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Preparation of New Optically Active Germylmethylamine Derivatives

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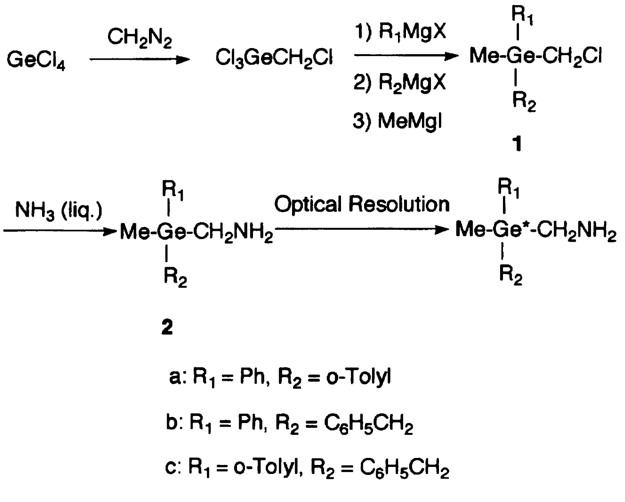
Synopsis. New optically active organogermanium compounds, such as [methylphenyl(*o*-tolyl)-, benzylmethylphenyl-, benzylmethyl(*o*-tolyl)-, and benzyl(*o*-methoxyphenyl)-methylgermyl]methylamine, were prepared in high optical purity.

A few optically active organogermanium compounds have been reported.[1] One of the problems in the preparation of asymmetric germanium compound is a difficulty to introduce different substituents on germanium. In the course of our interest concerning the preparation of optically active organometallic compounds,[2] new optically active organogermanium compounds were successfully obtained. Trichloro(chloromethyl)germane, prepared from the reaction of tetrachlorogermane with diazomethane, was treated stepwisely with Grignard reagents of aryl, benzyl, and methyl halides to give the corresponding (chloromethyl) germanium derivatives (**1a**, **1b**, **1c**, **1d**). Racemic organogermanium compounds, such as [methylphenyl(*o*-tolyl)germyl]methylamine (**2a**), (benzylmethyl phenylgermyl)methylamine (**2b**), [benzylmethyl(*o*-tolyl)germyl]methylamine (**2c**), and [benzyl(*o*-methoxyphenyl)methylgermyl]methylamine (**2d**), were prepared by treating the corresponding **1a**, **1b**, **1c** and **1d** with ammonia in an autoclave at 100°C (Scheme 1). The optical resolution of **2a** was carried out using 2-phenylpropanoic acid (PPA) as a resolving agent; **2b**, **2c**, and **2d** were resolved using tartaric acid as a resolving agent in a similar manner as that described for the preparation of their silicon analogues.[3,4] The optical purities of these amines were determined by measuring the NMR spectra of the amides of the optically active **2a**, **2b**, and **2c** with Mosher agent (MTPA)[5] (Table 1). In the case of the amide of racemic **2d** with MTPA, no diastereotopic separation of the signals was observed in its NMR spectrum, and optical purity of **2d** was determined by NMR spectrum using (benzylmethylphenylsilyl)acetic acid as an optical purity-determining reagent.[2]



Scheme 1.

Experimental

The melting points were uncorrected. The NMR spectra were recorded on a JEOL 60Si (60MHz), and a Bruker AM400 (400MHz) spectrometer in $CDCl_3$ using TMS as an internal standard. The optical rotations were measured with a JASCO DIP-360 polarimeter. All of the Grignard reactions were carried out under a dry-nitrogen atmosphere. Trichloro(chloromethyl)germane was prepared by the procedure described in the literature.[6]

Dichloro(chloromethyl)phenylgermane. Phenylmagnesium bromide prepared from bromobenzene (17.7 g, 113 mmol) and magnesium (3.0 g, 124 mmol) in dry ether (120 ml) was added to a solution of trichloro(chloromethyl)-germane (25.8 g, 113 mmol) in dry ether (120 ml) at 0°C with stirring. The reaction mixture was stirred for 1 h at 0°C and then refluxed for 1 h. After the addition of hexane (80 ml), the reaction mixture was kept at room temperature over night. Filtration, evaporation and distillation of the residue gave a colorless liquid. Yield 21.3 g (70%). Bp 140°C/12 Torr (1 Tor=133.322 Pa).

Dichloro(chloromethyl)(*o*- tolyl)germane and dichloro-(chloromethyl)(*o*-methoxyphenyl)germane were prepared in the similar manner described above in 90% (bp 118°C/0.18 Torr) and 60% (bp 138°C/0.11 Torr) yield, respectively.

(Chloromethyl)methylphenyl(*o*-tolyl)germane (1a). The *o*-tolylmagnesium bromide prepared from *o*-bromotoluene (13.5 g, 79 mmol) and magnesium (2.1 g, 87 mmol) in dry ether (80 ml) was added to a mixture of dichloro(chloromethyl)phenylgermane (21.3 g, 79 mmol) in dry ether (50 ml) at 0°C with stirring. The mixture was stirred at room

Table 1. Optically Active Organogermanium Compounds

	Yield %	Specific rotation °(c 2, CH_2Cl_2)	Optical purity % e.e.
2a	14	−7.1	99
2b	14	+10.0	99
2c	30	+6.0	98
2d	17	+21.1	97

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temperature for 3 h. A Grignard reagent prepared from iodomethane (13.3 g, 87 mmol) and magnesium (2.3 g, 95 mmol) in dry ether (70 ml) was added to the reaction mixture at 0°C with stirring. The mixture was stirred at room temperature for 3 h, and then refluxed for 1 h. An aqueous HCl solution (3 M, 40 ml, $1\,\mathrm{M}=1\ \mathrm{mol\,dm^{-3}}$) was added to the mixture at 0°C. The organic layer was separated and the aqueous layer were extracted with ether (30 ml×2). The combined organic layer and extracts were dried (Na_2SO_4). Evaporation and distillation of the residue gave a colorless liquid. Yield 17.2 g (71%). Bp 141°C/0.18 Torr. ^{1}H NMR ($CDCl_3$) $\delta=0.80$ (3H, s, Ge–CH_3), 2.28 (3H, s, Ar–CH_3), 3.38 (2H, s, CH_2Cl), 7.0—7.6 (9H, m, C_6H_5, C_6H_4).

The compound **1b**, **1c**, and **1d** were prepared in the similar manner described above. **1b**: Yield 62%. Bp 146°C/0.18 Torr. ^{1}H NMR ($CDCl_3$) $\delta=0.40$ (3H, s, Ge–CH_3), 2.55 (2H, s, Ge–CH_2–Ar), 3.00(2H, s, Ge–CH_2Cl), 6.6—7.6 (10H, m, Ph). **1c**: Yield 31%. Bp 128°C/0.15 Torr. ^{1}H NMR ($CDCl_3$) $\delta=0.48$ (3H, s, Ge–CH_3), 2.10 (3H, s, CH_3–Ar), 2.62 (2H, s, Ge–CH_2–Ar), 3.10 (2H, s, Ge–CH_2Cl), 6.6—7.6 (9H, m, C_6H_5, C_6H_4). **1d**: Yield 59%. Bp 140°C/0.14 Torr. ^{1}H NMR ($CDCl_3$) $\delta=0.45$ (3H, s, Ge–CH_3), 2.65 (2H, s, Ge–CH_2–Ar), 3.17 (2H, s, Ge–CH_2Cl), 3.79 (3H, s, OCH_3), 6.6—6.8 (9H, m, C_6H_5, C_6H_4).

Methylphenyl(*o*-tolyl)germylmethylamine (2a). In a stainless-steel autoclave, **1a** (17.2 g, 56 mmol) and liquid ammonia (96 g, 5.6 mol) were added under a nitrogen atmosphere. The autoclave was kept for 1.5 h at 100°C. The excess ammonia was liberated from the autoclave, and the contents were washed out with an aqueous alkali (6 M NaOH, 50 ml) and then benzene (100 ml). The organic layer was separated and the aqueous layer was extracted with ether (30 ml×3). The combined organic layer and extracts were dried (Na_2SO_4). Evaporation and distillation gave a colorless liquid. Yield 13.0 g (80%). Bp 142°C/0.18 Torr. ^{1}H NMR ($CDCl_3$) $\delta=0.75$ (3H, s, Ge–CH_3), 1.10 (2H, s, NH_2), 2.30 (3H, s, Ar–CH_3), 2.95 (2H, s, Ge–CH_2N), 7.0—7.6 (9H, m, C_6H_5, C_6H_4).

The compound **2b**, **2c**, and **2d** were prepared in the similar manner described above. **2b**: Yield 84%. Bp 138°C/0.11 Torr. ^{1}H NMR ($CDCl_3$) $\delta=0.31$ (3H, s, Ge–CH_3), 0.80 (2H, s, NH_2). 2.50 (2H, s, Ge–CH_2–Ar), 2.61 (2H, s, Ge–CH_2–N), 6.7—7.7 (10H, m, Ph). **2c**: Yield 73%. Bp 149°C/0.3 Torr. ^{1}H NMR ($CDCl_3$) $\delta=0.36$ (3H, s, Ge–CH_3), 0.80 (2H, s, NH_2), 2.35 (3H, s, Ar–CH_3), 2.53 (2H, s, Ge–CH_2–Ar), 2.63 (2H, s, Ge–CH_2N), 6.6—7.6 (9H, m, C_6H_5, C_6H_4). **2d**: Yield 68%. Bp 150°C/0.15 Torr. ^{1}H NMR ($CDCl_3$) $\delta=0.25$ (3H, s, Ge–CH_3), 0.75 (2H, s, NH_2), 2.50 (2H, s, Ge–CH_2–Ar), 2.56 (2H, s, Ge–CH_2N), 3.75 (3H, s, OCH_3), 6.5—7.5 (9H, m, C_6H_5, C_6H_4).

Optical Resolution of 2a. A solution of **2a** (10.0 g, 35 mmol) and (+)-PPA (5.25 g, 35 mmol) in benzene/hexane (1/1) mixture (122 ml) was kept overnight at room temperature. The crystalline precipitate was separated by filtration and recrystallized from benzene 10 times. Yield 2.5 g (16%). Mp 141—142°C. $[\alpha]_D+2.7°$ (*c* 1, MeOH). Found: C, 65.82; H, 6.65; N, 3.01%. Calcd for $C_{24}H_{29}NGeO_2$: C, 66.10; H, 6.70; N, 3.21%.

An aqueous solution of 10% NaOH was added to the crystals at 0°C. The liberated amine was extracted three times with ether (20 ml×3). The combined extracts were dried ($NaSO_4$). Evaporation and distillation gave a colorless oil. Yield 1.3 g (14%). $[\alpha]_D\ -7.1°$ (*c* 2, CH_2Cl_2) (99% e.e.). The (+)-rich **2a** recovered from the mother liquor was treated with an equimolar amount of (−)-PPA in the similar manner described above to give white crystals. Yield 3.6 g (24%). Mp 140—141°C. $[\alpha]_D-2.7°$ (*c* 1, MeOH).

Liberation gave a colorless oil. Yield 2.0 g (20%). $[\alpha]_D$ +6.9° (*c* 2, CH_2Cl_2) (97% e.e.). The optical resolutions of **2b**, **2c**, and **2d** were carried out in the similar manner to that described in the literature[2] using (+)-tartaric acid as a resolving reagent. **2b**: Yield 14%. $[\alpha]_D$ +10.0° (*c* 2, CH_2Cl_2) (99% e.e.). **2c**: YIeld 30%. $[\alpha]_D$ +6.0° (*c* 2, CH_2Cl_2) (98% e.e.). **2d**: Yield 17%. $[\alpha]_D$ +21.1° (*c* 2, CH_2Cl_2) (97% e.e.).

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