MECHANISM OF THE POLAROGRAPHIC REDUCTION OF 6-PYRIDAZONES

V. T. Glezer, Ya. P. Stradyn', and L. Ya. Avota

UDC 543.253:547.852.2

The mechanism of the polarographic reduction of substituted 6-pyridazones in acidic media depends substantially on the nature of the substituent in the 3 position. One reduction wave due to the reduction of the >C=C< bond is observed in the case of electron-donor substituents, whereas, further electrical reduction involving the system of >C=N-N< bonds with cleavage of the >N-N< bond is also observed in the case of electron acceptors. Only one two-electron wave, which reflects reduction at the >C=C< bond, is observed in alkaline media. The half-wave potentials of 3-substituted 6-pyridazones in both acidic and alkaline media correlate linearly with the Hammett σ constants. It is assumed that the transfer of the first electron in acidic media is realized at the quaternary nitrogen atom in the 2 position, whereas in alkaline media it is realized at the carbonyl group.

The polarographic study of 6-pyridazone derivatives has primarily been carried out within an analytical framework [1-3] to investigate the possibility of the quantitative determination of one of the derivatives of this series – the widely used herbicide fenazon (piramin, khlorazon) [4]. However, the mechanism of polarographic reduction is not completely clear. The first step in the electrochemical process in all cases reflects two-electron reduction of the <C=C> bond of the pyridazone system [5, 6]. The data are somewhat contradictory insofar as the subsequent reduction of the molecule is concerned. According to [5], the 3-methyl-4,5-dihydro-6-pyridazone formed during electrical reduction gives a second four-electron wave corresponding to cleavage of the <N-N> bond and saturation of the <C=N> bond in acidic media at more negative potentials. However, it follows from other studies [7] that this sort of trend in the case of further reduction is characteristic only for 3-phenyl-4,5-dihydro-6-pyridazone, whereas in the case of 3-methyl-4,5-dihydro-6-pyridazone the second wave, like the first, is a two-electron wave, since reduction of the azomethine bond does not occur at the potentials necessary for cleavage of the <N-N> bond, and the electrochemical reaction is accompanied by hydrolysis of this bond. Only two-electron reduction of the <C=C> bond was observed in the case of the polarographic reduction of 4- and 5-substituted 6-pyridazones over the entire pH range, and further reduction is not observed [6]. The goal of the present research was a systematic study of the polarographic behavior of the accessible 3-substituted 6-pyridazones and a comparison of the results related to their electrical reduction with the previously expressed assumptions regarding the mechanism of the electrical reduction of 6-pyridazone derivatives.

Compounds I and II are reduced on a dropping mercury electrode (DME) in the same way, in general features, as the previously studied 4,5-substituted 6-pyridazones [6] (Fig. 1). One wave, the half-wave potential ($E_{1/2}$) of which depends on the pH (about 80-85 mV/pH unit), is observed in acidic media. As the pH increases beyond three, the height of this wave begins to decrease, and a second wave, the height of which increases as the pH increases, appears simultaneously at more negative potentials, whereas the half-wave potentials no longer depend on the acidity of the medium. At pH values above six, the first wave vanishes, and the second wave remains the only one on the polarogram. A further increase in the basicity of the solution (pH > 10) leads to a decrease in the height of the second wave and, in addition, the half-wave potentials again begin to depend on the pH. The height of the first wave in media up to pH < 4 or the height of the second wave over the interval $7 \leq pH \leq 10$, as well as the overall height of both waves over the intermediate pH range, correspond to a

---

Institute of Organic Synthesis, Academy of Sciences of the Latvian SSR, Riga 226006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 668-673, May, 1977. Original article submitted May 12, 1976.

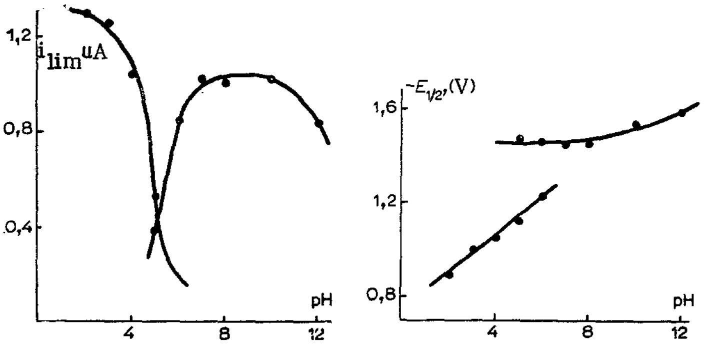
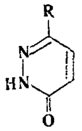
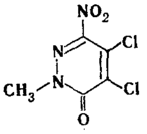


Fig. 1. Dependence of the half-wave potential and the limiting current on the pH of the medium for 3-methyl-6-pyridazone (II) [depolarizer concentration $2 \cdot 10^{-4}$ M, Britton–Robinson buffer (μ = 0.25), 10 vol.% dimethylformamide].

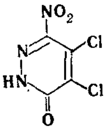
two-electron process; this was established by means of microcoulometric studies. This pattern can be explained by the amphoteric character of 6-pyridazone (see the scheme below), considering that form c is polarographically inactive.



I-IV



V



VI

I R=H; II R=CH_3; III R=OH; IV R=COOH

Our data on the polarographic reduction of II on both a short-period electrode (t = 0.2 sec) and on an electrode with a dropping period of 2.8 sec did not confirm further reduction of II, as indicated in [5, 7]. In addition, we did not observe reduction waves during a study of the model compound 3-methyl-4,5-dihydro-6-pyridazone, the hypothetical product of electrical reduction of II. The difference between our conclusion and the results in [7] is possibly explained by the fact that Lund did his research under conditions of prolonged preparative electrolysis, in the case of which the particles formed during electrical reduction have time to undergo more profound secondary changes.

Compound III gives three electrical reduction waves: the first in acidic media (pH 2-5), the second in weakly acidic and neutral media (pH 5-8), and the third in alkaline media (pH 7-9). Compound III is not reduced in media with pH > 9. Of interest is IV which, in contrast to the preceding compounds, gives two reduction waves in acidic media; the second wave is observed at pH < 4.

Additional reduction waves also appear in the case of 1-methyl-3-nitro-4,5-dichloro-6-pyridazone (V) and 3-nitro-4,5-dichloro-6-pyridazone (VI), in which case a wave whose height is doubled in acidic media and halved in alkaline media as compared with the height of the reduction wave of the nitro group follows the four-electron reduction wave of the nitro group. The dependence of the half-wave potentials of I-VI on the pH is presented in Table 1.

It follows from the dependence of the half-wave potential on the pH that I and II are reduced in acidic media in the protonated form a, which is formed as a result of the preceding protonation of 6-pyridazone molecules on the electrode surface. Evidence in favor of this is also provided by the previously established protonation constants of these compounds [8] (pK from −0.61 to −1.86). The second wave is the result of polarographic reduction of the principal form b of the molecule, whereas at pH > 10 it is probably a consequence of reduction of the previously protonated (on the electrode surface) form c, as a result of which a dependence on the pH is also again observed at these pH values of the medium. This trend in the electrical reduction is also in agreement with the deprotonation constants of these compounds [8]. In both acidic and basic media the electrochemical process consists in two-electron reduction of the <C=C> bond. This judgment was made on the basis of the IR spectrum of the product of preparative electrolysis (the band corresponding to absorption of the C=C bond vanishes) and also because of the absence of polarographic activity in the case of model compound 3-methyl-4,5-dihydro-6-pyridazone.

TABLE 1. Effect of the pH of the Medium on the Half-Wave Potentials [$-E_{1/2}$ (V) relative to a saturated calomel electrode] of Substituted 6-Pyridazones in Britton—Robinson Buffer Solutions (μ = 0.25)

Compound	pH										
	2	3	4	5	6	7	8	9	10	11	12
I	0,92	0,98	1,09	1,18 1,38	1,23 1,42	1,43	1,45	1,46	1,47	1,54	1,56
II	0,90	1,00	1,05	1,13 1,47	1,23 1,46	1,45	1,45	1,45	1,53	1,55	1,58
III	1,03	1,11	1,17	1,23 1,37	1,41	1,43 1,62	1,47 1,65	1,68			
IV	0,73 1,19	0,87 1,17	1,06 1,29	1,41	1,43		1,47		1,50		1.55
V	0,13 0,98	0,19 1,12	0,26 1,20 1,34	0,37 1,23 1,38	0,43 1,26 1,50	0,51 1,55		0,58 1,57		0,60 1,57	0,60 1,57
VI*	0,09 0,92	0,12 1,02	0,17 1,08	0,27 1,24	0,40 1,27 1,41	0,50 1,27 1,47		0,63 1,28 1,53		0,68 1,38 1,57	0,69 1,42 1,62

---

*An additional wave with $E_{1/2} = -1.13$ V appears at pH 11, 12.

The three waves on the polarogram of III can be ascribed to electrical reduction of three forms: the first wave corresponds to electrical reduction of the protonated cation (as in the case of I and II), the second corresponds to the molecular form, and the third wave corresponds to the basic form (the phenoxide anion). The absence of electrical reduction waves at pH > 9 can be explained by deprotonation of the nitrogen atom to give a polarographically inactive dianion. Thus, as in the case of compounds with R = OCH_3 and Cl, the presence of electron-donor substituents in the 3 position in the case of I-III does not lead to the appearance of waves of further reduction after saturation of the >C=C< bond.

A different pattern is observed when electron-acceptor substituents (IV-VI) are present in the 6-pyridazone molecule. The introduction of substituents of this type in the 3 position not only gives rise to a shift in $E_{1/2}$ to the positive side but also leads to the appearance of an additional wave in acidic media. Thus the pattern of reduction of IV in alkaline media is the same as for I and II, but another additional wave equal in height to the first and reflecting cleavage of the >N-N< bond of the heteroatom is observed on the polarograms in acidic media at pH $\leq$ 4. However, saturation of the azomethine bond does not occur in the case of IV over the accessible range of potentials.

In the case of V and VI, as a result of a four-electron process at the most positive potentials, the nitro group is reduced to a hydroxylamino group, which is protonated in acidic media and has pronounced acceptor properties. The second wave of pyridazones V and VI in acidic media, the height of which is twice as high, therefore corresponds to an eight-electron process and, in all likelihood, reflects a set of electrode reactions proceeding at extremely close potentials — it includes the further two-electron reduction of the $-NH_2OH^+$ group to $-NH_3^+$, two-electron reduction of the <C=C> bond, and subsequent four-electron reduction of the pyridazone system, which consists in cleavage of the >N-N< bond and saturation of the >C=N- bond. In alkaline media the second reduction wave of V and VI reflects only two-electron reduction of the >C=C< bond. More profound reduction of the pyridazone system does not occur under the given conditions, since in basic media the unprotonated hydroxylamino group is an electron donor rather than an electron acceptor, like $-NH_2OH^+$

Thus on the basis of the experimental data set forth above and our previous data [6] one may draw conclusions regarding some of the general principles of the polarographic reduction of 6-pyridazones. Whereas the two-electron reduction of the >C=C< bond is characteristic for all of the 6-pyridazones regardless of the nature and location of the substituent, subsequent reduction requires the presence of an electron-acceptor substituent in the 3 position, which reduces the electron density in the system of >C=N-N< bonds.

The extent of subsequent electrical reduction depends on the magnitude of the acceptor effect, as seen from a comparison of the data for IV and V and VI. Thus the introduction of

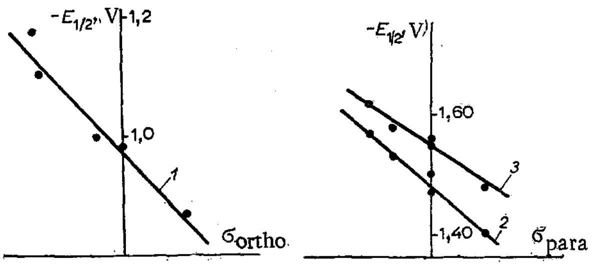


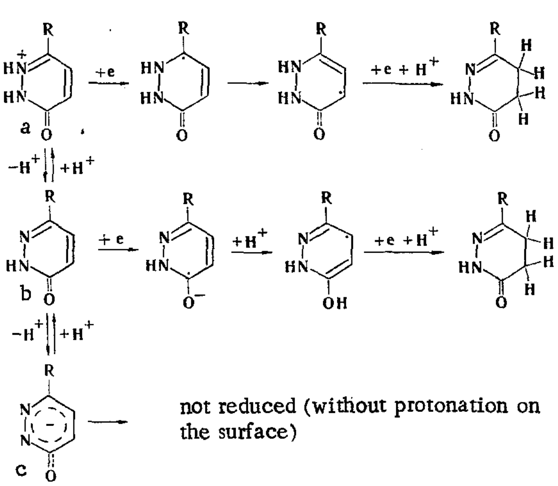
Fig. 2. Correlation of the Hammett σ constants with the half-wave potentials of 3-substituted 6-pyridazones: 1) pH 3, ρ = 0.43 V (r = 0.964); 2) pH 10, ρ = 0.33 V (r = 0.983); 3) pH 12, ρ = 0.27 V (r = 0.982).

a COOH group leads only to two-electron reduction of the >N-N< bond, whereas the $-NH_2OH^+$ group, by virtue of its considerably more pronounced acceptor properties, lowers the electron density of the azomethine bond to such an extent that reduction of the >C=N– bond proceeds at the same potentials as cleavage of the >N-N< bond; both reactions proceed at the same potentials as reduction of the >C=C< bond.

The indicated effect is observed only in acidic solutions (pH < 4) in which not only is the substituent present in the acidic form and acts as an electron acceptor but the nitrogen atom in the 2 position of the heteroring is also protonated (form a), as proved in [9].

We established a linear correlation between the Hammett σ substituent constants and the half-wave potential of the first wave of 3-substituted 6-pyridazones in both acidic and alkaline media (Fig. 2). The existence of this correlation indicates a single mechanism of primary electrical reduction for all of the investigated 3-substituted 6-pyridazones (the constants for COOH were used in acidic media, and the constants for COO^- were used in alkaline media).

The protonated form of the 6-pyridazone molecule undergoes reduction in acidic media, and it therefore seems likely that the electrochemical reaction is determined by electron transfer to the quaternary nitrogen atom in the 2 position. In alkaline media, in which this nitrogen atom is unprotonated, it is unlikely that the same electrophilic center is retained — the first electron most likely attacks the carbonyl group. A comparison of the correlations of the half-wave potentials by means of the σ_0 constants in one case and the σ_p constants in the other provides a certain confirmation of the latter. The values of these constants differ to the greatest extent from the number of the set of substituents that we investigated for the OCH_3 substituent ($\Delta\sigma \approx 0.12$). Whereas the $E_{1/2}$ value of the group in alkaline media fits on the $E_{1/2} = f(\sigma)$ dependence when the σ_p constants are used, in acidic media the $E_{1/2}$ value of this compound correlates only when σ_0 constants are used. The correlation of the half-wave potentials in acidic media with the σ_0 constants serves as yet another proof that the nitrogen atom in the 2 position of the heteroring is protonated in the 6-pyridazone molecule. The sensitivity (ρ) of a reaction series to substituent effects usually decreases as the protogenic character of the medium increases [10], but in this case, despite one's expectations, the regularity is reversed. However, one should take into account the fact that there are, in point of fact, two different reaction series: one, in acidic media, is electrical reduction of the N-protonated cations (a), and the other, in alkaline media, is electrical reduction of the molecular form (b), in which conjugation is realized to



not reduced (without protonation on the surface) a greater degree, and the sensitivity of the reaction center to the electronic effect of the substituent is consequently lower. The data set forth above make it possible to assume the mechanism (shown above) for the first step in the electrical reduction.

The subsequent steps in the electrode process are not indicated in this scheme, but if R is an electron acceptor, they lead to cleavage of the heteroring (cleavage of the >N-N< bond and reduction of the azomethine bond).

EXPERIMENTAL

The purity of the recrystallized I-VI was monitored by means of thin-layer chromatography; solutions with depolarizer concentrations of $2 \cdot 10^{-4}$ M were prepared for the polarographic studies, and the working solutions were prepared from Britton-Robinson buffer solutions containing 10% dimethylformamide (DMF). The ionic strength of the investigated solutions was held constant (0.25). The polarograms were recorded with LP-60 and OH-102 polarographs equipped with a thermostatted cell at 25.0 ± 0.2 deg. The cathode was a dropping mercury electrode with forced drop detachment with the characteristics m = 2.75 mg/sec and t = 0.2 sec (open circuit), and the anode was a saturated calomel electrode. The correlation equations were calculated by the method of least squares with a computer.

LITERATURE CITED

1. M. Gruca, Z. Janko, J. Kanty, and A. Kotarsky, Chem. Anal., 12, 1331 (1967).
2. M. Gruca, Z. Janko, and A. Kotarsky, Chem. Anal., 16, 91 (1971).
3. K. Dulak, J. Kovac, and P. Rapos, J. Chromatography, 31, 354 (1967).
4. L. Ya. Avota, N. Ya. Ozolin', and S. A. Giller, Izv. Akad. Nauk Latv.SSR, Ser. Khim., 347 (1967).
5. P. Pflegel, G. Wagner, and O. Manousek, Z. Chem., 6, 263 (1966).
6. V. T. Glezer, Ya. P. Stradyn', I. K. Tutane, L. Ya. Avota, and S. A. Giller, Zh. Obshch. Khim., 43, 1150 (1973).
7. H. Lund, Disc. Faraday Soc., 45, 193 (1968).
8. I. V. Turovskii, V. T. Glezer, L. Ya. Avota, Ya. P. Stradyn', and S. A. Giller, Khim. Geterotsikl. Soedin., No. 7, 993 (1973).
9. D. N. Miller and R. N. White, Can. J. Chem., 34, 1510 (1956).
10. S. G. Mairanovskii, Ya. P. Stradyn', and V. D. Bezuglyi, Polarography in Organic Chemistry [in Russian], Khimiya, Leningrad (1975), p. 116.

PYRIMIDINES.

LIX.* HYDROXYTETRAHYDROPYRIMIDINES — INTERMEDIATES IN THE SYNTHESIS OF PYRIMIDINES FROM α,β-UNSATURATED CARBONYL COMPOUNDS AND AMIDINES

A. L. Vais and V. P. Mamaev

UDC 547.853.5.07

It is shown in the case of condensation of benzamidine with cinnamaldehyde and benzalacetophenone that the synthesis of pyrimidines from α,β-unsaturated carbonyl compounds and amidines proceeds through a step involving the formation of hydroxytetrahydropyrimidines.

---

*See [1] for communication LVIII.

Novosibirsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR, Novosibirsk, 630090. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 674-677, May, 1977. Original article submitted July 26, 1976.