KINETICS AND MECHANISM OF REACTION OF N-(2,4-DINITROPHENYL)PYRIDINIUM CHLORIDE WITH PIPERIDINE. DETERMINATION OF REACTION PRODUCTS AND MECHANISM

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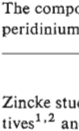
In mixture piperidine-piperidinium chloride in 50% by vol. ethanol N-(2,4-dinitrophenyl)pyridinium chloride (*I*) reacts with piperidine to give N-(2,4-dinitrophenyl)-5-piperidino-2,4-pentadienylideneimine (*V*) as intermediate, or it reacts with OH^- ion to give 5-(2,4-dinitrophenylamino)-2,4-pentadienal (*VII*) which reacts with piperidine to give the protonated intermediate *IV*. The both reactions are reversible. The reaction $V \rightleftharpoons I$ is faster under all reaction conditions. The compound *IV* reacts further with piperidine to give N-(5-piperidino-2,4-pentadienylidene)piperidinium chloride (*VI*) as the main reaction product.

Zincke studied the reactions of N-(2,4-dinitrophenyl)pyridinium chloride (*I*) with aniline derivatives[1,2] and N-methylaniline[3]. The reaction of the compound *I* with aniline produces N-phenyl-5-anilino-2,4-pentadienylideneimonium chloride (*IIa*) and its conjugated base which further undergoes ring-closure[1] to give N-phenylpyridinium chloride with simultaneous splitting off of an aniline molecule. The reaction of the compound *I* with N-methylaniline produces the imonium salt *IIb* which cannot undergo cyclization (Eq. (*A*)).



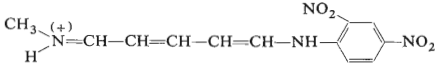
$$Cl^- + 2\,R^1R^2NH \rightarrow [R^1R^2N{=}CH{-}(CH{=}CH)_2{-}NR^1R^2]^{(+)}\,Cl^- + RNH_2 \qquad (A)$$

I *IIa–c*

R = 2,4-$(O_2N)_2C_6H_3$

IIa; $R^1 = C_6H_5$, $R^2 = H$
IIb; $R^1 = C_6H_5$, $R^2 = CH_3$
IIc; $R^1 = CH_3$, $R^2 = H$

Zincke tried to apply this reaction also to primary and secondary aliphatic amines[2]. From reaction of the compound *I* with methylamine he obtained a dark-red salt to which he ascribed the structure *III*. This intermediate gave dinitroaniline and N-methylpyridinium chloride on further reaction with another molecule of methylamine. Obviously this compound is formed by cyclization of the conjugated base of the primarily formed amonium salt *IIc*. The reaction with dimethylaniline gave another product which was not identified by Zincke and probably not even isolated. From this fact Zincke concluded that the reaction course is different in this case.



III

We have not found any further published works concerning the reaction of the compound *I* with aliphatic amines in available literature. As we do not know any reason why this reaction should not take the same course as that with aromatic amines, we decided to study its mechanism using the reaction of the compound *I* with piperidine. The work is divided into two parts: in this one isolation and identification of the reaction products and determination of the overall mechanism are described. Subsequent communication deals with the rate constants of the individual reaction steps and corresponding kinetic equations.

EXPERIMENTAL

N-(2,4-Dinitrophenyl)pyridinium chloride (*I*) and 5-(2,4-dinitrophenylamino)-2,4-pentadienal (*VII*) were prepared according to known procedures[1,2,4,5]. The other chemicals used were commercial reagents of analytical grade (Lachema, Brno).

Synthesis of Reaction Products

N-(2,4-*Dinitrophenyl*)-5-*piperidino*-2,4-*pentadienylideneiminium chloride* (IV). A mixture of 3 ml 1M piperidine hydrochloride solution and 2 ml 1M piperidine solution was injected into a mixture of 5 ml 0·25M solution of the compound *I* in 50% by vol. ethanol and 3 ml 1M piperidine hydrochloride solution in the same solvent. After 10 s the reaction mixture was acidified with 2 ml 2M-HCl and heated to about 60°C. After cooling the precipitated red crystals of the compound *IV* were collected by suction, washed with a mixture of 5 ml 96% ethanol and 0·2 ml 1M-HCl and dried in a desiccator. Yield 0·367 g (74% calculated on the compound *I*). Crystallization from 96% ethanol containing about 5% 1M-HCl gave a product melting at 140—141°C. For $C_{16}H_{19}N_4O_4Cl$ (366·79) calculated: 52·4% C, 5·2% H, 15·3% N; found: 52·3% C, 5·3% H, 15·2% N.

N-(5-*Piperidino*-2,4-*pentadienylidene*)*piperidinium chloride* (VI). A mixture of 100 ml 0·25M solution of the compound *I* in 50% ethanol and 10 ml 1M piperidine hydrochloride in the same solvent was added drop by drop to a mixture of 70 ml 1M piperidine hydrochloride and 70 ml 1M piperidine (both in 50% ethanol, too) during half an hour. Then the reaction mixture was acidified with 1M-HCl and the compound *VI* was isolated by repeated extraction with chloroform. Combined chloroform extracts were dried with sodium sulphate and chloroform was distilled off in vacuum. Yield of the raw product was 5·71 g (85%). This product was purified by dissolving 0·5 g in minimum amount of ethyl acetate and chromatography through an alumina column (4 × 30 cm, activity II according to Brockman) using the same solvent as eluent. The purified product melted within 81—88°C. For $C_{15}H_{25}N_2Cl$ (268·81) calculated: 67·0% C, 9·4% H; found: 67·80% C, 9·35% H.

5-*Piperidino*-2,4-*pentadienal* (VIII). The raw product *VI* (2 g) was dissolved in 100 ml 0·1M-Na_3PO_4 in 20% ethanol. After four hours the compound *VIII* was extracted with benzene which

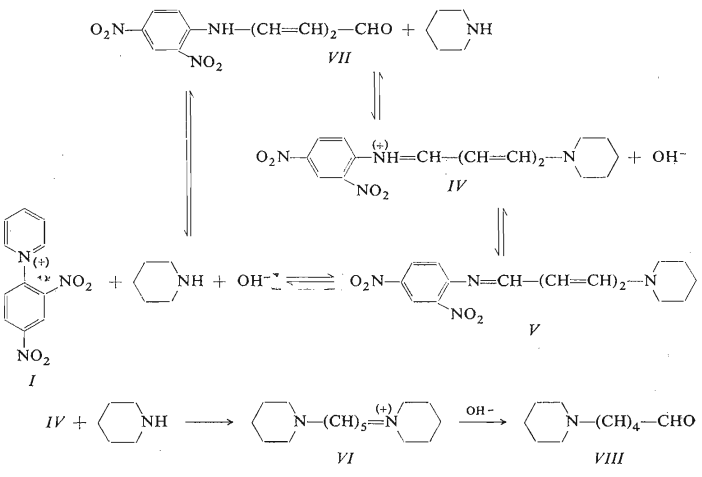
was then distilled off in vacuum. Yield of the compound *VIII* was 1·23 g (45% calculated on the compound *I*). M.p. 79—80°C. For $C_{10}H_{15}NO$ (165·20) calculated: 72·7% C, 9·2% H, 8·5% N; found: 72·2% C, 9·0% H, 8·8% N.

Spectrophotometric Measurements

^{1}H NMR *spectra* were measured with the use of a Tesla BS 487-B apparatus at 80 MHz at room temperature. Saturated solutions of the compounds in deuteriochloroform were used for the measurements containing hexamethyldisiloxane as an internal standard (9·95τ). In the case of the compound *VI* the spectrum in deuteriochloroform could not be simply interpreted. Therefore, spectrum of 10% solution of the same compound was measured in dimethyl sulphoxide using the solvent as internal standard (7·5τ).

Electronic spectra of the compounds *IV*, *VI*, *VII*, *VIII* and anion of the compound *VII* were measured with a Unicam SP 800 spectrophotometer at 20°C and are given in Fig. 1. The spectrum of the compound *V* was not measured because this substance was transformed relatively quickly ($t_{1/2} < 5$ min) into the compound *VII* resp. its anion. Electronic spectrum of the compound *V* is, however, very similar to that of the compound *VII* in both its character and the values of extinction coefficients. The difference in exctinction coefficients at λ_{max} 390 and 550 nm is maximum 5%.

Course of the reactions was followed by measuring the electronic spectra of the reaction solutions in 50% aqueous ethanol at 20°C. Conversion of the compound *I* (Scheme 1) resp. *VII* into a mixture of the intermediates *IV* and *V* and further to *VI* was carried out in mixtures of piperidine and its hydrochloride of various concentrations and ratios. The reverse reaction of the inter-



SCHEME 1

mediates *IV* and *V* into *I* and *VII* was measured in N-ethylpiperidinium and phosphate buffers (mixture of primary and secondary phosphates). The conversion of the compound *VI* into the compound *VIII* was followed spectrophotometrically in solution of sodium hydroxide in 50% ethanol in the range of concentrations 0·001 to 0·1M. The concentration changes of the compound *V* during the reactions of the compound *I* resp. *VI* with piperidine were followed with the use of a Zeiss VSU 2P spectrophotometer at λ 550 nm. The other reactions were studied with the use of the Unicam SP 800: the formation of the compound *VI* in the range 380 to 600 nm and conversion of the compound *VI* into *VIII* in the range 350 to 450 nm.

The pK_a *value* of N-(2,4-dinitrophenyl)-5-piperidino-2,4-pentadienylideneimonium chloride (*IV*) was determined spectrophotometrically. The time dependence of extinction of $2 . 10^{-5}$M solution of the compound *IV* was measured in N-ethylpiperidinium and phosphate buffers with ionic strength 0·2 at 20°C at 550 nm. The extinction values were extrapolated for zero time. Extinction of the protonated form was determined at pH 4, that of the unprotonated form *V* had to be determined by iteration method, because the compound *V* rapidly changes at higher pH values (>10·5), so that the extrapolation of the values measured to zero time would have been subject to a large error. The equation $pK_a = pH + \log((E_B - E)/(E - E_{BH+}))$ was used for calculation[6].

RESULTS AND DISCUSSION

Scheme 1 gives the reaction mechanism of action of piperidine on the compound *I* in 50% by vol. ethanol under the presence of piperidine hydrochloride.

Structures of the intermediate *IV*, product *VI* and aldehyde *VIII* were confirmed by the values of chemical shifts and coupling constants of the protons from NMR spectra. All the three compounds showed peaks about 6·7τ and 8·5τ corresponding to the protons of piperidine nuclei and, in the case of the compound *IV*, three spin-coupled peaks at 1·35τ (doublet), 1·73τ (double doublet) and 2·9τ (doublet) of the protons in positions 3, 5 and 6 of the aromatic nucleus, respectively. Spectra of the compounds *IV* and *VIII* showed peaks of five different protons of an unsaturated carbon chain split into doublets (terminal C—H groups) and double doublets. The symmetrical compound *VI* showed the peaks corresponding to only three different types of protons of an unsaturated carbon chain as it was expected.

Formation of the aldehyde *VII* from the compound *I* is independent of piperidine concentration; kinetics of this reaction was studied previously[7]. The reaction is reversible; at lower pH values the rate of formation of the aldehyde is second order in OH^- concentration; at higher pH values (>10) the reaction order gradually decreases to the value of 1. The compound *VI* is the final and practically the only product of the reaction of the compound *I* with piperidine under the reaction conditions used (pH 8 to 11). This compound *VI* reacts with OH^- ion to give the compound *VIII*, but the reaction is practically significant first at OH^- concentrations higher by several orders of magnitude.

In contrast to the reaction of the compound *I* with aromatic amines[1,2,5], a relatively great amount of the intermediates (*IV* and *V*) is formed in the course of the reaction

investigated in all the experiments. Time dependence of extinction of the product *VI* has an S-shape typical for a system of consecutive competitive reactions. The transient increase in concentration of the intermediates *IV* and *V* (Fig. 2) can be seen even by naked eye. The colour of the reaction product first turns to orange-red (pH < 9; the compound *IV* has pK_a 8·85) or purple (the compound *V*), and then the reaction solution gradually turns yellow (the compound *VI*). The maximum concentration of the intermediates increases with both piperidine concentration and pH (Fig. 2). In optimum cases it reaches almost 100%.

The reaction product *VI* is formed practically quantitatively also by reaction of the aldehyde *VII* with piperidine. In this case, besides the way through the compound *I*, the direct reaction of the aldehyde *VII* with piperidine *via* the intermediate *IV* is significant, too. This pathway was proved by the fact that, under selected reaction conditions (low pH value, high piperidine concentration), the found rate of formation of the product *VI* from the aldehyde *VII* was several times higher than the rate of conversion of the aldehyde *VII* into the compound *I*. However, the product *VI* is formed faster from the compound *I* than from the aldehyde *VII* under all reaction conditions. The reaction pathway *VII* → *VIII* → *VI* cannot be considered. Spectral record of the reaction course did not show any absorption at λ 390 nm corresponding to the compound *VIII*, and rate of the reaction *VIII*

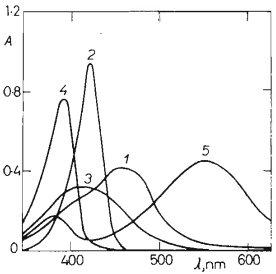


FIG. 1

Electronic Spectra of Compounds *IV* (*1*), *VI* (*2*), *VII* (*3*), *VIII* (*4*), and Anion of Compound *VII* (*5*) in 50% by Vol. Aqueous Ethanol

Concentration 1 . 10^{-5}M, 1 cm cell, *A* means absorbance.

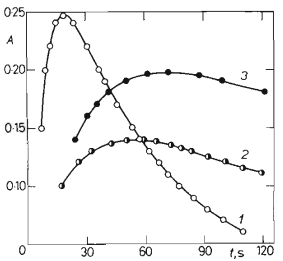


FIG. 2

Time Dependence of Absorbance at 550 nm Corresponding to Concentration of Intermediate *V*

The concentration ratio piperidine: piperidine hydrochloride (mol/l) 0·015 : 0·30 *1*, 0·0075 : 0·15 *2*, 0·0075 : 0·075 *3*; *A* absorbance.

→ *VI* investigated separately under the same reaction conditions was lower than that of the conversion *VII* → *VI* by several orders of magnitude.

The intermediates *IV* and *V* really lie on the reaction pathway *I* → *VI* (they are real intermediates and not products of the reversible side reaction). This statement was confirmed by the rate of formation of the product *VI* from the intermediates (*IV* and *V*) being substantially greater than that from the compound *I*. If we start from the intermediates *IV* and *V*, then, at the beginning, the rate of formation of the compound *VI* rapidly decreases till, after some time, it is the same as that of the conversion *I* → *VI*. It suggests that the reverse reactions (*IV* and *V*) ⇌ *I* + *VII* take place simultaneously, and after some time steady state is reached. The reverse reactions of the intermediates (*IV* and *V*) were followed in buffer media not containing piperidine, so that the product *VI* could not be formed. The reaction produces a mixture of the aldehyde *VII* and the compound *I* which at the given pH changes into the more stable aldehyde *VII*, too[7]. The compound *I* cannot be proved directly by the spectral method, as it does not practically absorb at 350 nm, and concentrations of individual components cannot be accurately determined from the spectral records at lower wavelengths. Therefore, formation of the compound *I* had to be proved in some other way. At pH < 9 the conversion *I* → *VII* is much slower than the measured reaction (*IV* and *V*) → *I* + *VII*. The amount of the aldehyde *VII* formed (determined spectrophotometrically) is lower than 15%. The remaining 85% are obviously represented by the compound *I*, which can be inferred from the following reasons: If the reaction mixture is alkalinized to pH 13–14, anion of the aldehyde *VII* is formed immediately in practically quantitative yield (calculated on the starting intermediate). The compound *I* gives the anion of the aldehyde *VII* quantitatively under these conditions, the half-life of the conversion being smaller than one second[7]. When piperidine is added to the mixture of products after finishing the reaction (*IV* and *V*) → *I* + *VII*, the product *VI* is formed again quantitatively. Here both the character of spectral records and rate of formation of the product *VI* are the same as those in the reaction of the compound *I* with piperidine studied separately under the same conditions.

The results of the above discussion can be summarized as follows. Reaction of the compound *I* with piperidine produces reversibly the intermediate *V* and its conjugated acid *IV*. At the same time the compound *I* reacts with OH^- to give the aldehyde *VII* which again reacts reversibly with piperidine to give the protonated intermediate *IV*. However, this reaction is slower than that of the compound *I* with piperidine. Obviously the product *VI* is formed by reaction of the protonated intermediate *IV* with piperidine, because at a constant piperidine concentration both the concentration of the intermediate *V* and t_{max} (Fig. 2) increase with increasing pH, which means that the subsequent reaction becomes slower. After completed reaction the reaction solution contains only the product *VI* which is stable under the given conditions. Its subsequent reaction with OH^- is practically significant first at much higher pH.

The reverse reaction *VIII* → *VI* is slower than *VII* → *VI* by several orders of magnitude, which excludes the pathway *VII* → *VIII* → *VI*.

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