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Synthesis of spirodienone derivatives and their conversion into dihydrobenzopyrans

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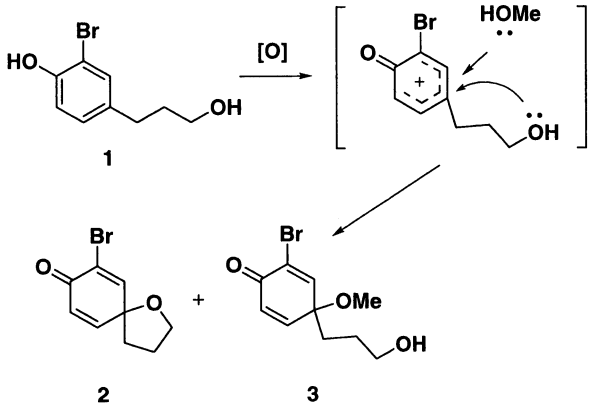
Abstract—The spirodienones **5**, **6**, and **12**–**14** including optically active ones were synthesized by anodic oxidation of the corresponding phenol derivatives. Although the asymmetric centers included in the substrates had little effect on the diastereomeric selectivity of the cyclization, the asymmetric structure of the products led to a regioselective conversion into dihydrobenzopyrans **16**, **17**, and **21**–**26** under mild Lewis acid-promoted conditions.

1. Introduction

In the preceding paper,[1] we reported the anodic oxidation of monohalogenated phenols, as part of our chemical investigation of isodityrosine-class bioactive substance. The chemical properties of the monohalogenated phenols have not been elucidated, contrary to the extensive studies on *o*,*o*′-dihalogenated phenols. Detailed inspection revealed that steric hindrance of alkyl substituents at the *p*-position of *o*-bromophenol derivatives effects preferentially two-electron oxidation rather than one-electron oxidation. Whereas anodic oxidation of phenol derivatives carrying Me or Et groups at the *p*-positions produced such intermolecular radical coupling products as diaryl ethers and diaryls, the spirodienone-type compounds **2** and **3** were obtained selectively via addition of appropriate nucleophiles to the cation center generated from the 3-hydroxypropyl derivative **1** (Scheme 1).



Scheme 1.

It was also of interest to investigate whether anodic oxidation of phenol derivatives possessing asymmetric centers would provide optically active spiro products or not. In relation to bromotyrosine-class natural products carrying spiroisoxazole moieties (e.g. araplysillin, hexadelin C),[2] Hoshino reported a chirality induction of spiro centers by using an optically active ester moieties, leading to the corresponding products in good diastereoselection.[3] Additionally, to understand their synthetic availability, the spirodienone derivatives would be submitted to Lewis acid conditions, which would effect rearrangement[4] to release a structural strain of the spiro five-membered rings. Influence of the stereogenic center on the reaction pathway would be another concern of this investigation. Accordingly, we describe herein the synthesis of several bicyclic-spiro compounds by anodic oxidation and their rearrangement into a dihydrobenzopyran-type compound.

2. Results and discussion

2.1. Anodic oxidation of bromophenols

To obtain the spiro compounds modified at the alkyl group of the *p*-positions type A, e.g. *N*-protected bromotyrosinols and type B, e.g. 3-hydroxypropyl-2-bromophenols were employed as substrates of the anodic oxidations: type A has an asymmetric center at the homobenzylic position towards the phenyl group, whereas type B possesses secondary alcohols at the C-3 position (Fig. 1).

When the tyrosinol derivatives (type A, **4a**–**4c**) prepared by a borane-reduction of the tyrosine derivative,[5] were

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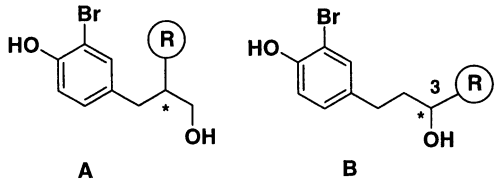


Figure 1.

submitted to the anodic oxidation, the phenols were converted into the spiro compounds as a 1:1 mixture of the corresponding diastereomers **5** and **6** (Table 1, Scheme 2).[6] The stereostructures of both products were confirmed by the NOE experiments. Unfortunately, the ratio of the products **5** and **6** indicated that existence of the *N*-protected amino groups at these positions could not effect stereochemical differentiation of the nucleophilic attack of the hydroxyl group to the cationic center, whereas it enabled chromatographic separation of both diastereomers.

To examine the effect of a hydroxyl group at the asymmetric C-3 position, synthesis of the corresponding phenol derivatives was commenced by benzylation of **7**,[1] followed by Swern oxidation to give aldehyde **8** (Scheme 3). Upon the Grignard reaction employing *i*-propyl magnesium bromide, **8** provided a chain-elongated product, which on TMSI-promoted deprotection gave the 3-hydroxyl-4-methylpentyl derivative **9**. A similar reaction cascade using *i*-butyl magnesium bromide, afforded **10** carrying a 3-hydroxyl-5-methylhexyl group. Additionally, the tertiary alcohol derivative **11** was also synthesized from methyl 3-(4-hydroxyphenyl)propionate in high yield in order to gain insight into the reaction trend of a relatively hindered nucleophile.

Anodic oxidations of **9**, **10**, and **11** were performed as shown in Table 2. In the case of the secondary alcohols **9** and **10**, nucleophilic attack of a small solvent molecule (MeOH) to the cationic intermediate increased at low reaction temperature, leading to the methoxy products **15a** and **15b**[7] (entries 1, 2 and 6). Preferential production of the cationic species under acidic conditions afforded spiro derivatives **12** and **13** in higher yields (entries 5, 8 and 9). Even the sterically hindered tertiary hydroxyl group of **11** gave the corresponding product **12** in high yields under acidic conditions (entries 10 and 11).

Table 1. Anodic oxidation of the tyrosinol derivatives (**4a**, **4b**, and **4c**)

Entry	Educt	Condition[a]	Potential (V)	Yield (%)[b]	
				5	**6**
1	**4a**	n	1.07–1.32	18	18
2	**4b**	n	1.15–1.39	8	8
3		a	1.10–1.80	9	9
4	**4c**	n	1.27–1.64	20	20

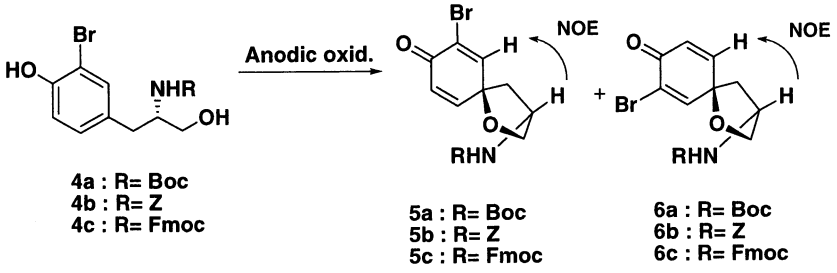
[a] Electrolyte ($LiClO_4$), C.C.E. at 0.13 mA/cm^2: 1.4 F/mol, substrate concentration=1 mM. n: neutral conditions in MeOH. a: acidic conditions in MeOH–aq. 60% $HClO_4$ (10/1).
[b] Conversion yield.

2.2. Lewis acid-promoted rearrangements

Since the required spiro compounds **2**, **4a–c**, **12**, **13ab**, and **14ab** were obtained, rearrangement reactions were carried out by employing $BF_3{\cdot}OEt_2$ as a Lewis acid. At the outset, the most primitive derivative **2**[1] was treated with $BF_3{\cdot}OEt_2$, to give dihydrobenzopyrans **16** and **17** in quantitative yields (Table 3).

In addition to the structural confirmation, the NOE experiments of the corresponding derivatives **18** and **19** of **16** and **17** elucidated the mechanistic features of the rearrangement: the reaction was induced by the electron-donation of lone pair electrons of the spiro-oxygen, and the electron-withdrawing effect of the carbonyl part interacted with a Lewis acid **20** (Scheme 4). Such a push–pull effect enabled a smooth reaction-process even under low temperature (entries 3 and 4).[4] In those entries, **17** was apparently produced in higher yield than **16** (Table 4, Scheme 5).

When the optically active spiro compounds **5b**, **5c**, **6b**, and **6c**[8] were submitted to the Lewis acid conditions, product distribution apparently depended on the stereochemistry of the spiro compounds: yields of **21** took preference over those of **22**, in contrast to definite production of **22** from **6b** and **6c**. The acid-labile property of Z (benzyloxycarbonyl) groups might cause low yields of **21** and **22** (entries 6 and 8). The same regioselectivity was also observed in the case of **13** and **14** carrying secondary alcohols as nucleophiles. Yields of compounds **23a** and **23b** produced from **13a** and **13b** were approximately two-fold higher than those of **24a** and **24b**, whereas **14a** and **14b** furnished **24a** and **24b** as the sole products monitored by TLC. In the case of **12** carrying a geminal dimethyl function, **26** was selectively obtained (entry 9). Based on these observations, bromo-substituents are deemed to be the controlling factors of reactions of the spiro derivatives to dihydrobenzopyrans. Thus, **2** and **12** possessing no asymmetric substituents gave rise to a rearrangement of the σ-bond directed to the opposite side of the Br groups, probably owing to avoidance of steric repulsion. However,

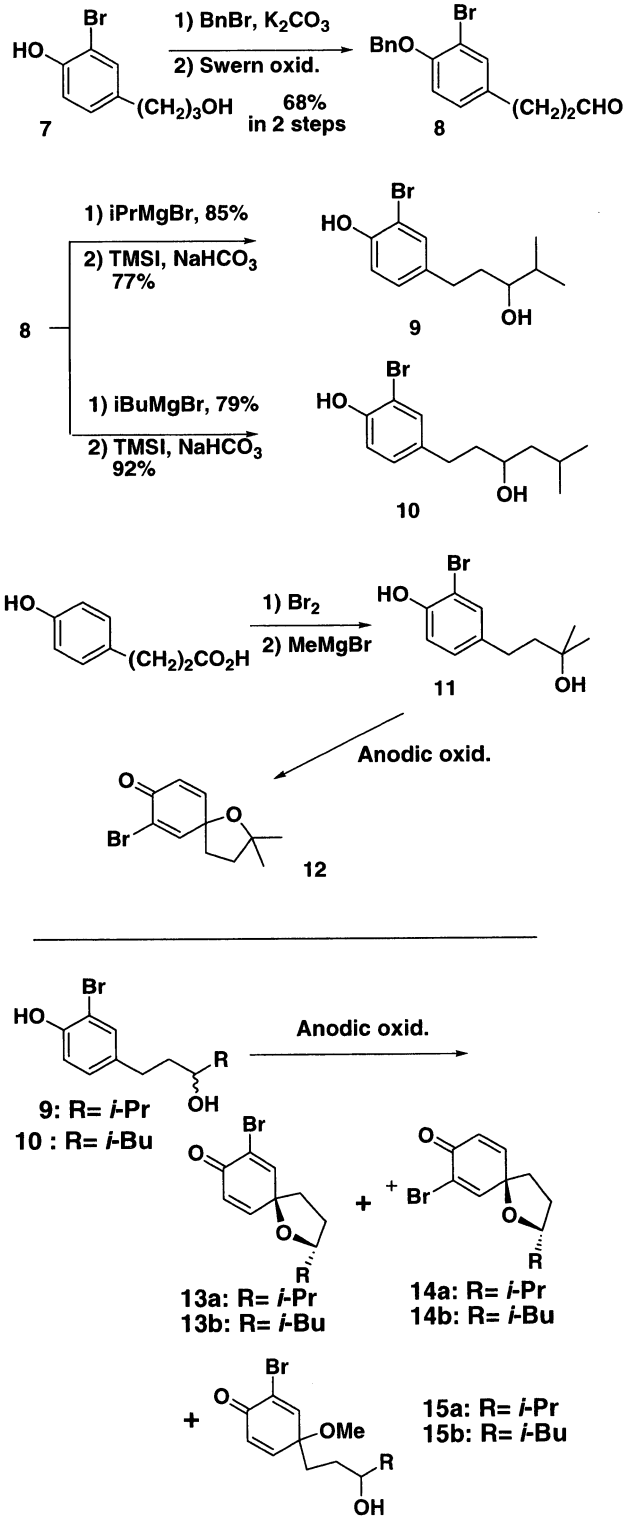


4a : R= Boc
4b : R= Z
4c : R= Fmoc

5a : R= Boc
5b : R= Z
5c : R= Fmoc

6a : R= Boc
6b : R= Z
6c : R= Fmoc

Scheme 2.



Scheme 3.

there would be an additional feature in the case of tyrosinol and *sec*-alcohols: **21** and **23** were preferred to **22** and **24** (entries 1, 2, 5 and 6). Structural comparison of both spirodienone derivatives indicated similar relative stereochemistry between Br and R or NHR′-substituents (**A** and **B**) (Scheme 6). In the direction of the gray arrow to the opposite side of the Br, there might be repulsion with the R-substituent, which might be a direction-controlled factor more influential than the Br group. Accordingly, the rearrangement proceeded to the Br side as indicated by the thick arrow, leading to **21** and **23**. In contrast to those cases, types C and D produced **24** without any stereochemical interruption.

In conclusion, introduction of asymmetric centers to the 3-hydroxypropyl group at the *p*-position provided spirodienone compounds including optically active derivatives, although no diastereoselectivity was observed. Conversion into the corresponding dihydropyrans was smoothly conducted under $BF_3{\cdot}OEt_2$ conditions. Whereas the σ-bonds were shifted usually to the opposite side of the Br group, repulsion with an alkyl or *N*-protected amino group causes rearrangement to the Br side. Further inspection of the synthetic potentials of the spiro derivatives will be reported.

3. Experimental

All of the melting points were obtained on a Yanaco MP-S3 melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO Model A-202 spectrophotometer. ^{1}H 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. Optical rotations were recorded on a JASCO DIP-360 digital polarimeter. High-resolution mass spectra were obtained on a Hitachi M-80 B GC-MS spectrometer operating at an ionization energy of 70 eV. Preparative and analytical TLC were carried out on silica gel plates (Kieselgel 60 F_{254}, E. Merck A.G., Germany) using UV light and/or 5% molybdophosphoric acid in ethanol for detection. Katayama silica gel (K 070) was used for column chromatography. The anodic oxidation was undertaken by the same procedures as described in the preceding paper.[1]

3.1. Data for compounds

3.1.1. *N*-(*tert*-Butyloxycarbonyl)-3-bromo-L-tyrosinol (4a). To a solution of *N*-(*tert*-butyloxycarbonyl)-L-tyrosinol (0.57 g, 2.1 mmol) and $NaHCO_3$ (0.18 g, 2.1 mmol) in THF (60 ml) was added bromine (0.1 ml, 2.1 mmol) at −78°C. After being stirred overnight, the reaction mixture was poured into aq. $Na_2S_2O_3$ (50 ml), and extracted with EtOAc (2×50 ml). The combined extracts were washed with brine, dried (Na_2SO_4), and then evaporated. The residue was purified by silica-gel column chromatography (hexane/EtOAc=1:1) to give **4a** (0.51 g, 71%) as a colorless oil: $[\alpha]_D^{22}=-17.0$ (*c* 1.00, $CHCl_3$); IR (film) 3346, 1682, and 1510 cm^{-1}; ^{1}H NMR: δ 1.41 (9H, s), 2.74 (2H, d, *J*=7.3 Hz), 3.56 (1H, m), 3.64 (1H, m), 3.78 (1H, m), 4.77 (1H, d, *J*=8.3 Hz), 5.75 (1H, s), 6.91 (1H, d, *J*=8.3 Hz), 7.05 (1H, dd, *J*=2.0, 8.3 Hz), and 7.32 (1H, d, *J*=2.0 Hz); ^{13}C NMR: δ 28.4, 36.2, 53.7, 63.9, 79.9, 110.0, 115.4, 116.0, 129.8, 130.2, 132.5, and 151.0. Found: *m/z* 347.0548. Calcd for $C_{14}H_{20}{}^{81}BrNO_4$: M, 347.0555.

3.1.2. *N*-(Benzyloxycarbonyl)-3-bromo-L-tyrosinol (4b). To a solution of **4a** (52 mg, 0.15 mmol) in CH_2Cl_2 (3 ml) was added TFA (1 ml, 14 mmol) at 0°C. After being stirred

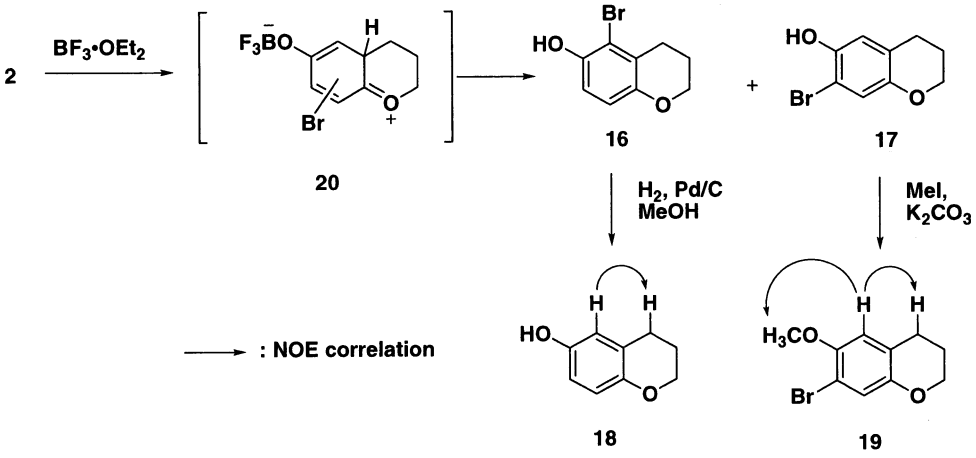
Table 2. Anodic oxidation of the halogenated phenol derivatives (**9**, **10**, and **11**)

Entry	Educt	Condition[a]	Temperature (°C)	Yield (%)[b]						
				12	**13a**	**13b**	**14a**	**14b**	**15a**	**15b**
1	**9**	n_1	−78		–		21		60	
2		n_1	−50		9		12		55	
3		n_1	23		15		21		–	
4		n_1	50		17		18		11	
5		a_1	23		25		25		13	
6	**10**	n_1	−78			11		11		42
7		n_1	23			16		23		20
8		a_1	23			21		27		–
9		a_2	23			38		25		–
10	**11**	n_2	23	16						
11		a_3	23	49						

[a] Substrate concentration 2 mM. n_1: neutral condition in MeOH. n_2: neutral condition in 1,4-dioxane–H_2O (5/1). a_1: acidic condition in MeOH–aq. 60% $HClO_4$ (10/1). a_2: acidic condition in dioxane–aq. 60% $HClO_4$ (10/1). a_3: acidic condition in dioxane–aq. 60% $HClO_4$ (5/1).
[b] Conversion yield. a=*i*-Pr; b=*i*-Bu.

Table 3. Lewis acid-promoted rearrangement reactions of the spiro derivative (**2**)

Entry	Solvent	Lewis acid concentration (M)	Reaction temperature (°C)	Products yield (%)	
				16	**17**
1	CH_2Cl_2	0.16	0	40	60
2	CH_2Cl_2	0.16	23	50	50
3	CH_2Cl_2	0.20	−20	33	55
4	$CH_2Cl_2/CHCl_3$ (7:1)	0.13	−78–23	37	61



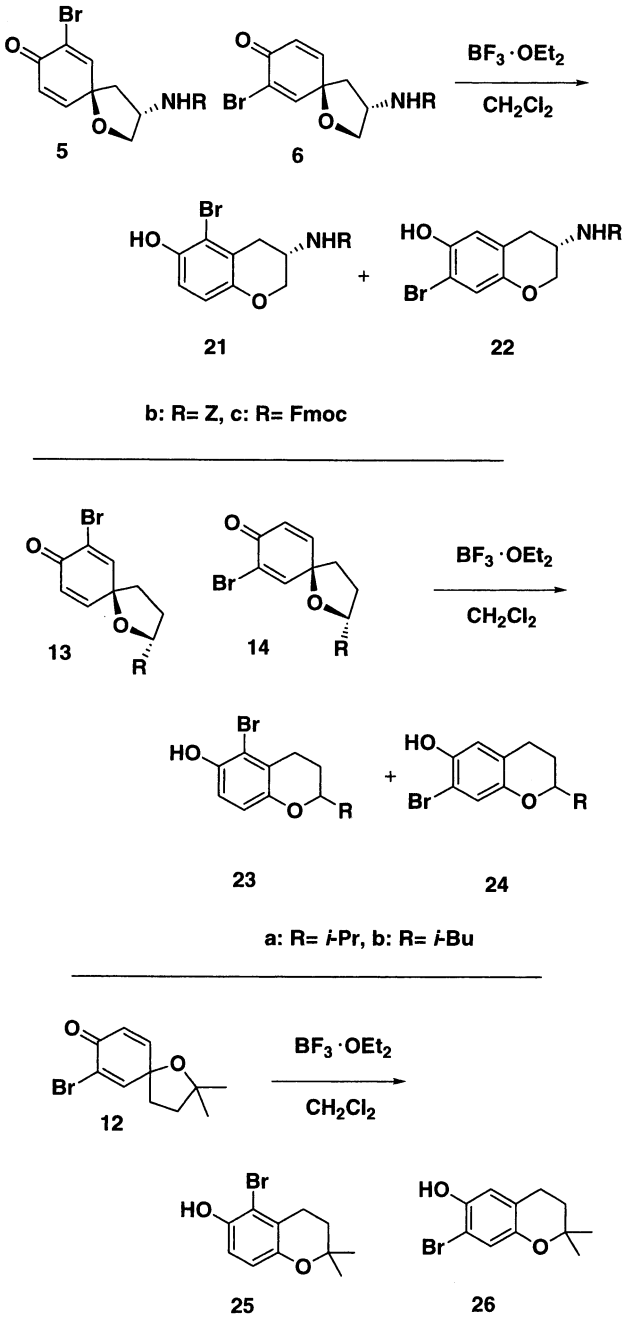
Scheme 4.

Table 4. Lewis acid-promoted rearrangement reactions of the spiro derivative (**5bc**, **6bc**, **13ab**, **14ab**, and **12**)

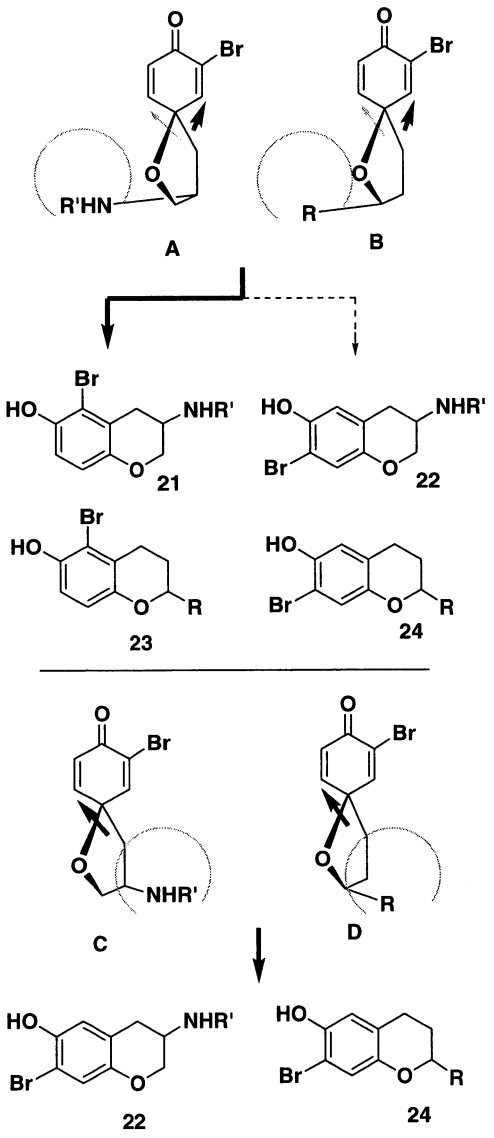
Entry	Educt	Products yield (%)			
		21b	**21c**	**22b**	**22c**
1	**5b**	22		8	
2	**5c**		70		27
3	**6b**	–		37	
4	**6c**		–		76
		23a	**23**b	**24a**	**24b**
5	**13a**	54		27	
6	**13b**		51		30
7	**14a**	–		74	
8	**14b**	–			74
		25	**26**		
9	**12**	1	77		

The reactions were carried out under $BF_3{\cdot}OEt_2/CH_2Cl_2$ conditions at −20–0°C.

for 2 h, the reaction mixture was concentrated in vacuo, then the residue was diluted with 1,4-dioxane (1 ml)–H_2O (1 ml). After the addition of $NaHCO_3$ (38 mg, 0.45 mmol) and benzyloxycarbonyl chloride (0.08 ml, 0.53 mmol) at 0°C, the reaction mixture was stirred overnight. The reaction mixture was poured into brine, and extracted with EtOAc (2×20 ml). The combined organic extracts were dried (Na_2SO_4), then evaporated. The residue was purified by PTLC (hexane/EtOAc=1:1) to give **4b** (59 mg, 100% in 2 steps) as a colorless oil: $[\alpha]_D^{20}=-26.3$ (*c* 1.00, $CHCl_3$); IR (film) 3314, 1691, and 1509 cm^{-1}; ^1H NMR: δ 2.76 (2H, d, *J*=6.9 Hz), 3.55 (1H, dd, *J*=4.6, 11 Hz), 3.65 (1H, dd, *J*=3.1, 11 Hz), 3.86 (1H, m), 5.07 (2H, s), 5.84 (1H, broad), 6.88 (1H, d, *J*=8.2 Hz), 7.04 (1H, dd, *J*=1.2, 8.2 Hz), and 7.26–7.36 (6H, complex); ^{13}C NMR: δ 36.0, 54.2, 63.7, 67.1, 110.3, 116.3, 128.2, 128.4, 128.7, 128.7, 130.1, 131.3, 132.7, 136.3, 151.2, and



Scheme 5.



Scheme 6.

156.6. Found: *m/z* 378.0314. Calcd for $C_{17}H_{17}{}^{79}BrNO_4$: M−H, 378.0340.

3.1.3. *N*-(9-Fluorenylmethyloxycarbonyl)-3-bromo-L-tyrosinol (4c). A hydrolyzed product obtained from **4a** (52 mg, 0.15 mmol) by the same procedure as in the case of **4b**, was diluted with DMF (3 ml), then Na_2CO_3 (24 mg, 0.23 mmol) and FmocOSu (74 mg, 0.23 mmol) were added at 0°C; the mixture was stirred for 4 h. The same workup as in the case of **4b** gave **4c** (70 mg, 100% in 2 steps) as colorless needles: mp 156–157°C (MeOH); $[\alpha]_D{}^{22}=-22.0$ (*c* 1.00, $CHCl_3$); IR (nujol) 3314, 1693, and 1534 cm^{-1}; ^1H NMR: δ 2.76 (2H, d, *J*=6.3 Hz), 3.57 (1H, m), 3.65 (1H, m), 3.84 (1H, m), 4.19 (1H, t, *J*=6.4 Hz), 4.40 (1H, m), 5.04 (1H, d, *J*=7.3 Hz), 5.78 (1H, s), 6.91 (1H, d, *J*=8.3 Hz), 7.04 (1H, dd, *J*=1.2, 8.3 Hz), 7.29 (3H, complex), 7.40 (2H, t, *J*=7.3 Hz), 7.54 (2H, t, *J*=7.3 Hz), and 7.76 (2H, d, *J*=7.3 Hz); ^{13}C NMR: δ 36.1, 47.2, 54.1, 63.5, 66.7, 110.1, 116.1, 119.9, 124.9, 127.0, 127.6, 129.8, 131.1, 132.4, 141.2, 143.6, 150.9, and 156.2. Found: *m/z* 470.0764. Calcd for $C_{24}H_{23}{}^{81}BrNO_4$: M+H, 470.0790.

3.2. Anodic oxidation of 4a

Electrolysis of **4a** (11 mg, 0.033 mmol) [C.C.E.: +1.07→+1.32 V vs SCE] provided **5a** (2.0 mg, 18%) and **6a** (2.0 mg, 18%).

3.2.1. Compound 5a. $[\alpha]_D{}^{23}=-62.7$ (*c* 1.00, $CHCl_3$); IR (film) 3346, 1674, and 1518 cm^{-1}; ^1H NMR: δ 1.47 (9H, s), 2.10 (1H, dd, *J*=4.9, 14 Hz), 2.47 (1H, dd, *J*=6.8, 14 Hz), 3.89 (1H, dd, *J*=4.4, 9.6 Hz), 4.20 (1H, dd, *J*=5.4, 9.6 Hz), 4.47 (1H, m), 4.75 (1H, m), 6.26 (1H, d, *J*=10 Hz), 6.90 (1H, dd, *J*=2.8, 10 Hz), and 7.25 (1H, d, *J*=2.8 Hz). Found: *m/z* 241.9801. Calcd for $C_9H_9{}^{79}BrNO_2$: M−Boc, 241.9817.

3.2.2. Compound 6a. $[\alpha]_D^{23}=+7.5$ (c 1.00, $CHCl_3$); IR (film) 3348, 1674, and 1517 cm^{-1}; ^1H NMR: δ 1.47 (9H, s), 2.13 (1H, dd, J=4.9, 14 Hz), 2.44 (1H, dd, J=7.3, 14 Hz), 3.87 (1H, dd, J=4.9, 9.8 Hz), 4.21 (1H, dd, J=5.9, 9.8 Hz), 4.44 (1H, m), 4.72 (1H, m), 6.26 (1H, d, J=10 Hz), 6.82 (1H, dd, J=2.9, 10 Hz), and 7.30 (1H, d, J=2.9 Hz). Found: m/z 343.0391. Calcd for $C_{14}H_{18}{}^{79}BrNO_4$: M, 343.0419.

3.3. Anodic oxidation of 4b

(a) *Neutral condition*: electrolysis of **4b** (20 mg, 0.053 mmol) [C.C.E.: +1.15→+1.39 V vs SCE] provided **5b** (1.0 mg, 5%), **6b** (1.0 mg, 5%), and recovered **4b** (8.0 mg, 40%).

(b) *Acidic condition*: electrolysis of **4b** (14 mg, 0.036 mmol) [C.C.E.: +1.10→+1.80 V vs SCE] provided **5b** (1.0 mg, 7%), **6b** (1.0 mg, 7%), and recovered **4b** (2.5 mg, 18%).

3.3.1. Compound 5b. IR (film) 3333, 1673, and 1530 cm^{-1}; ^1H NMR: δ 2.12 (1H, dd, J=4.8, 14 Hz), 2.47 (1H, dd, J=6.9, 14 Hz), 3.89 (1H, dd, J=4.6, 9.7 Hz), 4.18 (1H, dd, J=5.6, 9.7 Hz), 4.50 (1H, m), 4.93 (1H, m), 5.11 (2H, s), 6.24 (1H, d, J=9.9 Hz), 6.83 (1H, dd, J=3.0, 9.9 Hz), 7.23 (1H, d, J=3.0 Hz), and 7.34 (5H, broad s). Found: m/z 377.0273. Calcd for $C_{17}H_{16}{}^{79}BrNO_4$: M, 377.0262.

3.3.2. Compound 6b. IR (film) 3338, 1673, and 1528 cm^{-1}; ^1H NMR: δ 2.16 (1H, dd, J=4.4, 14 Hz), 2.45 (1H, dd, J=7.3, 14 Hz), 3.90 (1H, dd, J=4.4, 9.8 Hz), 4.21 (1H, dd, J=5.9, 9.8 Hz), 4.50 (1H, m), 4.98 (1H, m), 5.13 (2H, s), 6.26 (1H, d, J=9.8 Hz), 6.82 (1H, dd, J=2.6, 9.8 Hz), 7.32 (1H, d, J=2.6 Hz), and 7.37 (5H, s). Found: m/z 377.0247. Calcd for $C_{17}H_{16}{}^{79}BrNO_4$: M, 377.0262.

3.4. Anodic oxidation of 4c

Electrolysis of **4c** (18 mg, 0.038 mmol) [C.C.E.: +1.27→+1.64 V vs SCE] provided **5c** (2.0 mg, 11%), **6c** (2.0 mg, 11%), and recovered **4c** (8.0 mg, 44%).

3.4.1. Compound 5c. IR (film) 3332, 1715, 1672, and 1528 cm^{-1}; ^1H NMR: δ 2.11 (1H, m), 2.45 (1H, m), 3.89 (1H, m), 4.17 (1H, m), 4.40 (1H, d, J=5.9), 4.45–4.54 (3H, complex), 4.92 (1H, m), 6.25 (1H, d, J=9.8 Hz), 6.79 (1H, dd, J=2.4, 9.8 Hz), 7.24 (1H, d, J=2.4 Hz), 7.33 (2H, t, J=7.3 Hz), 7.42 (2H, t, J=7.3 Hz), 7.57 (2H, d, J=7.3 Hz), and 7.78 (2H, d, J=7.3 Hz). Found: m/z 465.0542. Calcd for $C_{24}H_{20}{}^{79}BrNO_4$: M, 465.0555.

3.4.2. Compound 6c. IR (film) 3328, 1700, 1675, and 1521 cm^{-1}; ^1H NMR: δ 2.10 (1H, m), 2.21 (1H, m), 3.89 (1H, m), 4.21 (1H, m), 4.50 (2H, complex), 4.85 (1H, m), 6.25 (1H, d, J=10 Hz), 6.81 (1H, dd, J=2.0, 10 Hz), 7.34 (3H, complex), 7.41 (2H, t, J=7.3 Hz), 7.57 (2H, d, J=7.3 Hz), and 7.78 (2H, d, J=7.3 Hz). Found: m/z 466.0672. Calcd for $C_{24}H_{21}{}^{79}BrNO_4$: M+H, 466.0653.

3.4.3. 3-[3-Bromo-4-(phenylmethoxy)phenyl]propanal (8). To a solution of **7** (2.3 g, 10 mmol) and K_2CO_3 (1.7 g, 12 mmol) in DMF (10 ml) was added benzyl bromide (1.2 ml, 10 mmol) at ambient temperature. After being stirred overnight, the reaction mixture was poured into aq. 5% $KHSO_4$ (30 ml), and extracted with EtOAc (2×50 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), and then evaporated. The residue was purified by silica-gel column chromatography (hexane/EtOAc=2:1) to give an alcohol (3.2 g, 100%) as a colorless oil: IR (film) 3347, 1604, and 1495 cm^{-1}; ^1H NMR: δ 1.87 (2H, tt, J=7.6, 6.3 Hz), 2.63 (2H, t, J=7.6 Hz), 3.66 (2H, t, J=6.3 Hz), 5.13 (2H, s), 6.85 (1H, d, J=8.3 Hz), 7.05 (1H, dd, J=8.3, 2.0 Hz), and 7.31–7.48 (6H, complex); ^{13}C NMR: δ 30.9, 34.1, 62.0, 70.9, 112.2, 113.8, 126.9, 127.7, 128.1, 128.4, 133.0, 135.7, 136.5, and 153.0. Found: m/z 322.0399. Calcd for $C_{16}H_{17}{}^{81}BrO_2$: M, 322.0392.

To a solution of $(COCl)_2$ (1.90 ml, 21.2 mmol) in CH_2Cl_2 (35 ml) was added a mixture of DMSO (1.90 ml, 26.5 mmol) and CH_2Cl_2 (7 ml) at −70°C under an argon atmosphere. After being stirred for 15 min, the alcohol (3.40 g, 10.6 mmol) in CH_2Cl_2 (23 ml) was added, and the reaction mixture was stirred for another 80 min. After the addition of Et_3N (7.0 ml, 53.0 mmol), the reaction mixture was warmed to 0°C. After being stirred for 30 min, the reaction mixture was poured into brine, and extracted with EtOAc (2×60 ml). The combined organic extracts were dried (Na_2SO_4), then evaporated. The residue was purified by silica-gel column chromatography (hexane/EtOAc=4:1) to give **8** (2.31 g, 68%) as a colorless oil: IR (film) 1722 and 1496 cm^{-1}; ^1H NMR: δ 2.74 (2H, t, J=7.3 Hz), 2.87 (2H, t, J=7.3 Hz), 5.13 (2H, s), 6.85 (1H, d, J=8.3 Hz), 7.05 (1H, dd, J=8.3, 2.0 Hz), 7.31–7.47 (6H, complex), and 9.80 (1H, s); ^{13}C NMR: δ 26.9, 45.3, 70.9, 112.4, 113.9, 126.9, 127.8, 128.1, 128.4, 133.0, 134.2, 136.4, 153.3, and 201.0. Found: m/z 318.0258. Calcd for $C_{16}H_{15}{}^{79}BrO_2$: M, 318.0255.

3.4.4. 2-Bromo-4-(3-hydroxy-4-methylpentyl)phenol (9). To a mixture of magnesium (110 mg, 4.5 mmol) and THF (10 ml) was added 2-bromopropane (0.45 ml, 4.8 mmol) at ambient temperature under an argon atmosphere. After being stirred for 30 min, **8** (520 mg, 1.6 mmol) in THF (10 ml) was added; the reaction mixture was stirred overnight. After the addition of MeOH (1 ml) and aq. 5% $KHSO_4$ (2 ml), the mixture was poured into brine, and extracted with EtOAc (2×20 ml). The combined organic extracts were dried (Na_2SO_4), then evaporated. The residue was purified by silica-gel column chromatography (hexane/EtOAc=4:1) to give an alcohol (490 mg, 85%) as a colorless oil: IR (film) 3398, 1496, and 1454 cm^{-1}; ^1H NMR: δ 0.91 (6H, d, J=6.8 Hz), 1.60–1.75 (3H, complex), 2.56 (1H, m), 2.76 (1H, m), 3.36 (1H, m), 5.13 (2H, s), 6.85 (1H, d, J=8.3 Hz), 7.06 (1H, dd, J=8.3, 1.5 Hz), and 7.29–7.48 (6H, complex); ^{13}C NMR: δ 17.4, 18.9, 31.5, 34.0, 36.1, 71.3, 76.3, 112.8, 114.4, 127.5, 128.4, 128.8, 129.1, 133.8, 137.0, 137.3, and 153.7. Found: m/z 362.0871. Calcd for $C_{19}H_{23}{}^{79}BrO_2$: M, 362.0881.

To a solution of the alcohol (120 mg, 0.33 mmol) and $NaHCO_3$ (28 mg, 0.33 mmol) in $CHCl_3$ (4 ml) was added TMSI (0.09 ml, 0.66 mmol) at ambient temperature under an argon atmosphere; the mixture was stirred overnight. After the addition of MeOH (2 ml), the reaction mixture was stirred another 5 min. The reaction mixture was poured into aq. $Na_2S_2O_3$ (10 ml), and extracted with EtOAc

(2×20 ml). The combined organic extracts were dried (Na_2SO_4) and then evaporated. The residue was purified by PTLC (hexane/EtOAc=3:1) to give **9** (69 mg, 77%) as a colorless oil: IR (film) 3349 and 1496 cm^{-1}; ^1H NMR: δ 0.91 (6H, d, J=6.8 Hz), 1.06–1.76 (3H, complex), 2.56 (1H, m), 276 (1H, m), 3.36 (1H, m), 5.42 (1H, s), 6.93 (1H, d, J=8.3 Hz), 7.05 (1H, dd, J=8.3, 2.0 Hz), and 7.30 (1H, d, J=2.0 Hz); ^{13}C NMR: δ 17.4, 18.9, 31.5, 34.0, 36.2, 76.3, 110.5, 116.4, 129.7, 132.1, 136.6, and 150.9. Found: m/z 272.0414. Calcd for $C_{12}H_{17}{}^{79}BrO_2$: M, 272.0412.

3.5. Anodic oxidation of 9

(a) *Neutral condition at −78°C*: electrolysis of **9** (16 mg, 0.058 mmol) provided **14a** (0.8 mg, 5%), **15a** (2.4 mg, 14%), and recovered **9** (12 mg, 76%).

(b) *Neutral condition at −50°C*: electrolysis of **9** (15 mg, 0.055 mmol) provided **13a** (0.4 mg, 3%), **14a** (0.6 mg, 4%), **15a** (2.4 mg, 16%), and recovered **9** (11 mg, 71%).

(c) *Neutral condition at 23°C*: electrolysis of **9** (15 mg, 0.055 mmol) provided **13a** (2.3 mg, 15%), **14a** (3.2 mg, 21%), and recovered **9** (0.8 mg, 5%).

(d) *Neutral condition at 50°C*: electrolysis of **9** (16 mg, 0.060 mmol) provided **13a** (2.7 mg, 17%), **14a** (2.9 mg, 18%), and **15a** (2.0 mg, 11%).

(e) *Acidic condition at 23°C*: electrolysis of **9** (17 mg, 0.061 mmol) provided **13a** (4.1 mg, 25%), **14a** (4.2 mg, 25%), and **15a** (2.3 mg, 13%).

3.5.1. Compound 13a. IR (film) 1673 cm^{-1}; ^1H NMR: δ 0.92 (3H, d, J=6.8 Hz), 0.99 (3H, d, J=6.8 Hz), 1.73–1.89 (2H, complex), 2.07–2.20 (3H, complex), 3.94 (1H, m), 6.23 (1H, d, J=10 Hz), 6.80 (1H, dd, J=10, 2.9 Hz), and 7.30 (1H, d, J=2.9 Hz); ^{13}C NMR: δ 18.6, 19.2, 29.7, 33.3, 36.9, 79.9, 86.7, 123.0, 125.4, 150.39, 150.41, and 178.2. Found: m/z 270.0257. Calcd for $C_{12}H_{15}{}^{79}BrO_2$: M, 270.0255.

3.5.2. Compound 14a. IR (film) 1673 cm^{-1}; ^1H NMR: δ 0.94 (3H, d, J=6.8 Hz), 1.00 (3H, d, J=6.8 Hz), 1.74–1.90 (2H, complex), 2.10–2.20 (3H, complex), 3.92 (1H, m), 6.25 (1H, d, J=10 Hz), 6.86 (1H, dd, J=10, 2.9 Hz), and 7.21 (1H, d, J=2.9 Hz); ^{13}C NMR: δ 18.6, 19.3, 29.8, 33.4, 37.0, 79.9, 87.0, 122.9, 125.4, 150.4, 150.6, and 178.2. Found: m/z 270.0228. Calcd for $C_{12}H_{15}{}^{79}BrO_2$: M, 270.0255.

3.5.3. Compound 15a isomer-1. IR (film) 3418 and 1672 cm^{-1}; ^1H NMR: δ 0.89 (6H, complex), 1.30–1.80 (4H, complex), 2.03 (1H, ddd, J=5.4, 12, 14 Hz), 3.26 (3H, s), 3.32 (1H, m), 6.48 (1H, d, J=10 Hz), 6.81 (1H, dd, J=2.9, 10 Hz), and 7.23 (1H, d, J=2.9 Hz); ^{13}C NMR: δ 17.3, 18.9, 28.1, 29.7, 33.7, 36.2, 53.5, 125.3, 129.6, 131.9, 151.0, and 151.5. Found: m/z 301.0446. Calcd for $C_{13}H_{18}{}^{79}BrO_3$: M−H, 301.0439.

3.5.4. Compound 15a isomer-2. IR (film) 3434 and 1673 cm^{-1}; ^1H NMR: δ 0.90 (6H, d, J=6.8 Hz), 1.37 (1H, m), 1.50 (1H, m), 1.62 (1H, m), 1.79 (1H, ddd, J=4.9, 11, 13 Hz), 2.02 (1H, ddd, J=5.1, 12, 13 Hz), 3.26 (3H, s), 3.32 (1H, m), 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); ^{13}C NMR: δ 17.2, 18.8, 28.1, 29.7, 33.7, 36.2, 53.5, 125.7, 129.6, 132.8, 151.1, and 151.4. Found: m/z 303.0641. Calcd for $C_{13}H_{20}{}^{79}BrO_3$: M+H, 303.0595.

3.5.5. 2-Bromo-4-(3-hydroxy-5-methylhexyl)phenol (10). To a mixture of magnesium (53 mg, 2.2 mmol) and THF (5 ml) was added 2-methyl-1-bromopropane (0.29 ml, 2.7 mmol) at ambient temperature under an argon atmosphere. After being stirred for 30 min, **8** (290 mg, 0.91 mmol) in THF (5 ml) was added, and the reaction mixture was stirred overnight. Essentially the same procedure as in the case of **9** gave an alcohol (260 mg, 79%) as a colorless oil: IR (film) 3398, 1496, and 1454 cm^{-1}; ^1H NMR: δ 0.90 (3H, d, J=6.4 Hz), 0.92 (3H, d, J=6.4 Hz), 1.25 (1H, m), 1.40 (1H, m), 1.62–1.79 (3H, complex), 2.59 (1H, m), 2.71 (1H, m), 3.68 (1H, m), 5.13 (2H, s), 6.85 (1H, d, J=8.3 Hz), 7.06 (1H, dd, J=8.3, 1.5 Hz), and 7.30–7.48 (6H, complex); ^{13}C NMR: δ 22.1, 23.5, 24.7, 30.8, 39.6, 46.8, 69.2, 70.8, 112.2, 113.8, 126.8, 127.7, 128.0, 128.4, 133.0, 136.1, 136.5, and 152.9. Found: m/z 377.1116. Calcd for $C_{20}H_{26}{}^{79}BrO_2$: M+H, 377.1115.

To a solution of the alcohol (350 mg, 0.93 mmol) and $NaHCO_3$ (170 mg, 2.0 mmol) in $CHCl_3$ (10 ml) was added TMSI (0.46 ml, 3.3 mmol) at ambient temperature under an argon atmosphere. The same workup as in the case of **9** gave **10** (250 mg, 92%) as a colorless oil: IR (film) 3334 and 1496 cm^{-1}; ^1H NMR: δ 0.90 (3H, d, J=6.3 Hz), 0.92 (3H, d, J=6.3 Hz), 1.27 (1H, ddd, J=3.9, 8.8, 13 Hz), 1.43 (1H, ddd, J=5.4, 13, 13 Hz), 1.65–1.80 (3H, complex), 2.59 (1H, ddd, J=6.8, 9.8, 14 Hz), 2.72 (1H, ddd, J=5.9, 9.8, 14 Hz), 3.70 (1H, m), 5.49 (1H, s), 6.93 (1H, d, J=8.3 Hz), 7.05 (1H, dd, J=8.3, 2.0 Hz), and 7.30 (1H, d, J=2.0 Hz); ^{13}C NMR: δ 22.2, 23.5, 24.7, 30.9, 39.7, 46.9, 69.26, 109.9, 115.8, 129.0, 131.4, 135.7, and 150.1. Found: m/z 288.0528. Calcd for $C_{13}H_{19}{}^{81}BrO_2$: M, 288.0548.

3.6. Anodic oxidation of 10

(a) *Neutral condition at −78°C*: electrolysis of **10** (18 mg, 0.062 mmol) provided **13b** (1.3 mg, 7%), **14b** (1.3 mg, 7%), **15b** (5.6 mg, 29%), and recovered **23b** (5.6 mg, 31%).

(b) *Neutral condition at 23°C*: electrolysis of **10** (25 mg, 0.087 mmol) provided **13b** (3.9 mg, 16%), **14b** (5.6 mg, 23%), and **15b** (5.5 mg, 20%).

(c) *Acidic condition at 23°C*: electrolysis of **10** (15 mg, 0.050 mmol) provided **13b** (3.0 mg, 21%), and **14b** (3.9 mg, 27%).

(d) *Acidic condition at 23°C in dioxane*: electrolysis of **10** (15 mg, 0.050 mmol) provided **13b** (2.5 mg, 17%), **14b** (1.7 mg, 11%), and recovered **10** (8.4 mg, 56%).

3.6.1. Compound 13b. IR (film) 1673 cm^{-1}; ^1H NMR: δ 0.93 (3H, d, J=5.4 Hz), 0.94 (3H, d, J=5.4 Hz), 1.38 (1H, ddd, J=5.4, 7.8, 13 Hz), 1.61 (1H, m), 1.73–1.80 (2H, complex), 2.13–2.18 (2H, complex), 2.26 (1H, m), 4.27 (1H, m), 6.23 (1H, d, J=10 Hz), 6.80 (1H, dd, J=10,

2.9 Hz), and 7.30 (1H, d, J=2.9 Hz); ^{13}C NMR: δ 22.7, 23.3, 25.7, 32.9, 36.9, 45.5, 80.2, 80.3, 123.5, 125.9, 151.2, 151.5, and 179.1. Found: m/z 284.0397. Calcd for $C_{13}H_{17}{}^{79}BrO_2$: M, 284.0412.

3.6.2. Compound 14b. IR (film) 1673 cm^{-1}; ^{1}H NMR: δ 0.94 (3H, d, J=6.4 Hz), 0.95 (3H, d, J=6.4 Hz), 1.40 (1H, ddd, J=5.9, 7.8, 14 Hz), 1.62 (1H, m), 1.72–1.81 (2H, complex), 2.13–2.29 (3H, complex), 4.27 (1H, m), 6.24 (1H, d, J=9.8 Hz), 6.85 (1H, dd, J=9.8, 2.9 Hz), and 7.21 (1H, d, J=2.9 Hz); ^{13}C NMR: δ 22.7, 23.3, 25.8, 33.0, 37.0, 45.6, 80.2, 80.4, 123.4, 126.0, 151.2, 151.6, and 179.1. Found: m/z 284.0405. Calcd for $C_{13}H_{17}{}^{79}BrO_2$: M, 284.0412.

3.6.3. Compound 15b isomer-1. IR (film) 3421 and 1673 cm^{-1}; ^{1}H NMR: δ 0.91 (6H, t, J=6.8 Hz), 1.16–1.55 (4H, complex), 1.71–1.85 (2H, complex), 2.00 (1H, ddd, J=5.4, 11, 13 Hz), 3.26 (3H, s), 3.65 (1H, m), 6.48 (1H, d, J=10 Hz), 6.80 (1H, dd, J=10, 2.9 Hz), and 7.22 (1H, d, J=2.9 Hz). Found: m/z 316.0682. Calcd for $C_{14}H_{21}{}^{79}BrO_3$: M, 316.0673.

3.6.4. Compound 15b isomer-2. IR (film) 3399 and 1672 cm^{-1}; ^{1}H NMR: δ 0.90 (3H, d, J=6.8 Hz), 0.92 (3H, d, J=6.8 Hz), 1.17–1.54 (4H, complex), 1.71–1.83 (2H, complex), 1.97 (1H, ddd, J=5.4, 11, 13 Hz), 3.26 (3H, s), 3.65 (1H, m), 6.50 (1H, d, J=10 Hz), 6.81 (1H, dd, J=10, 2.9 Hz), and 7.23 (1H, d, J=2.9 Hz). Found: m/z 317.0790. Calcd for $C_{14}H_{22}{}^{79}BrO_3$: M+H, 317.0751.

3.6.5. 2-Bromo-4-(3-hydroxy-3-methylbutyl)phenol (11). To a solution of methyl 3-(3-bromo-4-hydroxy-phenyl)-propionate (90 mg, 0.35 mmol) in THF (1.0 ml) was added methyl magnesium bromide (0.93 M solution in THF, 1.9 ml, 1.8 mmol) at 0°C under an argon atmosphere. After being stirred for 3.5 h, MeOH (1 ml) and aq. 5% $KHSO_4$ (2 ml) was added to the reaction mixture, then the reaction mixture was poured into brine, and extracted with EtOAc (2×20 ml). The combined organic layer was dried (Na_2SO_4), then evaporated. The residue was purified by PTLC (hexane/EtOAc=1:1) to give **11** (91 mg, 100%) as a colorless oil: IR (film) 3344 and 1496 cm^{-1}; ^{1}H NMR: δ 1.28 (6H, s), 1.74 (2H, m), 2.63 (2H, m), 6.92 (1H, d, J=8.3 Hz), 7.04 (1H, dd, J=8.3, 2.0 Hz), and 7.30 (1H, d, J=2.0 Hz); ^{13}C NMR: δ 29.5, 29.7, 45.9, 71.3, 110.4, 116.4, 129.5, 132.1, 136.7, and 150.9. Found: m/z 258.0234. Calcd for $C_{11}H_{15}{}^{79}BrO_2$: M, 258.0255.

3.7. Anodic oxidation of 11

(a) *Neutral condition in H_2O–dioxane*: electrolysis of **11** (10 mg, 0.039 mmol) provided **12** (1.6 mg, 16%).

(b) *Neutral condition in dioxane*: electrolysis of **11** (16 mg, 0.060 mmol) provided **12** (7.5 mg, 49%).

3.7.1. Compound 12. IR (film) 3360, 1672, 1459, and 1120 cm^{-1}; ^{1}H NMR: δ 1.37 (3H, s), 1.39 (3H, s), 2.04 (2H, t, J=6.8 Hz), 2.25 (2H, t, J=6.8 Hz), 6.23 (1H, d, J=10 Hz), 6.82 (1H, dd, J=2.4, 10 Hz), and 7.23 (1H, d, J=2.4 Hz); ^{13}C NMR: δ 29.22, 29.26, 36.8, 38.2, 80.4, 84.6, 122.7, 125.2, 151.06, 151.08, 178.0. Found: m/z 258.0083. Calcd for $C_{11}H_{13}{}^{81}BrO_2$: M, 258.0079.

3.8. General procedure for the dienone–phenol rearrangement of spirodienone compounds

To an ice-cooled (0°C) solution of spiro compound (0.02 mmol) in CH_2Cl_2 (2.0 ml) was added dropwise $BF_3{\cdot}OEt_2$ (0.04 ml, 0.32 mmol). The mixture was stirred at 0°C for 3 h, then the resulting mixture was evaporated to give a residue, which was chromatographically purified.

3.9. Rearrangement of 2

Reaction of **2** (4.9 mg, 0.021 mmol) provided **16** (2.0 mg, 40%) and **17** (2.9 mg, 60%) as colorless crystals, respectively.

3.9.1. Compound 16. Mp 124–124.5°C (sealed tube, from hexane–EtOAc); IR (nujol) 3276, 3179, and 1579 cm^{-1}; ^{1}H NMR: δ 2.02 (2H, dt, J=5.1, 6.8 Hz), 2.72 (2H, t, J=6.8 Hz), 4.07 (2H, t, J=5.1 Hz), 5.15 (1H, s), 6.72 (1H, d, J=8.9 Hz), and 6.80 (1H, d, J=8.9 Hz); ^{13}C NMR: δ 23.1, 27.1, 66.5, 113.2, 114.5, 117.5, 122.7, 146.6, and 150.0. Found: m/z 227.9779. Calcd for $C_9H_9{}^{79}BrO_2$: M, 227.9786.

3.9.2. Compound 17. Mp 110.5–111°C (sealed tube, from hexane–EtOAc); IR (nujol) 3432, 3183, 1507, and 1178 cm^{-1}; ^{1}H NMR: δ 1.95 (2H, dt, J=5.1, 6.4 Hz), 2.70 (2H, t, J=6.4 Hz), 4.10 (2H, t, J=5.1 Hz), 5.00 (1H, s), 6.69 (1H, s), and 6.90 (1H, s); ^{13}C NMR δ 22.9, 25.5, 67.1, 108.2, 116.5, 119.9, 123.9, 146.2, and 149.6. Found: m/z 227.9787. Calcd for $C_9H_9{}^{79}BrO_2$: M, 227.9786.

3.9.3. Debromination of 16. A solution of **16** (4.4 mg, 0.02 mmol) in MeOH (2.0 ml) in the presence of catalytic amounts of 10% Pd–C was stirred at room temperature for 3 h under a hydrogen atmosphere. The mixture was filtered, and the filtrate was evaporated to give a residue. Purification by preparative TLC (hexane/EtOAc=3:1) afforded **18** (0.6 mg, 21%) as an oil: IR (film) 3388 and 1496 cm^{-1}; ^{1}H NMR: δ 1.98 (2H, dt, J=5.4, 6.3 Hz), 2.74 (2H, t, J=6.3 Hz), 4.13 (2H, t, J=5.4 Hz), 4.34 (1H, s), 6.53 (1H, d, J=2.9 Hz), 6.58 (1H, dd, J=2.9, 8.8 Hz), and 6.67 (1H, d, J=8.8 Hz). Found: m/z 150.0683. Calcd for $C_5H_{10}O_2$: M, 150.0680.

3.9.4. Methylation of 17. To a mixture of **17** (12 mg, 0.05 mmol) and K_2CO_3 (7 mg, 0.05 mmol) in DMF (0.5 ml) at 0°C was added MeI (0.02 ml, 0.3 mmol); the mixture was stirred at room temperature overnight, then the resulting mixture was evaporated. The crude product was purified by preparative TLC (hexane/EtOAc=4:1) to give **19** (13 mg, quantitative) as an oil: IR (film) 1488, 1399, 1277, 1193, and 1048 cm^{-1}; ^{1}H NMR: δ 2.00 (2H, dt, J=5.1, 5.9 Hz), 2.74 (2H, t, J=5.9 Hz), 3.82 (3H, s), 4.12 (2H, t, J=5.1 Hz), 6.58 (1H, s), and 7.01 (1H, s); ^{13}C NMR: δ 22.3, 25.1, 56.9, 66.4, 109.3, 113.0, 121.1, 121.7, 149.1, and 149.5. Found: m/z 243.0013. Calcd for $C_{10}H_{12}{}^{79}BrO_2$: M, 243.0020.

3.10. Rearrangement of 5b

Reaction of **5b** (10 mg, 0.027 mmol) provided **21b** (2.3 mg, 22%) and **22b** (0.8 mg, 8%).

3.10.1. Compound 21b. IR (film) 3326, 1715, and 1472 cm^{-1}; ^1H NMR: δ 2.85 (1H, dd, J=1.5, 18 Hz), 3.02 (1H, dd, J=5.4, 18 Hz), 3.95–4.10 (4H, complex), 4.29 (1H, m), 5.05 (1H, s), 5.12 (2H, s), 6.75 (1H, d, J=9.8 Hz), 6.78 (1H, d, J=9.8 Hz), and 7.34 (5H, broad). Found: m/z 377.0257. Calcd for $C_{17}H_{16}{}^{79}BrNO_4$: M, 377.0262.

3.10.2. Compound 22b. IR (film) 3325, 1714, and 1493 cm^{-1}; ^1H NMR: δ 2.70 (1H, d, J=17 Hz), 3.05 (1H, dd, J=4.9, 17 Hz), 3.98–4.13 (4H, complex), 4.23 (1H, m), 5.05–5.11 (3H, complex), 6.56 (1H, s), 7.05 (1H, s), and 7.34 (5H, broad s). Found: m/z 379.0241. Calcd for $C_{17}H_{16}{}^{81}BrNO_4$: M, 379.0243.

3.11. Rearrangement of 6b

Reaction of **6b** (11 mg, 0.028 mmol) provided **22b** (3.9 mg, 37%).

3.12. Rearrangement of 5c

Reaction of **5c** (3.7 mg, 7.9 mmol) provided **21c** (2.6 mg, 70%) and **22c** (1.0 mg, 27%).

3.12.1. Compound 21c. IR (film) 3330, 1695, and 1478 cm^{-1}; ^1H NMR: δ 2.80 (1H, d, J=17 Hz), 3.01 (1H, dd, J=5.9, 17 Hz), 4.00 (1H, d, J=11 Hz), 4.12 (1H, m), 4.20 (1H, t, J=6.4 Hz), 4.26 (1H, m), 4.43 (2H, m), 5.12 (1H, d, J=6.8 Hz), 5.25 (1H, s), 6.81 (1H, d, J=8.8 Hz), 6.88 (1H, d, J=8.8 Hz), 7.30 (2H, t, J=7.3 Hz), 7.40 (2H, t, J=7.3 Hz), 7.57 (2H, d, J=7.3 Hz), and 7.76 (2H, d, J=7.3 Hz). Found: m/z 465.0545. Calcd for $C_{24}H_{20}{}^{79}BrNO_4$: M, 465.0575.

3.12.2. Compound 22c. IR (film) 3330, 1697, and 1507 cm^{-1}; ^1H NMR: δ 2.71 (1H, dd, J=2.4, 17 Hz), 3.04 (1H, dd, J=5.4, 17 Hz), 4.04 (1H, d, J=12 Hz), 4.15–4.23 (2H, complex), 4.40 (2H, d, J=6.8 Hz), 5.06 (1H, d, J=8.3 Hz), 5.13 (1H, s), 6.73 (1H, s), 7.00 (1H, s), 7.30 (2H, t, J=7.3 Hz), 7.39 (2H, t, J=7.3 Hz), 7.54 (2H, d, J=7.3 Hz), and 7.74 (2H, d, J=7.3 Hz). Found: m/z 465.0621. Calcd for $C_{24}H_{20}{}^{79}BrNO_4$: M, 465.0575.

3.13. Rearrangement of 6c

Reaction of **6c** (2.5 mg, 5.4 mmol) provided **22c** (1.9 mg, 76%).

3.14. Rearrangement of 13a

Reaction of **13a** (3.7 mg, 14 mmol) provided **23a** (2.0 mg, 54%) and **24a** (1.0 mg, 27%).

3.14.1. Compound 23a. IR (film) 3513 and 1474 cm^{-1}; ^1H NMR: δ 1.00 (3H, d, J=6.8 Hz), 1.04 (3H, d, J=6.8 Hz), 1.71 (1H, m), 1.90 (1H, m), 2.03 (1H, m), 2.66 (1H, ddd, J=6.1, 11, 17 Hz), 2.81 (1H, ddd, J=2.9, 5.9, 17 Hz), 3.58 (1H, ddd, J=2.0, 6.4, 10 Hz), 5.15 (1H, s), 6.72 (1H, d, J=8.8 Hz), and 6.81 (1H, d, J=8.8 Hz). Found: m/z 270.0231. Calcd for $C_{12}H_{15}{}^{79}BrO_2$: M, 270.0255.

3.14.2. Compound 24a. IR (film) 3520 and 1486 cm^{-1}; ^1H NMR: δ 0.98 (3H, d, J=6.8 Hz), 1.02 (3H, d, J=6.8 Hz), 1.68 (1H, m), 1.84–1.97 (2H, complex), 2.64–2.79 (2H, complex), 3.62–3.66 (2H, complex), 5.00 (1H, s), 6.71 (1H, s), and 6.93 (1H, s); ^{13}C NMR: δ 18.21, 18.24, 23.9, 25.0, 32.2, 80.8, 107.4, 115.4, 119.1, 123.2, 145.2, and 149.4. Found: m/z 272.0216. Calcd for $C_{12}H_{15}{}^{81}BrO_2$: M, 272.0235.

3.15. Rearrangement of 14a

Reaction of **14a** (2.7 mg, 10 mmol) provided **24a** (2.0 mg, 74%).

3.16. Rearrangement of 13b

Reaction of **13b** (5.3 mg, 19 mmol) provided **23b** (2.7 mg, 51%) and **24b** (1.6 mg, 30%).

3.16.1. Compound 23b. IR (film) 3334 and 1473 cm^{-1}; ^1H NMR: δ 0.95 (3H, d, J=6.8 Hz), 0.95 (3H, d, J=6.8 Hz), 1.34 (1H, ddd, J=4.9, 8.3, 13 Hz), 1.63–1.75 (2H, complex), 1.92 (1H, m), 2.02 (1H, m), 2.68 (1H, ddd, J=6.3, 10, 17 Hz), 2.79 (1H, ddd, J=3.4, 6.3, 17 Hz), 3.92 (1H, m), 5.16 (1H, s), 6.71 (1H, d, J=8.8 Hz), and 6.81 (1H, d, J=8.8 Hz). Found: m/z 284.0408. Calcd for $C_{13}H_{17}{}^{79}BrO_2$: M, 284.0412.

3.16.2. Compound 24b. IR (film) 3440 and 1486 cm^{-1}; ^1H NMR: δ 0.95 (3H, d, J=6.8 Hz), 0.95 (3H, d, J=6.8 Hz), 1.33 (1H, ddd, J=4.4, 8.3, 14 Hz), 1.62–1.70 (2H, complex), 1.85–1.96 (2H, complex), 2.66 (1H, ddd, J=3.9, 5.9, 17 Hz), 2.77 (1H, ddd, J=6.4, 11, 17 Hz), 3.98 (1H, m), 5.01 (1H, s), 6.70 (1H, s), and 6.92 (1H, s). Found: m/z 284.0393. Calcd for $C_{13}H_{17}{}^{79}BrO_2$: M, 284.0412.

3.17. Rearrangement of 14b

Reaction of **14b** (3.5 mg, 12 mmol) provided **24b** (2.6 mg, 74%).

3.18. Rearrangement of 12

Reaction of **12** (6.4 mg, 25 mmol) provided **25** (0.1 mg, 1%) and **26** (4.9 mg, 77%).

3.18.1. Compound 25. IR (film) 3445 cm^{-1}; ^1H NMR: δ 1.30 (6H, s), 1.80 (2H, t, J=6.9 Hz), 2.71 (2H, t, J=6.9 Hz), 5.15 (1H, s), 6.69 (1H, d, J=8.9 Hz), and 6.83 (1H, d, J=8.9 Hz). Found: m/z 256.0137. Calcd for $C_{11}H_{13}{}^{79}BrO_2$: M, 256.0099.

3.18.2. Compound 26. IR (film) 3427 cm^{-1}; ^1H NMR: δ 1.30 (6H, s), 1.77 (2H, t, J=6.9 Hz), 2.70 (2H, t, J=6.9 Hz), 5.00 (1H, s), 6.72 (1H, s), and 6.90 (1H, s); ^{13}C NMR: δ 22.5, 26.7, 32.6, 74.2, 107.7, 115.4, 119.7, 122.0, 145.1, and 148.0. Found: m/z 256.0137. Calcd for $C_{11}H_{13}{}^{79}BrO_2$: M, 256.0090.

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5. Although tyrosinol hydrochloride is commercially available, samples used in this investigation were prepared by diborane reduction of Boc-L-tyrosine.
6. As can be seen in Table 1, the relatively high electric potential under reaction conditions might give rise to overoxidation of the products or side reactions accompanied by oxidation of the solvent, which might cause low yields of the reaction products (entries 2 and 3).
7. Compounds **15a** and **15b** were obtained as diastereomeric mixtures which could be chromatographically separated.
8. Boc groups of **5a** and **6a** were too labile under the Lewis acid conditions to produce the rearranged products. It may be considered that removal of the protective groups was followed by production of a complicated mixture.