



1,1,2,2-Tetraphenyldisilane as a Diversified Radical Reagent

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Abstract: Reactivity of 1,1,2,2-tetraphenyldisilane as a radical reagent in ethanol was studied in reduction of alkyl bromides, addition to olefin and alkylation onto heteroaromatic bases with alkyl bromides. The present organodisilane showed moderate to good reactivities for these three types of radical reactions. © 1998 Elsevier Science Ltd. All rights reserved.

The importance of free radical reactions in organic synthesis has been greatly increasing in recent years.¹⁾ In synthetic organic chemistry, tributyltin hydride and hexabutylditin have been frequently used as radical mediators. However, it is well known that organotin compounds are highly toxic, and the complete removal of the tin species from the reaction products is difficult. Organosilanes, which generate silyl radicals²⁾, are shown to be highly efficient and superior radical reagents from both ecological and practical viewpoints. Thus, replacing organotin compounds, studies on monosilane compounds such as diphenylsilane³⁾ and polysilane compounds such as tris(trimethylsilyl)silane,⁴⁾ tetrakis(trimethylsilyl)silane,⁵⁾ etc., have been carried out. Namely, tris(trimethylsilyl)silane is effective for the reduction of alkyl bromides, addition to activated olefins and alkylation onto heteroaromatic bases with alkyl bromides,^{4,5)} while, tetrakis(trimethylsilyl)silane is effective only for the alkylation onto heteroaromatic bases with alkyl bromides.⁵⁾ However, tris(trimethylsilyl)silane is an oil and has not enough stability under aerobic conditions for the storage. Here, we would like to report on the utilization of 1,1,2,2-tetraphenyldisilane ($\text{Ph}_4\text{Si}_2\text{H}_2$), which is stable crystals under aerobic conditions, as a diversified reagent for the radical reduction and the C-C bond formations with alkyl bromides. Today, to our knowledge, the use of organodisilanes in organic synthesis has not been reported.

At first, the radical reduction of alkyl bromides with $\text{Ph}_4\text{Si}_2\text{H}_2$ which was prepared according to the procedures described in the literature,⁶⁾ was carried out, and the results are shown in Table 1. In the reduction of 2-bromoethyl phenyl ether with $\text{Ph}_4\text{Si}_2\text{H}_2$ and AIBN (α,α' -azobisisobutyronitrile) as a radical initiator under refluxing conditions, the yields of ethyl phenyl ether were 93% and 97%, with 1 equiv. and 2 equiv. of $\text{Ph}_4\text{Si}_2\text{H}_2$, respectively (Method A). However, in the reduction using 0.5 equiv. of $\text{Ph}_4\text{Si}_2\text{H}_2$ under the same conditions, the yield of ethyl phenyl ether was decreased to 49%. These results indicate that one of two hydrogen atoms bonded to silicon atoms in $\text{Ph}_4\text{Si}_2\text{H}_2$ participates in this reaction and, therefore, this radical reduction requires more than 1 equiv. of $\text{Ph}_4\text{Si}_2\text{H}_2$ to obtain the reduction product in good yield. On the other hand, the radical reduction of 2-bromoethyl phenyl ether with 1 equiv. of diphenylsilane (Ph_2SiH_2) initiated by AIBN was carried out to form ethyl phenyl ether in only 3% yield and the starting material was recovered in 95% yield. So, there is considerable difference in the reactivity between $\text{Ph}_4\text{Si}_2\text{H}_2$ and Ph_2SiH_2 . The reduction of bromo sugar with $\text{Ph}_4\text{Si}_2\text{H}_2$ was then carried out under the same conditions; however, the reduction product was not obtained due to decomposition under the present thermal

Table 1. Radical Reduction of Alkyl Bromides

$\text{RBr} \xrightarrow[\text{Solvent}]{\text{Ph}_4\text{Si}_2\text{H}_2, \text{ initiator}} \text{RH}$				
Entry	Substrate	Solvent	Method*	Yield / %
1		EtOH	A ₁	49
2		EtOH	A ₂	93
3		EtOH	A ₃	97
4		EtOH	B	89
5		EtOH	B	97
6		EtOH	C	88
7		EtOH	B	35
8		EtOH	C	99
9		EtOH	C	40
10		THF	C	68

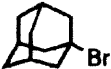


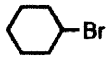
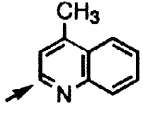
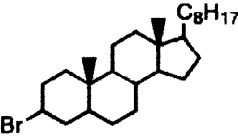
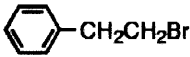
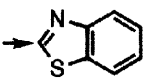
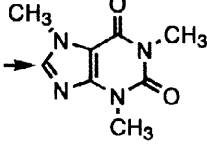

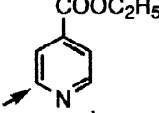
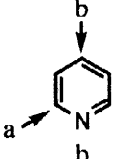
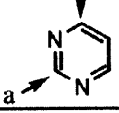
* Method A: A₁ (Ph₄Si₂H₂ 0.5 equiv., AIBN 0.15 equiv.), A₂ (Ph₄Si₂H₂ 1.0 equiv., AIBN 0.3 equiv.), A₃ (Ph₄Si₂H₂ 2.0 equiv., AIBN 0.6 equiv.). The reaction mixture was refluxed for 14 h.; Method B: triethylborane (2.4 equiv.) was added twice, and the reaction mixture was stirred overnight at RT.; Method C: triethylborane (2.4 equiv.) was added, and the reaction mixture was stirred for 4 h at RT.

Table 2. Radical Addition to Olefin

$\text{RBr} + \text{CH}_2=\text{CHSO}_2\text{Ph} \xrightarrow[\text{EtOH, reflux}]{\text{Ph}_4\text{Si}_2\text{H}_2, \text{ AIBN}} \text{R-CH}_2\text{-CH}_2\text{-SO}_2\text{Ph}$		
Entry	Substrate	Yield / %
1		88
2		78
3		62
4	CH ₃ (CH ₂) ₇ Br	43

A mixture of alkyl bromide, olefin (3 equiv.), Ph₄Si₂H₂ (2.5 equiv.), and AIBN (0.5 equiv.) in ethanol was refluxed for 14 h.

Table 3. Radical Alkylation of Heteroaromatic Bases

$\text{RX} + \text{H} \begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{N} \end{array} \begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{N} \end{array} \xrightarrow[\text{EtOH, reflux}]{\text{Ph}_4\text{Si}_2\text{H}_2, \text{AIBN}} \text{R} \begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{N} \end{array} \begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{N} \end{array}$ $\text{H}^+\text{CF}_3\text{COO}^-$			
Entry	Substrate	Heteroaromatic base	Yield / %
1			93
2			91
3			0
4			73
5			63
6	$\text{CH}_3(\text{CH}_2)_7\text{Br}$		31
7			32
<hr/>			
8			69
9			55
10			47
11			79 (a:b = 50:29)
12			54 (a:b = 13:41)

To a mixture of alkyl bromide, heteroaromatic base (5 equiv.), and $\text{Ph}_4\text{Si}_2\text{H}_2$ (1.5 equiv.) in ethanol at refluxing temperature, the same amount of $\text{Ph}_4\text{Si}_2\text{H}_2$ was added after 4 h. While AIBN (1.5 equiv.) was added 5 times over 8 h (2 h intervals). Then, the reaction mixture was stirred overnight at the same temperature.

conditions. Thus, triethylborane was employed as a radical initiator to carry out the radical reduction at room temperature under aerobic conditions (Methods B and C), and 6-bromo-6-deoxy- α -D-glucopyranoside was reduced in quantitative yield by this method. Cholestanyl bromide was also reduced to cholestane in quantitative yield. The reduction of 5'-bromo-5'-deoxythymidine and 2,3,4,6-tetra-O-acetyl- α -D-glucopyranosyl bromide also proceeded efficiently, though the yields were moderate.

Next, the radical addition of alkyl bromide to a carbon-carbon double bond with phenyl vinyl sulfone was carried out in the presence of $\text{Ph}_4\text{Si}_2\text{H}_2$ and AIBN in ethanol. As shown in Table 2, the radical addition to phenyl vinyl sulfone gave the corresponding reductive addition products in moderate to good yields. In this reaction, the reactivities of alkyl bromides increased in the following orders: primary < secondary < tertiary alkyl groups. Thus, the reactivity corresponds to the bond energies of the C-Br bond in alkyl bromides and the nucleophilicity of the formed carbon radical toward phenyl vinyl sulfone.

Finally, the radical alkylation onto heteroaromatic bases was investigated. A mixture of alkyl bromide, $\text{Ph}_4\text{Si}_2\text{H}_2$, AIBN, and a heteroaromatic base, which was activated by protonation with trifluoroacetic acid, was heated in ethanol at refluxing temperature to give the corresponding alkylated heteroaromatic bases in moderate to good yields. As shown in Table 3, the radical alkylation of 4-methylquinoline gave the corresponding alkylated products in good yields with secondary and tertiary alkyl bromides, while, in the alkylation of 4-methylquinoline with primary alkyl bromides, the corresponding alkylated product was obtained in low yields. The difference in these reactivities may be due to the same reason mentioned above in the addition reaction. Here, adamantyl iodide gave the alkylated product in good yield, while adamantyl chloride did not react at all. Many other types of heteroaromatic bases such as benzothiazole, caffeine, ethyl isonicotinate, pyridine, and pyrimidine were also effectively alkylated with 1-adamantyl bromide in the presence of $\text{Ph}_4\text{Si}_2\text{H}_2$ in good yields.

In conclusion, $\text{Ph}_4\text{Si}_2\text{H}_2$ is useful as a diversified radical reagent, *i.e.*, reduction of alkyl bromides, alkyl addition to activated olefin, and alkylation onto heteroaromatic bases. Further, the present reactions proceed in ethanol instead of other toxic organic solvents such as benzene, which is a common solvent in radical reactions with tin hydride. Further study of organodisilanes as a radical promoter is underway.

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References.

- 1) Giese, B. "Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds," Baldwin, J. E. ed., Pergamon Press, Oxford (1986); Fossey, J.; Lefort, D.; Sorba, J. "Free Radicals in Organic Chemistry," Wiley, Chichester (1995).
- 2) Speier, J. L.; Zimmerman, R.; Webster, J. *J. Am. Chem. Soc.*, **1955**, *78*, 2278-2281; Chatgililoglu, C. *Chem. Rev.*, **1995**, *95*, 1229-1251; Chatgililoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.*, **1982**, *114*, 5123-5127, and references cited therein.
- 3) Barton, D. H. R.; Jang, D. O.; Jaszberenyi, J. Cs. *Tetrahedron Lett.*, **1990**, *31*, 4681-4684; **1991**, *32*, 2569-2572; idem, *Synlett*, **1991**, 435-438; Smadja, W.; Zahouily, M.; Journet, M.; Malacria, M. *Tetrahedron Lett.*, **1991**, *32*, 3683-3686; Yamazaki, O.; Togo, H.; Nogami, G.; Yokoyama, M. *Bull. Chem. Soc. Jpn.*, **1997**, *70*, 2519-2523.
- 4) Chatgililoglu, C. *Acc. Chem. Res.*, **1992**, *25*, 188-194.
- 5) Togo, H.; Hayashi, K.; Yokoyama, M. *Bull. Chem. Soc. Jpn.*, **1994**, *67*, 2522-2527.
- 6) Steudel, W.; Gilman, H. *J. Am. Chem. Soc.*, **1960**, *82*, 6129-6132; Winkler, H. J. S.; Gilman, H. J. *Org. Chem.*, **1961**, *26*, 1265-1271; Schott, V. G.; Langecker, W. *Anorg. Allg. Chem.* **1968**, *358*, 210-218; Boudjouk, P.; Han, B. H. *Tetrahedron Lett.*, **1981**, *22*, 3813-3814; Nakano, T.; Nakamura, H.; Nagai, Y. *Chem. Lett.*, **1989**, 83-86.