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# ELECTROCHEMICAL DEHYDROGENATION OF 1,2,3,4-TETRAHYDROISOQUINOLINE TO 3,4-DIHYDROISOQUINOLINE

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**Abstract** - Dehydrogenation of 1,2,3,4-tetrahydroisoquinoline to 3,4-dihydroisoquinoline was carried out using an electrochemical method in the presence of KI. In this method, the iodide ion presumably played an important role as an electron carrier.

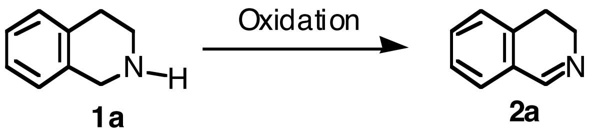
## INTRODUCTION

Oxidation of amines to the corresponding imines is not frequently encountered, and accordingly, the scope of these reactions is rather limited.[1] In the case of the oxidation of 1,2,3,4-tetrahydroisoquinoline (**1a**), a cyclic amine, to 3,4-dihydroisoquinoline (**2a**), the reported methods involve environmentally undesirable oxidants,[2] expensive catalysts,[3] and/or long reaction periods. In our laboratory, oxidation of several organic compounds, especially those containing a nitrogen atom, has been carried out using an electrochemical method in the presence of halogen ion.[4] Although it is well known that the use of electric current is one of the cleanest method for the oxidation of organic compounds,[5] to the best of our knowledge, the electrochemical method for the oxidation of **1a** to **2a** has not been reported. Herein, we report on the novel electrochemical dehydrogenation of **1a** using iodide ions as the electron carrier.

## RESULTS AND DISCUSSION

Initially, to optimize the reaction conditions, oxidation of **1a** was performed in the presence of various halogen ion sources and bases. The results of these reactions, along with the yields of **2a**, are listed in Table 1.

Table 1. Oxidation of 1,2,3,4-Tetrahydroisoquinoline (**1a**)[a]



| Run | Halogen ion source (3 mmol) | Base (5 mmol) | Yield of **2a**[b] (%) |
|---|---|---|---|
| 1 | none | NaOMe | 41 |
| 2 | KCl | NaOMe | 66 |
| 3 | KBr | NaOMe | 59 |
| 4 | KI | NaOAc | 76 |
| 5 | KI | NaOH | 87 |
| 6 | KI | NaOMe | 90 |
| 7 | NaI | NaOMe | 88 |

[a] Reaction conditions: **1a**, 10 mmol; MeOH, 40 mL; Constant current, 0.3 A; Current passed, 3.0 F/mol; *ca.*15 ℃.

[b] Determind by GC analysis.

When NaOMe was used as the lone supporting electrolyte, the yield of **2a** was merely 41% (Run 1). However, the addition of a catalytic amount of KI, along with a base (especially a strong base such as NaOMe) was favorable in affording higher yields of **2a** (Runs 4-6). When KCl (Run 2) or KBr (Run 3) was used instead of KI, the yields of **2a** were 66 and 59 %, respectively. Substitution of NaI for KI as the iodide ion source did not decrease the yield of **2a** (Run 7). Optimal amounts of KI and NaOMe for this electrooxidation were separately determined using **1a** as the substrate. On the other hand, as shown in the relationship between the current passed and yield (Figure 1), the yield of **2a** increased with an increase in amount of current passed until nearly 3 F/mol, and finally reached to just 90%. Current in excess of 3 F/mol resulted in a gradual decrease in the yield of **2a**. Because most of the substrate was consumed at the stage where 3 F/mol of electricity had been passed, the electrooxidation presumably involves a two-electron oxidation process.

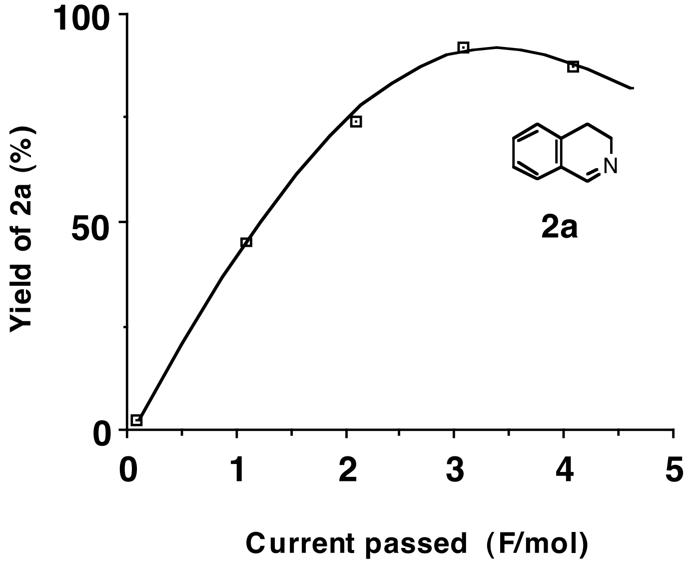
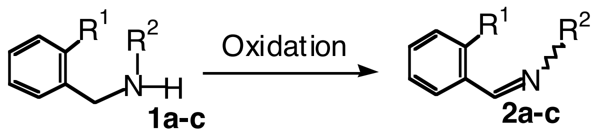


Figure 1. Relationship between current passed and yield of **2a**

Subsequently, based on the results obtained from the preliminary examinations, the electrochemical oxidation of **1a** and other benzylic amines (**1b**) and (**1c**) was carried out, and the results were shown in Table 2. The course of the electrochemical dehydrogenation was carefully monitored by analyzing the composition of the reaction mixture using silica gel TLC (ether/hexane 1:1) and GC. In each case, electrolytic current was applied until the substrate was nearly completely consumed. As in the case of **1a**, electrochemical dehydrogenation of **1b** and **1c** to the corresponding imines (**2b**) and (**2c**) was successful; the yields of isolated imines (**2b**) and (**2c**) were 76 and 81%, respectively. Unexpectedly, the electrochemical dehydrogenation of an alicyclic amine, such as dicyclohexylamine, was unsuccessful, resulting in a tar-like material that was difficult to purify.

Table 2. Oxidation of Benzylic Amines[a]

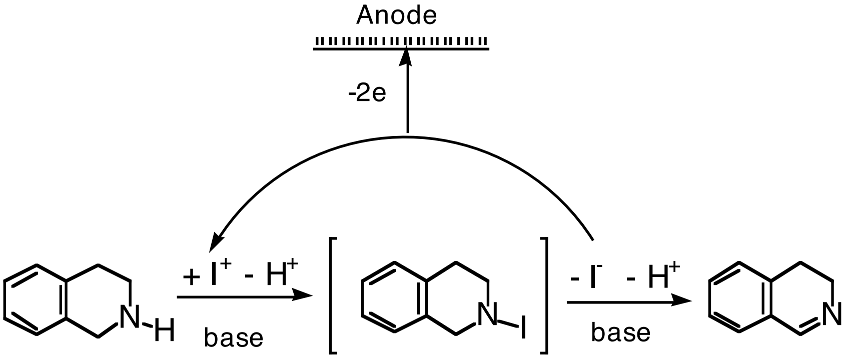


| | Substrate R1 | Substrate R2 | Current Passed (F/mol) | Yield of **2a-c**[b] (%) |
|---|---|---|---|---|
| **1a** | $-(CH_2)_2-$ | | 3.0 | 86 |
| **1b** | H | *tert*-Bu | 4.0 | 76 |
| **1c** | H | Cyclohexyl | 3.7 | 81 |

[a] Reaction conditions: **1a-c**, 10 mmol; KI, 3 mmol; NaOMe, 5 mmol; MeOH, 40 mL; Constant current, 0.3 A; *ca.*15°C.

[b] Isolated yields based on substrates.

Although the reaction mechanism remains unclear, it appears that the iodide ion plays an important role as the electron carrier in this system. Specifically, the iodide ion undergoes a two-electron oxidation process to form an iodonium ion, which then reacts with the substrate to give an intermediate (illustrated as the structure in brackets in Scheme 1).



Scheme 1

In this electrolysis system, the presence of a base such as NaOMe presumably facilitates the deprotonation of both the substrate and the intermediate to form the final product. Furthermore, the base can also function as an efficient supporting electrolyte (the terminal voltage of the electrolytic cell was always maintained at less than 10V). In conclusion, the electrooxidative transformation of some benzylic amines to the corresponding imines was achieved under very mild conditions, and without the use of environmentally undesirable reagent. In each case, isolation of the resulting imines was relatively simple.

## EXPERIMENTAL

The structure of the products was identified using their physical and spectral data. All reagents were obtained from commercial suppliers and were used without further purifications. Preparative-scale electrochemical oxidation was carried out in a tall 50-mL beaker, equipped with a fine frit cup as the cathode compartment, an insert cylindrical platinum net (diameter, 30 mm; height, 34 mm; 55 mesh) as the anode, and a nickel coil cathode. Amines (**1a** – **c**) were oxidized as follows: a solution of substrate **1a** – **c** (10 mmol), KI (3 mmol), and NaOMe (5 mmol) in MeOH (40 mL) was electrooxidized under a constant current (0.3 A). During the course of the reaction, the anolyte was magnetically stirred while maintaining the temperature of the cell at approximately 15±2 °C. GC analyses were performed with stainless steel column (length:1.5 m, diameter:5 mm) packed with 20% Apeazon L and 10% of KOH on Chromosorb W AW. $N_2$ served as the carrier gas. The gas chromatograph was equipped with a flame ionization detector. After completion of the electrochemical dehydrogenation, the reaction mixture was concentrated *in vacuo* at approximately 40 °C to roughly one-fifth of its original volume, and the resulting residue was treated with water (30 mL), then extracted with ether (3 × 40 mL). The combined ether extracts were washed with an aqueous sodium thiosulfate solution (20% w/w, 20 mL), and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was purified by distillation under reduced pressure.

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