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Anodic oxidation of monohalogenated phenols

Kazuki Mori, Masakatsu Takahashi, Shosuke Yamamura and Shigeru Nishiyama*

Department of Chemistry, Faculty of Science and Technology, Keio University, Hiyoshi 3-14-1, Kohoku-ku, Yokohama 223-8522, Japan

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Abstract—Anodic oxidation of simple *o*-halogenated phenol derivatives has been investigated. Among the oxidation products, tricyclic ketone **9** was obtained, along with both the corresponding diaryl ethers **3** and **4** and the diaryls **5**–**8**. Additionally, the effect of the alkyl substituent on the oxidation mode was inspected: anodic oxidation of phenols carrying *n*-propyl or 3-hydroxylpropyl groups **10b** and **10c** mainly provided the dienone compounds **11** and **15** through two-electron oxidation. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

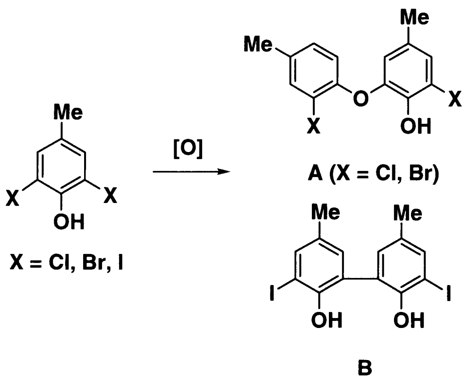
Diverse biological activities of such isodityrosine-class natural products as vancomycin, K-13 and OF-4949s might be expressed by peptide chain-backbones rigidly supported by the diaryl ether and diaryl moieties of the molecules. In our extensive synthetic investigation of these natural products, we have developed phenolic oxidation methodology by employing anodic and thallium (III) oxidations of *o*,*o*′-dihalogenated phenols.[1,2] In addition to an effect of lowering oxidation potentials, the halogen-substituents were observed to control the reaction pathway (Scheme 1): anodic oxidation of dibromo- and dichlorophenols specifically provide the corresponding diaryl ethers (**A**), whereas diaryl derivatives (**B**) are produced from diiodo-phenols.[3] In contrast to the synthetic availability of dihalogenated phenol derivatives, no significant information on monohalogenated derivatives has been reported, to our knowledge, with the exception of phenolic oxidation of bastadins.[4]

This paper describes anodic oxidation of monohalogenated phenol derivatives to understand the scope and limitation of the oxidation reaction, as well as to probe the synthetic availability of the oxidation products as building blocks towards complicated naturally occurring molecules.

2. Results and discussion

To investigate the detailed profile of the oxidation of monohalogenated phenols, compounds **1a**–**1c**[5] were submitted to anodic oxidation in the presence of $LiClO_4$ as an electrolyte in MeOH or CH_3CN (Table 1, Fig. 1). Upon comparison of the yields of the oxidation products, entries using the bromo substituents **1b** provided better results than those of chloro and iodo derivatives **1a** and **1c**. Accordingly, the phenolic oxidation was extensively inspected by using the bromo derivative **1b**. As can be seen in Table 1, all oxidation entries provided both the diaryl ethers **3** and **4** and the diaryls **5**–**8**. The reaction looked to be independent of the kind of halogen atoms in the present series, entirely different from the case of dihalogenated derivatives.[3] Additionally, the tricyclic derivative (Pummerer's ketone, **9**) was obtained in the monosubstituted halogen series.

To obtain further information on product distribution, the effect of the alkyl chain at the *p*-position of bromophenol derivatives was examined in the next stage. Thus, the derivatives **10a**–**10c** were submitted to the same anodic oxidation conditions (Fig. 2), and the results are summarized in Table 2. In contrast to the case of the ethyl derivative **10a** providing similar products distribution to that of **1b**, an obvious difference was observed in the propyl derivative **10b**: the dienone compound **11**, produced by the two-electron oxidation, was obtained in a comparable yield to



Scheme 1.

Keywords: diaryl ethers; diaryls; electrochemical reaction; phenolic oxidation.

* Corresponding author. Tel./fax: +81-45-566-1717; e-mail: nisiyama@chem.keio.ac.jp

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Table 1. Anodic oxidation of the halogenated cresols (**1a**, **1b**, and **1c**)

Entry	Educts	Conditions,[a] solvent	Products (%)[b]							
			Diaryl ethers			Diaryls				
			2	**3**	**4**	**5**	**6**	**7**	**8**	**9**
1	**1a** (X=Cl)	a, MeOH	–	–	2	–	10	1	–	7
2	**1b** (X=Br)	a, MeOH	–	–	7	–	19	2	–	20
3		a[c], MeOH	–	1	1	6	9	–	–	10
4		n, MeOH	–	3	4	1	6	–	–	9
5		n, CH_3CN	–	7	–	29	–	–	–	–
6		b, MeOH	–	–	–	15	–	–	–	3
7	**1c** (X=I)	a, MeOH	4	–	2	–	–	–	6	–

[a] Substrate-concentration, 10 mM. a: acidic conditions. n: neutral conditions. b: basic conditions.
[b] Conversion yields.
[c] Substrate-concentration, 58 mM.

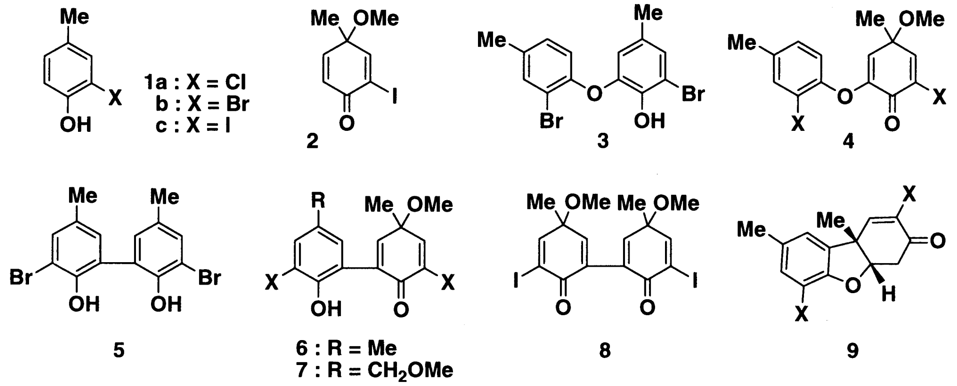


Figure 1. The oxidation products of the halogenated cresols (**1a**, **1b**, and **1c**).

that of **13**. Additionally, upon using the 3-hydroxypropyl derivative **10c**, the spiro compound **15** was produced as a main product, via intramolecular cycloadditions (entries 3–6). Based on these findings, it is deduced that intermolecular couplings between the radical species electrochemically generated, might be hampered by steric hindrance of the alkyl substituents at the *p*-position, and the following oxidation gave rise to production of the dienone compounds.

With respect to these results, a plausible reaction process can be depicted (Scheme 2): abstraction of electron and proton at the first stage of the anodic oxidation provides delocalization of the resultant radical, followed by intermolecular couplings at several positions on the phenol (Path I). The reactive points are apparently the phenolic oxygen and the *o*-position carrying no halogen substituent, as well as the *p*-position. These radicals produced the same diaryls as those obtained from iodo derivatives.[3] Whereas diaryl ether **3** (type A) and diaryl **5** (type B) undergo over-oxidation to **4** and **12** (diaryl ether), and **6**, **7**, **8**, and **13** (diaryl), the coupling between *o*- and *p*-positions (type C) effects the following Michael addition of a phenolic hydroxyl group, yielding the tricyclic product **14**.

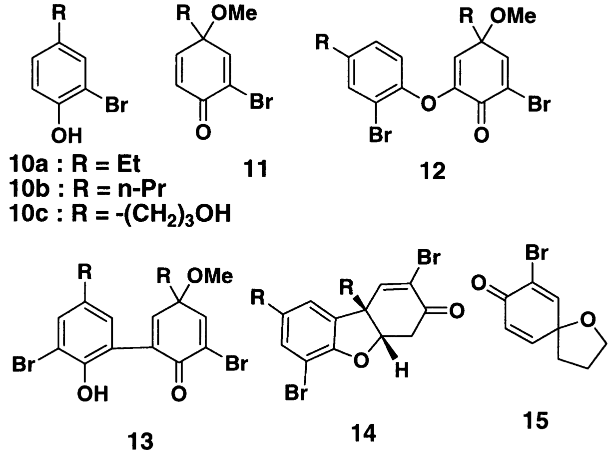
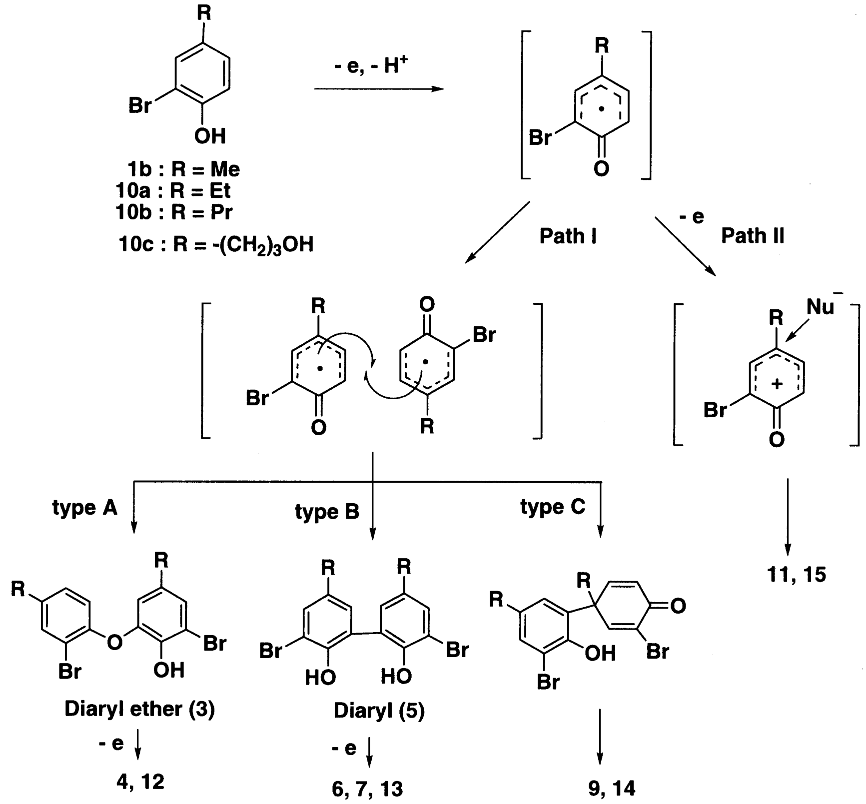


Figure 2. The oxidation products of the halogenated phenol derivatives (**10a**, **10b**, and **10c**).

Table 2. Anodic oxidation of the halogenated phenol derivatives (**10a**, **10b**, and **10c**)

Entry	Educts	Conditions,[a] solvent	Products (%)[b]				
			11	**12**	**13**	**14**	**15**
1	**10a** (R=Et)	a, 10 mM/MeOH	–	3	15	12	–
2	**10b** (R=nPr)	n, 10 mM/MeOH	13	6	12	–	–
3	**10c** (R=HOC_3H_5)	n, 10 mM/MeOH	5	–	–	–	16
4		n, 1 mM/CH_3CN	–	–	–	–	38
5		n, 1 mM/CH_3CN	–	–	–	–	56
6		a, 1 mM/MeOH	16	–	–	–	76

[a] Substrate concentration/solvent. a: acidic conditions. n: neutral conditions.
[b] Conversion yields.



Scheme 2.

In contrast to substrates carrying methyl and ethyl groups **1b** and **10a** leading to dimerization, the steric hindrance of propyl or 3-hydroxypropyl substituents seems to restrain the intermolecular radical coupling reactions (Path II). Since the radical species generated by the one-electron oxidation possessed poor possibilities for intermolecular reactions, they suffered the further abstraction of an electron. Attack of a nucleophile (MeOH or the hydroxyl group in the side chain) to the cation stabilized provides the dienone compounds **11** and **15** as two-electron oxidation products.

In conclusion, anodic oxidation of *o*-halogenated phenols produced diaryl ethers, diaryls, and Pummerer's ketone or dienone compounds. Whereas the oxidation mode seems to be independent of the kind of halogen atoms, elongation of the alkyl side chain at the *p*-position effected an increase of steric hindrance leading to the corresponding two-electron products such as **11** and **15**. Since the 3-hydroxypropyl derivative provided the corresponding spiro products **15** in good yield, conversion into dihydrobenzopyrans will be presented in the following paper,[6] as an example of its synthetic availability.

3. Experimental

IR spectra were recorded on a JASCO Model A-202 spectrophotometer. ^1H NMR and ^{13}C NMR spectra were obtained on a JEOL JNM EX-270, a JEOL JNM GX-400 or a JNM ALPHA-400 NMR spectrometers in a deuteriochloroform ($CDCl_3$) solution using tetramethylsilane as an internal standard. High-resolution mass spectra were obtained on a Hitachi M-80 B GC-MS spectrometer operating at the ionization energy of 70 eV. Preparative and analytical TLC were carried out on silica gel plates (Kieselgel 60 F_{254}, E. Merck AG., Germany) using UV light and/or 5% molybdophosphoric acid in ethanol for detection. Katayama silica gel (K 070) was used for column chromatography.

3.1. General procedure for anodic oxidation of *o*-halogenated cresol

A solution of a phenol derivative (0.25 mmol) in a solvent (MeOH (22.5 ml)– 60% $HClO_4$ (2.5 ml) for acidic conditions; MeOH (25 ml) for neutral conditions; 0.05 M NaOMe/MeOH for basic conditions) containing an electrolyte ($LiClO_4$) was electrolyzed (C.C.E. at 0.13 mA/cm^2: 1.4 F/mol), using a glassy carbon beaker as an anode and a platinum wire as a cathode. The reaction mixture was partitioned between an organic solvent and H_2O. The organic layer was dried over anhydrous Na_2SO_4, and concentrated to give a crude product, which was purified by preparative TLC.

3.2. Anodic oxidation of 2-chloro-4-methylphenol (1a)

Acidic condition: electrolysis of **1a** (23 mg, 0.16 mmol) [C.C.E.: +914→+963 mV vs SCE] provided **4a** (0.9 mg, 1.8%), **6a** (4.9 mg, 9.7%), **7a** (0.4 mg, 0.7%), **9a** (3.3 mg, 7.3%) and recovered **1a** (0.1 mg, 0.4%).

3.2.1. Compound 4a. IR (film) 1692, 1653, and 1611 cm^{-1}; ^1H NMR: δ 1.44 (3H, s), 2.35 (3H, s), 3.19 (3H, s), 5.51 (1H, d, *J*=2.8 Hz), 6.95 (1H, d, *J*=2.8 Hz), 6.98 (1H, d, *J*=8.3 Hz), 7.09 (1H, d, *J*=8.2 Hz), and 7.27 (1H, s). Found: *m/z* 312.0287. Calcd for $C_{15}H_{14}{}^{35}Cl_2O_3$: M, 312.0319.

3.2.2. Compound 6a. IR (film) 1678, 1583, and 1480 cm^{-1}; ^{1}H NMR: δ 1.55 (3H, s), 2.28 (3H, s), 3.32 (3H, s), 5.71 (1H, s), 6.84 (1H, d, *J*=3.0 Hz), 6.85 (1H, s), 7.01 (1H, d, *J*=3.0 Hz), and 7.18 (1H, s); ^{13}C NMR: δ 21.3, 25.2, 26.5, 29.8, 53.7, 120.3, 127.6, 129.7, 130.0, 142.7, 147.0, and 151.3. Found: *m/z* 312.0281. Calcd for $C_{15}H_{14}{}^{35}Cl_2O_3$: M, 312.0319.

3.2.3. Compound 7a. IR (film) 1727, 1678, and 1463 cm^{-1}; ^{1}H NMR: δ 1.56 (3H, s), 3.32 (3H, s), 3.38 (3H, s), 4.37 (2H, s), 5.88 (1H, s), 6.88 (1H, d, *J*=3.0 Hz), 7.02 (1H, d, *J*=3.0 Hz), 7.05 (1H, s), and 7.36 (1H, s). Found: *m/z* 342.0450. Calcd for $C_{16}H_{16}{}^{35}Cl_2O_4$: M, 342.0425.

3.2.4. Compound 9a. IR (film) 1702, 1610, and 1474 cm^{-1}; ^{1}H NMR: δ 1.62 (3H, s), 2.31 (3H, s), 2.92 (1H, dd, *J*=3.8, 18 Hz), 3.35 (1H, dd, *J*=2.8, 18 Hz), 4.75 (1H, complex), 6.60 (1H, d, *J*=2.0 Hz), 6.90 (1H, s), and 7.04 (1H, s). Found: *m/z* 283.0301. Calcd for $C_{14}H_{13}{}^{35}Cl_2O_2$: M+H, 283.0292.

3.3. Anodic oxidation of 2-bromo-4-methylphenol (1b)

(a) *Acidic condition*: electrolysis of **1b** (46 mg, 0.25 mmol) [C.C.E.: +910→+1056 mV vs SCE] provided **4b** (6.1 mg, 6.1%), **6b** (17 mg, 17%), **7b** (1.7 mg, 1.6%), **9b** (17 mg, 18%), and recovered **1b** (5.0 mg, 11%).

(b) *Acidic condition*: electrolysis of **1b** (270 mg, 1.5 mmol) [C.C.E.: +874→+1008 mV vs SCE] provided **3b** (2.7 mg, 0.5%), **4b** (7.0 mg, 1.2%), **5** (33 mg, 6.0%), **6b** (51 mg, 8.6%), **9b** (54 mg, 9.9%) and recovered **1b** (3.6 mg, 1.3%).

(c) *Neutral condition*: electrolysis of **1b** (50 mg, 0.27 mmol) [C.C.E.: +897→+1046 mV vs SCE] provided **3b** (2.8 mg, 2.8%), **4b** (4.1 mg, 3.8%), **5** (0.8 mg, 0.8%), **6b** (6.1 mg, 5.6%), **9b** (8.5 mg, 8.5%) and recovered **1b** (1.9 mg, 3.8%).

(d) *Neutral condition in CH_3CN*: electrolysis of **1b** (47 mg, 0.25 mmol) [C.C.E.: +1077→+1226 mV vs SCE] provided **3b** (5.4 mg, 5.8%), **5** (23 mg, 25%), and recovered **1b** (7.0 mg, 15%).

(e) *Basic condition*: electrolysis of **1b** (55 mg, 0.30 mmol) [C.C.E.: +298→+1321 mV vs SCE] provided **5** (17 mg, 15%), and **9b** (3.7 mg, 3.3%).

3.3.1. Compound 3b. IR (film) 3507, 1724, 1584, and 1487 cm^{-1}; ^{1}H NMR: δ 2.19 (3H, s), 2.27 (3H, s), 5.79 (1H, s), 6.46 (1H, d, *J*=1.7 Hz), 6.89 (1H, d, *J*=8.3 Hz), 7.06–7.11 (2H, complex), and 7.46 (1H, d, *J*=1.7 Hz). Found: *m/z* 369.9234. Calcd for $C_{14}H_{12}{}^{79}Br_2O_2$: M, 369.9204.

3.3.2. Compound 4b. IR (film) 1688, 1649, 1608, and 1487 cm^{-1}; ^{1}H NMR: δ 1.43 (3H, s), 2.35 (3H, s), 3.21 (3H, s), 5.51 (1H, d, *J*=2.6 Hz), 6.96 (1H, d, *J*=8.1 Hz), 7.13 (1H, d, *J*=8.1 Hz), 7.21 (1H, d, *J*=2.6 Hz), and 7.45 (1H, s). Found: *m/z* 399.9325. Calcd for $C_{15}H_{14}{}^{79}Br_2O_3$: M, 399.9310.

3.3.3. Compound 5. IR (film) 3409, 1720, 1572, and 1473 cm^{-1}; ^{1}H NMR: δ 2.31 (6H, s), 5.79 (2H, s), 7.01 (2H, d, *J*=1.8 Hz), and 7.35 (2H, d, *J*=1.8 Hz). Found: *m/z* 371.9178. Calcd for $C_{14}H_{12}{}^{79}Br^{81}BrO_2$: M, 371.9185.

3.3.4. Compound 6b. IR (film) 3446, 1687, 1650, 1607, and 1487 cm^{-1}; ^{1}H NMR: δ 1.54 (3H, s), 2.28 (3H, s), 3.34 (3H, s), 5.70 (1H, s), 6.84 (1H, d, *J*=2.8 Hz), 6.89 (1H, s), 7.28 (1H, d, *J*=2.8 Hz), and 7.32 (1H, s). Found: *m/z* 401.9292. Calcd for $C_{15}H_{14}{}^{79}Br^{81}BrO_3$: M, 401.9290.

3.3.5. Compound 7b. IR (film) 3453, 1686, 1608, and 1487 cm^{-1}; ^{1}H NMR: δ 1.54 (3H, s), 3.34 (3H, s), 3.38 (3H, s), 4.36 (2H, s), 5.87 (1H, s), 6.87 (1H, d, *J*=3.0 Hz), 7.07 (1H, d, *J*=2.2 Hz), 7.29 (1H, d, *J*=3.0 Hz), and 7.50 (1H, d, *J*=2.2 Hz). Found: *m/z* 429.9406. Calcd for $C_{16}H_{16}{}^{79}Br_2O_4$: M, 429.9415.

3.3.6. Compound 9b. IR (film) 1698, 1604, and 1470 cm^{-1}; ^{1}H NMR: δ 1.57 (3H, s), 2.31 (3H, s), 2.93 (1H, dd, *J*=3.5, 17 Hz), 3.39 (1H, dd, *J*=2.8, 17 Hz), 4.77 (1H, complex), 6.87 (1H, d, *J*=1.7 Hz), 6.93 (1H, d, *J*=0.7 Hz), and 6.93 (1H, dd, *J*=0.7, 1.7 Hz); ^{13}C NMR: δ 20.6, 21.4, 37.5, 49.3, 86.6, 103.3, 121.4, 122.2, 128.8, 132.3, 133.0, 133.3, 148.8, and 186.5. Found: *m/z* 373.9176. Calcd for $C_{14}H_{12}{}^{81}Br_2O_2$: M, 373.9165.

3.4. Anodic oxidation of 2-iodo-4-methylphenol (1c)

Acidic condition: electrolysis of **1c** (57 mg, 0.24 mmol) [C.C.E.: +906→+1473 mV vs SCE] provided **2c** (2.3 mg, 3.7%), **4c** (2.5 mg, 2.1%), **8c** (7.7 mg, 6.1%), and **9c** (0.4 mg, 0.4%).

3.4.1. Compound 2c. IR (film) 1666 cm^{-1}; ^{1}H NMR: δ 1.45 (3H, s), 3.24 (3H, s), 6.44 (1H, d, *J*=10 Hz), 6.83 (1H, dd, *J*=2.7, 10 Hz), and 7.56 (1H, d, *J*=2.7 Hz); ^{13}C NMR: δ 25.9, 53.8, 75.9, 105.1, 127.2, 151.9, 160.5, and 188.2. Found: *m/z* 263.9619. Calcd for $C_8H_9IO_2$: M, 263.9647.

3.4.2. Compound 4c. IR (film) 1682, 1645, 1596, and 1480 cm^{-1}; ^{1}H NMR: δ 1.43 (3H, s), 2.33 (3H, s), 3.23 (3H, s), 5.54 (1H, d, *J*=2.6 Hz), 6.89 (1H, d, *J*=8.3 Hz), 7.15 (1H, dd, *J*=1.7, 8.3 Hz), 7.53 (1H, d, *J*=2.6 Hz), and 7.68 (1H, d, *J*=1.7 Hz). Found: *m/z* 495.9009. Calcd for $C_{15}H_{14}I_2O_3$: M, 495.9034.

3.4.3. Compound 8c. IR (film) 1659, 1591, and 1456 cm^{-1}; ^{1}H NMR: δ 1.49 (3H, s), 1.51 (3H, s), 3.32 (3H, s), 3.36 (3H, s), 6.84 (2H, d, *J*=2.8 Hz), and 7.58 (2H, d, *J*=2.8 Hz). Found: *m/z* 525.9123. Calcd for $C_{16}H_{16}I_2O_4$: M, 525.9139.

3.4.4. Compound 9c. IR (film) 1689 and 1466 cm^{-1}; ^{1}H NMR: δ 1.58 (3H, s), 2.30 (3H, s), 2.29 (1H, dd, *J*=3.6, 17 Hz), 3.43 (1H, dd, *J*=3.0, 17 Hz), 4.79 (1H, complex), 6.95 (1H, d, *J*=1.7 Hz), 7.19 (1H, d, *J*=1.7 Hz), and 7.40 (1H, d, *J*=1.7 Hz); ^{13}C NMR: δ 20.8, 21.5, 37.9, 48.0, 86.6, 121.4, 129.4, 129.7, 130.1, 130.5, 132.7, 132.9, 144.4, and 186.5. Found: *m/z* 465.8915. Calcd for $C_{14}H_{12}I_2O_2$: M, 465.8928.

3.5. Anodic oxidation of 2-bromo-4-ethylphenol (10a)

Acidic condition: electrolysis of **10a** (51 mg, 0.25 mmol) [C.C.E.: +0.91→+0.97 V vs SCE] provided **12a** (1.3 mg, 2.4%), **13a** (7.7 mg, 14%), **14a** (5.5 mg, 11%), and recovered **10a** (3.7 mg, 7.3%).

3.5.1. Compound 12a. IR (film) 1688, 1648, 1607, 1488, 1243, and 1096 cm^{-1}; ^{1}H NMR: δ 0.84 (3H, t, J=7.6 Hz), 1.26 (3H, t, J=7.6 Hz), 1.73–1.78 (2H, complex), 2.65 (2H, q, J=7.6 Hz), 3.23 (3H, s), 5.44 (1H, d, J=2.6 Hz), 6.97 (1H, d, J=8.3 Hz), 7.15 (1H, dd, J=2.0, 8.3 Hz), 7.16 (1H, d, J=2.6 Hz), and 7.47 (1H, d, J=2.0 Hz). Found: *m/z* 427.9604. Calcd for $C_{19}H_{22}{}^{79}Br_2O_3$: M, 427.9623.

3.5.2. Compound 13a. IR (film) 3502, 1675, 1607, 1472, and 1086 cm^{-1}; ^{1}H NMR: δ 0.94 (3H, t, J=7.6 Hz), 1.21 (3H, t, J=7.6 Hz), 1.88 (2H, q, J=7.6 Hz), 2.58 (2H, q, J=7.6 Hz), 5.70 (1H, s), 6.81 (1H, d, J=2.8 Hz), 6.90 (1H, d, J=2.0 Hz), 7.24 (1H, d, J=2.8 Hz), and 7.33 (1H, d, J=2.0 Hz). Found: *m/z* 427.9630. Calcd for $C_{19}H_{22}{}^{79}Br_2O_3$: M, 427.9623.

3.5.3. Compound 14a. IR (film) 1697, 1604, 1469, and 1080 cm^{-1}; ^{1}H NMR: δ 1.05 (3H, t, J=7.6 Hz), 1.22 (3H, t, J=7.6 Hz), 2.01 (2H, q, J=7.6 Hz), 2.60 (2H, q, J=7.6 Hz), 2.90 (1H, dd, J=4.0, 18 Hz), 3.39 (1H, dd, J=2.8, 18 Hz), 4.91 (1H, m), 6.87 (1H, d, J=1.7 Hz), 6.91 (1H, d, J=1.7 Hz), and 7.21 (1H, d, J=1.7 Hz). Found: *m/z* 401.9485. Calcd for $C_{16}H_{16}{}^{81}Br_2O_2$: M, 401.9478.

3.6. Anodic oxidation of 2-bromo-4-propylphenol (10b)

(a) *Neutral condition*: electrolysis of **10b** (56 mg, 0.26 mmol) [C.C.E.: +0.93→+1.15 V vs SCE] provided **11b** (7.1 mg, 11%), **12b** (2.0 mg, 3.3%), and **13b** (5.4 mg, 9.1%).

(b) *Neutral condition*: electrolysis of **10b** (30 mg, 0.14 mmol) [C.C.E.: +1.02→+1.21 V vs SCE] provided **11b** (4.3 mg, 13%), **12b** (2.0 mg, 6.2%), and **13b** (3.8 mg, 12%).

3.6.1. Compound 11b. IR (film) 1674, 1601, 1459, and 1084 cm^{-1}; ^{1}H NMR: δ 0.89 (3H, t, J=7.3 Hz) 1.22–1.30 (2H, complex), 1.68–1.73 (2H, complex), 3.22 (3H, s), 6.45 (1H, d, J=10 Hz), 6.75 (1H, dd, J=2.5, 10 Hz), and 7.18 (1H, d, J=2.5 Hz). Found: *m/z* 244.0054. Calcd for $C_{10}H_{13}{}^{79}BrO_2$: M, 244.0099.

3.6.2. Compound 12b. IR (film) 1689, 1648, 1607, 1487, and 1240 cm^{-1}; ^{1}H NMR: δ 0.88 (3H, t, J=7.3 Hz), 0.96 (3H, t, J=7.3 Hz), 1.22–1.28 (2H, complex), 1.61–1.71 (4H, complex), 2.57 (2H, t, J=7.8 Hz), 3.22 (3H, s), 5.46 (1H, d, J=2.7 Hz), 6.96 (1H, d, J=8.3 Hz), 7.13 (1H, dd, J=2.0, 8.3 Hz), 7.19 (1H, d, J=2.7 Hz), and 7.44 (1H, d, J=2.0 Hz). Found: *m/z* 455.9934. Calcd for $C_{19}H_{22}{}^{79}Br_2O_3$: M, 455.9936.

3.6.3. Compound 13b. IR (film) 3503, 1674, and 1471 cm^{-1}; ^{1}H NMR: δ 0.93 (3H, t, J=7.3 Hz), 0.94 (3H, t, J=7.3 Hz), 1.36–1.39 (2H, complex), 1.61 (2H, dt, J=7.3, 7.8 Hz), 1.81 (2H, t, J=8.3 Hz), 2.50 (2H, t, J=7.8 Hz), 3.34 (3H, s), 5.72 (1H, s), 6.82 (1H, d, J=2.9 Hz), 6.87 (1H, d, J=2.0 Hz), 7.26 (1H, d, J=2.9 Hz), and 7.31 (1H, d, J=2.0 Hz). Found: *m/z* 455.9942. Calcd for $C_{19}H_{22}{}^{79}Br_2O_3$: M, 455.9936.

3.7. Anodic oxidation of 2-bromo-4-(1-hydroxypropyl)-phenol (10c)

(a) *Neutral condition*: electrolysis of **10c** (98 mg, 0.42 mmol) in MeOH (30 ml) containing an electrolyte (0.25 g, $LiClO_4$) [C.C.E.: +1.95→+1.30 V vs SCE] provided **11c** (6 mg, 5%) and **15** (15 mg, 16%).

(b) *Neutral condition in CH_3CN*: electrolysis of **10c** (59 mg, 0.26 mmol) in CH_3CN (25 ml) containing an electrolyte (0.25 g, $LiClO_4$) [C.C.E.: +1.16→+1.34 V vs SCE] provided **15** (6.0 mg, 10%), and recovered **10c** (43 mg, 73%).

(c) *Diluted neutral condition*: electrolysis of **10c** (9.3 mg, 0.04 mmol) in MeOH (30 ml) containing an electrolyte (0.25 g, $LiClO_4$) [C.C.E.: +1.08→+1.35 V vs SCE] provided **15** (5.1 mg, 56%).

(d) *Diluted acidic condition*: electrolysis of **10c** (9.9 mg, 0.043 mmol) in MeOH (27 ml) and aq. 60% $HClO_4$ (3 ml) containing an electrolyte (0.25 g, $LiClO_4$) [C.C.E.: +1.08→+1.50 V vs SCE] provided **11c** (1.4 mg, 12%), **15** (5.7 mg, 58%), and recovered **10c** (2.3 mg, 23%).

3.7.1. Compound 11c. IR (film) 3433, 1673, 1601, and 1455 cm^{-1}; ^{1}H NMR: δ 1.56–1.61 (2H, multiplex), 1.84–1.89 (2H, multiplex), 3.26 (3H, s), 3.66 (2H, t, J=6.3 Hz), 6.49 (1H, d, J=10 Hz), 6.81 (1H, dd, J=2.9, 10 Hz), and 7.23 (1H, d, J=2.9 Hz). Found: *m/z* 260.0039. Calcd for $C_{10}H_{13}{}^{79}BrO_3$: M, 260.0048.

3.7.2. Compound 15. IR (film) 2875, 1672, 1636, and 1600 cm^{-1}; ^{1}H NMR: δ 2.10–2.22 (4H, complex), 4.10 (2H, t, J=6.6 Hz), 6.27 (1H, d, J=10 Hz), 6.84 (1H, dd, J=2.4, 10 Hz) and 7.26 (1H, d, J=2.4 Hz); ^{13}C NMR: δ 26.8, 36.8, 69.5, 79.9, 123.1, 125.7, 149.8, and 178.1. Found: *m/z* 227.9802. Calcd for $C_9H_9{}^{79}BrO_2$: M, 227.9786.

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