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SILYL PHOSPHITES. 8. DEOXYGENATION REACTIONS BY MEANS OF TRIS(TRIMETHYLSILYL) PHOSPHITE[1]

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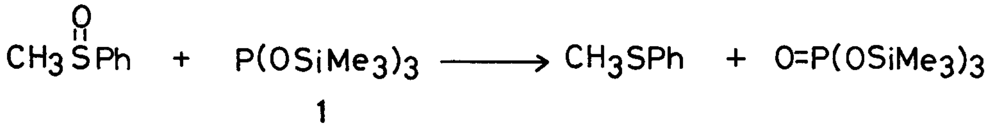
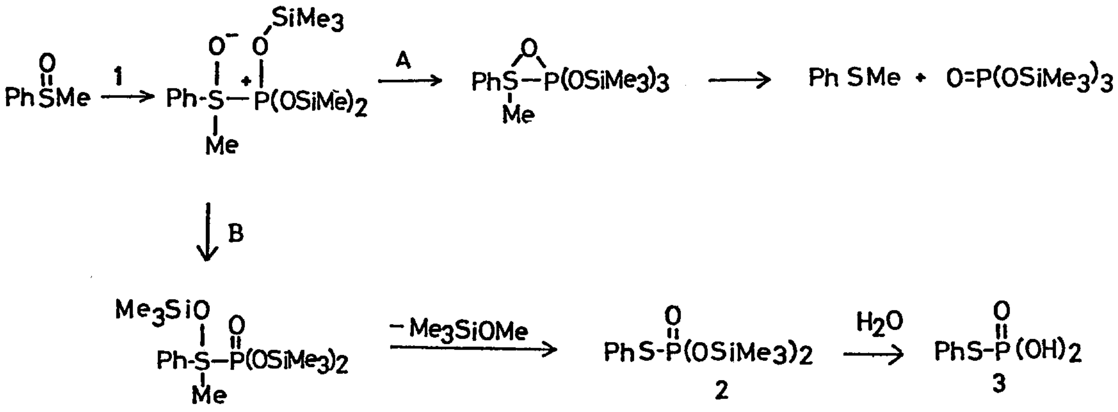
Deoxygenation reactions[2,3] using tervalent phosphorus compounds constitute one of important reactions in organic synthesis. In preceding papers[1], we have described versatile utilities of tris(trimethylsilyl) phosphite (1) in the synthesis of organophosphorus compounds. We now wish to report that 1 was found to be useful for deoxygenation reactions as a highly reactive agent comparing previously known agents, i.e., tervalent phosphorus compounds substituted with electron-donating groups such as dialkylamino groups.



$$CH_3\overset{O}{\overset{\|}{S}}Ph + \underset{1}{P(OSiMe_3)_3} \longrightarrow CH_3SPh + O{=}P(OSiMe_3)_3$$

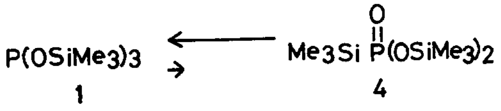
First, we examined the deoxygenation reaction of methyl phenyl sulfoxide with 1 in order to test the reactivity. When 1 was added to one equiv. of methyl phenyl sulfoxide, no reaction took place at room temperature, but at a higher temperature around 150°C, the deoxygenation reaction proceeded to give methyl phenyl sulfide in 72 % yield after 8.5 h. The prolonged heating of the mixture did not afford a better yield of the sulfide. In this reaction, bis(trimethylsilyl) S-phenyl phosphorothioate (2) was formed in 28 % yield as the sole phosphorus-containing by-product. The identification of 2 was carried out by comparing the corresponding free S-phenyl phosphorothioate (3) obtained by the hydrolysis of the reaction mixture with the authentic sample reported previously.[4]

The deoxygenation reaction might proceed through Path A as shown in Scheme I. The compound 2 would be probably formed with the elimination of a volatile methyl trimethylsilyl ether through Path B.



Scheme I

Commercially available triethyl phosphite is known to isomerize to diethyl ethylphosphonate at 150°C by the reaction with methyl phenyl sulfoxide losing its deoxygenating ability.[2,5] It is noteworthy that tris(trimethylsilyl) phosphite is substantially stable in the tervalent form 1 and even if 1 isomerized to the phosphonate form 4, 1 could be reversibly regenerated due to the strong affinity between the trimethylsilyl group and the neighboring oxygen atom of the O=P bond.



Smith[3] reported that tervalent phosphorus compounds substituted either with strong electron-withdrawing group or with strong electron-donating group such as dialkylamino groups were effective for the deoxygenation of sulfoxides, proposing the two types of reaction mechanisms in which the deoxygenation would be initiated by an attack of the phosphorus atom having a lone-pair of electrons on the sulfur atom of sulfoxides or by an attack of the oxygen atom of sulfoxides on vacant *d*-orbitals of the phosphorus atom.

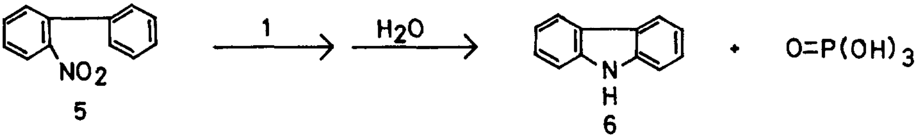
In order to compare the deoxygenating ability of 1 with those of aminophosphines known as strong deoxygenating agents, the deoxygenation reactions of methyl phenyl sulfoxide with aminophosphines were examined: The reactions of methyl phenyl sulfoxide with tris(dimethylamino)phosphine and with tris(diethylamino)phosphine gave

Table I Reactions of tervalent phosphorus compounds with methyl phenyl sulfoxide

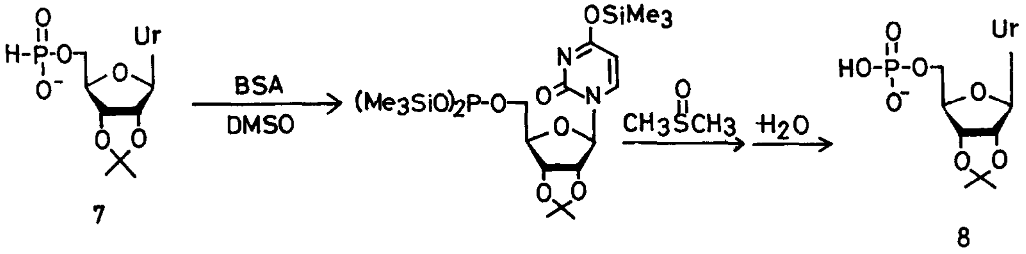
Compound	Time(h)	Yield of MeSPh (%)
$P(OSiMe_3)_3$	8.5	72 (NMR)
	20	65
$P(NMe_2)_3$	20	39
$P(NEt_2)_3$	20	31
$P(Bu\text{-}n)_3$	20	no reaction

methyl phenyl sulfide in poorer yields than with 1 even when the reactions were carried out at 150°C for prolonged periods of time. Tri-*n*-butylphosphine classified in the same category did not react with the sulfoxide under the same condition. Based on the strong deoxygenating ability of 1, the deoxygenation reaction of nitro-compounds was examined.

Nitrobenzene was allowed to react with 1 at 180°C for 30 min to afford an unidentified black mass and 8 % of nitrobenzene was recovered. Nitrosobenzene reacted violently with 1 even at room temperature. However, a similar black solid material was obtained. On the other hand, when 2-nitrobiphenyl (5) was heated with 3 equiv. of 1 at 130°C for 5 h, carbazole (6) was obtained in 84 % yield. According to this method, 6 was separated easily as a precipitate by addition of water after the reaction was completed.



In contrast to the previously reported carbazole synthesis[6] using triethyl phosphite or triphenylphosphine, the present method has two advantages; 1) the reaction proceeds much faster even at lower temperature, 2) the separation procedure is quite simple since simultaneously formed tris(trimethylsilyl) phosphate and an excess of 1 were immediately hydrolyzed to water-soluble phosphoric acid and phosphorous acid by addition of water, and extraction, distillation, or chromatographical procedure is not required after the reaction.[7]



Finally, it was shown that the deoxygenation reaction described herein was reversely applied to the oxidation of nucleoside phosphonates to nucleotides.[8] The reaction of fully trimethylsilylated nucleoside phosphonates with dimethyl sulfoxide (DMSO) was examined since 1 was found to be easily deoxygenated by DMSO even at room temperature and DMSO could be used as both the oxygen donor and the solvent.[9] For example, pyridinium 2', 3'-O-isopropyrideneuridine 5'-phosphonate (7) was treated with 6 equiv. of bis(trimethylsilyl)acetamide (BSA) in DMSO at room temperature for 24 h. After removal of trimethylsilyl groups by addition of water, 2',3'-O-isopropyridene-uridine 5'-phosphate (8) was isolated in 93 % yield by paper chromatography. A similar reaction by the use of nitrosobenzene (8 equiv.) in pyridine in place of DMSO gave 8 and an unidentified nucleotidic by-product in 80 % and 20 % yields, respectively. The use of nitrobenzene or isoamyl nitrite as the oxygen donor gave 8 in poorer yields.

The above application provides an improved method for the conversion of nucleoside phosphonates to nucleotides under completely neutral conditions.

References and Notes

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3) E. H. Amonoo-Neizer, S. K. Ray, R. A. Shaw, and B. C. Smith, J. Chem. Soc., 4296 (1965).
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5) In the case of the reaction of triethyl phosphite with DMSO, a rather reactive sulfoxide, triethyl phosphite is known to behave as a good deoxygenating agent to give dimethyl sulfide (see ref. 2).
6) J. I. G. Cadogan, M. Caeron-wood, R. K. Mackie, and R. J. G. Searle, J. Chem. Soc., 4831 (1965).
7) Diethyl methylphosphinite is known to be effective agent for the synthesis of carbazole and the deoxygenation reaction was carried out under relatively mild conditions; J. I. Cadogan and M. J. Todd, J. Chem. Soc., (C), 2808 (1969). Reagents other than tervalent phosphorus compounds have been used for the synthesis of carbazole; H. C. Watermann and D. L. Vivian, J. Org. Chem., **14**, 289 (1949) (FeC_2O_4); F. Tsui, T. M. Vogel and G. Zon, ibid., **40**, 761 (1975) ($Me_3SiSiMe_3$).
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9) In this case, a solvent such as pyridine was required to make the reaction homogeneous, since 1 was not miscible with DMSO so that the deoxygenation did not proceed smoothly.

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