as acids. This is in accordance with the mechanism found for the reaction of the compound *I* with aniline[2], where the reverse reaction (pH > 8) involved rate-determining splitting off of the proton from the protonated intermediate (corresponding to the compound *XIX*) by action of lyate ions or molecules of the amines.

When studying the reaction in phosphate buffers we found (by extrapolation to zero buffer concentration) the rate constant value $1 \,.\, 10^{-2}\ s^{-1}$ which is 4·6 times greater than the k_{03} value found in the above given buffers. The magnitude of this constant was independent of concentration of the acidic buffer component. It means that in phosphate buffers the protonation of the compound *XIII* is inasmuch fast that the



SCHEME 4

cyclization $V \rightarrow XIII$ becomes the rate-determining step. This fact again agrees with the mechanism of the reaction of the compound *I* with aniline where pyridine ring opening became rate-limiting at lower pH values. However, it was surprising to find that, in this case, the rate constant k_3 increased practically linearly with increasing concentration of secondary phosphate. Here obviously some specific salt effect is operating which was not further studied.

Kinetics of formation of the compound *V* from *I* (Scheme 3) was followed, on the one hand, at relatively low piperidine concentrations and low pH values, where the rate of formation of the intermediates (*IV* and *V*) and the rate of conversion of the compound *IV* into *VI* were comparable and, on the other hand, at relatively high piperidine concentrations where the rate of formation of the compound *V* is many times higher than the subsequent reaction. In the first case the reaction constant k_4 of Eq. (5) was calculated[3] from the measured t_{max} value according to Eq. (6) where k_{exp} means the rate constant of the reaction $IV \rightarrow VI$ determined before (see Eq. (1)).

$$v = k_4[I] = k_5[I][(CH_2)_5NH], \tag{5}$$

$$t_{max} = (1/(k_4 - k_{exp})) \ln (k_4/k_{exp}), \tag{6}$$

$$k_5 = k_6[RO^-] + k_7[(CH_2)_5NH]. \tag{7}$$

Under the conditions used k_5 depends on concentration of both piperidine and RO^- ion (Eq. (7)), *i.e.* splitting off of the proton from the intermediate *XIV* is the rate-determining step. The constants k_6 and k_7 were evaluated graphically from the dependence of k_5 on piperidine concentration at a constant pH ($[RO^-]$ = const.) according to Eq. (7): $k_6 = 7{\cdot}40 \,.\, 10^4\, l^2\, mol^{-2}\, s^{-1}$, $k_7 = 1{\cdot}89 \,.\, 10^2\, l^2\, mol^{-2}\, s^{-1}$. At higher piperidine concentrations the rate of formation of the intermediates (*IV* and *V*) is much higher than that of subsequent formation of the product *VI*, so that the both reactions can be studied separately. The rate constant k_4 values are given in Table I. At a constant concentration of piperidinium chloride the measured rate constant k_4 should increase with the square of piperidine concentration. From Table I it can be seen that the constant k_4 increases more and more slowly till it becomes practically independent of piperidine concentration. This limit concentration decreases with increasing pH value. At the same time a new absorption band at about 400 nm is formed. The half-life of the formation of the new compound corresponding to this absorption band must be substantially lower than 0·5 millisecond, as it could not be trapped on the screen of the Durrum apparatus. The initial extinction of the new substance gradually increases in the same way as the reaction order with respect to piperidine decreases. In the reaction course the extinction at λ 400 nm decreases proportionally to the concentration increase of the inter-

mediates (*IV* and *V*). This observation can be explained by a combined action of two factors. With increasing concentration of both piperidine and lyate ion the conversion *XIV* → *XIII* is inasmuch accelerated that the reaction of the compound *I* with piperidine becomes rate-limiting, so that neither piperidine nor lyate ion are further significant as catalysts. At the same time the reversible side reaction of the compound *I* with piperidine (Scheme 4) giving probably the products *XV* and *XVI* becomes increasingly significant.

Besides the compounds *XV* and *XVI* it is possible to consider other adducts of the compound *I* with piperidine. Bernasconi[3] studying the reaction of 1,3,5-trinitrobenzene with piperidine found that a side product is formed which was believed to be a product of addition of piperidine to one of the nitro groups. Such an addition product does not, however, absorb in the region about 400 nm. A further possibility is represented by a formation of charge-transfer complex, but its stability in 50% ethanol cannot be so great to correspond to the found kinetic relations; also the dependence on pH could not be explained in this case.

Formation of such compounds where the addition takes place predominantly in position 4 was proved *e.g.* in the reaction of pyridinium ions with cyanide ion[4]. This phenomenon results in decrease of concentration of the compound *I* and, hence, also decrease of the constant k_4. At the piperidine concentrations where k_4 reaches its limit value the equilibrium is shifted predominantly to the side of the products *XV* and *XVI*. The concentration of the compound *I* is inversely proportional to that of piperidine, the rate of its conversion into the compound *XIV*, however, is directly proportional to piperidine concentration, so that the rate constant k_4 becomes independent of piperidine concentration. The higher the pH value is, the more the equilibrium is shifted in favour of the neutral compound *XVI*, and the concentration

TABLE I

Dependence of Rate Constant k_4 (s^{-1}) on Concentration of Piperidine Hydrochloride [A], and Piperidine [B]

[A]	[B]	k_4	[A]	[B]	k_4
0·20	0·075	0·924	0·10	0·075	0·722
0·20	0·150	2·46	0·10	0·150	2·66
0·20	0·225	4·76	0·10	0·300	6·93
0·20	0·300	6·93	0·10	0·450	11·53
0·20	0·450	13·05	0·10	0·600	13·05
0·20	0·600	19·25	0·05	0·450	0·988
0·20	0·750	19·80	0·05	0·600	1·020
0·20	0·900	21·00			

of the compound *I* is lower and lower. Therefore, at higher pH values the limit value of k_4 is sooner reached, and its final value is smaller.

The reaction of the aldehyde *VII* with piperidine giving the intermediate *IV* belongs to a group of reactions of aldehydes with amines, and it can be supposed to have similar mechanism. Kinetics of this reaction was followed under the conditions of the conversion *VII* → *I* being slower than formation of the compound *IV* by more than one order of magnitude, and, on the contrary, the subsequent reaction (which gives the product *VI*) being faster by more than one order of magnitude. Under these conditions, soon after the beginning of reaction, the steady state is reached, so that the rate constant of the reaction *VII* → *IV* can be determined experimentally from the time dependence of extinction of the product *VI*. The constant is first order in piperidine and does not depend on pH so that the kinetic equation has the form (*8*). The calculated value of k_8 is $4{\cdot}54 \cdot 10^{-2}$ l mol^{-1} s^{-1}.

$$v = k_8[VII]\,[(CH_2)_5NH]\,. \qquad (8)$$

From the determined values of rate constants it follows that formation of the intermediates (*IV* and *V*) from the compound *I* is much faster than that from the aldehyde *VII* under all conditions. From these rates and known[5] equilibrium constant *I* ⇌ *VII* it follows that, under the conditions used, the reaction (*IV* and *V*) → *I* is much faster than that giving the compound *VII*. Thus the interpretation of the results of kinetic measurements of the reverse reaction by Scheme 3 is wholly justifiable.

One of the aims of this work was to explain the reasons of different behaviour of aromatic and non-aromatic amines in reaction with N-(2,4-dinitrophenyl)pyridinium chloride (*I*). N-(5-anilino-2,4-pentadienylidene)aniline (*II*) is practically the only product in reaction with aniline[6]. The primary intermediate reacts rapidly with a further aniline molecule, and its concentration is so low that it cannot even be traced spectrophotometrically. In reaction with aliphatic and alicyclic amines the intermediate is formed much faster than in the reaction with aniline, because these amines are stronger nucleophiles. However, the subsequent reaction is not accelerated, as the intermediate formed is much less reactive than that from aniline. Therefore, in the course of the reaction the intermediate is accumulated and can be isolated under suitable conditions in relatively high yield. The fact that in reactions of the compound *I* with aliphatic amines the substances of the type *II* were not isolated is caused by their much less tendency to crystallization than in the case of aromatic amines. The reaction product of the compound *I* and methylamine underwent ring closure (in the reaction mixture during reaction) to give N-methylpyridinium salt which was the final reaction product[7]. The products formed by reaction of the compound *I* with two molecules of secondary amine exist only in the form of amonium

ions of the type *VI*, so that they cannot undergo cyclization. However, a subsequent reaction with OH^- can be significant leading to monoaldehydes of the type *VIII* or even to glutaconic aldehyde.

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