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Activation of silylphosphines by diethyl azodicarboxylate: novel silylation of alcohols ☆

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Abstract—A novel activation mode of silylphosphines and an application of that to silylation of alcohols were described. Silylphosphines were found to be instantly activated by means of DEAD and PPTS to form reactive silyl cation equivalents. By using the activated species, silylation of alcohols successfully proceeded under mild acidic condition.

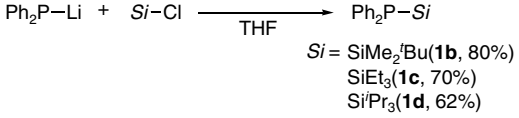
Silylphosphines are versatile reagents in inorganic and organometallic chemistry for the synthesis of various phosphorus compounds and metal complexes. Although a number of studies of the phosphorus–silicon linkage have appeared,[1] applications of silylphosphines in organic synthesis were quite limited probably due to their highly sensitive nature to oxygen and/or moisture.[2] Even in these limited uses, the silyl group in the silylphosphine tends to waste as byproduct.[2,3] Herein we wish to report a novel utility of silylphosphines as a silyl group source for silylation of a hydroxyl group, together with diethyl azodicarboxylate.

A phosphorus–silicon bond of a silylphosphine was known to be easily cleaved by a polar electrophile; for example, the reaction of trimethylsilyldiphenylphosphine **1a** with benzaldehyde gave the adduct as TMS ether via the silyl group migration to the oxygen atom during addition.[4] When an external nucleophile exists and the internal silyl group migration could be suppressed, silylation of the external nucleophile would proceed by the electrophile-activated silylphosphine.

Before testing our hypothesis, novel silylphosphines having ordinary protective silyl groups, that is, TBDMS (**1b**), TES (**1c**), and TIPS (**1d**) were prepared at first from the corresponding chlorosilanes and lithium diphenylphosphides by a slightly modified procedure reported for **1a** (Scheme 1).[5,6]

Survey on the reactivities of **1b–d** toward electrophiles revealed that these silylphosphines were more stable and much less reactive[7] than **1a**; reactions of **1b–d** required much longer time and gave the adducts in poor yields. As described above, **1a** reacted with benzaldehyde within 3 h to give the adduct in 80% yield, whereas the reaction of **1b** did not complete even after 18 h affording the adduct in only 56% yield. Among tested electrophiles, diethyl azodicarboxylate (DEAD) was the only electrophile, which reacted immediately with **1b** to give the corresponding adduct **2** in good yield (Scheme 2).[8]

When the reaction of **1b** with DEAD was conducted in the presence of alcohol **3** as an external nucleophile, competitive reactions occurred toward the silyl ether **4b** and the adduct **2**. Formation of **2** was still major at this stage (Fig. 1). The internal silyl group migration affording **2** could be suppressed by a protonation of the initially formed betaine intermediate.[9] Indeed, pyridinium *p*-toluenesulfonate (PPTS) and tetrazole were found to be effective for this purpose; the silyl ether **4b** was obtained from **3** and **1b** in the presence of PPTS and tetrazole in 95% and 85% yields, respectively (Fig. 1).



Scheme 1.

Keywords: Silylphosphine; Silylation; Silyl ether.
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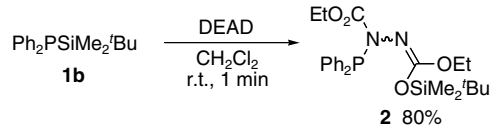


Scheme 2.

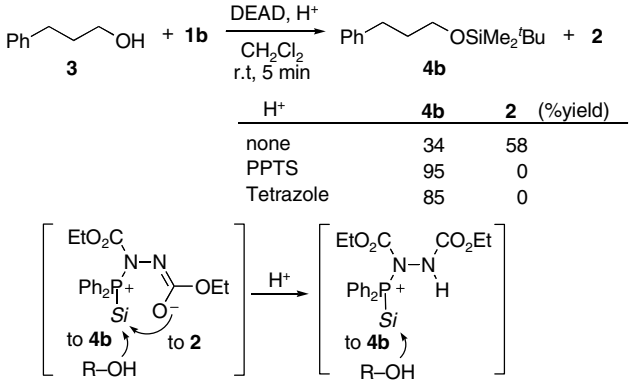


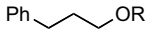
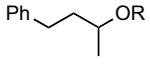
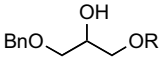
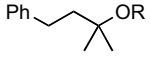
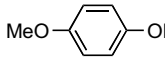
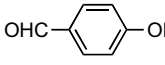
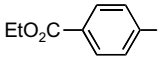
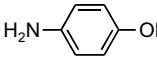
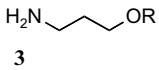
Figure 1. A plausible mechanism and an effect of protonation.

No silyl ether was formed from the adduct **2** or silylphosphine **1b** alone even in the presence of PPTS. Thus silylation through the adduct or silylphosphine itself can be ruled out. The silylation seemed to proceed through the activated silylphosphine, as shown in Figure 1.

Silylphosphines **1b–d** were then subjected to silylation of various alcohols using DEAD and PPTS. The results were shown in Table 1.

Incorporation of TBDMS and TES groups to primary, secondary alcohols and phenols, and TIPS group to primary alcohols and a phenol was successfully conducted in good yields within a few minutes, by using **1b–1d** with DEAD in the presence of PPTS (Table 1).[10] It should be noted that the present silylation proceeded under mild acidic condition, though silyl ethers usually prepared in the presence of base. The reaction was unaffected by other functional groups such as an amino group and carbonyl groups (entries 6–9). Steric hindrances of both an alcohol and a silyl group tend to prevent the present silylation; silylation of a secondary alcohol by **1b** and **1c** required an additional amount of the reagents to give the products in good yields. Under the standard condition, the silylated products were

Table 1. Silylation of alcohols by silylphosphine–DEAD–PPTS

Entry	Ph_2PSi	Alcohol (R = H)	Product (R = *Si*)	Yield (%)[a,b]
1	$Ph_2PSiMe_2{}^tBu$ **1b**	 **3**	**4b**	95
2		 **5**	**6b**	90[c]
3		 **7**	**8b**	84[d]
4		 **9**	**10b**	—[e]
5		 **11**	**12b**	86
6		 **13**	**14b**	71
7		 **15**	**16b**	73
8		 **17**	**18b**	68
9		 **19**	**20b**	74
10	Ph_2PSiEt_3 **1c**	**3**	**4c**	91
11		**5**	**6c**	84[c]
12		**7**	**8c**	81[d]
13		**11**	**12c**	84
14	$Ph_2PSi^iPr_3$ **1d**	**3**	**4d**	78[f]
15		**5**	**6d**	—[e]
16		**7**	**8d**	73[f]
17		**11**	**12d**	70[f]

[a] Conditions: **1b–d** (1.2 equiv), DEAD (1.2 equiv), PPTS (1.2 equiv) in CH_2Cl_2, rt, 5 min.
[b] Isolated yields. All products were identified by comparison with the authentic samples prepared by a generic silylation procedure.[11]
[c] 2.0 equiv of each reagent was used.
[d] Only the primary hydroxyl group was silylated.
[e] No silylation took place though silylphosphine and DEAD were consumed.
[f] 1.5 equiv of each reagent was used.

afforded in only 30–58% yields. Introduction of TIPS group also required slightly excess reagents for satisfactory results (entries 14, 16, and 17). No silylation occurred even under more drastic conditions with excess reagents in the reactions of tertiary alcohol **9** with **1b** (entry 4) and secondary alcohol **5** with **1d** (entry 15). A primary hydroxyl group was rapidly silylated in the presence of a secondary hydroxyl group in quite selective manner (entries 3, 12, and 16). In contrast, silylation of diol **7** by using common methods in short period resulted in low selectivity (TBDMSOTf/2,6-lutidine/DMF: **8b** 18%; bis-silyl ether 51%) or poor yield ($TBDMSCl/Et_3N/DMAP/CH_2Cl_2$: **8b** 33%) under similar conditions (1.2 equiv of each silylating agents, rt, 5 min). These results clearly showed the peculiar reactivity of the present reagents that differed from common silylating agents; silylation of a primary hydroxyl group proceeded quite rapidly as a silyl triflate with high selectivity.

In conclusion, we have discovered that silylphosphines were instantly activated by means of DEAD to form the reactive silyl cation equivalents. The present reaction provides a novel utility of silylphosphines toward organic synthesis as an acidic silylation procedure for hydroxyl groups. Further application of silylphosphines is now under investigation.

Acknowledgements

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6. Representative procedure for preparation of **1b**: To a solution of *tert*-butyldimethylchlorosilane (6.3 g, 42 mmol) in THF was added a THF solution of lithium diphenylphosphide (38 mmol) prepared from lithium, triphenylphosphine, and *tert*-butyl chloride under N_2 at rt. A distinct red color of lithium diphenylphosphide soon faded. After the mixture was refluxed for 30 min, the solvent was removed under reduced pressure, and the residue was directly distilled in vacuo affording **1b** (9.1 g, 80%); physical and spectral data for **1b**: bp 152 °C/1.5 mmHg. Anal. Calcd for $C_{18}H_{25}PSi$: C, 71.96; H, 8.39. Found: C, 72.00; H, 8.52. ^1H NMR (C_6D_6) δ 7.73–7.68 (m, 4H), 7.19–7.11 (m, 6H), 1.03 (s, 9H), 0.21 (s, 3H), 0.20 (s, 3H); ^{13}C NMR (C_6D_6) δ 136.30 (d, $J_{C-P} = 15.7$ Hz), 135.01 (d, $J_{C-P} = 18.5$ Hz), 128.33 (d, $J_{C-P} = 7.2$ Hz), 127.64 (d, $J_{C-P} = 0.8$ Hz), 27.38 (d, $J_{C-P} = 2.9$ Hz), 18.79 (d, $J_{C-P} = 13.1$ Hz), −4.98, −5.07; $^{31}P\{^1H\}$ NMR (C_6D_6) δ −61.2. **1c**: bp 140 °C/0.7 mmHg. ^1H NMR (C_6D_6) δ 7.78–7.67 (m, 4 H), 7.24–7.13 (m, 6 H), 1.04 (t, $J = 6.4$ Hz, 9 H), 0.84 (dq, $J = 3.2$, 6.4 Hz, 6 H); ^{13}C NMR (C_6D_6) δ 135.11 (d, $J_{C-P} = 15.7$ Hz), 134.01 (d, $J_{C-P} = 18.5$ Hz), 128.17 (d, $J_{C-P} = 7.3$ Hz), 127.64 (d, $J_{C-P} = 0.8$ Hz), 27.38 (d, $J_{C-P} = 2.4$ Hz), 14.42 (d, $J_{C-P} = 11.1$ Hz); $^{31}P\{^1H\}$ NMR (C_6D_6) δ −60.7. **1d**: bp 165 °C/0.6 mmHg. Anal. Calcd for $C_{21}H_{31}PSi$: C, 73.64; H, 9.12. Found: C, 73.80; H, 9.21. ^1H NMR (C_6D_6) δ 7.80–7.76 (m, 4 H), 7.19–7.11 (m, 6 H), 1.51–1.42 (dsept, $J = 7.6$, 2.0 Hz, 3 H), 1.21 (d, $J = 7.6$ Hz, 18H); ^{13}C NMR (C_6D_6) δ 136.05 (d, $J_{C-P} = 15.8$ Hz), 134.91 (d, $J_{C-P} = 18.6$ Hz), 128.37 (d, $J_{C-P} = 7.1$ Hz), 127.48, 19.48 (d, $J_{C-P} = 4.7$ Hz), 13.38 (d, $J_{C-P} = 10.5$ Hz); $^{31}P\{^1H\}$ NMR (C_6D_6) δ −57.8.
7. These silylphosphines are still somewhat sensitive to oxygen and should avoid contact with the air.
8. It was difficult to determine the accurate structure of the adduct **2** because it showed very broad signals in its NMR spectra. The FABMS spectrum of **2** showed a parent peak at $m/z = 475$, which corresponded to a simple sum of the molecular weights of **1b** and DEAD. In addition, **2** gave the corresponding desilylated phosphinohydrazinedicarboxylate product quantitatively by an acidic hydrolysis. These facts clearly indicated that **2** is a 1:1 adduct of **1b** and DEAD. The ^1H, ^{13}C, and ^{31}P NMR spectra of **2** at rt showed the presence of three isomers, which probably corresponded to one of the *E*/*Z* isomer and the rotamers of the other. It is in accord with the observation of the coalescence of three peaks in ^{31}P NMR to two peaks on heating. Thus, we represented tentatively the most plausible structure of **2** as in Scheme 2 speculating from the results described above and the mechanistic consideration of the Mitsunobu reaction.[9]
9. These betaines were speculated from the mechanism accepted for the Mitsunobu reaction, see: Hughes, D. L. *Org. React.* **1992**, *42*, 335.
10. A typical procedure of the silylation by a silylphosphine and DEAD is depicted as follows: to a mixture of **1b** (54 mg, 0.18 mmol), 3-phenyl-1-propanol **3** (20 mg, 0.15 mmol), and PPTS (45 mg, 0.18 mmol) in CH_2Cl_2 (1.5 mL) was added DEAD (31 mg, 0.18 mmol) dropwise at rt. A distinct yellow color of DEAD immediately dissappeared upon addition. After the addition was completed, the reaction mixture was concentrated and purified by a column chromatography on silica gel to afford the silyl ether **4b** (36 mg, 95%).
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