Generation of the 1,3-Phosphasilolene Skeleton from Ortho-Silylated Biarylphosphonates

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Treatment of diethyl 2-(3-trimethylsilyl)biphenylphosphonate **15** with excess methyllithium affords a mixture of the 2*H*-benzo[*d*]-1,3-phosphasilolen-1-one **16** together with the silyl transfer product **17**. Deuterium incorporation studies show that the mechanism involves the conversion from **15** to **19** and **20**, followed by formation of a siliconate intermediate **21**. Cleavage of an exocyclic Si−C bond affords **16** while endocyclic C−Si cleavage leads to **17**. The phosphasilolene structure **16** is confirmed by X-ray crystallography.

In the course of studies designed to prepare chiral phosphines as potential nucleophilic catalysts,[1] we have encountered an unusual series of heterocycles belonging to the 1,3-phosphasilolene family. This ring system is virtually unprecedented. The only prior report describes a structure where an analogous 1,3-phosphasilolane subunit is present as part of a 1,6-diphospha-4-sila-bicyclo[3.2.0]hept-6-ene skeleton.[2] In view of the unusual structure and the unexpected nature of the reaction that produced it from an ortho-trimethylsilylated arylphosphonate, we have investigated relevant structural and mechanistic aspects as described below.

In the initial experiments, the hydroxybinaphthyl phosphonate **1a**[3] was converted into **2** via O-methylation to **1b** followed by ortho lithiation and reaction with $ClSiMe_3$. An attempt was then made to convert **2** into the corresponding phosphine oxide **3** using excess methyllithium in ether (−10°, 40 min). However, **3** was not detected in the mixture of products obtained after aqueous workup. Instead, three products eventually identified as **4** (27%), **5** (13%), and **6** (37%) were obtained by chromatography. The structures were deduced from characteristic ^1H NMR signals (nonequivalent $Si-CH_3$ signals in **4** and **5**; ABX pattern for the $SiCH_2P$ subunit of **6**), and the detailed structure of **4** was established by X-ray methods. Support for the assignment of **5** was obtained after reduction ($CeCl_3 + LiAlH_4 + NaBH_4$)[4] to give the borane complex **7**, and the latter was characterized by X-ray crystallography.

The structures of **4** and **5** contain obvious clues regarding their origin, and the silicon transfer product **6** implicates the intermediacy of a pentavalent siliconate species.[5] However, the timing of the key C−P bond forming events was not clear, and was not convenient to study in the relatively inaccessible methoxybinaphthyl system. An investigation of simpler model compounds was therefore initiated.

Treatment of diethyl 2-(trimethylsilyl)phenylphosphonate **8** with excess methyllithium in THF was examined under the usual methyllithium−ether conditions. However, the heterocycles **9** or **10** were not detected among the products. On the other hand, a silicon migration product **11** (38%) was isolated, analogous to structure **6** in the binaphthyl series, and polar (unknown) decomposition products were noted. These results suggested that the phosphasilolene or its precursors may be sensitive to the presence of an aryl substituent next to phosphorus. Accordingly, a biphenyl structure was investigated that more closely resembles the original binaphthyl system. Phosphonate **14** was prepared from phenol **12** via the corresponding triflate **13**[6a] in 85% overall yield using a precedented method for palladium-catalyzed phosphonylation[3a] as the key step to prepare the known product **14**.[6b] Conversion to the trimethylsilyl derivative **15** was then performed via ortho lithiation and trapping with $ClSiMe_3$ (70−80% yield).

When **15** was reacted with methyllithium in ether, a complex mixture resulted that contained the characteristic NMR signals expected for **16** and **17**. However, cleaner product mixtures and faster reactions were noted in THF, and these conditions were adopted for subsequent investigations. The phosphasilolene **16** was more sensitive to decomposition than was the analogue **4** in the binaphthyl series, but it could be purified by rapid flash chromatography and was obtained in 42% yield. The silyl migration product **17** was also isolated (26%) and its structure was clear from NMR comparisons with **6**. The phosphasilolene **16** was fully characterized and was found to resemble the binaphthyl analogue **4** in key spectroscopic features. The crystal structure was also obtained for final confirmation.

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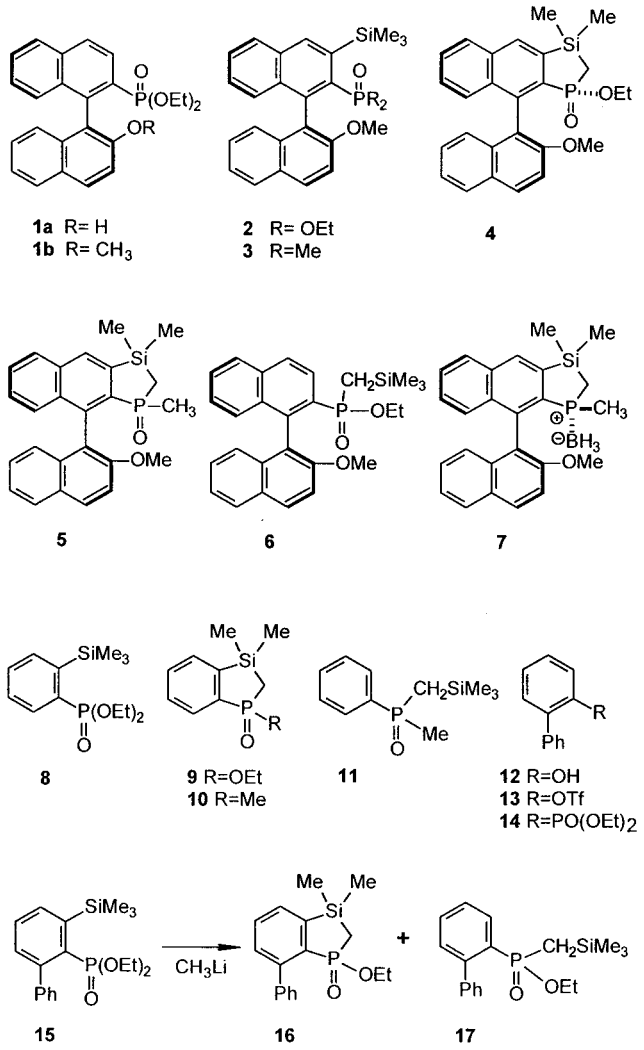
Scheme 1



With structural assignments in hand, we sought to define the sequence of bonding events leading to the phosphasilolene. Two distinct pathways were considered. The first pathway begins with the phosphonate-directed metalation of **15** to give **18** followed by cyclization (path a). A similar directed metalation−cyclization sequence has been proposed in the reaction of *N*,*N*-diisopropyl(2-trimethylsilyl)benzamide with methyllithium.[7] If **18** is formed, then conversion into the silyl migration product **17** might occur by the reaction of a second equivalent of methyllithium with **16** at the silicon atom. Alternatively (path b), initial displacement of an ethoxy group in **15** might form **19**, and metalation to **20** and cyclization via a siliconate **21** might also lead to **16**. According to path b, **21** would be the logical precursor of both of the principal products **16** and **17**, either of which could be formed via cleavage of a C−Si bond. If path a is correct, then the same intermediate **21** might be formed from the interaction of the phosphasilolene **16** with excess methyllithium, followed by cleavage of the Si−C aryl bond. In either case, cleavage at the stage of **21** might occur to generate the aryllithium species **22** or might take place during aqueous workup if **21** survives under the reaction conditions.

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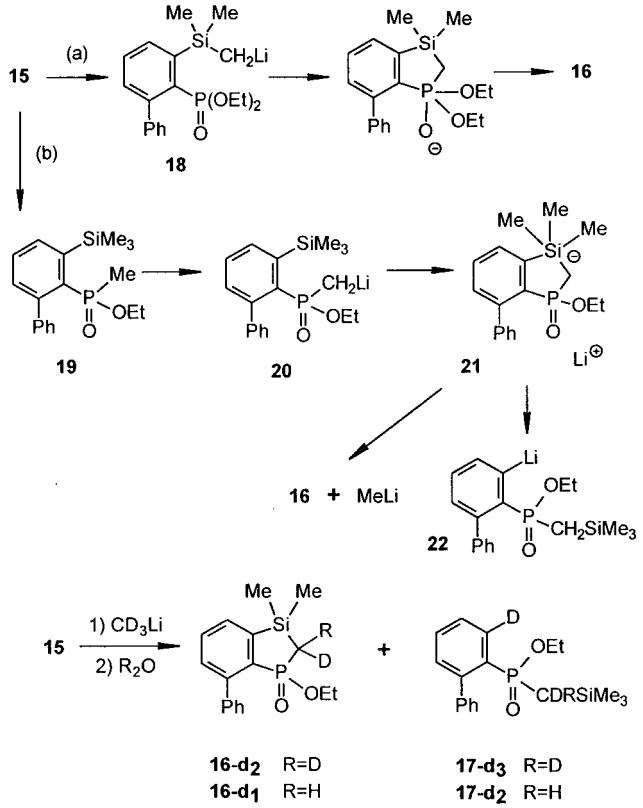
Scheme 2



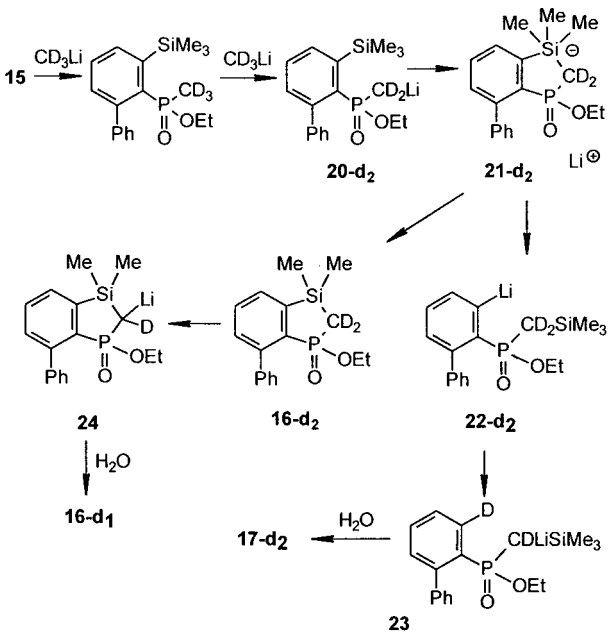
To probe the timing of these events and to distinguish between path a and path b, the experiment was repeated using CD_3Li followed by quenching with D_2O or with H_2O. The CD_3Li-D_2O sequence afforded the usual products, and inspection of the ^1H NMR spectra revealed the presence of a $P-CD_2Si$ group in both the phosphasilolene **16-d$_2$** and in the silyl transfer product. The latter was found to contain a third deuterium ortho to phosphorus on the aromatic ring, as shown in structure **17-d$_3$**.

When the experiment was repeated using CD_3Li followed by quenching with H_2O, the results were especially informative. Both of the principal products contained a P−CHDSi subunit, and the silyl transfer product still contained the ortho deuterium. These products are represented by structures **16-d$_1$** and **17-d$_2$** in Scheme 2.

The deuterium incorporation results argue against the directed metalation pathway a. This mechanism does not explain complete deuteration α to phosphorus in the CD_3Li-D_2O experiment as well as the clean monodeuteration using the CD_3Li-H_2O sequence. Path b is more consistent with the observations, but the deuterium incorporation pattern requires additional proton-transfer events after the formation of the initial products. The details are presented in the context of the CD_3Li-H_2O experiment as shown in Scheme 3.

Conversion from **15** via **19-d$_3$** and **20-d$_2$** affords the siliconate species **21-d$_2$** via path b, but the siliconate does not survive up to the aqueous quench. The labeling results require that **21-d$_2$** undergoes conversion into other organolithium intermediates prior to workup and via two different pathways. The first involves cleavage of an endocyclic C−Si bond to give an aryllithium species **22-d$_2$**, followed by conversion to **23**. The evidence does not prove whether **23** is formed via intramolecular

Scheme 3



deuterium−lithium exchange. That would be the simplest explanation, but an alternative is possible where **22-d$_2$** is deuterated by intermolecular deuterium transfer with subsequent intermolecular lithiation by excess CD_3Li to give the same intermediate **23**.

Alternatively, siliconate **21-d$_2$** can undergo exocyclic C−Si bond cleavage. This produces 1 equiv of methyllithium together with **16-d$_2$**, and lithiation of the latter leads to **24**. Finally, aqueous workup quenches the organolithium species **23** and **24**, resulting in the observed products **16-d$_1$** and **17-d$_2$**. A change to D_2O in the quenching step would incorporate an additional deuterium in each product, as observed in the experiment described earlier.

According to the evidence, the siliconate **21** is responsible for both of the major products. Similar intermediates have been invoked in prior studies,[5] and a recent report mentions the detection of an analogous structure containing five Si−C bonds as well as the further transformation into a neutral silane and an organolithium species.[5a] However, the prior reports deal with the interconversion of alkyllithium or aryllithium species via the siliconate. In the present case, a stabilized α-lithiophosphinate **20** would have to be sufficiently reactive to generate the siliconate **21**.

Conversion from **20** to **21** and eventually to **16** places two-third row elements into a five-membered ring. According to the X-ray data (Supporting Information; brief summary in Figure 1), this produces modest distortion from tetrahedral bond angles in the phosphasilolenes (structure **4**: endocyclic C−P−C, 102.3°; endocyclic C−Si−C, 98.2°; structure **16**: endocyclic C−P−C, 101.8°; endocyclic C−Si−C, 97.2°). Thus, it is unlikely that ring strain plays a substantial role in the final product ratio. More likely, the product ratio is related to the relative rates of C−Si bond cleavage, coupled with the rates for the final lithiation steps to **23** and **24**. The formation of these stabilized organolithium species from **16** probably terminates further opportunities for interconversion of organolithium species via the siliconate. However, it is possible that siliconate formation is reversible in some

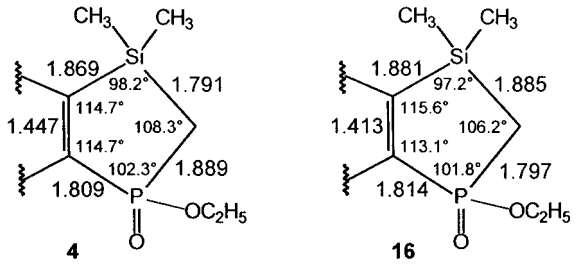


Figure 1. Summary of X-ray data for **4** and **16**: Bond lengths (Å) and angles.

of the earlier steps and that the relative rates for conversion to **23** and **24** influence the eventual product ratio.

In summary, the formation of phosphasilolenes (**4**, **16**) and silicon migration products (**6**, **11**, **17**) from orthosilylated arylphosphonates can be attributed to the intermediacy of a pentavalent, anionic siliconate species similar to **21**. Some of the siliconate undergoes endocyclic bond cleavage, leading to silicon migration products (as in the formation of **11** from **8**). If the adjacent aryl ring is present, as in the case of **2** or **15**, then the phosphasilolene derived from exocyclic C−Si cleavage can also be isolated. It is possible that the relatively compact cyclic structures **4** or **16** would have an advantage in terms of nonbonded interactions with the adjacent aryl ring compared to the alternatives **6** or **17**. This factor may be responsible for a lower tendency to form a phosphasilolene from the siliconate in substrates lacking the adjacent aryl ring.

Experimental Section

General. Merck silica gel plates with F-254 indicator were used in analytical TLC, and silica gel 60 from EM Science was used in flash column chromatography. Diethyl ether and THF were distilled from Na/benzophenone ketyl. Dichloromethane was distilled from P_2O_5. Acetonitrile and benzene were distilled from P_2O_5 and stored over 3 Å molecular sieves. Toluene was distilled over CaH_2. Pyridine, TMEDA, diethylamine, diisopropylethylamine, and triethylamine were distilled from CaH_2. Air and/or moisture sensitive reactions were performed with either flame or oven dried glassware under N_2 atmosphere.

Diethyl 3-(Trimethylsilyl)-2-biphenylphosphonate 15. To a cooled (−78 °C) solution of TMEDA (1.92 mL, 12.75 mmol, Aldrich, distilled from KOH) in Et_2O (40 mL) was added sec-BuLi (8.1 mL of a 1.38 M solution in cyclohexane, 11.2 mmol, Aldrich) followed by dropwise addition (2 min) of a solution of diethyl 2-biphenylphosphonate **14**[6a] (see Supporting Information for an improved preparation; 2.313 g, 7.97 mmol) in Et_2O (18 mL). The dark red solution was stirred for 4 min followed by dropwise addition of freshly distilled TMSCl (5.03 mL, 39.84 mmol, Aldrich). The light red solution was stirred for 40 min at −78 °C, slowly (1 h) warmed to room temperature, and stirred at room temperature for an additional 1 h. The reaction mixture was quenched with H_2SO_4 (6 mL of a 5% solution in water), and the ether layer was separated, washed with saturated $NaHCO_3$ and water, and dried ($MgSO_4$). After removal of solvent (aspirator), the residue was purified by flash chromatography on silica gel (13 × 2 cm), 1:5 EtOAc/hexane eluent; fraction 1 (25 mL) was blank, fractions 2−3 (15 mL ea) contained side products, fractions 4−5 (15 mL ea) product + trace of impurity (1.19 g; after recrystallization from hexanes 1.04 g of pure product was obtained), fractions 6−14 (15 mL ea) contained additional product (1.12 g) for a total yield of pure material of 2.16 g (75%). Analytical TLC on silica gel, 1:2.5 acetone/hexane, $R_f = 0.52$. Pure material was obtained by crystallization from hexane, mp 83−84 °C. The structure

was confirmed by X-ray crystallography. Anal. Calcd: C, 62.95; H, 7.52. Found: C, 63.19; H, 7.45. IR (KBr, cm^{-1}) 2958, C−H; 1243, P═O; 300 MHz NMR ($CDCl_3$, ppm) δ 7.80 (1H, ddd, J = 7.6, 4.1, 1.4 Hz) 7.49 (1H, ddd, J = 7.6, 7.6, 1.9 Hz) 7.39−7.23 (6H, m) 3.88 (2H, ddq, J = 7.0, 9.9, 7.0 Hz) 3.73 (2H, ddq, J = 7.0, 9.9, 7.0 Hz) 1.09 (6H, br d, J = 7.0, 7.0 Hz) 0.46 (9H, s). ^{31}P NMR (121.367 MHz, {H}, $CDCl_3$, ppm) δ 20.1.

Conversion of 15 into 16 and Silyl Transfer Product 17. 1-Ethoxy-3,3-dimethyl-7-phenyl-2*H*-benzo[*d*]-1,3-phosphasilolen-1-one (16). To a mixture of MeLi (3.6 mL of a 1.4 M solution in ether, 5 mmol, Aldrich) and THF (40 mL) was added silylated phosphonate **15** (300 mg, 0.83 mmol) as a solution in 10 mL of THF over 2 min at −20 °C. The reaction mixture was stirred for 40 min between −20 and −15 °C, resulting in a yellow solution. Next, H_2SO_4 (10 mL of 5% solution) was added at −15 °C followed by evaporation of the reaction mixture to ca. 20 mL and addition of ca. 30 mL of Et_2O. The ether layer was separated and washed with saturated $NaHCO_3$ and water and dried ($MgSO_4$). After removal of solvent (aspirator), the residue was purified by flash chromatography on silica gel (14 × 1.2 cm), 1:1.1:1 ether/hexane/acetonitrile eluent; fractions 1−5 (7.2; 4 × 5 mL respectively) were blank, fractions 6−9 (5 mL ea) contained silyl transfer product **17** (71 mg, 26%, analytical TLC on silica gel, 1:1:1 ether/hexane/acetonitrile, R_f = 0.54), and fractions 10−15 (5 mL ea) contained phosphasilolene **16** (113 mg, 42%, analytical TLC on silica gel, 1:1:1 ether/hexane/acetonitrile, R_f = 0.40). Pure **17** was obtained by crystallization from hexane, mp 52−53 °C. Molecular ion calcd for $C_{18}H_{25}O_2PSi$: 332.13617; found m/e = 332.1360, error = 1 ppm; base peak= 165 amu; IR (neat, cm^{-1}); 1217, P═O; 3055, ═C−H; 300 MHz NMR ($CDCl_3$, ppm) δ 8.26−8.18 (1H, m) 7.57−7.26 (8H, m) 4.09 (1H, ddq, J = 7.0, 9.9, 7.0 Hz) 3.77 (1H, ddq, J = 7.0, 9.9, 7.0 Hz) 1.27 (3H, dd, J = 7.0, 7.0 Hz) 0.79 (1H, dd, J = 14.4, 16.9 Hz) 0.73 (1H, dd, J = 14.4, 13.7 Hz) −0.05 (9H, s). ^{31}P NMR (121.367 MHz, {H}, $CDCl_3$, ppm) δ 44.0. Pure phosphasilolene **16** was obtained by crystallization from ether, mp 100−101 °C. The structure was verified by X-ray crystallography. Molecular ion calcd for $C_{17}H_{21}O_2PSi$: 316.10486; found m/e = 316.1050, error = 0 ppm. Anal. Calcd: C, 64.52; H, 6.7. Found: C, 64.24; H, 6.64. IR (KBr, cm^{-1}) 1214, P═O; 300 MHz NMR ($CDCl_3$, ppm) δ 7.66−7.52 (4H, m) 7.47−7.32 (4H, m) 3.75 (1H, ddq, J = 9.9, 7.2, 7.2 Hz) 3.57 (1H, ddq, J = 9.9, 8.6, 7.2 Hz) 1.46 (1H, dd, J = 17.9, 14.5 Hz) 1.29 (1H, dd, J = 17.0, 14.5 Hz) 0.93 (3H, dd, J = 7.2, 7.2 Hz) 0.50 (3H, s) 0.42 (3H, s). ^{31}P NMR (121.367 MHz, {H}, $CDCl_3$, ppm) δ 59.6.

Experiments Using CD_3Li. A. Quench with D_2O. The experiment was carried out as above for **16** and **17**. Instead of MeLi, CD_3Li−LiI (0.5 M solution in Et_2O, Aldrich) was used. The reaction mixture was quenched with 2.5% H_2SO_4/D_2O and compounds were separated on a silica gel plate (200 × 200 × 2 mm) in acetonitrile/hexane/Et_2O 1:1:1. Dideuterated phosphasilolene **16-d_2**: molecular ion calcd for $C_{17}H_{19}O_2D_2SiP$ 318.11740, found m/e = 318.1163, error = 3 ppm. Trideuterated silyl transfer product **17-d_3**: molecular ion calcd for $C_{18}H_{22}D_3O_2PSi$ 335.15498, found m/e = 335.1544, error = 2 ppm.

B. Quench with H_2O. The experiment was carried out as for part A, except that the reaction mixture was quenched with 5% H_2SO_4/H_2O. Monodeuterated phosphasilolene **16-d_1**: molecular ion calcd for $C_{17}H_{20}O_2DSiP$ 317.11112, found m/e = 317.1119, error = 2 ppm. The ring proton appeared as a broad doublet in the 300 MHz NMR spectrum in $CDCl_3$, δ = 1.46 ppm (^2J = 17.9 Hz). Dideuterated silyl transfer product **17-d_2**: molecular ion calcd for $C_{18}H_{23}D_2O_2PSi$ 334.14870, found m/e = 334.1486, error = 0 ppm. The proton between phosphorus and silicon appeared as two broad doublets in the 300 MHz NMR spectrum in $CDCl_3$ (due to the presence of two diastereomers formed in the reaction) at 0.73 ppm (^2J = 13.7 Hz) and 0.79 ppm (^2J = 16.9 Hz).

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Supporting Information Available: Experimental details and characterization for **1b**, **2**, **4**, **5**, **6**, **7**, **8**, **11**, and **14**. NMR spectra of new compounds and selectively deuterated **16** and **17**; X-ray data tables for **4**, **7**, and **16** (52 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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