Enantioselective, Electrocatalytic Oxidative Coupling of Naphthol, Naphthyl Ether and Phenanthrol on a TEMPO-modified Graphite Felt Electrode in the Presence of (−)-Sparteine (TEMPO = 2,2,6,6-tetramethylpiperidin-1-yloxyl)

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Constant potential electrolysis of 2-naphthol, 2-methoxynaphthalene and 10-hydroxyphenanthrene at 0.6 V *vs.* Ag/AgCl on a TEMPO-modified graphite felt electrode in the presence of (−)-sparteine in acetonitrile yields, enantioselectively, (*S*)-binaphthyl type dimers in >92% isolated yield and with >88% current efficiency with enantiomeric excesses of 98, 91 and 97% respectively for each dimer, respectively.

Since optically pure binaphthyls such as (*S*)-(−)- or (*R*)-(+)-2,2′-dihydroxy-1,1′-binaphthyl have been utilized in a variety of synthetic reactions to induce chirality,[1] much attention has been devoted to their synthesis. Optically active binaphthyls have been synthesized directly by three enantioselective routes: (*a*) an intermolecular Ullman coupling,[2] (*b*) a nucleophilic aromatic substitution[3,4] and (*c*) an oxidative dimerization of 2-naphthols with copper(II) amine complexes as oxidants.[5–8] We have recently reported that 2-naphthol,[9] 2-methoxynaphthalene[9] and 2- and 4-methylquinolines[10] in the presence of 2,6-lutidine are quantitatively oxidized to the corresponding binaphthyls and biquinolinyls with >90% current efficiency on a graphite felt (GF) electrode coated with a thin poly(acrylic acid) (PAA) layer bonded to 4-amino-2,2,6,6-tetramethylpiperidin-1-yloxyl (4-amino-TEMPO) by an amide bond. So far, few electrochemical coupling methods[11] have been reported, because electrolysis of naphthols deposits a polymer film on electrodes which halts the reaction. The use of the mediator-modified electrode in the presence of a deprotonation reagent such as 2,6-lutidine made the coupling reactions of binaphthyls possible and the use of a chiral alkaloids such as (−)-sparteine instead of 2,6-lutidine has now led to highly enantioselective oxidative couplings of naphthol, naphthyl ether, and phenanthrol.

The TEMPO-modified electrode was prepared according to our established procedure.[10] A layer of PAA (M 1.4 × 10^5) about 40 nm thick was deposited on the GF electrode (National Electric Carbon Corp., WDF graphite felt). This layer was bonded to 4-amino-TEMPO to give a coverage of about 64% (by titration), cross-linked with hexamethylenediamine to give a coverage of 16% and, finally, butylated with butyl sulfate to remove any remaining carboxylate groups. The concentration of TEMPO was 24 μmol cm^{-3}. The cyclic voltammogram of the TEMPO-modified electrode afforded a well defined electrocatalytic peak at *ca.* +0.55 V *vs.* Ag/AgCl in 0.2 mol l^{-1} $NaClO_4$ acetonitrile containing 10 mmol l^{-1} (−)-sparteine **1** and 10 mmol l^{-1} 2-naphthol **2** as shown in Fig. 1 (curve *a*).

Based on the cyclic voltammetry results, preparative, controlled-potential electrolysis was performed in MeCN solution, using an H type divided cell separated by cationic exchange membrane (Nafion 117). The anolyte contained 5 mmol of substrate, 2 mmol of tetralin as a chromatographic standard, 5 mmol of **1** and 1 mmol of $NaClO_4$ as a supporting electrolyte in a total volume of 5 cm^3. The catholyte was 5 cm^3 of an MeCN solution containing 1 mmol of $NaClO_4$. Controlled potential electrolysis was carried out at +0.60 V under an argon atmosphere. The size of the modified anode was 1.0 × 1.0 × 0.5 cm. The anolyte was sampled at appropriate intervals for GC analysis (Unicarbon A-100 3 m; column temp. 220 °C, inj. temp 240 °C, detn. temp 260 °C) and HPLC (Chiralcel-OT 0.46 ϕ cm × 25 cm; column temp. 30 °C; flow rate 0.5 cm^3 min^{-1}, solvent: methanol). The end of electrolysis was usually decided by disappearance of the substrate by GC or diminishing current (*ca.* 6 h of electrolysis). After the electrolysis was over, the anolyte was evaporated, dissolved in 30 cm^3 of ethyl acetate, and the mixture was washed with 0.1 mol l^{-1} HCl and H_2O, dried with sodium sulfate and concentrated. For example, the pale brown reaction mixture from **2** was fed onto a silica gel column (Wako Gel C-200, 3 cm ϕ × 50 cm) and eluted with light petroleum–ether (1 : 1 *v*/*v*). The eluted solution was evaporated and recrystallized from toluene. The product was identified by conventional methods. The reaction mixtures for the other substrates were treated similarly.

The purity of (*S*)-(−)-2,2′-dihydroxy-1,1′-binaphthyl **3** in the isolated product (669 mg, 93.6% yield) was found to be 99.4% (98.5% ee) from its $[\alpha]_D^{20}$ of −33.6 (*c* 1.25, THF) {$[\alpha]_D$ of pure **3** −34 (*c* 5.0, THF)[7]} and 99.7% (99.5% ee) from HPLC;[12] mp 209–212 °C (lit.[7] mp 210–214 °C). The current efficiency for **3** was 88.8%. The electrode maintained its oxidizability (see curve *c* in Fig. 1) even after electrolysis. Sparteine remained without decomposition (95% of **1** was recovered). On the other hand, a bare GF electrode in 0.2 mol l^{-1} $NaClO_4$–MeCN containing 5 mmol of **2**, 5 mmol of **1** and 0.5 mmol of 4-acetylamino-TEMPO yielded **3** with only 10% ee (92.4% current efficiency). Chemical oxidation of **2** with 5 mmol of the oxoammonium tosylate of 4-acetylamino-

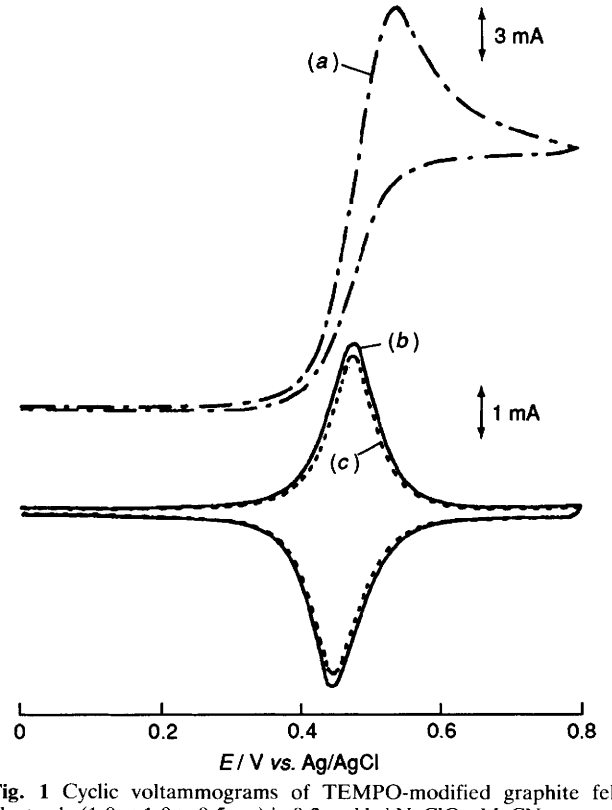


Fig. 1 Cyclic voltammograms of TEMPO-modified graphite felt electrode (1.0 × 1.0 × 0.5 cm) in 0.2 mol l^{-1} $NaClO_4$–MeCN at a scan rate of 10 mV s^{-1}. Curve (*a*) in the presence of 10 mmol l^{-1} 2-naphthol and 10 mmol l^{-1} (−)-sparteine; curve (*b*) in the absence of both 2-naphthol and (−)-sparteine; curve (*c*) electrode after one macroelectrolysis

TEMPO[13] dissolved in acetonitrile afforded the product[14] in 90.2% yield and 6% ee. These results are summarized in Table 1. It is clear that enantioselective coupling of **2** proceeds only on the TEMPO-modified electrode.

The results for electrolysis of 2-methoxynaphthalene and 10-hydroxyphenanthrene performed under the same conditions as for **2** are shown in Table 2. The coupling products also showed high enantiopurity: 93.3% ee by polarimetry[15] and 93.6% ee by HPLC for (*S*)-(−)-2,2′-dimethoxy-1,1′-binaphthyl from 2-methoxynaphthalene, and 97.9% ee by polarimetry {$[\alpha]_D^{23}$ ($CHCl_3$) of 98% purity compound; −71[5]} and 98.3% ee by HPLC for (*S*)-(−)-10,10′-dihydroxy-9,9′-biphenanthryl from 10-hydroxyphenanthrene.

The oxidation of **2** by means of copper(II) chiral amine complexes as oxidants has been reported[6–8] to yield enantioselectively 2,2′-dihydroxy-1,1′-binaphthyl which is formed by selective precipitation of the copper(II)-(+)-amphetamine-(*S*)-(−)-binaphthyl complex with a simultaneous enantiomerization of (+)-binaphthol when (+)-amphetamine is used as a chiral base (second-order transformation in the reaction). We confirmed that (*R*)-binaphthyl in MeCN solution kept at 0.6 V on the electrode was neither enantiomerized in the presence of **1** (0.2 C of electric charge was passed after 24 h and $[\alpha]_D^{20}$ of binaphthyl was +33.8), nor enantiomerized in the presence of the oxoammonium tosylate of 4-acetylamino-TEMPO. These results suggest that the asymmetric induction by the present electrochemical method does not arise from second-order transformations but arises from a direct electrochemical reaction though we have not investigated at a molecular level the behaviour in the modified layer of the electrode. The above highly enantioselective coupling reactions may result from a strong interaction between substrate, sparteine and mediator-TEMPO moiety in a suitably sized PAA domain formed by the cross-linking of hexamethylenediamine. Because the electrode is not deactivated during electrolysis, the binaphthyl and biphenanthryl formation can proceed *via* coupling of naphthyl[9] and phenanthryl radicals, respectively, formed by one-electron oxidation and deprotonation in which the reaction is enantiomerically controlled by the interaction of naphthyl and phenanthryl radicals with sparteine. Primary amines such as amphetamine cannot be used due to their reactivity with TEMPO.[16] Therefore, we have examined the enantioselective coupling reaction using (−)-strychnine as another chiral tertiary amine. The optical purity of **3** in the isolated product (656 mg, 91.8% yield) was found to be 71.9% (43.8% ee) from its $[\alpha]_D^{20}$ −14.8 (*c* 1.25, THF) and 72.4% (44.8% ee) from HPLC (90.5% current efficiency). The results suggest that the strength of interaction between the components of the reaction depends on the chiral bases. Possessing useful features such as full consumption of substrate, highly enantioselective product formation and easy isolation of product from reaction solution, this electrochemical process can be expected to be the simplest and most convenient way to synthesize optically pure binaphthyl and biphenanthryl derivatives from naphthols, naphthyl ethers and phenanthrols.

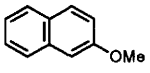
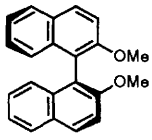
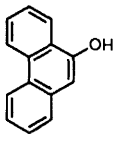
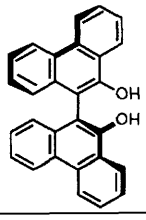
We thank Professor Kunio Ogasawara (Tohoku University) for helpful discussion on the enantioselective reactions. This research is supported, in part, by Grants-in-Aid for Scientific Research on Priority Areas (No. 05235102) and Encourage-

Table 1 Oxidative coupling reactions of 2-naphthol to 1,1′-binaphthol in the presence of (−)-sparteine[a]

Method	Charge passed/C	Current efficiency (%)	Isolated yield (%)	$[\alpha]_D^{20}$	*R* : *S*[d]	Ee[d] (%)	Turnover[e]
Electrocatalytic on TEMPO-modified GF	5132	88.8	93.6	−33.6	0.6 : 99.4 0.3 : 99.7	98.8 99.5	410
Electrocatalytic on bare GF[b]	5199	92.4	93.4	−3.4	45 : 55 44.5 : 55.5	10 11.1	10
Chemical oxidation[c]	—	—	90.2	−2.0	47 : 53 46.7 : 53.3	6 6.7	1

[a] In the presence of 5 mmol 2-naphthol and 5 mmol (−)-sparteine in each reaction. [b] 0.5 mmol of 4-acetylamino-TEMPO in 5 ml of 0.2 mol l^{-1} $NaClO_4$–MeCN. [c] 5 mmol of oxoammonium tosylate of 4-acetylamino-TEMPO in 5 ml of MeCN, 24 h. [d] Upper row: obtained by polarimetry (20 °C, *c* 1.25, THF), lower row: obtained by HPLC. [e] Calc. from [1,1′-binaphthyl (mol)] × 2]/TEMPO (mol).

Table 2 Enantioselective, electrocatalytic coupling reactions of 2-methoxynaphthalene and 10-hydroxyphenanthrene on TEMPO-modified GF electrode in the presence of (−)-sparteine[a]

Substrate	Product	Charge passed/C	Current efficiency (%)	Isolated yield (%)	$[\alpha]_D^{20}$	Ee[b] (%)	Turnover
		5215	91.0	92.3	−74.2	91.4 93.6	410
		5313	89.6	91.2	−69.5	97.9 98.3	410

[a] Carried out under the same electrolysis conditions as for 2-naphthol (Table 1). [b] Upper row: obtained by polarimetry (20 °C, *c* 1.25, THF), lower row: obtained by HPLC.

ment Research (No. 05855134), from the Ministry of Educaton, Science and Culture of Japan, and by a joint research grant between the Japan Society for the Promotion of Science and the National Science Foundation (T. O., J. M. B.) for 1990–1993.

Received, 9th August 1994; Com. 4/04897K

References

1 K. Narasaka, *Synthesis*, 1991, 1.
2 S. Miyano, M. Tobita and H. Hashimoto, *Bull. Chem. Soc. Jpn.*, 1981, **54**, 3522.
3 A. I. Meyers and K. A. Lutomsky, *J. Am. Chem. Soc.*, 1982, **104**, 879.
4 J. M. Wilson and D. J. Cram, *J. Am. Chem. Soc.*, 1982, **104**, 881.
5 Y. Yamamoto, H. Fukushima and M. Nakazaki, *J. Chem. Soc., Chem. Commun.*, 1984, 1490.
6 J. Brussee, J. L. C. Groenendijk, J. M. te Koppele and A. C. A. Jansen, *Tetrahedron*, 1985, **41**, 3313.
7 M. Smrčina, M. Lorenc, V. Hanuš, P. Sedmera and P. Kočovský, *J. Org. Chem.*, 1992, **57**, 1917.
8 M. Smrčina, J. Poláková, Š. Vyskočil and P. Kočovský, *J. Org. Chem.*, 1993, **58**, 4534.
9 Y. Kashiwagi, H. Ono and T. Osa, *Chem. Lett.*, 1993, 81.
10 Y. Kashiwagi, H. Ono and T. Osa, *Chem. Lett.*, 1993, 257.
11 L. Papouchado, R. W. Sandford, G. Petric and R. N. Adams, *J. Electroanal. Chem.*, 1973, **65**, 275.
12 Y. Okamoto, S. Honda, I. Okamoto, H. Yuki, S. Murata, R. Noyori and H. Takaya, *J. Am. Chem. Soc.*, 1981, **103**, 6971.
13 The reagent was isolated as a disproportionation product of 4-acetylamino-TEMPO through the oxidation of ethanol in the presence of toluene-*p*-sulfonic acid monohydrate in CH_2Cl_2: Z. Ma and J. M. Bobbitt, *J. Org. Chem.*, 1991, **56**, 6110.
14 Phenol coupling reactions with this reagent have been developed: *e.g.* J. M. Bobbitt and Z. Ma, *Heterocycles*, 1992, **33**, 641.
15 $[\alpha]_D^{21}$ (*c* 1, THF) of pure compound is −79.5: D. S. Lingenfelter, R. C. Helgeson and D. J. Cram, *J. Org. Chem.*, 1981, **46**, 393.
16 M. F. Semmelhack and C. R. Schmid, *J. Am. Chem. Soc.*, 1983, **105**, 6732.