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Electrocatalytic Oxidative Coupling of Methylquinolines on TEMPO-modified Graphite Felt Electrodes

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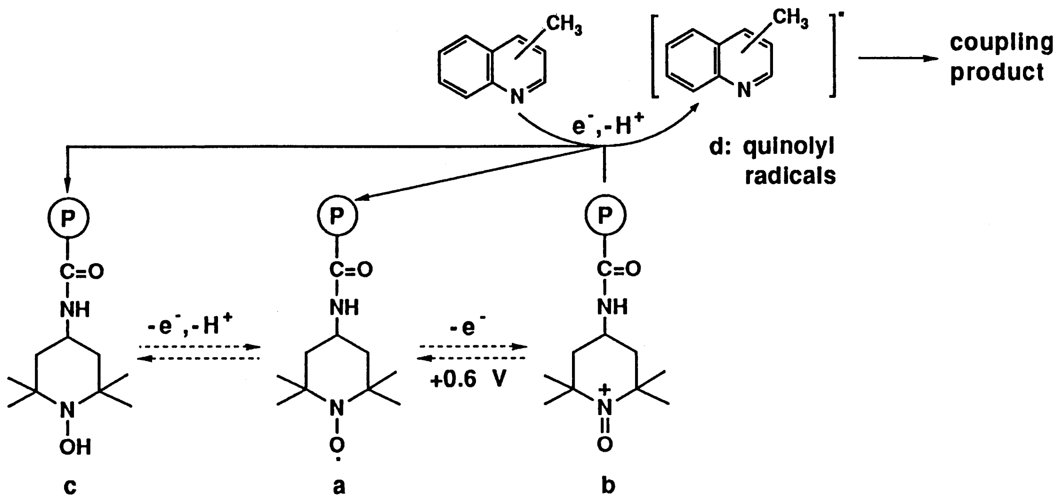
2- and 4-Methylquinolines were oxidized to 2,2'-dimethyl-4,4'-biquinolyl and 4,4'-dimethyl-2,2'-biquinolyl, respectively, both in ca. 94% isolated yield and ca. 90% current efficiency on a graphite felt electrode coated with a thin poly(acrylic acid) layer containing 4-amino-2,2,6,6-tetramethylpiperidinyl-1-oxyl (4-amino-TEMPO). The reaction proceeds via electrocatalytic oxidation of the modified-TEMPO species. The electrode was not inactivated during electrolysis and could be used repeatedly.

Organic oxoammonium salts,1) which can be prepared from nitroxide radicals such as 2,2,6,6-tetramethylpiperidinyl-1-oxyl (TEMPO) by a one-electron oxidation, have been explored as selective oxidizing agents for organic functional groups.2,3) This oxidation takes place by electron transfer, and its rate is usually dependent on deprotonation from substrate.4) In order to accelerate deprotonation, addition of basic materials in the reaction medium is effective.4) Though Hunter et al. have reported that oxoammonium salts oxidize naphthols to quinones and do not produce binaphthyls,2) Bobbitt succeeded in coupling a phenolic alkaloid, corypalline, with oxonium tetrafluoroborate of TEMPO in acetonitrile (CH_3CN)-H_2O solution in the presence of $KHCO_3$ (yield 81%).5,6) However, no coupling reactions of N-aromatic nucleus with oxoammonium ions have been reported, although other methods, such as Pd/C or Pd/Pt-C catalyst in the presence of tetra-amine-N-oxide7,8) or Grignard reagent with N-heteroaryl halides in the presence of triphenylphosphine Pd complex,9) afford coupling products.

Electrochemical oxidation using oxoammonium ions from nitroxide radicals has recently been developed (Scheme 1).4,5,10-17) When nitroxide radicals were immobilized on the electrode, catalytic amounts of nitroxide near the electrode surface could be used, since the oxoammonium ion could be electrochemically recycled.4,11-17) In our previous paper,17) we reported the electrocatalytic oxidative coupling reactions of naphthols and naphthol ethers on the TEMPO-modified graphite felt electrode. In this communication, we report the results of electrocatalytic oxidative coupling reaction of 2- and 4-methylquinolines on the same modified electrode.

The graphite felt electrodes (National Electric Carbon Corp. WDF, 5.0 x 2.0 x 0.5 cm^3) were coated with poly(acrylic acid) by immersion in a 0.25% methanol solution. This coated electrode was then treated with 41.6 mM ($M=mol \cdot dm^{-3}$) of 4-amino-TEMPO in dimethylformamide (DMF) in the presence of dicyclohexylcarbodiimide (DCC) (1.2 equiv. to 4-amino-TEMPO) for 72 hours at room temperature. The electrode was then crosslinked with 6.94 mM of hexamethylenediamine in DMF in the presence of DCC (2 equiv. to hexamethylenediamine) for 12 hours at 4 °C and 60 hours at room temperature. The remaining carboxyl groups were butylated with di-n-butyl sulfate and 1,8-diazabicyclo-[5,4,0]-7-undecene.18) Thus, the carboxyl groups of polymer layers on the graphite felt were attached to TEMPO (64%), crosslinked (16%) and butylated



Scheme 1. Mechanism of electrocatalytic oxidation of methylquinolines on TEMPO-modified electrode.

(20%).[19] No free carboxyl groups were remained. The density of TEMPO on the electrode was determined to be 24.4 μmol/cm^3 by elementary analysis, gravimetric analysis and titration. This modified electrode is better than the previous ones (the attached amount of TEMPO was 52%) that were crosslinked before TEMPO is modified.[14] In the electrocatalytic oxidation of nerol on this electrode, the turnover number was raised from 156 to 196, and the current efficiency was increased from 97.1% to 98.2% (Fig. 1).

Preparative, potential-controlled electrolysis was performed at + 0.60 V vs Ag/AgNO$_3$ in CH$_3$CN solution, using an H type divided cell separated by cationic exchange membrane (Nafion 117). The anolyte contained 50 mmol (7.15 g) of substrate, 20 mmol of tetralin as a gas chromatographic (GC) standard, 50 mmol of 2,6-lutidine and 8 mmol of sodium perchlorate (NaClO$_4$) as a supporting electrolyte in a total volume of 40 ml. The catholyte was 40 ml of CH$_3$CN solution containing 8 mmol of NaClO$_4$. The end of electrolysis was decided by disappearance of the substrate by GC (Unicarbon A-100, column temp 220 °C, inj. temp 260 °C).

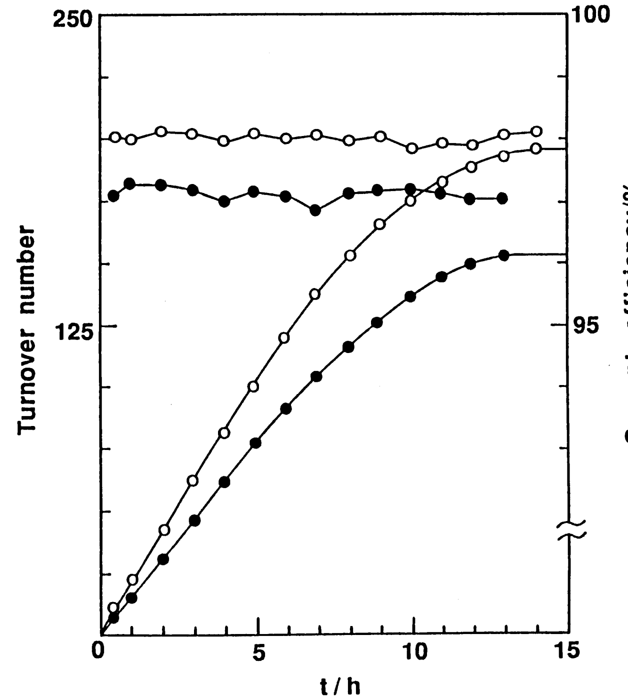
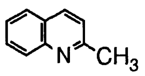
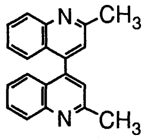
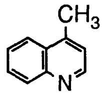
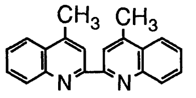


Fig. 1. Macroelectrolysis of nerol on TEMPO-modified electrodes. Turnover number is given by 2 x mol of nerol / mol of TEMPO. ○ : this electrode, ● : previous electrode.[14]

After the electrolysis was over, the anolyte was concentrated, dissolved in 100 ml of dichloromethane, washed with 0.1M HCl and H_2O, dried with sodium sulfate, and concentrated. Then, the solution was fed onto an alumina column (Aluminiumoxide H, 3 cm ϕ x 50 cm) and eluted with 1.5 l of benzene. Each fraction contained only one product. The crude yields of the reaction product from 2- and 4-methylquinolines were 6.82 and 6.96 g, respectively. The purified yield, recrystallized from chloroform, was 6.66 g of **1** (93.8% yield) and 6.71 g of **2** (94.5% yield), respectively. **1** : ^1H NMR ($CDCl_3$) δ 2.88 (6H, s, CH_3), 7.3-8.2 (10H, m, ArH); lit.[9] ^1H NMR ($CDCl_3$) δ 2.85 (6H, s, CH_3), 7.3-8.2 (10H, m, ArH). Mp. 241-243 °C (lit.[9] mp 242-244 °C). MS(EI) m/e 284 (M^+). Anal. Found : C, 84.52; H, 5.76; N, 9.63%. Calcd for $C_{20}H_{16}N_2$: C, 84.48; H, 5.67; N, 9.85%. **2** : ^1H NMR ($CDCl_3$) δ 2.82 (6H, s, CH_3), 7.2-8.1 (10H, m, ArH). Mp. 281-283 °C (lit.[8] mp 280 °C). MS(EI) m/e 284 (M^+). Anal. Found : C, 84.55; H, 5.78; N, 9.58%. Calcd for $C_{20}H_{16}N_2$: C, 84.48; H, 5.67; N, 9.85%.

Table 1. The Results of the Electrocatalytic Coupling of Methylquinolines on TEMPO-modified Electrode

Substrate	Product	Charge passed[a] C	Current efficiency/%	Isolated yield (mol x 2 %)	Selectivity %	Turnover number
	 **1**	5308	90.9	93.8	100	410
	 **2**	5256	91.8	94.5	100	410

a) Substrates were completely consumed (100% conversion).

The results are summarized in Table 1. As same with the naphthols and methoxynaphthalenes,[17] 2- and 4-methylquinolines were coupled cleanly to 2,2'-dimethyl-4,4'-biquinolyl and 4,4'-dimethyl-2,2'-biquinolyl, respectively. The coupling was selectively carried out at the 2- or 4-positions of the pyridine nucleus. In case of homogeneous reaction with oxoammonium salts, this coupling reaction was not carried out. The coupling mechanism is estimated to proceed via quinolyl radicals (**d**) which were formed by deprotonation following one electron transfer from the quinolines to oxoammonium salts. Blank electrolysis at + 0.6 V on the bare electrode did not yield any coupling product. Since the electrolysis was performed at + 0.6 V, it is clear that the oxoammonium ion (**b**) of TEMPO is formed in the domain of polymer layer on graphite felt (Scheme 1) and that it smoothly reacts with methylquinolines. If the TEMPO species is reduced to hydroxylamine (**c**), it is necessary to keep the oxidation potential more positive than + 0.6 V, because **c** is directly oxidized to the TEMPO radical (**a**) at +1.1 V. However, **c** may disproportionate with **b** to form **a**.[10] This reaction might be possible due to flexible moving of the TEMPO residues in the polymer layers. Therefore, the redox reaction of TEMPO might be recycled between **a** and **b**. It is concluded that the TEMPO-modified graphite felt is an excellent electrode for electrocatalytic coupling reaction of methylquinolines without deactivation of the electrode and can be used for macrosynthesis of biquinolyl compounds. Further coupling reactions of N-aromatic compounds on this electrode are now in progress.

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References

1) V. A. Golubev, E. G. Rozantsev, and M. B. Neiman, Bull. Acad. Sci. USSR, Div. Chem. Sci., **1965**, 1898.
2) D. H. Hunter, D. H. Barton, and W. J. Motherwell, Tetrahedron Lett., **25**, 603 (1984)
3) J. M. Bobbitt, Heterocycles, **27**, 509 (1988).
4) A. Deronzier, D. Limosin, and J.-C. Moutet, Electrochimica Acta, **23**, 1643 (1987).
5) J. M. Bobbitt, Heterocycles, **1**, 181 (1973).
6) J. M. Bobbitt and Z. Ma, Heterocycles, **33**, 641 (1992).
7) T. Haginiwa and Y. Higuchi, Yakugaku Zasshi, **93**, 140 (1973).
8) T. Haginiwa and Y. Higuchi, Yakugaku Zasshi, **93**, 144 (1973).
9) H. Yamanaka, M. An-naka, Y. Kondo, and T. Sakamoto, Chem. Pharm. Bull., **33**, 4309 (1985).
10) M. F. Semmelhack, C. R. Schmid, D. A. Cortes, and C. S. Chou, J. Am. Chem. Soc., **105**, 4492 (1983).
11) S. Cosnier, A. Deronzier, and J.-C. Moutet, J. Electroanal. Chem., **207**, 315 (1986); L. Coche, A. Deronzier, and J.-C. Moutet, ibid., **198**, 187 (1986); L. Coche and J.-C. Moutet, ibid., **224**, 111 (1987).
12) G. Bidan and D. Limosin, Ann. Phys. Paris, **11**, 5 (1986).
13) T. Osa, U. Akiba, I. Segawa, and J. M. Bobbitt, Chem. Lett., **1988**, 1423.
14) T. Osa, Y. Kashiwagi, K. Mukai, A. Ohsawa, and J. M. Bobbitt, Chem. Lett., **1990**, 75.
15) Y. Kashiwagi, A. Ohsawa, T. Osa, Z. Ma, and J. M. Bobbitt, Chem. Lett., **1991**, 581.
16) T. Osa, Y. Kashiwagi, J. M. Bobbitt, and Z. Ma, "Electroorganic Synthesis," ed by R. D. Little and N. L. Weinberg, Marcel Dekker, Inc. (1991), 343.
17) Y. Kashiwagi, H. Ono, and T. Osa, Chem. Lett., accepted.
18) F. H. Stodola, J. Org. Chem., **29**, 2490 (1964).
19) The values were determined by back titration with 0.2 M HCl.

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