Counterattack Reagents Sodium Trimethylsilanethiolate and Hexamethyldisilathiane in the Bis-O-demethylation of Aryl Methyl Ethers

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New methods were developed for removal of two methyl groups from aryl methyl ethers. Treatment of an aryl methyl ether containing two methoxy units (i.e., **1**, **3**, **5**, **7**, **9**, 11, or 13) with ~2.5 equiv of Me_3SiSNa in 1,3-dimethyl-2-imidazolidinone at 185 °C in a sealed tube gave the corresponding aryl alcohol (i.e., **2**, **4**, **6**, **8**, **10**, **12**, or **14**) in 78–96% yields after aqueous workup. Also, $Me_3SiSSiMe_3$ was found useful for bis-O-demethylation of aromatic compounds containing one free hydroxyl group and two methoxy units (e.g., 11 and 13). Thus 11 and 13 reacted with 1.5 equiv of NaH and then with 1.5 equiv of $Me_3SiSSiMe_3$ at 185 °C in a sealed tube to afford triols 13 (75%) and 14 (72%), respectively. In these bis-O-demethylations, Me_3SiSNa and $Me_3SiSSiMe_3$ act as counterattack reagents.

Introduction

Methylation of phenolic hydroxyl groups provides an important protection tool in organic synthesis.[1] Often the methyl group in the resulting anisole unit has to be removed later to liberate the desired phenols in multistep syntheses.[1] Commonly used reagents for demethylation of aryl methyl ethers include mineral acids,[2,3] Lewis acids,[4-6] alkaline reagents,[7,8] alkali metals,[9] silicon compounds,[10-13] oxidizing agents,[14] and reducing agents.[15] Most of these reagents give mono-O-demethylated products; a few of them can efficiently bis-O-demethylate substrates.[16,17]

Sequential demethylation of dimethoxybenzenes in one flask is difficult by use of nucleophilic reagents.[8,18-20] As shown in Scheme I, the first demethylation involves an attack of a nucleophilic reagent on a methyl group of dimethoxybenzenes (**15**) to give methoxy phenolates (**16**). Unlikely, nucleofuge **16** can be demethylated again by another nucleophile in an efficient manner (i.e., **16** → **17**) because the resulting species **17** would bear two negative charges.

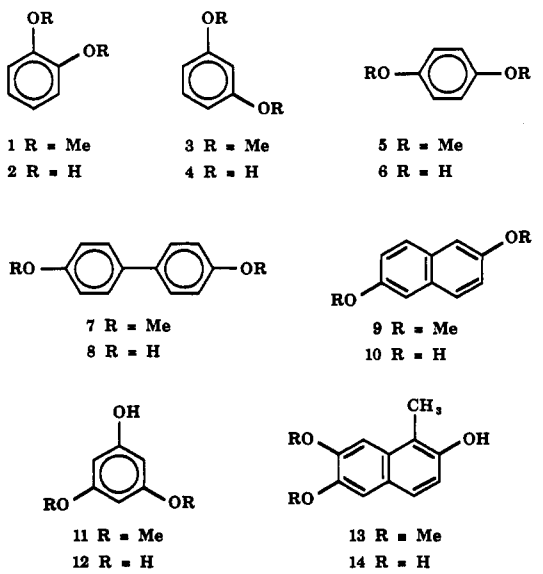
We sought a solution to this problem by applying the concept of "counterattack reagents".[21,22] We found that the use of sodium trimethylsilanethiolate (Me_3SiSNa) and hexamethyldisilathiane ($Me_3SiSSiMe_3$) as counterattack reagents was able to bis-O-demethylate aryl methyl ethers efficiently under alkaline conditions.

Results

We developed three methods for the bis-O-demethylation of dimethoxy aromatic compounds (see Scheme II and Table I, methods A–C). Using method A, we first generated an excess of Me_3SiSNa from $Me_3SiSSiMe_3$ (2.5 equiv) and NaOMe (2.5 equiv) in anhydrous 1,3-dimethyl-2-imidazolidinone at room temperature.[23] Then 1,2-, 1,3-, or 1,4-dimethoxybenzene (**1**, **3**, or **5**) was treated with Me_3SiSNa at 185 °C in a sealed tube to give the corresponding aryl diol (**2**, **4**, or **6**) in 86–92% yields after aqueous workup.

Likewise, aryl alcohols containing a biphenyl or a naphthalene unit were generated by the same procedure. Thus 4,4′-dimethoxybiphenyl (**7**) afforded 4,4′-biphenol (**8**) in 95% yield, and 2,6-dimethoxynaphthalene (**9**) provided 2,6-dihydroxynaphthalene (**10**) in 96% yield.

Method A was also applicable to aromatic compounds with one hydroxyl and two methoxy groups. We were able



to obtain phloroglucinol (**12**) in 83% yield from 3,5-dimethoxyphenol (**11**) and to isolate 1-methyl-2,6,7-tri-

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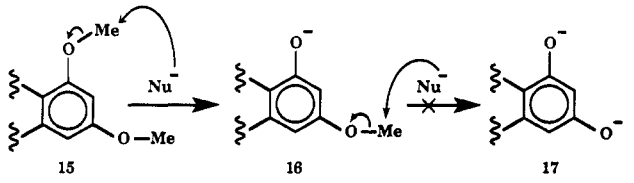
Scheme I



Scheme II

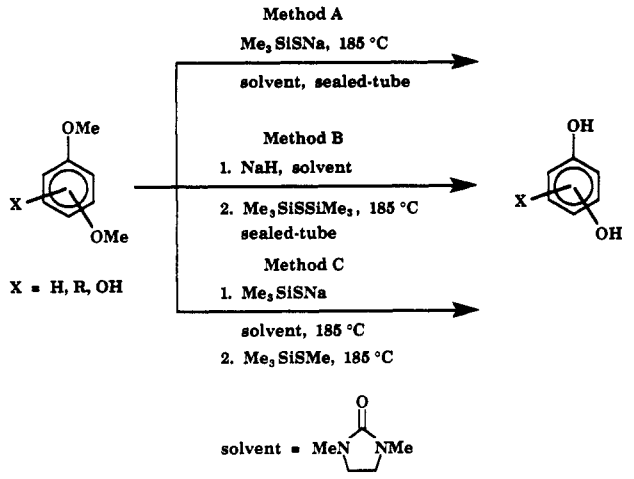


Table I. Bis-O-demethylation of Aryl Methyl Ethers To Give Diols or Triols by Methods A–C

aryl methyl ether	diol or triol	yield, %		
		method A	method B	method C
1	2	92	NA[a]	87
3	4	95	NA	81
5	6	86	NA	-
7	8	95	NA	82
9	10	96	NA	-
11	12	83	75	-
13	14	78	72	-

[a] NA = not applicable.

hydroxynaphthalene (**14**) in 78% yield from 6,7-dimethoxy-1-methyl-2-naphthol (**13**).

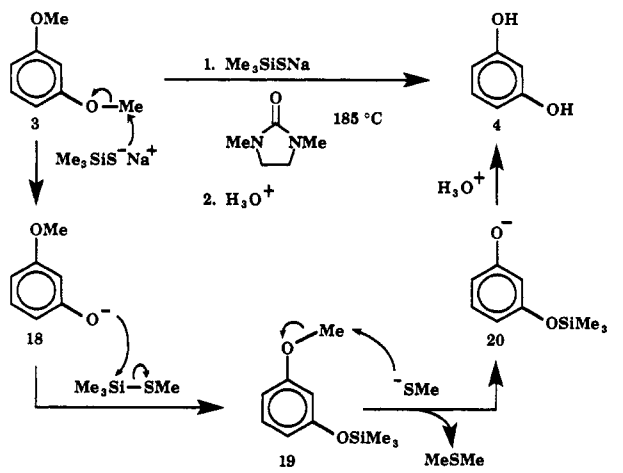
We developed method B for bis-O-demethylation of aromatic compounds containing one free hydroxyl group and two methoxy units. Treatment of alcohol **11** with 1.5 equiv of NaH in anhydrous 1,3-dimethyl-2-imidazolidinone at room temperature gave the corresponding phenoxide. This phenoxide then was allowed to react with 1.5 equiv of $Me_3SiSSiMe_3$ at 185 °C in a sealed tube to afford phloroglucinol (**12**) in 75% yield. By using the same procedure, we converted **13** to **14** in 72% yield.

Method C provided an alternative way to bis-O-demethylate dimethoxy aromatic compounds. By this method, we treated 1,2-dimethoxybenzene (**1**) with ~2.5 equiv of Me_3SiSNa in anhydrous 1,3-dimethyl-2-imidazolidinone at 185 °C under an atmosphere of nitrogen. After 12 h, Me_3SiSMe was added into the reaction flask at room temperature and the solution was stirred for 1.5 h. Then the mixture was heated at 185 °C for another 12 h. The desired diol **2** was isolated in 87% yield after aqueous workup. Similarly, bis-O-demethylation of methyl aryl ethers **3** and **7** provided the corresponding diols **4** and **8** in 81% and 82% yields, respectively.

Discussion

Design and Reaction Mechanism. Method A can be utilized to bis-O-demethylate various types of aryl methyl ethers. We illustrate its reaction mechanism in Scheme III by using 1,3-dimethoxybenzene (**3**) as an example.

Scheme III



The first step involves an S_N2 between **3** and Me_3SiSNa to give phenoxide **18** and Me_3SiSMe. Alkyl and aryl sulfides can demethylate aryl methyl ethers under alkaline conditions.[18-20] In addition, Hanessian and Guindon[24] found that (alkylthio)- and (arylthio)trimethylsilanes can effect mono-O-demethylation in the presence of ZnI_2 and n-Bu_4NI.

It would be difficult for phenoxide **18** to react with the second equivalent of Me_3SiSNa to give dianionic species—a bis-O-demethylated product. Nevertheless, the byproduct Me_3SiSMe was found to silylate **18** easily to give silyl phenol **19**: we applied the conditions of method A to **3** and stopped the reaction in 3 h instead of 24 h. 3-Methoxyphenol was obtained, via the corresponding silyl ether **19**, as the major product upon acidic workup.

Silylation of **18** to **19** with Me_3SiSMe produced methanethiolate anion (^-SMe) in situ. We believe that nucleofuge ^-SMe can demethylate **19** to afford **20** based upon Feutrill and Mirrington's results;[18,19] they reported a demethylation procedure by using ethanethiolate anion (^-SEt). Finally, acidic workup leads siloxyphenoxide **20** to the desired diol **4**.

In the conversion of **3** to **19**, one may claim that Me_3SiSNa is first attacked by **3** to give Me_3SiSMe and **18**.[21] Intermediate Me_3SiSMe then counterattacks **18** to give **19**. Therefore "**3** + Me_3SiSNa → **18** + Me_3SiSMe → **19** + NaSMe" constitutes the first counterattack process, in which Me_3SiSNa acts as a "counterattack reagent". Being a nucleophile, Me_3SiSNa is a "nucleophilic counterattack reagent".[21]

In the conversion of **18** to **20**, Me_3SiSMe is first attacked by **18**. The nucleofuge ^-SMe then counterattacks intermediate **19**. Therefore "**18** + Me_3SiSMe → **19** + NaSMe → **20** + MeSMe" constitutes the second counterattack process.

In the entire transformation of **3** to **4** shown in Scheme III, two counterattack procedures link together. This transformation exemplifies a "tandem double-counterattack process".[21]

Scheme IV depicts the reaction mechanism for method B by use of dimethoxyphenol **11** as an example. The steps from "**22** + $^-SSiMe_3$" to the final product **12** is similar to those from "**3** + $^-SSiMe_3$" to **4** shown in Scheme III.

In Scheme IV, $Me_3SiSSiMe_3$ is first attacked by alkoxide **21** to give $^-SSiMe_3$ and compound **22**. The nucleofuge

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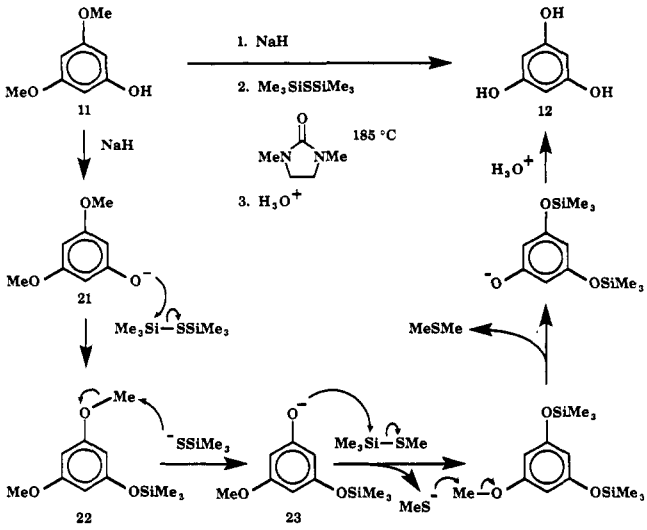
Scheme IV



$^-SSiMe_3$ then counterattacks **22** to afford phenoxide **23**. Reagent $Me_3SiSSiMe_3$ acts as an electrophile and contains a counterattacking unit. Therefore, $Me_3SiSSiMe_3$ is an "electrophilic counterattack reagent"[21] in the bis-O-demethylation of **11**.

Reactions shown in Schemes III and IV share common features—the design is complicated and the manipulation is simple. Counterattack reagents Me_3SiSNa and $Me_3SiSSiMe_3$ in each reaction use both their nucleophilic *S* centers (twice) and electrophilic *Si* centers.

Method C provides mechanistic information on the role of Me_3SiSMe in Scheme III. Under the conditions of method C, the sealed-tube technique was not applied. Intermediate Me_3SiSMe could be vaporized (bp 110–111 °C)[25] at 185 °C once it was generated. Thus we added 2.5 equiv of Me_3SiSMe into the reaction flask.

Reaction and Workup Conditions. In searching the best solvent[26] for bis-O-demethylation, we found that 1,3-dimethyl-2-imidazolidinone was superior to others, such as 1-methyl-2-pyrrolidinone, *N,N*-dimethylformamide, and *N,N*-dimethylpropionamide.[27] Although 1,3-dimethyl-2-imidazolidinone has a high boiling point (224–226 °C),[26] we were able to remove it easily from the ethereal solution of diols by washing with water.

We were able to generate Me_3SiSNa from commercially available $Me_3SiSSiMe_3$ with either NaOMe or NaOEt.[23] A dark blue solution of Me_3SiSNa was observed by use of 1,3-dimethyl-2-imidazolidinone or DMF as solvent.

For isolating highly water-soluble triols (i.e., **12** and **14**), we used EtOAc to extract the crude, desired products from the aqueous layer. Triols were then separated from 1,3-dimethyl-2-imidazolidinone with a column packed with basic aluminum oxide.

Conclusion

Reagents Me_3SiSNa and $Me_3SiSSiMe_3$ can sequentially remove two methyl groups from an aryl methyl ether under alkaline conditions. These newly developed bis-O-demethylations gave the parent aryl alcohols in good to excellent yields. In these transformations, reagents Me_3SiSNa and $Me_3SiSSiMe_3$ were utilized by an efficient manner: both of the nucleophilic center (i.e., *S*) and the electrophilic center (i.e., *Si*) were allowed to react with intermediates in individual steps. The design involves the concept of "counterattack reagents". In the bis-O-demethylations, Me_3SiSNa acts as a nucleophilic counterattack reagent and $Me_3SiSSiMe_3$ as an electrophilic counterattack reagent.

Experimental Section

General Procedure. All reactions were carried out in oven-dried glassware (120 °C) under an atmosphere of nitrogen, unless otherwise indicated. Ethyl acetate and hexanes from Tilley Chemical Co. were dried and distilled from CaH_2. 1,3-Dimethyl-2-imidazolidinone from Aldrich were dried and distilled from CaH_2 under reduced pressure and stored in serum capped bottles under argon over molecular sieves 4A. 1,2-Dimethoxybenzene, 1,3-dimethoxybenzene, 1,4-dimethoxybenzene, 4,4'-dimethoxybiphenyl, 2,6-dimethoxynaphthalene, 3,5-dimethoxyphenol, 6,7-dimethoxy-1-methyl-2-naphthol, sodium methoxide, and sodium hydride were purchased from Aldrich Chemical Co. Hexamethyldisilathiane and (methylthio)trimethylsilane from Fluka Chemical Co. were stored in serum capped bottles under argon over molecular sieves 4A. Reactions at 185 °C were carried out in an explosion-proof oven from Blue M. Electric Co.; the Pyrex combustion tubes (8 × 10 × 200 mm) used for high-temperature reactions were purchased from Corning Glass Works. Melting points were obtained with a Büchi 510 melting point apparatus. Analytical thin-layer chromatography (TLC) was performed on precoated plates (silica gel GHLF) purchased from Analtech Inc. Visualization of spots on TLC plates was done by use of UV light. Mixtures of ethyl acetate and hexanes were used as eluants. Gas chromatography analyses were performed on a Hewlett-Packard 5794 instrument equipped with a 12.5-m cross-linked methyl silicone gum capillary column (0.2-mm i.d.). Purification by gravity column chromatography was carried out by use of EM Reagents silica gel 60 (particle size 0.063–0.200 mm, 70–230 mesh ASTM) or activated aluminum oxide (basic or neutral Brockmann I, standard grade, ~150 mesh, 58 Å). Separations by radial thin-layer chromatography were performed on a Model 7924T Chromatotron from Harrison Research. The plates (1, 2, or 4 mm thickness) were coated with EM Reagents silica gel 60 PF_{254} containing gypsum. Infrared (IR) spectra were measured on a Perkin-Elmer 1600 Series FT-IR. The wavenumbers reported are referenced to the polystyrene 1601 cm^{-1} absorption. Absorption intensities are recorded by the following abbreviations: s, strong; m, medium; w, weak; br, broad. Proton NMR spectra were obtained on a Varian CFT-20 (80 MHz) spectrometer by use of chloroform-*d* and/or dimethyl-d_6 sulfoxide as solvent and tetramethylsilane as internal standard. Multiplicities are recorded by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; *J*, coupling constant (hertz). High-resolution mass spectra and electron impact mass spectra (EIMS) were obtained with a VG Analytical 70-S mass spectrometer.

Standard Procedure for the Bis-O-demethylation of Aryl Methyl Ethers. Method A. To a one-necked, pear-shaped flask equipped with a stirring bar and a rubber septum were added dry sodium methoxide (2.5 equiv), hexamethyldisilathiane (2.5 equiv), and anhydrous 1,3-dimethyl-2-imidazolidinone (2.0 mL). After 1 h of stirring at room temperature under an atmosphere of nitrogen, the mixture was transferred into a Pyrex combustion tube under argon. An aryl methyl ether (1.0 equiv) in 1,3-dimethyl-2-imidazolidinone (1.0 mL) was injected into the tube, which was then sealed by torch. The sealed tube was heated in an oven at 185 °C for 24 h, during which the tube was shaken once for 10 min at 60 °C. The reaction mixture was diluted with water at room temperature, neutralized with 10% HCl, and extracted with Et_2O (30 mL × 5) if a diol is desired or extracted with EtOAc (20 mL × 20) if a triol is desired. For isolation of diols, the combined ethereal solutions were washed with water and saturated aqueous NaCl, and then the mixture was dried over $MgSO_4$(s), filtered, and concentrated under reduced pressure. The residue was chromatographed to give pure diol. For isolation of triols, the combined EtOAc solutions were washed with saturated aqueous NaCl, dried over $MgSO_4$(s), filtered, and concentrated under reduced pressure. The residue was chromatographed through a column packed with basic or neutral aluminum oxide.

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1,3-Dimethyl-2-imidazolidinone was elutriated by use of Et_2O and the desired triol was then obtained by use of methanol as eluant.

Method B. In a one-necked, pear-shaped flask equipped with a stirring bar and a rubber septum, sodium hydride (1.5 equiv) was washed with hexanes (3 × 5 mL). Hexanes were removed to give NaH as a white powder. An aryl methyl ether (1.0 equiv) in 1,3-dimethyl-2-imidazolidinone was added to the flask. After 30 min of stirring at room temperature under an atmosphere of nitrogen, hexamethyldisilathiane (1.5 equiv) was added to the solution and stirring was continued at room temperature for 2 h. Then the reaction mixture was transferred, under argon, into a Pyrex combustion tube, which was then sealed by torch. The sealed tube was heated in an oven at 185 °C for 24 h, during which the tube was shaken once for 10 min at 60 °C. The reaction mixture was diluted with water at room temperature, neutralized with 10% HCl, and extracted with EtOAc (20 mL × 20). The combined organic layers were washed with saturated aqueous NaCl, dried over $MgSO_4$(s), filtered, and concentrated under reduced pressure. The residue was chromatographed through a column packed with basic or neutral aluminum oxide. 1,3-Dimethyl-2-imidazolidinone was elutriated by use of Et_2O, and the desired triol was then obtained by use of methanol as eluant.

Method C. To a one-necked, pear-shaped flask equipped with a stirring bar and a rubber septum were added dry sodium methoxide (2.5 equiv), hexamethyldisilathiane (2.5 equiv), and anhydrous 1,3-dimethyl-2-imidazolidinone (5.0 mL). After 1 h of stirring at room temperature under an atmosphere of nitrogen, an aryl methyl ether (1.0 equiv) in 1,3-dimethyl-2-imidazolidinone (1.0 mL) was injected into the flask, which was then immersed in an oil bath at 185 °C for 12 h. The reaction mixture was cooled down to room temperature, to which (methylthio)trimethylsilane (2.5 equiv) in 1,3-dimethyl-2-imidazolidione (1.0 mL) was added. After 1.5 h of stirring, the reaction mixture was heated at 185 °C for another 12 h. The mixture was quenched at room temperature with water, neutralized with 10% HCl, and extracted with Et_2O (30 mL × 5). The combined ethereal layers were washed with water and saturated aqueous NaCl. The solution was dried over $MgSO_4$(s), filtered, and condensed under reduced pressure. The residue was chromatographed to give a pure diol.

Catechol (2). Method A. The standard procedure was followed. Reagents added into the reaction flask were sodium methoxide (105 mg, 1.94 mmol, 2.5 equiv), 1.2-dimethoxybenzene (**1**, 107 mg, 0.777 mmol, 1.0 equiv), hexamethyldisilathiane (418 mg, 1.94 mmol, 2.5 equiv), and 1,3-dimethyl-2-imidazolidinone (3.0 mL). After workup and purification by use of a chromatotron (1-mm plate, 50% EtOAc in hexanes as eluant), catechol (**2**) was obtained as a tan solid (mp 104.0–105.0 °C; lit.[28a] mp 105.0 °C) in 92% yield (79 mg, 0.72 mmol): GC (injector temperature 260 °C; column program: initial temperature 70 °C, duration 2.00 min; increment rate 15 °C/min; final temperature 250 °C) t_R 5.06 min; TLC R_f 0.38 (40% EtOAc in hexanes); ^{1}H NMR ($CDCl_3$, 80 MHz) δ 4.30–5.55 (br, 2 H, 2 OH), 6.85 (br s, 4 H, C_6H_4); IR ($CHCl_3$) 3554 (s, OH), 3272 (br m, OH), 2978 (w), 1602 (m, C=C), 1508 (s, C=C), 1467 (m, C=C), 1361 (m), 1267 (s), 1249 (s, C—O), 1208 (s, C—O), 1149 (m), 1091 (s, C—O), 908 (m), 732 (s, =C—H) cm^{-1}. Its physical properties and spectroscopic characteristics are consistent with those of an authentic sample.[29a]

Method C. The standard procedure was followed. Reagents added into the reaction flask were sodium methoxide (105 mg, 1.94 mmol, 2.5 equiv), 1,2-dimethoxybenzene (**1**, 107 mg, 0.777 mmol, 1.0 equiv), hexamethyldisilathiane (418 mg, 1.94 mmol, 2.5 equiv), (methylthio)trimethylsilane (290 mg, 1.942 mmol, 2.5 equiv), and 1,3-dimethyl-2-imidazolidinone (7.0 mL). After workup and purification by use of a chromatotron (1-mm plate, 50% EtOAc in hexanes as eluant), catechol (**2**) was obtained as a tan solid in 87% yield (74 mg, 0.68 mmol). Its spectroscopic characteristics were identical with those listed above.

Resorcinol (4). Method A. The standard procedure was followed. Reagents added into the reaction flask were sodium methoxide (102 mg, 1.89 mmol, 2.5 equiv), 1,3-dimethoxybenzene (**3**, 104 mg, 0.756 mmol, 1.0 equiv), hexamethyldisilathiane (407 mg, 1.89 mmol, 2.5 equiv), and 1,3-dimethyl-2-imidazolidinone (3.0 mL). After workup and purification by use of a chromatotron (1-mm plate, 50% EtOAc in hexanes as eluant), resorcinol (**4**) was obtained as a white solid (mp 111.5–112.0 °C; lit.[28b] mp 111.2–111.6 °C) in 95% yield (80 mg, 0.72 mmol): GC (injector temperature 260 °C; column program: initial temperature 70 °C, duration 2.00 min; increment rate 15 °C/min; final temperature 250 °C) t_R 5.96 min; TLC R_f 0.35 (40% EtOAc in hexanes); ^{1}H NMR (DMSO-d_6 + $CDCl_3$, 80 MHz) δ 6.22–7.11 (m, 4 H, C_6H_4), 8.72 (br, 2 H, 2 OH); IR ($CHCl_3$) 3320 (s br, OH), 2978 (s), 2919 (m), 1602 (s, C=C), 1484 (s, C=C), 1381 (m), 1302 (m), 1160 (m, C—O), 1143 (s, C—O), 961 (s), 774 (s, =C—H), 741 (m), 680 (s, =C—H) cm^{-1}. Its physical properties and spectroscopic characteristics are consistent with those of an authentic sample.[29b]

Method C. The standard procedure was followed. Reagents added into the reaction flask were sodium methoxide (102 mg, 1.89 mmol, 2.5 equiv), 1,3-dimethoxybenzene (**3**, 104 mg, 0.756 mmol, 1.0 equiv), hexamethyldisilathiane (407 mg, 1.89 mmol, 2.5 equiv), (methylthio)trimethylsilane (282 mg, 1.89 mmol, 2.5 equiv), and 1,3-dimethyl-2-imidazolidinone (7.0 mL). After workup and purification by use of a chromatotron (1-mm plate, 50% EtOAc in hexanes as eluant), resorcinol (**4**) was obtained as a white solid in 81% yield (68 mg, 0.61 mmol). Its spectroscopic characteristics were identical with those listed above.

Hydroquinone (6). Method A. The standard procedure was followed. Reagents added into the reaction flask were sodium methoxide (106 mg, 1.97 mmol, 2.5 equiv), 1,4-dimethoxybenzene (**5**, 109 mg, 0.788 mmol, 1.0 equiv), hexamethyldisilathiane (424 mg, 1.97 mmol, 2.5 equiv), and 1,3-dimethyl-2-imidazolidinone (3.0 mL). After workup and purification by use of a chromatotron (1-mm plate, 50% EtOAc in hexanes as eluant), hydroquinone (**6**) was obtained as a white solid (mp 175.0–176.0 °C; lit.[28c] mp 175.4–176.6 °C) in 86% yield (75 mg, 0.68 mmol): GC (injector temperature 260 °C; column program: initial temperature 70 °C, duration 2.00 min; increment rate 15 °C/min; final temperature 250 °C) t_R 5.78 min; TLC R_f 0.34 (40% EtOAc in hexanes); ^{1}H NMR (DMSO-d_6 + $CDCl_3$, 80 MHz) δ 6.63 (s, 4 H, C_6H_4), 8.24 (s, 2 H, 2 OH); IR ($CHCl_3$) 3320 (br m, OH), 2955 (m), 2861 (m), 1555 (m, C=C), 1508 (s, C=C), 1455 (m, C=C), 1167 (s, C—O), 1108 (s, C—O), 1090 (m, C—O), 826 (m, =C—H), 767 (m, =C—H) cm^{-1}. Its physical properties and spectroscopic characteristics are consistent with those of an authentic sample.[29c]

4,4′-Biphenol (8). Method A. The standard procedure was followed. Reagents added into the reaction flask were sodium methoxide (69 mg, 1.3 mmol, 2.5 equiv), 4,4′-dimethoxybiphenyl (**7**, 109 mg, 0.508 mmol, 1.0 equiv), hexamethyldisilathiane (273 mg, 1.27 mmol, 2.5 equiv), and 1,3-dimethyl-2-imidazolidinone (3.0 mL). After workup and purification by use of a chromatotron (1-mm plate, 50% EtOAc in hexanes as eluant), 4,4′-biphenol (**8**) was obtained as a yellow solid (mp 282.0 °C dec; lit.[30] mp 275.0–278.0 °C (EtOH)) in 95% yield (90 mg, 0.48 mmol): GC (injector temperature 260 °C; column program: initial temperature 120 °C, duration 2.00 min; increment rate 15 °C/min; final temperature 250 °C) t_R 8.58 min; TLC R_f 0.35 (40% EtOAc in hexanes); ^{1}H NMR (DMSO-d_6 + $CDCl_3$, 80 MHz) δ 6.85 (d, J = 8.7 Hz, 4 H, 2 C_6H_2), 7.35 (d, J = 8.7 Hz, 4 H, 2 C_6H_2), 7.90–8.80 (br, 2 H, 2 OH); IR ($CHCl_3$) 3425 (m, OH), 3119 (br m, OH), 3002 (m, =C—H), 1608 (m, C=C), 1590 (w), 1496 (s, C=C), 1455 (w), 1261 (s, C—O), 1226 (m), 1167 (m), 1049 (s, C—O), 1026 (s, C—O), 1002 (s), 820 (s, =C—H), 756 (s, =C—H) cm^{-1}. Its physical properties and spectroscopic characteristics are consistent with those of an authentic sample.[29d]

Method C. The standard procedure was followed. Reagents added into the reaction flask were sodium methoxide (69 mg, 1.27 mmol, 2.5 equiv), 4,4′-dimethoxybiphenyl (**7**, 109 mg, 0.508 mmol, 1.0 equiv), hexamethyldisilathiane (273 mg, 1.27 mmol, 2.5 equiv), (methylthio)trimethylsilane (190 mg, 1.27 mmol, 2.5 equiv), and 1,3-dimethyl-2-imidazolidinone (7.0 mL). After workup and purification by use of a chromatotron (1-mm plate, 50% EtOAc in hexanes as eluant), 4,4′-biphenol (**8**) was obtained as a yellow solid in 82% yield (78 mg, 0.42 mmol). Its spectroscopic characteristics were identical with those listed above.

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(29) (a) *Catalog Handbook of Fine Chemicals*; Aldrich Chemical: Milwaukee, 1988–1989; p 311. (b) p 1311. (c) p 830. (d) p 175. (e) p 557.

(30) Carrick, W. L.; Karapinka, G. L. U.S. Patent 3 332 838, 1963.

2,6-Dihydroxynaphthalene (10). Method A. The standard procedure was followed. Reagents added into the reaction flask were sodium methoxide (77 mg, 1.42 mmol, 2.5 equiv), 2,6-dimethoxynaphthalene (**9**, 107 mg, 0.567 mmol, 1.0 equiv), hexamethyldisilathiane (305 mg, 1.42 mmol, 2.5 equiv), and 1,3-dimethyl-2-imidazolidinone (3.0 mL). After workup and purification by use of a chromatotron (1-mm plate, 50% EtOAc in hexanes as eluant), 2,6-dihydroxynaphthalene (**10**) was obtained as a white solid (mp 224.0–225.0 °C; lit.[29e] mp 223.0–225.0 °C) in 96% yield (87 mg, 0.54 mmol): GC (injector temperature 260 °C; column program: initial temperature 100 °C, duration 2.00 min; increment rate 15 °C/min; final temperature 250 °C) t_R 8.44 min; TLC R_f 0.35 (40% EtOAc in hexanes); ^{1}H NMR (DMSO-d_6 + $CDCl_3$, 80 MHz) δ 6.93–7.60 (m, 6 H, 2 C_6H_3), 8.21–8.85 (br, 2 H, 2 OH); IR (KBr) 3154 (s, OH), 3002 (s, =C—H), 2919 (s), 2872 (s), 1901 (w), 1664 (s), 1619 (s, C=C), 1519 (s, C=C), 1454 (s, C=C), 1449 (s), 1402 (m), 1367 (s), 1284 (s), 1243 (s, C—O), 1143 (m, C—O), 1120 (m, C—O), 1085 (w), 1038 (w), 967 (w), 934 (w), 873 (m), 808 (m), 773 (s), 744 (m), 685 (w) cm^{-1}. Its physical properties and spectroscopic characteristics are consistent with those of an authentic sample.[29e]

Phloroglucinol (12). Method A. The standard procedure was followed. Reagents added into the reaction flask were sodium methoxide (130 mg, 2.41 mmol, 2.5 equiv), 3,5-dimethoxyphenol (**11**, 149 mg, 0.963 mmol, 1.0 equiv), hexamethyldisilathiane (518 mg, 2.41 mmol, 2.5 equiv), and 1,3-dimethyl-2-imidazolidinone (3.0 mL). After workup, most of 1,3-dimethyl-2-imidazolidinone in the resulting mixture was removed by use of a column packed with basic aluminum oxide. Further purification was performed by use of a chromatotron (1-mm plate, 50% EtOAc in hexanes as eluant) to give phloroglucinol (**12**) as a yellow solid (mp 116.5–117.0 °C; lit.[28d] mp 117.0 °C) in 83% yield (101 mg, 0.799 mmol): GC (injector temperature 260 °C; column program: initial temperature 100 °C, duration 2.00 min; increment rate 15 °C/min; final temperature 250 °C) t_R 6.67 + 7.67 min; TLC R_f 0.37 (60% EtOAc in hexanes); ^{1}H NMR (DMSO-d_6 + $CDCl_3$, 80 MHz) δ 5.89 (s, 3 H, C_6H_3), 8.37 (br s, 3 H, 3 OH); IR (KBr) 3472 (s, OH) 3190 (br s, OH), 2931 (m), 2882 (w), 2684 (w), 1619 (s, C=C), 1531 (m), 1496 (s, C=C), 1414 (m), 1296 (m), 1155 (s, C—O), 1002 (s, C—O), 814 (m), 779 (m), 732 (m) cm^{-1}. Its physical properties and spectroscopic characteristics are consistent with those reported in literature.[31,32]

Method B. The standard procedure was followed. Reagents added into the reaction flask were sodium hydride (35 mg, 1.4 mmol, 1.5 equiv), 3,5-dimethoxyphenol (**11**, 149 mg, 0.963 mmol, 1.0 equiv), hexamethyldisilathiane (311 mg, 1.44 mmol, 1.5 equiv), and 1,3-dimethyl-2-imidazolidinone (3.0 mL). After workup and purification as described in method A, phloroglucinol (**12**) was obtained as a yellow solid in 75% yield (91 mg, 0.72 mmol). Its spectroscopic characteristics were identical with those listed above.

1-Methyl-2,6,7-trihydroxynaphthalene (14). Method A. The standard procedure was followed. Reagents added into the reaction flask were sodium methoxide (93 mg, 1.72 mmol, 2.5 equiv), 6,7-dimethoxy-1-methyl-2-naphthol (**13**, 150 mg, 0.688 mmol, 1.0 equiv), hexamethyldisilathiane (370 mg, 1.72 mmol, 2.5 equiv), and 1,3-dimethyl-2-imidazolidinone (3.0 mL). After workup, most of 1,3-dimethyl-2-imidazolidinone in the resulting mixture was removed by use of a column packed with neutral aluminum oxide. Further purification was performed by use of a chromatotron (1-mm plate, 50% EtOAc in hexanes as eluant) to give triol **14** as a yellow solid (mp 118.5–119.0 °C) in 78% yield (102 mg, 0.537 mmol): GC (injector temperature 260 °C; column program: initial temperature 140 °C, duration 2.00 min; increment rate 15 °C/min; final temperature 250 °C) t_R 8.22 min; TLC R_f 0.31 (50% EtOAc in hexanes); ^{1}H NMR (DMSO-d_6 + $CDCl_3$, 80 MHz) δ 2.41 (s, 3 H, CH_3), 6.60–7.46 (m, 4 H, $C_{10}H_4$), 7.85–8.61 (br s, 3 H, 3 OH); IR (KBr) 3401 (s, OH), 3295 (br s, OH), 3166 (s, =C—H), 2931 (m), 1643 (s, C=C), 1614 (s, C=C), 1537 (s, C=C), 1447 (w), 1411 (s), 1396 (s), 1342 (m), 1297 (w), 1264 (s), 1252 (s), 1204 (s, C—O), 1159 (m), 1076 (m, C—O), 1039 (w), 862 (m), 799 (m), 772 (w) cm^{-1}; exact mass calcd for $C_{11}H_{10}O_3$ 190.0630, found 190.0631.

Method B. The standard procedure was followed. Reagents added into the reaction flask were sodium hydride (25 mg, 1.03 mmol, 1.5 equiv), 6,7-dimethoxy-1-methyl-2-naphthol (**13**, 150 mg, 0.688 mmol, 1.0 equiv), hexamethyldisilathiane (222 mg, 1.03 mmol, 1.5 equiv), and 1,3-dimethyl-2-imidazolidinone (3.0 mL). After workup and purification as described in method A, triol **14** was obtained as a yellow solid in 72% yield (94 mg, 0.50 mmol). Its spectroscopic characteristics were identical with those listed above.

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The Stereochemistry of the Aryl Phosphate/Aryl Phosphonate Rearrangement in 1,3,2-Oxazaphospholidine 2-Oxides

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On treatment with LDA/THF (aryloxy)phospholidines in the pseudoephedrine/ephedrine series undergo P–O to P–C rearrangement to afford arylphospholidines with retention of configuration at phosphorus. The stereochemistry of each product was assigned by ^{1}H NMR chemical shift and C-4/C-5 vicinal proton coupling constant analysis and comparison with known phenylphospholidines.

Introduction

The base (LDA or *n*-BuLi) induced rearrangement of arylphosphate **1** to arylphosphonate **2** shown in Figure 1 was first reported by Melvin in 1981.[1] Since that time Cambie and Palmer[2] as well as Dhawan and Redmore[3] have demonstrated the usefulness of this synthetic method. In an effort to probe the stereochemistry of this reaction at the phosphorus atom, the base-initiated rearrangement

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