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N,N-BIS(HALOMETHYLDIMETHYLSILYL)ACETAMIDES AND THEIR REACTIONS

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Summary

N,N-Bis(halomethyldimethylsilyl)acetamides, $MeCON(SiMe_2CH_2X)_2$, (X = Cl, Br) were prepared by transsilylation of *N,O*-bis(trimethylsilyl)acetamide with halomethyldimethylchlorosilane. With water and methanol, instead of the expected Si—N cleavage, nucleophilic substitution of halogen took place and the products were 1-acetyl-2,2,6,6-tetramethyldisilamorpholine and *N,N*,-bis-methoxymethyldimethylsilyl)acetamide respectively. These compounds were shown by IR and ^1H NMR spectra to have the *N,N*-disilylacetamide structure. Thermodynamic, kinetic constants of hindered rotation around the C—N bond in these compounds were determined from their temperature-variable ^1H NMR spectra. The main products of thermolysis of the silylamides are α,ω-dichloropolydimethylsiloxanes and polydimethylcyclosiloxanes.

Introduction

N,O-Bis(trimethylsilyl)acetamide (BSA) is often used as a highly efficient silylating agent for hydroxylic compounds in conjunction with gas-chromatographic analysis [1]. Replacement of trimethylsilyl by a halomethyldimethylsilyl group allows use of an electron capture detector in the gas chromatography, and this has been the main reason for employing halomethyldimethylsilyl derivatives in GLC analysis of hormones, steroids etc. The substrates are reacted typically with halomethyldimethylsilyldiethylamine in the presence of halomethyldimethylchlorosilane [2,3] (eq. 1) or with 1,3-(chloromethyl)tetra-

$$XCH_2Me_2SiNEt_2 + ROH \xrightarrow{XCH_2Me_2SiCl} ROSiMe_2CH_2X \qquad (1)$$

$$ClCH_2Me_2SiNHSiMe_2CH_2Cl + ROH \rightarrow ROSiMe_2CH_2Cl \quad (2)$$

methyldisilazane [4] (eq. 2).

On account of the high reactivity of BSA it seemed interesting to synthesize the acetamide containing two halomethyldimethylsilyl groups, in order to study its structure and evaluate its potential as a silylating agent.

Results and discussion

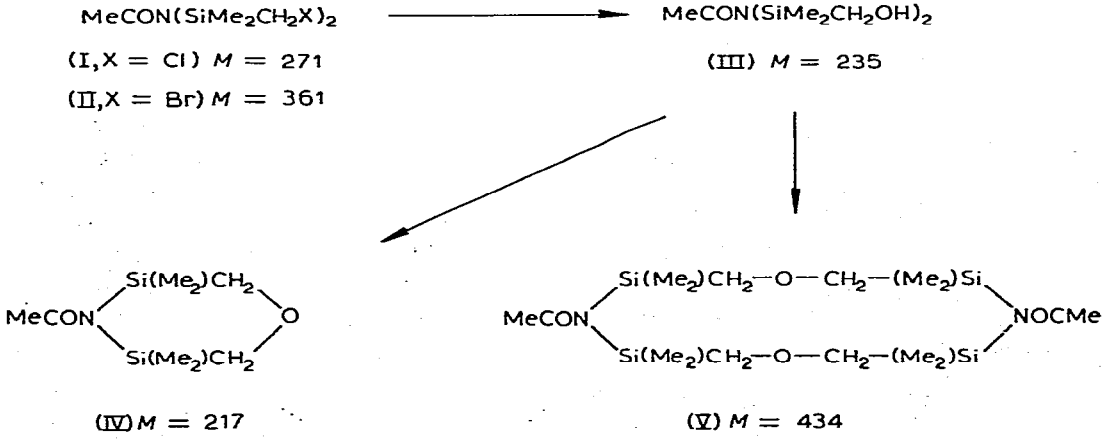
Attempts to prepare bis(chloromethyldimethylsilyl)-acetamide from chloromethyldimethylchlorosilane and acetamide, by a method analogous to that used for BSA [5], failed. For example, when chloromethyldimethylchlorosilane (2 moles), acetamide (1 mole) and triethylamine were heated together in boiling toluene, subsequent fractionational distillation gave unchanged materials. However, transsilylation of BSA with halomethyldimethylchlorosilane gave satisfactory yields of compounds I and II:

$$MeCON(SiMe_3)_2 + 2\ ClSiMe_2CH_2X \rightarrow MeCON(SiMe_2CH_2X)_2 + 2\ Me_3SiCl \quad (3)$$

(I, X = Cl;
II, X = Br)

Similar transsilylations have been used to replace trimethylsilyl units in hexamethyldisilazane by RMe_2Si groups (R = alkyl, aryl [6] or Cl_nSiMe_{3-n} [7]).

Compounds I and II are easily hydrolysed by water and preliminary experiments showed, surprisingly, that hydrogen halide is one of the products. Titrating aqueous solutions of I (or II) with silver nitrate or sodium hydroxide gave identical results showing that the CH_2—X bond is cleaved quantitatively. The high reactivity of the compounds hindered determination of their molecular weights by mass spectrometry. In the mass spectra (sample introduced by direct inlet) both parent bands and the $M - 15$ molecular ions were absent and, instead, characteristic bands at $m/e = 217$ and $m/e = 434$ were observed for both I and II. It is assumed therefore that bis(hydroxymethyldimethylsilyl)acetamide (III) is formed by hydrolysis and yields the cyclic compounds IV and V, respectively as a result of intramolecular and intermolecular condensation (Scheme 1).



Hydroxymethyl groups attached to silicon are known to condense readily [8] and this process may be facilitated by the conditions in the mass spectometer.

When a solution of bis(halomethyldimethylsilyl)acetamide in methylene chloride was introduced directly into the mass spectrometer, the spectrum contained parent as well as $M-15$ ions (i.e., $M-CH_3$) and $M-35$ for I or $M-79$ for II ($M-X$), isotopic patterns characteristic for two halogen atoms per molecule were also observed.

The hydrolysis process (Scheme 1) was further substantiated by the preparation of 1-acetyl-2,2,6,6-tetramethyldisilamorpholine (IV) when I was treated with water. This compound was found to be the main product irrespective of the method of hydrolysis employed. Another compound (10%) also present in the reaction products, was shown by gas chromatography coupled with mass spectrometry to have a molecular weight of 434. It is also formed on storage of IV and from its molecular weight it can be assigned formula V.

Upon methanolysis I or II, instead of Si—N bond cleavage, typical of silylation as with BSA, halogen is replaced by methoxyl:

$$MeCON(SiMe_2CH_2X)_2 + MeOH \xrightarrow{Et_3N} MeCON(SiMe_2CH_2OMe)_2 \qquad (4)$$

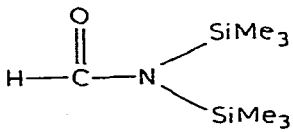
(I or II) (VI)

In halomethylsilylacetamides the most reactive center towards nucleophilic substitution is thus the halogenated carbon, The carbon—halogen bond in α-haloalkylsilanes is relatively stable [9], for example the carbon—chlorine bond in chloromethyl(trimethylsilane) is cleaved only by sodium methoxide in boiling methanol and the bromine derivatives react similarly with alcohols in the presence of amines. A typical reaction of α-halomethylsilicon compounds is the cleavage of the carbon—silicon bond with formation of methyl halide, but we were unable to detect by GLC any traces of methyl halide in either the hydrolysis or methanolysis of bis(halomethyldimethylsilyl)acetamides.

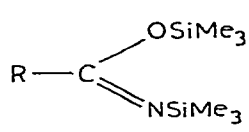
Spectra and structure of the silylacetamides

The structures of the compounds were determined by elemental analysis (Table 1), mass spectra, IR and ^1H NMR (Table 2).

Of the bis(trimethylsilyl)amides investigated so far only the formamide derivative is assigned the amide structure (A), all remaining compounds having the iminoether structure (B) [10—12].



(A)

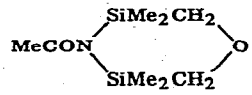


(B)

The spectral differences between both classes of compounds are significant. The band at 1659 cm^{-1} is assigned to carbonyl vibrations and that at 983 cm^{-1} to the Si—N—Si grouping in *N,N*-bis(trimethylsilyl)formamide (A) [11]. For *N,O*-bis(trimethylsilyl)acetamide (B, R = Me) the characteristic absorption is at 1698 cm^{-1} and can be assigned to O—C=N or C=N [12].

TABLE 1

PROPERTIES OF THE SILYLACETAMIDES

Compound [a]	Yield (%)	B.p./mmHg (m.p.)	Analysis found (calcd.) (%)			
			C	H	Si	Hal [b]
$MeCON(SiMe_2CH_2Cl)_2$ (I)	81	(128—131)			20.10 (20.63)	25.40 (26.03)
$MeCON(SiMe_2CH_2Br)_2$ (II)	80	(150—151)			15.30 (15.46)	42.10 (43.95)
 (IV)	48	72/1 (38—40)			21.33 (21.31)	
$MeCON(SiMe_2CH_2OMe)_2$ (VI)	46	108—112/5	44.30 (44.20)	8.72 (8.81)	26.08 (25.84)	

[a] All compounds gave the expected molecular ion in the mass spectrum. [b] Determined by potentiometric titration with 0.1 *M* NaOH.

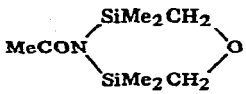
In the IR spectra of our compounds strong absorption bands characteristic of the amide grouping at 1603 cm^{-1} in I and 1640 cm^{-1} in IV and VI are present together with a medium absorption at 990 cm^{-1}. Comparison with the spectra of *N,N*-bis(trimethylsilyl)formamide leads us to conclude that our compounds have the *N,N*-disilylamide structure analogous to A.

The integrated ^1H NMR spectra are consistent with this formulation (Table 2) and the chemical shift values provide additional evidence for their *N,N*-disilylamide structure. There are significant differences between the chemical shifts in the solution spectra of our compounds in the non-aromatic and aromatic solvents, viz. chloroform and benzene. This was not observed for either BSA [11] or bis(*p*-tolyldimethylsilyl)acetamide [13] which were both shown to have *N,O*-disilyliminoether structure. It is known that such differences in chemical shifts are due to magnetic anisotropy of the aromatic solvent. In *N,N*-dialkylamides the difference between the chemical shifts of the magnetically non-equivalent alkyl protons is larger in benzene because of the formation of an oriented complex composed of a solute and solvent molecule [14]. In the present case the magnetic non-equivalency of the methylsilyl protons arises from hindered rotation around the carbon—nitrogen bond (restricted rotation is also observed in *N,N*-dialkylamides [15]).

In the ^1H NMR spectra the distance between the signals of the methylsilyl protons decreases with rising temperature and coalescence is ultimately observed as illustrated in Fig. 1 for compound VI. In Table 3 the rate constants of the rotation (k_c), the coalescence temperatures (T_c) and the free energies of activations ($\Delta G_c^{\ddagger}$) for that process are listed. The approximate method [16] was used for determining k_c, and $\Delta G_c^{\ddagger}$ was evaluated from the maximum difference between the chemical shifts of the methylsilyl protons at hindered rotation. The $\Delta G_c^{\ddagger}$ values are close to the 15.3 kcal mol^{-1} obtained for the internal silyl migration in BSA [17]. They are much higher than the value for the rotation around

TABLE 2

^{1}H NMR SPECTRAL DATA FOR THE SILYLACETAMIDES

Compound [a]	Solvent	δ values			
		CH_3Si	CH_3C	CH_2Si	CH_3O
$MeCON(SiMe_2CH_2Cl)_2$ (I)	$CHCl_3$	0.61(12H)	2.17(3H)	2.85(2H) 3.25(2H)	
	C_6H_6	0.20(6H) 0.97(6H)	1.53(3H)	2.63(2H) 2.81(2H)	
$MeCON(SiMe_2CH_2Br)_2$ (II)	$CHCl_3$	0.70(6H) 0.78(6H)	2.30(3H)	3.18(2H) 3.44(2H)	
	C_6H_6	0.35(6H) 1.03(6H)	1.54(3H)	2.80(2H) 3.04(2H)	
 (IV)	$CHCl_3$	0.22(12H)	2.07(3H)	2.83(2H) 3.05(2H)	
	C_6H_6	0.01 + 0.1 [b] (12H)	1.83(3H)	2.44(2H) 3.12(2H)	
$MeCON(SiMe_2CH_2OMe)_2$ (VI)	$CHCl_3$	0.21(12H)	2.05(3H)	2.66(2H) 2.93(2H)	3.39(3H) 3.48(3H)
	C_6H_6	0.02(6H) 0.45(6H)	1.76(3H)	2.60(4H)	3.20(3H) 3.40(3H)

[a] Tetramethylsilane as internal standard; room temperature. [b] Unresolved.

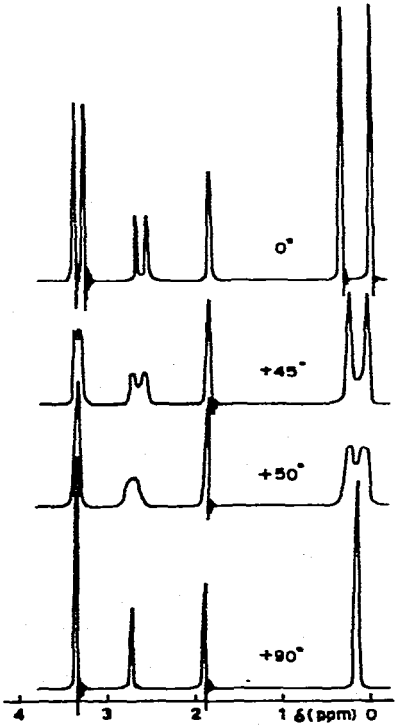
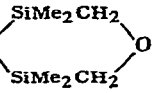


Fig. 1. Variable temperature proton NMR spectra of *N,N*-bis(methoxymethyldimethylsilyl)acetamide in chlorobenzene.

TABLE 3

KINETIC AND THERMODYNAMIC PARAMETERS OBTAINED BY VARIABLE TEMPERATURE NMR

Compound [a]	T_c (°C)	k_c (s^{-1})	$\Delta\nu$(Hz)	$\Delta G_c^{\ddagger}$ (kcal mol^{-1})
$MeCON(SiMe_2CH_2Cl)_2$ (I)	[b]	43.8	19.7	15.4 [c]
$MeCON(SiMe_2CH_2Br)_2$ (II)	[b]	32.2	14.5	15.5 [c]
 (IV)	28	14.9	6.7	16.0
$MeCON(SiMe_2CH_2OMe)_2$ (VI)	55	19.3	8.7	17.3

[a] Spectra taken in C_6H_5CN except IV ($C_6D_5CD_3$) at 60 MHz. [b] Coalescence temperatures (above 150°C) could not be determined because of the unstability of these compounds at high temperatures. [c] Values of free energy determined for 20°C.

C—N in *N,N*-bis(trimethylsilyl)formamide (11.6 kcal mol^{-1}) [11]. In *N,N*-dialkylacetamides increasing the size of alkyl substituents at nitrogen decreases the barrier to rotation [18]. In the present case changing from trimethylsilyl to halomethyldimethylsilyl groups brings about a change in structure (from *N,O*- to *N,N*-disilyl), and relative to the trimethylsilylformamide it increases considerably the free energy or activation for rotation. The reason lies in the inductive effect of α-halogen or α-methoxyl groups which will increase the π character of the carbonyl carbon—nitrogen bond. This will favour the *N,N*-disilylamide form of acetamide. A similar effect was observed in the series of trimethylsilylacetanilides, where electron supplying substituents in the benzene ring increased the proportion of the *N*-silylamide in its equilibrium mixture with the *O*-silylamide [19].

Thermal stability of N,N-bis(chloromethyldimethylsilyl)acetamide

In view of the structural difference between *N,N*-bis(chloromethyldimethylsilyl)acetamide and *N,O*-bis(trimethylsilyl)acetamide it is of interest to investigate the thermal decomposition of the former.

Compounds of two homologous series were found in the liquid product (approx. 40%) produced on heating I at 200°C for 20 h. They are: α,ω-dichloropoly(dimethylsiloxanes), $Cl(Me_2SiO)_nSiMe_2Cl$, ($n = 0$—5) and dimethylcyclosiloxanes $(Me_2SiO)_m$ (m = 4—6). Small amounts of acetonitrile and trimethylchlorosilane were also present. All these compounds were identified by GLC-MS. It was not possible to determine the composition of the charred residue.

From the nature of the thermolysis products it can be concluded, that a number of bond-breaking and bond-making processes occur when I is heated. The thermal disintegration of BSA appears to be a simpler process since the only products are acetonitrile and hexamethyldisiloxane [20]. On the other hand, *N,N*-bis(trimethylsilyl)formamide yields, on heating, hexamethyldisiloxane and a "charred residue" [10]. It has been noticed that the nature of the thermolysis

product depends on the structure of the silylamide [20], however, chemically-bonded nitrogen was always found in the identifiable compounds. In the present case all the original silylamide nitrogen must be in the non-identifiable charred mixture.

Experimental

N,N-bis(halomethyldimethylsilyl)acetamides

N,O-bis(trimethylsilyl)acetamide (0.05 mol) was added slowly with stirring to a solution of halomethyldimethylchlorosilane (0.11 mol) in 50 ml of solvent (n-heptane or diethyl ether). The process is exothermic and the reaction flask was cooled in ice during the addition. After a few hours precipitated bis(chloromethyldimethylsilyl)acetamide (I) or bis(bromomethyldimethylsilyl)acetamide (II) was filtered off, washed with ether, and dried under reduced pressure. The physical constants are listed in Table 1.

Reaction of bis(halomethyldimethylsilyl)acetamides with water

The reaction was carried out in two ways.

(a) The silylacetamide I or II (0.025 mol) was dissolved in chloroform (25 ml) and extracted with 2 ml portions of water until a neutral aqueous layer was obtained. The chloroform solution was dried over K_2CO_3 and filtered, chloroform was distilled off, and the residue was fractionally distilled to give 1-acetyl-2,2,6,6-tetramethyldisilamorpholine (IV) which crystallized on cooling. Yield 50%; purity 98% (by GLC).

(b) A solution of pyridine (0.052 mol) and water (0.025 mol) in diethyl ether (40 ml) was added to *N,N*-bis(chloromethyldimethylsilyl)acetamide (0.025 mol) in benzene (25 ml). Pyridine hydrochloride was filtered off and the filtrate was analyzed by GLC. The acetyldisilamorpholine (IV) and its dimer (V) were found in proportions of 10:1. Both these compounds were identified by GLC-MS analysis. After distillation of the solvents, the residual liquid was fractionally distilled to give 1-acetyl-2,2,6,6-tetramethyldisilamorpholine (IV) in 48% yield.

Reaction with methanol

A solution of methanol (0.066 mol) and triethylamine (0.066 mol) in 10 ml of benzene was added dropwise to *N,N*-bis(halomethyldimethylsilyl)acetamide (I or II) (0.03 mol) in 50 ml benzene, the reaction flask being cooled with water. After standing overnight the precipitated triethylamine hydrohalide was filtered off and after removal of the solvents the residual liquid was fractionally distilled in vacuo to give *N,N*-bis(methoxymethyldimethylsilyl)acetamide (VI).

Thermolysis of N,N-bis(chloromethyldimethylsilyl)acetamide

Approximately 0.5 g of I was heated at 200°C for 20 h in an evacuated, sealed ampoule. The liquid portion was then separated from the dark solid and analyzed by GLC (column 2 m, 10% OV-101, programmed temperature from 40°C to 250°C; carrier gas H_2, 40 ml/min) and by GLC-MS,

Mass spectra

The mass spectra were taken on a mass spectrometer LKB 9000 coupled with

a gas chromatograph. For mass analysis of I and II the samples were introduced by direct inlet in the form of solutions in methylene chloride which prevented their hydrolysis. In all other cases the samples were introduced through the gas chromatograph.

NMR and IR measurements

^{1}H NMR spectra were recorded on a JEOL C-60HL spectrometer equipped with a temperature controlling device. The temperatures of the samples were measured by using capillary tubes with methanol or ethylene glycol and Van Goets equation [21].

IR spectra were obtained with a Pye Unicam 1200 spectrometer.

Acknowledgement

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