ENAMINES.

9.* POLAROGRAPHIC REDUCTION OF ENAMINO KETONES IN AQUEOUS MEDIA

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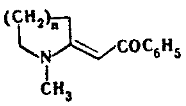
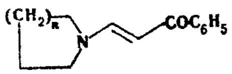
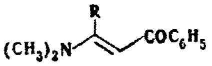
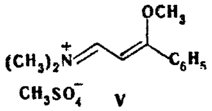
The mechanism of the polarographic reduction of cyclic enamino ketones of the pyrrolidine, piperidine, and hexahydroazepine series of two types, viz., compounds in which the α-carbon atom of the enamine is included in the azoheteroring, and enamino ketones in which the double bond is located outside the cyclic system, was investigated. The acyclic analogs were also studied. It is shown that the two- or four-electron reduction depends substantially on the structures of the investigated compounds and the pH of the medium; this in turn is associated with a change in the character, rate, and site of protonation of the enamino ketones and the compounds formed as a result of their reduction.

Relatively little research has been devoted to the polarographic reduction of enamino ketones [2-4]. It has been shown that protonation precedes electron transfer in acidic and neutral media, whereas the neutral enamino ketone molecules are reduced at high pH values [2, 4]. In anhydrous dimethylformamide (DMF) reduction takes place in two one-electron steps with the formation of unconjugated enamines [3]. The aim of the present research was to investigate the mechanism of the polarographic reduction of cyclic enamino ketones of two types, viz., compounds in which the α-carbon atom of the enamine is included in the azaheteroring (Ia-c), and enamino ketones in which the double bond is located outside the cyclic system (IIa-c). We simultaneously studied the acyclic analogs, viz., IIIb for the first group, and enamino ketone IIIa for the second group. It should be noted that the separation of the investigated compounds into two groups is not by chance — it has been previously shown that the indicated two types of enamino ketones differ substantially with respect to the character of protonation [5] and with respect to certain details of the mechanism of their hydrolysis in acidic media [1]. In the present research we carried out our study of the mechanism of the reduction of the enamino ketones in aqueous media over a broad range of pH values; the rather stable Ia and IIa were selected as the principal subjects of the study (see [1, 6]).


Ia-c


IIa-c


IIIa,b


V

I-II a n=1; b n=2; c n=3

One reduction wave is observed on the polarograms of enamino ketone Ia at pH 0-3 (Fig. 1). This wave has diffusion character and corresponds to the transfer of two electrons according to the results of coulometry at a controllable potential. The slope of the wave in semilogarithmic coordinates ranges from 32 to 43 mV, while an anode peak is absent on the cyclical volt—ampere curves at a rate of application of potentials up to 100 V/sec, i.e., this reduction wave is irreversible. Over the same pH range a second wave, which beginning with

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*See [1] for Communication 8.

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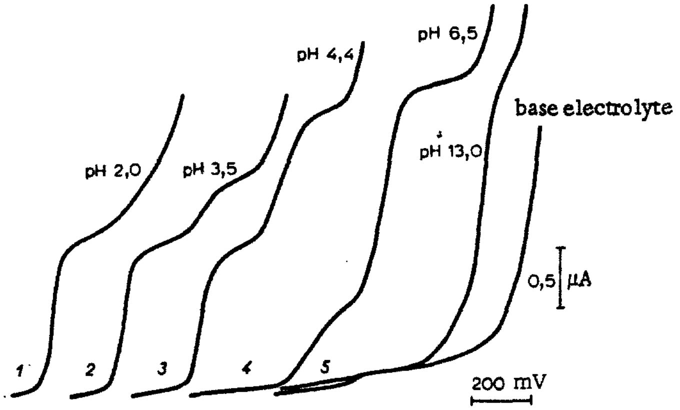
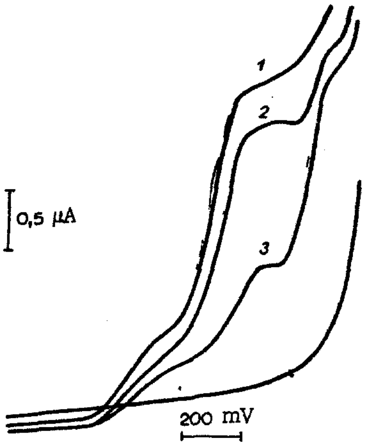


Fig. 1. Polarograms of enamino ketone Ia ($c = 0.5$ mmole/liter) in aqueous buffer solutions: 1), 2), 3), and 4) recorded from −0.8 V; 5) recorded from −1.1 V.



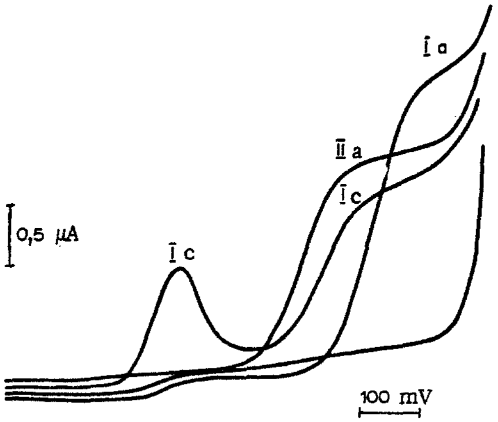


Fig. 2 Fig. 3

Fig. 2. Polarograms of enamino ketone Ia ($c = 0.5$ mmole/liter) in a citrate–phosphate buffer with pH 5.8 (1) and in acetate buffers with pH 5.8 (2) and 6.0 (3) (recorded from −0.8 V).

Fig. 3. Polarograms of enamino ketones Ia,c and IIa in 0.1 N KCl: $c_{Ia} = 0.5$, $c_{Ic} = 0.3$, and $c_{IIa} = 0.5$ mmole/liter (recorded from −1.2 V).

pH 3 increases sharply and reaches the two-electron level at pH 4.3, is also apparent at more negative potentials, in addition to the principal reduction wave. The height of the first wave is constant over this entire pH range, and at pH > 5 it begins to decrease, taking on kinetic character, and vanishes at pH ∿ 7.5. The second wave increases simultaneously and is split as the first reduction wave decreases, during which the overall current corresponds to the transfer of four electrons. The half-wave potentials ($E_{1/2}$) of both the first and second reduction waves of enamino ketone Ia are shifted to the negative potential region as the pH is increased ($\Delta E_{1/2}/\Delta pH$ is 50 mV for the first wave over the entire pH range, while $\Delta E_{1/2}/\Delta pH = 88$ mV for the second wave at pH 3.5-5). It may be assumed that the reduction of enamino ketone Ia takes place in the adsorbed state. The significant surface activity of this and the other investigated enamino ketones is evidenced, in particular, by the appreciable dispersion of the compacitive current at a depolarizer concentration of 10^{-4} mole/liter. In conformity with this, prior protonation has surface character; this is seen distinctly in the case of the second reduction wave of enamino ketone Ia. As the pH is increased, a second reduction wave consisting of two poorly separated waves appears on the plateau of the limiting current (see Fig. 2). The rate of the preceding protonation reaction depends on both the surface concentration of the depolarizer and on the proton donor concentration. In conformity with this, the height of the second reduction wave and the height of the drop are deter-

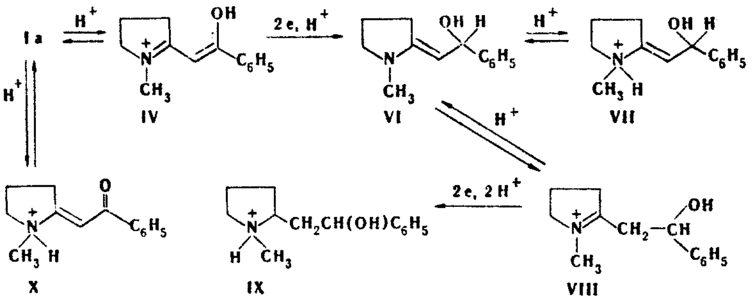
TABLE 1. Half-Wave Potentials and Overall Limiting Current Constants (χ) of Enamino Ketones in Aqueous Buffer Solutions

Compound		Indexes					
I a	pH	0	1,0	3,5	4,6	8,0	13
	$E_{1/2}$	−0,85	−0,87	−0,97 −1,22	−1,07 −1,31	−1,80	−1,80
	χ	2,0	2,0	3,5	4,0	4,1	3,7
I b	pH	0	1,0	3,0			13
	$E_{1/2}$	−0,84	−0,87	−0,95			−1,78
	χ	2,1	2,0	2,0			2,4
I c	pH	0	1,0	3,0	5,0		13
	$E_{1/2}$	−0,82	−0,85	−0,91	−1,05 −1,19 −1,36		−1,80
	χ	1,9	2,0	2,0	3,9		3,2
II a	pH	0	1,0	3,2	4,6	8,0	13
	$E_{1/2}$	−0,78 −0,89	−0,82 −0,92	−0,94 −1,16	−1,00 −1,15 −1,26	−1,54	−1,76
	χ	1,9	1,9	2,3	4,0	4,3	2,7
II b	pH	0			4,1	8,0	13
	$E_{1/2}$	−0,75 −0,85			−0,93 −1,14	−1,47	−1,73
	χ	2,0			4,0	4,2	2,2
II c	pH	0			4,1	8,0	13
	$E_{1/2}$	−0,82 −0,93			−1,10 −1,21	−1,57	−1,80
	χ	2,0			4,1	4,2	2,6
III a	pH	0			5,3	8,0	13
	$E_{1/2}$	−0,78 −0,88			−1,30	−1,54 −1,68	−1,73
	χ	2,1			4,3	4,3	2,1
III b	pH	0					13
	$E_{1/2}$	−0,85					−1,78
	χ	2,2					2,4
V	pH	0					
	$E_{1/2}$	−0,91					
	χ	1,9					

Note: χ is the overall limiting current constant (the overall limiting current in microamperes divided by the depolarizer concentration in millimoles per liter).

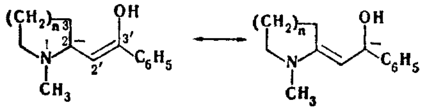
mined both by the volume concentration of the depolarizer and by the concentration and type of buffer solution. For example, whereas in an acetate buffer solution with pH 5.8 the limiting current does not reach a value that corresponds to the transfer of four electrons and there is a clearly expressed drop on the plateau of the limiting current (Fig. 2), while a third reduction wave appears at more negative potentials, in a citrate–phosphate buffer solution with the same pH there is no drop on the plateau of the limiting current, the overall wave corresponds to a four-electron process, and there is no third wave. As the pH is increased, a decrease in the second wave also occurs after a decrease in the first reduction wave of enamino ketone Ia (see Fig. 2). A third reduction wave, the $E_{1/2}$ value of which is independent of the pH, appears similtaneously and increases. The character of this change and the magnitude of the overall limiting current depend substantially on the size of the ring. Thus, whereas the second wave vanishes at pH 11-12 in the case of enamino ketone Ia, this wave can be observed even in a 0.1 N NaOH solution as the base electrolyte, and in this case water is a completely effective proton donor. In the case of nonbuffer KCl solutions as the base electrolyte the polarograms of enamino ketone Ic (Fig. 3) before the reduction wave of the basis form of the depolarizer contain a characteristic wave with a drop almost to the level of the current of the base electrolyte during desorption of the depolarizer, i.e., a wave of reduction of the protonated enamino ketone Ic. The adsorption character of this wave confirms a decrease in it as the ionic strength of the solution is increased, as well as on passing to aqueous alcohol media. As we have already noted, a decrease in the overall limiting current, which is manifested to the greatest degree for six-membered compound Ib and to the smallest extent for five-membered enamino ketone Ia, is observed in sufficiently alkaline media (see Table 1).

It is reasonable to assume that the first wave observed in strongly acidic media is related to the reduction of the O-protonated form (IV) of enamino ketone Ia; this opinion is confirmed by the similarity in the $E_{1/2}$ values of Ia and the model of the O-protonated form (V) at pH = 0 (see Table 1). The subsequent scheme of the process has the following form:

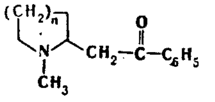


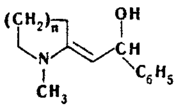
Cation IV is capable of undergoing reduction to unconjugated enamine VI, which in a strongly acidic medium is converted to N-protonated form VII, which is not capable of accepting an electron in the accessible range of potentials. The prototropic shift with the formation of an immonium cation of the VIII type is extremely slow under these conditions, and, as a result, at pH 0-3 the principal reduction wave for enamino ketone Ia (and the only such wave for Ic) corresponds to the process Ia → VII. As the pH is increased, the formation of cation VIII is accelerated (see [7] for the interpretation of this phenomenon), and a second wave corresponding to the process VIII → IX, which reaches the two-electron level as the pH is increased, appears. The picture is complicated somewhat when pH > 5. We assume that over this pH range the first reduction wave corresponds to the process Ia → VI, while the second wave corresponds to the process VIII → IX and to discharge of N-protonated form X. It may be assumed that the orientation of Ia on the electrode surface is such that it ensures faster N-protonation. This process can consequently be observed at higher pH values as compared with O-protonation, which is evidently the preferred process in the volume of the solution*.

It is quite clear that the reduction wave, the $E_{1/2}$ value of which is –1.8 V and is independent of the pH, is a wave of reduction of the unprotonated form of the depolarizer. In this case, as in the reduction of the N-protonated form, transfer of four electrons all at once is possible at a sufficiently high rate of protonation of the intermediately formed particles. The fact of the dependence of the limiting current in alkaline solutions on the size of the saturated azaheteroring is extremely interesting. Starting from general considerations [2] and data previously obtained during a study of the electrical reduction of enamino ketones in a nonaqueous solvent [3], one can give the following explanation for this phenomenon. An anion (XIa ↔ XIb) is formed after the transfer of the first two electrons; the protonation of this anion may take place at two centers — in the 2 position of the ring or at the carbon atom of the side chain (3' position) bonded to the hydroxy group and the phenyl substituent:


XIa XIb

Protonation in the 2 position leads to polarographically active ketone XII, while protonation at the 3' atom leads to unconjugated enamine XIII, which is not capable of accepting an electron over the accessible range of potentials. The stabilization of the enamine fragment as a function of the ring size changes in the order. 6 > 7 > 5; the tendency of the system to undergo protonation at the 3' atom decreases in the same order. Protonation primarily in the 2 position of the ring is therefore observed for five-membered ring Ia, and the


XII


XIII

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*We assume that in this case the formation of a C-protonated form can be disregarded, since this process is slow [8].

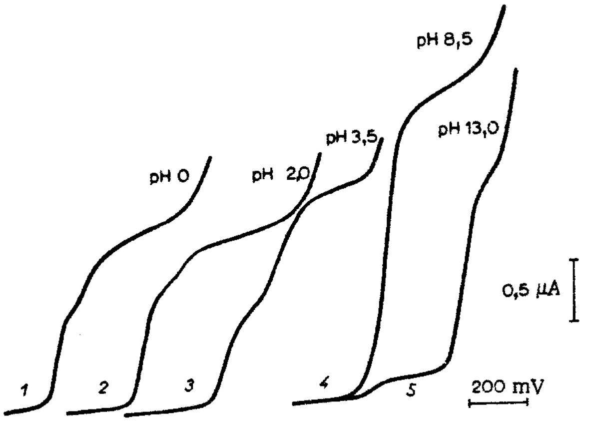


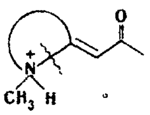
Fig. 4. Polarograms of enamino ketone IIa ($c = 0.5$ mmole/liter) in aqueous buffer solutions: 1), 2), and 3) recorded from –0.6 V; 4) and 5) recorded from –1.2 V.

limiting current is close to the four-electron level, whereas the degree of protonation at the 3' atom increases sharply for six-membered compound Ib, and this gives rise to the decrease in the limiting current for this compound (Ib) that is observed at pH 10-13. Seven-membered enamino ketone Ic occupies an intermediate position. Let us note that, in conformity with the generally accepted concepts, the behavior of noncyclic enamino ketone IIIb is similar to that of six-membered compound Ib.

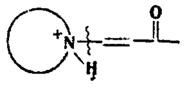
Experimental data that pertain to the first group of compounds and their interpretation are presented primarily in the case of enamino ketone Ia. However, the general pattern is also retained for other compounds of this group (Ib,c and IIIb); a complicating factor in this case is the hydrolysis of the indicated compounds in acidic media [6].

Two waves, the ratio of the heights of which depends on the pH of the medium, whereas the overall current corresponds to the transfer of two electrons, are observed for enamino ketone IIa (Fig. 4) at pH 0-3. By comparison with model compound V, the first wave was assigned to the reduction of the N-protonated form, while the second wave was assigned to the reduction of the O-protonated form [the fact that compounds of the second group (IIa-c, IIIa) undergo primarily N-protonation was established in [5]]. At pH 0-2 the height of the wave of the N-protonated form increases, after which it begins to decrease; the overall current at pH 0-3 remains constant. As the pH is increased further, the wave of the N-protonated form continues to decrease and vanishes completely at pH 5.2. Yet another wave, which increases as the pH is increased, so that at pH 4.6 the overall current reaches the four-electron level, appears in addition to the reduction wave of the O-protonated form at pH > 3. The $E_{1/2}$ values of all of the reduction waves are shifted to the negative potential region as the pH is increased; $\Delta E_{1/2}/\Delta pH$ is 56 mV for the wave of the N-protonated form, as compared with 64 mV for the wave of the O-protonated form. As a result, these waves become separated more distinctly as the pH is increased. The third wave depends on the pH to a lesser extent as compared with the wave of the O-protonated form, and this leads to merging of these waves; at pH > 5 one observes only one four-electron reduction wave, which continues to be shifted to negative potentials: $\Delta E_{1/2}/\Delta pH = 87$ mV at pH 5-8. The shift of $E_{1/2}$ slows down as the pH is increased further, whereas the height of the wave decreases somewhat commencing with pH 10.

In its general features the scheme presented above for the compounds of the first group (Ia-c, IIIb) describes the reduction of compounds of the second group (IIa-c, IIIa) also. However, it is apparent that there are also substantial differences. In our opinion, these differences are associated with the character of the protonation of the indicated groups of compounds [5], certain steric factors, and, as a consequence, with the different character of protonation in the adsorbed state. The more difficult reduction of the N-protonated form of the compounds of the first group as compared with the compounds of the second group is explained by the greater steric accessibility of the "enamine" α position of the latter. In addition, when one is dealing with cyclic compounds I and II, one may also cite the following circumstance: The endocyclic $C-N^+$ bond undergoes cleavage in the reduction of the N-protonated forms of enamino ketones of the I type (see [9] for data on the mechanism of the reduction of compounds with such structures), whereas the exocyclic bond is cleaved in the case of compounds of the II type (structures A and B, respectively).

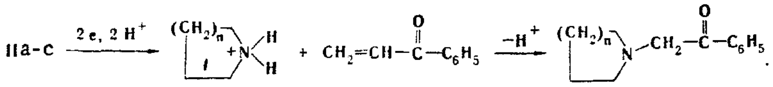


A



B

At the same time, it is known [10] that the ease of cleavage of the C–N bond depends substantially on whether this bond belongs to a cyclic system; cleavage of this bond in cations of the A type is hindered as compared with cations of the B type. In weakly acidic and neutral media cleavage of the $C–N^+$ bond of enamino ketones is accompanied by the process



and the resulting acetophenone derivative is reduced more easily than the starting depolarizer, which determines the four-electron character of the reduction wave. In strongly acidic media the reaction of the products of two-electron reduction of enamino ketones of the second group is hindered as a consequence of slowing down of the step involving deprotonation of the amine fragment; the resulting phenyl vinyl ketone is evidently consumed rapidly by undergoing other chemical transformations. In any case, as in the reduction of N,N,N-triethyl-N-β-formylvinylammonium perchlorate (XIV) [9] in strongly acidic media, waves of reduction of the corresponding vinyl ketones are absent in the case of enamino ketones of the second group. As a result, the reduction wave of the N-protonated form of compounds of the second group in acidic media corresponds to a two-electron process.

As demonstrated in [9], cation XIV, which can be regarded as a model of the N-protonated form of the enamino ketone, is reduced much more easily than β-dimethylaminoacrolein, which under these conditions should undergo reduction in the form of O-protonated form XV [8]. The same order is also observed in the reduction of the second group of enamino ketones (IIa-c, IIIa).

$$(C_2H_5)_3\overset{+}{N}-CH=CHCHO \qquad (CH_3)_2\overset{+}{N}=CH-CH=CH-OH$$

XIV XV

The fact that the reverse dependence is observed for compounds of the first group (Ia-c, IIIb) is determined primarily by the peculiarities of the three-dimensional structure. Let us note that N-protonation cannot be observed for the enamino ketones of the first group by direct methods (in contrast to the compounds of the second group [5]). The reduction of the N-protonated form of enamino ketones of the first group can be recorded only when protonation is possible only with the participation of depolarizer adsorbed on the electrode surface. On the other hand, in the case of compounds of the second group (IIa-c, IIIa) N-protonation in acidic media is observed also in the volume of the solution [5]. As the pH of the medium is increased, the equilibrium is shifted to favor the thermodynamically more favorable O-protonated form [2]. This character of the protonation is also retained in media in which the rate of protonation in the volume of the solution can be disregarded. This is probably determined by the planar structure of the enamino ketones of the second group and the smaller amount of steric hindrance (than for compounds of the first group) to O-protonation [5]. These factors evidently also ensure the better adsorbability of enamino ketones IIa-c and IIIa as compared with enamino ketones Ia-c and IIIb. As a result, in the case of compounds of the second group in nonbuffer solutions the drops on the plateau of the limiting current that are determined by desorption of the depolarizer as the potential is increased are absent. A prior protonation step for compounds of the II type can be observed up to pH 12, and water is a considerably more effective proton donor for them than for compounds of the I type. The overall height of the wave, i.e., the two- or four-electron character of the reduction, is determined by the same factors as for enamino ketones Ia-c and IIIb. This pattern may appear unexpected if one takes into account the fact that the pK values of enamino ketones of the I type are almost two orders of magnitude higher than for enamino ketones of the II type [5]. This contradiction is completely resolvable: When the rate of protonation in the volume of the solution is extremely low, we are dealing exclusively with "surface" protonation at the kinetically favorable center. At the same time, as demonstrated in [5], the high pK_a values of enamino ketones of the I type are determined by the substantial contribution of the thermodynamically most favorable C-protonation, which is a slow process and is not displayed in this case under polarographic conditions.

Thus the mechanism of the reduction of enamino ketones in aqueous media depends substantially on the structure of the investigated compounds and the pH of the medium; this is primarily associated with a change in the character, rate, and site of protonation of enamino ketones and the compounds formed in their reduction.

EXPERIMENTAL

The polarographic measurements were made in a thermostatted (25 ± 0.1°C) cell by means of a PAR-170 electrochemical system. The characteristics of the dropping mercury electrode with a blade for forced detachment of drops were as follows: m = 0.3 sec, and t = 1.0 mg. All of the solutions contained 10% by volume ethanol. The method for coulometry at a controllable potential on a mercury macrocathode is described in [11], while the method for coulometry on a dropping mercury electrode is described in [12]. The number of electrons (n) for enamino ketone Ia in 0.1 N HCl solution was 2.21 ± 0.40, as compared with 2.42 ± 0.58 in a buffer solution with pH 3.2.

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