Russian Journal of General Chemistry, Vol. 74, No. 9, 2004, pp. 1356–1358. Translated from Zhurnal Obshchei Khimii, Vol. 74, No. 9, 2004, pp. 1462–1465.

Reactivity of *N*-(Chlorodimethylgermyl)methyl and *N*-(Chlorodimethylsilyl)methyl Derivatives of Lactams and Amides toward Grignard Reagents

S. Yu. Bylikin, A. G. Shipov, E. P. Kramarova, O. B. Artamkina, Vad. V. Negrebetskii, and Yu. I. Baukov

Russian State Medical University, Moscow, Russia

Received Decmber 6, 2002

Abstract — *N*-[(Chlorodimethylgermyl)methyl]lactams and -amides containing a five-coordinate germanium atom react with Grignard reagents chemoselectively by the Ge–Cl bond to form four-coordinate germanium compounds. The method of competitive reactions was used to establish that respective five-coordinate germanium and silicon compounds are almost equally reactive toward Grignard reagents but much more reactive than model four-coordinate germanium and silicon compounds.

Five-coordinate silicon [1] and tin compounds [2] are characteristically more reactive in certain reactions compared with model compounds containing four-coordinate germanium and silicon. For instance, (O–Si)-chelate *N*-[(halodimethylsilyl)methyl]lactams exhibit a higher silylating activity toward carbonyl compounds compared with halotrimethylsilanes [3] and are more reactive than the latter in exchange reactions with compounds Me_3SiY (Y = OAc, Hlg) [4].

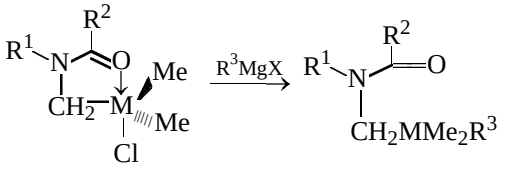
The method of competitive reactions was used to reveal a higher reactivity of *N*-[(chlorodimethylsilyl)-methyl]lactams compared with chlorotrimethylsilane toward benzylmagnesium chloride. Therewith, the relative reactivity of the lactams increases with increasing size of the lactam ring, i.e. with enhancing O→Si coordination interaction in the starting chloride [5].

Compared with five-coordinate silicon and tin compounds, there germanium analogs have received much less study [6], and relative reactivities of five- and four-coordinate germanium compounds, as well as of such germanium compounds and structurally related compounds of the other Group 14 elements have never been reported.

In the present work we studied the reactions of *N*-(chlorodimethylgermyl)methyl-substituted hexahydroazepin-2-ones **Ib** and **Id**[1] and *N*-(*S*)-(1-phenylethyl)-acetamide with Grignard reagents (methylmagnesium iodide and benzylmagnesium chloride), as well as compared the reactivities of these compounds with those of *N*-(chlorodimethylsilyl)methyl derivatives **Ia** and **Ic** and chlorotrimethylgermane toward the same Grignard reagents.

Germanium(V) chlorides **Ib** and **Id**, like their silicon analogs, chemoselectively react with Grignard reagents by the Ge–Cl bond to form *N*-(benzyldimethylgermyl)methyl and *N*-(trimethylgermyl)methyl derivatives **IIb** and **IId**, respectively, in which, according to the IR spectra, the intramolecular coordination O→Ge is lacking. Note that similar chemoselectivity have been observed in the reaction of *N*-[(chlorodimethylgermyl)methyl]-*N*-methylacetamide with butyllithium [8].

The facility of formation of germyl chlorides **Ib** and **Id** in the reactions of *N*-(trimethylsilyl)lactams and -amides with chloro(chloromethyl)dimethylgermane [8, 9] and the fairly high yields of compounds **IIb** and **IId** make us to consider this reaction feasible for preparative synthesis of *N*-[(organyldimethylgermyl)methyl]lactams and -amides.



Ia–**Id** **IIa**–**IId**

M = Si (**a, c**), Ge (**b, d**); R^1, R^2 = $(CH_2)_5$ (**a, b**); R^1 = Me(Ph)CH, R^2 = Me (**c, d**); R^3 = Bn (**a, b**), Me (**c, d**); Hlg = Cl (**a, b**), I (**c, d**).

[1] For preliminary commication on the reaction of *N*-[(chlorodimethylgermyl)methyl]hexahydroazepin-2-one with methylmagnesium iodide, see [7].

1070-3632/04/7409-1356 ©2004 MAIK "Nauka/Interperiodica"

By the method of competitive reactions we determined the relative reactivities of germyl chlorides **Ib** and **IId** and their silicon analogs **Ia** and **Ic** toward benzylmagnesium chloride and methylmagnesium iodide, respectively, as well as of germyl chloride **Ib** and chlorotrimethylgermane toward benzylmagnesium chloride. The product ratios were determined by GLC.

The resulting molar ratios of substituted benzyldimethyl and trimethylgermanes and -silanes at a 5:5:1 ratio of the starting reagents and Grignard reagent (solvent diethyl ether–benzene, 1:1) are listed in the table.

As seen from the table, five-coordinate silicon and germanium derivatives are much more reactive than their four-coordinate element analogs. With silicon derivatives, this effect is weaker, which is probably explained both by the larger size and higher polarizability of the germanium atom compared with silicon and by slightly different reaction conditions (the molar ratios of the reagents and Grignard reagent were 5:5:1 with germyl derivatives and 1:1:1 with silyl derivatives).

Replacement of the silicon atom by germanium, too, enhances the reactivity, but the molar ratio of the reaction products is markedly higher only for four-coordinate element derivatives [1:2.6 for Me_3SiCH_2Ph and Me_3GeCH_2Ph against 1:1.05 for compounds **IIa** and **IIb**]. The observed leveling of the reactivity of five-coordinate element derivatives probably results from the relatively stronger elongation of the M–Cl bond in silicon compounds on the extension of the coordination sphere of the central atom from 4 to 5 compared with their germanium analogs. The rate effect of such factors as the dependence of the coordination strength on the nature of the chelating ligand and the different solubility of the reagents under heterogeneous reaction conditions should also not be excluded. Apparently, there reasons explain the fact that the difference in the reactivities of compounds **Ic** and **Id** (1:1.13) toward the more active (and, consequently, less selective) methylmagnesium iodide is slightly larger that the difference in the reactivities of compounds **Ia** and **Ib** (1:1.05) toward benzylmagnesium chloride.

Thus, the resulting data suggest enhanced reactivity of five-coordinate germanium derivatives compared with chlorotrimethylgermane toward Grignard reagents, as well as an only slight difference in the reactivities of five-coordinate silicon and germanium compounds.

EXPERIMENTAL

The IR spectra of ~3% solutions in $CHCl_3$ were measured on a Specord IR-75 instrument. The ^1H and ^{13}C NMR spectra were obtained on a Varian XL-400 spectrometer (400.1 and 100.6 MHz, respectively) in the pulse mode with subsequent Fourier transform, internal reference TMS.

Competitive reactions of five-coordinate germanium chlorides **Ib** and **Id** with their silicon analogs **Ia** and **Ic** and chlorotrimethylgermane

Reagents	Grignard reagent	Molar ratio
Ia, Ib	$PhCH_2MgCl$	**IIa**:**IIb** = 1:1.05 ± 0.03
Ic, Id	MeMgI	**IIc**:**IId** = 1:1.13 ± 0.03
Me_3SiCl, **Ia**	$PhCH_2MgCl$[a]	Me_3SiCH_2Ph:**IIa** = 1:1.55[b]
Me_3GeCl, **Ib**	$PhCH_2MgCl$	Me_3GeCH_2Ph:**IIb** = 1:3.4 ± 0.1
Me_3SiCl, Me_3GeCl	$PhCH_2MgCl$	Me_3SiCH_2Ph:Me_3GeCH_2Ph = 1:2.6 ± 0.2

[a] Molar ratio 1:1:1. [b] Data of [5].

The specific rotations were measured on an A1-EPO polarimeter in 0.5-dm cells.

The products of competitive reactions were analyzed by GLC on a Chrom-4 chromatograph (column 1000 × 5 mm, packing 10% SE-30 on silica gel, carrier gas helium, thermal conductivity detector).

The starting (O–M)-chelate (M = Si, Ge) *N*-[(chlorodimethylsilyl)methyl]hexahydroazepin-2-one and *N*-[(chlorodimethylgermyl)methyl]hexahydroazepin-2-one (**Ia**, **Ib**) were prepared by the reactions of *N*-(trimethylsilyl)hexahydroazepin-2-one with chloro(chloromethyl)dimethylsilane and -germane [4, 10]. (O–Si)-Chelate *N*-(*S*)-[(chlorodimethylsilyl)methyl]-*N*-(1-phenylethyl)acetamide (**Ic**) was prepared by the reaction of *N*-(*S*)-(1-phenylethyl)acetamide with chloro(chloromethyl)dimethylsilane in the presence of triethylamine [11].

N-[(Benzyldimethylsilyl)methyl]hexahydroazepin-2-one (**IIa**) and benzyltrimethylgermane were synthesized as described in [5, 12], respectively.

(O→Ge)-Chelate *N*-(*S*)-[(chlorodimethylgermyl)methyl]-*N*-(1-phenylethyl)acetamide (Id). A solution of 1.3 g of chloro(chloromethyl)dimethylgermane and 1.63 g of *N*-(trimethylsilyl)-*N*-(*S*)-(1-phenylethyl)acetamide in 10 ml of *o*-xylene was heated under reflux for 3 h and then reduced by half in a vacuum. The crystals that formed were filtered off, washed with hexane, and dried to obtain 1.76 g (81%) of compound **Id**, mp 86–87°C (from toluene), $[\alpha]_D^{20}$ +42° (MeCN, 12 mg/ml). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1590 s, 1500 w. ^1H NMR spectrum ($CDCl_3$),

δ, ppm: 0.89 d (3H, $GeMe_2$), 1.68 d (3H, $^*C–CH_3$, $^3J_{HH}$ 6.9 Hz), 2.25 s (3H, CH_3CO), 2.51 d, 2.81 d (2H, NCH_2, $^2J_{HH}$ 14.0 Hz), 5.12 q (1H, $^*C–CH$, $^3J_{HH}$ 6.9 Hz), 7.2–7.4 m (5H, C_6H_5). Found, %: C 49.91; H 6.48; Ge 22.92. $C_{13}H_{20}ClGeNO$. Calculated, %: C 49.67; H 6.41; Ge 23.10.

***N*-[(Benzyldimethylgermyl)methyl]hexahydroazepin-2-one (IIb).** A solution of $PhCH_2MgCl$, obtained from 0.32 g of Mg and 1.5 ml of benzyl chloride in 15 ml of diethyl ether, was added to a solution of 2.64 g of germyl chloride **Ib** in 10 ml of benzene. The reaction mixture was heated under reflux for 10 min, cooled, and made weakly acidic with 10% HCl. The organic layer was separated, and the aqueous layer was treated with diethyl ether (2 × 10 ml). The combined organic layers were dried with $MgSO_4$, the solvent was removed in a vacuum, and the residue was fractionated to obtain 1.9 g (59%) of compound **IIb** as a colorless liquid, bp 201–202°C (7 mm Hg), n_D^{20} 1.5480. IR spectrum ($CHCl_3$), ν, cm^{-1}: 1620 s. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.16 s (3H, $GeMe_2$), 2.30 (2H, CH_2Ph), 2.49 m (2H, H 3), 1.56–1.69 (6H, H 4–6), 3.17 m (2H, H 7), 3.09 s (2H, NCH_2), 7.0–7.2 (5H, C_6H_5). Found, %: C 59.92; H 7.56; N 4.11. $C_{16}H_{25}GeNO$. Calculated, %: C 60.06; H 7.88; N 4.38.

***N*-(1-Phenylethyl)-*N*-(*S*)-[(trimethylsilyl)methyl]acetamide (IIc)** was synthesized similarly to compound **IIb** from a solution of 8.1 g of chlorosilane **Ic** in 50 ml of benzene and MeMgI obtained from 0.8 g of Mg and 2.1 ml of 35 ml of diethyl ether; yield 4.4 g (59%), colorless liquid, bp 155–156°C (7 mm Hg), n_D^{20} 1.5133, $[\alpha]_D^{20}$ –40° (MeCN, 14 mg/ml). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1630 s. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.05 s (3H, $SiMe_2$), 1.58 d (3H, $^*C–CH_3$, $^3J_{HH}$ 6.8 Hz), 2.25 s (3H, CH_3CO), 2.28 d, 2.44 d (2H, NCH_2, $^2J_{HH}$ 14.7 Hz), 5.09 q (1H, $^*C–CH$, $^3J_{HH}$ 6.8 Hz), 7.2?7.4 m (5H, C_6H_5). Found, %: C 67.29; H 9.30; N 5.47. $C_{14}H_{23}NOSi$. Calculated, %: C 67.41; H 9.29; N 5.62.

***N*-(1-Phenylethyl)-*N*-(*S*)-[(trimethylgermyl)methyl]acetamide (IId)** was prepared similarly to compound **IIb** from 3.14 g of germyl chloride **Id** in 25 ml of benzene and MeMgI (from 0.29 g of Mg and 0.75 g of MeI in 10 ml of diethyl ether), yield 1.7 g (58%), colorless liquid, bp 164–165°C (7 mm Hg), n_D^{20} 1.5252, $[\alpha]_D^{20}$ –41° (MeCN, 15 mg/ml). IR spectrum ($CHCl_3$), ν, cm^{-1}: 1625 s. ^1H NMR spectrum ($CD_3C_6D_5$), ν, ppm: 0.15 s (3H, $GeMe_2$), 1.15 d (3H, $^*C–CH_3$, $^3J_{HH}$ 6.8 Hz), 1.87 s (3H, CH_3CO), 2.36 d, 2.55 d (2H, NCH_2, $^2J_{HH}$ 13.9 Hz), 4.57 q (1H, $^*C–CH$, $^3J_{HH}$ 6.8 Hz), 6.9–7.1 m (5H, C_6H_5). Found, %: C 57.06; H 7.62; N 4.59. $C_{14}H_{23}GeNO$. Calculated, %: C 57.21; H 7.89; N 4.77.

Competitive reactions. A solution of 1 mmol of organomagnesium compound in 10 ml of diethyl ether was added dropwise to a mixture of 5 mmol of germyl chloride **Ib** or **Id** and 5 mmol of silyl chloride **Ia** or **Ic**, or 5 mmol of Me_3GeCl in 10 ml of benzene. The mixture was stirred for 0.5 h at room temperature and then decomposed with water. The aqueous layer was treated with 10 ml of diethyl ether. The combined organic layers were evaporated in a vacuum, and the residue was analyzed by GLC to determine the molar ratios of the reaction products (see table).

REFERENCES

1. Chuit, C., Corriu, R.J.P., Reye, C., and Young, J.C., *Chem. Rev.*, 1993, vol. 93, no. 4, p. 1371.
2. Jastrzebski, J.T.B.H. and Van Koten, G., *Adv. Organomet. Chem.*, 1993, vol. 35, p. 241.
3. Shipov, A.G., Kramarova, E.P., Artamkina, O.B., Oleneva, G.I., Nepomnyashchaya, N.A., and Baukov, Yu.I., *Zh. Obshch. Khim.*, 1995, vol. 65, no. 2, p. 272.
4. Baukov, Yu.I., Kramarova, E.P., Shipov, A.G., Oleneva, G.I., Artamkina, O.B., Albanov, A.I., Voronkov, M.G., and Pestunovich, V.A., *Zh. Obshch. Khim.*, 1989, vol. 59, no. 1, p. 127.
5. Shipov, A.G., Kramarova, E.P., Artamkina, O.B., and Baukov, Yu.I., *Metalloorg. Khim.*, 1991, vol. 4, no. 5, p. 1101.
6. Baukov, Yu.I., Shipov, A.G., Ovchinnikov, Yu.E., and Struchkov, Yu.T., *Izv. Ross. Akad. Nauk, Ser. Khim.*, 1994, no. 6, p. 982.
7. Kramarova, E.P., Khaustova, T.I., Zueva, G.Ya., Shipov, A.G., and Baukov, Yu.I., *Zh. Obshch. Khim.*, 1992, vol. 62, no. 9, p. 2156.
8. Shitaro, K. and Sato, Y., *J. Organomet. Chem.*, 1988, vol. 346, no. 1, p. 1.
9. Pestunovich, V.A., Kalikhman, I.D., Baukov, Yu.I., Bannikova, O.B., Albanov, A.I., Belousova, L.I., Kramarova E.P., Shipov, A.G., and Voronkov, M.G., *Metalloorg. Khim.*, 1988, vol. 1, no. 3, p. 719.
10. Kalikhman, I.D., Albanov, A.I., Bannikova, O.B., Belousova L.I., Pestunovich S.V., Voronkov, M.G., Pestunovich, V.A., Macharashvili, A.A., Shklover, V.E., Struchkov, Yu.T., Khaustova, T.I., Zueva, G.Ya., Kramarova, E.P., Shipov, A.G., Oleneva, G.I., and Baukov, Yu.I., *Metalloorg. Khim.*, 1989, vol. 2, no. 3, p. 637.
11. Baukov, Yu.I., Ovchinnikov, Yu.E., Shipov, A.G., Kramarova, E.P., Negrebetsky, Vad.V., and Struchkov, Yu.T., *J. Organomet. Chem.*, 1997, vol. 536, no. 2, p. 399.
12. Mironov, V.F., Dzhurinskaya, N.G., Gar, T.K., and Petrov, A.D., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1962, no. 3, p. 460.