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Synthesis of Methyl 2,3-Dihydro-2-benzofurancarboxylates from *o*-Allylphenols *via* 2-(Phenylthiomethyl)-2,3-dihydrobenzofurans

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A method for synthesizing methyl 2,3-dihydro-2-benzofurancarboxylates from *o*-allylphenols is described. The reaction of 6-allyl-2,3-dichlorophenol (3) with benzenesulfenyl chloride (PhSCl) in acetonitrile gave a mixture of PhSCl-adducts, which was heated in aqueous acetonitrile then with sodium bicarbonate to obtain 6,7-dichloro-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (6). α-Dichlorination of the phenylthiomethyl group of 6 and subsequent methanolysis gave the methyl ester 5 in high yield. The generality of this synthetic method was examined by the conversion of *o*-allylphenols 11 having various substituents on the benzene ring into the corresponding methyl esters 23. Cyclizations of 11 to the sulfides 12 could be achieved similarly to the case of 3. However, in the subsequent conversions of 12 to 23, selective α-dichlorination followed by methanolysis could be achieved only with 12 substituted with an electron-withdrawing group such as a chloro or nitro group.

Keywords *o*-allylphenol; methyl 2,3-dihydro-2-benzofurancarboxylate; 2-(phenylthiomethyl)-2,3-dihydrobenzofuran; benzenesulfenyl chloride; α-dichlorination; methanolysis

Recently, novel diuretics such as indacrinone[1] or tienilic acid,[2] which possess an aryloxyacetic acid structure, have attracted much interest in view of their uricosuric activities. Similar biological activities were reported for 2,3-dihydro-2-benzofurancarboxylic acid derivatives bearing an acyl functional group.[3] We examined carboxylic acids having a sulfamoyl group at the 5-position, and selected S-8666 (**1**) from among these derivatives as a candidate for a new uricosuric diuretic.[4] We sought a general method for synthesizing 2,3-dihydro-2-benzofurancarboxylic acids which would be suitable for industrial-scale preparation.

Methods for synthesizing 2,3-dihydro-2-benzofurancarboxylic acids have not been studied in detail. Harrison and Aelony[5] have reported the synthesis of the parent carboxylic acid from *o*-allylphenol *via* 2-(hydroxymethyl)-2,3-dihydrobenzofuran, and Hoffman *et al.*[3] applied this method to the synthesis of the 6,7-dichloro derivative **2**. Although this method is regarded as a good one by which the carboxylic acid **2** can be prepared from 6-allyl-2,3-dichlorophenol **3** in a short process, there are some problems in applying it to large-scale preparation of **2**. Peracetic acid is required for the oxidative cyclization of **3** to **4**, and chromium(VI) oxide, which would create a disposal problem if used on a large scale, is required for the oxidation of **4** to **2**.

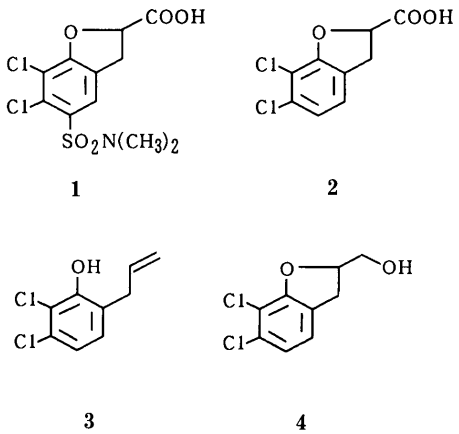


Chart 1

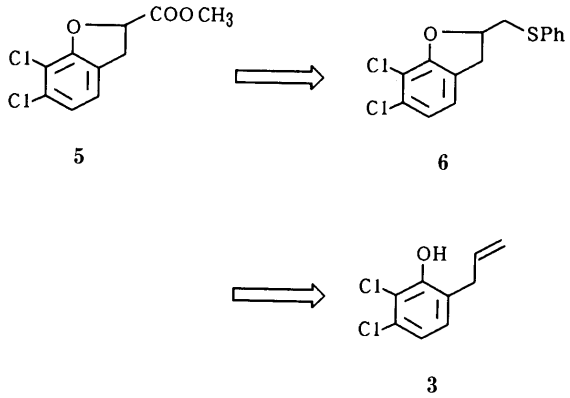


Chart 2

Mühlstädt *et al.*[6] reported that the reactions of *o*-allylphenols with benzenesulfenyl chloride (PhSCl) gave exclusively 2-(phenylthiomethyl)-2,3-dihydrobenzofuran derivatives. Fortes *et al.*[7] reported that the phenylthiomethyl group could be converted into a methoxycarbonyl group *via* α-dichlorination of the sulfide followed by methanolysis. Since the combination of these two procedures seemed to be suitable as a general procedure for obtaining 2,3-dihydro-2-benzofurancarboxylic acids having various substituents on the aromatic nucleus, we investigated its potential with respect to the 6,7-dichloro derivative **5**; the retrosynthetic pathway is shown in Chart 2. We also examined the applicability of this synthetic method by using *o*-allylphenols having various substituents on the benzene ring.

Results and Discussion

6-Allyl-2,3-dichlorophenol **3** was prepared from 2,3-dichlorophenol according to the method of Hoffman *et al.*[3] PhSCl was prepared by passage of chlorine gas through a solution of diphenyl disulfide in carbon tetrachloride (CCl_4).

In the procedure of Mühlstädt *et al.*,[6] the reactions of *o*-allylphenols with PhSCl are carried out in methylene chloride (CH_2Cl_2) at −40 °C. We tried to carry out this cyclization at ice-cooled temperature from a practical point of view. The reaction of **3** with an equimolar amount of

PhSCl in CH_2Cl_2 at 0 °C gave an inseparable mixture of PhSCl-adducts of **3** (the Markownikoff adduct **7** and anti-Markownikoff adduct **8**) and not the cyclized product **6**. The isomer ratio in this mixture was determined to be 2 : 1 by means of proton nuclear magnetic resonance (^{1}H-NMR) integration of the peaks due to phenolic hydroxy protons; δ 5.84 for the major isomer and δ 5.76 for the minor one. In order to assign these isomers, this mixture was treated with potassium carbonate (K_2CO_3) in acetonitrile (CH_3CN) to produce a chroman derivative **9** and the dihydrobenzofuran derivative **6** in 54% and 28% yields, respectively. Thus, the major PhSCl-adduct was assigned as **8** and the minor one as **7**. PhSCl addition to a terminal olefin is known to occur predominantly in an anti-Markownikoff sense rather than in a Markownikoff sense, and the anti-Markownikoff adduct can be isomerized to the Markownikoff adduct.[8] We found that heating the mixture of **7** and **8** in aqueous CH_3CN at 80 °C effectively caused isomerization of **8** to **7**, during which some cyclization to **6** also occurred. Although the cyclization to **6** was not completed under this condition, further heating with sodium bicarbonate ($NaHCO_3$) forced it to completion.

From an operational point of view, using CH_3CN as a solvent for PhSCl addition seemed to offer an advantage over CH_2Cl_2. PhSCl addition to **3** in CH_3CN proceeded similarly to that in CH_2Cl_2 and gave a 3 : 2 mixture of **8** and **7**. Therefore, without having to evaporate the solvent, the resulting mixture in CH_3CN had only to be heated at 80 °C after addition of water and then to be heated with $NaHCO_3$. In this one-pot procedure, the dihydrobenzofuran **6** was obtained from the *o*-allylphenol **3** in 74% yield.

Next, conversion of **6** into the ester **5** was attempted. In the procedure of Fortes *et al.*,[7] alkyl phenyl sulfide is chlorinated with 2 eq of sulfuryl chloride (SO_2Cl_2) in the presence of 2 eq of pyridine at −5 °C in CCl_4 then the crude dichlorosulfide is treated with methanol–water (1% (v/v)) and sodium carbonate at −5 °C for 30 min to obtain the corresponding methyl ester. Conditions suitable for the conversion of **6** to **5** were investigated. The di-chlorination of **6** was carried out using either 2.3 eq of SO_2Cl_2 in the absence of pyridine in CH_2Cl_2 or 2.3 eq of *N*-chlorosuccinimide (NCS) in chloroform to produce an α-dichlorosulfide **10**. However, the chlorination by SO_2Cl_2 proved to be superior to that by NCS in terms of the control of the reaction temperature and the post-treatment; chlorination of **6** by NCS is an exothermic reaction and removal of the deposited succinimide is troublesome. Subsequent methanolysis of the dichlorosulfide **10** was carried out by stirring in methanol containing an equimolar amount of water in the absence of a base such as sodium carbonate at room temperature for 1 d to obtain the methyl ester **5**, which could be easily separated from the reaction mixture and purified by crystallization, in 84% yield.

The synthesis of **5** from **3** was accomplished by using PhSCl and SO_2Cl_2 in the place of peracetic acid and chromium(VI) oxide, respectively, as oxidizing agents, and this procedure proved to be suitable for large-scale preparation of **5** from the viewpoints of the safety of the reagents used and isolation of the products. Thus, the potential of the method combining the approaches of Mühlstädt *et al.*[6] and Fortes *et al.*[7] was verified by the synthesis of the 6,7-dichloro derivative **5**.

We next examined the generality of this synthetic method by converting *o*-allylphenols having various substituents on the benzene ring into the corresponding methyl esters. The *o*-allylphenols used were a parent one (**11a**), monosubstituted ones possessing a methoxy, methyl, chloro, or nitro group at the *ortho*- or *para*-position to the hydroxy group (**11b**—**11i**), and three kinds of dimethyl-substituted ones (**11j**—**11l**). The reaction of *o*-allylphenols **11** with PhSCl is outlined in Chart 4, and the product yields are compiled in Table I.

When 1 eq of PhSCl was added to solutions of **11a**—**11j** in CH_3CN at 0 °C, the addition reaction proceeded rapidly and **11a**—**11j** were consumed completely. Next, the re-

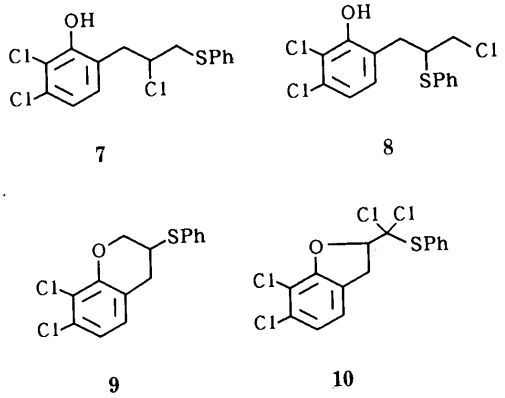


Chart 3

TABLE I. Cyclization of *o*-Allylphenols **11a**—**11l**

Compd.	X	Conditions		Yield (%)			
		PhSCl (eq)	$NaHCO_3$ (eq)	**12**	**13**	**14**	**15**
11a	H	1.1	1.2	87	<1	4.3	2.7
11b	6-CH_3O	1	1.5	79	—	3.5	2.8
11c	4-CH_3O	1.1	1.6	75	—	5	1.6
11d	6-CH_3	1.1	1.2	81	—	2.1	1.2
11e	4-CH_3	1	1.6	83	0.6	4.4	2.2
11f	6-Cl	1.1	1.1	88	1.5	2.8	2.0
11g	4-Cl	1	1.2	80	1	3.3	2.4
11h	6-NO_2	1	1.1	90	2.9	2.0	1.7
11i	4-NO_2	1	1.2	87	—	3.1	2.0
11j	4,6-diCH_3	1.1	1.2	89	—	1.8	1.0
11k	3,6-diCH_3	1.7	1.7	41	—	—	—
11l	3,5-diCH_3	1.7	1.7	19	—	—	—

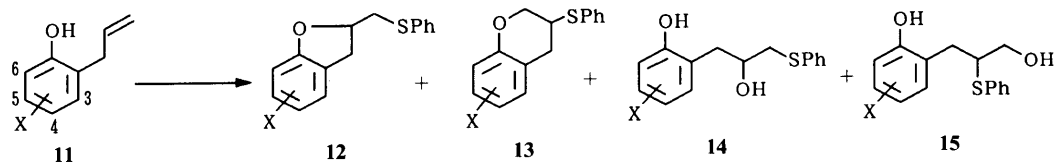


Chart 4

action mixture was heated at 80 °C for about 2 h after addition of water, and then with $NaHCO_3$ to obtain the dihydrobenzofuran derivatives **12a**—**12j** in high yields. In these reactions, chroman derivatives **13** and β-hydroxysulfides **14** and **15** were also obtained as by-products. However, in the case of **11k** and **11l**, the *o*-allylphenols were not completely consumed in the reaction with 1 eq of PhSCl. After PhSCl had been added to the reaction mixture until the *o*-allylphenols were consumed completely, the cyclization to **12** was carried out in a similar manner to the above. However, yields of the desired sulfides **12k** and **12l** were poor, and the sulfides **16k** and **16l** (Chart 5), which were substituted with a phenylthio group on the benzene ring of dihydrobenzofuran, were obtained in 45% and 65% yields, respectively, as major products. In the case of **11l**, an *o*-allylphenol **17**, which can be regarded as a precursor of **16l**, was also obtained in 8.6% yield. A similar substitution reaction by a methylthio group has been reported to occur only at the *para*-position to the hydroxy group in the reaction of *o*-allylphenol with methyl(bismethylthio)sulfonium hexachloroantimonate.[9] Thus, the position of the phenylthio group in **16k** and **16l**, which could not be determined by ^{1}H-NMR spectroscopy, was tentatively assigned as the *para*-position to the oxygen atom. Mühlstädt *et al.*[6] reported that the cyclizations of **11a**—**11g** using PhSCl gave **12a**—**12g** in 35—90% yield. Furthermore, they attempted the cyclization of 2-allyl-6-isopropyl-3-methylphenol, but obtained only a small amount of the corresponding sulfide **12**. This probably occurred due to the nucleophilic substitution reaction on the aromatic ring by the phenylthio group described above.

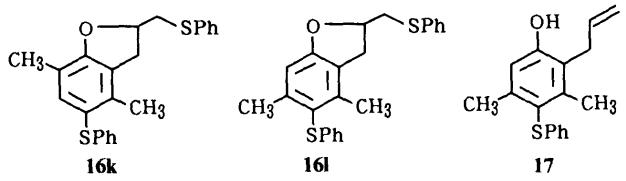


Chart 5

A mechanistic rationale for the cyclization of *o*-allylphenols (**11a**—**11l**) is suggested in Chart 6. The addition of PhSCl to *o*-allylphenols in CH_3CN probably affords a mixture of the Markownikoff adduct **18** and the anti-Markownikoff adduct **19** as in the case of the 2,3-dichloro derivative **3**. The subsequent heating in aqueous CH_3CN causes rearrangement of **19** to the thermodynamically more stable adduct **18** *via* an episulfonium ion intermediate of type **20**. In the course of this rearrangement, **20** is subjected to nucleophilic displacement by the internal phenolic hydroxy group to give the sulfide **12** *via* the preferred 5-*Exo*-*Tet* cyclization.[10] In the cases of **11h** and **11i**, the sulfides **12h** and **12i** did not form upon heating in aqueous CH_3CN, while heating with $NaHCO_3$ caused rapid cyclization to **12h** and **12i**. Consequently, in these cases, **12** was assumed to have been formed mainly *via* deprotonation of **18**, which had come to predominate over **19** by heating in aqueous CH_3CN, followed by internal displacement of the secondary chlorine by the resulting phenolate anion **21**. The chroman derivatives **13** obtained in only a trace amount were considered to be formed from **19** *via* **22** in a similar manner.

The formation of the β-hydroxysulfides **14** and **15** could be explained as a result of nucleophilic attack of water on the episulfonium ion **20**. The structure assignment of **14** and **15**, which were regioisomeric to each other, was done on the basis of the ^{1}H-NMR spectral data. In the ^{1}H-NMR spectra of the less polar isomers **14**, the α-methylene protons of the sulfide appeared at δ 2.6—3.3 ppm as a multiplet and the methine proton on the carbinol carbon at δ 3.7—4.2 ppm as a multiplet. On the other hand, in the case of the more polar isomers **15**, both the α-methine proton of the sulfide and the methylene protons on the carbinol carbon appeared at δ 3.3—3.8 ppm as a multiplet. The regioisomeric relationship between **14** and **15** was further supported by the acid-catalyzed cyclizations illustrated in Chart 7. Individual heating of the 6-chloro derivatives **14f** and **15f** in benzene in the presence of a

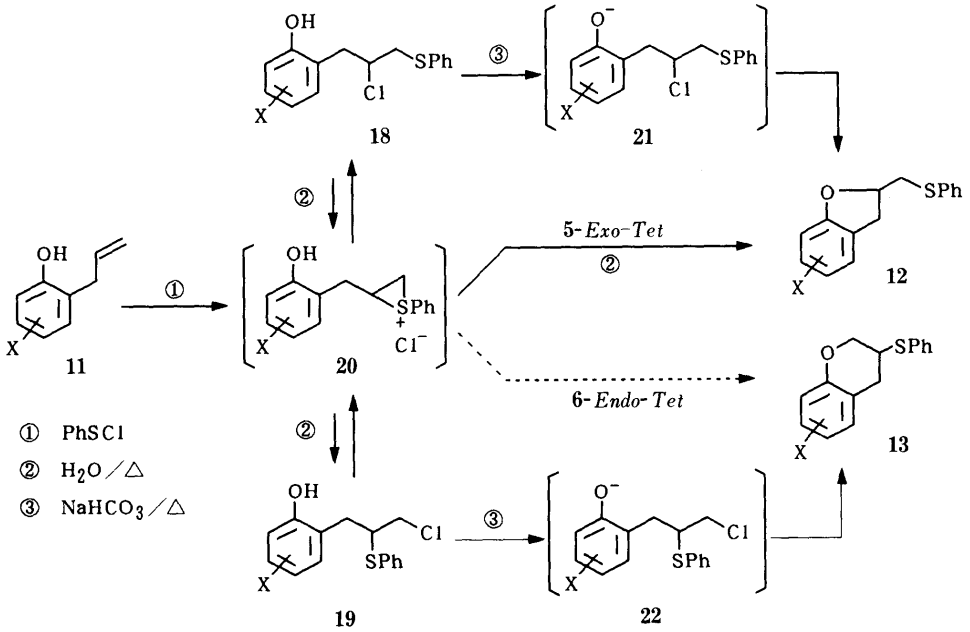


Chart 6

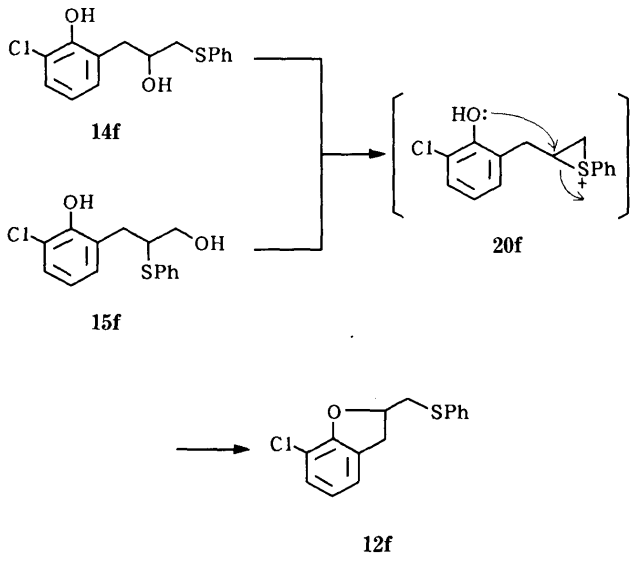


Chart 7

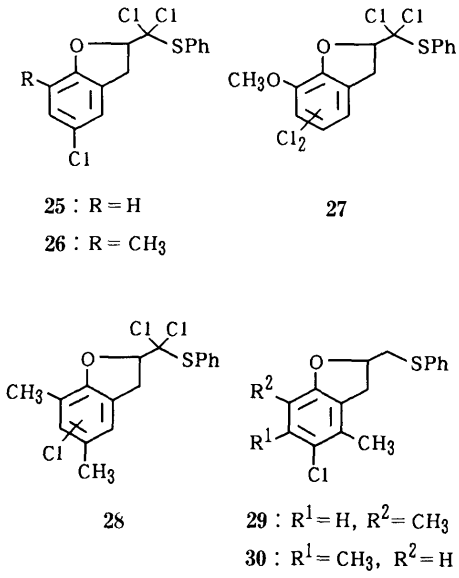
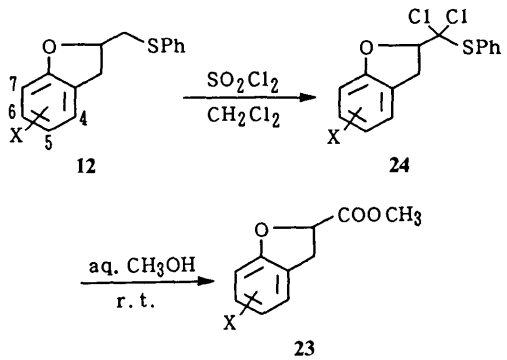


Chart 8

TABLE II. α-Dichlorination and Methanolysis of Sulfides **12f—12i**



Compd.	X	Conditions		Yield (%)
		12 **24**	**24** **23**	**23**
12f	7-Cl	Reflux, 1 h	19 h	87
12g	5-Cl	Reflux, 1 h	20 h	87
12h	7-NO_2	r.t.,[a] 80 min	68 h	91
12i	5-NO_2	Reflux, 3.5 h	27 h	90

a) Room temperature.

catalytic amount of *p*-toluenesulfonic acid (*p*-TsOH) afforded the same product **12f** in 87% and 88% yields, respectively, as a sole product. This result suggested the formation of an episulfonium ion **20f** as a common intermediate, which was then cyclized to **12f** *via* the preferred 5-*Exo*-*Tet* cyclization.

The chlorination and methanolysis of the sulfides **12** were investigated. Table II shows the conditions and results of the conversion of the sulfides having a chloro or nitro group (**12f—12i**) into the corresponding methyl esters **23**. Chlorination of **12f—12i** with 2.3 eq of SO_2Cl_2 in CH_2Cl_2 proceeded smoothly, and gave α-dichlorosulfides **24** as in the case of the 6,7-dichloro derivative **6**. The crude dichlorides **24** were dissolved or suspended in methanol containing an equimolar amount of water without purification, and stirred at room temperature to give the methyl esters **23f—23i**, respectively, in high yield.

In the cases of **12a—12e** and **12j—12l**, no selective chlorination of the α-position of the sulfur atom occurred because of competitive or exclusive chlorination of the aromatic ring of the dihydrobenzofuran moiety. Thus, these sulfides (**12a—12e**, **12j—12l**) could not be converted into the corresponding methyl esters **23**. The results of the chlorination of these sulfides are detailed below.

The reaction of **12a** with 2.3 eq of SO_2Cl_2 in CH_2Cl_2 at room temperature produced many spots on the thin-layer chromatogram. Further treatment with 1.1 eq of SO_2Cl_2 made these spots become almost a single spot. The ^{1}H-NMR spectrum of the crude product **25** showed that chlorination had occurred not only at the α-position of the sulfur atom but also at the aromatic ring of the dihydrobenzofuran moiety. In order to determine the position of the chloro group on the aromatic ring, the crude chloride **25** was subjected to methanolysis to obtain the ester **23g**, which was identical to that obtained from the chloro-substituted sulfide **12g**, in 86% yield. This showed that chlorination of the aromatic ring occurred at only the *para*-position to the oxygen atom. Chlorination of **12d** showed a reaction pattern similar to that of **12a** and gave the 5-chlorinated derivative **26**. Selective α-dihalogenation of **12d** with other halogenating reagents was not successful.[11] On the other hand, similar treatment of **12e** with 3.5 eq of SO_2Cl_2 resulted in a complex mixture. In the case of **12b**, reaction with 3.5 eq of SO_2Cl_2 afforded two spots on thin-layer chromatography (TLC), and further treatment with 1.2 eq of SO_2Cl_2 was required in order to obtain almost a single spot. The ^{1}H-NMR spectrum of the crude product **27** indicated that dichlorination on the aromatic ring had occurred, but did not show which positions on the aromatic ring were chlorinated. Treatment of **12c** with 4.6 eq of SO_2Cl_2 gave a complex mixture, similar to the case of **12e**. Chlorination of **12j** with 3.5 eq of SO_2Cl_2 gave **28**, in which the aromatic ring was mono-chlorinated. Reactions of the 4,7- and 4,6-dimethyl-substituted sulfides **12k** and **12l** with 1 eq of SO_2Cl_2 in CH_2Cl_2 provided almost a single spot on TLC. The ^{1}H-NMR spectra of the crude products **29** and **30** indicated that only the aromatic ring of dihydrobenzofuran was chlorinated; *i.e.*, chlorination of the aromatic ring took precedence over that of the α-position of the

sulfur atom in the case of **12k** and **12l**. These experimental results suggested that the ease or course of chlorination of the aromatic ring varied depending upon not only the kind of substituent but also its position.

Our consideration of the generality of the method for synthesizing methyl 2,3-dihydro-2-benzofurancarboxylates from *o*-allylphenols showed that cyclizations of *o*-allylphenols **11** to sulfides **12** proceeded regardless of the substituent on the benzene ring. However, in the subsequent conversions of **12** to **23**, selective α-dichlorination followed by methanolysis could be achieved only with **12** substituted with a chloro or nitro group. Therefore, substitution of an electron-withdrawing group such as a chloro or nitro group is needed to obtain a methyl ester **23** from an *o*-allylphenol *via* a sulfide **12** according to the present method.

Experimental

Melting points were determined on a Yanagimoto hot plate micro melting point apparatus and are uncorrected. The infrared (IR) spectra were recorded on a Hitachi 260-10 infrared spectrophotometer. The ^{1}H-NMR spectra were recorded on a Varian EM-390 spectrometer in $CDCl_3$, unless otherwise noted. Chemical shifts are reported as δ values with respect to Me_4Si used as an internal standard. Silica gel 60 (E. Merck, 0.063—0.200 mm) was used for column chromatography, unless otherwise noted. Organic extracts were dried over $MgSO_4$.

6-Allyl-2,3-dichlorophenol (3) Allyl bromide (145 g, 1.20 mol) was added dropwise over a period of 20 min to a stirred mixture of 2,3-dichlorophenol (163 g, 1.00 mol), K_2CO_3 (207 g, 1.50 mol), and CH_3CN (350 ml) (dried over molecular sieves 3A) under heating at 80 °C. The resulting mixture was stirred for 1 h at 90 °C. The insoluble materials were removed by filtration and the filtrate was concentrated *in vacuo* to give 203 g of allyl 2,3-dichlorophenyl ether as a pale-brown oil. This oil was dissolved in *N*-methylaniline (200 g), and heated at 187 °C for 4 h under an N_2 stream. The resulting mixture was diluted with AcOEt (750 ml), washed with a solution of concentrated HCl (250 ml) in ice water (750 ml) and then brine (4 times), dried, and concentrated *in vacuo*. The resultant oil was distilled under reduced pressure to give 187 g (92%) of **3** as a colorless oil: bp 95—102 °C (2.5 mmHg).[3]

PhSCl Chlorine gas was passed through an ice-cooled solution of diphenyl disulfide (5.02 g, 23.0 mmol) in CCl_4 (30 ml) until the disappearance of the diphenyl disulfide was confirmed by TLC (silica gel, CH_2Cl_2–hexane, 1 : 3, v/v), which was preceded by treatment of the reaction mixture with an excess amount of **3**. The reaction mixture was concentrated *in vacuo*, giving 7.3 g of PhSCl as a wine-red oil, which was immediately used for the reaction with *o*-allylphenols without purification.

6,7-Dichloro-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (6) a) A solution of PhSCl (57 mg, 0.39 mmol) in CH_2Cl_2 was added dropwise to an ice-cooled solution of *o*-allylphenol **3** (80 mg, 0.39 mmol) in CH_2Cl_2 (2 ml) with stirring. The resulting mixture was stirred for 10 min at 0 °C and for 10 min at room temperature, and then concentrated *in vacuo* to give a mixture of **7** and **8** as a pale-yellow oil (140 mg). The product ratio in this mixture was determined to be 2 : 1 by comparison of the area of the peak at δ 5.84 for the major isomer with that at δ 5.76 for the minor one in the ^{1}H-NMR spectrum of this mixture; δ: 2.73—3.05 (1H, m), 3.15—3.9 (3H + 2/3H, m), 4.15—4.50 (1/3H, m), 5.76 (1H, s, OH), 5.84 (2/3H, s, OH), 6.9—7.5 (7H, m, aromatic).

K_2CO_3 (57 mg, 0.41 mmol) was added to a solution of this mixture in CH_3CN, and the resulting mixture was stirred at room temperature for 7 h. The reaction mixture was concentrated *in vacuo*, and the residue was dissolved in Et_2O and water. The aqueous layer was separated and extracted with Et_2O. The ethereal extract was combined with the organic layer, and the resulting solution was washed with water and brine, dried and then concentrated *in vacuo*. The residue was chromatographed on silica gel (Merck Lobar B) with CH_2Cl_2–hexane (1 : 2, v/v) as an eluant to give 66 mg (54%) of **9** as colorless needles and 34 mg (28%) of **6** as colorless crystals. **9**: mp 88.5—89 °C (Et_2O–hexane). *Anal.* Calcd for $C_{15}H_{12}Cl_2OS$: C, 57.89; H, 3.89; Cl, 22.78; S, 10.30. Found: C, 57.91; H, 3.99; Cl, 22.58; S, 10.35. ^{1}H-NMR δ: 2.74 (1H, dd, J = 16.2, 10.2 Hz, 4-H), 3.12 (1H, ddm, J = 16.2, 5.1 Hz, 4-H), 3.55 (1H, tdd, J = 10, 5.1, 3.3 Hz, 3-H), 3.96 (1H, dd, J = 10.8, 9.6 Hz, 2-H), 4.45 (1H, ddd, J = 10.8, 3.3, 1.8 Hz, 2-H), 6.83 (1H, d, J = 8.6 Hz, 6-H), 6.96 (1H, d, J = 8.0 Hz, 5-H), 7.2—7.6 (5H, m, SPh). **6**: mp 69—70 °C (Et_2O–hexane). *Anal.* Calcd for $C_{15}H_{12}Cl_2OS$: C, 57.89; H, 3.89; Cl, 22.78; S, 10.30. Found: C, 57.79; H, 3.89; Cl, 23.01; S, 10.06. ^{1}H-NMR δ: 3.09 (1H, dd, J = 13.5, 8.1 Hz, 1H of C$\underline{H}_2$SPh), 3.12 (1H, dd, J = 16.1, 7.0 Hz, 3-H), 3.40 (1H, dd, J = 16.1, 8.7 Hz, 3-H), 3.44 (1H, dd, J = 13.5, 4.5 Hz, 1H of C$\underline{H}_2$SPh), 5.04 (1H, m, 2-H), 6.93 (2H, s, 4-H and 5-H), 7.5—7.1 (5H, m, SPh).

b) PhSCl (129 g, 0.891 mol) was added dropwise over 30 min to a stirred solution of **3** (181 g, 0.892 mol) in CH_3CN (400 ml) (dried over molecular sieves 3A). Water (100 ml) was added to the resulting solution, which was then heated at 80 °C for 2 h with stirring. Sodium bicarbonate (82.4 g, 0.981 mol) was added portionwise and the reaction mixture was heated at 80 °C for 2.5 h. The insoluble material that appeared was removed by filtration, and the filtrate was concentrated *in vacuo*. The residue was dissolved in AcOEt (1.5 l), and this solution was washed with water (5 times), dried, and concentrated *in vacuo*. The resultant solid was dissolved in Et_2O (200 ml) and hexane (200 ml) with heating and then left standing. The precipitated crystals, collected by filtration, gave 204 g of **6**. The mother liquor was concentrated and then treated with Et_2O–hexane to give 3.2 g of **6**. The combined first and second crops of crystals (207 g) were recrystallized from Et_2O–hexane to obtain 204 g (74%) of **6** as colorless crystals: mp 68—70 °C. The ^{1}H-NMR spectrum of the product agreed with that of **6** obtained in the above experiment.

6,7-Dichloro-2-[dichloro(phenylthio)methyl]-2,3-dihydrobenzofuran (10) a) With Sulfuryl Chloride: A solution of SO_2Cl_2 (194 g, 1.44 mol) in CH_2Cl_2 (200 ml) (dried over molecular sieves 4A) was added dropwise over 45 min to a stirred and heated (30—35 °C) solution of **6** (204 g, 0.656 mol) in CH_2Cl_2 (450 ml) under an N_2 stream. After additional stirring for 45 min at 30—35 °C, the resulting solution was diluted with CH_2Cl_2 (800 ml), washed with water (twice), aqueous $NaHCO_3$, and water, dried, and concentrated *in vacuo* to give 254 g of **10** as a colorless viscous oil, which was used for the subsequent methanolysis without further purification. In order to prepare an analytical sample, the oily α-dichlorosulfide **10** was solidified by trituration in methanol, and the resulting solid was then recrystallized from Et_2O–hexane to give white crystals: mp 73.5—74.5 °C. *Anal.* Calcd for $C_{15}H_{10}Cl_4OS$: C, 47.40; H, 2.65; Cl, 37.31; S, 8.43. Found: C, 47.17; H, 2.78; Cl, 37.04; S, 8.26. IR (film): 1600, 1580, 1455, 1440 cm^{-1}. ^{1}H-NMR δ: 3.46 (1H, dd, J = 17.0, 9.3 Hz, 3-H), 3.67 (1H, dd, J = 17.0, 6.8 Hz, 3-H), 5.16 (1H, dd, J = 9.3, 6.8 Hz, 2-H), 6.99 (2H, s, 4-H and 5-H), 7.2—7.6 (3H, m, 3H of SPh), 7.7—7.9 (2H, m, 2H of SPh).

b) With *N*-Chlorosuccinimide: *N*-Chlorosuccinimide (43.3 g, 0.324 mol) was added portionwise over 10 min to an ice-cooled solution of **6** (43.9 g, 0.141 mol) in $CHCl_3$ (150 ml) and the resulting mixture was stirred at room temperature. Since the reaction temperature rose rapidly after 5 min, the reaction mixture was cooled with an ice-water bath for 10 min and then stirred for 45 min at room temperature. The solvent was evaporated *in vacuo* and the residue was partially dissolved in AcOEt (300 ml). The insoluble succinimide was removed by exhaustive washing with water, and the resulting organic layer was washed with brine, dried, and concentrated *in vacuo* to give 63.7 g of **10** as a colorless viscous oil, which was used for the subsequent methanolysis without further purification. The ^{1}H-NMR spectrum of the oily product **10** agreed with that of **10** prepared by using sulfuryl chloride.

Methyl 6,7-Dichloro-2,3-dihydro-2-benzofurancarboxylate (5) The α-dichlorosulfide **10** (254 g, 0.656 mol) was dissolved in MeOH (1 l) with heating. After addition of water (12 ml, 0.667 mol), the resultant solution was stirred for 18 h at room temperature under an Ar atmosphere. The reaction mixture was concentrated *in vacuo* and the residue was dissolved in AcOEt (2 l), washed with water (twice), and extracted with cold 5% NaOH (200 ml × 3) to remove the thiophenol which formed during the methanolysis. The organic layer was washed with water, dried, and concentrated *in vacuo*. The resulting solid was triturated with hexane (400 ml) and gave 138.5 g of **5** as crude crystals, which when recrystallized from benzene gave 136.7 g (84%) of **5** as colorless crystals: mp 115—116 °C. *Anal.* Calcd for $C_{10}H_8Cl_2O_3$: C, 48.61; H, 3.26; Cl, 28.70. Found: C, 48.35; H, 3.38; Cl, 28.54. IR (Nujol): 1760, 1600, 1585 cm^{-1}. ^{1}H-NMR δ: 3.39 (1H, dd, J = 16.3, 7.0 Hz, 3-H), 3.63 (1H, dd, J = 16.3, 9.8 Hz, 3-H), 3.80 (3H, s, CH_3), 5.32 (1H, dd, J = 9.8, 7.0 Hz, 2-H), 6.99 (2H, s, aromatic).

***o*-Allylphenols 11** *o*-Allylphenols **11** were prepared from the corresponding phenols by *O*-alkylation with allyl bromide followed by the Claisen rearrangement, except for the commercially available unsubstituted (**11a**) and 6-methyl-substituted (**11d**) ones.

Reaction of *o*-Allylphenol (11a) with PhSCl Freshly prepared PhSCl (1.71 g, 11 mmol) was added dropwise to an ice-cooled solution of **11a** (1.38 g, 10.0 mmol) in CH_3CN (10 ml) with stirring. The resulting solution

was stirred for 1 h at room temperature. Water (2 ml) was added to the reaction mixture, which was then heated at 80 °C for 80 min. Sodium bicarbonate (924 mg, 11.0 mmol) was added portionwise to the reaction mixture without heating. The resulting mixture was heated at 80 °C for 9.5 h and concentrated *in vacuo*. The residue was dissolved in Et_2O, and this solution was washed with water and brine, dried, and concentrated *in vacuo*. The residue (2.61 g) was chromatographed on silica gel. Elution with CH_2Cl_2–hexane (1 : 1, v/v) gave 2.12 g (87%) of **12a** as colorless crystals and 16 mg (< 1%) of **13a** as white crystals. Continued elution with AcOEt–hexane (1 : 3, v/v) gave 112 mg (4.3%) of **14a** and 70 mg (2.7%) of **15a** as colorless oils.

The reactions of *o*-allylphenols **11b**—**11l** with PhSCl were carried out in a manner similar to that of **11a**. The ^{1}H-NMR spectra of **12a**—**12g** obtained here agreed with those reported in ref. 6.

2-(Phenylthiomethyl)-2,3-dihydrobenzofuran (**12a**): Colorless crystals. mp 56.5—57.5 °C (AcOEt–hexane) [lit.[6] mp 56—57 °C]. *Anal.* Calcd for $C_{15}H_{14}OS$: C, 74.35; H, 5.82; S, 13.23. Found: C, 74.06; H, 5.96; S, 13.16.

7-Methoxy-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**12b**): Colorless crystals. mp 94—95 °C (AcOEt–hexane) [lit.[6] mp 94.5—95.5 °C]. *Anal.* Calcd for $C_{16}H_{16}O_2S$: C, 70.56; H, 5.92; S, 11.77. Found: C, 70.51; H, 5.89; S, 11.65.

5-Methoxy-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**12c**): White solid. mp 36—37 °C (crude) [lit.[6] mp 36.5—37.5 °C]. *Anal.* Calcd for $C_{16}H_{16}O_2S$: C, 70.56; H, 5.92; S, 11.77. Found: C, 70.62; H, 6.00; S, 11.69.

7-Methyl-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**12d**): Colorless crystals. mp 54—56.5 °C (hexane) [lit.[6] mp 56—57 °C]. *Anal.* Calcd for $C_{16}H_{16}OS$: C, 74.96; H, 6.29; S, 12.51. Found: C, 74.85; H, 6.35; S, 12.43.

5-Methyl-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**12e**): White solid. mp 38.5—40 °C (crude) [lit.[6] mp 37—38 °C]. *Anal.* Calcd for $C_{16}H_{16}OS$: C, 74.96; H, 6.29; S, 12.51. Found: C, 74.88; H, 6.37; S, 12.37.

7-Chloro-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**12f**): Colorless crystals. mp 87—88 °C (AcOEt–hexane) [lit.[6] mp 87—88 °C]. *Anal.* Calcd for $C_{15}H_{13}ClOS$: C, 65.09; H, 4.73; Cl, 12.81; S, 11.58. Found: C, 65.07; H, 4.62; Cl, 13.04; S, 11.45.

5-Chloro-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**12g**): Colorless crystals. mp 62—63.5 °C (AcOEt–hexane) [lit.[6] mp 56—58 °C]. *Anal.* Calcd for $C_{15}H_{13}ClOS$: C, 65.09; H, 4.73; Cl, 12.81; S, 11.58. Found: C, 65.12; H, 4.84; Cl, 12.93; S, 11.67.

7-Nitro-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**12h**): Pale yellow crystals. mp 69.5—70.5 °C (AcOEt–hexane). *Anal.* Calcd for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.87; S, 11.16. Found: C, 62.76; H, 4.48; N, 4.92; S, 11.16. ^{1}H-NMR δ: 3.14 (1H, dd, J=13.8, 7.6 Hz, 1H of CH_2SPh), 3.17 (1H, dd, J=16.5, 6.9 Hz, 3-H), 3.43 (1H, dd, J=16.5, 10.3 Hz, 3-H), 3.44 (1H, dd, J=13.8, 4.6 Hz, 1H of CH_2SPh), 5.17 (1H, m, 2-H), 6.87 (1H, dd, J=8.2, 7.5 Hz, 5-H), 7.1—7.5 (6H, m, 4-H and SPh), 7.84 (1H, dm, J=8.2 Hz, 6-H).

5-Nitro-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**12i**): Pale yellow crystals. mp 78—79 °C (AcOEt–hexane). *Anal.* Calcd for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.87; S, 11.16. Found: C, 62.57; H, 4.57; N, 4.80; S, 10.95. ^{1}H-NMR δ: 3.09 (1H, dd, J=16.3, 7.2 Hz, 3-H), 3.11 (1H, dd, J=13.7, 7.2 Hz, 1H of CH_2SPh), 3.36 (1H, dd, J=13.7, 5.4 Hz, 1H of CH_2SPh), 3.40 (1H, dd, J=16.3, 9 Hz, 3-H), 5.06 (1H, m, 2-H), 6.72 (1H, d, J=9.8 Hz, 7-H), 7.1—7.5 (5H, m, SPh), 8.01 (1H, s, 4-H), 8.05 (1H, m, 6-H).

5,7-Dimethyl-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**12j**): Colorless crystals. mp 37—38 °C (crude). *Anal.* Calcd for $C_{17}H_{18}OS$: C, 75.52; H, 6.71; S, 11.86. Found: C, 75.40; H, 6.78; S, 11.76. ^{1}H-NMR δ: 2.09 and 2.21 (each 3H, s, CH_3), 2.98 (1H, dd, J=15.7, 7.0 Hz, 3-H), 3.02 (1H, dd, J=13.4, 7.6 Hz, 1H of CH_2SPh), 3.28 (1H, dd, J=15.7, 9 Hz, 3-H), 3.35 (1H, dd, J=13.4, 5.3 Hz, 1H of CH_2SPh), 4.85 (1H, m, 2-H), 6.71 and 6.76 (each 1H, br s, 4-H/6-H), 7.1—7.5 (5H, m, SPh).

4,7-Dimethyl-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**12k**): A colorless viscous oil. ^{1}H-NMR δ: 2.09 and 2.16 (each 3H, s, CH_3), 2.97 (1H, dd, J=15.2, 7.0 Hz, 3-H), 3.03 (1H, dd, J=13.6, 7.7 Hz, 1H of CH_2SPh), 3.23 (1H, dd, J=15.2, 9.0 Hz, 3-H), 3.36 (1H, dd, J=13.2, 5.1 Hz, 1H of CH_2SPh), 4.88 (1H, m, 2-H), 6.54 (1H, d, J=7.5 Hz, 5-H), 6.81 (1H, d, J=7.5 Hz, 6-H), 7.1—7.5 (5H, m, SPh).

4,6-Dimethyl-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**12l**): A colorless oil. ^{1}H-NMR δ: 2.16 and 2.23 (each 3H, s, CH_3), 2.8—3.5 (4H, m, 3-H_2 and CH_2SPh), 4.88 (1H, m, 2-H), 6.41 and 6.48 (each 1H, br s, 5-H/7-H), 7.1—7.5 (5H, m, SPh).

3-(Phenylthio)chroman (**13a**): A white solid. mp 59—62 °C (crude). ^{1}H-NMR δ: 2.75 (1H, dd, J=16.0, 10.2 Hz, 4-H), 3.12 (1H, ddm, J=16.0, 5.5 Hz, 4-H), 3.56 (1H, m, 3-H), 3.87 (1H, dd, J=10.4, 9.6 Hz, 2-H), 4.31 (1H, dm, J=10.4 Hz, 2-H), 6.7—7.6 (9H, m, aromatic).

6-Methyl-3-(phenylthio)chroman (**13e**): A colorless oil. ^{1}H-NMR δ: 2.23 (3H, s, CH_3), 2.6—3.7 (3H, m, 3-H and 4-H_2), 3.85 (1H, dd, J=10.2, 9.6 Hz, 2-H), 4.28 (1H, dm, J=10.2 Hz, 2-H), 6.6—7.0 (3H, m, 5-H, 7-H, and 8-H), 7.1—7.6 (5H, m, SPh).

8-Chloro-3-(phenylthio)chroman (**13f**): A colorless oil. ^{1}H-NMR δ: 2.74 (1H, dd, J=16.3, 10.2 Hz, 4-H), 3.12 (1H, ddm, J=16.3, 5.1 Hz, 4-H), 3.53 (1H, m, 3-H), 3.93 (1H, dd, J=10.5, 9.7 Hz, 2-H), 4.43 (1H, dm, J=10.5 Hz, 2-H), 6.6—7.6 (8H, m, aromatic).

6-Chloro-3-(phenylthio)chroman (**13g**): A colorless oil. ^{1}H-NMR δ: 2.5—3.7 (3H, m, 3-H and 4-H_2), 3.86 (1H, dd, J=10.2, 9.0 Hz, 2-H), 4.30 (1H, dm, J=10.2 Hz, 2-H), 6.71 (1H, d, J=8.4 Hz, 8-H), 6.99 (1H, s, 5-H), 7.05 (1H, d, J=8.4 Hz, 7-H), 7.2—7.5 (5H, m, SPh).

8-Nitro-3-(phenylthio)chroman (**13h**): A pale yellow oil. ^{1}H-NMR δ: 2.78 (1H, dd, J=16.5, 10.0 Hz, 4-H), 3.20 (1H, ddm, J=16.5, 5.0 Hz, 4-H), 3.56 (1H, m, 3-H), 3.96 (1H, dd, J=10.6, 9.6 Hz, 2-H), 4.46 (1H, dm, J=10.6 Hz, 2-H), 6.87 (1H, t, J=7.8 Hz, 6-H), 7.1—7.6 (6H, m, 5-H and SPh), 7.65 (1H, dm, J=7.8 Hz, 7-H).

2-[2-Hydroxy-3-(phenylthio)propyl]phenol (**14a**): A colorless oil. IR (film): 3600—2700 cm^{-1}. ^{1}H-NMR δ: 2.6—3.3 (4H, m, ArCH_2 and CH_2SPh), 3.7—4.1 (1H, m, CHOH), 6.6—7.5 (10H, m, ArOH and aromatic).

2-[2-Hydroxy-3-(phenylthio)propyl]-6-methoxyphenol (**14b**): A colorless oil. IR (film): 3600—2800 cm^{-1}. ^{1}H-NMR δ: 2.7—3.3 (5H, m, ArCH_2, CHOH, and CH_2SPh), 3.82 (3H, s, OCH_3), 3.9—4.2 (1H, m, CHOH), 6.1—6.7 (1H, br, ArOH), 6.74 (3H, s, 3-H, 4-H, and 5-H), 7.1—7.4 (5H, m, SPh).

2-[2-Hydroxy-3-(phenylthio)propyl]-4-methoxyphenol (**14c**): A pale brown oil. ^{1}H-NMR δ: 2.6—3.3 (4H, m, ArCH_2 and CH_2SPh), 3.72 (3H, s, OCH_3), 3.8—4.1 (1H, m, CHOH), 4.19 (1H, d, J=6 Hz, CHOH), 6.5—6.9 (3H, m, 3-H, 5-H, and 6-H), 7.1—7.5 (6H, m, ArOH and SPh).

2-[2-Hydroxy-3-(phenylthio)propyl]-6-methylphenol (**14d**): A pale orange oil. IR (film): 3600—2700 cm^{-1}. ^{1}H-NMR δ: 2.23 (3H, s, CH_3), 2.6—3.2 (4H, m, ArCH_2 and CH_2SPh), 3.53 (1H, br s, CHOH), 3.7—4.1 (1H, m, CHOH), 6.6—7.1 (3H, m, 3-H, 4-H, and 5-H), 7.1—7.5 (5H, m, SPh), 8.01 (1H, br s, ArOH).

2-[2-Hydroxy-3-(phenylthio)propyl]-4-methylphenol (**14e**): A pale yellow oil. ^{1}H-NMR δ: 2.20 (3H, s, CH_3), 2.6—3.2 (4H, m, ArCH_2 and CH_2SPh), 3.8—4.1 (1H, m, CHOH), 6.7—7.0 (3H, m, 3-H, 5-H, and 6-H), 7.1—7.5 (5H, m, SPh).

2-Chloro-6-[2-hydroxy-3-(phenylthio)propyl]phenol (**14f**): A colorless oil. IR (film): 3600—2500 cm^{-1}. ^{1}H-NMR δ: 2.6—3.2 (4H, m, ArCH_2 and CH_2SPh), 3.27 (1H, br s, CHOH), 3.8—4.2 (1H, m, CHOH), 6.72 (1H, t, J=7.5 Hz, 4-H), 6.94 (1H, dd, J=7.5, 2.0 Hz, 5-H), 7.1—7.4 (6H, m, 3-H and SPh), 7.54 (1H, br s, ArOH).

4-Chloro-2-[2-hydroxy-3-(phenylthio)propyl]phenol (**14g**): A pale yellow oil. ^{1}H-NMR δ: 2.5—3.3 (4H, m, ArCH_2 and CH_2SPh), 3.4—4.1 (2H, m, CHOH), 6.90 (1H, d, J=8.7 Hz, 6-H) 6.97 (1H, d, J=2.5 Hz, 3-H), 7.08 (1H, dd, J=8.7, 2.5 Hz, 5-H), 7.2—7.5 (5H, m, SPh), 7.9—8.4 (1H, br, ArOH).

2-[2-Hydroxy-3-(phenylthio)propyl]-6-nitrophenol (**14h**): Yellow crystals. mp 80.5—83 °C (crude). *Anal.* Calcd for $C_{15}H_{15}NO_4S$: C, 59.00; H, 4.95; N, 4.59; S, 10.50. Found: C, 59.17; H, 4.91; N, 4.48; S, 10.46. IR (Nujol): 3600—2800 cm^{-1}. ^{1}H-NMR δ: 2.58 (1H, br s, CHOH), 2.7—3.3 (4H, m, ArCH_2 and CH_2SPh), 3.8—4.2 (1H, m, CHOH), 6.88 (1H, dd, J=8.4, 7.5 Hz, 4-H), 7.1—7.5 (5H, m, SPh), 7.50 (1H, dd, J=7.5, 1.5 Hz, 3-H), 7.97 (1H, dd, J=8.4, 1.5 Hz, 5-H), 10.95 (1H, br s, ArOH).

2-[2-Hydroxy-3-(phenylthio)propyl]-4-nitrophenol (**14i**): A pale yellow solid. mp 123—125 °C (crude). *Anal.* Calcd for $C_{15}H_{15}NO_4S \cdot 1/4H_2O$: C, 58.15; H, 5.04; N, 4.52; S, 10.35. Found: C, 58.32; H, 4.90; N, 4.50; S, 10.16. ^{1}H-NMR δ: 2.6—3.3 (4H, m, ArCH_2 and CH_2SPh), 3.7—4.2 (2H, m, CHOH), 6.95 (1H, d, J=9.0 Hz, 6-H), 7.1—7.5 (5H, m, SPh), 7.9—8.2 (2H, m, 3-H and 5-H), 9.26 (1H, br s, ArOH).

2-[2-Hydroxy-3-(phenylthio)propyl]-4,6-dimethylphenol (**14j**): A pale brown oil. ^{1}H-NMR δ: 2.20 (6H, s, 2 × CH_3), 2.5—3.3 (4H, m, ArCH_2 and CH_2SPh), 3.40 (1H, br s, CHOH), 3.7—4.1 (1H, m, CHOH), 6.64 and 6.83 (each 1H, br s, 3-H/5-H), 7.1—7.5 (5H, m, SPh), 7.73 (1H, br s, ArOH).

2-[3-Hydroxy-2-(phenylthio)propyl]phenol (**15a**): A colorless oil. IR (film): 3600—2800 cm^{-1}. ^{1}H-NMR δ: 2.9—3.1 (2H, m, ArCH_2), 3.3—3.7 (3H, m, CHSPh and CH_2OH), 6.7—7.0 (2H, m, 4-H and 6-H), 7.0—7.5 (7H, m, 3-H, 5-H, and SPh).

2-[3-Hydroxy-2-(phenylthio)propyl]-6-methoxyphenol (**15b**): A colorless oil. IR (film): 3700—2800 cm^{-1}. ^{1}H-NMR δ: 2.6—3.2 (3H, m, ArCH_2 and CH_2OH), 3.4—3.7 (3H, m, CHSPh and CH_2OH), 3.80 (3H, s, OCH_3), 6.10 (1H, br s, ArOH), 6.74 (3H, s, 3-H, 4-H, and 5-H), 7.1—7.5 (5H, m, SPh).

2-[3-Hydroxy-2-(phenylthio)propyl]-4-methoxyphenol (**15c**): A pale brown oil. ^{1}H-NMR δ: 2.9—3.1 (2H, m, ArC$\underline{H}_2$), 3.3—3.6 (3H, m, C$\underline{H}$SPh and C$\underline{H}_2$OH), 3.72 (3H, s, OCH_3), 4.9—5.3 (1H, br, $CH_2O\underline{H}$), 6.5—6.9 (3H, m, 3-H, 5-H, and 6-H), 7.2—7.5 (6H, m, ArO$\underline{H}$ and SPh).

2-[3-Hydroxy-2-(phenylthio)propyl]-6-methylphenol (**15d**): A pale orange oil. IR (film): 3650—2800 cm^{-1}. ^{1}H-NMR δ: 2.23 (3H, s, CH_3), 2.7—3.1 (3H, m, ArC$\underline{H}_2$ and $CH_2O\underline{H}$), 3.2—3.7 (3H, m, C$\underline{H}$SPh and C$\underline{H}_2$OH), 6.6—7.1 (4H, m, 3-H, 4-H, 5-H, and ArO$\underline{H}$), 7.1—7.5 (5H, m, SPh).

2-[3-Hydroxy-2-(phenylthio)propyl]-4-methylphenol (**15e**): A colorless oil. ^{1}H-NMR δ: 2.21 (3H, s, CH_3), 2.8—3.1 (2H, m, ArC$\underline{H}_2$), 3.3—3.6 (3H, m, C$\underline{H}$SPh and C$\underline{H}_2$OH), 4.0—5.3 (1H, br, $CH_2O\underline{H}$), 6.6—7.0 (3H, m, 3-H, 5-H, and 6-H), 7.1—7.5 (5H, m, SPh).

2-Chloro-6-[3-hydroxy-2-(phenylthio)propyl]phenol (**15f**): A colorless oil. IR (film): 3600—2800 cm^{-1}. ^{1}H-NMR δ: 2.55 (1H, br s, $CH_2O\underline{H}$), 2.9—3.1 (2H, m, ArC$\underline{H}_2$), 3.4—3.7 (3H, m, C$\underline{H}$SPh and C$\underline{H}_2$OH), 6.20 (1H, br s, ArO$\underline{H}$), 6.77 (1H, t, J=7.6 Hz, 4-H), 7.05 (1H, dd, J=7.6, 1.6 Hz, 5-H), 7.1—7.5 (6H, m, 3-H and SPh).

4-Chloro-2-[3-hydroxy-2-(phenylthio)propyl]phenol (**15g**): A pale yellow oil. ^{1}H-NMR δ: 2.8—3.2 (2H, m, ArC$\underline{H}_2$), 3.3—3.8 (3H, m, C$\underline{H}$SPh and C$\underline{H}_2$OH), 6.76 (1H, d, J=9 Hz, 6-H), 7.0—7.5 (8H, m, 3-H, 5-H, ArO$\underline{H}$ and SPh).

2-[3-Hydroxy-2-(phenylthio)propyl]-6-nitrophenol (**15h**): A yellow oil. IR (film): 3700—2800, 2925, 2870 cm^{-1}. ^{1}H-NMR δ: 2.35 (1H, br s, $CH_2O\underline{H}$), 2.9—3.2 (2H, m, ArC$\underline{H}_2$), 3.5—3.8 (3H, m, C$\underline{H}$SPh and C$\underline{H}_2$OH), 6.90 (1H, dd, J=8.5, 7.4 Hz, 4-H), 7.1—7.4 (5H, m, SPh), 7.49 (1H, dd, J=7.4, 1.5 Hz, 3-H), 7.98 (1H, dd, J=8.5, 1.5 Hz, 5-H), 10.97 (1H, br s, ArO$\underline{H}$).

2-[3-Hydroxy-2-(phenylthio)propyl]-4-nitrophenol (**15i**): A pale yellow oil. ^{1}H-NMR δ: 2.9—3.2 (2H, m, ArC$\underline{H}_2$), 3.3—3.8 (3H, m, C$\underline{H}$SPh and C$\underline{H}_2$OH), 6.89 (1H, dm, J=8.6 Hz, 6-H), 7.2—7.5 (5H, m, SPh), 8.00 (1H, dm, J=8.4 Hz, 5-H), 8.05 (1H, s, 3-H).

2-[3-Hydroxy-2-(phenylthio)propyl]-4,6-dimethylphenol (**15j**): A pale brown oil. ^{1}H-NMR δ: 2.20 (6H, s, 2 × CH_3), 2.8—3.1 (2H, m, ArC$\underline{H}_2$), 3.3—3.6 (3H, m, C$\underline{H}$SPh and C$\underline{H}_2$OH), 6.7—6.9 (2H, m, 3-H and 5-H), 7.2—7.5 (5H, m, SPh).

4,7-Dimethyl-5-(phenylthio)-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**16k**): Colorless crystals. mp 70.5—71.5 °C. *Anal.* Calcd for $C_{23}H_{22}OS_2$: C, 72.98; H, 5.86; S, 16.94. Found: C, 72.83; H, 5.91; S, 16.87. ^{1}H-NMR δ: 2.07 and 2.19 (each 3H, s, CH_3), 2.97 (1H, dd, J=15.7, 6.7 Hz, 3-H), 3.07 (1H, dd, J=13.5, 7.5 Hz, 1H of C$\underline{H}_2$SPh), 3.28 (1H, dd, J=15.7, 9.0 Hz, 3-H), 3.39 (1H, dd, J=13.5, 5.1 Hz, 1H of C$\underline{H}_2$SPh), 4.95 (1H, m, 2-H), 6.9—7.5 (11H, m, 6-H and 2 × SPh).

4,6-Dimethyl-5-(phenylthio)-2-(phenylthiomethyl)-2,3-dihydrobenzofuran (**16l**): A colorless viscous oil. ^{1}H-NMR δ: 2.27 and 2.36 (each 3H, s, CH_3), 2.96 (1H, dd, J=15.9, 6.6 Hz, 3-H), 3.08 (1H, dd, J=13.5, 7.5 Hz, 1H of C$\underline{H}_2$SPh), 3.28 (1H, dd, J=15.9, 9.0 Hz, 3-H), 3.38 (1H, dd, J=13.5, 5.5 Hz, 1H of C$\underline{H}_2$SPh), 4.93 (1H, m, 2-H), 6.61 (1H, br s, 7-H), 6.8—7.5 (10H, m, 2 × SPh).

2-Allyl-3,5-dimethyl-4-(phenylthio)phenol (**17**): A colorless viscous oil. ^{1}H-NMR δ: 2.35 and 2.41 (each 3H, s, CH_3), 3.44 (2H, dm, J=5.7 Hz, CH_2), 4.95 (1H, dm, J=16.5 Hz, CH=C$\underline{H}_2$ (*trans*)), 5.02 (1H, dm, J=10.6 Hz, CH=C$\underline{H}_2$ (*cis*)), 4.8—5.3 (1H, br, OH), 5.95 (1H, ddt, J=16.5, 10.6, 5.7 Hz, C$\underline{H}$=CH_2), 6.67 (1H, s, 6-H), 6.8—7.3 (5H, m, SPh).

Acid-Catalyzed Cyclization of 14f A catalytic amount of *p*-TsOH was added to a solution of **14f** (435 mg, 1.47 mmol) in benzene, and the resulting solution was heated at reflux for 4.5 h. The reaction mixture was concentrated *in vacuo*. The residue was chromatographed on silica gel with CH_2Cl_2–hexane (1 : 2, v/v) as the eluant to give 356 mg (87%) of **12f** as a white solid: mp 86—86.5 °C (AcOEt–hexane). ^{1}H-NMR δ: 3.05 (1H, dd, J=13.5, 4.6 Hz, 1H of C$\underline{H}_2$SPh), 3.10 (1H, dd, J=15.8, 7.2 Hz, 3-H), 3.40 (1H, dd, J=15.8, 8.4 Hz, 3-H), 3.43 (1H, dd, J=13.5, 4.6 Hz, 1H of C$\underline{H}_2$SPh), 4.95 (1H, m, 2-H), 6.73 (1H, t, J=7.6 Hz, 5-H), 6.9—7.2 (2H, m, 4-H and 6-H), 7.1—7.5 (5H, m, SPh).

Acid-catalyzed cyclization of **15f** (241 mg, 0.81 mmol) was carried out in a similar manner to obtain 198 mg (88%) of **12f**: mp 86—87 °C.

Methyl 7-Chloro-2,3-dihydro-2-benzofurancarboxylate (23f) A solution of SO_2Cl_2 (7.42 g, 55.0 mmol) in CH_2Cl_2 (8 ml) was added dropwise to a refluxed solution of **12f** (6.92 g, 25.0 mmol) in CH_2Cl_2 with stirring. After the addition was completed, the resulting solution was heated at reflux for another 1 h. The reaction mixture was diluted with CH_2Cl_2, washed with water and brine, dried, and concentrated *in vacuo*. The residual yellow viscous oil (9.30 g) was dissolved in MeOH (100 ml), and then water (0.45 ml, 25 mmol) was added to the resulting solution, which was stirred for 19 h at room temperature. The reaction mixture was concentrated *in vacuo*, and the residue was diluted with AcOEt, washed with aqueous $NaHCO_3$, 5% NaOH, water, and brine, dried, and concentrated. The residue was chromatographed on silica gel with AcOEt–hexane (1 : 5 then 1 : 3, v/v) as the eluant to give 4.66 g (88%) of **23f** as a pale yellow oil. ^{1}H-NMR δ: 3.38 (1H, ddm, J=16.5, 7.5 Hz, 3-H), 3.61 (1H, ddm, J=16.5, 9.7 Hz, 3-H), 3.80 (3H, s, CH_3), 5.25 (1H, dd, J=9.7, 7.5 Hz, 2-H), 6.79 (1H, t, J=7.6 Hz, 5-H), 7.0—7.2 (2H, m, 4-H and 6-H).

α-Dichlorinations and methanolyses of **12g**—**12i** were carried out in a manner similar to that of **12f**.

Methyl 5-Chloro-2,3-dihydro-2-benzofurancarboxylate (**23g**): A colorless oil. *Anal.* Calcd for $C_{10}H_9ClO_3$: C, 56.49; H, 4.27; Cl, 16.67. Found: C, 56.24; H, 4.32; Cl, 17.44. ^{1}H-NMR δ: 3.31 (1H, ddm, J=16.1, 7.5 Hz, 3-H), 3.54 (1H, ddm, J=16.1, 9.8 Hz, 3-H), 3.79 (3H, s, CH_3), 5.20 (1H, dd, J=9.8, 7.5 Hz, 2-H), 6.78 (1H, d, J=9.2 Hz, 7-H), 7.0—7.2 (1H, m, 6-H), 7.13 (1H, s, 4-H).

Methyl 7-Nitro-2,3-dihydro-2-benzofurancarboxylate (**23h**): A pale yellow solid. mp 100.5—101.5 °C ($CHCl_3$–hexane). *Anal.* Calcd for $C_{10}H_9NO_5$: C, 53.82; H, 4.06; N, 6.28. Found: C, 53.62; H, 4.03; N, 6.33. ^{1}H-NMR δ: 3.42 (1H, ddm, J=16.2, 7.0 Hz, 3-H), 3.67 (1H, ddm, J=16.2, 10.0 Hz, 3-H), 3.80 (3H, s, CH_3), 5.45 (1H, dd, J=10.0, 7.0 Hz, 2-H), 6.98 (1H, dd, J=8.4, 7.5 Hz, 5-H), 7.44 (1H, dm, J=7.5 Hz, 4-H), 7.94 (1H, dm, J=8.4 Hz, 6-H).

Methyl 5-Nitro-2,3-dihydro-2-benzofurancarboxylate (**23i**): Pale yellow crystals. mp 100.5—101 °C ($CHCl_3$–hexane). *Anal.* Calcd for $C_{10}H_9NO_5$: C, 53.82; H, 4.06; N, 6.28. Found: C, 53.61; H, 4.06; N, 6.15. ^{1}H-NMR δ: 3.40 (1H, ddm, J=16.4, 7.5 Hz, 3-H), 3.65 (1H, ddm, J=16.4, 10.0 Hz, 3-H), 3.81 (3H, s, CH_3), 5.35 (1H, dd, J=10.0, 7.5 Hz, 2-H), 6.92 (1H, dm, J=9 Hz, 7-H), 8.0—8.2 (2H, m, 4-H and 6-H).

Chlorination and Methanolysis of 12a A solution of SO_2Cl_2 in CH_2Cl_2 (1.01 M, 6.15 ml) was added dropwise to a solution of **12a** (655 mg, 2.70 mmol) in CH_2Cl_2 at room temperature. The resulting mixture was stirred at room temperature for 1 h and heated at reflux for 85 min. Since the starting material was not completely consumed, additional SO_2Cl_2 (1.01 M in CH_2Cl_2, 3.0 ml) was added to the reaction mixture, which was then stirred for 45 min at room temperature. The reaction mixture was concentrated *in vacuo*, and the residue was diluted with $CHCl_3$ and concentrated to give 1.02 g of **25** as a yellow viscous oil. ^{1}H-NMR δ: 3.37 (1H, ddm, J=17.0, 9.4 Hz, 3-H), 3.60 (1H, ddm, J=17.0, 7.0 Hz, 3-H), 5.08 (1H, dd, J=9.4, 7.0 Hz, 2-H), 6.77 (1H, d, J=9.2 Hz, 7-H), 7.0—7.3 (2H, m, 4-H and 6-H), 7.3—7.6 (3H, m, 3H of SPh), 7.6—7.9 (2H, m, 2H of SPh). This oil was diluted with MeOH, and 1 drop of water was added to the resulting solution, which was stirred for 21 h at room temperature. The reaction mixture was concentrated *in vacuo*, and the residue was diluted with Et_2O, washed with water, 5% NaOH, water, and brine, dried, and concentrated *in vacuo*. The residue (593 mg, yellow oil) was chromatographed on silica gel with AcOEt–hexane (1 : 3, v/v) as the eluant to give 492 mg of **23g** as a colorless oil.

Chlorination of 12d A solution of SO_2Cl_2 in CH_2Cl_2 (1.01 M, 0.24 ml) was added to a solution of **12d** (27 mg, 0.11 mmol) in CH_2Cl_2 (1 ml), the resulting solution was stirred at room temperature for 2 h and heated at reflux for 1 h. SO_2Cl_2 (1.01 M in CH_2Cl_2, 0.10 ml) was added again to the reaction mixture. Stirring at room temperature for 1 h and evaporation of the solvent *in vacuo* gave 40 mg of **26** as a colorless oil. ^{1}H-NMR δ: 2.18 (3H, s, CH_3), 3.37 (1H, ddm, J=16.8, 9.3 Hz, 3-H), 3.60 (1H, ddm, J=16.8, 7.0 Hz, 3-H), 5.06 (1H, dd, J=9.3, 7.0 Hz, 2-H), 6.94 (2H, br s, 4-H and 6-H), 7.3—7.6 (3H, m, 3H of SPh), 7.6—7.9 (2H, m, 2H of SPh).

Chlorinations of **12b**, **12j**, **12k**, and **12l** were carried out in a manner similar to that used for **12d**.

27: A pale yellow oil. ^{1}H-NMR δ: 3.43 (1H, dd, J=17.0, 9.4 Hz, 3-H), 3.65 (1H, dd, J=17.0, 7.1 Hz, 3-H), 3.85 (3H, s, OCH_3), 5.16 (1H, dd, J=9.4, 7.1 Hz, 2-H), 6.85 (1H, s, 4-H or 6-H), 7.3—7.6 (3H, m, 3H of SPh), 7.6—7.9 (2H, m, 2H of SPh).

28: A pale yellow oil. ^{1}H-NMR δ: 2.24 and 2.27 (each 3H, s, CH_3), 3.2—3.7 (2H, m, 3-H_2), 5.04 (1H, m, 2-H), 6.86 (1H, br s, 4-H or 6-H), 7.3—7.6 (3H, m, 3H of SPh), 7.6—7.8 (2H, m, 2H of SPh).

29: A colorless oil. ^{1}H-NMR δ: 2.04 and 2.17 (each 3H, s, CH_3), 2.8—3.5 (4H, m, 3-H_2 and C$\underline{H}_2$SPh), 4.90 (1H, m, 2-H), 6.90 (1H, br s, 6-H), 7.1—7.5 (5H, m, SPh).

30: A colorless oil. ^{1}H-NMR δ: 2.22 and 2.29 (each 3H, s, CH_3), 2.8—3.5 (4H, m, 3-H_2 and C$\underline{H}_2$SPh), 4.88 (1H, m, 2-H), 6.49 (1H, br s, 7-H), 7.1—7.5 (5H, m, SPh).

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