

Total Synthesis of Norneolignans from *Krameria* Species

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The total synthesis of norneolignans isolated from *Krameria* species, 2-aryl-5-(*E*)-propenylbenzofurans (**5**, **11**), is described. The key step involves the one-pot reaction for 2-arylbenzofurans (**2**, **7**) from 4-hydroxyphenylacetone with 4'-acetoxy-2-chloro-2-(methylthio)acetophenone (**1**) and 2-chloro-2-methylthio-(2',4',6'-trimethoxy)acetophenone (**6**) under Friedel-Crafts reaction conditions.

Key words: Norneolignans, *Krameria* species, 2-Aryl-5-(*E*)-propenylbenzofurans, 4-Hydroxyphenylacetone, 4'-Acetoxy-2-chloro-2-(methylthio)acetophenone, 2-Chloro-2-methylthio-(2',4',6'-trimethoxy)acetophenone, Friedel-Crafts reaction

INTRODUCTION

2-(4-Hydroxyphenyl)-5-(*E*)-propenylbenzofuran (**5**) is a norneolignan isolated from *Krameria cystisoides* growing in central and south-west Mexico, and the root of this species is used for medicinal purposes including the treatment of stomach and bowel cancer. The structure of **5** was determined by its UV, ¹H- and ¹³C-NMR, and mass spectral characteristics (Achenbach *et al.*, 1987a). Also, 2-(2,4,6-trimethoxyphenyl)-5-(*E*)-propenylbenzofuran (**11**) is a constituent isolated from the Mexican *Krameria Ramosissima*, which is used to prepare a tea against diarrhoea and mild fevers. The structure of **11** was assigned through examination by its spectroscopic methods (Achenbach *et al.*, 1987b).

Among many procedures reported for the preparation of 2-arylbenzofuran ring, the route involving copper (I) arylacetylide substitution of an *o*-iodophenol is a relatively general good method (Lutjens and Scammells, 1998; Schreiber and Stevenson, 1976).

We recently reported that 2-arylbenzofurans could easily be produced by the Lewis acid-promoted reactions of substituted phenols with 1-acyl-1-chlorosulfides (Choi *et al.*, 1999; Seo *et al.*, 2000). Our method was applied to the total synthesis of a norneolignan (Choi *et al.*, 2002) from *Ratanhia radix* (Amone *et al.*, 1988).

In this paper, we describe the total synthesis of the naturally occurring norneolignans **5**, **11** isolated from the roots of the Mexican shrub, *Krameria* species (Achenbach *et al.*, 1987a, b).

MATERIALS AND METHODS

Chemical reagents and solvents were purchased from commercial supplies and used without purification. The melting points were determined by a Gallenkamp capillary melting point apparatus and were uncorrected. The IR spectra were obtained on a JASCO FT-IR 300E spectrophotometer. The ¹H-NMR (400 MHz) and ¹³C-NMR (100 MHz) spectra were recorded on a JEOL JNM-ECP 400 NMR spectrometer using tetramethylsilane as an internal standard. The MS spectra were measured on a Hewlett Packard 5973 GC/MS system by an electron impact method. Thin layer chromatography (TLC) was carried out using E. Merck silica gel 60 precoated plates. Silica gel 60 (70-230 mesh, E. Merck) was used for all column chromatographic separations.

4'-Acetoxy-2-chloro-2-(methylthio)acetophenone (**1**)

N-Chlorosuccinimide (2.67 g, 20 mmol) was added to a stirred solution of 4-acetoxy-2-(methylthio)acetophenone (4.48 g, 20 mmol) in carbon tetrachloride (90 mL) in small portions at 0°C, and with continuous stirring at room temperature for 10 h. The precipitated succinimide was filtered and the solvent was removed *in vacuo*. The residual solid was recrystallized from isopropyl ether to

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give **1** (3.18 g, 62%) as a white solid. mp 53–54°C; IR (KBr) 3060, 2979, 2925, 1762 (CO), 1688 (CO), 1594, 1501, 1419, 1366, 1276, 1195, 1002 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 2.25 (s, 3H), 2.33 (s, 3H), 6.30 (s, 1H), 7.23 (d, *J* = 8.76 Hz, 2H), 8.08 (d, *J* = 8.76 Hz, 2H); EI-MS (*m/z*) 260 (M⁺+2), 258 (M⁺), 178, 163, 151, 121 (100%), 107, 93, 79.

5-Acetylmethyl-2-(4-acetoxyphenyl)-3-(methylthio) benzofuran (**2**)

SnCl₄ (2.09 g, 8 mmol) was added to a stirred solution of compound **1** (2.07 g, 8 mmol) and 4-hydroxyphenylacetone (1.2 g, 8 mmol) in methylene chloride (40 mL) at 0°C under an Ar atmosphere, and the stirring was continued at the same temperature for 1 h. The reaction was quenched by adding water. The organic layer was separated and dried over anhydrous MgSO₄, and concentrated under the reduced pressure. The residue was purified by column chromatography (hexane/ethyl acetate = 1/1) to give **2** (1.45 g, 51%) as a white solid. mp 125–126°C; IR (KBr) 2927, 1749 (CO), 1713 (CO), 1470, 1366, 1202, 1165, 1075, 1016 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 2.19 (s, 3H), 2.33 (s, 3H), 2.36 (s, 3H), 3.83 (s, 2H), 7.15 (dd, *J* = 1.72, 6.72 Hz, 1H), 7.22 (d, *J* = 8.76 Hz, 2H), 7.46 (d, *J* = 8.44 Hz, 1H), 7.53 (br s, 1H), 8.33 (d, *J* = 6.84 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃) δ 18.39, 21.12, 29.22, 50.83, 108.98, 114.46, 120.58, 121.69, 126.46, 127.85, 128.34, 129.33, 131.54, 151.01, 152.27, 155.04, 169.18, 206.51; EI-MS (*m/z*) 354 (M⁺), 312, 269 (100%), 253, 237, 225, 194, 165, 126, 101, 89.

2-(4-Acetoxyphenyl)-5-(2-hydroxypropyl)benzofuran (**3**)

Compound **2** (1.13 g, 3.2 mmol) was heated under the reflux in ethanol (100 mL) containing Raney nickel (W-2, ca. 8 g) for 4 h. The Raney nickel was removed by filtration, and the solvent was allowed to evaporate. The residual solid was recrystallized from ethanol to give **3** (813 mg, 82%) as a white solid. mp 148–150°C; IR (KBr) 3357 (OH), 2966, 2928, 1757 (CO), 1463, 1371, 1236, 1116, 1023 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.27 (d, *J* = 6.08 Hz, 3H), 1.61 (br s, 1H), 2.32 (s, 3H), 2.82 (d, *J* = 5.95 Hz, 2H), 4.02–4.08 (m, 1H), 6.94 (s, 1H), 7.12 (dd, *J* = 1.76, 6.72 Hz, 1H), 7.18 (d, *J* = 8.72 Hz, 2H), 7.40 (s, 1H), 7.44 (d, *J* = 8.32 Hz, 1H), 7.86 (d, *J* = 8.68 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃) δ 21.12, 22.76, 45.64, 69.10, 101.17, 111.06, 121.37, 122.01, 125.74, 126.01, 128.22, 129.48, 133.16, 150.76, 153.89, 155.51, 169.29; EI-MS (*m/z*) 310 (M⁺), 268, 224 (100%), 194, 165, 152, 139, 116, 89.

2-(4-Acetoxyphenyl)-5-[2-(methylsulfinyloxy)propyl] benzofuran (**4**)

A solution of methanesulfonyl chloride (378 mg, 3.3 mmol) in methylene chloride (3 mL) was added to a

stirred solution of compound **3** (930 mg, 3 mmol) and triethylamine (334 mg, 3.3 mmol) in methylene chloride (20 mL) at 0°C, and the stirring was continued at the room temperature for 6 h. The reaction mixture was washed with 2% sodium carbonate (30 mL) and water (30 mL). The organic layer was separated and dried over anhydrous MgSO₄, and then concentrated under the reduced pressure. The residue was purified by column chromatography (hexane/ethyl acetate = 1/1) to give **4** (920 mg, 79%) as a white solid. mp 126–127°C; IR (KBr) 3024, 1761 (CO), 1498, 1465, 1353 (SO), 1200 (SO), 1020 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.49 (d, *J* = 6.32 Hz, 3H), 2.33 (s, 3H), 2.52 (s, 3H), 3.04 (d, *J* = 6.60 Hz, 2H), 4.90–4.95 (m, 1H), 6.95 (s, 1H), 7.14 (dd, *J* = 1.84, 6.60 Hz, 1H), 7.19 (d, *J* = 6.72 Hz, 2H), 7.43 (d, *J* = 1.42 Hz, 1H), 7.46 (d, *J* = 8.40 Hz, 1H), 7.86 (d, *J* = 8.84 Hz, 2H); ¹³C-NMR (100 MHz, CDCl₃) δ 21.13, 21.42, 37.81, 42.93, 81.67, 101.06, 111.16, 121.71, 122.07, 125.79, 126.07, 128.01, 129.54, 131.49, 150.92, 154.03, 155.85, 169.26; EI-MS (*m/z*) 338 (M⁺), 292, 250 (100%), 223, 202, 178, 165, 139, 121, 107.

2-(4-Hydroxyphenyl)-5-(*E*-propenyl)benzofuran (**5**)

A solution of compound **4** (970 mg, 2.5 mmol) and potassium *tert*-butoxide (337 mg, 3 mmol) in dimethylsulfoxide (15 mL) was stirred at room temperature for 20 h under an Ar atmosphere. The reaction mixture was acidified with 5% hydrochloric acid down to pH 3–4, and quenched by adding water (20 mL). The mixture was extracted with ethyl acetate (20 mL × 2). The combined extracts were dried over anhydrous MgSO₄, and evaporated off. The residue was purified by column chromatography (hexane/ethyl acetate = 1/1) to give **5** (531 mg, 85%) as a white solid. mp 208–209°C (Achenbach *et al.*, 1159–1156, 1987; 208–211°C); IR (KBr) 3408 (OH), 2918, 1607, 1503, 1437, 1254, 1110, 1033 cm⁻¹; ¹H-NMR (400 MHz, acetone-*d*₆) δ 1.81 (d, *J* = 6.72 Hz, 3H), 6.16–6.25 (m, 1H), 6.46 (br d, *J* = 15.76 Hz, 1H), 6.91 (d, *J* = 8.88 Hz, 2H), 6.98 (s, 1H), 7.26 (dd, *J* = 1.40, 7.28 Hz, 1H), 7.38 (br d, *J* = 8.44 Hz, 1H), 7.49 (br s, 1H), 7.73 (d, *J* = 8.72 Hz, 2H), 8.65 (s, 1H); ¹³C-NMR (100 MHz, acetone-*d*₆) δ 19.02, 100.66, 111.96, 117.16, 119.06, 123.33, 123.44, 125.24, 127.83, 131.36, 132.63, 134.72, 155.28, 158.20, 159.62; EI-MS (*m/z*) 250 (M⁺, 100%), 249, 231, 223, 202, 189, 178, 165, 129, 121, 107.

2-Chloro-2-methylthio-(2',4',6'-trimethoxy)acetophenone (**6**)

By the same procedure for the preparation of **1**, compound **6** was obtained from *N*-chlorosuccinimide (2.0 g, 15 mmol) and 2-methylthio-(2,4,6-trimethoxy)acetophenone (3.84 g, 15 mmol) as a white solid. yield 67% (2.92 g); mp 101–102°C (from isopropyl ether); IR (KBr) 2904, 1679 (CO), 1508, 1442, 1354, 1262, 1240, 1211, 1104, 1046

cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 2.19 (s, 3H), 3.81 (s, 6H), 3.83 (s, 3H), 6.09 (s, 1H), 6.11 (s, 2H); EI-MS (m/z) 292 (M⁺ + 2), 290 (M⁺), 229, 214, 195 (100%), 165, 152, 137, 109.

Acetylmethyl-2-(2,4,6-trimethoxyphenyl)-3-(methylthio)benzofuran (7)

By the same procedure for the preparation of 2, compound 7 was obtained from 6 (1.75 g, 6 mmol), 4-hydroxyphenylacetone (0.9 g, 6 mmol) and SnCl₄ (1.56 g, 6 mmol) as a white solid. yield 50% (1.16 g); mp 141-142 °C (from acetonitrile); IR (KBr) 2936, 2841, 1719 (CO), 1616, 1467, 1414, 1227, 1207, 1128, 1045 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 2.20 (s, 3H), 2.28 (s, 3H), 3.76 (s, 6H), 3.83 (s, 2H), 3.88 (s, 3H), 6.21 (s, 2H), 7.12 (dd, *J* = 1.80, 6.56 Hz, 1H), 7.46 (d, *J* = 8.36 Hz, 1H), 7.51 (br s, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 17.81, 21.19, 51.05, 55.41, 55.87, 90.65, 90.97, 100.58, 111.79, 112.56, 120.20, 125.37, 128.58, 130.53, 154.10, 160.43, 163.11, 206.89; EI-MS (m/z) 386 (M⁺, 100%), 343, 295, 267, 239, 193, 165, 139, 121, 105.

5-(2-Hydroxypropyl)-3-methylthio-2-(2,4,6-trimethoxyphenyl)benzofuran (8)

A solution of compound 7 (1.16 g, 3 mmol) in tetrahydrofuran (10 mL) was added to a stirred solution of LiAlH₄ (240 mg, 6 mmol) in tetrahydrofuran (30 mL) at room temperature, and the reaction mixture was refluxed for 2 h. The mixture was quenched by adding water (15 mL) and 10% H₂SO₄ (10 mL), and extracted with ethyl acetate (20 mL×2). The extracts were dried over anhydrous MgSO₄, and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/ethyl acetate = 1/1) to give 8 (1.07 g, 92%) in a white solid. mp 45-46°C; IR (KBr) 3410 (OH), 2925, 2833, 1618, 1577, 1458, 1419, 1227, 1155, 1128, 1047 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.29 (d, *J* = 6.12 Hz, 3H), 1.63 (br s, 1H), 2.29 (s, 3H), 2.87 (d, *J* = 4.64 Hz, 2H), 3.75 (s, 6H), 3.87 (s, 3H), 4.05-4.10 (m, 1H), 6.21 (s, 2H), 7.14 (dd, *J* = 1.72, 6.60 Hz, 1H), 7.45 (d, *J* = 8.28 Hz, 1H), 7.53 (d, *J* = 1.48 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 17.74, 22.73, 45.76, 55.37, 55.85, 69.18, 90.16, 100.70, 111.52, 112.44, 119.94, 125.40, 130.28, 132.73, 152.57, 153.86, 160.40, 163.04; EI-MS (m/z) 388 (M⁺, 100%), 370, 343, 297, 287, 221, 195, 177, 152, 121, 105.

5-(2-Hydroxypropyl)-2-(2,4,6-trimethoxyphenyl)benzofuran (9)

Compound 8 (854 mg, 2.2 mmol) was heated under the reflux in ethanol (50 mL) containing Raney nickel (W-2, ca. 2.5 g) for 2 h. The Raney nickel was removed by filtration, and the solvent was allowed to evaporate. The residue was purified by column chromatography (hexane/

ethyl acetate = 1/1) to give 9 (647 mg, 86%) as a high viscous oil. IR (neat) 3411 (OH), 2966, 2840, 1617, 1415, 1339, 1205, 1129, 1011 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.27 (d, *J* = 6.24 Hz, 3H), 2.17 (br s, 1H), 2.76 (d, *J* = 8.16 Hz, 2H), 3.80 (s, 6H), 3.87 (s, 3H), 4.01-4.06 (m, 1H), 6.21 (s, 2H), 6.75 (s, 1H), 7.08 (dd, *J* = 1.56, 8.32 Hz, 1H), 7.41 (br s, 1H), 7.45 (d, *J* = 8.36 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 22.61, 45.73, 55.38, 56.03, 69.17, 90.86, 102.18, 106.88, 111.05, 121.02, 124.69, 129.34, 132.17, 150.53, 153.71, 159.94, 162.26; EI-MS (m/z) 342 (M⁺, 100%), 297, 282, 267, 239, 209, 178, 163, 139, 115, 103.

5-[2-(Methylsulfinyloxy)propyl]-2-(2,4,6-trimethoxyphenyl)benzofuran (10)

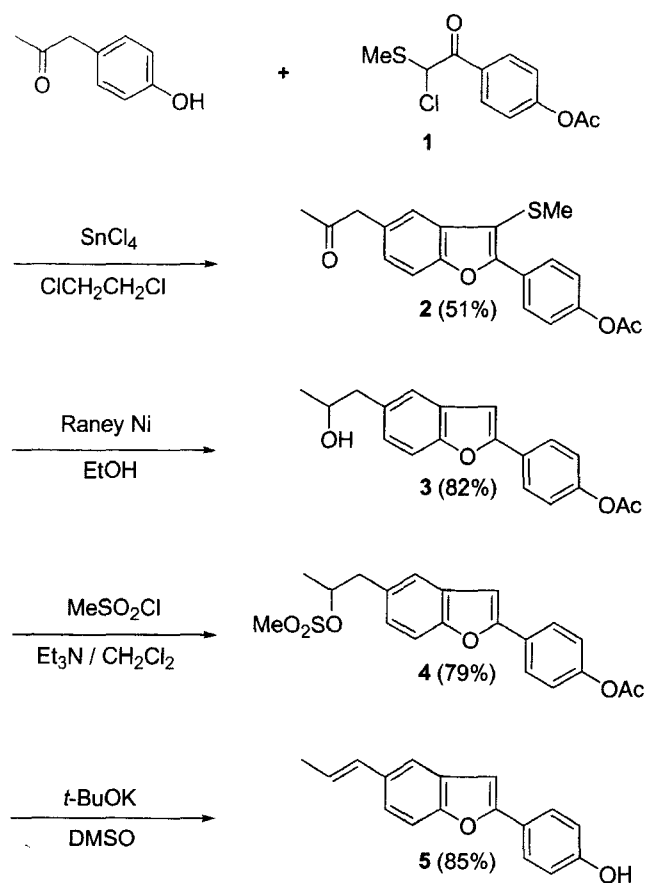
By the same procedure for the preparation of 4, compound 10 was obtained from 9 (684 mg, 2 mmol), methane-sulfonyl chloride (264 mg, 2.3 mmol) and triethylamine (233 mg, 2.3 mmol) as a white solid. yield 78% (655 mg); mp 140-141°C; IR (KBr) 2940, 2845, 1617, 1585, 1465, 1416, 1342 (SO), 1164 (SO), 1125, 1011 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.48 (d, *J* = 6.20 Hz, 3H), 2.56 (s, 3H), 3.08 (d, *J* = 7.08 Hz, 2H), 3.81 (s, 6H), 3.87 (s, 3H), 4.90-4.95 (m, 1H), 6.21 (s, 2H), 6.76 (s, 1H), 7.09 (dd, *J* = 1.76, 8.52 Hz, 1H), 7.42 (d, *J* = 1.4 Hz, 1H), 7.44 (d, *J* = 8.52 Hz, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 21.33, 37.88, 43.00, 55.41, 56.05, 81.87, 90.89, 102.01, 106.85, 111.06, 121.33, 124.71, 129.42, 130.49, 150.89, 153.81, 159.91, 162.29; EI-MS (m/z) 420 (M⁺), 324 (100%), 309, 281, 266, 178, 162, 129, 115, 103.

2-(2,4,6-Trimethoxyphenyl)-5-(*E*)-propenylbenzofuran (11)

By the same procedure for the preparation of 5, compound 11 was obtained from 10 (840 mg, 2 mmol) and *tert*-butoxide (270 mg, 2.4 mmol) as a white solid. yield 88% (570 mg); mp 140-141°C (Achenbach *et al.*, 2041-2043, 1987; 139-140°C); IR (KBr) 2936, 2844, 1614, 1583, 1462, 1197, 1127, 1052, 1001 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 1.88 (br d, *J* = 6.56 Hz, 3H), 3.79 (s, 6H), 3.86 (s, 3H), 6.08-6.23 (m, 1H), 6.20 (s, 2H), 6.49 (br d, *J* = 15.76 Hz, 1H), 6.74 (s, 1H), 7.24 (dd, *J* = 1.60, 8.28 Hz, 1H), 7.41 (br d, *J* = 8.32 Hz, 1H), 7.49 (br s, 1H); ¹³C-NMR (100 MHz, CDCl₃) δ 18.47, 55.38, 56.05, 90.89, 102.27, 107.15, 110.93, 117.71, 121.54, 123.81, 129.27, 131.41, 132.55, 150.46, 154.06, 159.97, 162.22; EI-MS (m/z) 324 (M⁺, 100%), 309, 281, 266, 178, 162, 129, 103.

RESULTS AND DISCUSSION

As shown in Scheme 1, we designed synthesis of target compound 5 starting from 4-hydroxyphenylacetone and 4'-acetoxy-2-chloro-2-(methylthio)acetophenone (1). The



Scheme 1. synthetic route of 2-(4-hydroxyphenyl)-5-(*E*)-propenylbenzofuran (**5**)

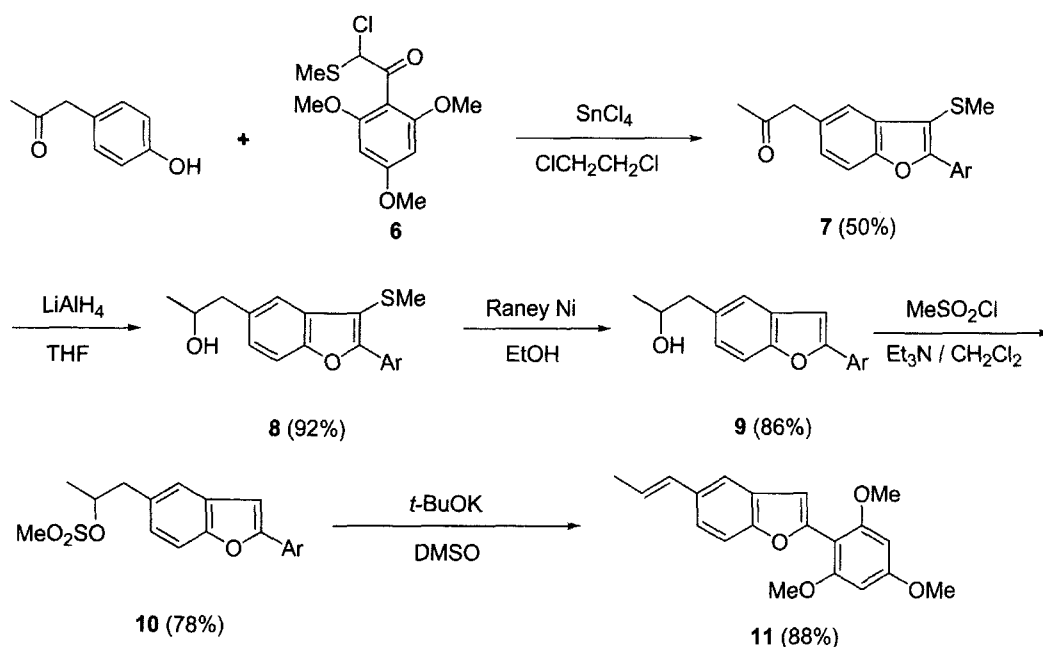
chloride **1** was prepared from 4'-acetoxy-2-(methylthio)acetophenone by the chlorination with *N*-chlorosuccinimide according to the procedure reported by Bohme and Krack in 1977.

The one-pot reaction of 4-hydroxyphenylacetone and the chloride **1** in the presence of SnCl_4 gave 5-acetylmethyl-2-(4-acetoxyphenyl)-3-(methylthio)benzofuran (**2**) in 51% yield. The structural assignment of **2** was made on the basis of spectroscopic evidence. The mass spectrum (M^+ , 354) of **2** showed the molecular ion peak to be $\text{C}_{20}\text{H}_{18}\text{O}_4\text{S}_1$. The IR spectrum of **2** revealed absorption bands for ketone (1713 cm^{-1}) and ester (1749 cm^{-1}). The ^1H - and ^{13}C -NMR spectra of **2** exhibited the corresponding signals due to its structural assignment.

For the reduction of ketone carbonyl group with the simultaneous desulfurization of carbon-sulfur bond in the compound **2**, the reaction of **2** was carried out under the conditions using a large excess Raney nickel in ethanol to give the reduced product **3** in 82% yield. The sulfonate **4** was obtained from the reaction of the alcohol **3** and methanesulfonyl chloride with triethylamine in 79% yield.

The desired norneolignan, 2-(4-hydroxyphenyl)-5-(*E*)-propenylbenzofuran (**5**), was produced by the elimination with concurrent hydrolysis of the sulfonate **4** using excess potassium *tert*-butoxide in 85% yield. The mp, ^1H - and ^{13}C -NMR data for **5** were in good agreement with those reported by Achenbach *et al.* in 1987a.

Next, 2-chloro-2-methylthio-(2',4',6'-trimethoxy)acetophenone (**6**) was used as the starting material in the synthesis of the target compound **11**. The chloride **6** was



Ar in **7**, **8**, **9**, **10** : 2,4,6-trimethoxyphenyl

Scheme 2. Synthetic route of 2-(2,4,6-trimethoxyphenyl)-5-(*E*)-propenylbenzofuran (**11**)

prepared from 2-methylthio-(2',4',6'-trimethoxy)acetophenone by the chlorination with *N*-chlorosuccinimide in 67% yield.

The one-pot reaction of 4-hydroxyphenylacetone with the chloride **6** in the presence of SnCl₄ afforded 5-acetylmethyl-2-(2,4,6-trimethoxyphenyl)-3-(methylthio)benzofuran (**7**) in 50% yield. The structure of **7** was assigned on the basis of spectroscopic data. The mass spectrum (M⁺, 386) showed the molecular formula to be C₂₁H₂₂O₅S. The infrared spectrum of **7** showed the presence of the carbonyl group (1719 cm⁻¹). The ¹H and ¹³C-NMR spectra of **7** appeared the corresponding signals due to its structural assignment. The reduction of carbonyl group in compound **7** with LiAlH₄ gave 5-(2-hydroxypropyl)-3-methylthio-2-(2,4,6-trimethoxyphenyl)benzofuran (**8**) in high yield. The reductive desulfurization of **8** with Raney nickel in ethanol afforded 5-(2-hydroxypropyl)-2-(2,4,6-trimethoxyphenyl)benzofuran (**9**) in 86% yield. The sulfonate **10** was obtained from the reaction of the alcohol **9** and methanesulfonyl chloride in 78% yield.

Finally the target compound, 2-(2,4,6-trimethoxyphenyl)-5-(*E*)-propenylbenzofuran (**11**) was produced by the elimination of the sulfonate **10** using potassium *tert*-butoxide in dimethylsulfoxide in 88% yield. The mp, ¹H- and ¹³C-NMR data for **11** were in good agreement with those of natural norneolignan reported in the literature (Achenbach *et al.*, 1987b).

Donnelly *et al.* in 1991 reported the first total synthesis of the norneolignan **11**, which proceeds in seven steps from *trans*-anethol in an overall yield of 14%. The key step of their method is arylation of benzofuranone by 2,4,6-trimethoxyphenyllead triacetate.

In conclusion, the total synthesis of a norneolignan (**5**) isolated from *Krameria cystisoides* was accomplished in four steps from 4-hydroxyphenylacetone in an overall yield 28%. Also, the total synthesis of a norneolignan **11** isolated *Krameria Ramosissima* was achieved in five steps from 4-hydroxyphenylacetone in an overall yield of 27%. Our preparation for 2-arylbenzofuran ring appears to provide a useful route for synthetic application of other natural products possessing substituted 2-arylbenzofurans.

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REFERENCES

- Achenbach, H., Gross, J., Dominguez, X. A., Cano, G., Star J. V., Brussolo, L. C., Munoz, G., Salgado, F., and Lopez L., Lignans, neolignans and norneolignans from *Krameria cystisoides*. *Phytochemistry*, 26, 1159-1166 (1987a).
- Achenbach, H., Gross, J., Dominguez, X. A., Star J. V., and Salgado, F., Ramosissin and othermethoxylated norneolignans from *Krameria Ramosissima*. *Phytochemistry*, 26, 2041-2043 (1987b).
- Amone, A., Modugno, V., Nasini, G., and Venturini, I., Isolation and structure determination of new active neolignans and norneolignans from *Ratanhia*. *Gazz. Chim. Ital.*, 118, 675-682 (1988).
- Bohme, H. and Krack, W., α -Chloroalkylsulfides and sulfoniumsalze. *Ann. Chem.*, 51-69 (1977).
- Choi, H. D., Seo, P. J., and Son, B. W., Synthesis of 2-arylbenzo[b]furan derivatives from substituted phenols. *J. Kor. Chem. Soc.*, 43, 606-608 (1999).
- Choi, H. D., Seo, P. J., and Son, B. W., Total synthesis of a norneolignan from *Ratanhia radix*. *Arch. Pharm. Res.*, 25, 786-788 (2002).
- Donnelly, D. M. X., Finet, J. P. and Kielty, J. M., Synthesis of a norneolignan from *Krameria Ramosissima*. *Tetrahedron Lett.*, 32, 3835-3836 (1991).
- Lutjens, H. and Scammells, P. J., Synthesis of natural products possessing a benzo[b]furan Skeleton. *Tetrahedron Lett.*, 39, 6581-6584 (1998).
- Schreiber, F. G. and Stevenson, R., Synthesis of benzofuran *Styrax* extractives. *J. Chem. Soc. Perkin Trans I*, 1514-1518 (1976).
- Seo, P. J., Ha, M. C., Choi, H. D., and Son, B. W., Synthesis of 2-(multimethoxyphenyl)benzo[b]furan derivatives from substituted phenols and application. *J. Kor. Chem. Soc.*, 44, 391-394 (2000).