[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, SAN JOSE STATE COLLEGE]

An Extension of and the Reversibility of the Silylamine-Amine Exchange Reaction[1,2]

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Hexamethyldisilazane was shown to undergo reaction with secondary amines, heterocyclic compounds containing an N—H function, and hydrazines. *N,N*-Di-*n*-butyltrimethylsilylamine and *N*-trimethylsilylpyrrole upon treatment with ammonia yielded hexamethyldisilazane and the corresponding amine. The catalytic effect of various salts and the influence of various solvent systems upon the silylamine-amine exchange reaction are presented.

The exchange reaction between a silylamine and an amine is a useful technique for the preparation of silylamines. The silicon moiety of this reaction has been extensively studied; silylamines,[3] silanediamines,[4] silanetriamines,[5] and disilazanes[6] all undergo this reaction. In general, the attacking nitrogen compound has been limited to primary amines.[7] In one study in which a secondary amine was used, the reaction of diethylamine with hexamethyldisilazane (I), it was reported that no silylamine could be detected.[8]

In this investigation, it has been observed that silylamines can be obtained by the exchange reaction between hexamethyldisilazane (I) and secondary amines. The amines investigated are summarized in Table I.

The reaction of di-*n*-butylamine with I, using ammonium sulfate as the catalyst, resulted in a 52% yield of *N,N*-di-*n*-butyltrimethylsilylamine (II), which, upon hydrolysis, yielded hexamethyldisiloxane and di-*n*-butylamine hydrochloride, the expected cleavage products. The identity of II was verified by its preparation from trimethylchlorosilane and di-*n*-butylamine in 44% yield.

TABLE I

REACTION OF HEXAMETHYLDISILAZANE WITH SECONDARY AMINES

Amine	% Yield of Silylamine	B.P.	n_D^{25}	Neut. Equiv. Calcd.	Neut. Equiv. Found
$(n\text{-}C_3H_7)_2NH$	35	163–164°	1.4218	173	173
$(n\text{-}C_4H_9)_2NH$	52	201–202°	1.4762	201	203[a]
$(i\text{-}C_4H_9)_2NH$	46	190–192°	1.4181	201	210[b]
$\underbrace{C_4H_8N}H$	61	139–140°	1.4297	143	143
$\underbrace{C_5H_{10}N}H$	56	158–160°	1.4403	157	157

[a] *Anal.* Calcd. for $C_{11}H_{27}SiN$: Si, 13.9. Found: Si, 13.9.
[b] *Anal.* Calcd. for $C_{11}H_{27}SiN$: Si, 13.9. Found: Si, 12.6.

$$\underset{\text{I}}{(CH_3)_3SiNHSi(CH_3)_3} + 2(n\text{-}C_4H_9)_2NH \longrightarrow \underset{\text{II}}{2(CH_3)_3SiN(C_4H_9\text{-}n)_2} + NH_3$$

Diisopropylamine and di-*sec*-butylamine both failed to react with I while di-*n*-propylamine and diisobutylamine underwent reaction to yield silylamines.

In considering the reaction of amines with I, it is evident that steric hindrance is a controlling factor. When primary amines are employed, the yields of silylamines are 60–90%.[7] Using secondary amines, the yields were 35 to 60%. Reaction failed when there was branching *alpha* to the amine nitrogen but did occur when branching was *beta* to the nitrogen.

Since other secondary amines gave successful results in the exchange reaction, the diethylamine case was re-investigated. Because of the proximity of the boiling points of I (125–126°)[9] and *N,N*-diethyltrimethylsilylamine (128°),[10] a purified sample of the silylamine was not obtained. Verification that the exchange reaction did occur to some extent

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(2) This work was supported by a grant (NSF-G14554) from the National Science Foundation.

(3) (a) M. Becke-Goehring and G. Wunsch, *Ann.*, **618**, 43 (1958). (b) L. Birkofer and A. Ritter, *Angew. Chem.*, **71**, 372 (1959). (c) P. L. DeBenneville and M. J. Hurwitz, U. S. Patent **2,906,756** (1959); *Chem. Abstr.*, **51**, 5480 (1960). (d) L. Birkofer and A. Ritter, *Chem. Ber.*, **93**, 424 (1960). (e) E. Larsson, *Kgl. Fysiograph. Sallskap. Lund, Forh.*, **24**, 139 (1954); *Chem. Abstr.*, **50**, 790 (1956). (f) E. Larsson and C. G. Carlsson, *Acta Chem. Scand.*, **4**, 45 (1950). (g) E. Larsson and R. E. I. Marin, *Acta Chem. Scand.*, **5**, 1173 (1951). (h) E. Larsson and O. Mjorne, *Svensk Kem. Tid.*, **61**, 59 (1949); *Chem. Abstr.*, **42**, 5739 (1949).

(4)(a) E. Larsson and B. Smith, *Acta Chem. Scand.*, **3**, 487 (1949). (b) E. Larsson, *Kgl. Fysiograph. Sallskap. Lund, Forh.*, **24**, 145 (1954); *Chem. Abstr.*, **50**, 791 (1956).

(5)(a) E. Larsson, *Kgl. Fysiograph. Sallskap. Lund, Forh.*, **24**, 149 (1954); *Chem. Abstr.*, **50**, 791 (1956). (b) L. Tansjo, *Acta Chem. Scand.*, **13**, 29 (1959).

(6)(a) Ref. 1d. (b) S. H. Langer, S. Connell, and I. Wender, *J. Org. Chem.*, **23**, 50 (1958). (c) O. Mjorne, *Svensk Kem. Tid.*, **62**, 120 (1950); *Chem. Abstr.*, **44**, 9342 (1950). (d) J. L. Speier, R. Zimmerman, and J. Webster, *J. Am. Chem. Soc.*, **78**, 2278 (1956).

(7) R. Fessenden and J. S. Fessenden, *Chem. Revs.*, **61**, 361 (1961).

(8) Ref. 6b.

(9) R. C. Osthoff and S. W. Kantor, *Inorg. Syntheses*, **5**, 55 (1957).

(10) R. O. Sauer and R. H. Hasek, *J. Am. Chem. Soc.*, **68**, 241 (1946).

was provided by the acid hydrolysis of the highest boiling distillation fraction, which resulted in 7.8% yield of the diethylamine hydrochloride.

The silylamine exchange reaction appears to be reasonably general for compounds containing an N—H function. Heterocyclic compounds containing this linkage react with I to yield the corresponding *N*-trimethylsilyl derivatives. Previously it had been observed that pyrrole reacts to yield the *N*-trimethylsilylpyrrole.[11] In this work, the reaction was extended to the preparation of the *N*-trimethylsilyl derivatives of indole and indoline, and a number of other heterocyclic compounds were also shown to undergo reaction. Since this work was completed, a more extensive investigation of the exchange reaction using heterocyclic compounds has appeared.[12]

The reaction of I with hydrazines provides a new route to the silylhydrazines. Phenylhydrazine yielded *N*-phenyl-*N'*-trimethylsilylhydrazine (III) in 87% yield. This compound has been previously prepared by the reaction of trimethylchlorosilane with phenylhydrazine.[13] Hydrazine itself gave *N,N'*-bis(trimethylsilyl)hydrazine in 13% yield.

$$\underset{\text{I}}{(CH_3)_3SiNHSi(CH_3)_3} + 2C_6H_5NHNH_2 \longrightarrow \underset{\text{III}}{2(CH_3)_3SiNHNHC_6H_5} + NH_3$$

The lower yield in this reaction is probably due to the formation of *N*-trimethylsilylhydrazine; however, this compound was not isolated. Its estimated boiling point falls in the range of that of I.

In synthetic work using the silylamine exchange reaction, a catalyst is employed. Reaction will occur in the absence of catalyst; however, the yields of silylamines obtained are poor (*e.g.*, di-*n*-butylamine in the absence of catalyst yielded 20% of the silylamine while 52% was obtained with the use of catalyst).

In Table II the effects of various catalysts upon the yield of product in the reaction between I and piperidine are summarized. Both trimethylchlorosilane[8] and amine salts[14] have been recommended as catalysts for the exchange reaction; however, in this study both were observed to be inferior to the ammonium salts. The comparable yields of silylamine when piperidine hydrochloride, trimethylchlorosilane, or aluminum chloride was used indicate that the latter two are acting through the generation of the amine salt.

The influence of solvent upon the yield of silylamine is summarized in Table III. In each reaction, ammonium sulfate was used as the catalyst. Control runs without catalyst failed to yield any silylamine except in the run with quinoline, in which case a 23% yield was obtained.

TABLE II

EFFECT OF CATALYST UPON THE EXCHANGE REACTION OF HEXAMETHYLDISILAZANE AND PIPERIDINE[a]

Catalyst	% Yield of *N*-Trimethylsilylpiperidine
None	16
$(NH_4)_2SO_4$	55
NH_4Cl	52
$NaHSO_4$	50
NaCl	12
Na_2SO_4	4
$NaHCO_3$	3
$C_5H_{10}NH\cdot HCl$	35
$(CH_3)_3SiCl$	35
$AlCl_3$	31
$ZnCl_2$	2

[a] Mixture of piperidine (0.20 mole), hexamethyldisilazane (0.10 mole), and catalyst (0.001 mole) was heated under reflux for 3 hr. The yield of the silylpiperidine was determined by isolation.

TABLE III

EFFECT OF SOLVENT UPON THE EXCHANGE REACTION OF HEXAMETHYLDISILAZANE AND PIPERIDINE[a]

Solvent	% Yield of *N*-Trimethylsilylpiperidine
Ether	0
p-Dioxane	35
Toluene	54
Decalin	54
Quinoline	61[b]

[a] A mixture of piperidine (0.20 mole), hexamethyldisilazane (0.10 mole), ammonium sulfate (0.001 mole), and 50 ml. of solvent was heated under reflux for 3 hr. The yield of product was determined by isolation. Control runs without catalyst yielded no product (see *b*). [b] Without catalyst a 23% yield of product was obtained.

Discussion of the role of the catalyst in the mechanism of the silylamine exchange reaction will be presented in another report.

Use of the silylamine exchange reaction using *N*-substituted silylamines has heretofore depended upon a difference in volatility between the attacking amine and the amine displaced.[7] The reaction has always been carried out under conditions where the most volatile component is continuously removed.

In this study the reversible nature of the silylamine exchange reaction has been demonstrated by the reaction of *N*-substituted silylamines with ammonia to yield I and the amine. In the reaction of *N,N*-di-*n*-butyltrimethylsilylamine (II) and ammonia in a sealed bomb a complete conversion was

$$\underset{\text{II}}{(CH_3)_3SiN(C_4H_9\text{-}n)_2} + NH_3 \longrightarrow \underset{\text{I}}{(CH_3)_3SiNHSi(CH_3)_3} + (n\text{-}C_4H_9)_2NH$$

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(11) R. Fessenden and D. F. Crowe, *J. Org. Chem.*, **25**, 598 (1960).

(12) L. Birkofer, P. Richter, and A. Ritter, *Ber.*, **93**, 2804 (1960).

(13) U. Wannagat and W. Liehr, *Z. anorg. u. allgem. Chem.*, **299**, 341 (1959).

(14) E. Larsson, Swedish Patent **130,374** (1950); *Chem. Abstr.*, **45**, 6654 (1951).

observed after twelve hours at room temperature. Of more significance, a 20% conversion was observed when II was stirred with liquid ammonia for one hour. *N*-Trimethylsilylpyrrole gave a 70% conversion in a sealed bomb after twenty-four hours.

Although trimethylsilylamine would be expected to result from this reaction, only I was obtained. It was not determined if condensation occurred during the ammonia reaction or during work-up.

EXPERIMENTAL[15]

Reaction of hexamethyldisilazane (I) *with secondary amines.* A. *With di-n-butylamine.* A mixture of 32.3 g. (0.25 mole) of di-*n*-butylamine, 40.2 g. (0.25 mole) of hexamethyldisilazane,[9] and 1.0 g. of ammonium sulfate was heated under reflux for 15 hr. Fractional distillation of the reaction mixture yielded 26.0 g. (52%) of *N*,*N*-di-*n*-butyltrimethylsilylamine (II). Physical constants may be found in Table I.

Another run, in which the same conditions were used except that no catalyst was employed, yielded 10 g. (20%) of II.

To a 10-g. sample of II was added 50 ml. of 1.5*N* hydrochloric acid (exothermic reaction), and the resulting mixture was extracted with two 25-ml. portions of ether. Gas phase chromatography (10′ Carbowax column, T = 105°) of the ether extract showed a peak at 1.75 min. An authentic sample of hexamethyldisiloxane had an identical retention time. A sample collected from the gas phase unit exhibited an infrared spectrum identical to that of hexamethyldisiloxane.

Evaporation of the aqueous acid layer yielded 7.5 g.. (91%) of di-*n*-butylamine hydrochloride. A portion of this was treated with sodium hydroxide to yield di-*n*-butylamine b.p. 158–159°, n_D^{25} 1.4158 (lit.[16] b.p. 159°).

B. *With diethylamine.* A mixture of 18.3 g. (0.25 mole) of diethylamine, 40.2 g. (0.25 mole) of hexamethyldisilazane, and 1.0 g of ammonium sulfate was heated under reflux for 24 hr. Fractional distillation yielded unchanged diethylamine, 5.5 g., b.p. 55–56°, and a mixture of hexamethyldisilazane and *N*,*N*-diethyltrimethylsilylamine, 42 g., b.p. 124–128°. A 10-g. cut of this fraction, boiling at 127–128°, was heated under reflux with 50 ml. of 95% ethanol for 5 hr., then mixed with 50 ml. of 1.5*N* hydrochloric acid and the resulting mixture evaporated to dryness, yielding 2.1 g. (7.8% based upon 0.25 molar reaction) of diethylamine hydrochloride, m.p. 227–228° (lit.[17] m.p. 228–229°). The melting point of this and an authentic sample showed no depression.

C. *With other secondary amines.* The reaction of I with other secondary amines was carried out using the procedure as outlined in part A. The physical constants of the products are summarized in Table I. Attempted reactions with diisopropylamine and di-*sec*-butylamine failed. The starting materials were recovered.

Reaction of trimethylcholorosilane and di-n-butylamine. To 64.5 g. (0.50 mole) of di-*n*-butylamine was added dropwise with cooling 27.0 g. (0.25 mole) of trimethylchlorosilane. The semisolid reaction mixture was then heated under reflux with stirring for 30 min., suction-filtered, and the filtrate washed with six 50-ml. portions of ether. Distillation of the ethereal extracts yielded 22.0 g. (44%) of II, b.p. 198–201°.

Reaction of hexamethyldisilazane with aromatic heterocyclic compounds. An apparatus was arranged so that the ammonia liberated by the boiling reaction mixture would pass through the reflux condenser and a take-off tube. The ammonia was swept through the tube by a gentle stream of air into 250 ml. of water. The course of the reaction was followed by titration of the ammonium hydroxide solution with 0.101*N* hydrochloric acid to the Congo Red end point. In a typical run, a mixture of 0.67 g. (0.01 mole) of pyrrole, 0.805 g. (0.005 mole) of hexamethyldisilazane, and 0.020 g. of ammonium sulfate was heated at 150° for 2 hr. During this time 33.6 ml. (68% of theory) of hydrochloric acid was consumed. *N*-Trimethylsilylpyrrole was previously isolated from this reaction in 51% yield.[11] In the reaction between hexamethyldisilazane and indole, *N*-trimethylsilylindole was isolated using gas phase chromatography. An infrared spectrum showed no band characteristic of an N—H linkage but did exhibit a band at 8.0 μ (Si—CH_3).

Anal. Calcd. for $C_{11}H_{15}NSi$: C, 69.7; H, 7.9; N, 7.4. Found: C, 69.4; H, 8.3; N, 7.6.

N-Trimethylsilylindoline was also isolated using gas phase chromatography. As in the case of indole, no N—H band was observed in the infrared spectrum, but a Si—CH_3 band at 8.0 μ was evident. This silyl derivative was highly unstable and no further characterization was accomplished.

The heterocyclic compounds studied are summarized in Table IV. Using the above procedure, no ammonia was liberated during attempted reactions with carbazole or *N*-methylaniline.

TABLE IV

REACTION OF HEXAMETHYLDISILAZANE WITH AROMATIC HETEROCYCLIC COMPOUNDS

Heterocyclic Compound	Ammonia Produced, % Yield
Pyrrole	68
Indole	80
Imidazole	64
3,5-Dimethylpyrazole	73
Benzimidazole	81
Indazole	48

Reaction of hexamethyldisilazane with hydrazines. A. *With phenylhydrazine.* A mixture of 27 g. (0.25 mole) of phenylhydrazine, 59.5 g. (0.37 mole) of hexamethyldisilazane, and 1.0 g. of ammonium chloride was heated under reflux for 12 hr., then fractionally distilled to yield 39.0 g. (89%) of *N*-trimethylsilyl-*N*′-phenylhydrazine, b.p. 111–115° (15 mm.), n_D^{24} 1.5229 [lit.[13] b.p. 115–116° (12 mm.)]; neut. equiv., calcd., 180; found, 175. Only one band appeared in the N—H region of the infrared spectrum.

In one run using ammonium sulfate as catalyst, sulfur-containing by-products interfered with isolation of the silylhydrazine. A run without catalyst resulted in a 12% yield of the silylhydrazine.

B. *With anhydrous hydrazine.* Using the same procedure as outlined above, there was obtained a 13% yield of *N*,*N*′ bis(trimethylsilyl)hydrazine, b.p. 153–154°, n_D^{26} 1.4177 [lit.[13] b.p. 69° (40 mm.)]; neut. equiv., calcd., 176; found, 179.

Reaction of N,N-di-n-butyltrimethylsilylamine with ammonia. A. *In a sealed bomb.* In a 360-ml. stainless steel bomb cooled with a Dry Ice–acetone bath were placed 17 g. (0.084 mole) of the silylamine (b.p. 201–203°) and 25 ml. of liquid ammonia. The bomb was sealed, allowed to warm to room temperature and stand for 12 hr., cooled, and opened. The excess ammonia was allowed to evaporate. Fractional distillation of the residue yielded 2.8 g. (41%) of hexamethyldisilazane, b.p. 124–126°, n_D^{21} 1.4045 (lit.[9] b.p. 125–126°,

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(15) All distillations were conducted at atmospheric pressure unless otherwise noted. Carbon, hydrogen, and nitrogen analyses were performed by the Berkeley Microanalytical Laboratory.

(16) *Lange's Handbook,* N. A. Lange, ed., Handbook Publishers, Inc., Sandusky, Ohio, Seventh Edition, 1949, p. 448.

(17) Ref. 16, p. 460.

n_{D}^{20} 1.4078) and 10.2 g. (94%) of di-*n*-butylamine, b.p. 158–160°, n_{D}^{20} 1.4171 (lit.[15] b.p. 159°). No unchanged silylamine was observed.

B. *With liquid ammonia.* To 50 ml. of liquid ammonia was added 17.0 g. (0.084 mole) of the silylamine. The two-phase system was stirred at Dry Ice–acetone temperature for 1 hr. The excess ammonia was allowed to evaporate and the residue was fractionally distilled to yield 1.3 g. (19%) of hexamethyldisilazane, b.p. 124–126°; 2.3 g. (21%) of di-*n*-butylamine, b.p. 158–159°; and 8.7 g. (51%) of recovered silylamine, b.p. 201–203°.

Reaction of N-trimethylsilylpyrrole with ammonia. Using the same procedure as outlined above, 71.8 g. (0.52 mole) of the silylpyrrole[11] (b.p. 152–154°) and 50 ml. of liquid ammonia were sealed in a bomb and allowed to stand at room temperature for 24 hr. Distillation yielded 16.2 g. (23%) of recovered silylpyrrole, b.p. 152–154° (lit.[11] b.p. 153°). Pyrrole and hexamethyldisilazane formed an azeotrope boiling at 113°. From gas chromatographic analysis (5′ silicone column, T = 111°) of the fractions boiling in this range, an estimated 65% yield of hexamethyldisilazane and 55% of pyrrole were obtained.

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[CONTRIBUTION FROM THE OLIN MATHIESON CHEMICAL CORP.]

Aromatic Fluorine Compounds. II. Synthesis of *p*-Fluorophenol by the Selective Hydrolysis of *p*-Bromofluorobenzene[1]

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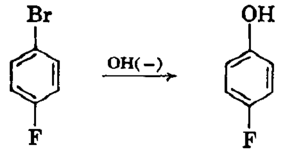
The selective alkaline (calcium hydroxide) hydrolysis of *p*-bromofluorobenzene at pressures of 500 p.s.i.g. (250°; one to three hours) in the presence of copper salts can provide up to 79% yields of *p*-fluorophenol. The main by-product of this reaction is *p,p′*-difluorodiphenyl ether. Evidence is presented to suggest that a nonrearranging S_N2-type mechanism is occurring for this reaction. No *m*-fluorophenol was found to suggest a benzyne intermediate.

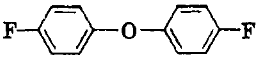
A novel method for the synthesis of *p*-fluorophenol (II) involves the alkaline hydrolysis of *p*-bromofluorobenzene (I). A survey of the literature reveals that a paucity of information is available on the selective alkaline hydrolysis of mixed *p*-dihalogenated benzenes. However, *p*-dihalogenated benzenes have been partially hydrolyzed under alkaline conditions to the *p*-halophenol, *e.g.*, *p*-chlorophenol from *p*-dichlorobenzene,[2] and *p*-fluorophenol from *p*-difluorobenzene.[3]



I II

Studies have been conducted with mixed *p*-dihalogenated benzenes and nucleophilic agents other than hydroxide ion. In most cases, the order of preferential halogen cleavage appeared to be a function of the electronegativity of the displaced halogen. Bergstrom and co-workers found the order of replacement, Br>Cl, in the reaction of *p*-bromochlorobenzene with potassium amide in ammonia.[4] Surprisingly, these investigators[4] found the order of replacement Br>I when *p*-bromoiodobenzene was treated with amide ion under similar conditions. Roberts and co-workers[5] noted a preferential cleavage of bromide ion when *p*-bromofluorobenzene was treated with potassium amide to give a mixture of *m*- and *p*-fluoroaniline.

With phenoxide ions, Leonard and Sutton[6] found that the reaction of *p*-bromofluorobenzene with potassium *p*-fluorophenate in the presence of copper bronze gave *p,p′*-difluorodiphenyl ether (III). The reaction of *p*-bromofluorobenzene with potassium phenate produced *p*-fluorodiphenyl ether as the sole product.[7,8]



III

With methoxide ion and mixed *p*-dihalogenated benzenes, the order of preferential halogen cleavage may be altered. De Crauw found that the reaction of *p*-chlorofluorobenzene with sodium methoxide

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[1] This work was supported by the Chemical Corps, Engineering Command, U. S. Army, Contract No. DA-18-064-CML-2696.

[2] D. R. Patent 284,533 (1915); W. J. Hale and E. C. Britton, *Ind. Eng. Chem.* **20**, 114 (1928).

[3] F. Swarts, *Bull. Acad. roy. Belg., Classe des sci.*, 241 (1913); *Chem. Zent.*, **II**, 760 (1913).

[4] F. W. Bergstrom, R. E. Wright, C. Chandler, and W. A. Gilkey, *J. Org. Chem.*, **1**, 170 (1936). These investigators noted the following sequence with unsubstituted aryl halides and amide ion in ammonia; Br > I > Cl. Fluorobenzene was inert under these conditions to amide ion.

[5] J. D. Roberts, C. W. Vaughan, L. A. Carlsmith, and D. R. Semenow, *J. Am. Chem. Soc.*, **78**, 611 (1956).

[6] N. J. Leonard and L. E. Sutton, *J. Am. Chem. Soc.*, **70**, 1564 (1948).

[7] J. Lichtenberger and R. Thermet, *Bull. soc. chim. France*, 318 (1951).

[8] R. L Huang, *J. Chem. Soc.*, 3725 (1958).