Selective Preparation of 1-Halo-2,6-dimethoxybenzenes from Bis(2,6-dimethoxyphenyl)dimethyltin

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With a hope to explore a facile method for preparation of 1-halo-2,6-dimethoxybenzenes, bis(2,6-dimethoxyphenyl)dimethyltin was prepared from 1,3-dimethoxybenzene, butyllithium, and dimethyltin dichloride or dimethyltin sulfide. The compound reacted with *N*-chlorosuccinimide and with *N*-bromosuccinimide in methanol to afford 1-chloro-2,6-dimethoxybenzene and 1-bromo-2,6-dimethoxybenezene, respectively. The dimethyltin by-product was obtained either as dimethyltin oxide or as dimethyltin sulfide. A reaction with iodine was performed in the presence of potassium sulfide to afford 1-iodo-2,6-dimethoxybenzene and dimethyltin sulfide. Preparation and reactions of analogous organosilanes also are described.

As an extension of our chemistry on 2,6-dimethoxyphenyl derivatives,[1-3] we are interested in the preparation of 1-halo-2,6-dimethoxybenzenes ΦX [X=Cl, Br, I; Φ=2,6-$(MeO)_2C_6H_3$, see Figure 1]. It is

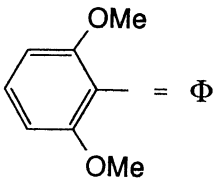

Fig. 1

well-known that the direct halogenation of 1,3-dimethoxybenzene ΦH affords a mixture of 1-halo-2,4-dimethoxybenzene and ΦX with the latter in poorer yields.[4-6] ΦX have been prepared, i) by the reactions of 2,6-dimethoxyphenyllithium ΦLi with elemental chlorine,[7,8] bromine,[7] iodine,[7,9] 1,2-dibromoethane,[7] or iodine cyanide;[7] ii) by methylation of 2-chloro-1,3-benzenediol;[10] iii) by decarboxylative bromination of 2,6-dimethyoxybenzoic acid;[11] iv) by the reaction of 2,6-dimethoxybenzenediazonium salt with pottasium iodide;[12] v) by the reaction of (2,6-dimethoxyphenyl)-trimethylsilane with *N*-bromosuccinimide (NBS);[5] or vi) by the reactions of 1,2,3-trimethoxybenzene with alkali metals followed by treatments with bromine or iodine.[13] The product yield by the method i) is not always satisfactory, as far as we have reexamined. The method v) is often accompanied by the protonation to afford ΦH. The other methods also require some special techniques, or the starting materials are often hard to obtain. In the present paper, we report a new and conventional preparative method of ΦX, which contains the preparation of bis(2,6-dimethoxyphenyl)dimethyltin $Me_2Φ_2Sn$ and its reactions with *N*-chlorosuccinimide (NCS), with NBS, or with elemental iodine in the presence of potassium sulfide (see Scheme 1).

Me_2SnCl_2 (or Me_2SnS) + 2ΦLi ⟶ $Me_2Φ_2Sn$

$Me_2Φ_2Sn$ + 2NCS + K_2S (or 2NaOH)
⟶ 2ΦCl + Me_2SnS (or Me_2SnO)

$Me_2Φ2Sn$ + 2NBS + K_2S (or 2NaOH)
⟶ 2ΦBr + Me_2SnS (or Me_2SnO)

$Me_2Φ_2Sn$ + $2I_2$ + K_2S ⟶ 2ΦI + Me_2SnS

Scheme 1.

Results and Discussion

The organolithium reagent ΦLi can be most easily prepared by mixing 15% hexane solution of butyllithium and ΦH in the presence of a catalytic amount of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) under argon.[3] The reagent is ready for the following reaction in less than 2 hours. Dimethyltin dichloride has been produced industrially for the use of electro-conducting glass (ITO) and is commercially available in pure grade. It can be handled in air and is soluble in diethyl ether and in water. The reaction of ΦLi with dimethyltin dichloride afforded $Me_2Φ_2Sn$ in 86% yield as air-stable crystals after recrystallization from alcohols or from hexane. Bis(2,6-dimethoxyphenyl)dimethylsilane and tris(2,6-dimethoxyphenyl)methylsilane also were prepared using dichlorodimethylsilane and trichloro-methylsilane, respectively, as crystalline compounds. The ^1H and ^{13}C NMR spectral data for the compounds obtained in the present study are summarized in Table 1 and 2, respectively.

The reaction $Me_2Φ_2Sn$ with NCS or NBS can be performed in air by stirring a 1 : 2 mixture of $Me_2Φ_2Sn$ and NCS or NBS (a slight excess) in methanol for one to two hours at room temperature. Addition of aqueous hydrochloric acid resulted in precipitation of ΦX in 79% (X=Cl) or 93% yield (X=Br). The acidic aqueous filtrate afforded white precipitates of dimethyltin oxide

Table 1. ^{1}H NMR Spectral Data[a] for 2,6-Dimethoxyphenyl Derivatives

Compounds	δ (ppm)[b]
$Me_2\Phi_2Sn$	7.21, 6.48, 3.63, 0.49[c]
$Me_2\Phi_2Si$	7.19, 6.44, 3.58, 0.57
$Me\Phi_3Si$	7.17, 6.43, 3.42, 0.81
ΦCl	7.18, 6.60, 3.90
ΦBr	7.23, 6.58, 3.90
ΦI	7.25, 6.50, 3.89
$Me[3\text{-}Br\text{-}2,6\text{-}(MeO)_2C_6H_2]_3Si$	7.44,[d] 6.46,[d] 3.44 and 3.41, 0.90

a) In $CDCl_3$; Φ=2,6-$(MeO)_2C_6H_3$. b) In the order of 4-H (triplet with J_H=8—9 Hz), 3,5-H (doublet with J_H=8—9 Hz), 2,6-CH_3O (singlet), and CH_3–Sn or –Si (singlet). c) The coupling constants with ^{117}Sn [59 Hz] and ^{119}Sn [62 Hz] were observed. d) Doublet.

Table 2. ^{13}C NMR Spectral Data[a] for 2,6-Dimethoxyphenyl Derivatives

Compounds	δ (ppm)[b]
$Me_2\Phi_2Sn$	118.9, 165.1, 103.6, 130.4, 55.6, −5.2
$Me_2\Phi_2Si$	117.2, 165.1, 104.1, 130.3 55.4, 2.5
$Me\Phi_3Si$	118.7, 165.1, 104.1, 129.4, 55.4, 3.2
ΦCl	110.7, 156.3, 104.7, 127.1, 56.4
ΦBr	101.0, 157.2, 104.7, 128.2, 56.5
ΦI	77.7, 159.6, 104.1, 129.8, 56.6
$Me[3\text{-}Br\text{-}2,6\text{-}(MeO)_2C_6H_2]_3Si$	124.4, 164.6 and 161.4, 107.8 and 107.5, 134.4, 60.6 and 55.2, 3.3

a) In $CDCl_3$; Φ=2,6-$(MeO)_2C_6H_3$. b) In the order of 1-C, 2,6-C, 3,5-C, 4-C, 2,6-CH_3O, and CH_3–Sn or –Si.

on treatment with aqueous sodium hydroxide, or it afforded dimethyltin sulfide on treatment with potassium sulfide. The sulfide is reusable for the preparation of the starting compound $Me_2\Phi_2Sn$.

The reaction of $Me_2\Phi_2Sn$ with iodine was performed in diethyl ether at room temperature in the presence of aqueous potassium sulfide. In the absence of potassium sulfide, the second Φ-group was inert. Crystals of ΦI were obtained in 83% yield, and the dimethyltin compound was recovered as crystals of dimethyltin sulfide in 69% yield.

The crystals of ΦX are in general very soluble in acetone, benzene, and tetrahydrofuran. They can be recrystallized from methanol, 2-propanol, and hexane, but are insoluble in water. The ^{1}H NMR spectra of ΦX (Table 1) show a very sharp resonance at δ=3.9 due to the two methoxyl protons, a triplet around δ=7.2, and a doublet in the region of δ=6.6—6.5. The ^{13}C NMR spectra of ΦX (Table 2) consist of five resonances, of which *ipso* carbon resonance is most sensitive to the change of halogen atom, appearing at higher magnetic field in the order of X=Cl<Br<H (δ=100.5)<I.

In our preliminary experiments, reactions of NCS with $Me_2\Phi_2Si$ and $Me\Phi_3Si$ resulted in the formation of ΦH. The reaction of NBS with $Me_2\Phi_2Si$ afforded ΦBr in 65—50% yield, while that of $Me\Phi_3Si$ resulted in bromination of Φ-groups to afford tris(3-bromo-2,6-dimethoxyphenyl)methylsilane.

Experimental

Physical Measurements. ^{1}H and ^{13}H NMR spectra were recorded for solutions in $CDCl_3$ using a JEOL model JNM-GX-270 spectrometer. IR spectra were recorded for Nujol mull using Shimadzu FTIR-4200 specrophotometer.

Preparation of Bis(2,6-dimethoxyphenyl)dimethyltin. The organolithium reagent ΦLi was prepared from 1,3-dimethoxybenzene (7.2 ml, 55 mmol), 15% hexane solution of butyllithium (34 ml, 55 mmol), and *N,N,N'N'*-tetramethylethylenediamine (TMEDA) (0.2 ml). The reagents were mixed under argon at 0°C, and the mixture was stirred at room temperature for 1—2 h to afford white suspension of ΦLi. The suspension was added under argon to a suspension of dimethyltin dichloride (5.49 g, 25 mmol) in diethyl ether (10 ml) at 0°C, and the mixture was stirred at room temperature for 3 h. It was washed with water, the organic layer was concentrated under reduced pressure, and the resultant precipitates were recrystallized from hexane or methanol to afford white crystals of $Me_2\Phi_2Sn$ 86% yield. Mp 93—94°C. Anal. ($C_{18}H_{25}O_4Sn$) C, H.

$Me_2\Phi_2Sn$ also was obtained by analogous treatments of ΦLi suspension (11 mmol) with dimethyltin sulfide (0.905 g, 5 mmol) in diethyl ether (50 ml in total). The mixture was stirred at room temperature for 5 h under argon. It was washed with water, the volatile materials in organic layer were removed under reduced pressure, and the residue was recrystallized from methanol to give $Me_2\Phi_2Sn$ in 64% yield.

Preparation of 2,6-Dimethoxyphenylsilanes. $Me_2\Phi_2Si$. To a suspension of ΦLi, prepared as aboved from 1,3-dimethoxybenzene (50 mmol), 15% hexane solution of butyllitium (50 mmol), and TMEDA (0.15 ml) in diethyl ether (100 ml), was added dichlorodimethylsilane (2.7 ml, 22.3 mmol) under argon at 0°C, and the mixture was stirred at room temperature overnight. It was washed with a saturated aqueous solution (100 ml) of ammonium chloride and then with water. The organic layer was concentrated under reduced pressure to ca. one third volume. The resultant precipitates were recrystallized from methanol to afford white crystals of $Me_2\Phi_2Si$ in 82% yield. Mp 104—105°C. Anal. ($C_{18}H_{24}O_4Si$) C, H.

$Me\Phi_3Si$. A suspension of ΦLi was prepared as above from 1,3-dimethoxybenzene (50 mmol), 15% hexane solution of butyllithium (50 mmol), and TMEDA (0.15 ml) in diethyl ether (100 ml), to which was added trichloromethylsilane (1.5 ml, 14.8 mmol) under argon at 0°C, and the mixture was stirred at room temperature overnight. Methanol (150 ml) was added, and the mixture was concentrated under reduced pressure to ca. one third volume. The resultant precipitates were recrystallized from methanol or hexane to afford $Me\Phi_3Si$ in 53% yield. Mp 130—131°C. Anal. ($C_{25}H_{30}O_6Si$) C, H.

Reactions of Bis(2,6-methoxyphenyl)dimethyltin. With NCS. To a suspension of $Me_2\Phi_2Sn$ (2.12 g, 5 mmol) in methanol (20 ml) was added NCS (1.64 g, 12 mmol). The

mixture was stirred at room temperature for 1 h to afford a yellow solution. Hydrochloric acid (6 M (1 M=1 mol dm^{-3}), 2 ml) was added to afford white precipitates of ΦCl in 79% yield. Mp 68—69 °C (reported[8] 69—71 °C). The fitrate was treated with aqueous sodium hydroxide (an excess) to afford white precipitates of dimethyltin oxide[14] in 63% yield; IR 480 cm^{-1} (Sn–O–Sn). In another experiment, aqueous potassium sulfide (1 M, 10 ml) was added to the filtrate. The resultant solution was kept at room temperature for two days to afford colorless crystals of dimethyltin sulfide in 69% yield; mp 149—150 °C (reported[15] 149 °C).

With NBS. An analogous mixture of $Me_2Φ_2Sn$ (5 mmol) and NBS (2.14 g, 12 mmol) in methnol (20 ml) was stirred at room temperature for 1—2 h. The resultant suspension was poured into 0.3 M hydrochloric acid (40 ml) to afford white precipitates of ΦBr in 95% yield. Mp 90—92 °C (reported 91—93 °C[13]; 93—94 °C[7]). The filtrate was treated with aqueous sodium hydroxide (an excess) to afford white precipitates of dimethyltin oxide[14] in 75% yield. In another experiment, the filtrate was treated with aqueous potassium sulfide, as above, to afford crystals of dimethyltin sulfide in 78% yield.

With Iodine in the Presence of Potassium Sulfide. To a two-layer mixture of a solution of $Me_2Φ_2Sn$ (5 mmol) in diethyl ether (5 ml) and 1 M aqueous solution of potassium sulfide (6 ml) was added under stirring at room temperature a solution of iodine (2.33 g, 11 mmol) dissolved in diethyl ether (35 ml). The mixture was stirred vigorously at room temperature for 24 h. The ethereal layer was concentrated to ca. one forth volume under reduced pressure to afford white precipitates of ΦI in 83% yield. Mp 101—102 °C (reported 102—103 °C;[13] 103 °C[7]). Volatile materials of the filtrate were removed under reduced pressure. The residue was dissolved in methanol (40 ml), and 1 M hydrochloric acid (5 ml) was added. The solution was kept at −30 °C overnight as above to afford colorless crystals of dimethyltin sulfide in 69% yield.

Reactions of 2,6-Dimethoxyphenylsilane. $Me_2Φ_2Si$ with NBS. A mixture of $Me_2Φ_2Si$ (0.332 g, 1 mmol) and NBS (2.1 mmol) in acetone (6 ml) was stirred at room temperature overnight. The solvent was removed under reduced pressure, and the residue was washed with hexane to leave ΦBr in 64% yield.

$MeΦ_2Si$ with NBS. A mixture of $MeΦ_3Si$ (0.454 g, 1 mmol) and NBS (3 mmol) in acetone (20 ml) was stirred for 1 h. The solvent was removed under reduced pressure, and the residual materials were treated with hexane (10 ml) and water. From the organic layer on cooling to −30 °C, white crystals of Me[3-Br-2,6-$(MeO)_2C_6H_2]_3Si$ were obtained in 63% yield. Mp 140—142 °C. Anal. ($C_{25}H_{27}Br_3O_6Si$) C, H.

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