

Novel method for preparing bis(trimethylsilyl) amines via treatment with trimethylsilylamines and methyl iodide

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Abstract

A convenient method for the synthesis of *N,N*-bis(trimethylsilyl)alkylamines has been reported. *N*-(Trimethylsilyl)diethylamine incorporated with a stoichiometric amount of methyl iodide was effective to convert primary amines, especially aromatic amines, and their monotrimethylsilyl derivatives into the corresponding *N,N*-bis(trimethylsilyl)amine derivatives in high yields. In the case of *N*-trimethylsilyl derivatives of aliphatic primary amines, a half-amount of silylamines served as a silylation agent against another half-amount of silylamines in the presence of 0.5 equivalent of methyl iodide to give *N,N*-bis(trimethylsilyl)alkylamines in good yield. Allyl iodide, allyl bromide and benzyl bromide were also effective to promote the silylation activity of silylamines.

Keywords: Silicon; Trimethylsilyl; *N*-(Trimethylsilyl)diethylamine; Bissilylation; Bis(trimethylsilyl)amine

1. Introduction

Several methods to prepare *N*-(trimethylsilyl)amines are known, some of which are useful as protecting methods of amino groups in many synthetic reactions [1]. Usually *N*-(trimethylsilyl)amines can be easily synthesized from the corresponding amines by treatment with trimethylsilyl chloride. However, a few effective methods to prepare *N,N*-bis(trimethylsilyl)amines have been reported. The silylation of ethylamine with trimethylsilyl chloride in the presence of pyridine produces *N,N*-bis(trimethylsilyl)ethylamine in only 13% yield in addition to the main product, *N*-(trimethylsilyl)ethylamine [2]. *N,N*-Bis(trimethylsilyl) amines can be synthesized by silylation of monosilylamines with *N*-(trimethylsilyl)diethylamine in the presence of ammonium sulfate or ammonium chloride as catalyst [3]. In this case, however, it is necessary to remove the resulting ethylamine to promote the reaction. As common methods to prepare *N,N*-bis(trimethylsilyl)amines, conversions of N–H to metal amide with alkyllithium [4] or Grignard reagents [5], followed by

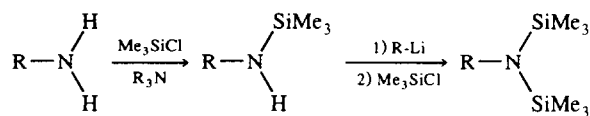
treatment with trimethylsilyl chloride, as shown in Scheme 1, are well used.

In this paper, we would like to report a synthetic method of *N,N*-bis(trimethylsilyl)amines using a monosilylated aliphatic amine and reactive alkyl halides such as methyl iodide, allyl iodide, allyl bromide and benzyl bromide.

2. Results and discussion

Derivatization of primary amines and their *N*-(trimethylsilyl) derivatives to *N,N*-bis(trimethylsilyl) amines with a combination of *N*-(trimethylsilyl)ethylamine and alkyl halides was studied. Conversion of *N*-(trimethylsilyl)alkylamines themselves into *N,N*-bis(trimethylsilyl)alkylamines assisted by methyl iodide was also carried out. The results are summarized in Table 1. To a toluene (500 ml) solution of 82.5 g (499 mmol) of *N*-(trimethylsilyl)aniline and 87.2 g (600 mmol) of *N*-(trimethylsilyl)diethylamine, 85.8 g (604 mmol) of methyl iodide was added. A silylation reaction proceeded mildly during stirring at 50°C or a higher temperature accompanying with black salt formation. *N,N*-Bis(trimethylsilyl)aniline [4a] was isolated with an

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Scheme 1.

86% yield by decantation, followed by concentration and fractional distillation under reduced pressure (Scheme 2, run 5).

N-(Trimethylsilyl)-*p*-bromoaniline and *N*-(trimethylsilyl)-*m*-bromoaniline were also silylated by *N*-(trimethylsilyl)diethylamine and methyl iodide in toluene to give the corresponding *N,N*-bis(trimethylsilyl)bromoaniline derivatives with 93% and 93% yields respectively (runs 8 and 10). Hexane could be also used as a solvent although the reaction was slightly slow compared with toluene (run 7). On the contrary, the same reaction using tetrahydrofuran (THF) as a solvent gave a polymeric complex mixture instead of an *N,N*-bis(trimethylsilyl)amine (run 9).

When aliphatic mono(trimethylsilyl)amines such as *N*-(trimethylsilyl)butylamine and *N*-(trimethylsilyl)allylamine were incorporated with 0.5 equivalent of methyl iodide, a half-amount of the mono(trimethylsilyl)alkylamines were used to form adducts [6] which worked as the silylation reagents of the remaining silylamines to give the respective *N,N*-bis(trimethylsilyl)amines [3] along with ammonium salt (runs 1 and 2).

The generation of silylation ability depends on the basicity of silylamines. Although thus aliphatic *N*-(trimethylsilyl)amines incorporated with methyl iodide could silylate the remaining hydrogen of monosilylated primary amines, in the case of *N*-(trimethylsilyl)derivatives of aromatic amines, which are weaker bases, the silylation ability was not generated by combination with alkyl halide. Namely, *N*-(trimethylsilyl)aniline was not activated by methyl iodide to produce *N,N*-bis(trimethylsilyl)aniline (run 4).

Treatment of cyclohexylamine with 2.0 equivalents of *N*-(trimethylsilyl)diethylamine and methyl iodide in toluene gave *N,N*-bis(trimethylsilyl)cyclohexylamine with a 70% yield together with a small amount of *N*-(trimethylsilyl)cyclohexylamine (run 12). The silylation of isopropylamine with *N*-(trimethylsilyl)diethylamine and methyl iodide in the similar condition gave a bis(trimethylsilyl) product in 99%, but the silylation of tert-butylamine was unsuccessful because of the steric hindrance (runs 13 and 14).

Not only methyl iodide but also allyl iodide, allyl bromide and benzyl bromide are useful for this reaction (runs 6, 15 and 16) (Scheme 3). Anyhow, a stoichiometric amount of halides is necessary toward this silylation, because the halides are consumed as ammonium salts. When ethyl bromide was used instead of the above-described halides, the silylation was very slow and im-

practical, although bis(trimethylsilyl)amines were produced similarly. It seems that the reactivity of these silylation reagents depends on the reactivity of halides with the silylamines in the formation process of adducts [6].

3. Experimental section

3.1. General remarks

All commercially available chemicals, i.e. primary amines and halides, were used as purchased. All solvents were dried over benzophenone ketyl and distilled before use. *N*-(Trimethylsilyl)diethylamine and other monosilylamines were synthesized from corresponding amines by the reaction with trimethylsilyl chloride in the presence of triethylamine or other tertiary amines. All silylation reactions were carried out under an atmosphere of dry nitrogen. ¹H NMR spectra were obtained using a JEOL JNM-PMX60SI spectrometer. IR spectra were recorded on a Perkin-Elmer 1600 Fourier transform IR spectrometer. Gas chromatography (GC)-mass spectroscopy was carried out with a Hewlett-Packard 5970 mass selective detector with a Hewlett-Packard 5890 gas chromatograph. *N,N*-Bis(trimethylsilyl)amines were identified by the comparison of their IR, NMR and mass spectra with those of authentic samples or those reported in literature [3–5].

3.2. Reaction of *N*-(trimethylsilyl)butylamine with methyl iodide

In a 500 ml four-necked flask, equipped with a mechanical stirrer, a reflux condenser, a dropping funnel and a thermometer, were placed 145.3 g (1000 mmol) of *N*-(trimethylsilyl)butylamine and 100 ml of hexane. To this solution, 85.7 g (604 mmol) of methyl iodide was added at 65–70°C over a period of 1.5 h, and the mixture was stirred for 10.5 h at the same temperature. After ammonium salt was separated by decantation, the solvent was distilled off and the residue was fractionally distilled under a reduced pressure to give 77.0 g (89% yield) of *N,N*-bis(trimethylsilyl)butylamine [3a] as a colorless liquid (boiling point (b.p.), 79°C (20 Torr)).

3.3. Reaction of *N*-(trimethylsilyl)allylamine with methyl iodide

In a 500 ml four-necked flask was placed 117.4 g (908 mmol) of *N*-(trimethylsilyl)allylamine and 100 ml of petroleum ether. To this solution, 71 g (500 mmol) of methyl iodide was added at room temperature over a period of 1.0 h, and the mixture was stirred at reflux

temperature for 26 h. After ammonium salt was separated, the solvent was distilled off and the residue was fractionally distilled under a reduced pressure to give 63.5 g (77% yield) of *N,N*-bis(trimethylsilyl)allylamine [3b] as a colorless liquid (b.p., 70°C (40 Torr)).

3.4. Reaction of *N*-(trimethylsilyl)benzylamine with methyl iodide

In a flask was placed 196.9 g (1098 mmol) of *N*-(trimethylsilyl)benzylamine and 100 ml of toluene.

Table 1
Preparation of bis(trimethylsilyl)amines

Run	Amines	Silanes	Halides	Solvents	Products	Yields (isolate) (%)
1			Me-I	Petroleum ether		77%
2			Me-I	Hexane		89%
3			Me-I	Toluene		76%
4			Me-I	Toluene	No reaction	—
5			Me-I	Toluene		86%
6				Toluene		85%
7			Me-I	Hexane		91%
8			Me-I	Toluene		93%
9			Me-I	THF	Complex mixture	—
10			Me-I	Toluene		93%
11			Me-I	Toluene		88%
12			Me-I	Toluene		70%
13			Me-I	Toluene		99% ^a

Table 1 (continued)

Run	Amines	Silanes	Halides	Solvents	Products	Yields (isolate) (%)
14			Me-I	Toluene	Complex mixture	—
15				Toluene		90% ^a
16				Toluene		80% ^a

^a Yields were measured by G.C.

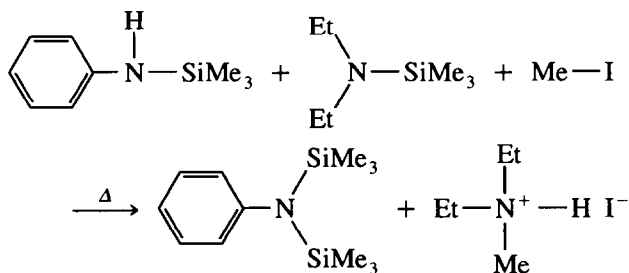
To this solution, 85.2 g (600 mmol) of methyl iodide was added over a period of 1.0 h at 65–75°C and the mixture was stirred at the same temperature for 8 h. After ammonium salt was separated, the solvent was distilled off and the residue was fractionally distilled under a reduced pressure to give 95.2 g (76% yield) of *N,N*-bis(trimethylsilyl)benzylamine [4d] (b.p., 76°C (1 Torr)).

3.5. Reaction of *N*-(trimethylsilyl)aniline with *N*-(trimethylsilyl)diethylamine and methyl iodide

In a flask was placed 82.5 g (499 mmol) of *N*-(trimethylsilyl)aniline, 87.0 g (599 mmol) of *N*-(trimethylsilyl)diethylamine and 100 ml of hexane. To this solution, 85.7 g (604 mmol) of methyl iodide was added at room temperature over a period of 1.0 h and the mixture was stirred at reflux temperature for 20 h. During the reaction, the conversion was monitored by GC. After ammonium salt was separated, solvent was distilled off and the residue was fractionally distilled under a reduced pressure to give 101.6 g (86% yield) of *N,N*-bis(trimethylsilyl)aniline [4a] (b.p., 68–69°C (2 Torr)).

3.6. Reaction of *N*-(trimethylsilyl)aniline with *N*-(trimethylsilyl)diethylamine and allyl iodide

In a flask was placed 24.8 g (150 mmol) of *N*-(trimethylsilyl)aniline, 26.1 g (180 mmol) of *N*-(trimethyl-



Scheme 2.

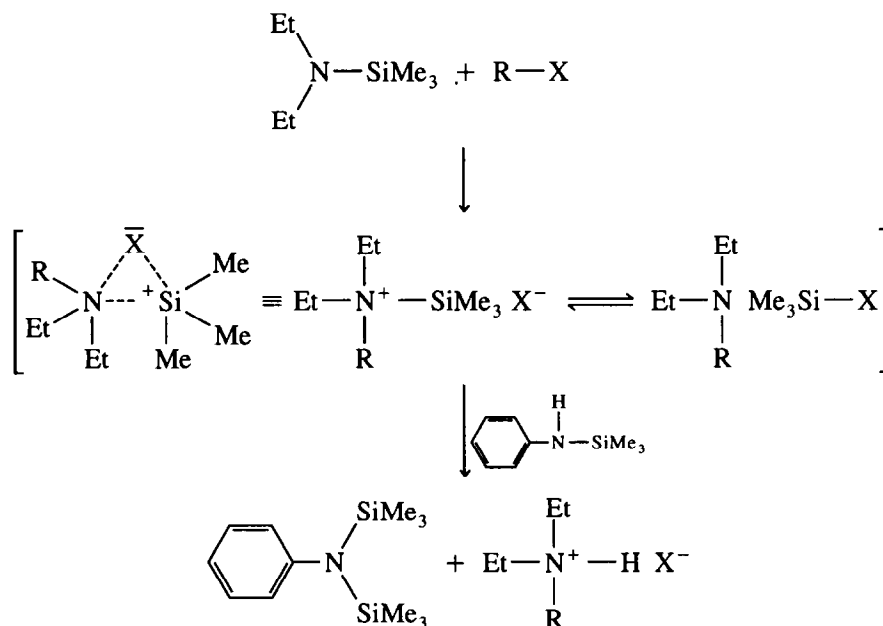
silyl)diethylamine and 60 ml of toluene. To this solution, 30.2 g (180 mmol) of allyl iodide was added at room temperature, and the mixture was stirred at 70–75°C. After *N*-(trimethylsilyl)aniline was consumed, ammonium salt was separated by decantation, the solvent was distilled off and the residue was fractionally distilled under a reduced pressure to give 30.3 g (85% yield) of *N,N*-bis(trimethylsilyl)aniline [4a].

3.7. Reaction of *N*-(trimethylsilyl)-*p*-bromoaniline with *N*-(trimethylsilyl)diethylamine and methyl iodide

In a flask was placed 56.2 g (230 mmol) of *N*-(trimethylsilyl)-*p*-bromoaniline, 35.0 g (241 mmol) of *N*-(trimethylsilyl)diethylamine and 100 ml of hexane. To this solution, 35.0 g (247 mmol) of methyl iodide was added at room temperature and the mixture was stirred at 80°C for 10 h. After *N*-(trimethylsilyl)-*p*-bromoaniline was consumed, ammonium salt was separated, the solvent was distilled off and the residue was fractionally distilled under a reduced pressure to give 66.2 g (91% yield) of *N,N*-bis(trimethylsilyl)-*p*-bromoaniline [4c] (b.p., 130°C (3 Torr)).

3.8. Reaction of *N*-(trimethylsilyl)-*m*-bromoaniline with *N*-(trimethylsilyl)diethylamine and methyl iodide

In a flask was placed 168 g (688 mmol) of *N*-(trimethylsilyl)-*m*-bromoaniline, 110 g (757 mmol) of *N*-(trimethylsilyl)diethylamine and 300 ml of toluene. To this solution, 110 g (775 mmol) of methyl iodide was added at room temperature and the mixture was refluxed for 5 h. After a GC peak of *N*-(trimethylsilyl)-*m*-bromoaniline disappeared, ammonium salt was separated, the solvent was distilled off and the residue was fractionally distilled under a reduced pressure to give 202 g (93% yield) of *N,N*-bis(trimethylsilyl)-*m*-bromoaniline [4c] (b.p. 23°C (2 Torr)).



Scheme 3.

3.9. Reaction of aniline with *N*-(trimethylsilyl)diethylamine and methyl iodide

In a flask was placed 52.2 g (359 mmol) of *N*-(trimethylsilyl)diethylamine and 60 ml of toluene. To this solution, 51.1 g (360 mmol) of methyl iodide was added at room temperature and the mixture was stirred at 50°C for 4 h. Then 14.0 g (150 mmol) of aniline was added to this solution and the mixture was stirred for another 6 h at 75°C. The progress of this reaction was monitored by GC, and the conversion of aniline to *N,N*-bis(trimethylsilyl)aniline via *N*-(trimethylsilyl)aniline was observed. After ammonium salt was separated, the solvent was distilled off and the residue was fractionally distilled under a reduced pressure to give 31.3 g (88% yield) of *N,N*-bis(trimethylsilyl)aniline [4a].

3.10. Reaction of cyclohexylamine with *N*-(trimethylsilyl)diethylamine and methyl iodide

In a flask was placed 10.0 g (101 mmol) of cyclohexylamine, 30.0 g (206 mmol) of *N*-(trimethylsilyl)diethylamine and 50 ml of toluene. To this solution, 30.0 g (211 mmol) of methyl iodide was added at room temperature and the mixture was refluxed for 4 h. After separation of ammonium salt, the solvent was distilled off and the residue was fractionally distilled under a reduced pressure to give 17.2 g (70% yield) of *N,N*-bis(trimethylsilyl)cyclohexylamine, along with a small amount of *N*-(trimethylsilyl)cyclohexylamine.

3.11. Reaction of isopropylamine with *N*-(trimethylsilyl)diethylamine and methyl iodide

In a flask was placed 5.3 g (89.7 mmol) of iso-propylamine, 30.0 g (206 mmol) of *N*-(trimethylsilyl)diethylamine and 50 ml of toluene. To this solution, 30.0 g (211 mmol) of methyl iodide was added at room temperature and the mixture was refluxed for 4 h. *N,N*-Bis(trimethylsilyl)isopropylamine was obtained with a 99% GC yield.

3.12. Reaction of *N*-(trimethylsilyl)aniline with *N*-(trimethylsilyl)diethylamine and allyl bromide

In a flask was placed 15.0 g (91 mmol) of *N*-(trimethylsilyl)aniline, 15.0 g (103 mmol) of *N*-(trimethylsilyl)diethylamine and 50 ml of toluene. To this solution, 13 g (107 mmol) of allyl bromide was added at room temperature and the mixture was refluxed for 8 h. *N,N*-bis(trimethylsilyl)aniline [4a] was obtained with a 90% GC yield.

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References and notes

- [1] H.H. Anderson, *J. Am. Chem. Soc.*, **73** (1951) 5802.
- [2] E.W. Abel and G.R. Willey, *J. Chem. Soc.*, (1964) 1528.
- [3] (a) J. Hils, V. Hagen, H. Ludwig and K. Rühlmann, *Chem. Ber.*, **99** (1966) 776; (b) J.L. Speier, R. Zimmerman and J. Webster, *J. Am. Chem. Soc.*, **78** (1956) 2278.
- [4] (a) J.F. Klebe, J.B. Bush, Jr., and J.E. Lyons, *J. Am. Chem. Soc.*, **86** (1964) 4400; (b) W. Broser and W. Harrer, *Angew. Chem., Int. Edn. Engl.*, **4** (1965) 1081; (c) J.R. Pratt, W.D. Massey, F.H. Pinkerton and S.F. Thames, *J. Org. Chem.*, **40** (1975) 1090; (d) K. Rühlmann, *Chem. Ber.*, **94** (1961) 2311.
- [5] (a) D.R.M. Walton, *J. Chem. Soc., C*, (1966) 1706; (b) R.B. Weisenfeld, *J. Org. Chem.*, **51** (1986) 2434.
- [6] The toluene solution of *N*-(trimethylsilyl)diethylamine and methyl iodide gave a non-volatile residue, which seems to be an adduct of *N*-(trimethylsilyl)diethylamine and methyl iodide, by removing the solvent under reduced pressure. ¹H NMR of the residue in C₆D₆ gave a new singlet of SiMe₃ at 0.56 ppm, while a signal of SiMe₃ arising from *N*-(trimethylsilyl)diethylamine was observed at 0.21 ppm. It seems that the silylation ability of *N*-(trimethylsilyl)diethylamine was increased by interaction with methyl iodide.