The Germanium–Carbon Bond Cleavage Reaction of (Germylmethyl)amine Derivatives. Mechanism and Stereochemistry

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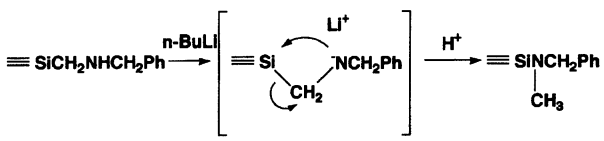
A facile cleavage reaction of the germanium–carbon bond of (germylmethyl)amine derivatives to give a germyl anion and an azomethine derivative was developed. The effects of substituents such as phenyl, benzyl, and ethyl groups on the germanium and nitrogen atoms of the (germylmethyl)amine derivatives on the cleavage reaction, were investigated. The mechanism was also investigated based on the stereochemistry of the cleavage reaction using an optically active organogermanium compound.

One of the most active areas of interest in the chemistry of the group 14 elements is the investigation of the similarities or differences in the reactivities among carbon, silicon, and germanium.

It is known that treatment of a (silylmethyl)amine derivative with a catalytic amount of *n*-BuLi in tetrahydrofuran (THF) gives an aminosilane derivative (Brook rearrangement) in a good yield, and that the reaction proceeds with retention of the configuration on the silicon center in a high stereospecificity (Scheme 1).[1] It has been shown that the rearrangement reaction is one of the most useful methods for the preparation of optically active sila-functional compounds from optically active (silylmethyl)amine derivatives, which were resolved using tartaric acid.[2]

On the other hand, in the course of our investigations of the preparation and reactions of optically active organosilanes and organogermanes, we investigated the reaction of (germylmethyl)amine derivatives with *n*-BuLi. In the case of the (germylmethyl)amine derivatives, it was found that Ge–C bond cleavage rather than Brook rearrangement occurred[3] to give the germyl anion under similar reaction conditions to those described for the Brook rearrangement of (silylmethyl)amine derivatives. In this reaction, 2 molar amounts of *n*-BuLi per mole of (germylmethyl)amine derivative were required to complete the cleavage reaction.

In this report, we wish to describe the effects of the substituents on the germanium and nitrogen atoms of the (germylmethyl)amine derivatives, and the mechanism of the Ge–C bond cleavage reaction.



Scheme 1.

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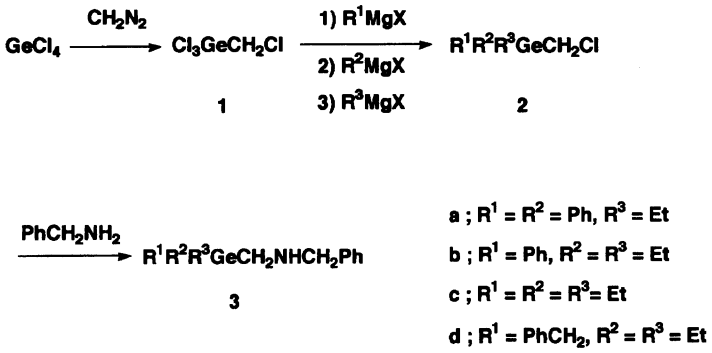
Results and Discussion

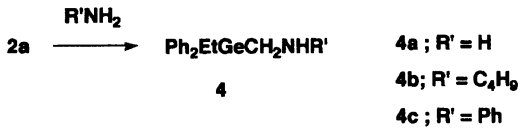
Preparation of the (Germylmethyl)amine Derivatives. (Chloromethyl)germanium derivatives such as (chloromethyl)ethyldiphenyl- (**2a**), (chloromethyl)diethylphenyl- (**2b**), (chloromethyl)triethyl- (**2c**), and benzyl(chloromethyl)diethylgermane (**2d**), were prepared by treating trichloro(chloromethyl)germane[4] with the corresponding Grignard reagents. Compounds **2a**—**2d** were treated with a large excess of benzylamine to give the corresponding benzylamine derivatives *N*-[(ethyldiphenyl- (**3a**), diethylphenyl- (**3b**), triethyl- (**3c**), and benzyldiethylgermyl)methyl]benzylamine (**3d**) (Scheme 2). Compound **2a** was also treated with ammonia, butylamine, and aniline under ambient conditions to give the corresponding amine derivatives (ethyldiphenylgermyl)methylamine (**4a**), *N*-[(ethyldiphenylgermyl)methyl]butylamine (**4b**), and *N*-[(ethyldiphenylgermyl)methyl]aniline (**4c**) (Scheme 3).

Reaction of the (Germylmethyl)amine Derivatives with *n*-BuLi. A solution of the (germylmethyl)amine derivatives in THF was treated with a solution of *n*-BuLi in hexane at 0 °C. The reaction mixture was stirred for 1 h at 0 °C and an additional hour at room temperature. After hydrolysis, the solution was dried, and the products were isolated by TLC. The results are summarized in Table 1.

It was shown that the reactions of **3a** with *n*-BuLi yielded ethyldiphenylgermane (**5a**) and *N*-pentylbenzylamine (**6**) (Scheme 4), and the yields of the products were affected remarkably by the amount and kind of the base used (Table 1, Entries 1 and 2). Namely, the use of a slight molar excess of *n*-BuLi with **3a** gave **5a** and **6** in 63 and 33% yields, respectively, in addition to 27% recovery of **3a** (Entry 1). On the other hand, the use of 2 molar equivalents of *n*-BuLi for **3a** improved the yields of **5a** and **6** to 91 and 84%, respectively (Entry 2). Furthermore, the use of a large excess of lithium diisopropylamide (LDA) as a base, which is not able to add to the N=C bond of *N*-methyleneamine produced in the reaction mixture, yielded only **5a** in a 68% yield (Entry 3). These results support the suggested reaction



Scheme 2.



Scheme 3.

mechanism[3] that one mole of *n*-BuLi extracts the hydrogen on the nitrogen, and another one mole excess of *n*-BuLi adds to the *N*-methyleneamine produced in the reaction mixture, and the equilibrium moves to the right side to increase the yields of **5** and **6** (Scheme 5).

The substituents on the germanium also play important roles in the Ge–C bond cleavage reaction. It seems that at least one phenyl substituent on germanium is required for obtaining sufficient yields of hydrogermane derivatives (Entries 2, 4, and 5). An exception is that the reaction of **3d**, which has benzyl and ethyl substituents on the germanium, with 2 molar equivalents of *n*-BuLi gave benzyldiethylgermane in a high yield (Entry 6). We have no clear explanation for the effects of the benzyl substituent on the germanium.

Furthermore, the substituents on the nitrogen affected the cleavage reaction. Not only a benzyl group but also hydrogen and alkyl groups could be available as a substituent on the nitrogen for the Ge–C bond cleavage reaction (Entries 7 and 8). However, a phenyl substituent on the nitrogen gave a complete recovery of starting material **4c** (Entry 9). It may be suggested that the nitrogen anion produced from the reaction of **4c** with *n*-BuLi is too stable to the cleavage reaction, because of the resonance of the anion with a phenyl group on the nitrogen.

Stereochemistry of the Ge–C Bond Cleavage. The stereochemical course of the Ge–C bond cleavage reaction was investigated using optically active *N*-[(benzylmethylphenylgermyl)methyl]-benzylamine (**8**).[5] That is, the cleavage reaction was restored to the original (germylmethyl)amine **7** (Scheme 6).

It is clear that the reactions proceed with a high stereospecificity, and with retention of the configuration of the germanium center, because the compound (**7**) finally obtained had a high optical purity [$[\alpha]_{435}$ +19.7°, (*c* 1, CH_2Cl_2)], and the same sign of rotation as that of the starting **7** [$[\alpha]_{435}$ +20.5°, (*c* 1, CH_2Cl_2)].

Among these 6 reaction steps, only 3 steps are concerned with the configuration of the asymmetric center. Furthermore, it is already known that the hydrolysis of germyllithium to give hydrogermane[6] and the insertion of dichlorocarbene in the Ge–H bond to give the dichloromethylgermane derivative[7] proceed with retention of the configurations. So it is clear that Ge–C bond cleavage proceeds with retention of the configuration of the asymmetric germanium center.

These observations support the intramolecular rearrangement mechanism proposed for the Ge–C bond cleavage reaction.[3] The possibility of a mechanism for the Ge–C bond cleavage similar to the Brook rearrangement proposed for the (silylmethyl)amine derivatives can be excluded. The Ge–C bond cleavage reaction was never completed in the presence of a catalytic amount of *n*-BuLi as the silicon analogue reaction was, and the reaction required 2 molar amounts of *n*-BuLi to obtain a satisfactory yield of the hydrogermane derivatives. These results show that no carbon anion intermediate, which would extract a proton from the amine group of another molecule, is existent in the Ge–C bond cleavage reaction.

On the other hand, it is clear that these Ge–C bond cleavage reactions provide a useful method for the preparation of new optically active germyl anions, and germa-functional compounds. These observations also show that the chloromethyl substituent on an organogermanium compound is a suitable and convenient equivalent for the preparation of optically active hydrogermane, as well as the chloromethyl substituent on an organosilicon compound.

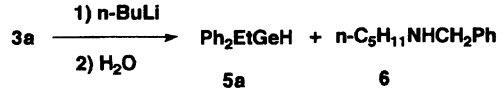
Experimental

The melting points are uncorrected. The NMR spectra were determined at 60 and 400 MHz with a JEOL 60Si and a Bruker AM400 spectrometer in $CDCl_3$, respectively, using TMS as an internal standard. The mass spectra were measured with a JEOL DX303 mass spectrometer. The optical rotations were measured with a JASCO DIP-360 polarimeter. All the Grignard and Ge–C bond cleavage reactions were carried out under a dry nitrogen atmosphere. Trichlo-

Table 1. Results of the Reaction of **3** and **4** with *n*-BuLi

Entry	Germylmethylamine/mmol		*n*-BuLi/mmol	Product yield/%		
				≡Ge-H		**6**
1	**3a**	1.3	1.5	$EtPh_2GeH$	63	33
2	**3a**	1.3	2.9	$EtPh_2GeH$	91	84
3	**3a**	1.3	4.0[a]	$EtPh_2GeH$	68	0
4	**3b**	1.3	2.9	Et_2PhGeH	68	83
5	**3c**	1.3	2.9	Et_3GeH	13	15
6	**3d**	1.3	2.9	Et_2PhCH_2GeH	83	67
7	**4a**	1.3	2.9	$EtPh_2GeH$	56	—[b]
8	**4b**	1.3	2.9	$EtPh_2GeH$	65	—[b]
9	**4c**	1.3	2.9	$EtPh_2GeH$	0	—[b]

a) LDA was used instead of *n*-BuLi. b) The yield was not estimated.



Scheme 4.

ro(chloromethyl)germane was prepared by the procedure described in the literature.[4]

(Chloromethyl)ethyldiphenylgermane (2a). Phenylmagnesium bromide prepared from bromobenzene (12.2 g, 78 mmol) and magnesium (2.0 g, 85 mmol) in dry ether (80 ml) was added to a solution of trichloro(chloromethyl)-germane (8.1 g, 35 mmol) in dry ether (50 ml) during 1 h at 0 °C. This reaction mixture was stirred for 4 h at 0 °C. Ethylmagnesium bromide prepared from bromoethane (4.6 g, 42 mmol) and magnesium (1.2 g, 49 mmol) in dry ether (60 ml) was then added to the reaction mixture during 1 h at 0 °C. The mixture was left at room temperature overnight with stirring. After the mixture was hydrolyzed, the organic layer was separated and the aqueous layer was extracted with ether (30 ml×3). The combined organic layer and extracts were then dried (Na_2SO_4). Evaporation and distillation of the residue gave a colorless oil. Yield, 7.4 g (69%); bp 142 °C/0.3 Torr (1 Torr=133.322 Pa); ^{1}H NMR (CCl_4) δ=1.0—1.7 (5H, m, CH_2CH_3), 3.30 (2H, s, CH_2Cl), and 7.1—7.6 (10H, m, C_6H_5).

(Chloromethyl)germane derivatives **2b**, **2c**, and **2d** were prepared by using the corresponding Grignard reagents in a manner similar to that described above.

2b, Yield, 57%; bp 90 °C/0.6 Torr; ^{1}H NMR (CCl_4) δ= 1.10 (10H, s, CH_2CH_3), 3.08 (2H, s, CH_2Cl), and 7.1—7.6 (5H, m, C_6H_5).

2c, Yield, 71%; bp 85 °C/26 Torr; ^{1}H NMR (CCl_4) δ= 0.7—1.5 (15H, m, CH_2CH_3), and 2.93 (2H, s, CH_2Cl).

2d, Yield, 24%; bp 130 °C/4.5 Torr; ^{1}H NMR (CCl_4) δ=0.7—1.5 (10H, m, CH_2CH_3), 2.30 (2H, s, CH_2Ph), 2.90 (2H, s, CH_2Cl), and 6.8—7.4 (5H, m, C_6H_5).

***N*-[(Ethyldiphenylgermyl)methyl]benzylamine (3a).** A mixture of **2a** (3.7 g, 1.2 mmol) and benzylamine (13.1 g, 122 mmol) was stirred for 16 h at 80 °C. Aqueous 2 M NaOH (9 ml) (1 M=1 mol dm^{-3}) was added to the mixture. The organic layer was separated and the aqueous layer was extracted with ether (10 ml×3). The combined organic layer and extracts were then dried (Na_2SO_4). Evaporation and preparative silica-gel chromatography (hexane : ethyl acetate=5 : 1) gave an oil. Yield, 4.3 g (94%); ^{1}H NMR (CCl_4) δ=0.8—1.4 (6H, m, NH, CH_2CH_3), 2.76 (2H, m, $GeCH_2N$), 3.70 (2H, s, NCH_2Ph), and 6.7—7.6 (10H, m, C_6H_5). Found: *m/z* 377.1211. Calcd for $C_{22}H_{25}GeN$: M, 377.1200.

(Germylmethyl)amine derivatives **3b**, **3c**, **3d**, **4a**, **4b**, and **4c** were prepared using the corresponding (chloromethyl)-germanes and amines.

3b, Yield, 58%; ^{1}H NMR (CCl_4) δ=0.8—1.2 (11H, m, NH, C_2H_5), 2.45 (2H, s, $GeCH_2N$), 3.70 (2H, s, NCH_2Ph), and 6.9—7.6 (5H, m, C_6H_5). Found: *m/z* 329.1209. Calcd for $C_{18}H_{25}GeN$: M, 329.1200.

3c, Yield, 87%; ^{1}H NMR (CCl_4) δ=0.5—1.3 (16H, m, NH, C_2H_5), 2.28 (2H, s, $GeCH_2N$), 3.70 (2H, s, NCH_2Ph), and 7.1—7.3 (5H, m, C_6H_5). Found: *m/z* 281.1212. Calcd for $C_{14}H_{25}GeN$: M, 281.1200.

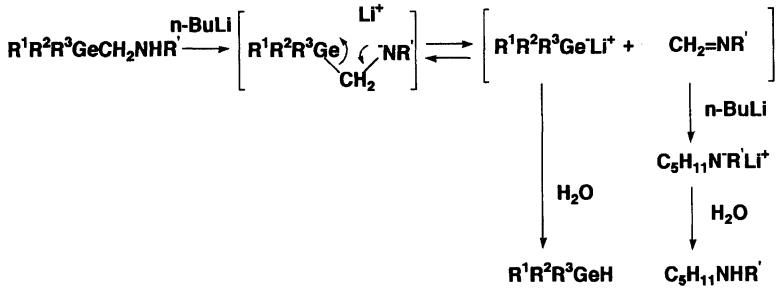
3d, Yield, 80%; ^{1}H NMR (CCl_4) δ=0.7—1.3 (11H, m, NH, C_2H_5), 2.25 (2H, s, $GeCH_2N$), 3.64 (2H, s, NCH_2Ph), and 6.8—7.5 (10H, m, C_6H_5). Found: *m/z* 343.1348. Calcd for $C_{19}H_{27}GeN$: M, 343.1357.

4a, Yield, 64%; bp 145—150 °C/0.4 Torr; ^{1}H NMR (CCl_4) δ=1.0—1.4 (5H, m, C_2H_5), 1.60 (2H, broad s, NH_2), 2.85 (2H, s, $GeCH_2N$), and 7.0—7.6 (10H, m, C_6H_5). Found: *m/z* 287.0725. Calcd for $C_{15}H_{19}GeN$: M, 287.0731.

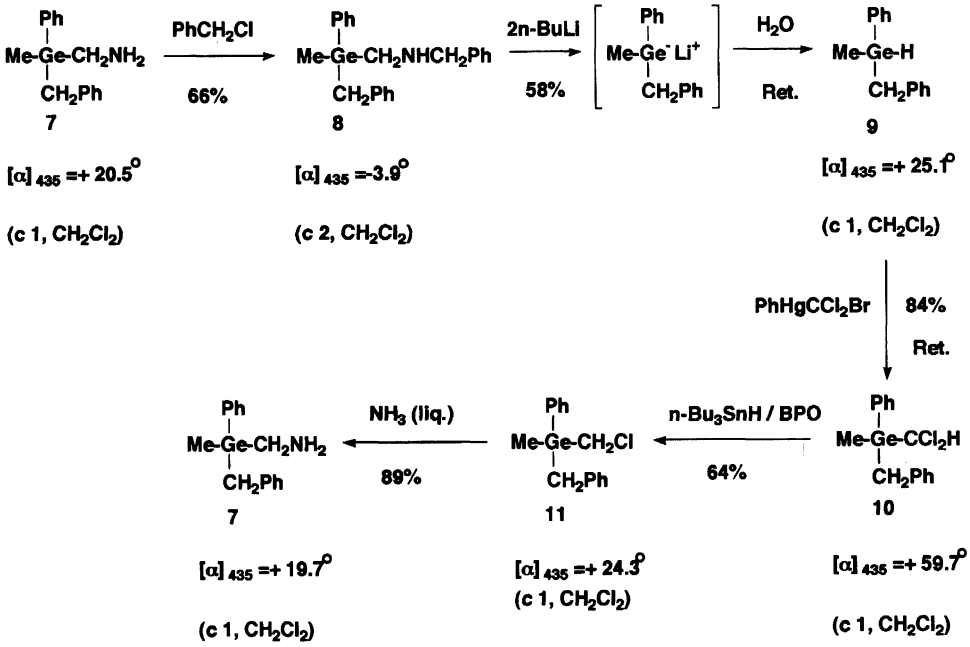
4b, Yield, 59%; ^{1}H NMR (CCl_4) δ=0.6—1.6 (13H, m, NH, C_2H_5, $NCCH_2CH_2CH_3$), 2.65 (2H, t, J=7.0 Hz, NCH_2), 2.85 (2H, s, $GeCH_2N$), and 7.0—7.6 (10H, m, C_6H_5). Found: *m/z* 343.1350. Calcd for $C_{19}H_{27}GeN$: M, 343.1357.

4c, Yield, 24%; bp 155—160 °C/0.3 Torr; ^{1}H NMR (CCl_4) δ=1.1—1.5 (5H, m, C_2H_5), 3.15 (2H, s, $GeCH_2N$), 3.35 (1H, broad s, NH), and 6.3—7.7 (15H, m, C_6H_5). Found: *m/z* 363.1040. Calcd for $C_{21}H_{23}GeN$: M, 363.1044.

Reaction of 3a with 2 Molar Equivalents of *n*-BuLi. To a solution of **3a** (0.50 g, 1.3 mmol) in THF (4 ml) was added *n*-BuLi (1.9 ml, 1.55 M hexane solution, 2.9 mmol) at 0 °C. After stirring the solution for 1 h at 0 °C, the reaction was quenched with distilled water (20 ml). The reaction mixture was extracted with ether (10 ml×4), and the combined extracts were dried (Na_2SO_4). Evaporation and preparative silica-gel chromatography (a mixture of benzene and ethyl acetate) gave **5a** and **6** in 91 and 84% yields, respectively. **5a**, ^{1}H NMR (CCl_4) δ=1.0—1.7 (5H, m, C_2H_5), 4.9—5.1 (1H, m, GeH), and 7.0—7.5 (10H, m, C_6H_5). Found: *m/z* 258.0464. Calcd for $C_{14}H_{16}Ge$: M, 258.0465.



Scheme 5.



Scheme 6.

The reactions of the other (germylmethyl)amine derivatives with *n*-BuLi were carried out in a manner similar to that described above, and the results are summarized in Table 1.

Diethylphenylgermane (**5b**), ^{1}H NMR (CCl_4) δ=0.9—1.5 (10H, m, C_2H_5), 4.2—4.5 (1H, m, GeH), 7.1—7.5 (5H, m, C_6H_5). Found: *m/z* 210.0461. Calcd for $C_{10}H_{16}Ge$: M, 210.0465.

Triethylgermane (**5c**), ^{1}H NMR (CCl_4) δ=0.6—1.3 (15H, m, C_2H_5) and 3.7—3.9 (1H, m, GeH). Found: *m/z* 162.0458. Calcd for $C_6H_{16}Ge$: M, 162.0465.

Benzyldiethylgermane (**5d**), ^{1}H NMR (CCl_4) δ=0.6—1.3 (10H, m, C_2H_5), 2.30 (d, *J*=4 Hz, 2H, $GeCH_2Ph$), 3.7—4.0 (1H, m, GeH), and 6.7—7.3 (5H, m, C_6H_5). Found: *m/z* 224.0618. Calcd for $C_{11}H_{18}Ge$: M, 224.0621.

Preparation of Optically Active *N*-[(Benzylmethylphenylgermyl)methyl]benzylamine (8). A solution of (+)-[(benzylmethylphenylgermyl)methyl]amine (**7**)[5] [$[\alpha]_{435}$ +20° (*c* 1, CH_2Cl_2)] (0.99 g, 3.5 mmol), and benzyl chloride (0.53 g, 4.2 mmol) in triethylamine (3 ml) was stirred for 8 h at 100 °C. 1 M aqueous NaOH (3 ml) and hexane (3 ml) were added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with ether (5 ml×3). The combined organic layer and extracts were then dried (Na_2SO_4). Evaporation and preparative chromatogrphy (hexane : ethyl acetate=1 : 1) gave an oil. Yield, 0.86 g (66%); $[\alpha]_{435}$ −3.9° (*c* 2, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ=0.30 (3H, s, $GeCH_3$), 0.90 (1H, broad s, 1H, NH), 3.40 (2H, s, $GeCH_2N$ or $GeCH_2Ph$), 3.48 (2H, s, $GeCH_2N$ or $GeCH_2Ph$), 3.67 (2H, s, $PhCH_2N$), and 6.6—7.6 (15H, m, C_6H_5). Found: *m/z* 377.1192. Calcd for $C_{22}H_{25}GeN$: M, 377.1200.

Reaction of (−)-8 with *n*-BuLi. A solution of *n*-BuLi (4.0 ml, 1.55 M in hexane, 6.2 mmol) was added to a solution of (−)-**8** (0.86 g, 2.3 mmol) in THF (9 ml) at 0 °C, and the reaction mixture was stirred for 4 h at room temperature. Distilled water (5 ml) was added to the mixture with external cooling. A usual workup followed by preparative chromatography (hexane) gave (+)-benzyl(methyl)-phenylgermane (**9**). Yield, 0.34 g (58%); $[\alpha]_{435}$ +25.1° (*c* 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ=0.40 (3H, d, *J*=6.0 Hz, $GeCH_3$), 2.45 (2H, d, *J*=4.0 Hz, $GeCH_2Ph$), 4.4—4.7 (1H, m, GeH), and 6.6—7.6 (10H, m, C_6H_5). Found: *m/z* 258.0470. Calcd for $C_{14}H_{16}Ge$: M, 258.0465.

Reaction of (+)-9 with Dichlorocarbene. A solution of (+)-**9** (0.34 g, 1.3 mmol) and (bromodichloromethyl)phenylmercury (0.65 g, 1.5 mmol) in dry benzene (14 ml) was refluxed for 2 h with stirring. The solid precipitate was filtered off, the solvent was evaporated, and the residue was purified by chromatography (benzene : hexane=1 : 1) to

give (+)-benzyl(dichloromethyl)methylphenylgermane (**10**). Yield, 0.38 g (84%); $[\alpha]_{435}$ +59.7° (*c* 1, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ=0.53 (3H, s, $GeCH_3$), 2.75 (2H, s, $GeCH_2Ph$), 5.48 (1H, s, $GeCHCl_2$), and 6.8—7.8 (10H, m, C_6H_5). Found: *m/z* 339.9850. Calcd for $C_{15}H_{16}Cl_2Ge$: M, 339.9843.

Reaction of (+)-10 with Tributylstannane. A solution of **(+)-10** (0.38 g, 1.1 mmol), tributylstannane (0.49 g, 1.7 mmol), and a catalytic amount of benzoyl peroxide (15 mg) in dry benzene (14 ml) was refluxed for 10 h with stirring. Evaporation and preparative chromatography (hexane : benzene=10 : 1) gave (+)-benzyl(chloromethyl)methylphenylgermane (**11**). Yield, 0.18 g (64%); $[\alpha]_{435}$ +24.3° (*c* 1, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ=0.40 (3H, s, $GeCH_3$), 2.55 (2H, s, $GeCH_2Ph$), 3.00 (2H, s, $GeCH_2Cl$), and 6.6—7.0 (10H, m, C_6H_5); MS (70 eV) *m/z* (rel intensity) 306 (9%).

Reaction of (+)-11 with Ammonia. A solution of optically active **(+)-11** (0.18 g, 0.60 mmol) in liq. NH_3 (7 g, ca. 400 mmol) in an autoclave was maintained for 1.5 h at 100 °C. The excess ammonia was liberated from the autoclave, and the contents were washed out with aqueous alkali (6 M NaOH, 3 ml×2) and benzene (8 ml). The organic layer was separated and the aqueous layer was extracted with ether (5 ml×2). The combined organic layer and extracts were then dried (Na_2SO_4). Evaporation and Kugelrohr distillation of the residue gave **(+)-7**. Yield, 0.15 g (89%); $[\alpha]_{435}$ +19.7° (*c* 1, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ=0.31 (3H, s, $GeCH_3$), 0.83 (2H, s, NH_2), 2.50 (2H, s, $GeCH_2Ph$), 2.61 (2H, s, $GeCH_2N$), and 6.7—7.7 (10H, m, C_6H_5).

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