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NUCLEOPHILIC SUBSTITUTION AT SILICON: SYNTHESIS OF STERICALLY-HINDERED BIS(2,6-DI-t-BUTYLARYLOXY)SILANES

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Summary

The reaction of the monomethylsilane (**8a**) with two equivalents of the 4-(carboalkoxy)-2,6-di-t-butyl-substituted phenol (**7b**) in toluene using triethylamine as an acid acceptor gave the bis(aryloxy) adduct (**9a**). The analogous reaction of the dimethylsilane (**8b**) with sodium 2,6-di-t-butyl-4-(methoxycarboxyl)-phenolate (**7a**) gave only the monosubstitution product (**10a**). The reaction of the corresponding phenolate (**7e**) with **8b** gave a mixture of **7a**, **10a**, and bis-adduct (**9b**), whereas, in the presence of 15-crown-5, the bis-adduct **9b** was obtained. The bis-adducts **9c**–**e** were prepared in an analogous manner. The reaction of n-hexyl 3,5-di-t-butyl-4-hydroxylbenzoate (**7h**) with the diphenylsilane (**8c**) gave only the monosubstitution product **12**, while forcing conditions gave, unexpectedly, the methyl ether **13**. The reaction of 4-(carboalkoxyethyl)-2,6-di-t-butylphenol (**16a**) with **8a** gave the bis adduct. The reaction of **16a** with **8b** in THF, without a crown ether, gave a low yield of the monosubstitution product. The bis-adducts **17b**–**c** were obtained by the reaction of **8b** with the corresponding phenolates (**16a**–**b**) in tetraglyme. Compound **17b** was also obtained by the reaction of **8b** with **16a** in THF with a crown ether. These results are discussed in terms of charge dispersal in the phenolate ion and the corresponding effect upon both ion-pairing and aggregation in solution.

Introduction

The study of reactions involving silicon has encompassed a multitude of chemical disciplines. In particular, both the study of the nucleophilic substitution of halogen at silicon and the resultant silylated molecules have received considerable attention in the chemical literature [1]. Despite the importance of substitution reactions at silicon, the substitution of halogen at silicon by sterically-hindered aryloxy nucleophiles has received scant mention in the chemical literature [2], although reports are found in the patent literature [3].

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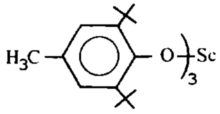

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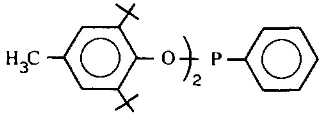

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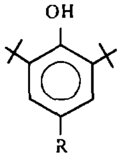
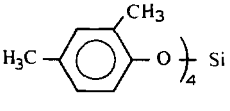


(3a, R = methyl ; 3b, R = t-butyl)



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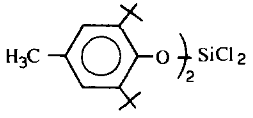

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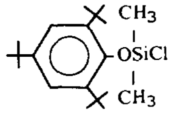

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Recently, considerable attention has been given to the reaction of sterically-hindered phenols with metal halides to prepare aryloxymetal derivatives of both the main group elements and transition metals [4]. The scandium derivative **1**, for example, is monomeric in solution and exhibits an unusual coordination number of three [5]. Quite recently, we reported the preparation of the sterically-hindered phosphonite **2** by the reaction of phenyldichlorophosphine with **3a** [6].

Considerably less is known about the reaction of sterically-hindered phenols with chlorosilanes. Liu and Lin reported the 2,4-dimethylphenoxysilane derivative **4** [7]. Gümrükçüoğlu reported the synthesis of **5** by the reaction of silicon tetrachloride with the lithium salt of **3a** in the presence of 18-crown-6 [8]. The 2,4,6-tri-t-butyl derivative **6**, recently employed by House, was shown by Manis and Rathke to be superior to t-butyldimethylsilyl chloride as a protecting group for enol ethers [9]. Our laboratory has reported the synthesis of the dibenzo[*d*,*f*][1,3,2]dioxasilepin, dibenzo[*d*,*g*][1,3,2]dioxasilocin, and dibenzo[*d*,*g*][1,3,6,2]dioxathiasilocin ring systems by the reaction of sterically-hindered bisphenols with chlorosilanes [10].

We report in this paper a systematic study of the reaction of sterically-hindered 2,6-di-t-butyl phenols with chlorosilanes.

Experimental

All melting points were determined in open capillary tubes with a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra (1% solution in sodium chloride cells) were recorded on a Perkin-Elmer Model 710 or 1300 spectrophotometer. ^1H NMR spectra were taken on either a Varian Model XL-100, XL-200, or CFT-20 spectrometer. All ^1H chemicals shifts are reported in ppm relative to tetramethylsilane.

Whatman DCS-1F silica gel was used for dry-column chromatography [11]. Merck 9385 silica gel-60 (230–400 mesh) was used for flash chromatography [12]. Merck pre-coated (0.25 mm) silica-gel 60 F-254 plates were used for TLC.

Mass spectra were obtained on a Finnigan Model 8200 mass spectrometer. All solvents were dried prior to use. THF was distilled immediately prior to use from a deep blue solution of sodium ketyl (sodium/benzophenone). Toluene was dried over 4Å molecular sieves. Tetraglyme was dried by passing through a column of alumina.

Reagents were purchased from commercial laboratory supply houses. Reactions were carried out in flame-dried apparatus under a dry-nitrogen atmosphere. Elemental analyses were performed by Analytical Research Services, Ciba-Geigy.

n-Hexyl 3,5-di-t-butyl-4-hydroxybenzoate (7a)

In a flask equipped with a Dean-Stark trap, a mixture of 100.1 g (0.4 mol) of 3,5-di-t-butyl-4-hydroxybenzoic acid, 63.1 g (0.6 mol) of *n*-hexyl alcohol, and 7.6 g (40 mmol) of *p*-toluenesulfonic acid was heated to 100 ° C over a 40 min period. The reaction mixture was heated from 100 to 142° C over a 3-h period during which time the water of reaction was collected in the Dean-Stark trap. The excess hexyl alcohol was removed by bulb-to-bulb (Kugelrohr) distillation (80–90 ° C/0.8 mmHg) and the residue was recrystallized from methyl alcohol to give 95.9 g (72%) of fine white needles: m.p. 73.0–73.5 ° C (lit. [13] 70–72° C); IR (CH_2Cl_2) ν 3620 (OH), 1705 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (t, 3H), 1.25 (complex m, 8H), 1.48 (s, $C(CH_3)_3$, 18H), 4.26 (t, OCH_2, 2H), 5.60 (s, OH, 1H), 7.85 (s, 2H). Anal. Found: C, 75.3; H, 10.0. $C_{12}H_{34}O_3$ calc: C, 75.4; H, 10.3%.

n-Dodecyl-3,5-di-t-butyl-4-hydroxybenzoate (7b)

Following the method used to prepare **7a**, compound **7b** was prepared from 100.1 g (0.40 mol) of 3,5-di-t-butyl-4-hydroxybenzoic acid, 100.6 g (0.54 mol) of *n*-dodecyl alcohol and 7.6 g (40 mmol) of *p*-toluenesulfonic acid [14]. After removal of excess *n*-dodecyl alcohol by bulb-to-bulb (Kugelrohr) distillation, the residue was recrystallized from methyl alcohol and the product was washed with cold ethyl alcohol. The product was triturated with cold methanol to give a white solid: m.p. 56.0–56.5 ° C (lit. [13] 47–53° C); IR (CCl_4) ν 3620 (OH), 1715 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (t, 3H), 1.25 (complex m, 20H), 1.48 (s, $C(CH_3)_3$, 18H), 4.21 (t, OCH_2, 2H), 5.60 (s, OH, 1H), 7.82 (s, 2H), Anal. Found: C, 77.5; H, 11.1. $C_{27}H_{46}O_3$ calc: C, 77.5; H, 11.1%.

n-Octadecyl-3,5-di-t-butyl-4-hydroxybenzoate (7c)

To a solution of 25.39 g (0.2 mol) of oxalyl chloride in 200 ml of dichloromethane was added 50.07 g (0.2 mol) of 3,5-di-t-butyl-4-hydroxybenzoic acid. The reaction mixture was stirred 3 h at r.t. To the reaction mixture at 0 ° C was added sequentially 54.10 g (0.2 mol) of *n*-octadecyl alcohol and 15.82 g (0.2 mol) of pyridine and the resultant mixture was stirred overnight. The reaction mixture was extracted sequentially with 10% aqueous potassium carbonate (2 ×) and with water, and the organic phase was dried over anhydrous sodium sulfate.

The solvent was removed in vacuo and the residue was recrystallized from methyl alcohol to give 82.67 g (82%) of a white solid: m.p. 68–69 ° C (lit. [13] 65–67 ° C): IR ($CHCl_3$) ν 3630 (OH), 1705 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, 3H), 1.28 (complex m, 32 H), 1.47 (s, $(CH_3)_3C$, 18H), 4.28 (t, OCH_2, 2H), 5.66 (s, OH, 1H), 7.94 (s, 2H). Anal. Found: C, 78.6; H, 11.8. $C_{33}H_{58}O_3$ calc: C, 78.8; H, 11.6%.

Methyl 3,5-di-t-butyl-4-hydroxybenzoate (7d)

To 1.6 l of methyl alcohol saturated with anhydrous hydrogen chloride at 15 ° C was added 500 g (2 mol) of 3,5-di-t-butyl-4-hydroxybenzoic acid. The resultant heterogeneous mixture was heated at reflux for 10 h. The reaction mixture was cooled overnight and the resultant crystals were collected by filtration. The crude product was dissolved in 1.25 l of hot chloroform and any insolubles were removed by filtration. The solvent was removed in vacuo and the residue was recrystallized from a 20/1 mixture of isopropyl alcohol and water to give 447 g (84%) of a white solid: m.p. 163–164 ° C (lit. [15] 162–164 ° C): IR (CH_2Cl_2) ν 3620 (OH), 1710 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (s, $C(CH_3)_3$, 18H), 3.89 (s, 3H), 5.71 (s, 1H), 7.96 (s, 2H). Anal. Found: C, 72.8; H, 9.4. $C_{16}H_{24}O_3$ calc: C, 72.7; H, 9.2%.

*Bis[2,6-di-t-butyl-4-(n-dodecyloxycarbonyl)phenoxy]methylsilane (**9a**)*

To a solution of 4.04 g (40 mmol) of triethylamine in toluene cooled with an ice bath was added dropwise sequentially 2.30 g (20 mmol) of **8a** and a solution of 16.7 g (40 mmol) of **7b** in 100 ml of toluene. The reaction mixture was stirred at r.t. for 48 h and then the suspension of triethylamine hydrochloride was removed by filtration. The solvent was removed in vacuo and the residue was recrystallized twice from a mixture of acetonitrile and toluene to give 2.70 g (8%) of a white solid: m.p. 55.5–56.5 ° C; IR (CCl_4) ν 2200 (SiH), 1715 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.27 (d, $SiCH_3$, 3H), 0.83 (t, CH_3, 6H), 1.29 (complex m, 40H), 1.49 (s, $C(CH_3)_3$, 36H), 4.29 (t, OCH_2, 4H) 5.65 (q, SiH, 1H), 7.95 (s, 4H).

*Reaction of 2 / 1 molar ratio of **7a** / **8b** in toluene*

To a stirred solution of 3.23 g (25 mmol) of **8b** in 50 ml of toluene at 5–10 ° C was added dropwise a solution of 16.73 g (50 mmol) of **7a** and 5.06 g (50 mmol) of triethylamine in 75 ml of toluene. The reaction mixture was heated at 85–90 ° C for 10 h. The TLC of the reaction mixture (7/3 heptane/ethyl acetate eluent) showed a spot corresponding to starting **7a** ($R_f = 0.51$) and a new slower moving spot which was assigned to **10a** ($R_f = 0.43$). In the IR spectrum of the reaction mixture, an absorption was observed at 3620 cm^{-1} corresponding to starting benzoate **7a**. The suspension was filtered to give 3.76 g (55% of theory) of triethylamine hydrochloride. The filtrate was concentrated in vacuo. The ^1H NMR of the residue showed a singlet resonance at δ 7.85 corresponding to the aromatic protons of **7a** and two new singlet resonances at δ 0.68 and 7.94 which were assigned to the protons of the methyl group bonded to silicon and the aromatic protons, respectively, of **10a**.

*2,6-di-t-butyl-4-(n-hexyloxycarbonyl)phenoxychlorodimethylsilane (**10a**)*

To a solution of 3.23 g (25 mmol) of **8b** in 50 ml of toluene was added dropwise a solution of 8.36 g (25 mmol) of **7a** and 2.52 g (25 mmol) of triethylamine in 50 ml of toluene. The reaction mixture was heated at 77 ° C for 26 h and then the triethylamine hydrochloride was removed by filtration. The solvent was removed in vacuo [16] and the residue was bulb-to-bulb distilled (Kugelrohr) to give 7.83 g (73%) of a lt. amber liquid: b.p. 140–147 ° C/0.1 mmHg; IR(CH_2Cl_2) ν 1710 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.68 (s, $Si(CH_3)_2$, 6H), 0.90 (t, CH_3, 3H), 1.34 (complex m, 8H), 1.45 (s, $C(CH_3)_3$, 18H), 4.23 (t, OCH_2, 2H), 7.94 (s, 2H). Anal. Found: C, 64.9; H, 9.5. $C_{23}H_{39}O_3SiCl$ calc: C, 64.7; H, 9.2%.

*Bis[2,6-di-t-butyl-4-(n-hexyloxycarbonyl)phenoxy]dimethylsilane (**9b**)*

To a suspension of 1.20 g (50 mmol) of sodium hydride in 100 ml of THF was added dropwise a solution of 16.73 g (50 mmol) of **7a** in 50 ml of THF. After hydrogen evolution was complete, 1.1 g (5 mmol) of 15-crown-5 was added to the reaction mixture. To the reaction mixture was added dropwise a solution of 3.23 g (25 mmol) of **8b** in 25 ml of THF. The reaction mixture was heated at 45–50 ° C for 20 h and then the suspension of sodium chloride was removed by filtration. The solvent was removed in vacuo and the residue was purified by flash chromatography (1/1 heptane/toluene eluent) to give 7.37 g (41%) of a colorless viscous liquid: IR (CCl_4) ν 1705 (C=O), 900 ($SiOC_{Ar}$) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.18 (s, $Si(CH_3)_2$, 6H), 0.89 (t, 6H), 1.46 (complex m, $C(CH_3)_3$ and CH_2, 52H) 4.27 (t, OCH_2, 4H), 8.02 (s, 4H). Anal. Found: C, 73.1; H, 9.9. $C_{44}H_{72}O_6Si$ calc: C, 72.9; H, 10.0%.

*Bis[2,6-di-t-butyl-4-(n-dodecyloxycarbonyl)phenoxy]dimethylsilane (**9c**)*

Following the method used to prepare **9b**, compound **9c** was prepared from 1.32 g (55 mmol) of sodium hydride, 20.93 g (50 mmol) of **7b**, 1.1 g (5 mmol) of 15-crown-5, and 3.23 g (25 mmol) of **8b** [17a]. The residue was purified by flash chromatography (95/5 heptane/ethyl acetate eluent) to give 8.4 g (38%) of a colorless viscous liquid: IR (CCl_4) ν 1705 (C=O), 900 ($SiOC_{Ar}$) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.20 (s, $Si(CH_3)_2$, 6H), 0.87 (t, 6H), 1.27 (complex m, 40H), 1.46 (s, $C(CH_3)_3$, 36H), 4.30 (t, OCH_2, 4H), 7.96 (s, 4H). Anal. Found: C, 75.5; H, 10.9. $C_{56}H_{96}O_6Si$ calc: C, 75.3; H, 10.8%.

*Bis[2,6-di-t-butyl-4-(n-octadecyloxycarbonyl)phenoxy]dimethylsilane (**9d**)*

Following the method used to prepare **9b**, compound **9d** was prepared from 2.64 g (110 mmol) of sodium hydride, 50.28 g (100 mmol) of **7c**, 1.1 g (5 mmol) of 15-crown-5, and 6.40 g (50 mmol) of **8b** [17b]. The residue was recrystallized from a 2.5/1 mixture of acetonitrile/toluene to give 45.02 g (85%) of a white solid. The analytical sample was purified by flash chromatography (9/1 heptane/toluene eluent): m.p. 68.5–69.5 ° C; IR (CCl_4) ν 1710 (C=O), 900 ($SiOC_{Ar}$) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.21 (s, $Si(CH_3)_2$, 6H), 0.90 (t, 6H), 1.30 (complex m, 64H), 1.49 (s, $C(CH_3)_3$, 36 H), 4.30 (t, OCH_2, 4H), 8.00 (s, 4H). Anal. Found: C, 77.0; H, 11.4. $C_{68}H_{120}O_6Si$ calc: C, 76.9; H, 11.4%.

*Bis[2,6-di-t-butyl-4-(methoxycarbonyl)phenoxy]dimethylsilane (**9e**)*

Method A: THF with crown ether. Following the method used to prepare **9b**, compound **9e** was prepared from 5.28 g (220 mmol) of sodium hydride, 52.87 g (200 mmol) of **7d**, 2.2 g (10 mmol) of 15-crown-5, and 12.90 g (100 mmol) of **8b** [17c]. The residue was recrystallized from a 1/1 mixture of acetonitrile and toluene to give 34.43 g (59%) [17d] of a white solid: m.p. 197–198 ° C; IR (CCl_4) ν 1710 (C=O), 910 ($SiOC_{Ar}$) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.21 (s, $Si(CH_3)_2$, 6H), 1.46 (s, $C(CH_3)_3$, 36H), 3.89 (s, OCH_3, 6H), 7.99 (s, 4H). Anal. Found: C, 70.2; H, 9.1. $C_{34}H_{52}O_6Si$ calc: C, 69.8; H, 9.0%.

Method B: THF without crown ether. Following the procedure of Method A, compound **9e** was prepared from 5.28 g (220 mmol) of sodium hydride, 52.87 g (200 mmol) of **7d**, and 12.98 g (100 mmol) of **8b** [17e]. The residue was recrystallized from a mixture of acetonitrile and toluene to give 33.18 g (57%) of **9e** identical in every respect to that prepared by Method A.

2,6-Di-t-butyl-4-(methoxycarbonyl)phenoxychlorodimethylsilane (10b)

Following the method used to prepare **9b**, compound **10b** was prepared from 1.20 (50 mmol) of sodium hydride, 13.20 g (50 mmol) of **7d**, and 6.45 g (50 mmol) of **8b** in 100 ml of THF. The solvent was removed in vacuo to give a colorless liquid. The spectral data were obtained without attempted purification: IR (CH_2Cl_2) ν 1715 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80 (s, Si$(CH_3)_2$, 6H), 1.52 (s, C$(CH_3)_3$, 18H), 3.96 (s, OCH_3 3H), 8.08 (s, ArH, 2H).

Reaction of 7h with 8c: Isolation of methyl 3,5-di-t-butyl-4-methoxybenzoate (13)

To a suspension of 5.28 g (220 mmol) of sodium hydride in 100 ml of THF was added dropwise a warm solution of 52.87 g (200 mmol) of **7d** in 150 ml of THF. After phenolate formation was complete as evidenced by cessation of hydrogen evolution, 2.2 g (10 mmol) of 15-crown-5 and a solution of 25.32 g (100 mmol) of **8c** in 25 ml of THF were sequentially added dropwise to the reaction mixture. The reaction mixture was stirred at r.t. for 48 h. The TLC of the reaction mixture (7/3 heptane/ethyl acetate showed a spot corresponding to starting benzoate **7d** (R_f = 0.46) and a new slower moving spot which was assigned to **12** (R_f = 0.31). The ^{1}H NMR spectrum of the reaction mixture showed a singlet resonance at δ 1.43 corresponding to the t-butyl protons of **7d** and a new singlet resonance at δ 1.30 which was assigned to the t-butyl protons of **12**.

The reaction mixture was heated at 55 ° C for 15 h and then 200 ml of tetraglyme was added. The reaction mixture was heated at reflux (78 ° C) for 15 h. The reaction mixture was diluted with diethyl ether and extracted with water (3 × 250 ml). The organic phase was dried over anhydrous sodium sulfate and it was concentrated in vacuo until crystallization occurred. The solid, which was collected by filtration, was identified as starting benzoate **7d** [18]. The filtrate was concentrated in vacuo and the residue was purified by flash chromatography (97.5/2.5 heptane/ethyl acetate eluent) to give 6.52 g of **13** as a colorless liquid which crystallized on standing: m.p. 61–64 ° C; IR (CCl)$_4$ ν 1715 (C=O) cm^{-1}; TLC (80/20 heptane/ethyl acetate eluent) R_f = 0.62; ^{1}H NMR ($CDCl_3$) δ 1.46 (s, C$(CH_3)_3$, 18H), 3.74 (s, OCH_3, 3H), 3.89 (s, C(=O)OCH_3, 3H), 8.02 (s, ArH, 2H). Anal. Found: C, 73.4; H, 9.5. $C_{17}H_{26}O_3$ calc: C, 73.3; H, 9.4%.

Bis[2,6-di-t-butyl-4-(2-(methoxycarbonyl)ethyl)phenoxy]methylsilane (17a)

Following the procedure used to prepare **9b**, compound **17a** was prepared from 1.44 g (60 mmol) of sodium hydride, 17.55 g (60 mmol) of **16c** [13], and 3.45 g (30 mmol) of **8a** [17f]. The residue was purified by dry-column chromatography (xylene eluent) to give 6.44 g (34%) of a white solid: m.p. 92–97 ° C; IR (CCl_4) ν 2200 (SiH), 1745 (C=O), 940 (SiOC$_{Ar}$) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.21 (d, $SiCH_3$, 3H), 1.45 (s, C$(CH_3)_3$, 36H), 2.62 (t, 4H), 2.90 (t, 4H), 3.72 (s, OCH_3, 6H), 5.31 (q, SiH, ^3J(HSiCH) 1.6 Hz, 1H), 7.09 (s, 4H). Anal. Found: C, 71.3; H, 9.0. $C_{37}H_{58}O_6$ Si calc: C, 70.9; H, 9.3%.

Bis[2,6-di-t-butyl-4-(2-(methoxycarbonyl)ethyl)phenoxy]dimethylsilane (17b)

Method A: Tetraglyme reaction medium. To a suspension of 1.80 g (75 mmol) of sodium hydride in 25 ml of tetraglyme was added dropwise a solution of 22.69 (75 mmol) of **16c** in 115 ml of tetraglyme. After phenolate formation was complete as evidenced by the cessation of hydrogen evolution (ca. 2 h), 4.84 g (37.5 mmol) of **8b** was added dropwise to the reaction mixture at 10 ° C and then the reaction mixture was heated at 55 ° C for 14 h. The cooled reaction mixture was diluted with 500 ml of water and it was extracted with diethyl ether. The combined ether extracts were extracted with water (2 × 150 ml) and the organic phase was dried over anhydrous sodium sulfate. The solvent was removed in vacuo and the residue was recrystallized from acetonitrile to give 12.6 (52%) of a white solid: m.p. 129–131.5 ° C; IR (CH_2Cl_2) ν 1735 (C=O), 900 ($SiOC_{Ar}$) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.21 (s, $Si(CH_3)_2$, 6H), 1.46 (s, $(CH_3)_3C$, 36H), 2.71 (t, 4H), 2.83 (t, 4H), 3.71 (s, OCH_3, 6H), 7.08 (s, 4H). Anal. Found: C, 71.5; H, 9.3. $C_{38}H_{60}O_6Si$ calc: C, 71.2; H, 9.4%.

Method B: 15-crown-5 in THF. Following the method used to prepare **9b**, compound **17b** was prepared from 1.80 g (75 mmol) of sodium hydride, 22.69 g (75 mmol) of **16c**, 1.65 g (7.5 mmol) of 15-crown-5 (added after phenolate formation was complete), and 4.84 g (75 ml) of **8b** [17g]. The residue was recrystallized from acetonitrile to give 8.67 g (36%) of **17b** identical in every respect to that prepared by Method A.

Bis[2,6-di-t-butyl-4-(2-(n-octadecyloxycarbonyl)ethyl)phenoxy]dimethylsilane (17c)

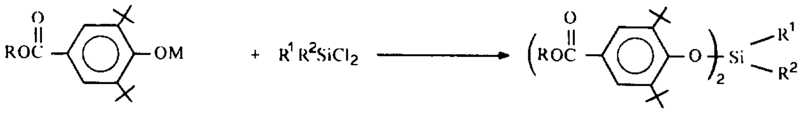
Following the procedure (Method A) used to prepare **17b**, compound **17c** was prepared from 1.80 g (75 mmol) of sodium hydride, 39.82 g (75 mmol) of **16d** [13], 1.65 g (7.5 mmol) of 15-crown-5, and 4.84 g (75 mmol) of **8b** [17h]. Unreacted **16d** was removed by bulb-to-bulb distillation (Kugelrohr; 250 ° C/0.1 mmHg) to give 26.40 g (63%) of crude product. The product was recrystallized from 2-propyl alcohol to give 13.93 g (34%) of a white solid: m.p. 53–55 ° C; IR ($CDCl_3$) ν 1730 (C=O), 900 ($SiOC_{Ar}$) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.21 (s, $Si(CH_3)_2$, 6H), 0.96 (t, 6H), 1.33 (complex m, 64H), 1.52 (s, $C(CH_3)_3$, 36H), 2.64 (t, 4H), 2.83 (t, 4H), 4.08 (t, OCH_2, 4 H) 7.08 (s, 4H). Anal. Found: C, 77.1; H, 11.2. $C_{72}H_{128}O_6Si$ calc: C, 77.4; H, 11.5%.

2,6-Di-t-butyl-4-[2-(methoxycarbonyl)ethyl]phenoxychlorodimethylsilane (18)

Following the method used to prepare **9b**, compound **18** was prepared from 0.90 (37.5 mmol) of sodium hydride, 11.34 g (37.5 mmol) of **16c**, 0.82 g (3.8 mmol) of 15-crown-5, and 4.84 g (37.5 mmol) of **8b**. The product was obtained as a colorless liquid. The spectral data were obtained without attempted purification: IR (CH_2Cl_2) ν 1735 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.27 (s, $Si(CH_3)_2$, 6H) 1.30 (s, $C(CH_3)_3$, 18 H), 2.61 (t, 2H), 2.83 (t, 2H), 3.64 (s, OCH_3, 3H), 7.05 (s, 2H).

Results and discussion

The reaction of **8a** with two equivalents of **7b** using triethylamine as an acid acceptor in a toluene reaction medium gave the expected bis(aryloxy) derivative **9a**, albeit in low yield (see Scheme 1). The reaction of **8b** with two equivalents of **7a** using triethylamine as an acid scavenger in toluene did not give the expected bis(aryloxy) derivative **9b**, but rather the product of mono-substitution **10a** was obtained. The ^1H NMR and IR spectra of the reaction mixture were consistent with a mixture of both starting **7a** and **10a**. Indeed, **10a** was prepared in high yield by the reaction of **7a** with one equivalent of **8b** using triethylamine as an acid acceptor (73% distilled). These observations are consistent with the work of Eaborn and Walton, who demonstrated that the rate of nucleophilic substitution at silicon was monotonically reduced as the size of the alkyl substituents on silicon increased



(7)

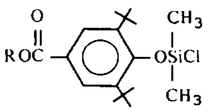
(a, M = H; R = n - hexyl ;
b, M = H; R = n - dodecyl ;
c, M = H; R = n - octadecyl ;
d, M = H; R = methyl ;
e, M = Na; R = n - hexyl ;
f, M = Na; R = n - dodecyl ;
g, M = Na; R = n - octadecyl ;
h, M = Na; R = methyl)

(8)

(a, R^1 = H; R^2 = methyl ;
b, R^1 = R^2 = methyl ;
c, R^1 = R^2 = phenyl)

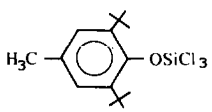
(9)

(a, R = n - dodecyl; R^1 = H; R^2 = methyl ;
b, R = n - hexyl; R^1 = R^2 = methyl ;
c, R = n - dodecyl; R^1 = R^2 = methyl ;
d, R = n - octadecyl; R^1 = R^2 = methyl ;
e, R = R^1 = R^2 = methyl ;
f, R = methyl; R^1 = R^2 = phenyl)



(10)

(a, R = n - hexyl ;
b, R = methyl)



(11)

SCHEME 1

[19,20].

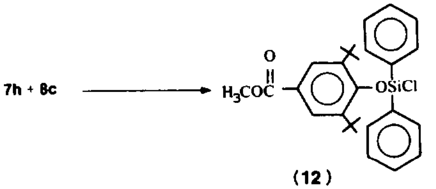
The reaction of the sodium phenolate **7e** with **8b** in a tetrahydrofuran (THF) reaction medium at r.t. gave a mixture of starting phenol **7a**, monosubstitution product **10a**, and the desired bis-adduct **9b**. Gümrükçüoğlu, however, reported that the reaction of the lithium phenolate of **3a** with silicon tetrachloride in THF at reflux gave only the product of monosubstitution, **11** [8]. In light of our results this may appear surprising since silicon tetrachloride would be expected to be more reactive than **8b** both on inductive and steric grounds [21]. However, the nucleophilicity of the phenolate anion is strongly dependent on the degree of ion pairing, which is in turn dependent on the nature of the substituents on the phenol (vide infra).

The reaction of **8b** with two equivalents of **7e** in THF in the presence of a crown ether (1,4,7,10,13-pentaoxacyclopentadecane; 15-crown-5) gave the bis-adduct **9b** (41% recrystallized). A reasonable explanation of this observation is that the phenolate anion **7e** exists either as an aggregate or a tight-ion pair in THF solution in the absence of a crown ether with a concomitant decrease in nucleophilicity towards the sterically encumbered substrate **10a**. This interpretation is supported by X-ray crystallography studies which show that the molecular structure of the sodium phenolate of **3b** in the solid state is a dimer with a molecule of diethyl ether in the coordination sphere of each sodium atom [22]. In a similar manner **9c–e** were prepared by the reaction of **8b** with the corresponding phenolates **7f–h**.

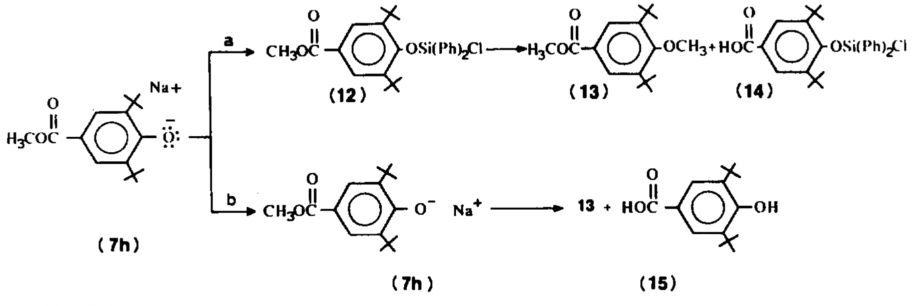
The reaction of **7h** with **8b** was studied in more detail. The reaction of two equivalents of **7h** with **8b** in THF with and without a crown ether was carried out concurrently at room tmperature. In both reactions after stirring for 45 min, a mixture of **7d**, **10b**, and **9e** was obtained. After stirring for 20 h at room temperature, however, only **9e** was observed by TLC in the reaction with crown ether, which upon workup **9e** was isolated in 62% yield (recrystallized). After 20 h, the reaction without crown ether still contained a mixture of **7d**, **10b**, and **9e**. After 4 d at room temperature, **9e** was the major component as indicated by both TLC, ^{1}H NMR, and the IR spectra of the reaction mixture. Upon workup **9e** was isolated in 57% yield (recrystallized). An authentic sample of **10b** was prepared by the reaction of one equivalent of **7h** with **8b** in THF. These observations support the proposal of a slower rate of substitution by a phenolate nucleophile existing as either a tight-ion pair or aggregate.

The reaction of the diphenylsilane **8c** with two equivalents of **7h** in THF with 15-crown-5 at reflux did not give the bis-adduct **9f**. In the ^{1}H NMR spectrum of the reaction mixture were observed resonances corresponding to **7d** and new resonances which were assigned to the monosubstitution product **12**. The addition of tetraglyme (tetraethyleneglycol dimethyl ether), which we previously demonstrated to be effective in generating unsolvated thiolate anions [23], to the reaction mixture and heating the reaction mixture at 78 °C for 15 h did not result in the formation of **9f**. Surprisingly, the methyl ether **13** (23% based upon **7d**) was isolated by flash chromatographic workup.

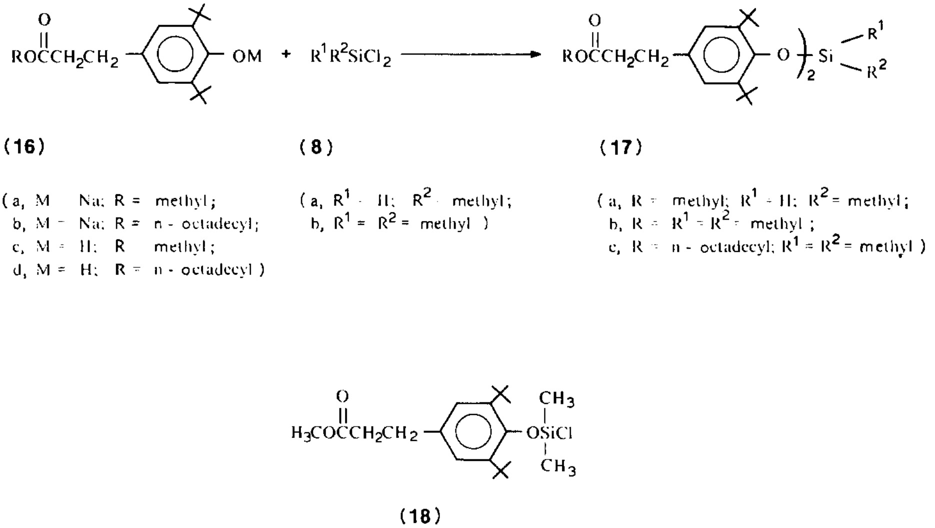
A plausible mechanism for the formation of **13** is illustrated in Scheme 2. Nucleophilic attack of the phenolate ion **7h** at the carbon atom of the methyl ester of either **12** (path a) or another molecule of **7h** (path b) would give **13**. Although neither the isolation of **14** nor **15** was attempted, the IR spectrum of the reaction mixture prior to chromatography displayed both a broad absorption between 3300–2500 and a band at 1680 cm^{-1} which is consistent with a carboxylic acid conjugated with an aryl group. Whatever the precise mechanism for the formation of **13**, however, this result demonstrates the difficulty encountered in attempting to substitute the chlorine atom in the sterically-hindered substrate **12** by the hindered nucleophile **7h**.



(12)



SCHEME 2



(16)

(a, M = Na; R = methyl;
b, M = Na; R = n - octadecyl;
c, M = H; R = methyl;
d, M = H; R = n - octadecyl)

(8)

(a, R^1 = H; R^2 = methyl;
b, R^1 = R^2 = methyl)

(17)

(a, R = methyl; R^1 = H; R^2 = methyl;
b, R = R^1 = R^2 = methyl ;
c, R = n - octadecyl; R^1 = R^2 = methyl)

(18)

SCHEME 3

The reaction of two equivalents of **16a** with **8a** in THF gave the bis-adduct **17a** (Scheme 3). The analogous reaction of **16a** with **8b** in THF without 15-crown-5 gave only a low yield the monosubstitution product **18** after 2 d at r.t. as determined by the TLC and ^{1}H NMR spectrum of the reaction mixture. The ^{1}H NMR spectrum of the reaction mixture showed resonances corresponding to both **16c** and **18** in a 4.5/1 ratio by integration of the corresponding aromatic peak areas. In the presence of a crown ether, the bis-adduct **17b** was obtained (36% recrystallized). The bis-adduct **17b** was also obtained at elevated reaction temperatures in tetraglyme reaction medium without a crown ether (52% recrystallized). The monoadduct **18** was obtained by the reaction of **8b** with one equivalent of **16a** in THF with 15-crown-5. These observations are consistent with the previous work of Gümrükçüoğlu where only monosubstitution was observed with silicon tetrachloride (vide ante) in THF. The bis-adduct **17c** was prepared in an analogous manner from **16b** with **8b** in tetraglyme.

The difference in nucleophilicity of the 4-(carboalkoxy)phenolates **7e–h** relative to the 4-(β-carboalkoxyethyl)phenolates **16a–b** in THF is clearly not what would be expected based solely upon the electronic effect of the *para* substituent. This would be the case since resonance delocalization of the negative charge on oxygen into the electron-accepting ester group would reduce the nucleophilicity of **7e–h** relative to **16a–b** where direct resonance delocalization into the ester group is not possible. The results of this study strongly suggest that resonance delocalization of charge in **7e–h** leading to a charge dispersed ion reduces either the degree of aggregation or ion pairing in solution resulting in increased nucleophilicity over that of **16a–16b**. Delocalization leading to charge dispersal would be expected to reduce the interaction of the phenolate oxygen with the sodium counterion resulting in a reduction of ion pairing. Nucleophilicity of anions in solution has been shown previously to be dependent on both the degree of ion pairing and aggregation [24] even in the presence of a crown ether [25].

The results of this study also further demonstrate the usefulness of tetraglyme as a reaction medium for nucleophilic substitution reactions [23,26].

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