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Synthesis of optically active germane carrying γ-butyrolactones

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Abstract

Threo and *erythro*-4-hydroxymethyl-γ-butyrolactones comprising germane were obtained in optically active form by the addition of trichlorogermane to (*Z*)-(*S*)-1-ethoxycarbonyl-3,4-*O*-isopropylidene-1-butene-3,4-diol which was derived from D-mannitol.

Introduction

Very few reports on the synthesis of organogermanium compounds containing chiral carbon skeletons have appeared [1]. We describe here synthesis of 3-trihydrogermyl-4-hydroxymethyl-γ-butyrolactones in optically active form.

Trichlorogermane adds to multiple bonds without catalyst or initiator, especially to α,β-unsaturated ketone, in a regioselective manner (in Michael fashion) [2]. So, we synthesized chiral α,β-unsaturated esters and allowed them to react with trichlorogermane.

Results and discussion

Michael acceptors, (*S*)-1-ethoxycarbonyl-3,4-*O*-isopropyridene-1-butene-3,4diols **2** and **3** were prepared from D-mannitol by glyceraldehyde [3]. Wittig reaction of **1** with (carbethoxymethylene)triphenylphosphorane in benzene afforded two unsaturated esters [4*] (**2**, 59%, ^{1}H NMR; 6.87 (dd, J_{12} 12 Hz, J_{23} 6.0 Hz, 1H, H-2), 5.81 (dd, J_{12} 12 Hz, J_{13} 1.5 Hz, 1H, H-1] and [**3**, 19%, ^{1}H NMR; 6.87 (dd, J_{12} 15 Hz, J_{23} 8.4 Hz, 1H, H-2), 6.07 (dd, J_{12} 15 Hz, J_{23} 2.4 Hz, 1H, H-1)).

(*Z*)-Unsaturated ester **2** was allowed to react with trichlorogermane in diethylether at 5°C. Treatment of the products with t-BuOK [5*] and KBH_4 in ethanol gave germanes **4** (25%) and **5** (26%) in a ratio of 1 to 1. On the other hand, the

* A reference number with an asterisk indicates a note in the list of references.

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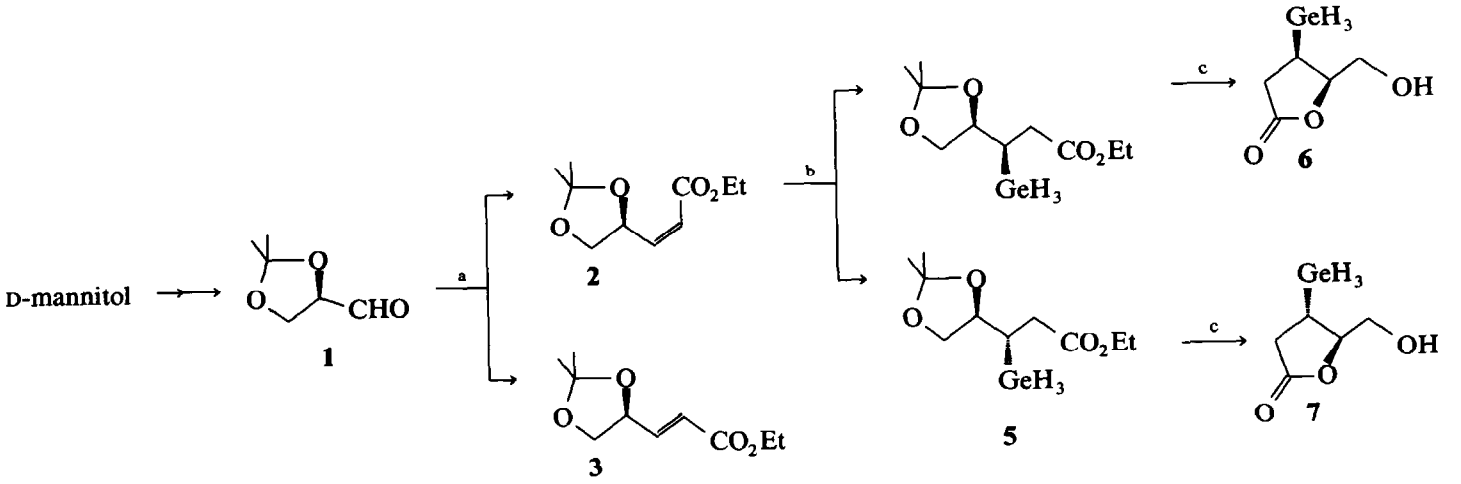

Scheme 1. (a) Ph_3PCHCO_2Et, benzene, (b) $HGeCl_3$, ether, then t-BuOK, KBH_4, EtOH, (c) Amberlyst 15, dioxane–H_2O

Table 1

^{1}H NMR chemical shifts in **6** and **7**

	H-3	H-4	H-5	H-5′
6	1.447	3.940	3.390	3.147
7	1.904	4.224	3.802	3.544

reaction of *E*-isomer **3** with trichlorogermane in the same condition gave **4** and **5** in a ratio of 2 to 1, but with poor yield (total yield was about 20%). Treatment of **4** with Amberlyst 15 in dioxane–water 5 : 1 gave *threo*-γ-lactone **6** (48%), and similar treatment of **5** gave *erythro* **7** (54%).

Optical purity of these compounds was determined by HPLC analysis of MTPA esters which were prepared from (+)- and (−)-MTPACI in pyridine [6]. From this measurement, optical purity of **6** and **7** was determined to be 99%ee and 98%ee, respectively.

Structural assignments were achieved by decoupling experiments and by comparing them with corresponding acetates prepared by standard procedures. The stereochemistry of **6** and **7** was assigned to be *threo* and *erythro*, respectively, on the basis of Karplus' rule. Coupling constants show the dihedral angles for H-3/H-4 to be near to 0° (**6**) and near to 180° (**7**). These results were confirmed by ^{1}H NMR NOE difference experiments. In the case of **6**, irradiation of H-3 induced NOE to H-4(5%). Another case **7**, irradiation of H-3 resulted in an NOE (1%) at H-4. As regards **6**, chemical shifts of H-3 and H-4 represent these protons are crowded each other compared with **7**. (Table 1, Fig. 1).

The absolute configurations of **6** and **7** were determined to be (3*R*,4*R*) and (3*S*,4*R*), respectively for the following reasons: (i) from the results of enantiomeric excess determinations, racemization scarcely occurs during the reactions; (ii) the stereochemistry of C-4(*R*) is derived from natural D-mannitol; (iii) relative configurations of **6** and **7** are *threo* and *erythro*, respectively.

Experimental

General. Melting points were measured on Meihoh Sharp Melting Point apparatus. Optical rotations were determined with a Perkin–Elmer Model 241 MC polarimeter, for solutions in methanol at 20 °C, unless noted otherwise. ^{1}H NMR spectra were measured on either Varian EM390 or JEOL JNM-GX500 spectrometers. ^{13}C NMR spectra were recorded with a JEOL JNM-GX500 NMR spectrometer operated at 125.65 MHz. Chemical shifts are expressed in ppm (δ) downfield from

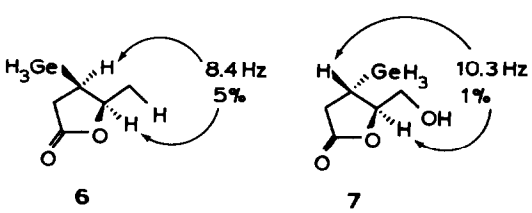

Fig. 1. Depiction of the germanes. Values denote coupling constants in Hz and observed NOE, respectively.

the tetramethylsilane, for solution in C_6D_6, unless noted otherwise. Flash chromatography was carried out in columns of Wako gel C-300 (200-300mesh). TLC was performed on Silica gel 60 F_{254} (Merck). IR spectra were recorded with a Shimadzu IR 440, in KBr pellets for the crystalline samples and films for the liquid samples. Liquid chromatographic analysis was conducted with a Tosoh CCPE instrument. Mass spectra were recorded with a Hitachi M-80 mass spectrometer.

The enantiomeric excess of **6** and **7** was determined by HPLC analysis as follows: To a solution of γ-butyrolactone in pyridine was added MTPACI which was obtained from the reaction of MTPA with oxalylchloride. After stirring for 2 h at room temperature, the mixture was concentrated in vacuo. Chromatography of the residue over SiO_2 in 6 : 1 hexane-ethylacetate afforded MTPA ester of γ-butyrolactone. The MTPA ester was analyzed by HPLC [column, Senshu pak Silica 1251-N; eluent, 4 : 1 hexane–ethyl acetate; flow rate 0.7ml/min; detection, 254 nm; t_R, 33.6 min[(+)-MTPA ester of *threo*-γ-butyrolactone **6**], and 37.6 min[(−)-MTPA ester of *threo*-γ-butyrolactone **6**]]. A similar procedure was used for *erythro*-γ-butyrolactone **7** [eluent, 6 : 1 hexane–ethyl acetate; flow rate, 1.0 ml/min; t_R, 29.6 min[(+)-MTPA ester of *erythro*-γ-butyrolactone **7** and 30.4 min[(−)-MTPA ester of *erythro*-γ-butyrolactone **7**]].

*Ethyl-(3R,4R)-3-trihydrogermyl-4,5-O-isopropylidene-4,5-dihydroxy-pentanoate (**4**) and ethly-(3S,4R)-3-trihydrogermyl-4,5-O-isopropylidene-4,5-dihydroxypentanoate (**5**)*

To a solution of 5.37 g(26.8 mmol) of *Z*-enoate **2** in 30ml of diethyl ether cooled to 5 °C was added 8.17 g(45.4 mmol) of trichlorogermane. After stirring for 2 h at 5 °C, to the reaction mixture was added 15.8 g(0.14mol) of t-BuOK in 20ml of ethanol. Then 7.0 g(0.13mol) of potassium borohydride was added. After the mixture had been stirred for 18 h at room temperature the reaction was quenched with acetic acid. The solution was filtered through Celite, and concentrated in vacuo. A solution of the residue in ethyl acetate was washed with aq; $NaCO_3$, H_2O, dried ($MgSO_4$), and evaporated in vacuo. Flash chromatography of the residue over SiO_2 in 5 : 1 hexane–ethyl acetate and then over Lober LiChroprep Si 60 size C in 5 : 1 hexane–ethyl acetate afforded *threo*-**4** (1.87 g 25% based on **2**) and *erythro*-**5** (1.93 g 26% based on **2**) as an oil, respectively.

Compound **4**: $[\alpha]_D = -1.4°$ ($c = 1.22$), $R_F = 0.50$ in 5 : 1 hexane–ethyl acetate, ν_{max} 1735 cm^{-1} (s,CO), 2090cm^{-1}(s,GeH). NMR data: δ_H 4.050 (dt, $J_{34} = 6.6$ Hz, J_{45} 6.23 Hz, 1H, H-4), 3.744 (dd, ^2J 8.06 Hz, J_{45} 6.23 Hz, 1H, H-5), 3.745(d, J 2.56 Hz, 3H, GeH_3), 3.366 (dd, ^2J 8.1 Hz, $J_{45'} = 7.33$ Hz, 1H, H-5′), 2.456 (dd, ^2J 16.49 Hz, J_{23} 7.33 Hz, 1H, H-2), 2.314 (dd, ^2J 16.5 Hz, $J_{2'3}$ 7.7 Hz, 1H, H-2′), 1.948 (m, 1H, H-3), 1.370 (s, 3H, C(CH_3)$_2$), 1.224 (s, 3H, C(CH_3)$_2$). δ_C 172.1(C-1), 109.0(CMe$_2$), 78.1(C-4), 68.8(C-5), 60.4(CH$_2$CH$_3$), 35.6(C-2), 26.6(CCH$_3$), 25.5(CCH$_3$), 24.2(C-3), 14.2(CH$_2$$CH_3$).

CI MS: found: m/z 277 ($M^+ - 1$). $C_{10}H_{20}O_4Ge$ calc: m/z 278.

Compound **5**: $[\alpha]_D = -4.1°$ ($c = 1.29$), $R_F = 0.55$ in 5 : 1 hexane–ethyl acetate, ν_{max} 1730cm^{-1}(bs,CO), 2100 cm^{-1}(s,GeH). NMR data: δ_H 4.045(ddd, J_{34} 8.8 Hz, J_{45} 7.33 Hz, $J_{45'}$ 5.86 Hz, H-4), 3.797 (dd, ^2J 8.06 Hz, J_{45} 6.23 Hz, 1H, H-5), 3.639 (d, J 2.56 Hz, 3H, GeH_3), 3.369 (t, J 7.69 Hz, 1H, H-5′), 2.674 (dd, ^2J 19 Hz, J_{23} 5.15 Hz, 1H, H-2), 2.740 (dd, ^2J 16.9 Hz, $J_{2'3}$ 8.43 Hz, 1H, H-2′), 1.354 (s, 3H, C(CH_3)$_2$), 1.258 (s, 3H, C(CH_3)$_2$). δ_C 172.3(C-1), 109.1(CMe$_2$), 78.0(C-4), 68.9(C-5), 60.3(CH$_2$CH$_3$), 35.1(C-2), 27.0(CCH$_3$), 25.8(CCH$_3$), 24.6(C-3), 14.2(CH$_2$$CH_3$).

CI MS: Found: m/z 277 ($M^+ - 1$). $C_{10}H_{20}O_4Ge$ calc: m/z 278.

(3R,4R)-3-Trihydrogermyl-4-hydroxymethyl-γ-butyrolactone (6)

To a solution of 2.68 g(9.7 mmole) of *threo*-**4** in 4:1 dioxane–H_2O(25ml) was added 1 g of Amberlyst 15. After stirring for 2 h at 80 °C, the product was filtered off and evaporated in vacuo. Flash chromatography of the residue over SiO_2 in 1:1 hexane–ethyl acetate afforded *threo*-γ-butyrolactone **6** (0.89 g, 48%), $[\alpha]_D$ +32.1° ($c = 1.12$), $R_F = 0.45$ in 1:1 hexane–ethyl acetate, mp 75.5–76.5 °C (hexane–ethyl acetate), ν_{max} 1760cm^{-1}(bs,CO), 2090 cm^{-1}(s,GeH). NMR data: δ_H(C_6D_6–D_2O) 3.940 (dt, J_{45} 3.3 Hz, J_{34} 8.4 Hz, 1H, H-4), 3.486 (d, J 2.9 Hz, 3H, GeH_3), 3.390 (dd, J_{45} 3.3 Hz, ^2J 12.5 Hz, 1H, H-5), 3.173 (dd, ^2J 12.5 Hz, $J_{45'}$ 3.3 Hz, 1H, H-5′), 2.264 (dd, J_{23} 11.5 Hz, ^2J 17.2 Hz, 1H, H-2), 2.052 (dd, ^2J 17.2 Hz, $J_{2'3}$ 9.7 Hz, 1H, H-2′), 1.447 (m, 1H, H-3). δ_C 177.2 (C-1), 83.0 (C-4), 63.7 (C-5), 33.9 (C-2), 19.9 (C-3).

CI MS: Found: m/z 191 ($M^+ - 1$), $C_5H_{10}O_3Ge$ calc: m/z 192; Anal. Found: C, 31.47: H, 5.34. calc: C, 31.49; H, 5.29%.

(3S,4R)-3-Trihydrogermyl-4-hydroxymethyl-γ-butyrolactone (7)

To a solution of 1.0 g (3.6 mmol) of *erythro*-**5** in 4:1 dioxane–H_2O (10ml) was added 0.5 g of Amberlyst 15. After stirring for 2 h at 80 °C, the product was filtered off and evaporated in vacuo. Flash chromatography of the residue over SiO_2 in 1:1 hexane–ethyl acetate afforded erythro-γ-butyrolactone **7** (0.35g, 54%), $[\alpha]_D$ +59.4° (c 1.10), R_F 0.34 in 1:1 hexane-ethylacetate, mp 60.0–62.0 °C(hexane–ethyl acetate), ν_{max} 1770 cm^{-1}(bs,CO), 2100cm^{-1}(s,GeH). NMR data; δ_H (C_6D_6–D_2O) 4.224 (ddd, J_{45} 2.9 Hz, $J_{45'}$ 4.8 Hz, J_{34} 10.3 Hz, 1H, H-4), 3.802 (dd, ^2J 12.8 Hz, J_{45} 2.9 Hz, 1H, H-5), 3.544 (dd, ^2J 12.5 Hz, $J_{45'}$ 4.8 Hz, 1H, H-5′), 3.499 (d, J 2.6 Hz, 3H, GeH_3), 2.472 (dd, J_{23} 8.8 Hz, ^2J 17.4 Hz, 1H, H-2), 2.088(dd, $J_{2'3}$ 12.5 Hz, ^2J 17.4 Hz, 1H, H-2′), 1.904(m, 1H, H-3).

δ_C 177.3 (C-1), 86.2 (C-4), 62.8 (C-5), 34.6 (C-2), 18.6 (C-3). CI MS: Found: m/z 191 ($M^+ - 1$), $C_5H_{10}O_3Ge$ calc: m/z 192; Anal. Found: C,32.17: H, 5.27. $C_5H_{10}O_3Ge \cdot 0.05$AcOEt calc.: C, 32.01; H, 5.37%.

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References

1 M. Lesbre, P. Mazerolles and J. Satge, The Organic Compounds of Germanium, John Wiley & Sons, 1971.

2 V.F. Mironov, E.M. Berlinner, and T.K. Gar, Zh. Obsch. Khim., 37, (1967) 962.

3 E.C. Herbert, Biochemical Preparations, Vol. 2, John Wiley & Sons 1949, p. 32.

4 Kishi reported that the *Z* isomer was selectively synthesized by performing the Horner–Emmons reaction and the *E* isomer was preferentially obtained from the Wittig reaction of **1** with (carbmethoxymethylene)triphenylphosphorane in methanol as a 7:1 mixture of *Z* and *E* unsaturated esters. During these reactions, no racemization was observed; (a) N. Minami, S.S. Ko and Y. Kishi, J. Am. Chem. Soc, 104 (1982) 1109; (b) B.M. Trost and S.M. Mignani, Tetrahedron Lett., 27 (1986) 4137.

5 The reduction of the trichlorogermyl moiety might proceed via alkoxygermane. S. Richelme, M. Andrianarison, C. Couret, J. Escudie and J. Satge., Main Group Metal Chemistry, 10 (1987) 69.

6 J.A. Dale, D.L. Dull and H.S. Mosher, J. Org. Chem., 34 (1969) 2543.