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Trimethylgermylation and trimethylsilylation of *N,N*-dialkylacetamides and application of their anions to the Peterson-type reaction

Shin'ichi Urayama, Sumie Inoue, and Yoshiro Sato *

Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467 (Japan)

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Abstract

Base-assisted trimethylsilylation and trimethylgermylation of *N,N*-dimethylacetamide (**1a**) or 1-acetylpiperidine (**1b**) were carried out. The germyl group was introduced stepwise onto the methyl carbon of the acetyl group to give mono- (**3**), bis- (**6**), or tris(trimethylgermyl)acetamides (**9b**), respectively, in high yields, whereas under similar conditions the second silyl group was usually introduced at the carbonyl-oxygen. The Peterson-type reaction of *N,N*-dimethyl(trimethylgermyl)(trimethylsilyl)acetamide (**5a**) with aldehydes gave preferentially *N,N*-dimethyl-2-(trimethylgermyl)-2-alkenamides (**13**).

Introduction

When acetic acid esters or ketones are deprotonated with a base followed by quenching with chlorotrimethylsilane or chlorotrimethylgermane, the germyl group is preferentially introduced onto the α-carbon whereas the trimethylsilyl group is introduced onto the carbonyl-oxygen [1,2]. In the Peterson-type reaction of (trimethylgermyl)(trimethylsilyl)acetates and (trimethylgermyl)(trimethylsilyl)acetonitrile anions with aldehydes, the germyl group remained in the reaction products with elimination of the siloxy group [1,3]. In the present study, a comparison was made of trimethylgermylation and trimethylsilylation of *N,N*-dialkylacetamides, and of the way in which the resulting compounds participate in the Peterson-type reaction.

Results and discussion

Treatment of *N,N*-dimethylacetamide (**1a**) or 1-acetylpiperidine (**1b**) with lithium diisopropylamide (LDA) followed by chlorotrimethylsilane or chlorotrimethylgermane at $-78°C$ in THF gave (trimethylsilyl)acetamides (**2**) or (trimethylgermyl)acetamides (**3**), respectively, in high yields (Table 1).

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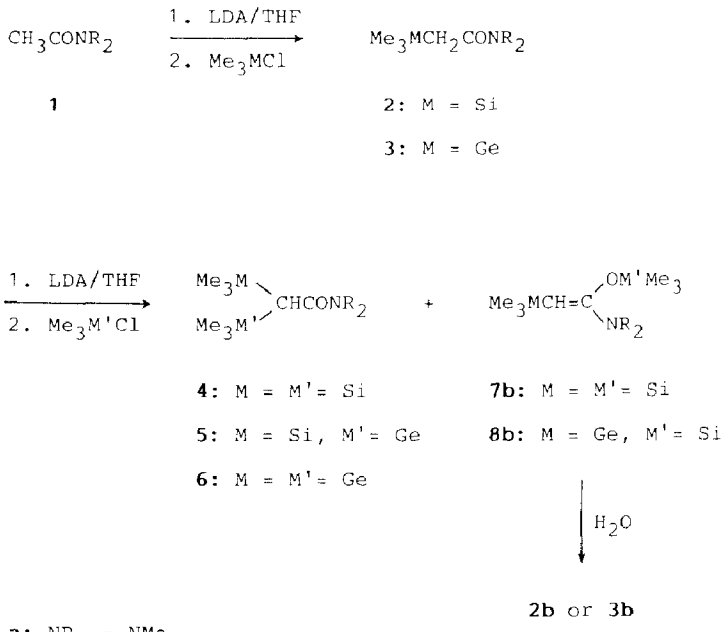


Scheme 1

Trimethylgermylation of **2** or **3** gave (trimethylgermyl)(trimethylsilyl)acetamides (**5**) or bis (trimethylgermyl)acetamides (**6**), respectively, in high yields under the same reaction conditions as above (entries 3, 4, 6, and 7 in Table 2). However, trimethylsilylation afforded bis(trimethylsilyl)acetamide (**4b**) and (trimethylgermyl)-(trimethylsilyl)acetamide (**5b**) in low yields (entries 2 and 5), apparently due to the competitive formation of the *O*-silylated products **7b** and **8b**. Indeed, GLC analysis of the reaction mixtures after the addition of chlorotrimethylsilane indicated the presence of **7b** and **8b** as the main products, which disappeared after aqueous work-up.

Table 1

(Trimethylsilyl or trimethylgermyl)acetamides (**2** or **3**)

Entry		M	NR_2	Yield (%)
1	**2a**	Si	NMe_2	91
2	**2b**	Si	cyclo-$C_5H_{10}N$	80
3	**3a**	Ge	NMe_2	95
4	**3b**	Ge	cyclo-$C_5H_{10}N$	88

Table 2

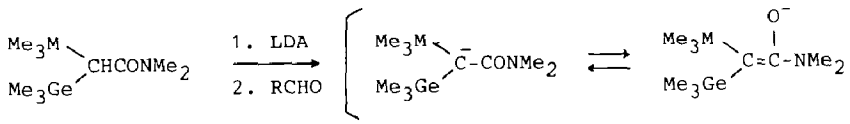
Bis(trimethylsilyl or trimethylgermyl)acetamides (**4** or **6**) and (trimethylsilyl)(trimethylgermyl)acetamides (**5**)

Entry		M	M′	NR_2	Yield (%)	
					from **2** or **3**	from **1**
1	**4a**	Si	Si	NMe_2	–	10
2	**4b**	Si	Si	cyclo-$C_5H_{10}N$	31	21
3	**5a**	Si	Ge	NMe_2	95	
4	**5b**	Si	Ge	cyclo-$C_5H_{10}N$	84	
5	**5b**	Ge	Si	cyclo-$C_5H_{10}N$	50	
6	**6a**	Ge	Ge	NMe_2	96	91
7	**6b**	Ge	Ge	cyclo-$C_5H_{10}N$	82	82

Although bis(trimethylsilyl or trimethylgermyl)acetamides (**4** or **6**) were obtained directly by treatment of **1** with two equivalents of the base and chlorotrimethylsilane or chlorotrimethylgermane, their silylation and germylation yields were markedly different (entries 1, 2, 6, and 7 in Table 2). Trimethylgermylation of **6b** gave 1-[tris(trimethylgermyl)acetyl]piperidine (**9b**) in good yield.

When **5a** or **6a** was treated with either 2-ethylhexanal or benzaldehyde after addition of LDA, at −78 °C in THF, *N*,*N*-dimethyl-4-ethyl-2-(trimethylgermyl)-2-octenamide (**13a**), or *N*,*N*-dimethyl-3-phenyl-2-(trimethylgermyl)propenamide (**13b**) was obtained as the main expected product (Table 3). However, appreciable amounts of starting material were recovered from the reaction mixtures. The amount of starting compound recovered was constant, even after prolonged reaction. Only small amounts of *N*,*N*-dimethyl-2-(trimethylsilyl)-2-alkenamides (**14**) were isolated from the reaction mixture of **5a**.

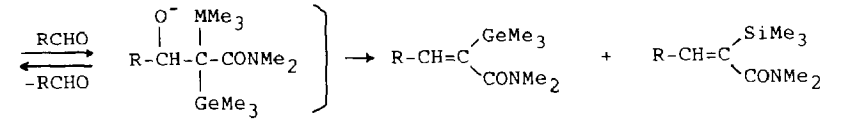
Thus, the silyl group is also preferentially eliminated in this Peterson-type reaction. The reaction may be equilibrated between the intermediate anion **10** and



5a: M = Si

6a: M = Ge

10 **11**



12 **13** **14**

Scheme 2

Table 3

Reaction of *N,N*-dimethyl[(trimethylsilyl)(trimethylgermyl) or bis(trimethylgermyl)]acetamide (**5a** or **6a**) with aldehydes

Entry	Starting compound	R	Products (%) (*E*/*Z*)		Recovery of **5a** or **6a** (%)
1	**5a**	n-Bu(Et)CH	**13a**, 53 (95/5)	**14a**, 3	15
2	**5a**	Ph	**13b**, 63 (86/14)	**14b**, 5	12
3	**6a**	n-Bu(Et)CH	**13a**, 38 (99/1)		47
4	**6a**	Ph	**13b**, 40 (98/2)		43

adduct **12** (Scheme 2). With this equilibrium, it is possible to bring about high selectivity which affords the thermodynamically stable *E*-isomer of **13**.

Experimental

All reactions were carried out under nitrogen or argon. Tetrahydrofuran was dried by distillation from sodium benzophenone ketyl. ^{1}H NMR and ^{13}C NMR spectra were recorded on JEOL JNM-MH-100 and JNM-PMX-60 spectrometers using Me_4Si as internal standard. IR spectra were recorded on a JASCO IRA-2 spectrometer. Mass spectral data were obtained by use of a JEOL JMS-DX 300 GC/MS system (70 eV). Gas chromatographic analyses were performed carried out with a Gasukuro Kogyo Model 370 equipped with FID and TCD detectors using 10% Tergitol NP-35 and 10% Silicone SE-30 columns. All melting and boiling points are uncorrected.

*Trimethylsilylation or trimethylgermylation of N,N-dimethylacetamide (**1a**) and 1-acetylpiperidine (**1b**): general procedure*

To a solution of diisopropylamine (5.26 g, 52 mmol) in THF (60 ml) was added n-BuLi (10 w/v% in hexane, 34 ml, 52 mmol) at 0 °C with continuous stirring over a period of 0.5 h. The LDA solution thus prepared was cooled at −78 °C and a solution of *N,N*-dimethylacetamide (**1a**) or 1-acetylpiperidine (**1b**) (57.5 mmol) in THF (20 ml) was added dropwise. After 1 h, a solution of chlorotrimethylsilane (5.60 g, 51.5 mmol) or chlorotrimethylgermane (7.89 g, 51.5 mmol) in THF (20 ml) was added dropwise, and stirring was continued for 2 h at the same temperature. The resulting solution was quenched with saturated aqueous NH_4Cl (100 ml) and the products were extracted with benzene (30 ml × 3). The organic layer was dried ($MgSO_4$), concentrated, and distilled to give (trimethylsilyl)acetamides (**2a** and **2b**) or (trimethylgermyl)acetamides (**3a** and **3b**). The yields are shown in Table 1 and the spectral data are summarized in Table 4.

*Trimethylsilylation or trimethylgermylation of **2** and **3**: general procedure*

A solution of **2** and **3** (45 mmol) in THF (20 ml) was added to a solution of LDA (50 mmol) in THF (60 ml) at −78 °C. After 2 h of stirring, a solution of chlorotrimethylsilane (5.87 g, 54 mmol) or chlorotrimethylgermane (8.29 g, 54 mmol) in THF (20 ml) was added and the mixture was stirred for an additional 2 h. The resulting solution was quenched with saturated aqueous NH_4Cl solution and extracted with benzene. The extract was dried ($MgSO_4$), concentrated, and distilled

Table 4

(Trimethylsilyl or trimethylgermyl)acetamides (**2** or **3**), bis(trimethylsilyl)- or bis(trimethylgermyl)-acetamides (**4** or **6**), and (trimethylsilyl)(trimethylgermyl)acetamides (**5**)

Compound	B.p. (°C/Torr) [m.p.]	IR (cm^{-1})	^1H NMR ($CDCl_3$): δ (ppm)			Elemental analysis (found (calcd.) (%))			High-resolution MS (*m/z*) (found (calcd.) (%))
			Me_3Si	Me_3Ge	CH_2CO or CHCO	C	H	N	
2a	67–69/4	1620	0.12		1.97	ref. 4			
2b	55–64/0.08	1610	0.12		2.04				199.13918 (199.13912)
3a	75–77/2	1620		0.27	2.06				205.05183 (205.05191)
3b	94–97/1	1610		0.26	2.70	49.13 (48.96)	8.85 (8.64)	5.73 (5.71)	
4a	80–85/0.7	1610	0.12		1.89				271.17912 (271.17860)
4b	85–90/1	1600	0.12		1.90				231.14694 (231.14732)
5a	56–59/0.2	1610	0.10	0.27	1.88				277.09269 (277.09164)
5b	[64–65]	1600	0.07	0.27	1.89				317.12264 (317.12267)
6a	79–80/3	1610		0.25	1.97	37.17 (37.48)	7.84 (7.86)	4.26 (4.37)	
6b	[65–66]	1600		0.26	2.05	43.18 (42.97)	8.29 (8.05)	3.93 (3.86)	

to give 1-[bis(trimethylsilyl)acetyl]piperidine (**4b**), *N*,*N*-dimethyl(trimethylgermyl)-(trimethylsilyl)acetamide (**5a**), 1-[(trimethylgermyl)(trimethylsilyl)acetyl]piperidine (**5b**), *N*,*N*-dimethyl[bis(trimethylgermyl)]acetamide (**6a**), and 1-[bis(trimethylgermyl)acetyl]piperidine (**6b**). The results are summarized in Tables 2 and 4.

*Direct synthesis of **4a**, **4b**, **6a**, and **6b** from **1**: general procedure*

A solution of **1a** or **1b** (10 mmol) in THF (10 ml) was added to a solution of LDA (22 mmol) in THF (30 ml) at −78°C. After 1 h of stirring, a solution of chlorotrimethylsilane or chlorotrimethylgermane (25 mmol) in THF (10 ml) was added with continuous stirring during 2 h. Saturated aqueous NH_4Cl was added and the mixture was extracted with benzene. The extract was dried ($MgSO_4$), concentrated, and distilled to give **4a**, **4b**, **6a** and **6b**. The results are shown in Tables 2 and 4.

*N-[Tris(trimethylgermyl)acetyl]piperidine (**9b**)*

To a solution of **6b** (360 mg, 1.0 mmol) in THF (10 ml) was added t-BuLi (1.7 *M* pentane solution, 0.9 ml, 1.5 mmol) at 0°C. After 1 h of stirring, chlorotrimethylgermane (247 mg, 1.6 mmol) was added and the mixture was stirred for an additional 3 h. The resulting solution was quenched with saturated aqueous NH_4Cl and extracted with hexane. The extract was dried ($MgSO_4$) and concentrated. The residue was chromatographed on a silica gel column (benzene/ether 8/1) to give **9b** (225 mg, 72%): b.p. 140°C (10 Torr, oven temperature of Kugelrohr distillation

Table 5

2-(Trimethylgermyl or trimethylsilyl)-2-alkenamides (**13** or **14**)

Compound	B.p. (°C/Torr)	^{1}H NMR ($CDCl_3$): δ		High resolution mass (m/z) (found (calcd.))
		MeSi or MeGe	-CH=	
E-**13a**	125–130/4	0.27	5.46(d)	315.16235 (315.16139)
Z-**13a**	125–130/4	0.33	5.85(d)	315.16364 (315.16139)
E-**13b**	135–140/3	0.37	6.61(s)	293.08513 (293.08319)
Z-**13b**	135–140/3	0.24	[a]	293.08514 (293.08319)
14a	125–130/4	0.12	[b]	269.21678 (269.21732)
14b	135–140/3	0.23	[b]	247.13928 (247.13912)

[a] Amounts too small to be detected. [b] Coalescence with aromatic protons.

apparatus). ^{1}H NMR ($CDCl_3$): δ 0.16 (s, 9H, Me_3Ge), 0.25 (s, 18H, $Me_3Ge \times 2$), 1.3–1.7 (m, 6H, $CH_2 \times 3$), 3.45 (br, 4H, $NCH_2 \times 2$). IR (film): 1605 (CO), 825, 600 cm^{-1} (MeGe). Anal. Found: C, 40.52; H, 7.51; N, 2.85. $C_{16}H_{37}Ge_3NO$ calc: C, 40.27; H, 7.81; N, 2.93%.

Peterson-type reaction of ***5a*** *and* ***6a*** *with aldehydes: general procedure*

To a solution of LDA (4.3 mmol) in THF (10 ml) was added dropwise **5a** or **6a** (3.1 mmol) at 0 °C. After 2 h of stirring, 2-ethylhexanal or benzaldehyde (4.5 mmol) was added dropwise, and stirring was continued for 2 h at the same temperature. The resulting solution was quenched with saturated aqueous NH_4Cl and extracted with benzene. The extract was dried ($MgSO_4$) and concentrated. Distillation of the residual oil gave a mixture of (*E*)- and (*Z*)-*N*,*N*-dimethyl-4-ethyl-2-(trimethylgermyl)-2-octenamides (*E*-**13a** and *Z*-**13a**) or (*E*)- and (*Z*)-*N*,*N*-dimethyl-3-phenylpentenamides (*E*-**13b** and *Z*-**13b**), and small amounts of the silaanalogue (**14a** or **14b**).

Assignment of *E* and *Z* geometrical isomers, making use of published procedures [3,5,6], was carried out by comparison of the chemical shifts of olefinic protons and trimethylgermyl group in their ^{1}H NMR spectra and retention times from GLC. The ratio of *E* to *Z* was calculated on the basis of the integrated values of GLC peaks of the mixtures. The yields and spectral data are listed in Tables 3 and 5.

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