Tetrahedron Vol. 37, No 18, pp 3221 to 3225, 1981
Printed in Great Britain

0040-4020/81/183221-05$02.00/0
Pergamon Press Ltd.

SYNTHESIS OF THREE STEREOISOMERIC FORMS OF 2,8-DIMETHYL-1,7-DIOXASPIRO[5.5]UNDECANE, THE MAIN COMPONENT OF THE CEPHALIC SECRETION OF *ANDRENA WILKELLA*†

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(*Received in Japan* 26 *February* 1981)

Abstract—Three stereoisomers of 2,8-dimethyl-1,7-dioxaspiro[5,5]undecane were synthesized from acetoacetic ester by utilizing its yeast reduction and dianion alkylation.

SPIROACETALS have been isolated by Francke *et al.* as pheromones of several insect species.[1] These include 1,6-dioxaspiro[4.4]nonanes **A**[2,3], 1,6-dioxaspiro[4.5]decanes **B**,[4,5] and 1,7-dioxaspiro[5.5]undecanes **C**.[3,6] This evoked considerable interest among synthetic chemists to carry out syntheses of spiroacetals either as racemates[2,6-10] or as optically active forms.[11-16] As to the six existing chiral syntheses, four of them[11-14] are the preparations of optically active 2-ethyl-1,6-dioxaspiro[4.4]nonane (chalcogran),[2] while the remaining two describe the syntheses of some 1,6-dioxaspiro[4.5]decanes.[15,16] Hitherto synthesized chiral spiroacetals are restricted to those with only one asymmetric carbon atom besides the spiro carbon. In continuation of our own work on the chiral synthesis of chalcogran using dianion alkylation,[12] we report here a chiral synthesis of 2,8-dimethyl-1,7-dioxaspiro[5.5]undecane **1** with two asymmetric C atoms besides the spiro C atom.

The mandibular gland secretion of *Andrena* bees plays an important role in the communication between the sexes. The main component in *Andrena wilkella* caught in Öland, Sweden, was identified as **1** by mass spectral comparison with a racemic reference compound.[3] There are six stereoisomers for **1** as shown in Fig. 1, if we assume the two Me groups of **1** to prefer the equatorial positions which should be energetically more favorable. Two of them [(2*S*, 6*S*, 8*S*)-**1** and (2*R*, 6*R*, 8*R*)-**1**], however, are unstable owing to the oxygen anomeric effect (*vide infra*). The synthesis of the remaining stereoisomers [(2*S*, 6*R*, 8*S*)-**1** (2*R*, 6*S*, 8*R*)-**1** and a racemic mixture of (2*S*, 6*S*, 8*R*)-**1** and (2*R*, 6*R*, 8*S*)-**1**] will be detailed below.[17]

The chiral starting material in our synthesis was ethyl (*S*)-(+)-3-hydroxy-butanoate **2**, which was readily obtainable in 92% optical purity by the reduction of ethyl acetoacetate with baker's yeast.[18] Conversion of **2** into the (*S*)-tosylate **3b** was carried out as described previously.[18] The key iodide (*S*)-**4** was obtained in 80.4% yield by treating (*S*)-**3b** with NaI in acetone in the presence of a small amount of $NaHCO_3$.

The antipodal iodide (*R*)-**4** was prepared in the following manner. The alcohol (*S*)-**3a** was converted to the corresponding benzyl ether (*S*)-**3c** in 90.5% yield by

†Pheromone Synthesis—XLVI. Part XLV, K. Mori and H. Ueda, *Tetrahedron* **37**, 2581 (1981).

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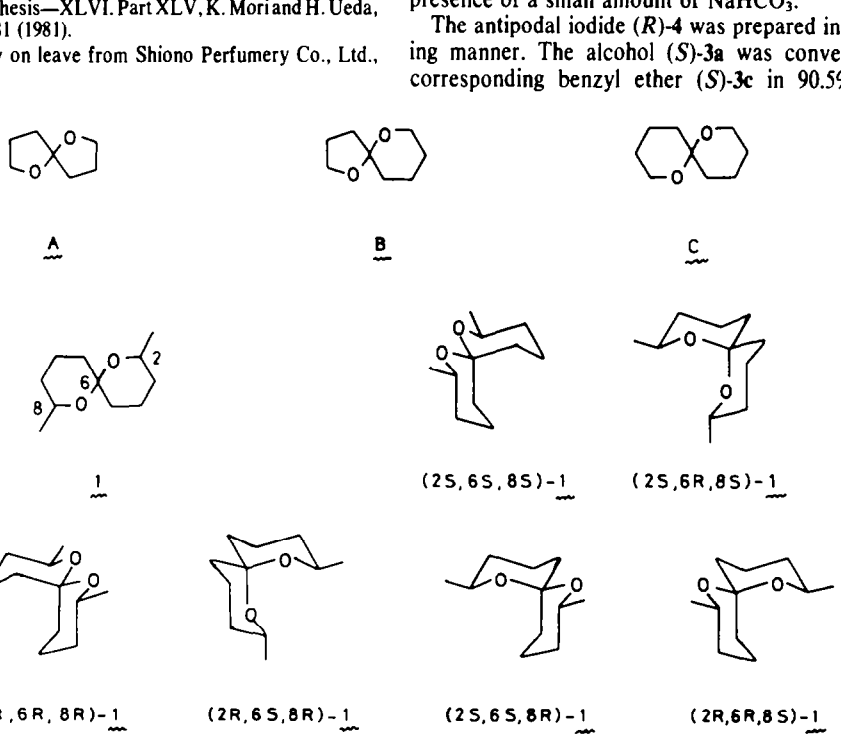
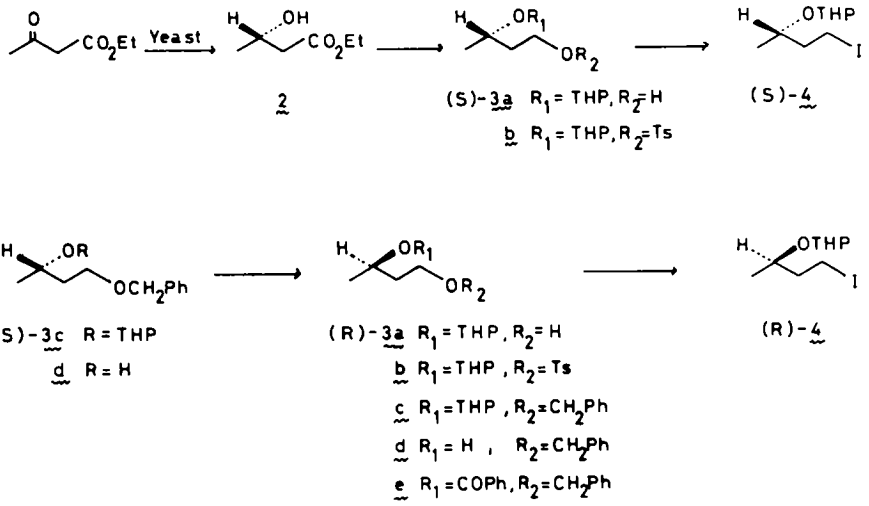




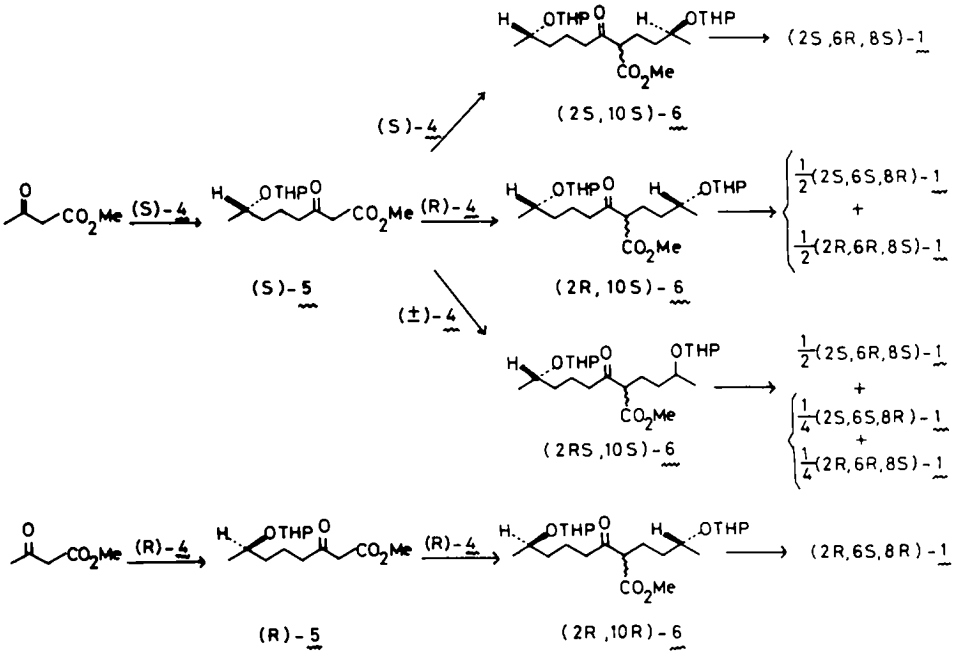
treatment with $PhCH_2Cl$-NaH in THF. Removal of the tetrahydropyranyl (THP) protective group with dil HCl yielded (*S*)-**3d**, $[\alpha]_D^{24}$ −2.12°($CHCl_3$), in 88% yield. Then the configuration of the OH group of (*S*)-**3d** was inverted by Mitsunobu's method.[19,20] Thus (*S*)-**3d** was treated with $PhCO_2H$-Ph_3P-$EtO_2CN{=}NCO_2Et$ in THF to give crude (*R*)-**3e**. This was hydrolyzed with KOH to give the desired (*R*)-diol monobenzyl ether **3d**,† $[\alpha]_D^{24}$ +2.08° ($CHCl_3$), in 72.7% yield. After protecting the OH group as a THP ether (*R*)-**3c**, the benzyl group was removed by hydrogenolysis to give (*R*)-**3a** in 82% yield from (*R*)-**3d**. This gave the (*R*)-iodide **4** via the tosylate (*R*)-**3b**.

The chiral iodide **4** was linked with $-CH_2COCH_2-$ unit in two steps. Firstly a dianion derived from methyl acetoacetate‡ (NaH-n-BuLi/THF)[22] was alkylated with 1 eq of either (*S*)-**4** or (*R*)-**4**. By employing (*S*)-**4**, a β-keto ester (*S*)-**5** was obtained in 75% yield. This was further alkylated with (*S*)-**4** in the presence of K_2CO_3/acetone-DMF to give (2*S*, 10*S*)-**6**. In the same manner (2*R*, 10*R*)-**6** was obtained by using (*R*)-**4** for alkylation. For the synthesis of (2*S*, 10*R*)-**6**, the first alkylation was carried out with (*S*)-**4** and the second was done with (*R*)-**4**.

Finally the keto ester **6** was converted to 2,8-dimethyl-1,7-dioxaspiro[5.5] undecane **1** by hydrolysis (KOH) and decarboxylation followed by deprotection and intramolecular acetalization (dil HCl). Starting from (2*S*, 10*S*)-**6**, a volatile spiroacetal **1**, $[\alpha]_D^{23}$ −51.6° (n-pentane), was obtained, which was homogeneous upon capillary GLC analysis. Its six-line ^{13}C-NMR spectrum [δ 19.7, 22.6, 33.7, 36.0, 66.0 (C–C–O), 97.1 (O–C–O)] suggested a

†These enantiomers of **3d** were converted to the corresponding (*S*)-(−)-α-methoxy-α-trifluoromethylphenylacetic acid (MTPA) esters to check their optical purities.[21] However, neither NMR nor glc analyses of them yielded useful results. Upon GLC analysis, the two diastereomers showed only very small difference in their R_t and no clear separation of the contaminating diastereomer was observed.

‡In our preliminary communication[17] we erroneously described this as ethyl acetoacetate. The Et esters **5** and **6** in Ref. 17 should be regarded as Me esters.



structure with a C_2-axis of symmetry. Both (2*S*, 6*S*, 8*S*)-**1** and (2*S*, 6*R*, 8*S*)-**1** possess a C_2-axis of symmetry. In connection with their synthetic works on the antibiotic A23187, Evans *et al.*[23] and Cresp *et al.*[24] synthesized crystalline 2,8-dialkyl-1,7-dioxaspiro[5.5] undecanes and found them to possess structures similar to (2*S*, 6*R*, 8*S*)-**1** by X-ray crystallographic analyses.[23,25] We therefore assign *R*-configuration to C-6 of our (2*S*, 8*S*)-**1**. The oxygen anomeric effect seems to be operating to make (2*S*, 6*S*, 8*S*)-**1** less stable than (2*S*, 6*R*, 8*S*)-**1**. Similarly (2*R*, 10*R*)-**6** yielded (2*R*, 6*S*, 8*R*)-**1**, $[\alpha]_D^{24}$ +51.7° (n-pentane), whose chromatographic and spectral data coincided with those of (2*S*, 6*R*, 8*S*)-**1**. Although the optical purities of (2*S*, 6*R*, 8*S*)-**1** and (2*R*, 6*S*, 8*R*)-**1** could not be determined directly, simple calculation suggested the optical purity of chemically pure (2*S*, 6*R*, 8*S*)-**1** prepared from (*S*)-**4** should be $96^2/(96^2+4^2)\times 100 = 99.8\%$, if the chiral center of 92% optically pure (*S*)-(+)-**2** survived without any appreciable racemization during the synthetic sequence.

The third stereoisomer of **1** was prepared from (2*R*, 10*S*)-**6**. In this case a homogeneous racemic mixture of (2*S*, 6*S*, 8*R*)-**1** and (2*R*, 6*R*, 8*S*)-**1** was obtained. The lack of a C_2-axis symmetry in this isomer was manifested by its eleven-line ^{13}C-NMR spectrum [δ 18.9, 20.2, 22.3, 22.6, 29.7, 33.1, 34.0, 36.9, 66.9 (C–C–O), 69.4 (C–C–O), 98.3 (O–C–O)].

The comparison of the optically active (2*S*, 6*R*, 8*S*)-**1** with the racemate [50% (2*S*, 6*S*, 8*R*)-**1** + 50% (2*R*, 6*R*, 8*S*)-**1**] revealed that the former is less polar than the latter, and they seemed to be separable by chromatography. To test this possibility, (*S*)-**5** was alkylated with (±)-**4** to give (2*RS*, 10*S*)-**6**. This was converted to **1** as usual and the resulting stereoisomeric mixture was separated by silica gel chromatography to give (2*S*, 6*R*, 8*S*)-**1**, $[\alpha]_D^{24}$ −51.0° (*n*-pentane), and the racemic mixture of (2*S*, 6*S*, 8*R*)-**1** and (2*R*, 6*R*, 8*S*)-**1**, $[\alpha]_D^{24}$ ±0.00° (*n*-pentane). The optical purity of thus obtained (2*S*, 6*R*, 8*S*)-**1** should be 96% on the assumption that the configuration of the starting (*S*)-**2** (92% optical purity) was retained throughout the synthesis.

In conclusion all the energetically possible sterisomers of 2,8-dimethyl-1,7-dioxaspiro[5.5] undecane were synthesized. The optical resolution of the racemic mixture of (2*S*, 6*S*, 8*R*)-**1** and (2*R*, 6*R*, 8*S*)-**1** remains to be achieved.[cf 13,15,16] The biological activity of these spiroacetal stereoisomers will be reported in due course by Drs. W. Francke (Hamburg) and J. Tengö (Öland).

EXPERIMENTAL

All b.ps were uncorrected. IR spectra were determined as film on a Jasco A-102 spectrometer. NMR spectra were recorded at 60 MHz with TMS as an internal standard on a Hitachi R-24A spectrometer unless otherwise stated. Optical rotations were measured on A Jasco DIP-4 polarimeter. GLC analyses were performed on a Yanaco GCG-550F gas chromatograph.

Ethyl (S)-(+)-3-*hydroxybutanoate* **2**. The following modified procedure gave optically purer **2** than the previously reported one.[18] Dry yeast (18 g, Oriental Yeast Co., Ltd., containing 98.5% yeast and 1.5% sorbitan fatty acid ester) was dispersed to tap water (300 ml) at 30–33° and sucrose (48 g) was added to it. The flask was shaken at 30–33° for 10 min, when brisk fermentation took place. Ethyl acetoacetate (3 g) was added to the fermentation mixture and the shaking culture was continued for 4 hr. Then ether (50 ml) was added to the fermentation broth and the mixture was filtered through Celite. Two batches of the fermentation broth were combined and extracted with ether (200 ml × 3). The ether soln was washed with water, dried ($MgSO_4$) and concentrated to give 5.5 g of crude **2**. This was distilled to give 4.5 g of **2**, b.p. 80–85°/18 mm. This contained a small amount of the starting material. After chromatographic purification (Merck Kieselgel 60), 3.3 g (54.3%) of (*S*)-**2** was obtained, b.p. 90–92°/20 mm, n_D^{24} 1.4159; $[\alpha]_D^{24}$ +37.6° (c = 1.57, $CHCl_3$).

This was converted to the corresponding (*S*)-(−)-MTPA ester. Its GLC analysis revealed the optical purity of **2** to be 92%. GLC (Yanaco YHP 5840A, SF96-CR19 column 40 m × 0.28 mm at 70–220° (+3°/min); Carrier gas, N_2 at 1.0 kg/cm^2): R_t 54.07 min (96.0%) 54.23 min (4.0%).

Ethyl (S)-3-*hydroxybutanoate THP ether*. The previous procedure[18] was modified as follows. Pyridinium *p*-toluenesulfonate (200 mg) was added to a soln of dihydropyran (9.4 g) and **2** (10 g) in CH_2Cl_2 (100 ml). The mixture was stirred for 18 hr at 25–30°, washed with Na_2CO_3aq and water. The aq layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 soln was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 14.0 g (85.9%) of the THP ether, b.p. 85–90°/1.5 mm, ν_{max} 1730 cm^{-1}; δ ($CDCl_3$) 1.25 (6H, m), 1.4–1.9 (6H, br), 2.5 (2H, m), 3.3–4.3 (3 H, m), ~4.7 (1 H).

(S)-1,3-*Butanediol* 3-*THP ether* (S)-**3a**. This was prepared according to the previous procedure[18] in 82.5% yield, b.p. 85–90°/1 mm, n_D^{24} 1.4511; $[\alpha]_D^{24}$ +26.0 (*c* = 1.69, $CHCl_3$); MS: m/z 174 (M^+, 2%), 173 (M-1, 10%), 85 (base peak).

(S)-1-*Iodo*-3-*butanol THP ether* (S)-**4**. NaI (5.2 g) and $NaHCO_3$ (3.0 g) were added to a soln of (*S*)-**3b** (7.6 g) in acetone (80 ml). The mixture was stirred at 25–30° for 24 hr. Then it was concentrated *in vacuo*. The residue was diluted with water and extracted with C_6H_6. The C_6H_6 soln was washed with water, 10% $Na_2S_2O_3$ aq and water, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography (Merck Kieselgel 60) to give 5.3 g (80.4%) of (*S*)-**4**, ν_{max} 2950 (s), 2870 (m), 1130 (s), 1075 (s), 1020 (s), 990 (s) cm^{-1}; δ ~1.18 (3 H, m), 1.3–1.7 (6 H, br.), 1.7–2.2 (2 H, m), 3.0–3.4 (2 H, m), 3.4–4.1 (3 H, m), 4.65 (1 H, br. s). This was employed for the next step without further purification.

(S)-1,3-*Butanediol* 1-*benzyl ether* 3-*THP ether* (S)-**3c**. A soln of (*S*)-**3a** (4.0 g) in dry THF (20 ml) was added dropwise to a stirred suspension of 50% NaH (1.6 g) in dry THF (30 ml) at room temp. The mixture was stirred and heated under reflux for 1 hr. Then a soln of $PhCH_2Cl$ (3.7 g) in dry THF (10 ml) was added dropwise to the stirred and heated mixture at reflux temp. The mixture was stirred and heated under reflux for 4 hr after the addition. Then it was cooled, poured into ice-water and extracted with C_6H_6. The C_6H_6 soln was washed with sat Na_2CO_3 aq and water, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 5.5 g (90.5%) of (*S*)-**3c**, b.p. 135–140°/1 mm, ν_{max} 2925 (s), 2850 (m), 1450 (m), 1360 (m), 1200 (m), 1110 (m), 1070 (s), 1020 (s), 995 (s), 730 (m), 695 (m) cm^{-1}; δ ($CDCl_3$ ~1.15 (3 H, m), 1.3–2.0 (8 H, br. m), 3.3–4.2 (5 H, m), 4.45 (2 H, s), ~4.65 (1 H, br. s), 7.25 (5 H, s).

(S)-(−)-1,3-*Butanediol* 1-*benzyl ether* (S)-**3d**. 6N HCl (0.1 ml) was added to a soln of (*S*)-**3c** (5.5 g) in MeOH (100 ml). The soln was stirred for 3 hr at room temp. Then it was mixed with sat Na_2CO_3aq (10 ml) and concentrated *in vacuo* to remove MeOH. The residue was diluted with water and extracted with ether. The ether soln was washed with water, dried ($MgSO_4$) and concentrated *in vacuo*. The rsidue was distilled *in vacuo* to give 3.3 g (88%) of (*S*)-**3d**, b.p. 98–102°/1.5 mn, n_D^{24} 1.5025; $[\alpha]_D^{24}$ −2.12° (*c* = 1.13, $CHCl_3$); ν_{max} 3400 (m), 3020 (w), 2950 (m), 2920 (m), 2850 (m), 1450 (m), 1360 (m), 1130 (m), 1095 (s), 1025 (m), 910 (m), 735 (m), 695 (m) cm^{-1}; δ 1.15 (3 H, d, J = 6 Hz), 1.70 (2 H, dt, J_1 = 6, J_2 = 5.5 Hz), ~2.8 (1 H, br. s), 3.60 (2 H, t, J = 6 Hz), 3.95 (1 H, m), 4.45 (2 H, s), 7.25 (5 H, s). Found: C, 72.83; H, 8.93. Calc. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95%. GLC of the (*S*)-(−)-MPTA ester of (*S*)-**3d** (Yanaco YHP 5840A gas chromatograph; Column: SF-96 CR-19, 40 m × 0.28 mm at 70–220° (+3°/min); carrier gas, N_2 at 1.0 kg/cm^2) R_t 84.08 min.

(R)-1,3-*Butanediol* 1-*benzyl ether* 3-*benzoate* (R)-**3e**. A soln of $EtO_2CN{=}NCO_2Et$ (6.4 g) in dry THF (30 ml) was added dropwise to a stirred soln of (*S*)-**3d** (3.3 g), Ph_3P (9.64 g) and $PhCO_2H$ (4.5 g) in dry THF (80 ml) maintaining the inner temp below 35°. After the addition the mixture was stirred overnight at room

temp. Then THF was removed *in vacuo* and the residue was dissolved in ether (50 ml). After a while precipitated materials were filtered off. The solid was washed with ether (50 ml × 2). The combined ether soln was washed with water, dried ($MgSO_4$) and concentrated *in vacuo*. The residual oil (11.0 g) was chromatographed over Merck Kieselgel 60. Elution with *n*-hexane-ether (10:1) yielded 5.0 g of crude (*R*)-**3e** contaminated with benzoic anhydride, ν_{max} 1710 (s), 1270 (s), 1090 (s), 710 (s) cm^{-1}; $\delta(CDCl_3)$ 1.32 (3 H, d, J = 6 Hz), 1.96 (2 H, q, J = 6 Hz), 3.50 (2 H, t, J = 6 Hz), 4.40 (2 H, s), 5.20 (1 H, m), 7.16 (5 H, s), 7.2–7.6 (3 H, m), 7.7–8.2 (2 H, m). This was employed for the next step without further purification.

(R)-(+)-1,3-*Butanediol* 1-*benzyl ether* (R)-**3d**. KOHaq (2.3 g in 70 ml) was added to a soln of (*R*)-**3e** (5.0 g) in MeOH (20 ml) and the mixture was stirred and heated under reflux for 2 hr. MeOH was removed *in vacuo* and the residue was extracted with ether. The ether soln was washed with water, dried ($MgSO_4$) and concentrated *in vacuo* to give 3.0 g of crude (*R*)-**3d**. This was distilled to afford 2.4 g (72.7%) of pure (*R*)-**3d**, b.p. 99–102°/1.5 mm, n_D^{24} 1.5027; $[\alpha]_D^{24}$ +2.08° (*c* = 1.11, $CHCl_3$). The IR and NMR spectra were identical with those of (*S*)-**3d**. Found: C, 72.80; H, 8.94. Calc for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95%. GLC of the (*S*)-(−)-MTPA ester of (*R*)-**3d** (conditions of the measurement were same as those described for the (*S*)-(−)-MTPA ester of (*S*)-**3d**) R_t 85.87 min.

(R)-1,3-*Butanediol* 1-*benzyl ether* 3-*THP ether* (R)-**3c**. Pyridinium *p*-toluenesulfonate (200 mg) was added to a soln of (*R*)-**3d** (2.4 g) and dihydropyran (1.4 g) in CH_2Cl_2 (50 ml). The mixture was stirred for 18 hr at room temp. Then it was mixed with sat Na_2CO_3aq (50 ml) and the organic soln was separated. The aq layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 soln was washed with water, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 3.2 g (91%) of (*R*)-**3c**, b.p. 135-140°/1 mm. The IR and NMR spectra were identical with those of (*S*)-**3c**.

(R)-(−)-1,3-*Butanediol* 3-*THP ether* (R)-**3a**. 10% Pd–C (1 g) was added to a soln of (*R*)-**3c** (3.2 g) in 99% EtOH (50 ml) and the mixture was shaken under H_2. When the H_2 uptake ceased, the catalyst was filtered off. The filtrate was concentrated *in vacuo*. The residue was distilled to give 1.9 g (90%) of (*R*)-**3a**, b.p. 83–88°/1.5 mm, n_D^{24} 1.4513; $[\alpha]_D^{24}$ −24.5° (*c* = 1.32, $CHCl_3$). The IR and NMR spectra were identical with those of (*S*)-**3a**.

(R)-1,3-*Butanediol* 1-*tosylate* 3-*THP ether* (R)-**3b**. This was prepared in the usual manner as described before for (*S*)-**3b**[18] to give 2.9 g (81.9%) of (*R*)-**3b** from 1.9 g of (*R*)-**3a**. The spectral data were identical with those of (*S*)-**3b**.

(R)-1-*Iodo*-3-*butanol THP ether* (R)-**4**. This was prepared in the same manner as described for (*S*)-**4** to give 1.9 g (81.5%) of (*R*)-**4** after chromatographic purification starting from 2.7 g of (*R*)-**3b**.

Methyl (S)-3-*oxo*-7-*hydroxyoctanoate* 7-*THP ether* (S)-**5**. A soln of $AcCH_2CO_2Me$ (1.02 g, 8.8 mmol) in dry THF (20 ml) was added dropwise to a stirred suspension of 50% NaH (465 mg, 9.7 mmol) in dry THF (30 ml) at −10 ~ 0° under Ar. After the addition the mixture was stirred for 30 min. Then *n*-BuLi in *n*-hexane (9.7 mmol) was added with stirring at −10 ~ −5°. The stirring was continued for 1 hr at 0–20°. Subsequently a soln of (*S*)-**4** (2.5 g, 8.8 mmol) in dry THF (10 ml) was added dropwise with stirring. After stirring for 1 hr at room temp, the reaction was quenched at 0° by addition of 30% AcOHaq (2.0 g, 10 mmol). The mixture was diluted with water and extracted with C_6H_6. The C_6H_6 soln was washed with water, dried ($MgSO_4$) and concentrated *in vacuo* to give 1.8 g (75%) of crude (*S*)-**5**, ν_{max} 2950 (s), 2875 (m), 1745 (s), 1720 (s), 1135 (s), 1080 (s), 1035 (s), 1025 (s), 1000 (m) cm^{-1}; $\delta(CDCl_3)$, 1.02–1.30 (3 H, 1.04, 1.15, 1.25), 1.35–1.80 (10 H, br.), 2.55 (2 H, t, J = 6 Hz), 3.40 (2 H, s), 3.67 (3 H, s), 3.1–3.9 (3 H, m), 4.6 (1 H, br. s). This was employed for the next step without further purification.

Methyl (R)-3-*oxo*-7-*hydroxyoctanoate* 7-*THP ether* (R)-**5**. In the same manner as described above 500 mg of (*R*)-**4** yielded 470 mg (98%) of (*R*)-**5**. The spectral data were identical with those described for (*S*)-**5**.

(2S, 10S)-5-*Methoxycarbonyl*-6-*oxo*-2, 10-*undecanediol di-THP ether* (2S, 10S)-**6**. A mixture of (*S*)-**4** (1.9 g), (*S*)-**5** (1.8 g) and K_2CO_3 (1.8 g) in dry acetone (50 ml) and DMF (2 ml) was stirred and heated under reflux for 5 hr. Then acetone was removed *in vacuo*. The residue was diluted with water and extracted with C_6H_6. The C_6H_6 soln was washed with water, dried ($MgSO_4$) and concentrated to give 2.5 g (89%) of crude (2S, 10S)-**6**, ν_{max} 2925 (s), 2860 (m), 1740 (m), 1710 (s), 1200 (s), 1130 (s), 1075 (s), 1030 (s, sh), 1020 (s), 995 (s) cm^{-1}; δ ($CDCl_3$ 1.00–1.30 (6 H, 1.02, 1.12, 1.24), 1.3–2.0 (~20 H, br), 2.45 (2 H, t), 3.67 (3 H, s), 3.2–4.2 (7 H, m), 4.6 (2 H, s). This was employed for the next step without further purification.

(2R, 10R)-5-*Methoxycarbonyl*-6-*oxo*-2,10-*undecanediol di-THP ether* (2R, 10R)-**6**. In the same manner as described above (*R*)-**4** (470 mg) and (*R*)-**5** (470 mg) yielded 470 mg (67%) of (2*R*, 10*R*)-**6**. The spectral data were identical with those of (2*S*, 10*S*)-**6**.

(2R, 10S)-5-*Methoxycarbonyl*-6-*oxo*-2, 10-*undecanediol di-THP ether* (2R, 10S)-**6**. In the same manner (*R*)-**4** (1.0 g) and (*S*)-**5** (1.0 g) yielded 1.5 g (97%) of crude (2*R*, 10*S*)-**6**. The IR and NMR spectra were very similar to those of (2*S*, 10*S*)-**6** with only very small differences in the finger-print region of the IR spectrum.

(2RS, 10S)-5-*Methoxycarbonyl*-6-*oxo*-2, 10-*undecanediol di-THP ether* (2RS, 10S)-**6**. In the same manner (±)-**4** (2.0 g) and (*S*)-**5** (2.0 g) yielded 2.4 g (77.8%) of crude (2*RS*, 10*S*)-**6**. The spectral data were almost identical with those of (2*S*, 10*S*)-**6**.

(2*S*, 6*R*, 8*S*)-(−)-2, 8-*Dimethyl*-1, 7-*dioxaspiro*[5.5]*undecane* (2S, 6R, 8S)-**1**. A soln of (2*S*, 10*S*)-**6** (2.5 g) in MeOH (20 ml) was added to 3% KOHaq (25 ml) and the mixture was stirred and heated under reflux for 2 hr. MeOH was removed *in vacuo*. The residue was extracted with C_6H_6. The C_6H_6 soln was washed with water, dried ($MgSO_4$) and concentrated *in vacuo* to give 1.8 g (84%) of (2*S*, 10*S*)-2,10-dihydroxy-6-undecanone di-THP ether, ν_{max} 2950 (s), 2860 (m), 1710 (m), 1200 (m), 1130 (s), 1080 (s), 1020 (s), 1000 (s) cm^{-1}; $\delta(CDCl_3)$ 1.00–1.30 (3 H, 1.02, 1.14, 1.24), 1.3–1.8 (~20 H, br), 2.35 (4 H, br. m), 3.2–4.1 (6 H, m), 4.6 (2 H, br. s), 6N HCl (0.2 ml) was added to a soln of the above ketone (1.8 g) in MeOH (30 ml) and the soln was stirred for 2 hr at room temp. Then sat Na_2CO_3aq (30 ml) was added and the mixture was concentrated *in vacuo* to remove MeOH below 25°. The residue was extracted with *n*-pentane. The pentane soln was washed with water, dried ($MgSO_4$) and concentrated. The residual oil (800 mg) was chromatographed over Merck Kieselgel 60. Thus obtained oil was distilled to give 200 mg of pure (2*S*, 6*R*, 8*S*)-**1**, b.p. 150–160°, n_D^{23} 1.4465; $[\alpha]_D^{23}$ −51.6° (c = 1.27, *n*-pentane); ν_{max} 2950 (s), 2870 (m), 1440 (m), 1390 (m), 1285 (w), 1260 (w), 1230 (m), 1210 (w), 1190 (w), 1180 (w), 1150 (w), 1130 (w), 1095 (m), 1075 (m), 1040 (w), 1000 (s), 960 (m), 900 (w), 840 (w), 805 (w), 785 (w) cm^{-1}; ^{1}H-NMR: δ(60 MHz, $CDCl_3$) 1.10 (6 H, d, J = 6 Hz), 1.2–2.0 (12 H, br), ~3.4–3.9 (2 H, m); ^{13}C-NMR: δ(25.05 MHz, $CDCl_3$) 19.7, 22.6, 33.7, 36.0, 66.0, 97.1; MS: m/z 69 (40%), 97 (56%), 112 (98%), 114 (36%), 115 (100%, base peak), 125 (10%), 140 (16%), 169 (19%), 184 (18% = M^+); GLC (Column, CF 96-CR19, 40 m × 0.28 mm at 70–220° (+3°/min); Carrier gas, N_2, 1.0 kg/cm^2); Rt 26.22 min (98% purity). *Anal.* M^+ = 184.1446 ($C_{11}H_{20}O_2$).

(2R, 6S, 8R)-(+)-2, 8-*Dimethyl*-1, 7-*dioxaspiro*[5.5]*undecane* (2R, 6S, 8R)-**1**. This was prepared in the same manner as described above starting from 470 mg of (2*R*, 10*R*)-**6** to give 36 mg (21%) of (2*R*, 6*S*, 8*R*)-**1**, b.p. 150–155°, n_D^{24} 1.4463; $[\alpha]_D^{24}$ +51.7° (c = 1.72, *n*-pentane). The spectral data were identical with those of (2*S*, 6*R*, 8*S*)-**1**.

A racemic mixture of (2S, 6S, 8R)-2, 8-*dimethyl*-1, 7-*dioxaspiro*[5.5]*undecane and its antipode* [50% (2S, 6S, 8R)-**1** + 50% (2R, 6R, 8S)-**1**]. This was prepared in the same manner as described for (2*S*, 6*R*, 8*S*)-**1** starting from 1.5 g of (2*R*, 10*S*)-**6** to give 185 mg (30.8%) of the racemate, b.p. 170–175°, n_D^{24} 1.4555; $[\alpha]_D^{24}$ ±0.00° (*c* = 1.87, *n*-pentane); ν_{max} 2950 (s), 2870 (m), 1440 (m), 1385 (m), 1370 (m), 1350 (w), 1330 (w), 1275 (w), 1260 (w), 1230 (s), 1210 (m), 1195 (w), 1180 (w), 1160 (w), 1140 (m), 1120 (w), 1085 (s), 1060 (w), 1050 (m), 1030 (m), 1005 (s), 990 (m), 970 (m), 945 (w), 915 (w), 895 (w), 870 (w), 850 (w), 840 (w), 830 (w), 810 (w), 780 (w) cm^{-1}; ^{1}H-NMR: δ(60 MHz, $CDCl_3$) 1.08 (3 H, d, J = 6 Hz), 1.09 (3 H, d, J = 6 Hz), 1.3–2.0 (12 H, br), ~3.3–3.8 (1 H, m), ~3.8–4.3 (1 H, m); ^{13}C-NMR: δ(25.05 MHz, $CDCl_3$) 18.9, 20.2, 22.3, 22.6, 29.7, 33.1, 34.0, 36.9, 66.9, 69.4, 98.3;

MS: *m/z* 69 (56%), 97 (60%), 112 (55%), 114 (37%), 115 (100%, base peak), 125 (12%), 140 (8%), 169 (7%), 184 (15% = M^+); GLC (Column, CF 96-CR19, 40 m × 0.28 mm at 70–220° (+3°/min); Carrier gas, N_2, 1.0 kg/cm^2: Rt 29.66 min (100% purity). *Anal.* M^+ = 184.1472 ($C_{11}H_{20}O_2$).

A stereoisomeric mixture of (2S, 6R, 8S)-, (2S, 6S, 8R)- *and* (2R, 6R, 8S)-**1**. The stereoisomeric mixture was prepared in the same manner as described for (2*S*, 6*R*, 8*S*)-**1** starting from 2.4 g of (2*RS*, 10*S*)-**6** to give 500 mg (83%) of a crude **1**. This was chromatographed over Merck Kieselgel 60 and eluted with *n*-pentane. The (2*S*, 6*R*, 8*S*)-isomer (55 mg) was eluted earlier, $[\alpha]_D^{24}$ −51.0° (*c* = 1.35, *n*-pentane). The later fraction yielded a racemic mixture (70 mg) of (2*S*, 6*S*, 8*R*)-**1** and (2*R*, 6*R*, 8*S*)-**1**, $[\alpha]_D^{24}$ ±0.00° (*c* = 1.21, *n*-pentane). TLC (Merck Silica gel GF_{254}; *n*-hexane-THF 10:1) Rf 0.85 [(2*S*, 6*R*, 8*S*)-**1**]; 0.70 [50% (2*S*, 6*S*, 8*R*)-**1** + 50% (2*R*, 6*R*, 8*S*)-**1**].

Acknowledgements—K. M. thanks Dr. W. Francke, Universität Hamburg, for arousing his interest in this problem. We are indebted to Dr. A. Echigo, Oriental Yeast Co., Ltd., for his kind gift of baker's yeast. This work was partly supported by a Grant-in-Aid for Scientific Research (No. 547107) from Ministry of Education, Science and Culture, Japan. We are grateful to Shiono Perfumery Co., Ltd. for financial support.

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