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Synthesis of heterocyclic compounds containing germanium and nitrogen as hetero-atoms. II *

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Abstract

The reaction of chloro(chloromethyl)dimethylgermane (**1**) with *N*-(trimethylsilyl)acetamides (**2**) gave *N*-[(chlorodimethylgermyl)methyl]acetamides (**3**). The amides **3** were converted to heterocyclic compounds containing both germanium and nitrogen as heteroatoms.

Introduction

We previously reported the synthesis of several new five- and six-membered heterocyclic compounds containing both germanium and nitrogen in the same ring. Their syntheses all involved the initial formation of a Ge–C bond by attack of carbon nucleophiles on the germanium atom of chloro(chloromethyl)dimethylgermane (**1**) [1].

Yoder et al. reported that the reaction of chloro(chloromethyl)dimethylsilane with *N*-trimethylsilylacetamides gives *N*-[(chlorodimethylsilyl)methyl]acetamides in high yields, without affecting the Si–Cl bond [2–4]. Application of this reaction to the preparation of the germanium analogue **1** should provide a new synthetic route to heterocyclic compounds containing a Ge–C–N bond. Herein we report on the study.

Results and discussion

The reactions of chloro(chloromethyl)dimethylgermane (**1**) with three acetamides, *N*,*N*-bis(trimethylsilyl)acetamide (**2a**), *N*-methyl-*N*-(trimethylsilyl)acetamide (**2b**), or *N*-allyl-*N*-(trimethylsilyl)acetamide (**2c**) gave *N*,*N*-bis[(chlorodimethylgermyl) methyl]acetamide (**3a**), *N*-[(chlorodimethylgermyl)methyl]-*N*-methylacetamide (**3b**),

* For part I see ref. 1.

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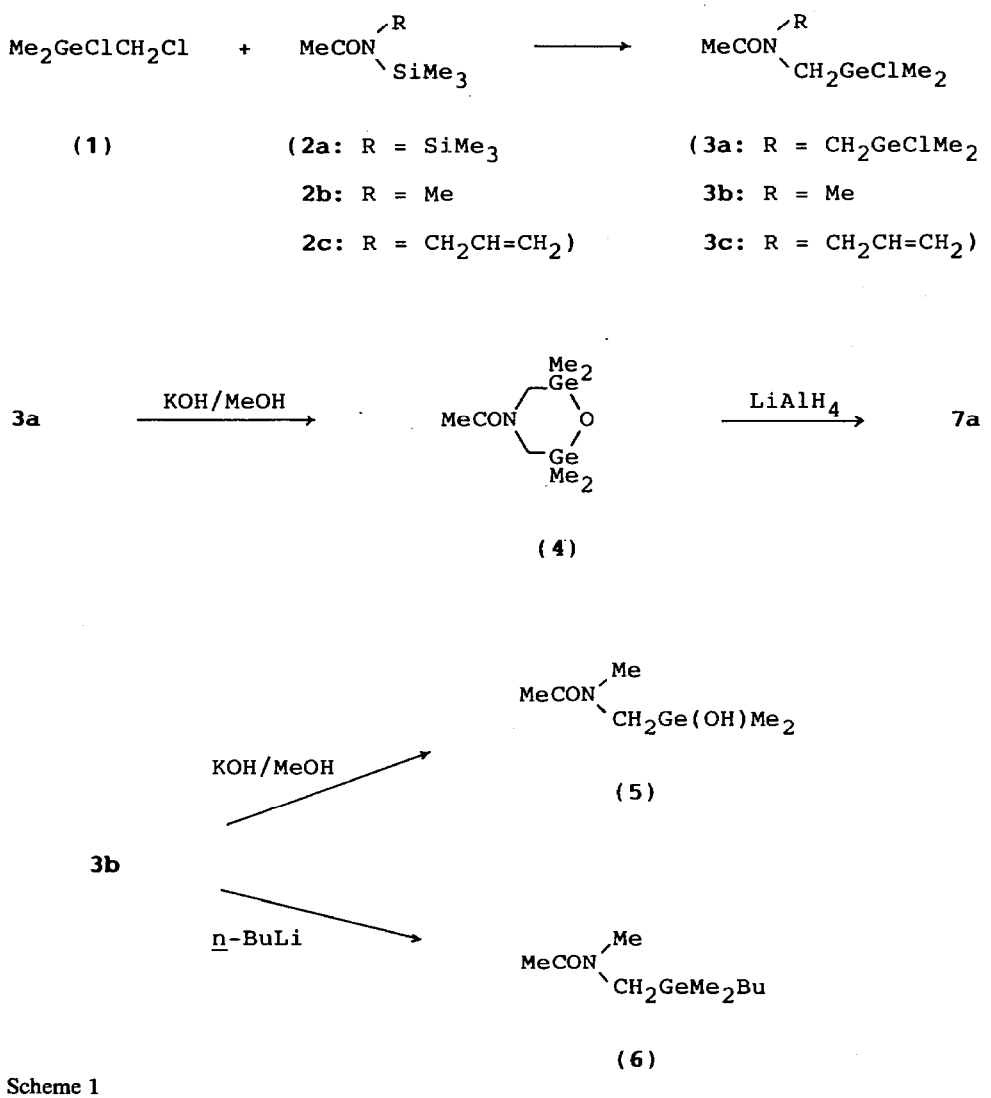
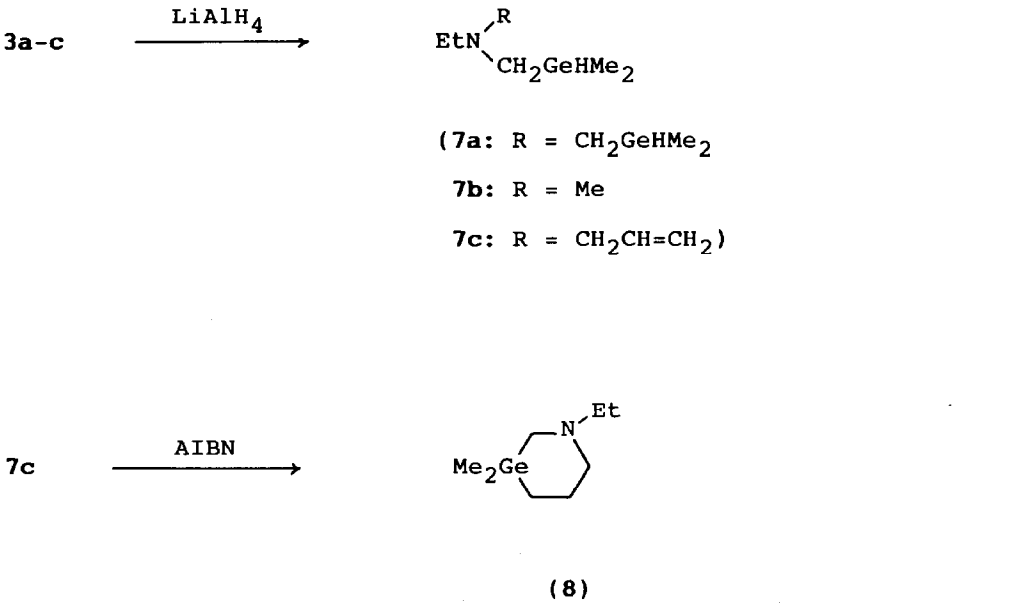


Scheme 1

and *N*-allyl-*N*-[(chlorodimethylgermyl)methyl]acetamide (**3c**), respectively in good yields. All our reactions were carried out in solvent under reflux, whereas the silicon-analogues had been allowed to react at room temperature [3]. Our products thus obtained were isolated by distillation under reduced pressure whereas the corresponding silicon-analogues of **3a** and **3b** were purified by sublimation [3]. Their structures were determined on the basis of spectroscopic and elemental analyses (see experimental section).

Treatment of **3a** with potassium hydroxide gave a new heterocyclic compound, 4-acetyl-2,2,6,6-tetramethylperhydro-1,4,2,6-oxazadigermine (**4**), similar treatment of **3b** yielded *N*-(dimethylhydroxygermyl)methyl-*N*-methylacetamide (**5**). Reduction of **3a**–**3c** with lithium aluminum hydride gave *N*-ethyl-bis[(dimethylgermyl)methyl] amine (**7a**) and *N*-methyl- or *N*-allyl-*N*-ethyl[(dimethylgermyl)methyl]amine (**7b** or **7c**), respectively. Compound **7a** was also obtained by the reduction of **4**.



Scheme 2

The intramolecular cyclization reaction of **7c** using a radical initiator AIBN gave a six-membered heterocyclic compound, 1-ethyl-3,3-dimethylperhydro-1,3-azagermine (**8**). Another possible cyclization product with a five-membered ring, 1-ethyl-3,3,4-trimethyl-1,3-azagermolidine was not detected in the reaction mixture. Treatment of **3b** with n-butyllithium gave *N*-(n-butyldimethylgermyl)methyl-*N*-methylacetamide (**6**).

Experimental

All reactions were carried out under nitrogen. Diethyl ether and tetrahydrofuran were dried by distillation from sodium benzophenone ketyl before use. ^{1}H NMR spectra were recorded on a JEOL JNM-MH-100 spectrometer using Me_4Si as internal standard. ^{13}C NMR spectra were taken on a JEOL JNM FX-100 spectrometer. IR spectra were recorded on a JASCO IRA-2 spectrometer. Mass spectral data were obtained by use of a JEOL JMS-DX300 GC/MS system (70 eV). Gas chromatographic analyses were carried out with Gasukuro Kogyo Model 370 equipped with FID and TCD detectors. All melting points and boiling points are uncorrected.

N-Allyl-N-(trimethylsilyl)acetamide (2c)

To a solution of *N*-allylacetamide (10.19 g, 103 mmol) in triethylamine (60 ml) was added chlorotrimethylsilane (14.24 g, 131 mmol). The reaction mixture was refluxed for 20 h and then filtered. The filtrate was distilled to give 13.20 g (75%) of **2c**: b.p. 85–87°C (27 Torr). ^{1}H NMR ($CDCl_3$): δ 0.27 (9H, s, $SiCH_3$), 2.03 (3H, s, CH_3CO), 3.7–3.8 (2H, m, CH_2), 4.9–5.2 (2H, m, $=CH_2$), 5.5–6.1 (1H, m, =CH). IR (film): 1640 (CO) cm^{-1}.

N,N-Bis[chlorodimethylgermyl)methyl]acetamide (3a)

A solution of chloro(chloromethyl)dimethylgermane (**1**, 4.41 g, 23.5 mmol) and bis(trimethylsilyl)acetamide (**2a**, 2.20 g, 10.8 mmol) in toluene (40 ml) was heated under reflux for 70 h. After evaporation of the solvent, the residue was distilled under reduced pressure or recrystallized from hexane to give 2.97 g (76%) of **3a**: b.p. 110°C (0.15 Torr, at oven temperature of Kugelrohr distillation apparatus), m.p. 99–101°C. ^{1}H NMR ($CDCl_3$): δ 0.89 (6H, s, $GeCH_3$), 0.92 (6H, s, $GeCH_3$), 2.13 (3H s, CH_3CO), 2.80 (2H, s, CH_2), 3.40 (2H, s, CH_2). IR (Nujol): 1580 (CO) cm^{-1}. Anal. Found: C, 26.58; H, 5.17; N, 3.89. $C_8H_{19}Cl_2Ge_2NO$ calc: C, 26.59; H, 5.30; N, 3.88%.

N-(Chlorodimethylgermyl)methyl-N-methylacetamide (3b)

A solution of **1** (4.78 g, 25.5 mmol) and *N*-methyl-*N*-(trimethylsilyl)acetamide (**2b**, 3.97 g, 27.3 mmol) in benzene (20 ml) was heated under reflux for 4 h. After removal of the solvent, the residue was distilled to give 4.50 g (79%) of **3b**: b.p. 172–174°C (43 Torr), m.p. 45–47°C. ^{1}H NMR ($CDCl_3$): δ 0.92 (6H, s, $GeCH_3$), 2.11 (3H, s, CH_3CO), 2.91 (2H, s, CH_2), 3.15 (3H, s, NCH_3). IR (Nujol): 1585 (CO) cm^{-1}. Anal. Found: C, 32.02; H, 6.36; N, 6.05. $C_6H_{14}ClGeNO$ calc: C, 32.14; H, 6.29; N, 6.25%.

N-Allyl-N-[(chlorodimethylgermyl)methyl]acetamide (3c)

A solution of **1** (9.75 g, 52.0 mmol) and **2c** (11.21 g, 65.4 mmol) in benzene (40 mol) was heated under reflux for 4 h, concentrated, and distilled to give 7.05 g (57%) of **3c**: b.p. 104–114°C (0.25 Torr), m.p. 59–61°C. ^{1}H NMR ($CDCl_3$): δ 0.92 (6H, s, $GeCH_3$), 2.10 (3H, s, CH_3CO), 2.89 (2H, s, NCH_2Ge), 3.99 (2H, br. d, J 5 Hz, NCH_2C), 5.1–5.4 (2H, m, $=CH_2$), 5.6–6.0 (1H, m, =CH). IR (Nujol): 1575 (CO) cm^{-1}. Anal. Found: C, 38.46; H, 6.43; N, 5.63. $C_8H_{16}ClGeNO$ calc: C, 38.39; H, 6.44; N, 5.60%.

4-Acetyl-2,2,6,6-tetramethylperhydro-1,4,2,6-oxazadigermine (4)

A solution of **3a** (765 mg, 2.12 mmol) in benzene (15 ml) was stirred with 5% KOH-MeOH (15 ml) for 30 min. The mixture was neutralized with 10% citric acid in MeOH, concentrated under reduced pressure, and then extracted with $CHCl_3$. Distillation of the extract gave 589 mg (91%) of **4**: b.p. 105°C (0.9 Torr, Kugelrohr), m.p. 101–103°C. ^{1}H NMR ($CDCl_3$): δ 0.48 (6H, s, $GeCH_3$), 0.51 (6H, s, $GeCH_3$), 2.12 (3H, s, CH_3CO), 3.18 (2H, s, CH_2), 3.37 (2H, s, CH_2). IR (Nujol): 850 (GeOGe), 1610 cm^{-1} (CO). Anal. Found: C, 31.14; H, 6.15; N, 4.54. $C_8H_{19}Ge_2NO_2$ calc: C, 31.36; H, 6.25; N, 4.57%.

N-(Dimethylhydroxygermyl)methyl-N-methylacetamide (5)

A solution of **3b** (605 mg, 2.70 mmol) in ether (10 ml) was treated with 5% KOH-MeOH (10 ml) in a manner similar to that described for **4**, to give 471 mg (85%) of **5**: b.p. 150°C (0.3 Torr, Kugelrohr). ^{1}H NMR ($CDCl_3$): δ 0.42 and 0.44 (6H, s ×2, $GeCH_3$), 2.05 (3H, s, CH_3CO), 2.81 and 2.93 (2H, s ×2, CH_2), 3.08 (3H, s, NCH_3). IR (film): 1620 (CO), 3400 cm^{-1} (OH). Anal. Found: C, 35.20; H, 7.38; N, 6.84. $C_6H_{15}GeNO_2$ calc: C, 35.02; H, 7.35; N, 6.81%.

N-(n-Butyldimethylgermyl)methyl-N-methylacetamide (6)

To a stirred solution of **3b** (338 mg, 1.51 mmol) in THF (10 ml) was added slowly

n-BuLi (10 w/v% in hexane, 1 ml, 1.56 mmol) during 1.5 h at −65 °C. After 5 h at room temperature, a saturated aqueous solution of NH_4Cl (10 ml) was added and the mixture was extracted with ether. The extract was dried ($MgSO_4$), concentrated, and distilled to give 264 mg (71%) of **6**: b.p. 150 °C (10 Torr, Kugelrohr). ^1H NMR ($CDCl_3$): δ 0.18 and 0.24 (6H, s ×2, CH_3Ge), 0.6–1.5 (9H, m, C_4H_9), 2.06 (3H, s, CH_3CO), 2.9–3.1 (5H, m, CH_2N and CH_3N). IR (film): 1635 cm^{-1} (CO). Exact mass calcd. for $C_{10}H_{23}GeNO$ 247.09927, observed 247.10134.

N-Ethyl[bis(dimethylgermyl)methyl]amine (7a) [1]

(*A*) To a mixture of $LiAlH_4$ (503 mg, 13.3 mmol) in THF (10 ml) was added a solution of **3a** (1.17 g, 3.25 mmol) in THF (10 ml) and heated under reflux for 2 h. The mixture was then cooled in an ice bath and AcOEt (0.5 ml), 10% NaOH (0.5 ml) and H_2O (1.5 ml) were added. After the mixture had been filtered, the filter cake was washed with ether, and the filtrate and washings were combined, dried over anhydrous $MgSO_4$, and concentrated. Distillation of the residue gave 811 mg (90%) of **7a**: b.p. 100 °C (18 Torr, Kugelrohr)

(*B*) In a manner similar to that described above, **4** (315 mg, 1.03 mmol) was treated with $LiAlH_4$ (166 mg, 4.37 mmol) in THF (10 ml), to give 217 mg (76%) of **7a**.

N-Ethyl-N-methyl(dimethylgermyl)methylamine (7b)

To a mixture of $LiAlH_4$ (157 mg, 4.14 mmol) in ether (6 ml) was added a solution of **3b** (374 mg, 1.67 mmol) in ether (8 ml). After 2 h of heating at reflux, work-up of the reaction mixture was similar to that described for **7a**. Distillation of the ethereal extract gave 264 mg (90%) of **7b**: b.p. 80 °C (Kugelrohr). ^1H NMR ($CDCl_3$): δ 0.27 (6H, d, *J* 3 Hz, $GeCH_3$), 1.05 (3H, t, *J* 7 Hz, CH_3C), 2.24 (3H, s, CH_3N), 2.26 (2H, d, *J* 3 Hz, CH_2Ge), 2.39 (2H, q, *J* 7 Hz, CH_2C), 3.9–4.1 (1H, m, GeH). IR (film): 2020 cm^{-1} (GeH). Anal. Found: C, 40.66; H, 9.49; N, 7.78. $C_6H_{17}GeN$ calc: C, 40.99; H, 9.75; N, 7.97%.

N-Allyl-N-ethyl(dimethylgermyl)methylamine (7c)

In a manner similar to that described for **7b**, **3c** (2.71 g, 10.8 mmol) was treated with $LiAlH_4$ (1.08 g, 28.3 mmol) in ether (30 ml). Distillation of the ethereal extract afforded 1.87 g (86%) of **7c**: b.p. 100 °C (40 Torr, Kugelrohr). ^1H NMR ($CDCl_3$): δ 0.26 (6H, d, *J* 4 Hz, CH_3Ge), 1.03 (3H, t, *J* 7 Hz, CH_3C), 2.36 (2H, d, *J* 4 Hz, CH_2Ge), 2.51 (2H, q, *J* 7 Hz, CH_2CH_3), 3.08 (2H, d, *J* 6 Hz, CH_2CH=), 3.9–4.1 (1H, m, GeH), 5.1–5.3 (2H, m, $=CH_2$), 5.7–6.1 (1H, m, =CH). IR (film): 2020 cm^{-1} (GeH). Anal. Found: C, 47.45; H, 9.45; N, 7.06. $C_8H_{19}GeN$ calc: C, 47.61; H, 9.49; N, 6.94%.

1-Ethyl-3,3-dimethylperhydro-1,3-azagermine (8)

A solution of **7c** (351 mg, 1.74 mmol) and AIBN (28 mg, 10 mol%) in benzene (7 ml) was heated at 75 °C for 18 h, it then was extracted with 10% HCl (10 ml ×3). The acid extract was made alkaline with NaOH and extracted with ether. The ethereal extract was dried ($MgSO_4$), concentrated, and distilled to give 185 mg (53%) of **8**: b.p. 130 °C (76 Torr, Kugelrohr). ^1H NMR ($CDCl_3$): δ 0.21 (6H, s, CH_3Ge), 0.7–1.2 (7H, m, CH_3C and CH_2CH_2Ge), 2.05 (2H, s, $GeCH_2N$), 2.3–2.5 (4H, m, CH_2CH_3 and NCH_2C). Anal. Found: C, 47.32; H, 9.31; N, 7.19. $C_8H_{19}GeN$ calc: C, 47.61; H, 9.49; N, 6.94%.

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