The authors are indebted to Prof. K. Takiura and Dr. T. Kametani for valuable suggestions and encouragements. The authors also wish to thank Mr. Y. Sanno for gifts of samples.

Summary

The polarographic behavior of α,β-unsaturated nitro compounds was studied by comparison with corresponding saturated nitro compounds and the reduction process were considered. The electrode reaction in acid medium was presumed to be a six-electron reduction and its process to be as follows:

$$\text{R-CH=CH-NO}_2 \xrightarrow[2\text{H}^+]{2\text{e}} \text{R-CH=CH-N=O} \xrightarrow[2\text{H}^+]{2\text{e}} \text{R-CH}_2\text{-CH=N-OH} \xrightarrow[2\text{H}^+]{2\text{e}} \text{R-CH}_2\text{-CH}_2\text{-NHOH}$$

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64. Masaichiro Masui, Hiroteru Sayo, and Yukio Nomura: Controlled Potential Electrolysis. III.[1] Controlled Potential Electrolysis of ω-Nitrostyrene.

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In the previous paper[1] α,β-unsaturated nitro compounds were studied by polarography, comparing with the corresponding saturated nitro compounds, and it was presumed that they would undergo six-electron reduction at electrode and the process in acid medium might be expressed by the following equation:

$$\text{R-CH=CH-NO}_2 \xrightarrow[2\text{H}^+]{2\text{e}} \text{R-CH=CH-N=O} \xrightarrow[2\text{H}^+]{2\text{e}} \text{R-CH}_2\text{-CH=N-OH} \longrightarrow \text{R-CH}_2\text{-CH}_2\text{-NHOH} \quad \ldots\ldots(1)$$

In the present series of experiments, we studied the controlled potential coulometric analysis and controlled potential electrolytic preparation of the reduction intermediates of ω-nitrostyrene and determined the number of electrons, *n*, involved in the electrode reaction and reduction process.

Determination of the Number of Eloctrons, *n*

To determine the *n* value, a controlled potential coulometric analysis with counter millicoulometer was applied. The results are shown in Table I. From these results it is evident that the first wave of ω-nitrostyrene in acid medium is a four-electron and the second two-electron reduction. The first wave of 1-phenyl-2-nitroethane in

Table I. Determination of the Number of Reduction Electrons

pH	EtOH present (%)	Cathode potential vs. S.C.E.	Sample taken (mg.)	Electricity required (coulombs)	Number of electrons
ω-nitrostyrene					
2.00	1	0.40	0.92	2.45	4.12
2.00	1	1.00	0.75	3.03	6.25
50% AcOH	1	0.40	0.92	2.50	4.20
6.00	1	0.60	0.75	1.83	3.77
1-phenyl-2-nitroethane					
2.00	1	0.90	0.92	2.28	3.88
6.00	1	1.00	0.92	2.16	3.67

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[1] Part II: This Bulletin, **4**, 332(1956).

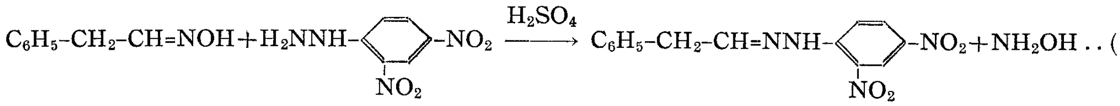
[2] M. Masui, H. Sayo: J. Pharm. Soc. Japan, **75**, 1515(1955).

acid medium is also evident as a four-electron reduction.

Controlled Potential Electrolytic Synthesis

ω-Nitrostyrene is only slightly soluble in water and soluble in ethanol and acetic acid, necessitating the use of a supporting electrolyte containing a large proportion of nonaqueous solvent. Otherwise only a very dilute solution could be made and it is not suitable for the preparation. Suspension is also not suitable for it, as it may take a very long time to complete the electrolysis. When the proportion of ethanol or acetic acid is increased, the resistance of the solution becomes very high and, especially in the case of the former, the form of polarographic wave is seriously affected. After various experiments, 50% acetic acid solution containing $0.2\,M$ potassium chloride was selected as a base solution. The polarogram of ω-nitrostyrene in the base solution shows an intermediate form between those of pH 2 and pH 3. Though lithium chloride added to the concentration of $1M$ in 50% acetic acid solution makes the resistance of the solution low, the effect does not appeare to be much preferable.

ω-Nitrostyrene was electrolyzed at -0.55 v. vs. S. C. E., a potential on the plateau of the first wave, and after completing the electrolysis, an oxime was detected from a small portion of the solution by the method expressed in equation (2).


..(2)

On the other hand, a large residual portion of the electrolyzed solution was neutralised and extracted several times with ether and phenylacetaldoxime was obtained.

In the same manner, ω-nitrostyrene was electrolysed on another sample at -1.15 v. vs. S. C. E., a potential on the plateau of the second wave. In this case, oxime was not detected and it was thought that the hydroxylamine derivative might be produced. However, the probable product, N-alkylhydroxylamine, was not found in any literature and attempt was made to obtain it as β-phenylethylamine. After the electrolysis was completed, its catalytic reduction with palladium-charcoal was carried out immediately by which one mole of hydrogen was absorbed and β-phenylethylamine was obtained.

$$C_6H_5\text{-}CH{=}CH\text{-}NO_2 \xrightarrow[6H^+]{6e} C_6H_5\text{-}CH_2\text{-}CH_2\text{-}NHOH \xrightarrow[H_2]{Pd\text{-}C} C_6H_5\text{-}CH_2\text{-}CH_2\text{-}NH_2 + H_2O \ldots\ldots\ldots (3)$$

From these experiments, therefore, it was determined that the reduction process of ω-nitrostyrene in acid medium occurs according to equation (1), and it was also concluded that ω-nitrostyrene could not be reduced to β-phenylethylamine only by the electrode reaction in such a medium.

Experimental

Apparatus—Potentiostat used was Yanagimoto Potentiostat Model-3. The coulometer was a counter millicoulometer.[2]

Cell—H-Type cell holding sintered glass disk and agar gel plug saturated with KCl between the cathode and anode compartments. Cathode compartment was closed with a rubber stopper and a gas delivery tube was provided for removing dissolved air from the solution with nitrogen or hydrogen. The volume of the cathode solution used, in general, was about 60 cc. The area of mercury pool was about $18\,cm^2$. Glass propeller partly immersed in the mercury was used.

Reagents—ω-Nitrostyrene and 1-phenyl-2-nitroethane used were the same as those described in the previous paper.[1]

Buffer solutions—Prepared according to the universal Britton-Robinson mixtures and their pH determined with Towa-Dempa Glass Electrode pH Meter Model HM-5. They contained $0.1M$ KCl.

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3) O. L. Brady, F. H. Peakin : J. Chem. Soc., **1929**, 478.

4) K. Nagasawa, S. Ohkuma : J. Pharm. Soc. Japan, **74**, 410(1954).

Determination of *n*—The buffer solution or 50% AcOH solution was placed in the cell and hydrazine hydrate was added to the anolyte as an anodic depolarizer. After dissolved oxygen was removed satisfactorily by bubbling hydrogen through the solution, the potentiostat was adjusted to maintain the desired control potentials (see Table I). The solution was then electrolyzed, with hydrogen passing continuously, until the current decreased to a background current, and the counter rate of millicoulometer was counted for the background. One cc. of EtOH solution of the sample, prepared by dissolving a known weight of the sample in 10 cc. EtOH, was pipetted into the cell, and the electrolysis was allowed to proceed until the current decreased again to the same background current observed with the base solution alone. Ordinarily, the electrolysis was completed within 1 hr. The total count of millicoulometer was then read and the count due to the background current during the electrolysis was subtracted. Coulombs required by the reduction was computed from the relation of counts-coulombs.

Phenylacetaldoxime—0.45 g. of ω-nitrostyrene was dissolved in 60 cc. of 50% AcOH solution containing 0.2*M* KCl and placed in the cathode compartment. In the anode compartment 0.1*M* KCl solution containing hydrazine hydrate was placed and Pt anode was settled. Electrolysis was continued for about 5 hrs. at −0.55 v. vs. S.C.E., controlling the temperature of the solution under 30° during the electrolysis.

Detection of Phenylacetaldoxime—To a few drops of the electrolyzed solution, a few drops of 1.5% 2,4-dinitrophenylhydrazine solution in 15% H_2SO_4 in EtOH (1:3) was added and heated in a water bath for about 2 mins. By adding 6.5% KOH solution to the orange precipitates produced, a red color appeared (aldehyde). The centrifugate was extracted with ether, the aqueous layer was acidified, and after oxidizing with I_2 solution, Griess reaction was carried out. Clear pink color developed (hydroxylamine).

Phenylacetaldoxime—After neutralising the electrolysed catholyte with Na_2CO_3, the solution was extracted several times with ether. The ether solutions were combined and after drying over anhyd. K_2CO_3, the ether was evaporated. A faint brown needles were obtained. The amount of the crystals was too small to allow recrystallization from EtOH that it was sublimed under a reduced pressure in oil bath. The melting point of the crystals adhering on the upper part of the vessel was 89~91°. Resublimed crystals showed m.p. 98~99°(microscopic determination) (reported m.p. 98.5°[5]).

1-Phenyl-2-aminoethane—0.43 g. of ω-nitrostyrene was dissolved in 60 cc. of 50% AcOH solution containing 0.2 *M* KCl and placed in the cathode compartment. Anode conditions were the same as those for phenylaldoxime. Electrolysis was continued for about 4.5 hrs. and after completion, the catholyte was reduced immediately by catalytic reduction with Pd-C, absorbing 58 cc. (calcd. for 1 mole, 66.8 cc. at 10°) of H_2. After filtering off the catalyst, the filtrate was neutralised with Na_2CO_3 and extracted several times with ether. The ether extracts were combined, dried over anhyd. K_2CO_3, and the solvent distilled off, leaving a slightly yellowish oil. Addition of saturated EtOH solution of oxalic acid gave the oxalate as colorless needles, m.p. 177~180°. Yield, 250 mg. Recrystallization from water afforded colorless needles, m.p. 180~181°(reported m.p. 181°[6]). The electrolyzed solution did not show any reaction as described in the detection of phenylacetaldoxime.

Discussion

Since 1-phenyl-2-nitroethane was an oil at room temperature and the purification was probably not sufficient, the number of reduction electrons at pH 2 was somewhat lower than the theoretical value of 4. If the purity was 95%, the value almost agrees with the theoretical one. In the case of ω-nitrostyrene, the number was larger than the theoretical value in acid medium. The reason was not clear, but, in general, when the wave form of polarogram was not good, the quantity of electricity required for the reduction varied slightly with varying settled potentials.

At pH 6, the value was lower in both cases. These might depend on the fact that the formation of aci-form of nitro group and the reverse reaction might not be sufficiently completed within the duration of electrolysis described above.

The authors are indebted to Prof. K. Takiura and Dr. T. Kametani for valuable suggestions and encouragements.

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5) Heilbron, Bunbury: Dictionary of Organic Compounds, Eyre & Spottiswood, London, **4**, 95 (1953).
6) Beilstein, **12**, 1096 (1929).

Summary

The two waves in the polarogram of ω-nitrostyrene in acid medium were determined to be four- and two-electron reductions by coulometric analysis using a large mercury pool cathode, and the reduction process was concluded, by the controlled potential electrolytic preparations, affording intermediate products, to be as shown by equation (1).

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65. **Manabu Fujimoto** : Application de la 2, 6-Lutidine au Médicament. II.*

Sur la synthèse des dérivés 3, 5-disulfanilamido substitués de lutidone-4 et de pyridone-4.

(*Larboratoire de Recherches, Shionogi & Co., S. A.***)

La nitration de 4-pyridone (I) est déjà exécutée par Crowe,[1] mais 3, 5-dinitropyridone (Ⅱ) lui-même est décrit récemment par Ochiai et Futaki, de son oxidure d'azote.[2] Selon nos résultats, (I) est capable de fournir (Ⅱ) en 63% rendement en milieu de l'acide sulfrique, en faisant réagir d'acide nitrique fumant. Mais dans cette condition, nous avons aussi gagné 3-nitropyridone-4 à 23% de la théorie.

On sait que 3, 5-diaminopyridone-4 (Ⅲ) est trés instable et se colore en rouge foncé, en exposant sout l'influence d'air.[3] En effet, après la réduction catalytique (10%-PdC-H_2), nous n'avons pas réussi à en isoler (Ⅲ), au départ de (Ⅱ). Nous avons pu le gagner seulement en solution éthanolique, avec un rendement peu satisfaisant. D'autre part, dans le but d'une comparaison, nous avons préparé, au départ de 3, 5-dinitrolutidone-4 (Ⅳ), le corps (Ⅴ) : 3, 5-diaminolutidone-4 qui diffère de (Ⅲ) par excellente stabilité contre l'air. La méthode de hydrogénation est catalytique ci-dessus (96% Rdt.) ou électrolytique (86% Rdt.), avec la solution aqueuse du sel de (Ⅳ).

A l'occasion de la même réduction catalytique de 4-chloro-3, 5-dinitrolutidine (Ⅵ), le chlore en position-4 a été non-séparable. En conséquence, (Ⅵ) se fournit 4-chloro-3,5-diaminolutidine (Ⅶ) en absorbant 6 mol. d'hydrogène, tandis que (Ⅵ) se forme, en aiguille jaune, 5-amino-4-chloro-3-hydroxyaminolutidine (Ⅷ), dans le cas de 5 mol. H_2.

La réaction entre (Ⅵ) et thiourée, fournit bis(3, 5-dinitrolutidyl)-sulfide (Ⅸ), au lieu de dinitrothiolutidone corresponde, en étant sous l'action de la solution aqueuse d'ammoniaque.

Encouragés par ces résultats, qui prouvent les propriétés des dérivés de 3, 5-diaminopyridine, nous avons décidé d'attacher le sulfanilamide à ces molécules : (Ⅲ), (Ⅴ), et (Ⅶ). Les corps ainsi obtenus sont (XIII), (XIV), et (XV). Ils ont été préparés en faisant réagir ordinairement le chlorure de *p*-acétamidobenzènesulfonyle sur (Ⅲ), (Ⅴ), ou (Ⅶ), en faveur de solvant de pyridine, et en procédant ensuite à la désacétylation en milieu alcalin.

L'expérimentation bactériologique des composés décrits ci-dessus sera dans le travail en cours.

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* Partie I : Ce Bulletin, **4**, 77(1956).

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[1] W. H. Crowe : J. Chem. Soc., **127**, 2028(1925).

[2] E. Ochiai, K. Futaki : J. Pharm. Soc. Japan, **72**, 274(1952).

[3] E. Hayashi : *Ibid.*, **70**, 142(1950).