— Note —

Electrochemical Reduction of 2-Hydroxyimino-2-phenylacetonitrile. A New Synthetic Route of 2-Phenylglycine from Styrene

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1 INTRODUCTION

2-Phenylglycine (**1**) is an important material in synthetic chemistry. Although 2-phenylglycine is synthesized by Strecker method¹⁾, this method starts from the expensive material, benzaldehyde. In this paper, we discuss a synthetic route of 2-phenylglycine, which starts from a cheaper material, styrene. Since the key step in our route is the conversion of 2-hydroxyimino-2-phenylacetonitrile (**2**) to 2-amino-2-phenylacetonitrile (**3**), electrochemical reduction is examined in detail.

2 EXPERIMENTAL

2.1 Preparation of the oxime **2**

2.1.1 Nitration of styrene

To a solution of styrene (10 mmol) in dichloromethane (50 cm³), was added NaNO₂ (80 mmol) with stirring. Acetic acid (80 mmol) was then added over 30 min. After 2 h, 6% HCl (30 cm³) was added and the solution was stirred overnight. By usual work-up, 4-nitro-3-phenylfurazan 2-oxide (**4**), mp 100.5–101.5 °C; lit.²⁾ 100 °C, was obtained (68%).

2.1.2 Substitution of nitro group in **4** with azide ion

To a solution of NaN₃ (0.5 mmol) in DMSO (2 cm³), was added the oxide **4** (0.25 mmol). After 10 min, the solution was poured into a phosphate buffer solution.

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By extraction and subsequent TLC, 4-azido-3-phenylfurazan 2-oxide (**5**), mp 95 °C, was obtained (94%).

2.1.3 Photolysis of **5**

A solution of the azide **5** (1 mmol) in dichloromethane-ethanol (7:3, 50 cm³) was irradiated through a Pyrex filter by a 500 W high-pressure mercury lamp under a nitrogen atmosphere for 30 min. Only the single isomer, (**E**)-2-hydroxyimino-2-phenylacetonitrile (**2**), mp 100 °C; lit.³⁾ 97 °C, was obtained (94%).

2.2 Synthesis of phenylglycine from **2**

2.2.1 Reduction of **2**

Electrochemical reduction was carried out with use of a graphite rod as a cathode and a platinum plate as an anode in an H-shaped electrolytic cell divided with a sintered-glass frit. Base solution was water or a mixture of water and ethanol containing 1 M (M = mol dm⁻³) hydrochloric acid. Amounts of the aminonitrile formed were determined by HPLC analysis with use of a Merck Hibar column (RP-18) as the stationary phase and phosphate solution of pH 3.5 as the eluent.

The oxime **2** (1 mmol) was taken in the cathode compartment of the cell together with 50 cm³ of the base solution and electrolyzed at a current density of 3.5 mA cm⁻². After passing 6 F mol⁻¹ (F=96480 C) of the electricity, the catholyte was condensed *in vacuo*. The aminonitrile **3** (91% yield by HPLC) was crystallized and isolated by filtration in 87% yield.

2.2.2 Hydrolysis of **3** to 2-phenylglycine

To the catholyte described in the above,

was added conc. HCl and the solution was heated under reflux for 3 h. 2-Phenylglycine (85% yield by HPLC) was isolated as its hydrochloride salt by filtration from the condensed solution in 44% yield.

3 RESULTS AND DISCUSSION

The starting material, 2-hydroxyimino-2-phenylacetonitrile (2), was easily prepared from styrene. Styrene was converted to 4-nitro-3-phenylfuran 2-oxide (4) in 68% yield. This was further converted to 4-azido-3-phenylfuran 2-oxide (5) (94%) and then to the oxime 2 (94%).

The electrochemical reduction of the oxime 2 was carried out on the graphite cathode in 1 M aqueous hydrochloric acid until most of the oxime disappeared. The amounts of the aminonitrile formed were monitored by HPLC. Results are exhibited in Fig. 1.

First, the oxime was reduced in water (curve a). When the theoretical amount of the electricity (4 F mol⁻¹) was supplied, the aminonitrile was produced in 65% yield. Further electrolysis up to 8 F mol⁻¹ gave the yield of 89%. Although the chemical yield was excellent in this case, much electricity was necessary for the completion of the reaction. This might be due to the hydrogen evolution which increases gradually with the decrease of the oxime concentration.

We next tried to use 50% aq. ethanol as the base solution in order to suppress the hydrogen evolution (curve b). In this case, however, the current efficiency (ce) rather decreased.

Improved current efficiency was obtained by the use of 20% ethanol (curve c). In this case, the aminonitrile formed with 94% ce at the point of 2 F mol⁻¹ of the electrolysis. By passing the theoretical amount of the electricity (4 F mol⁻¹), the chemical yield amounted to 82% (82% ce). After 6 F mol⁻¹ of the electrolysis, the

Fig. 1. Reduction of 2. Curves stand for reactions in a:0%, b:50%, and c:20% aqueous ethanol solutions.

aminonitrile was produced in 91% yield (61% ce).

The aminonitrile 3 was then hydrolyzed to 2-phenylglycine (1). The electrolyzed solution containing the aminonitrile 3 was heated for 3 h. The analysis by HPLC showed that 2-phenylglycine was produced in 85% yield from the oxime 2.

As mentioned above, the electrochemical reduction of the oxime 2 was carried out with good selectivity and current efficiency. Our route may be utilized as a new synthetic method for 2-phenylglycine.

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