The benzodifuran ring system has been known to exhibit interesting biological properties, and another important applications of these compounds are in the field of photosensitizers and fluorescent probes.

With our ongoing research for the synthetic method of various arene ring-fused furan derivatives, we describe here one-pot synthesis of substituted benzodifurans from benzene diols and α-chloro-α-(methylthio)acetone (1).

The chloride 1 was prepared from α-(methylthio)acetone by chlorination with N-chlorosuccinimide according to the reported method. Initially, a methylene chloride-tetrahydrofuran solution of hydroquinone and an excess of the chloride 1 was treated with zinc chloride at room temperature. The crude material was chromatographed to give substituted benzodifurans (2,3) in 29% and 33% yields, respectively. The formation of isomers (2,3) could be due to the presence of the two hydroxyl groups on the para position of hydroquinone ring. Therefore, we concluded that the type A and B denoted in Scheme 1 lead to 2,5-dimethyl-3,4-dimethylthiobenzof[1,2-b:4,3-b]difuran (2) and 2,6-dimethyl-3,7-dimethylthiobenzof[1,2-b:4,5-b']difuran (3).

Next, we examined the reaction of other benzene diols and methylresorcinols on the base of reaction conditions for the compounds (2,3). The results are summarized in Scheme 1. The reactions of resorcinol and 2-methylresorcinol took place smoothly at room temperature to give the adducts (4,6) in ca. 50% yields. In the case of catechol, 2,7-dimethyl-3,6-dimethylthiobenzof[1,2-b:6,5-b']difuran (5) was obtained in 17% yield. We assumed that the attack of incoming groups toward electrophilic substitution could not easily be accomplished due to the adjacent two hydroxyl groups in catechol.

The reaction of 5-methylresorcinol with an excess of the chloride 1 afforded substituted benzodifurans (7,8) in 27% and 24% yields, respectively. We could confirmed that the type C and D denoted in Scheme 1 lead to 2,4,6-trimethyl-3,5-dimethylthiobenzof[1,2-b:5,4-b']difuran (7) and 2,4,7-trimethyl-3,8-dimethylthiobenzof[1,2-b:5,6-b']difuran (8).
Like our previous report,\textsuperscript{4,5} The mechanism for the one-pot synthesis of benzodifurans 2-8 is similarly explained by a successive dehydrocyclization of Friedel-Crafts intermediate being obtained under Lewis acid conditions. The structures of the above new compounds 2-8 were determined by well-defined \textsuperscript{1}H and \textsuperscript{13}C NMR spectra, and mass spectra (see “Experimental”).

As shown in Table 1, the adducts (2-4, 6-8) obtained by the Lewis acid catalyzed reaction could easily be desulfurized into the corresponding benzodifurans (9-14) by heating with excess Raney nickel in ethanol.

A few synthetic methods for benzodifuran nucleus have so far been reported in the literature. The following methods are representative: 1) alkylation of 4,6-diacetylresorcinol with ethyl bromoacetate followed by saponification of the resulting ester and decarboxylative cyclization;\textsuperscript{6} 2) photocyclization of 1,2-di(2-furyl)ethene;\textsuperscript{8} 3) the double photocyclization of 1,5-dibenzoyl-2,4-dialkoxycyclohexene followed by dehydration;\textsuperscript{9} 4) the base-catalyzed dehydrative cyclization of an appropriate dialdehydodibenzyloxybenzene prepared from dimethoxybenzene with benzoyl chloride.\textsuperscript{9} Thus, these reports are rather limited on the synthesis of various benzodifuran isomers.

In summary, we developed a new route for synthesizing substituted benzodifuran derivatives using benzene diols with excess α-chloro-α-(methylthio)-
acetone (1) in the presence of zinc chloride. The advantages of the present method are as follows: the diverse and available benzene diols are directly utilized as the starting materials, and the sequence of reactions can be performed under rather mild conditions.

**EXPERIMENTAL**

**General.** Melting points were measured by an electrothermal digital melting point apparatus IA 9100 and uncorrected. IR spectra were obtained on a JASCO FT IR-300E spectrometer. NMR spectra were recorded on a JNM-ECP 400 spectrometer using tetramethylsilane as an internal standard. Mass spectra were obtained by electron impact (EI) method using a Hewlett Packard 5970 GC-MS system. TLC was run on a Merck precoated silica gel plates. Silica gel 60 (70-230 mesh, E. Merck) was used for all column chromatographic separations.

**α-Chloro-α-(methylthio)acetone (1):** N-Chloro-succinimide (10.5 g, 0.08 mol) was added to a stirred solution of α-(methylthio)acetone (8.2 g, 0.08 mol) in CCl₄ (40 mL) in small portions at 0 °C and the stirring was continued at room temperature for 3 h. The precipitated succinimide was filtered off and the solvent was removed in vacuo. The residual oil was distilled to give 1 (6.8 g, 63%), bp 55-56 °C/7 mmHg (lit. 76-77 °C/15 mmHg); ¹H NMR (400 MHz, CDCl₃) δ 2.19 (s, 3H), 2.37 (s, 3H), 5.38 (s, 1H).

**Typical procedure for the synthesis of substituted benzodifurans (2,3):** To a stirred solution of 1 (1.53 g, 11.0 mmol) and hydroquinone (550 mg, 5.0 mmol) in CH₂Cl₂ (30 mL) and THF (5 mL) was added ZnCl₂ (1.50 g, 11.0 mmol) at room temperature, and the stirring was continued at the same temperature for 40 min. The mixture was quenched with water and organic layer was separated. The organic layer was dried over anhydrous MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography (CCl₄) to afford 2 (348 mg) and 3 (458 mg) as white solids in 25% and 33%, respectively. The other compounds 4-8 were synthesized similarly and the spectroscopic data of the products 2-8 are as follows.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product (%)</th>
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<tbody>
<tr>
<td>2</td>
<td>9 (85)</td>
</tr>
<tr>
<td>3</td>
<td>10 (85)</td>
</tr>
<tr>
<td>4</td>
<td>11 (82)</td>
</tr>
<tr>
<td>6</td>
<td>12 (87)</td>
</tr>
<tr>
<td>7</td>
<td>13 (88)</td>
</tr>
<tr>
<td>8</td>
<td>14 (85)</td>
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*Reaction conditions: excess Raney nickel, EtOH, 60-70°C, 3 h. *Isolated yields.

**Table 1. The synthesis of desulfitized benzodifuran derivatives 9-14**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product (%)</th>
</tr>
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<tbody>
<tr>
<td>9 (83)</td>
<td></td>
</tr>
<tr>
<td>10 (85)</td>
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<td>11 (82)</td>
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<td>12 (87)</td>
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<td>13 (88)</td>
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<td>14 (85)</td>
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</table>
27-Dimethyl-3,6-dimethylthiobenzol[1,2-b:6,5-b']difuran (4): Rf=0.65 (CCL3); 52%; white solid, mp 94-95 °C; IR (KBr) 2983, 2919, 1595, 1431, 1374, 1274, 1173, 1113, 1067 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.19 (s, 6H), 2.38 (s, 6H), 7.36 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 12.56, 18.58, 94.20, 107.65, 108.39, 126.52, 151.96, 158.34; EI-MS (m/z) 278 (M⁺, 100%), 263, 248, 216, 203, 187, 159, 124, 115, 98, 69.

2.6.8-Trimethyl-3,5-dimethylthiobenzol[1,2-b:4,5-b']difuran (6): Rf=0.70 (CCl₃); 17%; white solid, mp 96-97 °C; IR (KBr) 2919, 2859, 1644, 1442, 1390, 1354, 1282, 1182, 1124 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.29 (s, 6H), 2.47 (s, 6H), 2.53 (s, 3H), 2.64 (s, 3H), 2.89 (s, 3H), 7.09 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 11.44, 12.37, 20.99, 91.62, 108.55, 123.28, 123.58, 151.86, 159.18; EI-MS m/z 292 (M⁺, 100%), 277, 262, 245, 230, 217, 201, 171, 131, 115, 95, 69.

2.4.6-Trimethyl-3,5-dimethylthiobenzol[1,2-b:5,4-b']difuran (7): Rf=0.71 (CCL3); 27%; white solid, mp 121-122 °C; IR (KBr) 2916, 1592, 1430, 1382, 1215, 1136, 1072 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.30 (s, 6H), 2.55 (s, 6H), 3.37 (s, 3H), 7.28 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 11.44, 12.37, 20.99, 91.62, 108.55, 123.28, 123.58, 151.86, 159.18; EI-MS m/z 292 (M⁺, 100%), 277, 262, 245, 229, 201, 187, 171, 146, 115, 87, 59.

Typical procedure for the synthesis of desulfurized benzdifuran (9):

Compound 2 (195 mg, 0.7 mmol) was heated under reflux in ethanol (40 mL) containing Raney nickel (W-2, ca. 2.5 g) for 3h. The Raney nickel was removed by filtration and the solvent was evaporated off. The residue was purified by column chromatography (CCl₃) to afford 9 (106 mg) as white solid in 83%. The other compounds 10-14 were prepared similarly from substituted benzdifulurans (3-4, 6-8) and the spectroscopic data 9-14 are as follows.

2.5-Dimethylbenzo[1,2-b:4,3-b']difuran (9): Rf=0.66 (CCL3); 83%; white solid, mp 109-110 °C; IR (KBr) 3114, 2913, 1585, 1419, 1269, 1221, 1155, 1043 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.49 (s, 6H), 6.50 (s, 2H), 7.25 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 12.42, 101.60, 105.74, 120.79, 151.16, 155.40; EI-MS m/z 186 (M⁺, 100%), 171, 157, 128, 115, 92, 77.

2.6-Dimethylbenzo[1,2-b:4,5-b']difuran (10): Rf=0.61 (CCL3); 85%; white solid, mp 117-118 °C; IR (KBr) 2957, 2912, 1612, 1428, 1374, 1283, 1171, 1112 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 2.45 (s, 6H), 6.38 (s, 2H), 7.40 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 14.27, 100.46, 102.74, 125.98, 151.74, 155.49; EI-MS m/z 186 (M⁺, 100%), 171, 157, 128, 115, 92, 77.

2.6-Dimethylbenzo[1,2-b:5,4-b']difuran (11): Rf=0.71 (CCL3); 82%; white solid, mp 83-84 °C; IR (KBr) 2964, 2914, 1609, 1435, 1349, 1277, 1125, 1084 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.45 (s, 6H), 7.37 (s, 2H), 4.23 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 13.21, 103.49, 93.41, 102.31, 109.04, 125.45, 152.47, 155.21; EI-MS m/z 186 (M⁺, 100%), 171, 157, 143, 128, 115, 92, 77.

2.6-Dimethylbenzo[1,2-b:5,4-b']difuran (12): Rf=0.69 (CCL3); 87%; white solid, mp 94-95 °C; IR (KBr) 2917, 1605, 1436, 1372, 1270, 1202, 1144, 1099 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.45 (s, 6H), 7.37 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 8.62, 14.25, 102.61, 103.89, 105.99, 125.01, 151.32, 154.95; EI-MS m/z 200 (M⁺, 100%), 185,
2,4,6-Trimethylbenzo|1,2-b:5,4-b’|difuran (13): $R_f = 0.64$ (CCl$_4$); 86%; white solid, mp 88-90°C; IR (KBr) 2916, 2856, 1599, 1436, 1366, 1269, 1211, 1092, 1049 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 2.45 (s, 6H), 2.54 (s, 3H), 6.40 (s, 2H), 7.28 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 14.23, 15.42, 90.92, 100.84, 118.97, 124.76, 152.28, 154.47. EIMS m/z 200 (M$^+$, 100%), 185, 171, 167, 128, 115, 100, 77.

2,4,7-Trimethylbenzo|1,2-b:5,6-b’|difuran (14): $R_f = 0.65$ (CCl$_4$); 85%; white solid, mp 64-65°C; IR (KBr) 2918, 2736, 1587, 1439, 1395, 1271, 1200, 1067 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 2.49 (s, 3H), 2.52 (s, 3H), 6.42 (s, 1H), 6.54 (s, 1H), 7.09 (s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 1406, 14.09, 18.88, 98.64, 101.75, 106.32, 111.89, 123.39, 124.60, 144.17, 153.25, 153.56, 154.02; EIMS m/z 200 (M$^+$, 100%), 185, 171, 157, 128, 115, 100, 84, 63.

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