Synthesis of *S*-2-Hydroxyphenyl Monothioacetals

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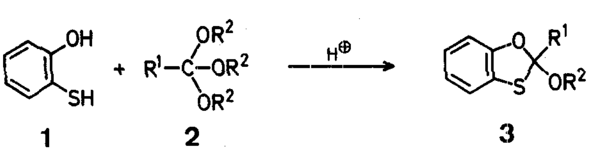
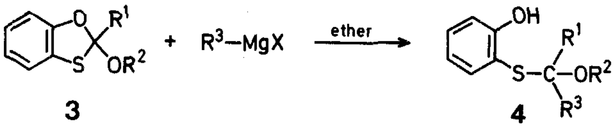
In a previous paper[1], we reported the synthesis of ethers by reaction of 2-OR-1,3-benzodioxoles with Grignard reagents. Analogous compounds containing C-S or C-N bonds are known to undergo selective cleavage of the C-O bond upon reaction with organomagnesium compounds[2, 3].

In the present paper, we report the synthesis of the hitherto unknown *S*-(2-hydroxyphenyl) *O*,*S*-acetals (**4**) from 2-alkoxy-1,3-benzoxathioles (**3**) and organomagnesium halides. Compounds **3** were obtained in good yields from 2-hydroxybenzenethiol and trialkyl orthocarboxylates.



	R^1	R^2
a	H	C_2H_5
b	CH_3	C_2H_5
c	C_6H_5	CH_3



	R^1	R^2	R^3
a$_1$	H	C_2H_5	CH_3
a$_2$	H	C_2H_5	C_6H_5
b$_1$	CH_3	C_2H_5	CH_3
b$_2$	CH_3	C_2H_5	C_6H_5
b$_3$	CH_3	C_2H_5	C_2H_5
c$_1$	C_6H_5	CH_3	CH_3

In contrast to our earlier experience in the series of the 2,2-dialkyl- and 2-aryl-1,3-benzoxathioles[4], the C—O bond cleavage in the monothioorthoesters **3** proceeds readily in diethyl ether and good yields are obtained. The 2-alkoxy-1,3-benzoxathioles **3** are probably more basic than diethyl ether; thus, the formation of the 1,3-benzoxathiole-Grignard complex is not inhibited[1]. Furthermore, performance of the cleavage reaction in ether prevents elimination side-reactions to a large extent and confines the bond cleavage to the 1,2-O-C bond of the heterocyclic ring[1].

All products **3** and **4** prepared gave satisfactory elemental analyses. The I.R.-and ^{1}H-N.M.R. spectra were in agreement with the proposed structure.

Microanalyses for C and H were carried out on a Perkin-Elmer Model 240 Elemental Analyzer; analyses for S were performed by the literature procedure[5, 6]. I.R. spectra were recorded on a Perkin-Elmer model 325 spectrophotometer, and ^{1}H-N.M.R. spectra were determined with a JEOL C-60 HL spectrometer. Tables 1 and 2 contain some characteristic I.R. and N.M.R. data for compounds **3** and **4**, respectively.

Preparation of 2-Alkoxy-1,3-benzoxathiols (3); General Procedure: A mixture of the trialkyl orthocarboxylate **2** (25.5 mmol), 2-hydroxybenzenethiol[7] (25 mmol), and conc. sulfuric acid (0.1 ml) is heated at 100° (oil bath) under a nitrogen atmosphere for 15 min. Then, a distillation device with a Vigreux column is attached. The mixture is heated at initially 120° and the temperature then raised to 180°. Ethanol (or methanol) (0.5 mol) distils over and is collected. The residual product in the flask is allowed to cool, diluted with ether, the solution washed successively with 10% sodium hydroxide solution and water, and dried with calcium chloride. The solvent is removed and the residue distilled under reduced pressure.

Preparation of *O*-Alkyl *S*-(2-Hydroxyphenyl) *O*,*S*-Acetals (4); General Procedure:
The Grignard reagent is prepared from the respective alkyl- or aryl halide (28 mmol) and magnesium turnings (29 mg-atom) in diethyl ether under a nitrogen atmosphere. A solution of the 2-alkoxy-1,3-benzoxathiole **3** (25.5 mmol) in ether (20 ml) is added dropwise with stirring and the mixture refluxed for ~24 h. The mixture is then poured into an ice-cold buffered solution (pH

Table 1. 2-Alkoxy-1,3-benzoxathioles (**3**) from 2-Hydroxybenzenethiol (**1**) and Trialkyl Orthocarboxylates (**2**)

3	Yield [%]	b.p./torr	n_D^{24}	Brutto formula[a]	I.R. (film) ν_{C-O} [cm^{-1}]	^{1}H-N.M.R. (CCl$_4$, HMDS) δ[ppm]
a	70	94–95°/1	1.5730	$C_9H_{10}O_2S$ (182.2)	1120, 1065, 960	6.85 (m, 4H$_{arom}$), 5.60 (s, 1H, $\geqslant C\underline{H}$), 3.50 (m, 2H, $-C\underline{H}_2-CH_3$), 1.15 (t, 3H, $-CH_2-C\underline{H}_3$).
b	77	95–96°/2	1.5542	$C_{10}H_{12}O_2S$ (196.3)	1125, 1070, 960	6.70 (m, 4H$_{arom}$), 3.40 (m, 2H, $-C\underline{H}_2-CH_3$), 1.90 (s, 3H, $\geqslant C-C\underline{H}_3$), 1.05 (t, 3H, $-CH_2-C\underline{H}_3$).
c	73	110/111°/1	1.5202	$C_{14}H_{14}O_2S$ (244.3)	1115, 1075, 970	7.20 (m, 9H$_{arom}$), 3.80 (s, 3H, $-C\underline{H}_3$).

[a] The elemental analyses (C, H, S) were in good agreement with the calculated values.

Table 2. *O*-Alkyl *S*-(2-Hydroxyphenyl) *O*,*S*-Acetals (**4**) from 2-Alkoxy-1,3-benzoxathioles (**3**) and Organomagnesium Halides

4	X	Yield [%]	b.p./torr	n_D^{24}	Brutto formula[a]	I.R. (film) ν_{OH} [cm^{-1}]	ν_{C-O} [cm^{-1}]	^{1}H-N.M.R. (CCl$_4$, HMDS) δ[ppm]
a$_1$	Br	75	155–156°/8	1.5619	$C_{10}H_{14}O_2S$ (198.3)	3410	1065, 960	6.90 (m, 4H$_{arom}$), 6.70 (s, 1H, O$\underline{H}$, D$_2$O exchanged), 5.10 (s, 1H, $\geqslant$C$\underline{H}$), 3.40 (m, 2H, —C$\underline{H}_2$—CH$_3$), 1.80 (s, 3H, $\geqslant$C—C$\underline{H}_3$), 1.20 (t, 3H, —CH$_2$—C$\underline{H}_3$).
a$_2$	Br	60	170–171°/7	1.5981	$C_{15}H_{16}O_2S$ (260.3)	3410	1065, 955	7.00 (m, 9H$_{arom}$), 6.90 (s, 1H, O$\underline{H}$, D$_2$O exchanged), 5.10 (s, 1H, $\geqslant$C$\underline{H}$), 3.40 (m, 2H, —C$\underline{H}_2$—CH$_3$), 1.15 (t, 3H, —CH$_2$—C$\underline{H}_3$).
b$_1$	J	70	158–159°/9	1.5614	$C_{11}H_{16}O_2S$ (212.3)	3410	1055, 970	6.80 (m, 4H$_{arom}$), 6.70 (s, 1H, O$\underline{H}$, D$_2$O exchanged), 3.45 (m, 2H, —C$\underline{H}_2$—CH$_3$), 2.00 (s, 3H, $\geqslant$C—C$\underline{H}_3$), 1.20 (t, 3H, —CH$_2$—C$\underline{H}_3$).
b$_2$	Br	58	167–168°/9	1.6181	$C_{16}H_{18}O_2S$ (274.4)	3410	1050, 965	7.10 (m, 9H$_{arom}$), 6.90 (s, 1H, O$\underline{H}$, D$_2$O exchanged), 3.40 (m, 2H, —C$\underline{H}_2$—CH$_3$), 1.20 (t, 3H, —CH$_2$—C$\underline{H}_3$).
b$_3$	Br	65	145–146°/4	1.5610	$C_{12}H_{18}O_2S$ (226.3)	3400	1055, 970	6.90 (m, 4H$_{arom}$), 6.65 (s, 1H, O$\underline{H}$, D$_2$O exchanged), 3.45 (m, 2H, —OC$\underline{H}_2$—CH$_3$), 2.55 (m, 2H, $\geqslant$C—C$\underline{H}_2$—CH$_3$), 1.90 (s, 3H, $\geqslant$C—C$\underline{H}_3$), 1.15 (m, 6H, —O—CH$_2$—C$\underline{H}_3$ and $\geqslant$C—CH$_2$—C$\underline{H}_3$).
c$_1$	J	72	100–102°/10	1.5280	$C_{15}H_{16}O_2S$ (260.3)	3400	1055, 970	7.20 (m, 9H$_{arom}$), 7.00 (s, 1H, O$\underline{H}$, D$_2$O exchanged), 3.75 (s, 3H, —OC$\underline{H}_3$), 1.50 (s, 3H, $\geqslant$C—C$\underline{H}_3$).

[a] The elemental analyses (C,H,S) were in good agreement with the calculated values.

10) of Titriplex II[8] and extracted with ether. The extract is dried with sodium sulfate, the solvent evaporated, and the residue distilled in vacuo.

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