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SELECTIVE ELECTROCATALYTIC OXIDATION OF AMINES MEDIATED BY DECAHYDROQUINOLINYL-*N*-OXYL RADICAL

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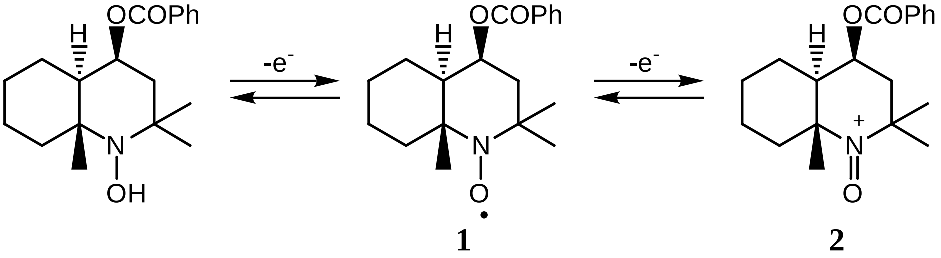
Abstract — Electrocatalytic oxidation of amines was studied using (±)-*trans,cis*-4-benzoyloxy-2,2,8a-trimethyldecahydroquinolinyl-*N*-oxyl. The reaction with amines led to direct formation of carbonyl compounds in aqueous media in adequate conversion (> 78 %), high current efficiency (> 90 %) and high selectivity (100 %). Under anhydrous conditions, primary amines were also oxidized to the corresponding nitriles in satisfactory conversion (> 76 %), high current efficiency (> 89 %) and high selectivity (> 95 %).

Oxoammonium ions such as **2** can be easily prepared electrochemically by one-electron oxidation of nitroxyl radicals such as **1** (Scheme 1),[1] and they are powerful and selective oxidants for the oxidation of several functional groups.[2] Semmelhack and Schmid have reported the electrooxidation of amines to nitriles and carbonyl compounds with 2,2,6,6-tetramethylpiperidinyl-*N*-oxyl (TEMPO) as a stable organic nitroxyl radical catalyst.[3] MacCorquodale *et al.* have demonstrated that, based on ESR and cyclic voltammetry, poly(TEMPO-4-acrylic ester) acts as an efficient catalytst for electrochemical oxidation of amines.[4] We have also achieved the electrocatalytic oxidation of amines to nitriles on a graphite felt (GF) electrode coated with a thin poly (acrylic acid) (PAA) layer immobilizing 4-amino-TEMPO.[5] However, a considerable body of these works has used TEMPO derivatives as an effective redox mediator. More recently, we have reported the electrocatalytic behavior of (±)-*trans,cis*-4-benzoyloxy-2,2,8a-trimethyl-decahydroquinolinyl-*N*-oxyl (**1**)[6] in the electrooxidation reactions of alcohols to aldehydes or ketoness.[7] To examine the wide applicability of this nitroxyl radical to the electrocatalytic oxidation of substrates other



Scheme 1. A reversible redox system based on **1**.

than alcohol, we report here a preparative electrocatalytic oxidation of amines using **1**.

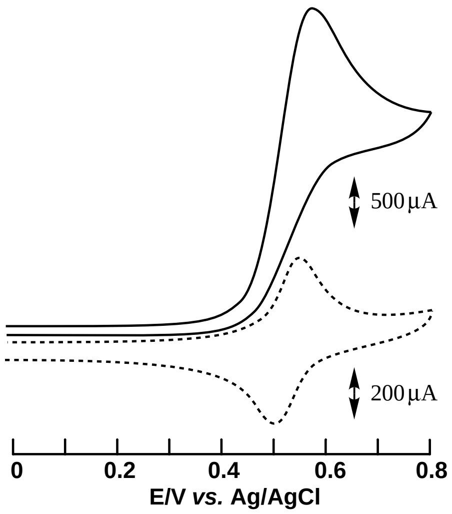


Figure 1. Cyclic voltammograms of 0.02 M of **1** in the presence (———) and absence (- - - - -) of 0.2 M of benzylamine and 1.6 M of 2,6-lutidine in 0.1 M of $NaClO_4/CH_3CN$ at scan rate of 50 mV sec^{-1}.

Cyclic voltammetry was used to check whether electrontransfer from oxidatively generated **2** to benzylamine occurred.[8] The cyclic voltammogram of **1** in the presence of benzylamine and 2,6-lutidine in anhydrous CH_3CN solution is shown in Figure 1. The reversible wave at + 0.55 V *vs*. Ag/AgCl which corresponds to the **1**/**2** couple became irreversible; an increase of the catalytic peak height corresponded to oxidation of **1**, although benzylamine is not electroactive below + 0.8 V *vs*. Ag/AgCl at a glassy carbon electrode. This means that **1** is electrocatalytically active for the oxidation of benzylamine. Based on the cyclic voltammmetry results, we have used two procedures for the oxidation of benzylamine.[9] In the first procedure (method A), the preparative electrolysis reaction of benzylamine was performed at + 0.6 V *vs*. Ag/AgCl in anhydrous CH_3CN solution. During electrolysis, the substrate and product were occasionally analyzed by gas chromatography (GC).[10] A time course of the electrooxidation of benzylamine by **1** is shown in Figure 2. One mmol of benzylamine reacted almost completely in about 5 h to yield benzonitrile. The current efficiency in the electrolysis is 93.5 % during the course of electrolysis, and a small amount of benzaldehyde was observed (95.6 % selectivity). The turnover number based on **1** (given by ratio of mole of product x 2 / mole of **1**) was calculated to be 19.0 at 5 h of electrolysis. On the contrary, the use of 4-benzoyloxy-TEMPO in place of **1** yielded benzonitrile low conversion (18.2 %) at 5 h of electrolysis, because the electrolysis potential was more negative than the oxidation peak potential 4-benzoyloxy-TEMPO (+ 0.66 V *vs*. Ag/AgCl). The nitroxyl radical compounds having benzoyloxy group has been smoothly electron transfer between electrode and substrate than other nitroxyl radical derivatives.[11] In the second procedure (method B), the reaction was carried out in mixtures of H_2O and CH_3CN. The consumption of benzylamine and formation of benzaldehyde are plotted against electrolysis time in Figure 3. After 5 h of electrolysis, benzylamine was oxidized to benzaldehyde in

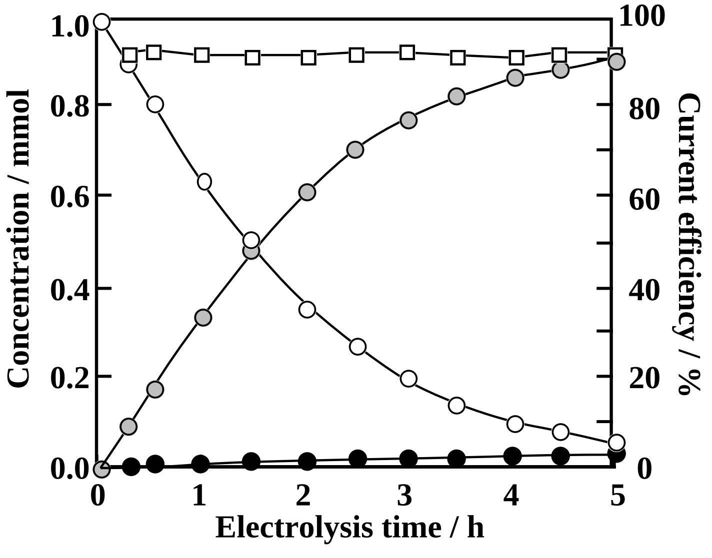


Figure 2. Macroelectrolysis of benzylamine by **1** in the presence of 2,6-lutidine in 0.1 M of $NaClO_4$ / CH_3CN. ○ : benzylamine, ◍ : benzonitrile, ● : benzaldehyde and □: current efficiency.

95.3 % yield, and no by-product was observed (100 % selectivity). The current efficiency and turnover number were 96.2 % and 19.1, respectively, at 5 h of electrolysis.

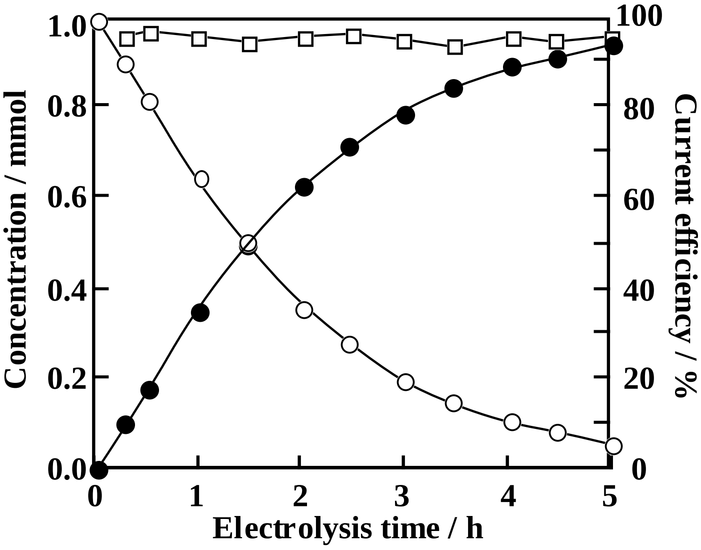
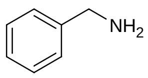
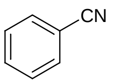
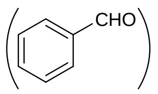
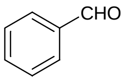
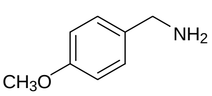
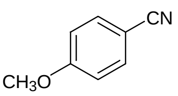
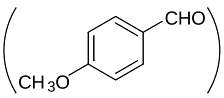
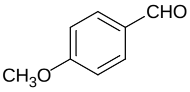
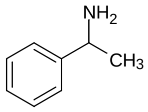
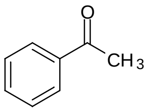
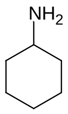
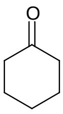
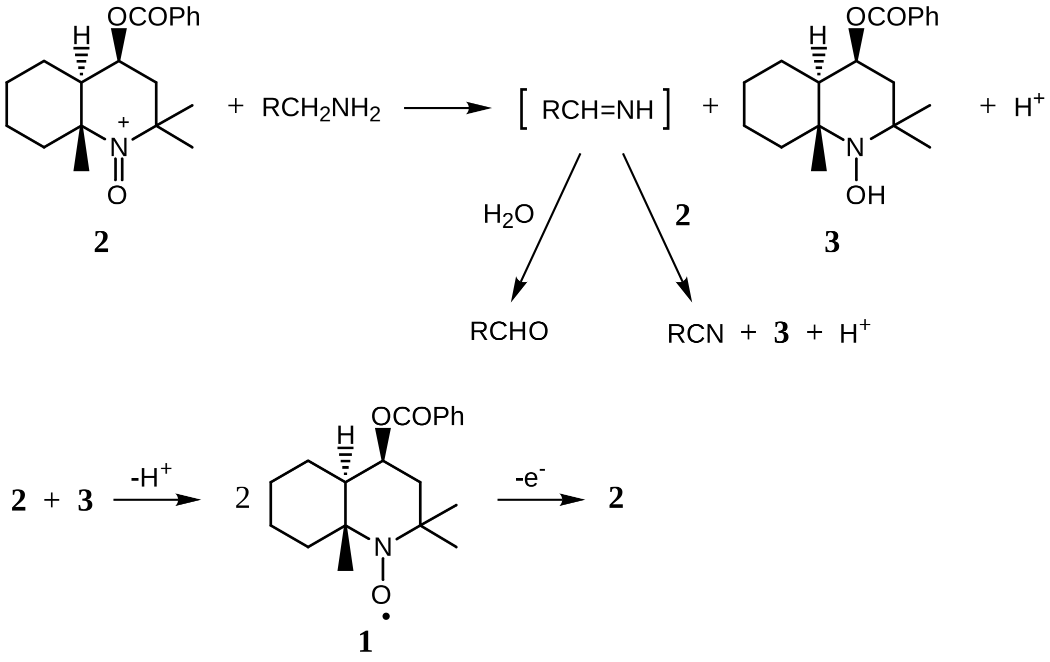


Figure 3. Macroelectrolysis of benzylamine by **1** in the presence of 2,6-lutidine in 0.1 M of $NaClO_4$ / CH_3CN-H_2O (4:1 v/v). ○ : benzylamine, ● : benzaldehyde and ☐ : current efficiency.

The preparative results of oxidation for five kinds of amines (benzylamine, *p*-methoxybenzylamine, nonylamine, 1-phenylethylamine and cyclohexylamine) are shown in Table 1. Under anhydrous condition, nitriles were the major products from RCH_2NH_2. After 5 h of electrolysis, amines were oxidized to the corresponding nitriles in adequate current efficiency (89.1-93.5 %) and yield (76.6 - 92.8 %). A slightly lower selectivity (95.6 - 96.8 %) is ascribable to the formation of small amounts (2.5 - 4.2 %) of aldehyde induced by H_2O. The turnover numbers are larger than 15. Shono *et al.* have reported the electrooxidation of amines to nitriles using halogen ions as mediators.[12] However, the use of halogen ions required more charge passed than that of nitroxyl radicals such as **1**. On the other hand, as long as some water was present, the products from RCH_2NH_2 and R_2CHNH_2 were aldehydes and ketones, respectively. After 5 h of electrolysis, amines were oxidized to the corresponding carbonyl compounds in 90.2 – 98.4 % current

Table 1. Electrocatalytic Oxidation of Amines to Nitriles and Carbonyl Compounds on **1**

Substrate	Method	Product	Charge passed / C	Current efficiency / %	Conversion %	Selectivity %	Turnover number
	A	 	195.9	93.5	90.7 (4.2)	95.6	19.0
	B		191.2	96.2	95.3	100	19.1
	A	 	200.5	92.6	92.8 (3.4)	96.5	19.2
	B		192.6	98.4	98.2	100	19.6
$CH_3(CH_2)_8NH_2$	A	$CH_3(CH_2)_7CN$ ($CH_3(CH_2)_7CHO$)	171.3	89.1	76.6 (2.5)	96.8	15.8
	B	$CH_3(CH_2)_7CHO$	167.7	90.2	78.4	100	15.7
	B		184.8	91.8	87.9	100	17.6
	B		185.5	95.7	92.0	100	18.4



Scheme 2. A proposed mechanism of oxidation of amine to nitrile and carbonyl compound with **2**.

efficiency, 78.4 – 98.2 % yield and 100 % selectivity. (*R*)- and (*S*)-forms of racemic 1-phenethylamine were equally oxidized to acetophenone, though **1** contains chiral centers. This fact means that **1** is non-enantioselective for the oxidation of optically active amines.

The mechanism of electrocatalytic oxidation of amines to nitriles and carbonyl compounds with **1** is proposed in Scheme 2. The oxoammonium ion (**2**) is expected at first to react with the amine, that is, to eliminate a proton from the amine, then to change to the hydroxylamine (**3**). The disproportionation of **2** and **3** produces **1**, which is re-oxidized electrochemically to complete a catalytic cycle.[3] Imines are the expected unstable intermediates, which can react again with **2** to produce stable nitriles or can be hydrolyzed to carbonyl compounds.

In conclusion, the compound (**1**) catalyzed the oxidation reaction of RCH_2NH_2 and R_2CHNH_2 to aldehydes and ketones, respectively, in an aqueous media. Under anhydrous conditions, RCH_2NH_2 were converted to the corresponding nitriles. During electrolysis, the oxoammonium ion (**2**) slowly decomposes. We are now trying to clarify the decomposition mechanism of **2**.

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8. A glassy carbon disk electrode (3 mm diameter) and a platinum wire were employed as the working electrode and the counter electrode, respectively. The anode potentials were referred to Ag/AgCl (saturated AgCl and $(CH_3)_3C_2H_5NCl$ in acetonitrile). Cyclic potential sweeps were generated by a Hokuto Denko Model HABF-501 potentiostat/galvanostat. Cyclic voltammograms were recorded on a Graphtec Model WX1200 X-Y recorder. All electrochemical measurements were carried out at room temperature (*ca.* 20 ℃).
9. Preparative potential-controlled electrolysis was performed in an anhydrous CH_3CN (method A) or 4:1 CH_3CN/H_2O (v:v) (method B) solution, using an ‘H’ type divided cell separated by a cationic exchange membrane (Nafion 117). The anolyte contained 1 mmol of substrate, 0.1 mmol of **1**, 0.5 mmol of tetralin as gas chromatographic standard, 8 mmol of 2,6-lutidine and 0.5 mmol of $NaClO_4$ as a supporting electrolyte in a total volume of 5 mL. The catholyte was 5 mL of anhydrous CH_3CN (method A) or 4:1 CH_3CN/H_2O (v:v) (method B) containing 0.5 mmol of $NaClO_4$. Controlled potential electrolysis was carried out at + 0.6 V *vs.* Ag/AgCl. The GF electrode (Nippon Kynol Inc.), the size of 5 x 5 x 5 mm, was used as a working anode electrode.
10. The GC analysis was carried out using CP-Cyclodextrin-B-2,3,6-M-19 capillary column (0.25 mm ϕ x 25 m). The column temperature was increased at 3 ℃ min^{-1} from 80 ℃ to 150 ℃. The injection and detector temperatures were 200 °C and 240 °C, respectively.
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