# Anodic Fluorination of 4-Methoxy-1-naphthol and 4-Nitroanisole Using Et<sub>3</sub>N·5HF in Mixed Nonaqueous Solvent

A. Saraswat, L.K. Sharma, S. Singh, I.R. Siddiqui, and R.K.P. Singh

Electrochemical Laboratory of Green Synthesis, Department of Chemistry, University of Allahabad, Allahabad, 211002 India e-mail: rkp.singh@rediffmail.com

#### Received April 30, 2012

**Abstract**—Anodic fluorination of 4-methoxy-1-naphthol and 4-nitroanisole has been investigated in a mixed nonaqueous solvent using  $Et_3N \cdot 5HF$  as supporting electrolyte as well as fluorine source. In order to avoid the formation of polymer on the anode, pulse electrolysis was carried out without exchanging the electrodes. The proposed procedure ensures excellent yield at room temperature, shortest reaction time, and easy work-up which provide additional advantages in the context of green chemistry. Experimental parameters of the reaction are discussed.

## DOI: 10.1134/S107042801309008X

Selective electrochemical fluorination has recently been shown to be a new highly efficient tool for synthesizing various organofluorine compounds because of their unique chemical, physical, and biological properties [1]. In addition, introduction of fluorine atoms into organic compounds often enhances or changes their biological activity [2, 3]. From the atom economy aspect, direct selective fluorination is an ideal method for the preparation of organofluorine compounds. Direct fluorination requires special equipments and techniques since many fluorinating reagents are usually explosive, toxic, unstable, and hygroscopic [4-6]. Anodic fluorination has recently been shown to be a useful method for selective direct fluorination because it can be performed in only one step under safe and mild conditions using relatively simple equipments. Hazardous or toxic reagents are not required; instead, less corrosive fluoride salts are used.

Anodic fluorination of various organic compounds, such as organosulfur, organonitrogen, and heterocyclic compounds has been reported by several research groups [7–11]. Sawaguchi et.al. [12] described anodic fluorination of substituted phenols with subsequent reduction with Zn in acidic aqueous solution; however, the reproducibility of intermediate and final products was poor due to formation of a considerable amount of polymer-like product deposited on the anode surface. In our study, anodic fluorination was performed with the use of pulse electrolysis. Fukuhara et al. [13] synthesized difluorinated derivatives by electrochemical oxidation of phenols using a variety of electrodes such as graphite, glassy carbon, and carbon felt. In our work, mono-ortho-substituted products were obtained at a platinum electrode in fair yield. The possibility of introducing fluorine atoms into aromatic compounds by anodic oxidation of substrate in the presence of fluorine source was first shown in 1969 by Domijan et al. [14] who obtained 9,10-difluoroanthracene by electrochemical oxidation of anthracene in the presence of NH<sub>4</sub>F. Rozhkov et al. [15–19] found that anodic oxidation of benzene, naphthalene, and its derivatives in the presence of fluoride ion results in fluoroaromatic compounds rather than fluorine addition products. They also found that radical cation intermediate was generated during the reaction.

These reactions were also examined in more detail by Eberson [20–22]; it was found that anodic oxidation reactions involve direct electrode attack on the sub-





1287



strate with subsequent ionic steps responsible for the formation of substitution products (Scheme 1).

Our objective was to find out a new general ecofriendly route in which the use of toxic, corrosive, and hazardous reagents could be minimized or eliminated. All these reasons prompted us to try to evaluate the scope of electrochemical fluorination of arenes. The electrochemical reaction proceeds with electron transfer between an electrode and a substrate, and the direct electrochemical oxidation or reduction of substrate utilizes mass-free electron as reagent [23]. Removal of aromatic  $\pi$ -electron system may be achieved by electrochemical oxidation in which radical cation or other cationic species undergoes a variety of reactions, e.g., aromatic substitution [24–27]. Seedi et al. [28] reported that attack by nucleophile on the ortho position of a monosubstituted aromatic compound bearing a hydroxy group follows Scheme 2.

Cyclic voltammograms of 4-methoxy-1-naphthol (I) were obtained at a  $1.0 \times 1.0$ -cm platinum electrode in CH<sub>3</sub>CN/DME containing 1 mol/l of Et<sub>3</sub>N · 5 HF as supporting electrolyte and fluorine source; Ag/AgCl (0.1 M) was used as reference electrode; scan rate  $v = 50 \text{ mV s}^{-1}$ . The corresponding voltammogram exhibits an anodic peak at 2.20 V indicating electrochemical fluorination of 4-methoxy-1-naphthol (I) to 2-fluoro-4-methoxy-1-naphthol (Ia) (see table).

Proper choice of supporting electrolyte was of special importance in this reaction. Both  $Et_3N \cdot 5$  HF and  $Et_3N \cdot 3$  HF are commercially available, but  $Et_3N \cdot 5$  HF was used since it is more stable than  $Et_3N \cdot 3$  HF and its anodic potential [29] is over 2.8 V which is suitable for our reactions. The best results were obtained under the following conditions: temperature 25–30°C, amount of electricity 3–4 F per mole of substrate, supporting electrolyte concentration 3–5%.

The yield of **Ia** in MeCN was lower than in a mixture of MeCN with DME because DME has a much higher donor number (23.9) than MeCN (14.1). No acetamidation of the naphthalene core occurred, as followed from the absence of C=O peak in the IR spectrum of the product. A plausible mechanism for the formation of 2-fluoro-4-methoxy-1-naphthol [28] conforms to that shown in Scheme 2, and analogous mechanism of anodic fluorination of 2-fluoro-4-nitro-anisole [30] is depicted in Scheme 3.



It is obvious from the results of our study that the anodic fluorination of 4-methoxy-1-naphthol and 4-nitroanisole provides a good method for selective fluorination at the *ortho* position. Less corrosive fluoride is used in electrolytic fluorination rather than other toxic reagents. Thus it is a part of green chemistry, where secondary pollution can be avoided by using electricity as oxidizing agent.

## **EXPERIMENTAL**

The <sup>1</sup>H, <sup>13</sup>C, and <sup>19</sup>F NMR spectra were recorded on a Bruker DRX 300 spectrometer (300 MHz for <sup>1</sup>H) in CDCl<sub>3</sub>, using TMS (<sup>1</sup>H, <sup>13</sup>C) or C<sub>6</sub>F<sub>6</sub> (<sup>19</sup>F) as internal

Compound no.	Supporting electrolyte	Solvent	$E_{\rm P}^{\rm ox, a}$ V	Current, A	Time, h	Yield, %
Ι	$Et_3N \cdot 5 HF$	MeCN	2.20	0.35	4	78
Ι	$Et_3N \cdot 5 HF$	MeCN/DME	2.20	0.38	3	88
II	$Et_3N \cdot 5 HF$	MeCN	1.99	0.29	4	80
II	$Et_3N \cdot 5 HF$	MeCN/DME	1.99	0.33	3	90

Current–potential data recorded during anodic fluorination of 4-methoxy-1-naphthol (I) and 4-nitroanisole (II) at a platinum electrode using  $Et_3N \cdot 5HF$  in non-aqueous solvent

<sup>a</sup> Oxidation potential of the substrate relative to SCE.

standard. The mass spectra (electron impact) were obtained on a Jeol SX-1020/PA-6000 spectrometer. The IR spectra were measured in KBr on a Shimadzu 8201 PC IR spectrometer. The melting points were determined in open capillaries and are uncorrected.

Cyclic voltammetry was performed using a CH Instruments Model 600A electrochemical analyzer. The controlled-potential electrolysis [31-40] was carried out in a three-electrode cell assembly with a  $1.0 \times 0.1$ cm platinum plate as working and counter electrode and a saturated calomel electrode (SCE) as reference electrode. The reference electrode was kept in close proximity to the working electrode to minimize ohmic drop. A powerful magnetic stirrer was used for efficient stirring of the reaction mixture.

**CAUTION!** Triethylamine–hydrogen fluoride salts  $Et_3N \cdot nHF$  (n = 3, 4, 5) are toxic and strong skin irritants. Therefore, proper safety precautions should be taken at all times, and it is recommended to use rubber gloves.

All chemicals used in reaction were of analytical grade (purchased from Merck and Loba Chemie) and were used without additional purification. Water was doubly distilled before use.

Anodic synthesis of 2-fluoro-4-methoxy-1-naphthol (Ia). 4-Methoxy-1-naphthol (I, 10 mmol) was electrolyzed on a platinum electrode at a constant potential (2.20 V relative to SCE) in MeCN/DME (40 ml) containing 1 mol/l of Et<sub>3</sub>N·5HF under nitrogen atmosphere at room temperature. The mixture was continuously stirred with a magnetic stirrer until the substrate was completely consumed. To avoid polymer formation on the anode, pulse electrolysis was applied with a pulse width of 2 s without exchanging the electrode. The progress of the reaction was monitored by TLC. The current-potential data were recorded with the aid of a potentiostat at 15-min intervals (see table). After electrolysis, the mixture was extracted with diethyl ether (3×10 ml), the extract was washed with water (3×10 ml), dried over MgSO<sub>4</sub>, and evaporated, and the crude product was purified by column chromatography on silica gel and identified by  ${}^{1}$ H,  ${}^{19}$ F, and  ${}^{13}$ C NMR.

**2-Fluoro-4-methoxynaphthalen-1-ol (Ia).** <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 4.98 s (1H, OH), 6.88– 8.08 m (6H, H<sub>arom</sub>). <sup>13</sup>C NMR spectrum,  $\delta_{C}$ , ppm: 56.0 (OCH<sub>3</sub>), 93.9, 120.1, 121.5, 123.5, 124.8, 125.8, 126.6, 127.6, 143.4, 150.4 (C<sub>arom</sub>). <sup>19</sup>F NMR spectrum:  $\delta_{F}$ -145.8 ppm.

Anodic synthesis of 2-fluoro-4-nitroanisole (IIa). 4-Nitroanisole (II, 10 mmol) was electrolyzed on a platinum electrode at a constant potential (1.99 V relative to SCE) in MeCN/DME (40 ml) containing 1 mol/l of Et<sub>3</sub>N  $\cdot$  5 HF under nitrogen atmosphere at room temperature. The mixture was continuously stirred with a magnetic stirrer until the substrate was completely consumed. To avoid polymer formation on the anode, pulse electrolysis was applied with a pulse width of 2 s without exchanging the electrode. The progress of the reaction was monitored by TLC. The current–potential data were recorded with the aid of a potentiostat at 15-min intervals (see table). The product was isolated and purified as described above for Ia.

**2-Fluoro-4-nitroanisole (IIa).** <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 3.76 s (3H, CH<sub>3</sub>), 7.01–7.86 m (3H, H<sub>arom</sub>). <sup>13</sup>C NMR spectrum,  $\delta_{C}$ , ppm: 56.0 (OCH<sub>3</sub>), 111.6, 116.6, 120.2, 142.3, 148.6, 155.1 (C<sub>arom</sub>), <sup>19</sup>F NMR spectrum:  $\delta_{F}$  –131.4 ppm.

The authors are thankful to the Head of the Department of Chemistry, University of Allahabad for providing necessary facilities, SAIF (IIT Bombay) for recording the <sup>19</sup>F NMR spectra, SAIF (Chandigarh) for recording the <sup>1</sup>H and <sup>13</sup>C NMR and IR spectra, and UGC (New Delhi) for financial support.

#### REFERENCES

1. Hiyama, T., Organofluorine Compounds: Chemistry and Applications, Berlin: Springer, 2000, p. 1.

- Kobayashi, Y. and Taguchi, T., *Biomedical Aspects of Fluorine Chemistry*, Filler, R. and Kobayashi, Y., Eds., Amsterdam: Elsevier Biomedical, 1982, p.30.
- 3. Welch, J.T., *Fluorine in Bioinorganic Chemistry*, Eswarakrishnan, S., Ed., New York: Wiley, 1991.
- 4. Wilkinson, J.A., Chem. Rev., 1992, vol. 92, p. 505.
- 5. McClinton, M.A., Aldrichim. Acta, 1995, vol. 28, p. 31.
- 6. Haufe, G., J. Prakt. Chem., 1996, vol. 338, p. 99.
- Noel, M.V. and Suryanarayanan, S., J. Fluorine Chem., 1997, vol. 83, p. 31.
- Fuchigami, T., Advances in Electron Transfer Chemistry, Mariano, P.S., Ed., Greenwich, CT: JAI, 1999, vol. 6, p. 41.
- Fuchigami, T., Organic Electrochemistry, Lund, H. and Hammerich, O., Eds., New York: Marcel Dekker, 2001, 4th ed., chap. 25.
- Fuchigami, T. and Tajima, T., *Fluorine-Containing Synthons* (ACS Symposium Series, vol. 911), Soloshonok, V.A., Ed., Washington DC: Am. Chem. Soc., 2005, chap. 15.
- 11. Bensadat, G., Bodennec, E., and Laurent, R.T., *Tetrahedron Lett.*, 1977, vol. 18, p. 3799.
- 12. Sawaguchi, M., Fukuhara, T., and Yoneda, N., *J. Electroanal. Chem.*, 2001, vol. 507, p. 66.
- 13. Fukuhara, T., Akiyama, Y., Yoneda, N., Tada, T., and Hara, S., *Tetrahedron Lett.*, 2002, vol. 43, p. 6583; Fukuhara, T., Sawaguchi, M., and Yoneda, N., *Electrochem. Commun.*, 2000, vol. 2, p. 259.
- Domijan, J.D., Ludman, C J., O'Malley, R.F.E.M., and Roman, V., *J. Inorg. Chem.*, 1969, vol. 8, p. 1534.
- Rozhkov, I.N., Bukhtiyarov, A.V., Kuleshova, N.D., and Knunyants, I.L., *Dokl. Akad. Nauk SSSR*, 1970, vol. 193, p. 1322.
- Knunyants, I.L., Rozhkov, I.N., Bukhtiyarov, A.V., Goldin, M.M., and Kudryavtsev, R.V., *Izv. Akad. Nauk* SSSR, Ser. Khim., 1972, p. 1207.
- 17. Rozhkov, I.N., Bukhtiyarov, A.V., and Knunyants, I.L., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1972, vol. 5, p.1130.
- 18. Rozhkov, I.N., Usp. Khim., 1976, vol. 45, p. 1222.
- Rozhkov, I.N., Bukhtiyarov, A.V., and Knunyants, I.L., Dokl. Akad. Nauk SSSR, 1971, vol. 199, p. 369.
- Eberson, L. and Nyberg, K., J. Am. Chem. Soc., 1966, vol. 88, p. 1686.
- 21. Eberson, L., J. Am. Chem. Soc., 1967, vol. 89, p. 4669.

- Rozhkov, I.N., Usp. Khim., 1976, vol. 45, p. 1222;
  Eberson, L., Blum, Z., Helgée, B., and Nyberg, K., Tetrahedron, 1978, vol. 34, p. 731.
- 23. Feroci, A.M., Orisni, M., Palombi, L., and Inesi, A., *Green Chem.*, 2007, vol. 9, p. 323.
- 24. Bockmain, G. and Fritz, H.P., *Electrochim. Acta*, 1976, vol. 21, p. 1099.
- 25. Evans, D.A., Tanis, S.P., and Hart, D.J., *J. Am. Chem. Soc.*, 1981, vol. 103, p. 5813.
- Johnson, R.W., Bendnarski, M.D., Leary, B.F.O., and Grower, E.R., *Tetrahedron Lett.*, 1981, vol. 22, p. 3751.
- Achord, J.M. and Hussey, C.L., J. Electrochem. Soc., 1981, vol. 128, p. 2556.
- Heshman, R., Seedi, E.I., Yamamura, S., and Nishiyama, S., *Tetrahedron Lett.*, 2002, vol. 43, p. 3301.
- 29. Chen, S.Q., Hatakeyama, T., Hara, S., and Yoneda, N., *Electrochim. Acta*, 1997, vol. 42, p. 13.
- Lerman, O., Tor, Y., Hebal, D., and Rozen, S., J. Org. Chem., 1984, vol. 49, p. 806.
- Srivastav, M.K., Saraswat, A., Sharma, L.K., and Singh, R.K.P., *J. Indian Chem. Soc.*, 2010, vol. 87, p. 1131.
- 32. Sharma, L.K., Kumar, S., Singh, S., and Singh, R.K.P., *Elektrokhimiya*, 2010, vol. 46, p. 37.
- Sharma, L.K., Singh, S., and Singh, R.K.P., J. Indian Chem. Soc., 2011, vol. 88, p. 155.
- 34. Sharma, L.K., Saraswat, A., Srivastav, M.K., Kumar, H., and Singh, R.K.P., *J. Indian Chem. Soc.*, 2011, vol. 88, p. 727.
- 35. Sharma, L.K., Singh, S., and Singh, R.K.P., *Indian J. Chem., Sect. B*, 2011, vol. 50, p. 110.
- Saraswat, A., Sharma, L.K., Srivastav, M.K., Siddiqui, I.R., and Singh, R.K.P., *J. Appl. Polym. Sci.*, 2012, vol. 123, p. 1479.
- Singh, S., Sharma, L.K., Saraswat, A., and Singh, R.K.P., Monatsh. Chem., 2012, vol. 143, p. 1427.
- Saraswat, A., Sharma, L.K., Singh, S., Siddiqui, I.R., and Singh, R.K.P., *Res. Chem. Intermed.*, 2013, vol. 39, p. 1393.
- Singh, S., Sharma, L.K., Saraswat, A., and Singh, R.K.P., *Res. Chem. Intermed.* (in press). doi 10.1007/s11164-012-1013-z
- 40. Saraswat, A., Sharma, L.K., Singh, S., Siddiqui, I.R., and Singh, R.K.P., *Synth. Met.*, 2013, vol. 167, p. 31.