ACETALS OF LACTAMS AND ACID AMIDES

XXI.* POLAROGRAPHIC STUDY OF ENAMINO KETONES OF THE PYRROLIDINE, PIPERIDINE, AND HEXAHYDROAZEPINE SERIES

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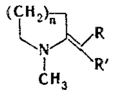
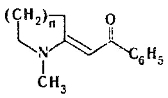
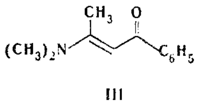
The reduction of 1-methyl-2-(2-benzoyl)methylenepyrrolidine, hexahydroazepines IIa-c, and (β-dimethylamino-β-methyl)methyleneacetophenone III in aprotic media on a dropping mercury electrode proceeds in two one-electron steps to give the corresponding enamines with a benzhydryl residue in the 2' position. The regular dependence of the $E_{1/2}$ values of the first waves in the reduction of enamino ketones IIa-c on the ring size is discussed: six-membered enamino ketone IIb is reduced most easily, while five-membered IIa is reduced with the greatest difficulty. It is shown that the ring size of the enamino compounds affects the $E_{1/2}$ values only in those cases in which a change in the hybridization of the ring carbon atom occurs during electrical reduction.

It has previously been shown [2] that the reduction of enamines – 1-methyl-2-(2'-R'-2'-R-methylene)-hexahydroazepine derivatives (I, n = 3) – on a dropping mercury electrode in dimethylformamide (DMF) in a 0.1 M tetrabutylammonium perchlorate base electrolyte proceeds in one one-electron step with subsequent dimerization of the resulting anion radicals.

The aim of the present research was to study the mechanism of the electrical reduction of a number of enamino ketones (IIa-c, III) in DMF. In addition to this, for the indicated compounds, as for other substances containing an enamino fragment, we examined the dependence of the half-wave potentials on the size of the saturated aza heteroring; this is essential in the solution of the structural and analytical problems that arise during the study of the reactions of compounds of this type.

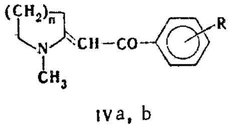

I




III

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

Two polarographic waves correspond to enamino ketones II and III in an aprotic medium (Table 1). The first waves are distinctly expressed, whereas the second waves are stretched out and evidently consist of a series of poorly resolved steps. As seen from Table 1, the first waves of IIa-c and III have coefficients of proportionality in the Ilkovič equation (ϰ) ranging from 1.19 to 1.47. The one-electron waves of the reduction of the nitro group of enamino ketones IVa, b under the same conditions have ϰ values of 1.19 and 1.16, respectively.


IVa, b

IV a n=1, R=p-NO$_2$;
b n=3, R=m-NO$_2$

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*See [1] for communication XX.

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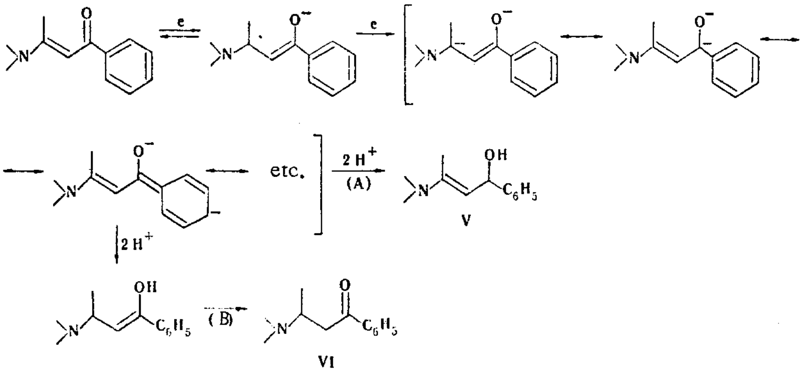
TABLE 1. Polarographic Characteristics of II and III

Compound	$-E_{1/2}$, V (saturated calomel elec)	$\varkappa = \frac{i_{\lim}}{c}$
IIa	2,30	1,47
	2,8	1,85
IIb	2,20	1,30
	2,7	1,34
IIc	2,25	1,19
	2,8	1,39
III	2,21	1,26
	2,7	1,69

TABLE 2. Polarographic Characteristics of I in a 0.1 M Solution of Bu_4NClO_4 in DMF

R	R′	n	$-E_{1/2}$, V (saturated calomel electrode)	$\varkappa = \frac{i_{\lim}}{c}$
CN	COOEt	1	2,44	1,58
CN	COOEt	2	2,34	1,14
CN	COOEt	3	2,36	1,11
CN	$CONH_2$	1	2,65	1,37
CN	$CONH_2$	2	2,46	1,15
CN	$CONH_2$	3	2,46	1,06

Consequently, the first waves of enamino ketones IVa-c and III correspond to transfer of one electron. The slopes of these waves attest to the reversibility of the process, in which the resulting anion radical is quite stable: an anode peak of oxidation of the anion radical that is approximately equal in height to the cathode peak of reduction of IIb is observed during recording of the cyclical voltamperograms of IIb on a hanging mercury drop in DMF in a 0.1 M BuNI base electrolyte at a potential scanning rate of less than 0.1 V/sec, and the difference in the potentials of the anode and cathode peaks is 69 mV and is practically independent of the scanning rate. The second waves in the reduction of enamino ketones II and III, as we have already stated above, are not distinctly expressed. Judging from the $\varkappa$ value, it may be assumed that these waves are also one-electron waves for IIb, c; this corresponds to reduction of the anion radicals to dianions. The certain overstatement of the height of the second waves for IIa and III is probably associated with side processes. Proceeding from the data presented above, one may conclude that the principal pathway in the electrical reduction of enamino ketones II and III is pathway A, which involves the formation of enamine V, which is not reduced in the accessible range of potentials, since even reduction of enamines I with strongly electron-acceptor substituents (R, R') is observed at extremely negative potentials [2] (Table 2).



Compound VI, which is formed through side process B, should not differ appreciably with respect to polarographic behavior in aprotic media from acetophenone, which under these conditions gives two one-electron $E_{1/2}$ waves of −2.12 and −2.7 V; consequently, at the potentials of the second wave ketone VI should undergo reduction rapidly with the consumption of two electrons. An increase in the second wave above the one-electron level also determines the occurrence of this process, and the relatively small magnitude of this increase indicates that the dominant process is reduction of the anion radical to enamine V.* Thus, as in the case of enamines I [2] and α,β-unsaturated ketones [4], the first step in the electrical reduction of enamino ketones is reversible transfer of one electron to give a quite stable anion radical. However, in contrast to enamines I, waves involving the reduction of these anion radicals are observed in the case of II and III.

It follows from an examination of the data in Table 1 that there are significant differences in the $E_{1/2}$ values of the first waves in the reduction of the investigated enamino ketones as a function of the ring size; six-membered enamino ketone IIb is reduced most easily, while five-membered IIa is reduced with the greatest difficulty. Noncyclic III is reduced in the same way as IIb. Since the first wave in the reduction is reversible, whereas the resulting anion radical is quite stable and does not undergo any further transformations at measur-

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*The final result of the reduction, i.e., the formation of enamine V, is in good agreement with the data in [3] on the electrical reduction of some enamino ketones in protogenic media.

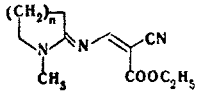
able rates under the given conditions, the $E_{1/2}$ values are associated with a difference in the stabilities of the ground states of II and III and anion radical VII:

VII

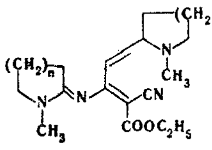
There is a basis to suppose [5] that the unshared pair of electrons of the ring amino groups is best conjugated with the exocyclic double bond in the case of the six-membered ring. Hence under the condition of equality of the energies of final state VII, IIb should undergo reduction with the greatest difficulty; this is not in agreement with the experimental results.

Thus in the case of an examination of the effect of the ring size of enamino ketones II on the $E_{1/2}$ values one must take into account the differences in the energies of the final states – anion radicals in this series of compounds.

The results made it possible to assume that the addition of an electron to the 2 position of the ring leads to an increase in the p character of the C_2 atom. It is well known [6] that a change in the character of the hybridization from sp^2 to sp^3 is most favorable for a six-membered ring and least favorable for a five-membered ring; this is in good agreement with the results presented above (Table 1). If the assumption expressed above is correct, facilitation of the reduction of six-membered compounds as compared with five-membered compounds should be retained in those cases in which the C_2 atom of the saturated ring is involved. In fact, a comparison of the $E_{1/2}$ values for enamino esters (I, n = 1-3, R = CN, R' = COOEt) [7] and enamino amides (I, n = 1, 3, R = CN, R' = $CONH_2$) confirms the assumptions expressed above (Table 2). The regularity found in this case may evidently serve as an indicator method for the determination of the nature of the reduced groups (or the structure of the anion radical) in complex systems with a large number of functional groups. Thus, for example, the $E_{1/2}$ values of the first waves in the reduction of the enamidines (VIII, n = 1-3) [7] are, respectively, −1.43, −1.42, and −1.41 V (with respect to a silver electrode in a 0.1 M solution of Bu_4NClO_4 in DMF as the base electrolyte); this makes it possible to conclude that in this case substantial changes in the character of the hybridization of the ring C_2 atom do not occur during attack of the electron.

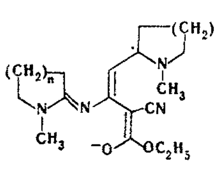


VIII



IX

On the other hand, in the case of IX one observes a distinct dependence of the $E_{1/2}$ values of the first waves on the ring size (the $E_{1/2}$ values for IX (n = 1-3) are, respectively, −1.70, −1.59, and −1.66 V [7]), which makes it possible to assume that structure X with increased p character (as compared with C_2 in IX) of the hybridization of the radical center (the ring C_2 atom) makes the greatest contribution to the resonance hybrid of the corresponding anion radical:



X

Thus the set of results obtained constitute evidence that the ring size of enamines, enamino ketones, and related compounds has an effect on the $E_{1/2}$ value only in those cases in which a change in the hybridization of the ring carbon atom occurs during electrical reduction.

EXPERIMENTAL

The polarographic measurements were made in a thermostatted (25 ± 0.1°C) cell. The working electrode was a dropping mercury electrode with characteristic values m = 0.73 mg/sec and t = 0.3 sec. A silver electrode submerged in the test solution was used as the comparison electrode. The half-wave potentials of the investigated compounds were reckoned relative to a saturated calomel electrode with respect to a "standard" (potassium) scale [8]. The polarograms were recorded with a Radiometer PO-4 polarograph.

The DMF was dried with fused KOH and vacuum distilled.

LITERATURE CITED

1. V. G. Granik, A. M. Zhidkova, R. G. Glushkov, A. B. Grigor'ev, M. K. Polievktov, T. F. Vlasova, and O. S. Anisimova, Khim. Geterotsikl. Soedin., No. 10, 1348 (1977).
2. A. B. Grigor'ev, V. G. Granik, and M. K. Polievktov, Zh. Obshch. Khim., 46, 404 (1976).
3. Ya. F. Freimanis, Ya. P. Stradyn', and I. Ya. Kravis, Zh. Obshch. Khim., 39, 631 (1969).
4. J. Zimmer, J. Richards, J. Turner, and D. Evans, Anal. Chem., 43, 1000 (1971).
5. R. Huisgen, H. Braude, H. Walz, and I. Glogger, Ber., 90, 1437 (1957).
6. Y. L. Gol'dfarb, and L. M. Belen'kii, Usp. Khim., 29, 470 (1970).
7. V. G. Granik, I. B. Marchenko, E. O. Sochneva, T. F. Vlasova, A. B. Grigor'ev, M. K. Polievktov, and R. G. Glushkov, Khim. Geterotsikl. Soedin., No. 11, 1505 (1976).
8. A. A. Vlced, Chem. Listy, 48, 1863 (1954).

SYNTHESIS OF HYDROGENATED HETEROCYCLIC COMPOUNDS BY THE ADDITION OF NUCLEOPHILIC REAGENTS TO SEMICYCLIC α-METHENYL 1,5-DIKETONES*

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The addition of primary and secondary amines and hydrogen cyanide to semicyclic α-methenyl 1,5-diketones of the 1,3-diphenyl-1-(2-oxocyclohexyl)-2-methenyl-3-propanone type leads, respectively, to compounds with hydrogenated quinoline, γ-flavenone, and chroman structures.

The study of reactions with nucleophilic reagents [3] was begun for semicyclic α-methenyl 1,5-diketones in [1, 2]. We present here the results of our studies of the addition of primary amines to semicyclic α-methenyl 1,5-diketones Ia-c and IV and of secondary amines and HCN to diketone Ia.

The reaction with primary amines leads to the hydrochlorides of IIa-d and V, and the reaction with ethanolamine leads to perhydrooxazolinoquinolines IIIa, b. The latter could be formed from both N,O-hemiacetals of the A form (R' = CH_2CH_2OH) by splitting out of a molecule of water through the hemiacetal and alcohol hydroxyl groups and from enamines II (R' = CH_2CH_2OH) by intramolecular addition of alcohol to the double bond of the enamine.

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