Tetrahedron Vol. 40, No. 2, pp. 299 to 303, 1984
Printed in Great Britain.

0040-4020/84 $3.00 + .00

SYNTHESIS OF THE PROPIONATES OF (2*R*, 8*R*)- AND (2*S*, 8*R*)-8-METHYL-2-DECANOL, THE PHEROMONE OF THE WESTERN CORN ROOTWORM, EMPLOYING CHIRAL COMPOUNDS OF MICROBIAL ORIGIN AS STARTING MATERIALS†

KENJI MORI* and HIDENORI WATANABE
Department of Agricultural Chemistry, The University of Tokyo, Yayoi 1-1-1, Bunkyo-ku, Tokyo 113, Japan

(*Received in Japan* 19 *April* 1983)

Abstract—The attractants of the western corn rootworm (*Diabrotica virgifera virgifera* Le Conte), the propionates of (2*R*, 8*R*)- and (2*S*, 8*R*)-8-methyl-2-decanol, were synthesized from (*R*)-(+)-citronellol and the enantiomers of ethyl β-hydroxybutryate of microbial origin.

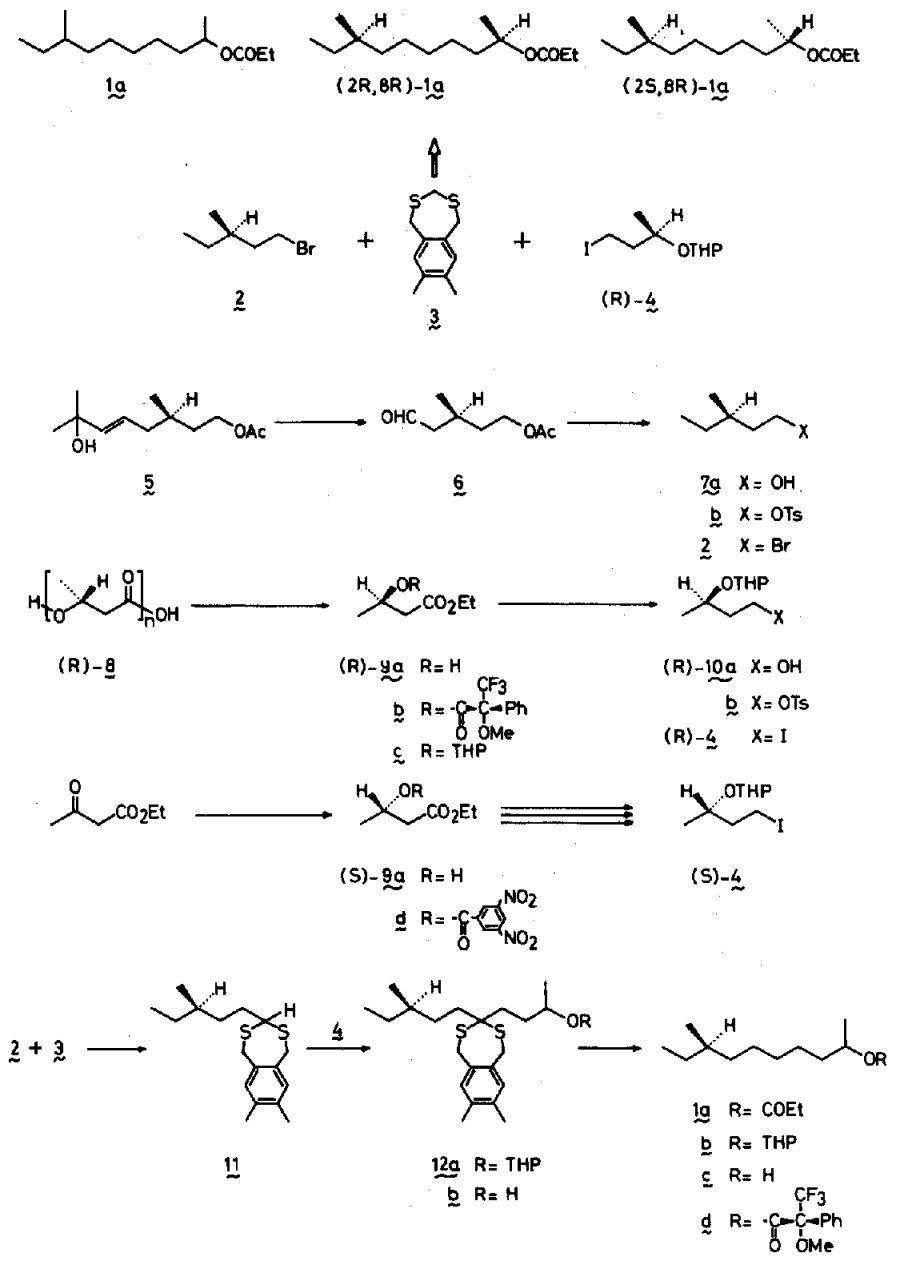
Recently the pheromone of the western corn rootworm, *Diabrotica virgifera virgifera* Le Conte was identified as the propionate of 8-methyl-2-decanol **1a**.[1,2] When the four stereoisomers of this compound were synthesized and tested in traps in the field, males of the western corn rootworm were captured only in traps baited with the (2*R*, 8*R*)- and (2*S*, 8*R*)-isomers. Thus, these males appear to be able to distinguish the (8*R*)- from the (8*S*)- isomers and reject the (8*S*). Whether or not the natural pheromone of this insect contains both isomers has not yet been determined.[2,3] The existing synthetic route for (2*R*, 8*R*)- and (2*S*, 8*R*)-**1a** is rather lengthy and includes the HPLC separation of the C-2 stereoisomers. We therefore became interested in developing another route for the pheromone. Herein we report a synthesis of both (2*R*, 8*R*)- and (2*S*, 8*R*)-**1a**. Our plan was to put two chiral building blocks [(*R*)-**2** and (*R*)-**4**] together on a dithiane **3** previously reported by us[4] yielding the desired carbon skeleton of (2*R*, 8*R*)-**1a**.

The synthesis of **2** was straightforward starting from the known allylic alcohol **5**,[5] which in turn was prepared from 100% optically pure pulegone.[6,7] Ozonolysis of **5** gave an aldehyde **6**. The Wolff-Kishner reduction of **6** yielded an alcohol **7a**. The desired bromide **2**, $[\alpha]_D^{21.5}$-18.9° (ether), was obtained in the usual manner from **7a** *via* **7b**.

Although both (*R*)- and (*S*)-**4** are the known compounds (~ 92% ee),[8] we decided to develop better methods for obtaining optically pure enantiomers of **4**. For the synthesis of (*R*)-**4**, the so-called "poly-β-hydroxybutyrate" [PHB, (*R*)-**8**] seemed to be an ideal chiral starting material. A wide variety of microorganisms accumulate granules composed of the polymeric ester of (*R*)-β-hydroxybutyric acid as their unique intracellular reserve of organic carbon and/or chemical energy. Recently Tomita and his co-workers studied the enzymatic synthesis of PHB in *Zoogloea ramigera* I-16-M (ATCC 19623), a flock-forming microorganism isolated from activated sludge.[9] *Z. ramigera* was reported to accumulate as high as 60–70% per dry weight of PHB after flocculation.[9] If PHB of this bacterium is highly optically pure, it will give (*R*)-**4** readily. PHB **8** separated from the flocculated cells of *Z. ramigera* or, more conveniently, the cells themselves were submitted to ethanolysis in the presence of a small amount of H_2SO_4 to give (*R*)-**9a**, $[\alpha]_D^{24} - 43.6°$ ($CHCl_3$). The optical purity of (*R*)-**9a** was shown to be 100% by the HPLC analysis of its MTPA (α-methoxy-α-trifluoromethylphenylacetic acid) ester **9b** (see Ref. 10). PHB of *Z. ramigera* was therefore shown to be a very convenient starting material for our synthesis. We obtained 4.7 g of (*R*)-**9a** starting from 4.0 g of PHB **8**, or 5.0 g of the flocculated cells afforded 3.3 g of (*R*)-**9a**. Direct use of the flocculated cells was more convenient. By growing the bacteria in a 5-l flask, we readily obtained 28 g of the flocculated cells within four days. Seebach and Züger very recently reported the preparation of (*R*)-**9a** from PHB of *Alcaligenes eutrophus*.[10] Our procedure seems to be less time-consuming than theirs (see Experimental). In a separate paper (in Japanese) we described a detailed study of the PHB production by *Z. ramigera*.[11] Conversion of (*R*)-**9a** to (*R*)-**4** was carried out *via* (*R*)-**9c**, (*R*)-**10a** and (*R*)-**10b** as reported previously.[8] For the preparation of (*S*)-**4**, we employed the reduction of ethyl acetoacetate to (*S*)-**9a** by baker's yeast as the key-step.[8] In a large-scale preparation of (*S*)-**9a**, however, its optical purity was often 83–87%.[12,13] It was therefore necessary to improve the optical purity of (*S*)-**9a** by recrystallizing its 3,5-dinitrobenzoate (*S*)-**9d** as reported by Seebach.[14] The purified (*S*)-**9a**, $[\alpha]_D^{20.5} + 43.9°$ ($CHCl_3$), was shown to be of 100% optical purity by the HPLC analysis of its MTPA ester.

With those chiral building blocks in hand, our next task was the alkylation of **3** with **2**. The dithiane **3** is a non-odoriferous and highly crystalline substance.[4] A carbanion generated by the addition of n-BuLi to **3** in THF was alkylated with **2** to give a crystalline dithiane **11**, which could be purified by chromatography and recrystallization. Further alkylation with (*R*)-**4** of a carbanion derived from **11** under carefully controlled condition yielded an oily dithiane (2*R*, 8*R*)-**12a**. This was reduced with Raney Ni to give (2*R*, 8*R*)-**1b**, whose acid hydrolysis gave

†Pheromone Synthesis—60. Part 59: K. Mori and T. Otsuka, *Tetrahedron* **39**, 3267 (1983). The experimental part of this work was taken from the BSc thesis of H.W. (March 1983).



(2*R*, 8*R*)-8-methyl-2-decanol **1c**, $[\alpha]_D^{23.5}$ −14.9° ($CHCl_3$). Finally acylation of **1c** with EtCOCl yielded (2*R*, 8*R*)-**1a**, $[\alpha]_D^{23}$ −7.57° ($CHCl_3$). For the preparation of (2*S*, 8*R*)-**1a**, **11** was alkylated with (*S*)-**4** to give (2*S*, 8*R*)-**12a**. Raney Ni desulfurization of (2*S*, 8*R*)-**12a** gave (2*S*, 8*R*)-**1b**. (Desulfurization of **12b** with Raney Ni caused partial racemization at C-2 to give (2*S*, 8*R*)-**1c** with 89% optical purity at C-2.) This yielded, upon acid hydrolysis, (2*S*, 8*R*)-**1c**, $[\alpha]_D^{21.5}$ −1.32° ($CHCl_3$), whose acylation with EtCOCl gave (2*S*, 8*R*)-**1a**, $[\alpha]_D^{21}$ −4.25° ($CHCl_3$). Both (2*R*, 8*R*)- and (2*S*, 8*R*)-**1a** showed the EI-MS identical to that reported for the natural pheromone.[2]

Since there was no synthetic step where racemization might be possible at C-8, the 100% optical purity of (*R*)-(+)-pulegone was retained throughout the synthesis. The high optical purities of (*R*)- and (S)-4 as secured by our bioorganic synthesis reflected in the high optical purities at C-2 (~100%) of (2*R*, 8*R*)- and (2*S*, 8*R*)-**1c** as revealed by both the NMR (in the presence of $Eu(fod)_3$-d_{27}) and the HPLC analysis of their corresponding MTPA esters (2*R*, 8*R*)- and (2*S*, 8*R*)-**1d**.

In conclusion the pheromone of the western corn rootworm was prepared in high optical purity employing (*R*)-(+)-pulegone and both the enantiomers of ethyl β-hydroxybutyrate **9a** as the starting materials.

EXPERIMENTAL

All mps and bps are uncorrected. IR spectra were recorded as films on a Jasco A-102 spectrometer. NMR spectra were measured on a Hitachi R-24 spectrometer at 60 MHz as CCl_4 soln with TMS as an internal standard. Optical rotations were measured on a Jasco DIP-140 polarimeter. GLC analyses were performed on a Jeol JGC-20K

or a Hitachi 163 gas chromatograph. Preparative GLC was carried out on a Yanaco G 80 gas chromatograph.

(S)-(−)-5-*Acetoxy*-3-*methylpentanal* **6**

O_3 was bubbled into a stirred and cooled mixture of **5** (59.3 g) and $NaHCO_3$ (5.6$_g$) in MeOH (450 ml) for 6 h at −60°. The mixture was cooled to −65° and N_2 instead of O_3 was bubbled for 10 min to remove the excess O_3. Me_2S (56.4 ml) was added dropwise to the stirred soln and temp was gradually raised to room temp. After stirring overnight, the mixture was poured into water (1000 ml) and extracted with ether. The ether soln was washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 32.4 g (74%) of **6**. A portion of it was distilled to give pure **6**, whose spectral data were identical to those reported earlier:[5] b.p. 107–112°/20 mm, n_D^{23} 1.4265; $[\alpha]_D^{18.5}$ − 10.0° (neat, $d_4^{18.5}$ 1.004); ν_{max} 1735 (s), 1725 (s), 1240 (s) cm^{-1}; δ (100 MHz) 1.03 (3H, d, J = 6Hz), 1.2–2.7 (5H, m), 2.02 (3H, s), 4.12 (2H, t, J = 6Hz), 9.86 (1H, s).

(R)-(−)-3-*Methyl*-1-*pentanol* **7a**

A soln of **6** (28 g) and $N_2H_4 \cdot H_2O$ (78 ml) in diethylene glycol (104 ml) was stirred and heated under reflux for 30 min. A soln of KOH (52 g) in water (65 ml) was added to the mixture. It was stirred and heated under reflux for 30 min. The bath temp was gradually raised to 200°. The mixture was kept under reflux for 1 h. Then the product was steam-distilled by the dropwise addition of water (260 ml) to the heated mixture to give *ca* 300 ml of distillate, which was extracted with ether. The ether soln was washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 8.6 g (48%) of **7a**, b.p. 84–88°/71 mm, n_D^{20} 1.4153; $[\alpha]_D^{20}$ − 8.5° (neat, d_4^{20} 0.8227); ν_{max} 3340 (s), 1060 (s) cm^{-1}; δ 0.90 (6H, m), 1.10–1.80 (5H, m), 3.10 (1H, s), 3.46 (2H, t, J = 6Hz). The IR and NMR data were identical with those reported earlier.[5]

(*R*)-3-*Methylpentyl tosylate* **7b**

p-TsCl (7.4 g) was added to a stirred and ice-cooled soln of **7a** (3.2 g) in dry C_5H_5N (31 ml). The mixture was stirred for 2 h at room temp. It was then poured into ice-dil HCl and extracted with ether. The ether soln was washed with N HCl, $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 7.8 g (quantitative) of crude **7b**, ν_{max} 1600 (m), 1185 (s), 1175 (s), 940 (s) cm^{-1}. This was directly used in the next step.

(R)-(−)-3-*Methylpentyl bromide* **2**

LiBr (7.6 g) was added to a soln of **7b** (7.8 g) in dry acetone (46 ml). The mixture was stirred overnight at room temp under Ar. It was then concentrated *in vacuo*. The residue was diluted with water and extracted with ether. The ether soln was washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 4.2 g (81% from **7a**) of **2**, b.p. 71–72.5°/63 mm, n_D^{23} 1.4436; $[\alpha]_D^{22}$ − 19.9° (c=1.72, ether); ν_{max} 2960 (s), 2920 (s), 2870 (m), 1455 (m), 1375 (m), 1250 (m), 1210 (m) cm^{-1}; $\delta \sim$ 0.95 (6H, m), 1.0–2.0 (5H, m), 3.36 (2H, t, J = 7Hz). (Found: C, 43.26; H, 7.88. Calc for $C_6H_{13}Br$: C, 43.65; H, 7.94%).

Poly-β-*hydroxybutyrate* (*PHB*)(*R*)-**8**

Stock cultures of *Zooglea ramigera* I-16-M (ATCC 1923) were maintained on agar slants containing 1.5% Trypticase soy agar (BBL) and 1.0% agar (Difco) at 4° after incubating at 30° for 1 day. The stock cultures were transferred every two weeks in order to obtain optimal growth. The basal glucose-starved medium for the dispersed growth of the cells was prepared as described by Tomita[9] and contained 0.5% casamino acids (Difco), 0.5% yeast extract (Oriental yeast), 0.2% K_2HPO_4 and 0.1% KH_2PO_4 in pure water. The basal medium (50 ml each) was put into two 500-ml Sakaguchi flasks and inoculated. The medium was then incubated at 30° for 24 h on a reciprocal shaker (130 strokes/min). This was transferred to a 5L Erlenmeyer flask containing 2L of the medium and incubated at 30° for 24 h on a rotary shaker (150 rpm). The above process was carried out under sterilized conditions. The culture broth was then transferred by rinsing with pure water (500 ml) to a 5L four-necked flask provided with a glass tube for aeration, a thermometer, air-tight sealed mechanical stirrer and a glass tube for evacuation. Glucose (100 g) was added to the medium and the mixture was stirred (360-400 rpm) for 24 h at 30° with aeration (16 L/min) by evacuation with an aspirator. During that period *Z. ramigera* cells flocculated. The culture broth was filtered under suction. At the time when about 2/3 of the broth was filtered, the filtration was interrupted. The broth remaining on a Buchner funnel was poured into acetone (1 L) with stirring. The filter cake was added into the aqueous acetone mixture by washing with acetone. Then the mixture was filtered. The collected cells were washed with water and acetone, dried *in vacuo* to give 28.3 g (13.5 g/l) of the dry cells of *Z. ramigera*. PHB granules could be prepared from the dry cells according to Tomita.[9]

Ethyl (*R*)-(−)-β-*hydroxybutyrate* (*R*)-**9a**

(a) *From PHB*. Ethanolysis of PHB was carried out essentially according to Seebach.[10] PHB (**8**, 4.0 g) was suspended in dry EtOH (29 ml) and $ClCH_2CH_2Cl$ (29 ml). Ultrasonic treatment of the mixture effected the swelling of PHB. To this was added conc H_2SO_4 (0.9 ml) and the mixture was stirred and heated under reflux for 37 h. After cooling, it was diluted with 18% NaCl soln (14 ml) and extracted with ether. The ether soln was washed with $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 4.7 g (80%) of (*R*)-**9a**, b.p. 84–85°/20 mm, n_D^{24} 1.4158; $[\alpha]_D^{24}$ − 43.6° (c = 1.34, $CHCl_3$); ν_{max} 3450 (m), 1740 (s), 1185 (s)cm^{-1}; δ 1.18 (3H, d, J = 6 Hz), 1.27 (3H, t, J = 7 Hz), 2.38 (2H, d, J = 6 Hz), 3.35 (1H, d, J = 4 Hz), 3.9-4.4 (1H, m), 4.15 (2H, q, J = 7 Hz). Found: C, 54.21; H, 9.01. Calc for $C_6H_{12}O_3$: C, 54.53; H, 9.15%.

(b) *Directly from Z. ramigera cells*. A suspension of dry cells of *Z. ramigera* (5.0 g) in dry EtOH (30 ml) and $ClCH_2CH_2Cl$ (36 ml) containing conc H_2SO_4 (1.1 ml) was stirred and heated under reflux for 57 h. After cooling, the mixture was diluted with sat brine and filtered through Celite. The filtrate was extracted with ether (70 ml × 1, 20 ml × 3). The residue was stirred with ether (100 ml) for 30 min, filtered through Celite and the ether layer was separated. The combined ether soln was washed with sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 3.3 g of (*R*)-**9a**, b.p. 86.0–86.5°/22 mm, n_D^{21} 1.4164; $[\alpha]_D^{21}$ − 43.4° (c = 1.36, $CHCl_3$).

The optical purity of (*R*)-**9a** was determined by the HPLC analysis of (*R*)-**9b** prepared by the acylation with (*R*)-MTPA Cl or (*S*)-MTPA Cl. The MTPA ester **9b** was analyzed on Shimadzu LC-2 (Column: Partisil 25 cm × 4.6 mm; solvent *n*-hexane–THF–MeOH 6000 : 100 : 1 ; 30 kg/cm^2; detector: SPD-1 at 217 nm): R_t 52.6 min [(*S*)-MTPA ester of (*R*)-**9a**], 40.6 min [(*R*)-MTPA ester of (*R*)-**9a**].

Ethyl (R)-β-*tetrahydropyranyloxybutyrate* (*R*)-**9c**

Pyridinium p-toluenesulfonate (PPTS, 0.7 g) was added to a soln of (*R*)-**9a** (3.7 g) and dihydropyran (3.5 g) in dry CH_2Cl_2 (37 ml). The mixture was stirred for 3 hr at room temp. It was then washed with 10% Na_2CO_3 soln and water, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 5.6 g (92.5%) of (*R*)-**9c**, b.p. 85–89°/2 mm, $n_D^{22.5}$ 1.4368; $[\alpha]_D^{22.5}$ − 15.9° (c = 1.00, $CHCl_3$). Found: C, 61.14; H, 9.27. Calc for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32%. The IR and NMR spectra were identical with those reported for (*S*)-**9a**.[8]

(R)-3-*Tetrahydropranyloxy*-1-*butanol* (R)-**10a**

A soln of (*R*)-**9c** (5.4 g) in dry ether (10 ml) was added to an ice-cooled and stirred suspension of LAH (0.8 g) in dry ether (65 ml) at 0–5°. After the addition, the mixture was

stirred for 2.5 h at room temp. It was then ice-cooled and the excess LAH was destroyed by the addition of water (0.8 ml), 10% NaOH (0.8 ml) and water (0.8 ml). After stirring for 1 h, the mixture was filtered and the filter cake was washed with THF. The combined filtrate and washings were concentrated *in vacuo*. The residue was distilled to give 3.9 g (91%) of (*R*)-**10a**, b.p. 69–76°/0.55 mm, n_D^{25} 1.4501; $[\alpha]_D^{25} - 33.6°$ (c=1.58, $CHCl_3$). The IR and NMR spectra were identical with those reported for (*S*)-**10a**.[12]

(R)-3-*Tetrahydropyranyloxybutyl tosylate* (R)-**10b**

p-TsCl (6 g) was added to a soln of (*R*)-**10a** (3.8 g) in dry C_5H_5N (20 ml) with stirring and ice-cooling. The stirring was continued for 4.5 h at 0–5°. The mixture was then poured into iced-water and extracted with ether. The ether soln was washed with water, sat $CuSO_4$ soln and sat $NaHCO_3$ soln, dried ($MgSO_4$), and concentrated *in vacuo* to give 7.1 g (quantitative) of crude (*R*)-**10b**. This was used in the next step without further purification.

(R)-3-*Tetrahydropyranyloxybutyl iodide* (R)-**4**

A mixture of crude (*R*)-**10b** (6.8 g), NaI (4.7 g) and $NaHCO_3$ (2.7 g) in dry acetone (71 ml) was stirred for 27 h at room temp. It was then concentrated *in vacuo*. The residue was diluted with water and extracted with benzene. The benzene soln was washed with water, 10% $Na_2S_2O_3$ and water, dried ($MgSO_4$) and concentrated *in vacuo* to give 6.2 g of crude **4**. This was chromatographed (Merck Kieselgel 60) to give 5.6 g (89.5% from (*R*)-**10a**) of (*R*)-**4**, whose IR and NMR spectra were identical to those reported previously.[8]

Ethyl (*S*)-*β*-(3′,5′-*dinitrobenzoyloxy*)*butyrate* (S)-**9d**

Reduction of ethyl acetoacetate by baker's yeast gave (*S*)-**9a** of 83% optical purity.[8,11,12] Its enantiomeric excess was enhanced by recrystallizing (*S*)-**9d** by essentially the same procedure as reported by Seebach.[14] To a soln of (*S*)-**9a** (83%e.e. 8.5 g), N,N-dicyclohexylcarbodiimide (DCC, 16.1 g) and N,N-dimethylaminopyridine (DMAP, 646 mg) in CH_2Cl_2 (127.5 ml) was added 3,5-dinitrobenzoic acid (20.6 g). The mixture was stirred for 16 hr at room temp, diluted with n-pentane (32 ml) and filtered. The filtrate was concentrated *in vacuo*. The residue was mixed with CH_2Cl_2–n-pentane (1 : 1) and left to stand at 0° for 3 h. The precipitate was filtered off and the filtrate was concentrated *in vacuo*. The similar treatments were repeated with CH_2Cl_2-*n*-pentane (96.6 ml) and ether (90 ml). A yellow oil obtained by concentrating the ether soln was chromatographed over Merck Kieselgel 60 to give 18.7 g (89%) of crude (*S*)-**9d**. This (16.3 g) was recrystallized from *n*-pentane–ether (4 : 1) to give 7.8 g (45% recovery) of pure (*S*)-**9d**, m.p. 38.5–39.0°, $[\alpha]_D^{20} + 26.1°$ (c=1.31, $CHCl_3$) [lit.[14] m.p. 40–41°, $[\alpha]_D^{25} + 26°$ (c = 1.37, $CHCl_3$)]. The spectral data were identical with those reported by Seebach.[14]

Ethyl (S)-*β*-*hydroxybutyrate* (S)-**9a**

N-KOH aq soln (16 ml) was added dropwise during 30 min to a stirred and cooled soln of (*S*)-**9d** (5.0 g) in THF–EtOH (1 ; 1, 63 ml) at $-5 \sim 0°$. The mixture was stirred for 30 min at 0° and then diluted with ether (150 ml) and sat $NaHCO_3$ soln (60 ml). The ether layer was separated and the aq layer was extracted with CH_2Cl_2. The combined organic soln was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled to give 1.8 g (89%) of (*S*)-**9a**, b.p. 94–95°/30 mm, $n_D^{21.5}$ 1.4385; $[\alpha]_D^{21.5} + 43.9°$ (c = 1.35, $CHCl_3$). This was shown to be 100% optically pure by analyzing its (*R*)-MTPA ester.

Ethyl (S)-*β*-*tetrahydropyranyloxybutyrate* (*S*)-**9c**

This was prepared in the same manner as described for (*R*)-**9c** in quantitative yield, b.p. 84.5–88.5°/3 mm, $n_D^{21.5}$ 1.4379; $[\alpha]_D^{21.5} + 17.8°$ (c=1.09, $CHCl_3$).

(S)-3-*Tetrahydropyranyloxy*-1-*butanol* (S)-**10a**

This was prepared in the same manner as described for (*R*)-**10a** in 87% yield, b.p. 76–82°/0.35 mm, n_D^{22} 1.4507; $[\alpha]_D^{22} + 45.2°$ (c = 1.58, $CHCl_3$).

(S)-3-*Tetrahydropyranyloxybutyl iodide* (S)-**4**

This was prepared in the same manner as described for (*R*)-**4** in 94% yield from (*S*)-**10a**.

(R)-(−)-7,8-*Dimethyl*-3-(3-*methylpentyl*)-1,5-*dihydro*-2,4-*benzodithiepin* **11**

n-BuLi in *n*-hexane (1.6 N, 9.9 ml) was added dropwise to a stirred and cooled soln of **3** (2.8 g) in dry THF (40 ml) at $-10 \sim -5°$ under Ar. The mixture was stirred for 3 h at 0–5° to give a wine-red soln of the carbanion. It was then cooled to $-10 \sim -5°$ and a soln of **2** (2.3 g) in dry THF (15 ml) was added dropwise with stirring. After the addition, the temp was raised gradually to room temp. The stirring was continued for 6 h. The mixture was poured into water and extracted with EtOAc. The EtOAc soln was washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 4.7 g of crude **11**. This was chromatographed over Merck Kieselgel 60. The eluted crystalline **11** was recrystallized from 99% EtOH to give 3.0 g (79%) of **11**, m.p. 88.0–88.5°; $[\alpha]_D^{23} - 9.98°$ (c = 1.01, $CHCl_3$); ν_{max} 1510 (m), 1430 (s), 1180 (m), 1020 (m), 905 (m), 890 (m)cm^{-1}; δ 0.89 (6H, br), 1.0–2.0 (7H, br), 2.21 (6H, s), 3.83 (4H, s), 3.91 (1H, t, J = 6Hz), 6.90 (2H, s). Found: C, 69.36; H, 8.73. Calc for $C_{17}H_{26}S_2$: C, 69.33; H, 8.90%.

7,8-*Dimethyl*-3-[(R)-3-*methylpentyl*]-3-[(R)-3-*tetrahydropyranyloxybutyl*]-1,5-*dihydro*-2,4-*benzodithiepin* (R, R)-**12a**

n-BuLi in n-hexane (1.6N, 2.75 ml) was added dropwise to a stirred and cooled soln of **11** (1.00 g) in dry THF (12 ml) at $-10 \sim -5°$ under Ar. The soln immediately turned red by the formation of the carbanion. The stirring was continued for 30 min at 0–5°. A soln of (*R*)-**4** (1.20 g) in dry THF (4 ml) was added dropwise to a stirred soln at $-10 \sim -5°$. The stirring was continued for 2 h gradually raising the reaction temp to room temp. The soln was then poured into water and extracted with EtOAc. The EtOAc soln was washed with water, $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 2.0 g of an oil. This was chromatographed over Merck Kieselgel 60 to give 0.85 g (56%) of (*R*, *R*)-**12a**, ν_{max} 1510 (w), 1200 (m), 1130 (m), 1075 (m), 1030 (s), 1020 (s), 995 (s) cm^{-1}; δ 0.90 (6H, m), 1.12 (1.5H, d, J = 6Hz), 1.22 (1.5H, d, J-6Hz), 1.10–2.05 (17H), 2.19 (6H, s), 3.20–4.20 (3H, m), 3.80 (4H, s), 4.68 (1H, br), 6.85 (2H, s). This was employed in the next step without further purification.

7,8-*Dimethyl*-3-[(R)-3-*methylpentyl*]-3-[(S)-3-*tetrahydropyranyloxybutyl*]-1,5-*dihydro*-2,4-*benzodithiepin* (S, R)-**12a**

In the same manner as described for the preparation of (*R*, *R*)-**12a**, alkylation of **11** (2.49 g) with (*S*)-**4** (2.4 g) yielded (*S*, *R*)-**12a** (2.25 g, 59.1%), ν_{max} 1510 (w), 1200 (m), 1130 (m), 1070 (m), 1030 (s), 1020 (s), 995 (s) cm^{-1}; δ 0.89 (6H, m), 1.10 (1.5 H, d, J = 6 Hz), 1.20 (1.5H, d, J = 6Hz), 1.0–2.05 (17H), 2.16 (6H, s), 3.15–4.15 (3H, m), 3.78 (4H, s), 4.64 (1H, br), 6.80 (2H, s).

(2R, 8R)-8-*Methyl*-2-*decanol THP ether* (R, R)-**1b**

A mixture of (*R*, *R*)-**12a** (1.5 g) and Raney Ni (W-7, 20 g) in 99% EtOH (200 ml) was stirred and heated under reflux for 8 h. It was then filtered and the filtrate was concentrated *in vacuo*. The residue was diluted with ether and filtered. The filter cake was washed with THF. The combined ether-THF soln was concentrated *in vacuo* to give 1.0 g of an oil. This was chromatographed over Merck Kieselgel 60 to give 0.40 g (47%) of (*R*, *R*) – **1b**, ν_{max} 1130 (m), 1080 (m), 1020 (s), 995 (m) cm^{-1}. This was employed in the next step without further purification.

(2S, 8R)-8-*Methyl*-2-*decanol THP ether*, (S, R)-**1b**

A mixture of (*S*, *R*)-**12a** (2.0 g) and Raney Ni W-7 (14 g) in 99% EtOH (270 ml) was stirred and heated under reflux

for 1 h. Subsequent treatments as described for the preparation of (*R*, *R*)-**1b** yielded 960 mg (84%) of (*S*, *R*)-**1b**, ν_{max} 1135 (s), 1080 (s), 1030 (sh), 1020 (s), 995 (s) cm^{-1}.

(2*R*, 8*R*)-(−)-8-*Methyl*-2-*decanol* (R, R) − **1c**

A soln of (*R*, *R*)-**1b** (400 mg) in THF (5 ml)–AcOH (10 ml)–water (5 ml) was stirred overnight at room temp. It was then neutralized with solid Na_2CO_3 and extracted with ether. The ether soln was washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue (400 mg) was chromatographed over Merck Kieselgel 60 to give 248 mg (92%) of (*R*, *R*)-**1c**, b.p. 87–95° (bath temp)/5 mm, $n_D^{23.5}$ 1.4337; $[\alpha]_D^{23.5} - 14.9°$ (c=1.01, $CHCl_3$); ν_{max} 3360 (m), 1120 (m) cm^{-1}; δ 0.88 (6H, m), 1.13 (3H, d, $J = 6$ Hz), 1.0–1.7 (13 H), 2.83 (1H, br), 3.70 (1H, m). Found: C, 76.78; H, 13.86. Calc for $C_{11}H_{24}O$: C, 76.67; H, 14.04%. Its (*R*)-MTPA ester **1d** was prepared as usual and analyzed by NMR and HPLC: δ [60MHz, MTPA ester (42.1 mg) and Eu(fod)$_3$-d_{27} (15 mg) in CCl_4 (0.25 ml)] 4.96 (3H, OMe); HPLC (Shimadzu LC-2, column: Partisil 5, 25cm × 4.6 mm; solvent: n-hexane–$ClCH_2CH_2Cl$–MeOH (90 : 1 : 1/90), 30 kg/cm^2; detector: SPD-1, 217 nm): R_t 46.1 min (single peak). (R, R)-**1c** was therefore 100% optically pure at C-2.

(2S, 8R)-(−)-8-*Methyl*-2-*decanol* (S, R)-**1c**

In the same manner as described for the preparation of (*R*, *R*)-**1c**, 960 mg of (*S*, *R*)-**1b** yielded 555 mg (86%) of (*S*, *R*)-**1c**. This was further purified by preparative GLC (column: 5% PEG 20M, 2m × 6mm at 130°; carrier gas: N_2, 33 ml/min): R_t: *ca* 8 min) to give 339 mg of pure (*S*, *R*)-**1c**, bp 104° (bath temp)/10 mm, $n_D^{21.5}$ 1.4339; $[\alpha]_D^{21.5} - 1.32°$ (c = 1.19, $CHCl_3$); ν_{max} 3350 (m), 1120 (m) cm^{-1}; δ 0.88 (6H, m), 1.12 (3H, d, $J = 6$Hz), 1.0–1.9 (13H, m), 2.80 (1H, br), 3.70 (1H, m). Found: C, 76.74; H, 14.09. Calc for $C_{11}H_{24}O$: C, 76.67; H, 14.04%. Its (*R*)-MTPA ester **1d** was prepared as usual and analyzed by NMR and HPLC: δ [60MHz, MTPA ester (42.4 mg) and Eu(fod)$_3$-d_{27} (15 mg) in CCl_4 (0.25 ml)] 4.71 (3H, OMe); HPLC (Shimadzu LC-2, column: Partisil 5, 25 cm × 4.6 mm; solvent: *n*-hexane–$ClCH_2CH_2Cl$–MeOH (90 : 1 : 1/90), 30 kg/cm^2; detector: SPD-1, 217 nm): R_t 40.9 min (single peak). (*S*, *R*)-**1c** was therefore 100% optically pure at C-2.

The propionate of (2R, 8R)-8-*methyl*-2-*decanol* (R, R)-**1a**

EtCOCl (0.139 ml, 148 mg) was added to a stirred soln of (*R*, *R*)-**1c** (200 mg) in dry C_5H_5N (11 ml). After stirring overnight at room temp, the mixture was poured into N HCl and extracted with ether. The ether soln was washed with water, sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed over Merck Kieselgel 60 to give 241 mg (88.9%) of pure (*R*, *R*)-**1a**, b.p. 95–98° (bath temp)/5 mm, n_D^{23} 1.4248; $[\alpha]_D^{23} - 7.57°$ (c = 1.05, $CHCl_3$); ν_{max} 2970 (s), 2940 (s), 2860 (s), 1740 (s), 1460 (m), 1375 (m), 1335 (w), 1270 (w), 1195 (s), 1125 (m), 1080 (m), 1075 (sh), 1005 (w), 920 (w), 805 (w) cm^{-1}: δ 0.89 (9H, m), 1.18 (3H, d, $J = 7$Hz), 1.05–1.80 (13H, m), 2.26 (2H, q, $J = 7$Hz), 4.96 (1H, m); MS: *m*/*z* 57 (100%, base peak), 70 (50%), 75 (17%), 83 (31%), 101 (26%), 125 (31%), 139 (4%), 154 (9%). Found: C, 73.75; H, 12.31. Calc for $C_{14}H_{28}O_2$: C, 73.63; H, 12.36%. GLC analysis revealed this to be 98.8% pure.

The propionate of (2S, 8R)-8-*methyl*-2-*decanol* (S, R)-**1a**

In the same manner as described above for the preparation of (*R*, *R*)-**1a**, 270 mg of (*S*, *R*)-**1c** gave 314 mg (88%) of (*S*, *R*)-**1a**, bp 104°/5 mm; n_D^{21} 1.4249; $[\alpha]_D^{21} - 4.25°$ (c = 1.11, $CHCl_3$); ν_{max} 2950 (s), 2930 (s), 2850 (s), 1740 (s), 1460 (m), 1375 (m), 1335 (w), 1270 (w), 1190 (s), 1120 (m), 1080 (m), 1070 (sh), 1005 (w), 920 (w), 800 (w) cm^{-1}; δ 0.88 (9H, m), 1.15 (3H, d, $J = 7$Hz), 1.00–1.80 (13H, m), 2.28 (2H, q, $J = 7$Hz), 4.88 (1H, m); MS: *m*/*z* 57 (100%, base peak), 70 (55%), 75 (17%), 83 (28%), 101 (33%), 125 (31%), 139 (2%), 154 (10%). (Found: C, 73.41; H, 12.32. Calc for $C_{14}H_{28}O_2$: C, 73.63; H, 12.36%). GLC analysis revealed this to be 99.5% pure.

Acknowledgements—We thank Prof K. Tomita, Kyoto University, for kindly providing his strain of *Z. ramigera* to us. We also thank Prof D. Seebach, Swiss Federal Institute of Technology, for informing us of his own work on the utilization of PHB. Mr T. Sugai's assistance in the microbial work is gratefully acknowledged. This work was supported by a Grant-in-Aid for Special Project Research from the Japanese Ministry of Education, Science and Culture.

REFERENCES

[1]J. H. Tumlinson, *Les Médiateurs Chimiques Agissant sur le Comportement des Insectes* (Les colloques de l'INRA, N° 7), pp. 193-201. Institut National de la Recherche Agronomique, Paris (1982).
[2]P. L. Guss, J. H. Tumlinson, P. E. Sonnet and A. T. Proveaux, *J. Chem. Ecol.* **8**, 545 (1982).
[3]P. E. Sonnet and R. R. Heath, *Chiral Insect Sex Pheromones: Some Aspects of Synthesis and Analysis, A. C. S. Symposium Series* No. 190, Edited by B. A. Leonhardt and M. Beroza, American Chemical Society, Washington, D.C. (1982). pp. 61–85.
[4]K. Mori, H. Hashimoto, Y. Takenaka and T. Takigawa, *Synthesis* 720 (1975).
[5]K. Mori, T. Suguro and M. Uchida, *Tetrahedron* **34**, 3119 (1978).
[6]K. Mori and S. Kuwahara, *Ibid.* **38**, 521 (1982).
[7]K. Mori, S. Kuwahara, H. Z. Levinson and A. R. Levinson, *Ibid* **38**, 2291 (1982).
[8]K. Mori and K. Tanida, *Ibid.* **37**, 3221 (1981).
[9]T Fukui, A. Yoshimoto, M. Matsumoto, S. Hosokawa, T. Saito, H. Nishikawa and K. Tomita, *Arch. Microbiol.* **110**, 149 (1976).
[10]D. Seebach and M. Züger, *Helv. Chim. Acta* **65**, 495 (1982).
[11]T. Sugai, M. Fujita and K. Mori, *Nippon Kagakukaishi* (*J. Chem. Soc. Japan*), 1315 (1983).
[12]K. Mori, *Tetrahedron* **37**, 1341 (1981).
[13]K. Hintzer, B. Koppenhoefer and V. Schurig, *J. Org. Chem.* **47**, 3850 (1982).
[14]E. Hungerbühler, D. Seebach and D. Wasmuth, *Helv. Chim. Acta* **64**, 1467 (1981).