A series of benzofuran ring system bearing various substituents at the C-2 position is widely distributed in nature and has recently become of interest in biological properties. There are well-known natural products having related benzofuran ring structures, particularly those isolated from Maderia gianescens.\(^1\) Ophryosporus chamae.\(^1\) Ophryosporus lorentzi.\(^1\) Krameria ramossissima.\(^1\) and Zanthoxylum atlanthondal.\(^1\)

For the carbon-carbon bond formation using 1-acyl-1-thiocarboxylations, we found that 2-methyl- and arylbenzofurans were easily prepared by the one-pot reaction of substituted phenols with 1-acyl-1-chlorosulfides in the presence of a Lewis acid.\(^4\) Also a facile one-pot procedure was developed, which offers 2-arylbenzofurans from substituted phenols using α-acylsulfides in the presence of p-toluenesulfonic acid.\(^7\)

In this paper, we report a new route for synthesizing of 2-arylbenzofuran derivatives from substituted phenols with α-acylsulfides (1,3,4) under Pummerer reaction conditions.

As preparation of the starting materials, α-(methylsulfinyl)acetophenone (1) was obtained from the oxidation of 2-(methylthio)acetophenone with sodium metaperiodate in aqueous methanol in 80% yield. The reactions of ethyl p-toluate and ethyl p-chlorobenzoate with methylsulfinyl carbanion\(^6\) afforded α-methylsulfinyl-p-methylacetophenone (3) and α-methylsulfinyl-p-chloroacetophenone (4) in 74% and 79% yields, respectively.

On the basis of our synthetic method\(^2\) for 2-arylbenzofurans using α-(methylsulfinyl)acetone under Pummerer reaction conditions, we first attempted the synthesis of 2-phenylbenzofurans 2 as illustrated in Scheme 1. Thus, treatment of equimolar amounts of substituted phenols and the sulfoxide 1 in 1,2-dichloroethane with three equivalents of anhydrous p-toluenesulfonic acid under reflux gave the compounds 2a-f in moderate yields. The spectroscopic data (mp, IR, and \(^1\)H NMR) were in good agreements with those reported by our pre-

\[\text{Scheme 1}\]
Scheme 2. Reagents and conditions: (i) MeSCH₂COAr, CH₂Cl₂, reflux, 1 h; (ii) Raney-Ni (W-2), EtOH, 60-65 °C, 1 h.

vious work on the synthesis of 2-methylthio-2-phenylbenzofurans under Friedel-Crafts reaction conditions. The procedure for desulfurization of the adducts 2a-f by heating with Raney nickel in ethanol was reported previously.

Secondly, we applied the above method to syntheses of 3-methylthio-2-(p-tolyl)benzofurans (5) and 3-methylthio-2-(p-chlorophenyl)benzofurans (6), in which the sulfoxides 3 and 4 are employed as electrophiles in place of 1. The Pummerer reactions of para-substituted phenols with 3 and 4 were carried out as shown in Scheme 2.

The treatment of equimolar amounts of para-substituted phenols and the sulfoxide 3 in the presence of three equivalents of p-toluene sulfonic acid afforded the compounds 5a-e in satisfactory yields. Also the compounds 6a-e were obtained from the reactions of para-substituted phenols and the sulfoxide 4 in the presence of p-toluene sulfonic acid.

The adducts (5, 6) given by the above Pummerer reaction can easily be desulfurized into the corresponding 2-arylbenzofurans (7, 8) by heating Raney nickel in ethanol. Thus, the adducts 5a-e and 6a-e were converted into 2-(p-tolyl)benzofurans 7a-e and 2-(p-chlorophenyl)benzofurans 8a-e, respectively, in high yields.

Of the many methods for the preparation of 2-arylbenzofuran ring, the route through the coupling reaction of an α-halophenol with a cuprous arylethylene has been regarded as an efficient procedure. This method requires uncommon starting materials and lengthy reaction time.

In conclusion, we developed a new one-pot method for the construction of 2-arylbenzofurans (2, 5, 6) using substituted phenols and α-acylsulfoxides (1, 3, 4) in the presence of anhydrous p-toluene sulfonic acid. This method is generally applicable to benzofuran moieties having various aryl groups at the C-2 position.

The Pummerer reactions for utilizing α-acylsulfoxides has been proved to be useful to synthesize the naturally occurring products possessing 2-arylbenzofuran skeleton.

**EXPERIMENTAL**

**General.** All reagents and solvents were used without further purification. Melting points were determined with a Gallenkamp capillary melting point apparatus and are uncorrected. 1H NMR spectra were recorded on a Hitachi R-1500 (TFT, 60 MHz) spectrometer. Chemical shifts are expressed in 8 units relative to tetramethylsilane as internal standard. IR spectra were recorded by using a JASCO FT IR-300E spectrometer. Mass spectral data were obtained on a Hewlett Packard 5700 GC MS system. Silica gel 60 (70-230 mesh, E. Merck) was used for all column chromatographic separations.

**5-(Methyl sulfonyl)acetophenone (1).** A solution of sodium metaperiodate (5.14 g, 24 mmol) in water (30 mL) was added in small portions to a stirred solution of 2-(methylthio)acetophenone (4 g, 24 mmol) in methanol (60 mL) at 0 °C and the mixture was further stirred at room temperature for 12 h. Inorganic materials were filtered off and the filtrate was extracted with chloroform (3 x 30 mL). The combined organic layer was dried over MgSO₄, and concentrated under reduced pressure. The residual solid was recrystallized from ethyl acetate to give 1 in 80% yield (3.49 g), mp. 86-87 °C (lit. 86-86.5 °C); IR (KBr) 3044, 2933, 1675 (C=O), 1577, 1422, 1299, 1193, 1030 (S=O), 978 cm⁻¹. 1H NMR (CDCl₃) 8 2.77 (s. 31), 4.39 (d, J=3.5 Hz, 211), 7.48-7.62 (m, 311), 7.98 (d, J=7.6 Hz, 211).

**General procedure for the synthesis of 3-methylthio-2-phenylbenzofuran (2).** A solution of 1 (1.1 mmol), substituted phenol (1.1 mmol), and anhydrous p-toluene sulfonic acid (3.3 mmol) in 1,2-dichloroethane (15 mL) was refluxed for 1 h. Then the mixture was cooled at room temperature, washed with water to remove p-toluene sulfonic acid, and dried over MgSO₄. The solvent was evaporated off, and the residue was purified by column chromatography (hexane:ethyl acetate=6:1) to give...
2a: Yield 80%, mp 67-68°C; 1H NMR (CDCl3) δ 2.37 (s, 3H), 2.48 (s, 3H), 6.80-8.37 (m, 8H).
2b: Yield 79%, mp 57-58°C; 1H NMR (CDCl3) δ 1.31 (t, J=7.6 Hz, 3H), 2.38 (s, 3H), 2.89 (q, J=7.6 Hz, 2H), 7.06-8.37 (m, 8H).
2c: Yield 82%, colorless liquid. 1H NMR (CDCl3) δ 81.33 (d, J=6.5 Hz, 6H), 2.38 (s, 3H), 2.84-3.31 (m, 1H), 7.10-8.36 (m, 8H).
2d: Yield 85%, colorless liquid. 1H NMR (CDCl3) δ 2.38 (s, 3H), 2.47 (s, 3H), 2.53 (s, 3H), 6.98-8.33 (m, 7H).
2e: Yield 53%, colorless liquid. 1H NMR (CDCl3) δ 2.32 (s, 3H), 2.42 (s, 3H), 2.49 (s, 3H), 6.86-8.22 (m, 7H). The above spectral data for 2 are in accord with those reported.

α-Methylsulfinyl-γ-methylecetoephene (3). A suspension of NaI (60% mineral oil dispersion, 2 g, 50 mmol) in DMSO (30 mL) was heated with stirring at 70-75°C for 40 min under Ar. After cooling to room temperature, THF (15 mL) was added to the reaction mixture. Ethyl p-toluene (3.28 g, 20 mmol) was added to the mixture at 0°C, and the stirring was continued for 90 min at the room temperature. The reaction mixture was poured into water (150 mL), acidified with aqueous HCl to pH 3-4, and then thoroughly extracted with chloroform (3 x 30 mL). The combined organic layer was washed with water (3 x 30 mL), dried over MgSO4, and evaporated off. The residual solid was recrystallized from ethyl acetate to give 3 in 74% yield (2.9 g), mp 113-114°C; IR (KBr) 2998, 2911, 2362, 2344, 1671 (C=O), 1605, 1569, 1411, 1278, 1186, 1131, 1044 (S=O), 961 cm⁻¹; 1H NMR (CDCl3) δ 2.44 (s, 3H), 2.75 (s, 3H), 4.33 (d, J=4.1 Hz, 2H), 7.31 (d, J=8.2 Hz, 2H), 7.89 (d, J=8.2 Hz, 2H); MS m/z 196 (M⁻).

α-Methylsulfinyl-p-chlorocetoephene (4). By the same procedure as described above for the preparation of 3, compound 4 was obtained from ethyl p-chloroacetate (3.69 g, 20 mmol). NaI (60% mineral oil dispersion, 2 g, 50 mmol), and DMSO (30 mL) in 79% yield (3.42 g). mp 126-127°C; IR (KBr) 3033, 2989, 2921, 2377, 2344, 1665 (C=O), 1588, 1422, 1288, 1033 (S=O), 767 cm⁻¹; 1H NMR (CDCl3) δ 2.76 (s, 3H), 4.36 (d, J=3.9 Hz, 2H), 7.49 (d, J=8.2 Hz, 2H), 7.94 (d, J=8.2 Hz, 2H); MS m/z 216 (M⁻).

General procedure for the synthesis of 3-methylthio-2-(p-tolyl) benzofuran (5). By the same procedure as described above for the preparation of 3, compound 5 was obtained from 3 (2 mmol), substituted phenol (2 mmol), and anhydrous p-toluene sulfonic acid (6 mmol). 5a: Yield 78%, mp 97-98°C; IR (KBr) 2918, 1499, 1472, 1332, 1272, 1256, 1202, 1187, 1078, 1016, 980 cm⁻¹; 1H NMR (CDCl3) δ 2.46 (s, 3H), 2.40 (s, 3H), 2.48 (s, 3H), 7.15-7.57 (m, 5H), 8.17 (d, J=8.2 Hz, 2H); MS m/z 286 (M⁻). 5b: Yield 83%, mp 66-67°C; IR (KBr) 2959, 2918, 1498, 1468, 1412, 1275, 1252, 2802, 1185, 1081, 1021, 969 cm⁻¹; 1H NMR (CDCl3) δ 2.31 (t, J=7.6 Hz, 2H), 2.37 (s, 3H), 2.41 (s, 3H), 2.79 (q, J=7.6 Hz, 2H), 7.11-7.54 (m, 5H), 8.17 (d, J=8.2 Hz, 2H); MS m/z 282 (M⁻). 5c: Yield 82%, colorless liquid. IR ( neat) 2952, 2920, 1613, 1511, 1470, 1420, 1352, 1204, 1184, 1078, 966 cm⁻¹; 1H NMR (CDCl3) δ 81.33 (d, J=7-0 Hz, 6H), 2.38 (s, 6H), 2.82-3.38 (m, 1H), 7.02-7.54 (m, 5H), 8.17 (d, J=8.2 Hz, 2H); MS m/z 296 (M⁻). 5d: Yield 68%, colorless liquid. IR ( neat) 2916, 2920, 2867, 1501, 1471, 1363, 1332, 1278, 1259, 1205, 1185, 1077, 1019, 969 cm⁻¹; 1H NMR (CDCl3) δ 1-42 (s, 9H), 2.37 (s, 6H), 7.11-7.69 (m, 5H), 8.17 (d, J=8.2 Hz, 2H); MS m/z 310 (M⁻). 5e: Yield 67%, mp 125-126°C; IR (KBr) 2971, 1497, 1465, 1442, 1254, 1126, 1187, 1076, 1065, 1012, 971 cm⁻¹; 1H NMR (CDCl3) δ 2.96 (s, 3H), 2.42 (s, 3H), 7.15-7.68 (m, 5H), 8.17 (d, J=8.2 Hz, 2H); MS m/z 288 (M⁻).

General procedure for the synthesis of 3-methylthio-2-(p-chlorophenyl) benzofuran (6). By the same procedure as described above for the preparation of 2, compound 6 was obtained from 4 (2 mmol), substituted phenol (2 mmol), and anhydrous p-toluene sulfonic acid (6 mmol). 6a: Yield 87%, mp 107-108°C; IR (KBr) 2920, 1486, 1470, 1401, 1254, 1202, 1090, 1074, 1010, 971 cm⁻¹; 1H NMR (CDCl3) δ 2.35 (s, 3H), 2.49 (s, 3H), 7.07-7.52 (m, 5H), 8.26 (d, J=8.7 Hz, 2H); MS m/z 288 (M⁻). 6b: Yield 90%, mp 64-65°C; IR (KBr) 2955, 2925, 2865, 1544, 1485, 1467, 1400, 1337, 1254, 1202, 1092, 1076, 1009, 969 cm⁻¹; 1H NMR (CDCl3) δ 1.31 (t, J=7.6 Hz, 3H), 2.37 (s, 3H), 2.79 (q, J=7.6 Hz, 2H), 7.11-7.52 (m, 5H), 8.25 (d, J=8.7 Hz, 2H); MS m/z 302 (M⁻). 6c: Yield 84%, mp 81-82°C; IR (KBr) 2952, 2919, 2862, 1543, 1463, 1422, 1402, 1383, 1254, 1204, 1177, 1094, 1077, 1012, 969 cm⁻¹; 1H NMR (CDCl3) δ 1.33 (d, J=7.0 Hz, 6H), 2.38 (s, 3H), 2.71-3.19 (m, 1H), 7.10-5.53 (m, 5H), 8.25 (d, J=8.72 Hz, 2H); MS m/z 316 (M⁻). 6d: Yield 90%, mp 83-84°C; IR (KBr) 2959.
General procedure for the synthesis of 2-(p-toly)benzofuran (8). By the same procedure as described above for the preparation of 7, compound 8 was obtained from 6 (1 mmol). Raney nickel (1.5 g), and ethanol (25 mL). The residual solid was reocrystallised from ethanol to give 8. 8a: Yield 88%, mp 186-187°C.

REFERENCES

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