ISSN 1070-3632, Russian Journal of General Chemistry, 2009, Vol. 79, No. 11, pp. 2367–2372. © Pleiades Publishing, Ltd., 2009.
Original Russian Text © G.S. Posyagin, M.A. Vikhareva, O.A. Bystritskaya, A.E. Rubtsov, P.G. Neifeld, V.V. Zalesov, 2009, published in Zhurnal Obshchei Khimii, 2009, Vol. 79, No. 11, pp. 1845–1850.

Polarographic Behavior of 4-Aryl-2-(1,2-diphenyl-2-oxoethylidenehydrazino)-4-oxo-2-butenoic Acids

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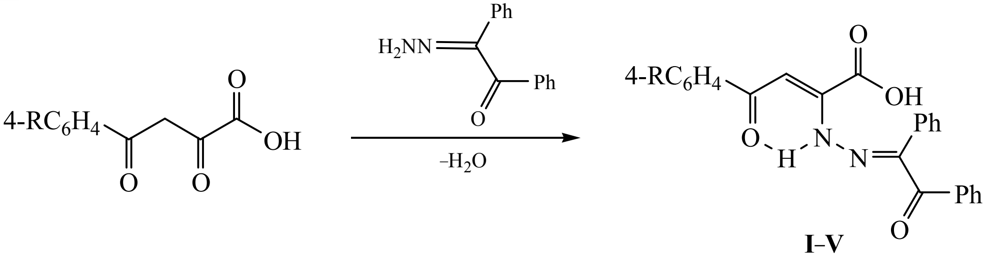
Received July 7, 2008

Abstract—Polarographic reduction of 4-aryl-2-(1,2-diphenyl-2-oxoethylidenehydrazino)-4-oxo-2-butenoic acids in 2-propanol–water solutions proceeds with the formation of two or three irreversible cathode waves and leads to 4-aryl-2-(1,2-diphenyl-2-hydroxyethylhydrazino)-4-hydroxybutanoic acids. The latter suffer hydrolysis with the rupture of the C^2–NH bond and the formation of 4-aryl-2,4-dihydroxybutanoic acids.

DOI: 10.1134/S1070363209110140

In continuation of the previous studies [1] on the polarographic reduction of derivatives of 4-aryl-2,4-dioxobutanoic acids we have investigated the polarographic reduction of 4-aryl-2-(1,2-diphenyl-2-oxoethylidenehydrazino)-4-oxo-2-butenoic acids (**I**–**V**). Compounds **I**–**V** belong to N-substituted α-aminoacids based on aroylpyruvic acid, that is, are potentially biologically active compounds. From this point of view the examination of their polarographic reduction is not only of theoretical but also of practical interest.

Compounds **I**–**V** were first synthesized by the reaction of 4-aryl-2,4-dioxobutanoic acids with benzil monohydrazone according to the scheme:



I–**V**

R = Cl (**I**), Me (**II**), MeO (**III**), EtO (**IV**), H (**V**).

Their physicochemical properties are presented in Table 1.

The polarographic behavior of compounds **I**–**V** was studied in aqueous 2-propanol (25% vol. of *i*-PrOH) in the pH range from 3 to 12. In the polarograms we reliably detect two or three irreversible cathode waves whose half-wave potentials ($E_{1/2}$) and limiting currents (i_d) depend on the pH of the solution.

In Table 2 are given the parameters of the polarographic waves for the studied compounds (values of $E_{1/2}$ and i_d), the limiting current constants $J_d = i_d c^{-1} m^{-2/3} \tau^{-1/6}$, where c is concentration of depolarizer with due regard to the effect of dilution with buffer solutions (0.5 mmol l^{-1}); m is the weight of mercury dropping in unit time (2.60 mg s^{-1}), τ is the dropping period (5.40 s).

Compound **I** shows three irreversible cathode waves which manifest themselves in the whole range of pH from 3 to 12 and which are characterized by a shift of the half-wave potentials towards more negative

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[†] Deceased.

Table 1. Physicochemical properties of compounds **I–V**

Comp. no.	R	Yield, %	mp, °C	IR spectrum, ν, cm^{-1}	R_f
I	Cl	79	147–148	3257 (NH), 1705 (COO), 1662 (CO)	0.08
II	Me	47	139–140	3246 (NH), 1700 (COO), 1655 (CO)	0.13
III	MeO	44	168–171	3275 (NH), 1700 (COO), 1660 (CO)	0.07
IV	EtO	41	157–159	3239 (NH), 1665 br (COO, CO)	0.11
V	H	21	134–136	3258 (NH), 1707 (COO), 1658 (CO)	0.06

Table 2. Characteristics of polarographic waves for compounds **I–V**

pH	Compound **I**								
	1st wave			2nd wave			3nd wave		
	$-E_{1/2}$, V	i_d, μA	J_d[a]	$-E_{1/2}$, V	i_d, μA	J_d[a]	$-E_{1/2}$, V	i_d, μA	J_d[a]
3.76	0.50	3.00	2.40	0.82	3.90	3.12	1.30	2.90	2.32
4.68	0.52	3.20	2.56	0.90	4.40	3.51	1.31	3.20	2.56
5.34	0.54	3.10	2.48	0.92	3.50	2.80	1.33	3.00	2.40
6.08	0.65	2.34	1.87	0.98	2.50	2.00	1.34	3.40	2.72
6.77	0.74	2.20	1.76	1.00	2.20	1.76	1.36	3.30	2.64
7.35	0.74	2.20	1.76	1.02	1.50	1.20	1.38	1.90	1.52
8.24	0.78	2.10	1.68	1.06	1.90	1.52	1.47	1.30	1.04
8.94	0.79	1.50	1.20	1.07	2.09	1.67	1.47	0.84	0.67
9.92	0.83	0.88	0.70	1.12	2.23	1.78	1.50	0.16	0.13
10.73	0.85	0.66	0.53	1.14	2.29	1.83	1.55	0.86	0.69
11.63	0.86	0.44	0.35	1.18	2.16	1.73	1.56	1.10	0.88
11.96	0.87	0.28	0.22	1.20	2.10	1.68	1.60	2.44	1.95
pH	Compound **II**								
3.76	0.39	1.40	1.12	0.82	2.70	2.16	–	–	–
4.68	0.47	1.32	1.05	0.87	3.32	2.65	1.30	0.92	0.73
5.34	0.51	1.72	1.37	0.93	3.28	2.62	1.31	1.12	0.89
6.08	0.57	1.48	1.18	0.95	3.16	2.52	1.32	2.08	1.66
6.77	0.60	1.68	1.34	0.97	2.92	2.33	1.34	1.56	1.25
7.35	0.64	1.68	1.34	1.01	2.56	2.04	–	–	–
8.24	0.72	1.72	1.37	1.07	0.96	0.77	1.47	0.68	0.54
8.94	0.73	1.32	1.05	1.15	0.48	0.38	1.49	0.74	0.59
9.92	0.73	0.88	0.70	1.20	0.88	0.70	1.55	0.80	0.64
10.73	0.72	0.60	0.48	1.42	0.78	0.62	1.58	0.68	0.54
11.63	0.82	0.44	0.35	1.43	0.60	0.48	1.60	0.80	0.64
11.96	0.86	0.34	0.27	1.43	0.72	0.58	1.64	0.64	0.51
pH	Compound **III**								
3.76	0.36	1.28	1.02	0.76	2.28	1.82	–	–	–
4.68	0.46	1.64	1.31	0.90	3.00	2.40	1.33	1.16	0.93
5.34	0.52	1.84	1.47	1.00	3.52	2.82	1.37	1.12	0.90
6.08	0.58	1.56	1.25	1.06	4.28	3.42	1.39	0.80	0.64
6.77	0.60	1.84	1.47	1.11	3.72	2.98	1.40	0.68	0.54
7.35	0.67	1.80	1.44	1.16	2.84	2.27	1.60	0.44	0.35
8.24	0.73	1.88	1.50	1.23	1.96	1.57	1.62	1.72	1.38
8.94	0.74	1.72	1.37	1.24	1.73	1.38	1.63	1.91	1.53
9.92	0.76	0.84	0.67	1.24	2.68	2.14	1.64	2.16	1.73
10.73	0.78	0.60	0.48	1.25	3.04	2.43	1.64	1.92	1.54
11.63	0.79	0.32	0.26	1.25	2.28	1.82	1.65	1.32	1.05
11.96	0.80	0.16	0.13	1.25	2.24	1.79	1.65	0.80	0.64

Table 2. (Contd.)

pH	Compound **IV**								
	1st wave			2nd wave			3nd wave		
	$-E_{1/2}$, V	i_d, μA	J_d[a]	$-E_{1/2}$, V	i_d, μA	J_d[a]	$-E_{1/2}$, V	i_d, μA	J_d[a]
3.76	0.38	1.36	1.09	0.77	2.68	2.14	1.28	0.92	0.73
4.68	0.47	1.64	1.31	0.90	3.32	2.65	1.33	1.28	1.02
5.34	0.50	1.40	1.12	1.00	3.40	2.72	1.36	0.90	0.72
6.08	0.63	1.36	1.09	1.10	3.52	2.81	1.36	1.04	0.83
6.77	0.70	1.36	1.09	1.14	3.56	2.85	1.36	0.80	0.64
7.35	0.72	1.26	1.01	1.17	3.12	2.50	1.38	0.20	0.16
8.24	0.76	1.22	0.98	1.18	2.04	1.63	–	–	–
8.94	0.78	1.16	0.93	1.22	1.68	1.34	–	–	–
9.92	0.80	1.12	0.90	1.24	0.76	0.61	1.39	1.20	0.96
10.73	0.80	0.40	0.32	1.24	0.98	0.78	1.40	1.27	1.01
11.63	0.82	0.48	0.38	1.25	2.44	1.95	1.59	1.28	1.02
11.96	0.83	0.16	0.13	1.26	2.48	1.98	1.61	1.68	1.34
	Compound **V**								
3.76	0.24	1.00	0.80	0.70	3.56	2.85	1.27	1.60	1.28
4.68	0.46	1.48	1.18	0.89	2.36	1.89	1.28	1.44	1.15
5.34	0.54	1.64	1.31	0.94	1.84	1.47	1.28	1.96	1.57
6.08	0.56	1.64	1.31	0.99	1.64	1.31	1.29	2.00	1.60
6.77	0.60	1.12	0.89	1.04	1.52	1.21	1.29	1.84	1.47
7.35	0.67	1.24	0.99	1.20	1.28	1.02	1.54	1.64	1.31
8.24	0.70	1.23	0.98	1.21	1.24	0.99	1.55	1.76	1.41
8.94	0.73	1.12	0.89	1.21	1.14	0.91	1.55	1.80	1.44
9.92	0.75	0.48	0.38	1.22	0.84	0.67	1.56	2.88	2.30
10.73	0.78	0.40	0.32	1.23	0.88	0.70	1.57	2.24	1.79
11.63	0.80	0.20	0.16	1.23	0.76	0.61	1.57	1.98	1.58
11.96	0.82	0.08	0.06	1.24	0.88	0.70	1.59	1.72	1.37

[a] J_d in μA l $s^{1/2}$ mol^{-1} $mg^{-2/3}$

values with increasing pH. The angular coefficients $dE_{1/2}/d$pH of the first wave have different values in different intervals of pH: at pH 3–5 it is 25 mV/pH unit, at pH 5–7 it is >100 mV/pH unit, and at pH > 7 it is 43 mV/pH unit. For the second and the third cathode waves the dependences of $E_{1/2}$ on pH do not vary in the whole range of pH. For the second wave $dE_{1/2}/d$pH = 44 mV/pH unit, for the third it is 40 mV/pH unit. The limiting current for the first wave tends to decrease with increasing pH, for the second cathode wave the i_d has a minimum in the neutral medium, for the third wave the minimum is reached in alkaline media.

Compounds **II–V** undergo reduction on a mercury electrode also in three steps. Certain differences in the polarographic behavior of the studied compounds are negligible.

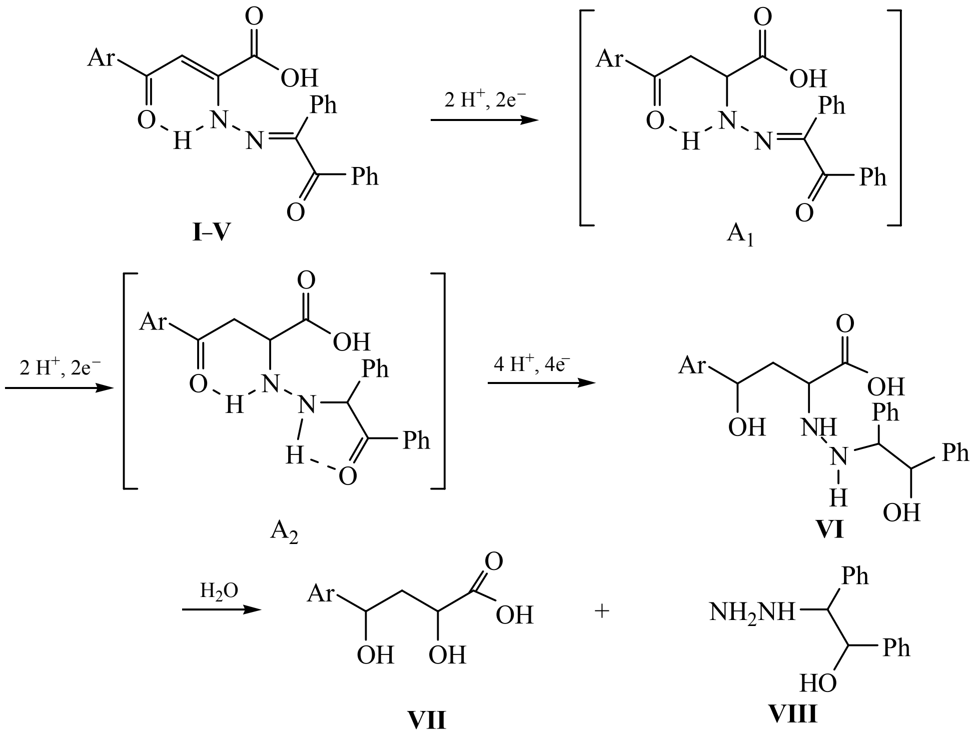
Investigation of the nature of the limiting current (i_l) was performed for compounds **I** and **III** at three values of pH of the solution, 3.76, 6.77, and 11.96, and gave the following results: (1) for compound **I** for the first wave in all media and for the second and the third waves in acidic and neutral media the dependence of i_l on concentration (c) is linear, whereas for the latter two in alkaline media a deviation from the linear dependence is observed and the values of i_l become independent of the concentration of depolarizer when certain concentrations c are attained; (2) for compound **III** the dependence of i_l on c is linear for the first and the third waves in all media and for the second wave in acidic and neutral media, whereas in alkaline media a deviation of i_l from linearity is observed for the second wave, similar to the aforementioned for compound **I**. Therefore, the polarographic method can be used for quantitative determination of the compounds under consideration in acidic and neutral media.

The shape of the dependence of the limiting current on the height of mercury column and the temperature allows a conclusion that for compounds **I** and **III** in acidic and neutral media it is a diffusion-controlled limiting current. However, in an alkaline medium the limiting current for the second and the third waves for compound **I** and that for the second wave for compound **III** have an adsorption character.

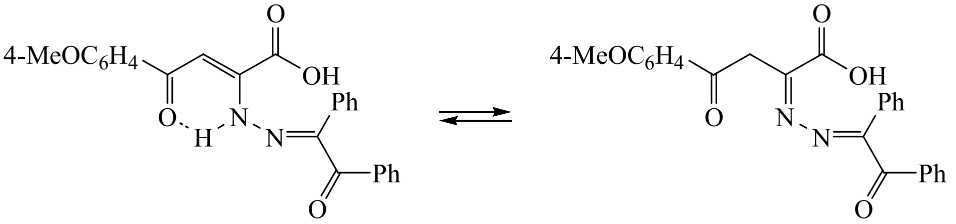
To elucidate the mechanism of reduction of the studied compounds on a mercury electrode we have determined the number of electrons (n) consumed by the molecule of depolarizer (compound **III**) upon reduction in neutral medium (pH 8.24). Using the method of electrolysis at the controlled potential of the working electrode (CPE) corresponding to the plateau of the limiting current for each of the waves, the following data have been obtained: for $E = -0.97$ V, $n = 2.12$; $E = -1.41$ V, $n = 4.21$, $E = -1.83$ V, $n = 8.22$. The products of electrolysis were isolated and identified by the methods of TLC, IR and NMR spectroscopy.

Based on the obtained electrochemical and spectral data, it is possible to suggest the following mechanism of reduction of compounds **I–V** on a mercury electrode.

First, apparently, the polarographic reduction of the $C^2=C^3$ double bond occurs with consumption of two electrons and two protons and the formation of 4-aryl-2-(1,2-diphenyl-2-oxoethylidenehydrazino)-4-oxobutanoic acids (intermediate A_1). This process corresponds to the first two-electron cathode wave. Apparently, A_1 is reduced also with the consumption of two electrons and two protons and the formation of 4-aryl-2-(1,2-diphenyl-2-oxoethylhydrazino)-4-oxobutanoic acids (intermediate A_2). This process corresponds to the second two-electron cathode wave. In intermediate A_2, two similar in nature carbonyl groups are present, which, most probably, are involved in intramolecular hydrogen bonds. Due to the similarity of their properties both carbonyl groups are probably reduced simultaneously with the consumption of four electrons and four protons to form eventually 4-aryl-2-(1,2-diphenyl-2-hydroxyethylhydrazino)-4-hydroxybutanoic acids (**VI**). This process corresponds to the third four-electron cathode wave.



Judged from the ^{1}H NMR spectrum recorded in a polar solvent, DMSO-d_6, compound **III** exists in solution in two forms, the *Z*-enehydrazine and β-ketohydrazone.



The *Z*-enehydrazine form of compound **III** is characterized by the following signals in the proton spectrum: a singlet of three protons of the methoxy group at 3.76 ppm, a singlet of the vinyl proton at 6.36 ppm, a singlet of the NH group involved in the intramolecular hydrogen bond at 12.71 ppm. In the spectrum is also observed a multiplet of aromatic protons centered at 7.55 ppm.

The β-ketohydrazone form is characterized by a singlet of protons of the methoxy group at 3.81 ppm and a singlet of protons of the methylene group at 4.49 ppm.

According to the integral intensity of the signals in the ^{1}H NMR spectrum, the *Z*-enehydrazine form dominates and the ratio of the forms is 9:1.

Since the polarographic reduction of compounds **I**–**V** also was studied in a polar medium it is presumable that just the *Z*-enehydrazine form undergoes the reduction.

^{1}H NMR spectra recorded from the products of electrolysis of compound **III** carried out at pH = 8.24, *E* = –0.97 V, and pH = 8.24, *E* = –1.41 V, have complex character and contain a set of signals from the mixture of the products of electrolysis and the starting compound (the *Z*-enehydrazine form is registered in the spectra).

In the ^{1}H NMR spectrum recorded from the product of electrolysis carried out at pH = 8.24 and *E* = –1.83 V the signals of the starting compound **III** are absent and the signals of 2-[N^2-(1,2-diphenyl-2-hydroxy)ethyl]hydrazino-4-hydroxy-4-(4-methoxyphenyl)-butanoic acid (**VI**) are present. In the spectrum apart from the multiplet of aromatic protons centered at 7.48 ppm a triplet of the methine proton of the C^{4}H group at 4.31 ppm (J = 6.9 Hz), a doublet of the C^{2}H methine proton of the ethyl group at the oxygen atom at 4.28 ppm (J = 9.3 Hz), a singlet of three protons of the methoxy group at 4.27 ppm, a doublet of doublets of the methine proton of the C^{2}H group at 4.15 ppm, a doublet of the C^{2}H methine proton of the ethyl group at the nitrogen atom at 3.84 ppm (J = 9.3 Hz), four broadened singlets of the NH and OH groups at 2.98, 3.10, 3.63, 3.79 ppm, and a complex multiplet of the CH$_2$ group at 2.2–2.4 ppm are observed. The signal of the carboxyl group could not be detected in the spectrum, apparently due to its strong broadening.

Compound **VI** is the final product of the electrolysis, although we failed to isolate it intact from the solution. Its formation, however, is corroborated by the fact that 2,4-dihydroxy-4-(4-methoxyphenyl)butanoic acid (**VII**) was identified as the product of electrolysis of compound **III**.

The formation of compound **VII** is quite possible to occur in the process of isolation as a result of hydrolysis of compound **VI** with the rupture of the C^2–NH bond. A structurally close to compound **VII** ethyl 2-hydroxy-4-phenylbutanoate was obtained earlier also by stepwise reduction of ethyl 2,4-dioxo-4-phenylbutanoate over palladium catalysts [2].

EXPERIMENTAL

IR spectra were recorded on a FSM–1201 instrument in mineral oil. ^{1}H NMR spectra were registered on a Mercury plus 300 spectrometer in CDCl$_3$ or DMSO-d_6 with HMDS as an internal reference.

Polarographic measurements were performed in 25% aqueous 2-propanol in the range of pH from 3 to 12. The Britton-Robinson buffer solutions were used to keep a constant pH. Polarograms were recorded on a PU-1 polarograph in a three-electrode cell by means of classical polarography.

To determine the number of electrons consumed by the molecule of the depolarizer the CPE was performed in a YaCE cell with separated cathode and anode spaces, with platinum wire anode, mercury cathode at the bottom, and a saturated silver chloride reference electrode. The cathode potential was kept constant by means of a P–5848 potentiostat. The amount of electricity passed was determined by an IPT-1 constant current integrator. CPE, as well as all polarographic measurements, were performed in a buffer solution in 25% aqueous 2-propanol at pH 8.24. The products of electrolysis were extracted with chloroform.

Thin layer chromatography was performed on standard Silufol UV-245 plates in the system of solvents ether–benzene–acetone (10:9:1) after 10 cm run of the solvent front. The spots were visualized by iodine vapor.

2-(1,2-Diphenyl-2-oxoethylidenehydrazino)-4-oxo-4-(4-chlorophenyl)-2-butenoic acid (I). To the solution of 2.26 g (0.1 mol) of 2-hydroxy-4-oxo-4-(4-chlorophenyl)-2-butenoic acid in 20 ml of ethanol the solution of 2.24 g (0.1 mol) of benzil monohydrazone in 20 ml of ethanol was added, the mixture was kept at 20–25°C for 24 h, cooled to 0°C, the precipitate formed was filtered off, crystallized from acetonitrile. Yield 3.4 g (79%), mp 147–148°C. Compounds **II–V** were prepared similarly.

2,4-Dihydroxy-4-(4-methoxyphenyl)butanoic acid (VII). 2-Propanol–water solution after preparative electrolysis of compound **III** at pH 8.24 and E = –1.83 V was twice extracted with equal volume of $CHCl_3$ and the combined chloroform extracts were evaporated. The oily residue was refluxed in ethanol with charcoal. After filtration and removal of solvent an oily substance was obtained. According to TLC it was an individual compound with R_f 0.99. ^{1}H NMR, δ, ppm: 2.21 m (2H, CH_2), 3.85 t (1H, C^2H), 3.95 s (3H, CH_3), 4.09 t (1H, C^4H), 4.26 s (1H, OH) 4.70 s (1H, OH), 7.11 d (2H, C_6H_4), 7.54 d (2H, C_6H_4).

ACKNOWLEDGMENTS

This work was financially supported by the Russian Foundation for Basic Research (grant no. 08-03-00488a).

REFERENCES

1. Posyagin, G.S., Posyagina, E.Yu., Zalesov, V.V., and Kataev, S.S., *Russ. J. Gen. Chem.*, 2001, vol. 71, no. 10, p. 1574.
2. Slavinska, V., Sile, Dz., Rozenthal, G., Maurops, G., Popelis, J., Katkevich, M., Stonkus, V., and Lukevics, E., *Chem. Heterocycl. Comp.*, 2006, vol. 42, no. 5, p. 570.