Acknowledgment. This work was supported by the Italian CNR (Progetto Chimica Fine e Secondaria).

Registry No. Gr-xZn, 69704-06-9; Gr, 7782-42-5; K, 7440-09-7; C_8K, 12081-88-8; $ZnCl_2$, 7646-85-7; ethyl bromoacetate, 105-36-2; trumethylsily bromoacetate, 18291-80-0; ethyl α-bromopropanoate, 535-11-5; α-bromo-γ-butyrolactone, 5061-21-2; methyl 4-bromocrotonate, 1117-71-1; allyl bromide, 106-95-6; 1-bromo-3-methyl-2-butene, 870-63-3; trimethylsilyl α-(bromomethyl)acrylate, 87070-51-7; nonanal, 124-19-6; cyclohexanone, 108-94-1; 6-methyl-5-hepten-2-one, 110-93-0; acetophenone, 98-86-2; ethyl 4-oxovalerate, 539-88-8; fluorenone, 486-25-9; Eschenmoser's salt, 33797-51-2; benzaldehyde, 100-52-7; 2-octanone, 111-13-7; camphor, 464-49-3; ethyl 3-hydroxyundecanoate, 87070-52-8; ethyl 1-hydroxycyclohexaneacetate, 5326-50-1; ethyl 3,7-dimethyl-3-hydroxy-6-octenoate, 54211-39-1; ethyl 3-phenyl-3-hydroxybutanoate, 2293-60-9; 1-hydroxycyclohexaneacetic acid, 14399-63-4; ethyl α,2-dimethyl-5-oxotetrahydrofuran-2-acetate, 87070-53-9; 9-hydroxy-9-(tetrahydro-2-oxo-3-furyl)fluorene, 87070-54-0; 3-[(dimethylamino)methyl]dihydro-2(3*H*)-furanone, 42023-17-6; 3-[(dimethylamino)methyl]dihydro-2(3*H*)-furanone hydrochloride, 87070-55-1; ethyl *erythro*-2-ethenyl-3-hydroxy-3-phenylpropanoate, 65203-03-4; ethyl *threo*-2-ethenyl-3-hydroxy-3-phenylpropanoate, 65203-02-3; 4-methyl-1-decen-4-ol, 38564-33-9; 3,3,4-trimethyl-1-decen-4-ol, 74120-67-5; 3-methylene-1-oxaspiro[4.5]decan-2-one, 52978-85-5; dihydro-4′-methylene-1,7,7-trimethylspiro[bicyclo[2.2.1]heptane-2,2′(5′*H*)-furan]-5′-one (isomer 1), 87070-56-2; dihydro-4′-methylene-1,7,7-trimethylspiro[bicyclo[2.2.1]heptane-2,2′(5′*H*)-furan]-5′-one (isomer 2), 87099-34-1.

Cleavage of Silicon–Nitrogen Bonds by Acid Chlorides: An Unusual Synthetic Route to Amides

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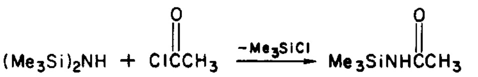
Received August 23, 1982

It has long been known that a wide variety of covalent halides react with silylamines under mild conditions to cleave the silicon–nitrogen bond (eq 1).


(1)

This reaction has been extensively used in organometallic synthesis;[1] however, the C–Cl bond of alkyl and aryl chlorides is generally inert toward silylamines. Early exceptions were observed by Anderson[2] and by Pump and Wannagat,[3] who converted an acid halide into a silyl-substituted amide by this method (eq 2).


(2)

$$(Me_3Si)_2NH + ClC(=O)CH_3 \xrightarrow{-Me_3SiCl} Me_3SiNHC(=O)CH_3 \quad (2)$$

This reaction should in theory be useful for the preparation of amides that retain silicon in their structures as well as those that do not; however, it does not appear that a detailed study of its utility has ever been reported. We have therefore determined the generality of this reaction and explored some of its possible synthetic applications; herein are reported our results.

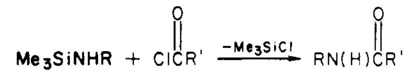
Table I. Products from the Reactions of Silylamines with Monoacid Chlorides ($R_1R_2NC(=O)R_3$)

R_1	R_2	R_3	yield,[a] %
Et	H	Me	71
Et	H	Et	68
Et	H	Ph	74
i-Pr	H	Me	82
i-Pr	H	Et	78
i-Pr	H	Ph	86
t-Bu	H	Me	90
t-Bu	H	Et	72
t-Bu	H	Ph	64
Ph	H	Me	61
Ph	H	Et	74
Ph	H	Ph	75
Et	Et	Me	67
Et	Et	Et	71
Et	Et	Ph	67

[a] Isolated yields of purified products; reported values represent an average of two or more trials.

Results and Discussion

Generality of the Reaction. To determine whether this reaction is a general one, and to evaluate the effect of varying the substituents of the silylamines, a series of reactions was performed in which N-substituted acetamides, propionamides, and benzamides were produced (eq 3).


(3)

$$Me_3SiNHR + ClC(=O)R' \xrightarrow{-Me_3SiCl} RN(H)C(=O)R' \quad (3)$$

R = Et, *i*-Pr, *t*-Bu, Ph, Me_3Si; R′ = Me, Et, Ph

It was found in each case that the reaction proceeded smoothly at or near room temperature to form the amide, usually as a crystalline precipitate from hexane or diethyl ether solvent. Those cases where R = Me_3Si were exceptional, as these silyl amides have somewhat higher solubilities in nonpolar solvents; this, coupled with their sensitivity toward hydrolysis, decreased the isolated yields unless special precautions (i.e., in-line filtration and removal of solvent under N_2) were taken.

The presence of bulky substituents on the nitrogen atom diminished the reaction rate; this is consistent with previous suggestions[3,4] that the mechanism is probably a simple nucleophilic displacement at the carbonyl carbon. It was also not surprising that the poorest nucleophiles, (trimethylsilyl)aniline and bis(trimethylsilyl)amine, often required some heating to allow the reaction to proceed at a reasonable rate. There were no significant differences in reactivity among acetyl, propionyl, and benzoyl chlorides.

The sterically hindered tertiary amine Me_3SiNEt_2 was used to convert monoacid chlorides to the corresponding *N,N*-diethyl amides in moderate yields (typically 60–70% after purification). The reaction conditions and observations generally paralleled those involving alkyl(trimethylsilyl)amines, indicating that both secondary and tertiary amides are readily synthesized by this process.

The individual results of these reactions are summarized in Table I.

Reactions of Diacid Chlorides with Alkyl(trimethylsilyl)amines. A. Formation of Diamides. As an extension of the above, it was found that mixing a 2:1 or greater molar ratio of diethyl(trimethylsilyl)amine with various diacid chlorides in an inert solvent results in the

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[1] See references in Lappert, M. F.; Power, P. P.; Sanger, A. R.; Srivastava, R. C. "Metal and Metalloid Amides: Synthesis, Structures, and Physical and Chemical Properties"; Wiley: New York, 1980.

[2] Anderson, H. H. *J. Am. Chem. Soc.* **1952**, *74*, 1421.

[3] Pump, J.; Wannagat, U. *Monatsh. Chem.* **1962**, *93*, 352.

[4] Gasparini, J. P.; Gassend, R.; Maire, J. C.; Elguero, J. *J. Organomet. Chem.* **1980**, *188*, 141.

0022-3263/83/1948-4111$01.50/0

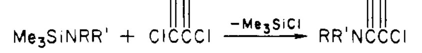
Table II. Products from the Reactions of Diacid Chlorides with Alkyl(trimethylsilyl)amines

amine	acid chloride	mole ratio	yields,[a] % amidoyl chloride	diamide
Me_3SiNEt_2	ClC(=O)C(=O)Cl	1:1	36	
		2:1		61
Me_3SiNEt_2	$ClC(=O)CH_2C(=O)Cl$	1:1	39	
		2:1		69
Me_3SiNEt_2	*o*-$C_6H_4(COCl)_2$	1:1	32	
		2:1		71
Me_3SiNEt_2	*p*-$C_6H_4(COCl)_2$	1:1	41	
		2:1		75
Me_3SiNH-*i*-Pr	ClC(=O)C(=O)Cl	1:1	29	
Me_3SiNH-*t*-Bu	ClC(=O)C(=O)Cl	1:1	39	

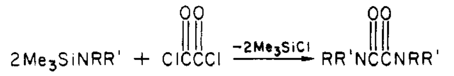
[a] Isolated yields of purified products.

smooth conversion to diamides in good to moderate (60–75%) yields; both aliphatic (oxalyl and malonyl) and aromatic (phthaloyl and terephthaloyl) chlorides were used. The results are compiled in Table II.

B. Formation of Amidoyl Chlorides. The preparation and/or purification of compounds having both amide and acid chloride functionalities is often difficult; it was therefore of interest to determine the conditions under which stoichiometric control leading to monosubstitution might be achieved. It was found that the reaction of oxalyl chloride with three different alkyl(trimethylsilyl)amines resulted in the formation of either mono- or disubstituted products depending on the stoichiometry and reaction conditions (eq 4 and 5).



$$\mathrm{Me_3SiNRR' + Cl\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}Cl \xrightarrow{-Me_3SiCl} RR'N\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}Cl} \qquad (4)$$



$$\mathrm{2Me_3SiNRR' + Cl\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}Cl \xrightarrow{-2Me_3SiCl} RR'N\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}NRR'} \qquad (5)$$

R = R′ = Et
R = H; R′ = *i*-Pr, *t*-Bu

The reproducible yields of reaction 4 are only about 40%, although higher yields have been observed in individual experiments. It does not appear that any significant disubstitution occurs when a 5% excess of oxalyl chloride is used and the temperature is maintained at −23 °C. These reactions typically occur with precipitation of amidoyl chloride from hexane solvent; in all cases care must be taken to avoid hydrolysis. Two of the amidoyl chlorides (R = H; R′ = *i*-Pr and *t*-Bu) do not appear to have previously been reported; they were fully characterized by NMR and IR spectroscopy and by elemental analysis, and a study of their conversion to unsymmetrically substituted diamides and other derivatives is in progress.

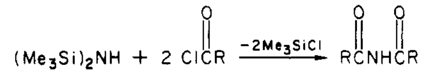
Reactions of Acid Chlorides with Bis(trimethylsilyl)amine. A. Formation of Silyl Amides. Trimethylsilyl amides are of major importance as silylating agents,[5] and their large-scale synthesis is of obvious significance. These compounds are generally prepared by the reaction of a primary amine with a chlorosilane in the presence of triethylamine, followed by isolation of the product through extraction, solvent removal, and purification.[6] Reactions between $(Me_3Si)_2NH$ and acid chlorides provide an attractive alternative route to some such compounds. In particular, we have found that the preparation of large quantities of *N*-(trimethylsilyl)benzamide by this method is especially convenient; it precipitates quantitatively as a virtually pure crystalline solid from hexane solutions of the two reagents. Aliphatic silyl amides can also be formed by this method, although their isolation and purification are less facile due to the solubilities of these compounds in nonpolar solvents.

Table III. Products from the Reaction of Bis(trimethylsilyl)amine with Acid Chlorides

acid chloride	mole ratio	yields, % silyl amide	imide
$CH_3C(=O)Cl$	1:1	88	
	1:2		51
$CH_3CH_2C(=O)Cl$	1:1	76	
	1:2		48
$C_6H_5C(=O)Cl$	1:1	84	
	1:2		54
ClC(=O)C(=O)Cl	1:1	57[a]	
$ClC(=O)CH_2C(=O)Cl$	1:1	68[a]	
p-$C_6H_4(COCl)_2$	1:1	76[a]	

[a] Polymeric material; see text.

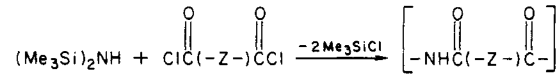
B. Formation of Imides. In the reactions described above care must be taken to add the acid chloride into a stirred solution containing an equimolar amount of $(Me_3Si)_2NH$; otherwise the yields may be decreased due to the formation of imides according to the reaction



$$\mathrm{(Me_3Si)_2NH + 2\ Cl\overset{O}{\overset{\|}{C}}R \xrightarrow{-2Me_3SiCl} R\overset{O}{\overset{\|}{C}}NH\overset{O}{\overset{\|}{C}}R} \qquad (6)$$

If desired, the yield of imide can be maximized by slow addition of $(Me_3Si)_2NH$ to a stirred solution of excess acid chloride in refluxing ether or THF; typical yields under these conditions are 50–60%.

C. Formation of Polyimides. Reactions between three diacid chlorides—oxalyl, malonyl, and terephthaloyl chlorides—and bis(trimethylsilyl)amine resulted in the formation of polymers (eq 7).



$$\mathrm{(Me_3Si)_2NH + Cl\overset{O}{\overset{\|}{C}}(-Z-)\overset{O}{\overset{\|}{C}}Cl \xrightarrow{-2Me_3SiCl} \left[-NH\overset{O}{\overset{\|}{C}}(-Z-)\overset{O}{\overset{\|}{C}}-\right]_x} \qquad (7)$$

The mixing of equimolar quantities of diacid chloride and disilylamine in hot hexane gave a white, primarily crystalline precipitate; these products had high melting points (over 200 °C) and were insoluble in water and in most organic solvents. The proposed structures are supported by spectroscopic data. Preliminary viscosity experiments suggest typical molecular weights of 10^3–10^4 g/mol; more accurate determinations are in progress.

The results of all reactions involving $(Me_3Si)_2NH$ are given in Table III.

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[5] See, for example, Green, T. "Protective Groups in Organic Synthesis"; Wiley: New York, 1981.

[6] Klebe, J. F.; Finkbeiner, H.; White, D. M. *J. Am. Chem. Soc.* **1966**, *88*, 3390.

Experimental Section

The alkyl(trimethylsilyl)amines and (trimethylsilyl)aniline were all prepared according to the literature;[1] bis(trimethylsilyl)amine was purchased (Fisher Scientific) and distilled prior to use. Acid chlorides were purchased (Aldrich) and checked for purity by NMR and IR spectroscopy; if necessary they were purified by distillation or recrystallization. All solvents were distilled from calcium hydride immediately prior to use. All reactions were performed under an atmosphere of dry nitrogen with the aid of a vacuum manifold.

Products were characterized by ^{1}H NMR (Varian EM 360L) and IR (Perkin Elmer 735B) spectroscopy; melting points were taken with a Fisher-Johns melting point apparatus and checked against published values, agreeing in all cases to within ±3 °C. Elemental analyses were performed by Micanal of Tucson, AZ.

Preparation of Monofunctional Amides. A representative procedure for reactions of this type is given here for the synthesis of *N-tert*-butylacetamide. A 250-mL two-necked flask equipped with a magnetic stirrer and an addition funnel was evacuated and filled with dry N_2. *tert*-Butyl(trimethylsilyl)amine (5.81 g, 0.040 mol) was added along with 120 mL of hexane. Acetyl chloride (2.9 mL, 0.041 mol) was added dropwise to the room-temperature solution, resulting in the formation of a white precipitate; stirring was continued for 5 h. Vacuum filtration, washing with hexane to remove residual chlorotrimethylsilane, and recrystallization from isopropyl alcohol yielded 4.05 g (88%) of the product amide [mp 97–98 °C (lit.[7] mp 97 °C)].

Reactions of Diacid Chlorides with Alkyl(trimethylsilyl)amines. A. Preparation of Diamides. A typical reaction is described here for the synthesis of *N,N,N′,N′*-tetraethyloxamide. Oxalyl chloride (4.68 g, 0.0369 mol) in 10 mL of hexane was slowly added to diethyl(trimethylsilyl)amine (10.90 g, 0.0750 mol) in 90 mL of hexane at room temperature under an atmosphere of N_2, *resulting in the formation of an orange-red liquid mixture.* Rotary evaporation of solvent and Me_3SiCl left a colored oily residue, which was recrystallized twice from CCl_4 to give the diamide [4.06 g = 55%; mp 33–35 °C (lit.[8] mp 35–36 °C)].

B. Preparation of *N-tert*-Butyloxamoyl Chloride. A solution of Me_3SiNH-*t*-Bu (3.78 g, 0.0260 mol) in 10 mL of hexane was added dropwise over a 15-min period to a stirred solution of oxalyl chloride (3.55 g, 0.0280 mol) in 35 mL of hexane under a nitrogen atmosphere at −23 °C; this temperature was maintained with a CCl_4/liquid N_2 slurry. Stirring was continued for 1.5 h as precipitation occurred. Solvent and Me_3SiCl were removed by low-pressure distillation under N_2 at 0 °C; the crystalline residue was washed with hexane and recrystallized from CCl_4 to give the product (1.83 g, 43%, mp 90–91 °C). Anal. Calcd for $C_6H_{10}ClNO_2$: C, 44.05; H, 6.16; N, 8.56. Found: C, 44.14; H, 6.28; N, 8.65.

C. Preparation of *N*-Isopropyloxamoyl Chloride. In a procedure similar to that described above, Me_3SiNH-*i*-Pr (4.61 g, 0.0351 mol) and $(COCl)_2$ (4.59 g, 0.0362 mol) were reacted to give a white precipitate identified as the expected product (1.89 g, 36%, mp 113 °C). Anal. Calcd for $C_5H_8ClNO_2$: C, 40.15; H, 5.39; N, 9.36. Found: C, 40.11; H, 5.37; N, 9.44.

Reactions of Bis(trimethylsilyl)amine with Acid Chlorides. A. Preparation of *N*-(Trimethylsilyl)benzamide. A solution of benzoyl chloride (34.71 g, 0.247 mol) in 50 mL of hexane was added dropwise to stirred $(Me_3Si)_2NH$ (40.35 g, 0.250 mol) in 90 mL of hexane, resulting in the formation of a white precipitate. Following reflux for 2 h under nitrogen, the mixture was cooled and filtered; the solid product was recrystallized from hot CCl_4 and identified as the desired silyl amide by NMR and IR spectroscopy. The yield was 40.69 g (85% based on C_6H_5COCl).

B. Preparation of Polyimides. In a representative procedure oxalyl chloride (4.82 g, 0.0380 mol) and $(Me_3Si)_2NH$ (6.13 g, 0.0380 mol) were mixed at room temperature in 20 mL of hexane under an atmosphere of dry N_2, resulting in the precipitation of a white solid. After stirring of the mixture for 5 h, volatile materials were removed by rotary evaporation, and the residue was washed several times with hexane, CCl_4, and $CHCl_3$. This crystalline solid did not melt below 240 °C and was insoluble in water and most organic solvents; it gave NMR and IR spectra consistent with those expected for a polyimide.

Registry No. EtNHCOMe, 625-50-3; EtNHCOEt, 5129-72-6; EtNHCOPh, 614-17-5; *i*-PrNHCOMe, 1118-69-0; *i*-PrNHCOEt, 10601-63-5; *i*-PrNHCOPh, 5440-69-7; *t*-BuNHCOMe, 762-84-5; *t*-BuNHCOEt, 1118-32-7; *t*-BuNHCOPh, 5894-65-5; PhNHCOMe, 103-84-4; PhNHCOEt, 620-71-3; PhNHCOPh, 93-98-1; $(Et)_2NCOEt$, 1114-51-8; $(Et)_2NCOPh$, 1696-17-9; EtNHTMS, 1735-00-8; *i*-BuNHTMS, 5577-65-1; *t*-BuNHTMS, 5577-67-3; PhNHTMS, 3768-55-6; $(Et)_2NTMS$, 996-50-9; MeCOCl, 75-36-5; EtCOCl, 79-03-8; PhCOCl, 98-88-4; $(Et)_2NCOCOCl$, 87039-68-7; $(Et)_2NCOCH_2COCl$, 87039-69-8; *o*-$(Et)_2NCOC_6H_4COCl$, 79422-68-7; *p*-$(Et)_2NCOC_6H_4COCl$, 87039-70-1; *i*-PrNHCOCOCl, 87039-71-2; *t*-BuNHCOCOCl, 87039-72-3; $((Et)_2NCO)_2$, 14288-05-2; $((Et_2NCO)_2CH_2$, 33931-42-9; *o*-$((Et)_2NCO)C_6H_4$, 83-81-8; *p*-$((Et)_2NCO)_2C_6H_4$, 15394-30-6; $(ClCO)_2$, 79-37-8; $(ClCO)_2CH_2$, 1663-67-8; *o*-$C_6H_4(COCl)_2$, 88-95-9; *p*-$C_6H_4(COCl)_2$, 100-20-9; TMSNHCOMe, 13435-12-6; TMSNHCOEt, 18140-08-4; TMSNHCOPh, 1011-57-0; $((ClCO)_2)\cdot$(TMSNHTMS) (copolymer), 87039-67-6; $((ClCO)_2CH_2)\cdot$(TMSNHTMS) (copolymer), 87050-06-4; (*p*-$(ClCO)_2C_6H_4)\cdot$(TMSNHTMS) (copolymer), 87050-07-5; $(MeCO)_2NH$, 625-77-4; $(EtCO)_2NH$, 6050-26-6; $(PhCO)_2NH$, 614-28-8; $(TMS)_2NH$, 999-97-3.

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[7] Ritter, J. J.; Minieri, P. P. *J. Am. Chem. Soc.* **1948**, *70*, 4048.

[8] Barre, R. *C. R. Hebd. Scances Acad. Sci.* **1927**, *185*, 1051.

Stereospecific Synthesis of Hydroxyl-Differentiated (*E*)- and (*Z*)-1,4-Enediols

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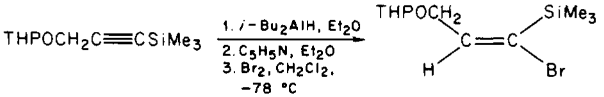
Received March 14, 1983

Hydroxyl-differentiated 1,4-enediols have significant potential as intermediates in the synthesis of complex organic molecules. Recently, Masamune and Sharpless[1] demonstrated the utility of such compounds in the synthesis of saccharides and related polyhydroxylated natural products via assymetric epoxidation. Also the potential exists for ultimate control of regiochemistry in Diels–Alder reactions by selective oxidation of the enediols to give regiocomplementary dienophiles. Therefore a general, stereospecific synthesis of hydroxyl-differentiated 1,4-enediols would be most useful; such a process is described in this paper.

The key compounds for this study were the tetrahydropyranyl ethers of (*E*)- and (*Z*)-3-bromo-3-(trimethylsilyl)-2-propen-1-ol. The *E*-isomer 1 was prepared stereospecifically by hydroalumination–bromination[2] of the tetrahydropyranyl ether of 3-(trimethylsilyl)-2-propyn-1-ol.[3] The product 1 was obtained in 80% isolated yield.



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It was observed that ~5% cleavage of the tetrahydropyranyl ether was obtained in the crude reaction product. This material could either be separated from 1 by distillation or reprotected by treating the crude reaction product with dihydropyran and a catalytic amount of phosphorus oxychloride. In an attempt to suppress the cleavage of the tetrahydropyranyl ether, use of an equivalent amount of

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[1] Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373.

[2] Zweifel, G.; Lewis, W. *J. Org. Chem.* **1978**, *43*, 2739.

[3] Miller, R. B. *Synth. Commun.* **1972**, *2*, 267.