ELECTROCHEMICAL DECHLORINATION OF SOME DERIVATIVES OF 1-CHLOROPHTHALAZINE IN DIMETHYLFORMAMIDE

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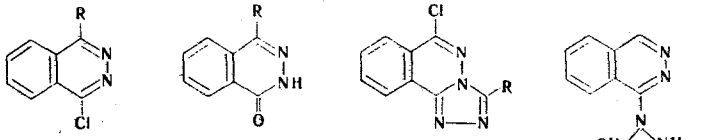
The electrochemical reduction of some chlorophthalazine derivatives that differ with respect to the nature of the substituent and the heteroring (phthalazines, phthalazones, and 1,2,4-triazolo[3,4-a]phthalazines) on a dropping mercury electrode in dimethylformamide was studied by polarography, coulometry, and preparative electrolysis with isolation and identification of the electrolysis products. It is shown that the carbon–chlorine bond is cleaved initially in the cathode reduction of the investigated compounds to give the corresponding dehalogenated heterocycles.

The electrochemical reduction of halogen-containing heterocycles in an aprotic medium has been studied only in the case of a small number of heterocyclic systems [1-3] and proceeds in the same way as the electrochemical reduction of aryl halides, although the effect of not only the nature of the halogen [1, 3] but also the nature of the heteroring [1] is observed distinctly.

In the present research we studied the electrochemical reduction of some 1-chlorophthalazine derivatives that differ with respect to the nature of the substituent and the nature of the heteroring — phthalazine (I-III), phthalazone (IV, V), and 1,2,4-triazolo[3,4-a]phthalazine (VI-IX) derivatives — on a dropping mercury electrode in dimethylformamide (DMF).



I–III IV, V VI–IX X

I, V, VI R = H; II, IV R = Cl; III R = NNH_2 (|, CH_3); VII R = CH_3; VIII R = C_6H_5; IX R = $C_6H_4NO_2$-4

The reduction of all of the investigated compounds is a multistep process. The half-wave potentials and limiting currents are presented in Table 1. The first waves on the polarograms of phthalazines I-III are two-electron waves and are irreversible, as evidenced by the absence of an oxidation peak on the cyclical volt–ampere graphs (v = 400 mV/min) recorded with a stationary electrode. With respect to their form and potentials, the second and third waves of II correspond to the reduction waves of 1-chlorophthalazine. These data indicate that cleavage of the C–Cl bond occurs at the potentials of the first wave in the electrochemical reduction of II and that 1-chlorophthalazine is formed as a result of successive electrode (E) and chemical (C) reactions, probably via an ECEC mechanism (see the scheme below).

The picture of the electrochemical reduction of 1-chlorophthalazine is not as clear, since the second wave does not coincide with the first wave in the reduction of phthalazine and requires special study. The electrochemical reduction of phthalazine in DMF takes place in two steps and is evidently similar to the electrochemical reduction in alkaline-buffered media [4].

According to the coulometric data, 2 faradays of electricity per mole of substance are consumed in the electrolysis of III at the potentials of the limiting current of the first wave, and 1-(α-methylhydrazino)phthalazine (X), the structure of which was confirmed by data

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TABLE 1. Half-Wave Potentials and Limiting Currents in the Electrochemical Reduction of Phthalazine, Phthalazone, and 1-Chlorophthalazine Derivatives in a 0.1 M $(C_2H_5)_4NBr$-Base Electrolyte in Dimethylformamide (the reference electrode was the mercury sludge)

Compound	R	mp, °C	$-E_{1/2}$, V	i, μA
Phthalazine	—	90	1,48 2,02	2,03 3,53
I	H	115	1,15 1,97	2,20 2,00
II	Cl	165	0,95 1,15 1,94	2,07 1,27 2,67
III	$-N<^{NH_2}_{CH_3}$	141—141,5	1,39 2,04	2,40 2,66
IV	Cl	274	1,30 1,65*	1,13 0,40
V	H	183	1,62*	0,80
VI	H	164—165	0,98 1,42 1,87	2,30 0,60 1,15
VII	CH_3	196	1,02 1,44 2,00	2,21 1,12 1,40
VIII	C_6H_5	168—170	0,97 1,47 2,00	2,07 0,64 1,65
IX	$C_6H_4NO_2$-4	232	0,50 1,02 2,00	1,09 3,30 2,18

*A wave that merges with the discharge of the base electrolyte appears at −1.8 V.

from IR, UV, and PMR spectroscopy, was isolated preparatively. Consequently, reductive cleavage of the C—Cl bond to give a dechlorinated product via the ECEC mechanism also occurs in the case of III in the first step. A comparison of the $E_{1/2}$ values of II and III shows that the transition to a stronger electron-donor group in the 4 position of the phthalazine ring hinders electrochemical reduction.

The preparative isolation of X made it possible to unambiguously solve the problem of the structure of the product of the reaction of 1-chlorophthalazine with methylhydrazine. It was recently shown [5] that phthalazone methylhydrazone rather than X, as assumed in [6, 7], is formed in this reaction.

The polarographic picture for 4-chlorophthalazone IV differs from that for I-III. Its first reduction wave is a one-electron wave, although it is also irreversible (on the basis of the cyclical volt—ampere graph, v = 400 mV/min). The second wave corresponds to reduction of phthalazone V and increases when it is added to the solution undergoing polarography. In the case of electrolysis at the potentials of the limiting current of the first wave 2 faradays of electricity per mole of substance are consumed in 2 h, and phthalazone V is formed; the latter was isolated and identified by thin-layer chromatography (TLC) and UV spectroscopy. Consequently, the splitting out of chlorine in the electrochemical reduction of 1-chlorophthalazone proceeds via an ECC mechanism and is analogous to the similar process in the electrochemical reduction of 2-chloro- and 2-bromopyridines [2] or chloro- and bromobenzophenones [8].

A study of the electrochemical reduction of 3-substituted 6-chloro-1,2,4-triazolo[3,4-a]phthalazines VI-IX showed that VI-VIII behave like II and III. The first polarographic wave is a two-electron wave and is irreversible.

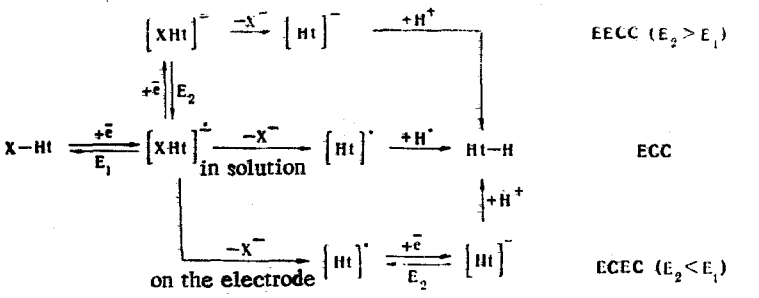
In the case of electrolysis at a controllable potential of the limiting current of the first wave 2 faradays of electricity per mole of substance are consumed, and a dechlorinated product is isolated; this was illustrated by the isolation of 3-phenyl-1,2,4-triazolo[3,4-a]-phthalazine XI in the preparative electrolysis of VIII. The structure of the dehalogenated

electrolysis product was confirmed by the spectral data and alternative synthesis from phthalazone hydrazone and benzoyl chloride by the method in [9]. Consequently, in this case the initial splitting out of halogen takes place via an ECEC mechanism. It should be noted that the nature of the substituent in the 3 position of the triazolophthalazine ring, judging from the $E_{1/2}$ values, has virtually no effect on the electrochemical reduction of these compounds.

Nitro-substituted IX takes on the first electron reversibly, which is apparent from the anode oxidation peak on the cyclical volt–ampere graph (ΔE_n = 60 mV, $i_{n,k}/i_{n,a}$ = 1 at scanning rate v = 400 mV/min). An anion radical, which is generated on the cathode (the solution near the cathode is green) and disappears as it is stirred into solution, is recorded in the case of the electrochemical reduction of IX directly in the resonator of the EPR spectrometer. The observed spectrum is rather complex and differs from the EPR spectra of p-substituted nitrobenzenes; this makes it possible to assume the participation of the triazolophthalazine ring in delocalization of the unpaired electron.

Thus in the case of aromatic character of the heteroring (II, III, and VI-VIII) the electrochemical splitting out of chlorine proceeds via an ECEC mechanism, whereas the mechanism changes to an ECC mechanism on passing to the phthalazone system.

On the basis of the literature data [1-3] and our data one may draw the generalizing conclusion that the character of the electrochemical reduction of halogen-containing heterocycles in aprotic media, as in the case of aryl halides, is determined by the stability of the C–Hal bond in the anion radical formed after the addition of the first electron and depends on both the nature of the heteroring and the nature of the halogen atom. The dehalogenation of haloheterocycles to heterocycles during electrochemical reduction in nonaqueous media may proceed via three mechanisms:



If the strain radical is stable, in the case of a more negative E_2 potential by taking on an electron it forms a dianion, which splits out a halide ion and is protonated to give the heterocycle (the EECC mechanism). The unstable anion radical splits out a halide ion on the electrode, and the resulting σ radical immediately takes on a second electron (the ECEC mechanism). An anion radical with intermediate stability has time to diffuse into the solution, where the subsequent chemical reactions occur (the ECC mechanism).

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EXPERIMENTAL

The classical and cyclical polarograms were recorded with an LP-7 polarograph with 0.1 M $(C_2H_5)_4NBr$ in DMF as the base electrolyte. The indicator electrodes were a dropping mercury electrode with forced detachment of the drops (τ = 0.5 sec, m = 0.7 mg/sec) and a stationary mercury electrode in the form of a hanging drop. The reference electrode in the recording of the polarograms was the mercury sludge, the potentials of which in 0.1 M $(C_2H_5)_4NBr$ in DMF is −0.44 V relative to the saturated calomel electrode (SCE); the reference electrode for electrolysis was the SCE. The number of electrons transferred was determined by the comparison method from the height of the first one-electron wave of nitro derivative IX. The depolarizer concentration during polarography was 10^{-3} mole/liter. The dissolved oxygen was removed by passing argon through the solutions. The half-wave potentials are presented relative to the mercury sludge. Electrolysis at a controllable potential was carried out in a three-electrode cell with separated anode and cathode spaces. The cathode was the stirred mercury sludge (S = 7 cm^2), and the anode was a platinum plate. The anolyte was 0.5 M $(C_2H_5)_4NClO_4$ in DMF, and the catholyte was 200 mg of the compound to be reduced and 2.1 g of $(C_2H_5)_4NBr$ in 20 ml

of DMF. The cathode potential was held constant by means of an II-5848 potentiostat. The electrolysis products were separated by column chromatography and were identified by IR, UV, and mass spectrometry and elementary analysis, as well as by comparison with samples with known structures. The melting points were determined with a Boetius microscope stage.

1-(α-Methylhydrazino)phthalazine (X). The electrolysis of 1-(α-methylhydrazino)-4-chlorophthalazine was carried out at E = −1.9 V (relative to the saturated calomel electrode), and the solutions from four experiments were combined [the overall weight of III was 0.8 g (0.004 mole)] and neutralized to pH 7 with 5% hydrochloric acid. The water and DMF were removed in vacuo, and the pasty residue was treated with hot benzene (seven 40-ml portions). The benzene solution was dried with Na_2SO_4, the benzene was removed by distillation, and the residual oil was separated with a column [on Brockmann activity II Al_2O_3 (neutral) with elution with petroleum ether–diethyl ether (1:2)] to give 0.32 g (0.002 mole) (48%) of colorless needles of X with mp 89-81°C (CCl_4). IR spectrum: ν_{NH} 3462, 3379; δ_{NH} 1624 cm^{-1} (petrolatum). UV spectrum (acetonitrile), λ_{max} (log ε): 218 (4.44), 262 sh (3.43), and 322 nm (3.66). PMR spectrum (d_6-DMSO), δ: 7.55 m (1H, 8-H), 7.08 m (2H), 6.77 m (2H)(4-H–7-H), 5.28 br s (2H, HN_2), and 3.66 s ppm (3H, NCH_3). Found: M 174 (by mass spectrometry). $C_9H_{10}N_4$. Calculated: M 174.

3-Phenyl-1,2,4-triazolo[3,4-a]phthalazine (XI). Solutions from two experiments on the electrolysis of phthalazine VIII at E = −1.6 V (relative to a saturated calomel electrode) were combined [the average weight of VIII was 0.43 g (0.0015 mole) and neutralized to pH 7 with 5% hydrochloric acid, and the solvent was removed in vacuo. The residue was treated with warm water to remove the base electrolyte, and the organic part was extracted with chloroform. The chloroform was removed, and the residue was chromatographed with a column filled with Brockmann activity II Al_2O_3 (neutral) (elution with methanol) to give 0.3 g (1.3 mmole) (70%) of white crystals of XI with mp 215-216°C. UV spectrum, λ_{max} (log ε): 265 (4.53) in acetonitrile, and 262 nm (4.53) in ethanol. Found: C 72.0; H 4.3; N 23.0%. Calculated: C 71.8; H 4.3; N 24.0%. Compound XI was obtained by alternative synthesis from phthalazone hydrazone and benzoyl chloride by the method in [9] and had mp 215-216°C (80% AcOH) (mp 208-209°C [9]).

LITERATURE CITED

1. K. Alwair and J. Grimshaw, J. Chem. Soc., Perkin II, 1811 (1973).
2. J. E. O'Reilly and P. J. Elving, J. Electroanal. Chem., 75, 507 (1977).
3. I. M. Sosonkin, G. N. Strogov, V. N. Novikov, and T. K. Ponomareva, Khim. Geterotsikl. Soedin., No. 1, 23 (1977).
4. H. Lund and E. T. Jensen, Acta Chem. Scand., 24, 1867 (1970).
5. B. I. Buzykin, N. N. Bystrykh, A. P. Stolyarov, S. A. Flegontov, V. V. Zverev, and Yu. P. Kitaev, Khim. Geterotsikl. Soedin., No. 3, 402 (1976).
6. K. T. Potts and C. Lovelette, J. Org. Chem., 34, 3221 (1969).
7. K. Ueno, R. Moroi, M. Kitagawa, K. Asano, and S. Miyazaki, Chem. Pharm. Bull., 24, 1068 (1976).
8. L. Nadjo and J. M. Saveant, J. Electroanal. Chem., 30, 41 (1971).
9. J. Druey and B. H. Ringier, Helv. Chim. Acta, 34, 197 (1951).