EFFECTIVE SYNTHESIS OF (4R,8R)- AND (4R,8S)-ENANTIOMERS of 4,8-DIMETHYLDECANAL, THE AGGREGATIONAL PHEROMONE OF THE BEETLES *TRIBOLIUM CONFUSUM* AND *TRIBOLIUM CASTANEUM*

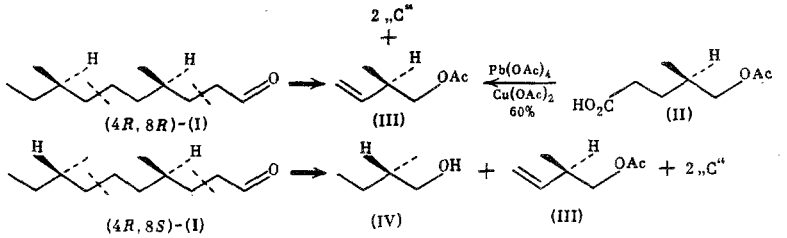
B. A. Cheskis, K. V. Lebedeva, and A. M. Moiseenkov

UDC 542.91:547.281.76:632.936.2

The small meal worm *Tribolium confusum* and the tenebrionid beetle *T. castaneum* are among the most dangerous and widely distributed grain and grain product pests. Their aggregational pheromone has been identified as 4,8-dimethyldecanal (I) [1]. When the racemic compound (I) was synthesized [1], it was found that its attractant properties were lower by an order of magnitude than those of the natural product. The four possible optical isomers of (I) were synthesized starting from (R)-citronellol and (R)-citronellic acid [2, 3]. Their bioassay showed that the pheromone has the (4R,8R)-configuration [2, 3]. Moreover, it was shown that a 4:1 isomeric mixture of (4R,8R)-(I) and (4R,8S)-(I) is by about an order of magnitude more active than the individual (4R,8R)-(I) [3, 4].

The aim of the present work was to synthesize optically pure (4R,8R)- and (4R,8S)-(I) starting from acetoxy acid (II), which is formed in the oxidative cleavage of the side chain of several (25R)-sapogenins [5] and industrial (S)-2-methylbutanol (IV).

Retrosynthetic analysis showed that both isomers (I) can be constructed by first generating the C_{10}-fragment of these molecules through the single syntone (III) and then introducing two additional carbon atoms:



In accordance with accepted procedure, optically pure acid (II) was subjected to oxidative decarboxylation in the presence of $Pb(OAc)_4$, pyridine, and catalytic amounts of $Cu(OAc)_2$ [6] to give the previously unreported acetate (III). The maximum yield(60%) was obtained by using an almost two-fold [with respect to (II)] excess of $Pb(OAc)_4$. Hydroboration — oxidation of olefin (III) with 9-borabicyclo[3.3.1]nonane (BBN) and H_2O_2 in acetate buffer — gave a quantitative yield of the previously unknown hydroxyacetate (V). At this stage the use of $n\text{-}Pr_2BH$ instead of BBN sharply lowers the yield of (V), probably because of the partial reduction of the acetoxy group. Oxidation of (V) with pyridinium chlorochromate (XXII) readily afforded one of the required fragments, the previously unknown acetoxyaldehyde (VI).

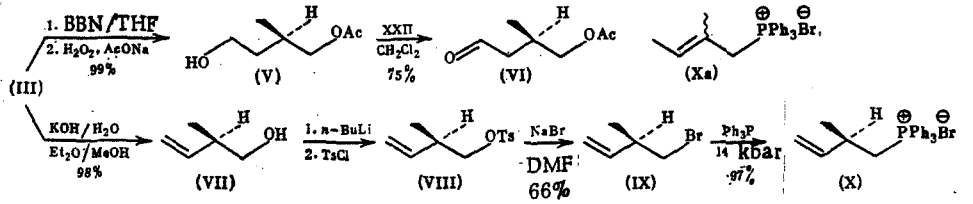
To obtain the second structural unit (X) in the synthesis of (4R,8R)-(I), acetate (III) was first saponified to alcohol (VII). The attempt to convert it directly to bromide (IX) in the presence of PBr_3 and pyridine afforded the corresponding phosphite as the major product. Therefore, the desired bromide (IX) was obtained by means of tosylate (VIII), which was used without further purification in an exchange reaction with NaBr to give bromide (IX) in a yield of 66%, based on (VII). The physicochemical characteristics of these two very volatile substances coincided with those published earlier for their racemates [7, 8].

The reaction of bromide (IX) with Ph_3P under standard conditions for obtaining phosphonium salts unexpectedly produced allyl salt (Xa) as the major product (as a mixture of

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow.
Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 4, pp. 865-871, April, 1988. Original article submitted May 19, 1986.

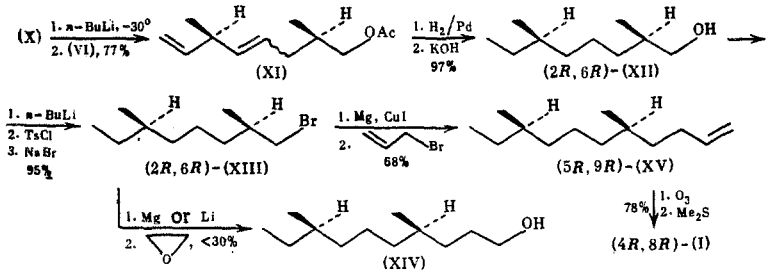
0568-5230/88/3704-0745$12.50

Z/E-isomers in a ratio of about 1:1). This was determined by comparing the integral intensities of the CH_3-group signals (δ 1.32 and 1.34 ppm) and of the CH_2-group doublets (δ 4.25 and 4.30 ppm) in the PMR spectrum of the reaction products. On the basis of the same spectrum, the required phosphonium salt (X) was formed in a yield of only about 30%; therefore, it was obtained by using the high pressure method [9]. Thus sodium bromide salt (IX), in the presence of a 10% excess of Ph_3P at 80°C and 14 kbar, afforded an almost quantitative yield of salt (X) in 5 h. The yield of the salt at a pressure of 5 kbar did not exceed 50% after 20 h at the same temperature.



The observed conversion sequence of acetoxy acid (II) to the previously unreported key syntones (VI) and (X) opens the possibility that they may be coupled by the Wittig reaction without affecting the chiral centers to yield the monoterpene fragment (XI) of the desired molecule (4R,8R)-(I). The previously unknown diene (XI) was obtained as an admixture of geometric isomers Z/E ≈ 85:15, which was determined by the NMR method. Specifically, the PMR spectrum (250 MHz) of the mixture contains two multiplets of the bis-allyl methine proton HC^6 at δ 3.15 and 2.83 ppm with the specified integral intensity ratio, and also two corresponding doublets of the CH_3—C^6 group at δ 1.06 and 1.09 ppm. The correlation between these signal pairs was confirmed by the double resonance method. The configuration of isomers (XI) was assigned on the basis of the ^{13}C NMR spectrum of the mixture. In accordance with results of partial proton uncoupling and ^{13}C NMR data [10, 11] for 1,2-disubstituted olefins, the intense signals at δ 31.1 and 35.5 ppm were assigned to allyl atoms C^3 and C^6 of the Z-isomer, and the low-intensity signals at δ 36.4 and 40.2 ppm were assigned to the same carbon atoms of the E-isomer.

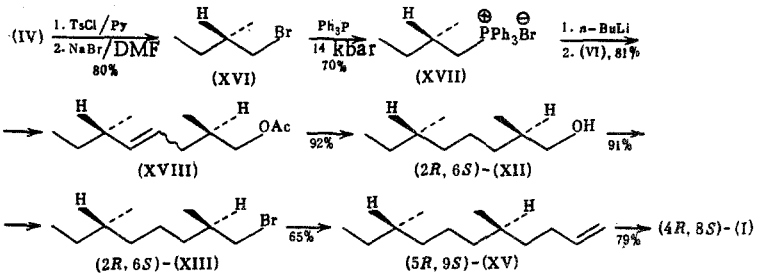
Hydrogenation of compound (XI) on a Pd catalyst and subsequent saponification of the unseparated saturated acetate afforded alcohol (2R,6R)-(XII) [12] as a racemate. This compound was converted, in a manner similar to (VII), to the previously unreported bromide (2R,6R)-(XIII) in a high overall yield.



The final stage in the synthesis of (4R,8R)-(I) required extending the carbon chain of the (2R,6R)-(XIII) molecule by adding a CH_2CHO fragment. For this purpose we planned to obtain racemic alcohol (XIV) [13] by the reaction by ethylene oxide with the Mg or Li derivative of bromide (2R,6R)-(XIII). However, this reaction afforded compound (XIV) in a yield of up to 30%. The condensation of the Grignard reagent prepared from (2R,6R)-(XIII) with allyl bromide, catalyzed by CuI, proved to be a much more effective method, readily affording the previously unreported olefin (5R,9R)-(XV). Ozonolysis of the latter afforded the desired aldehyde (4R,8R)-(I) in an overall yield of 10% with respect to the original acid (II).

Compound (4R,8S)-(I) was synthesized in a similar manner from alcohol (IV) and acid (II). Compound (IV) was converted in sequence to bromide (XVI) [14] and phosphonium salt (XVII) [15], from which the previously unreported olefin (XVIII) was obtained as a Z/E ≈ 9:1 mixture

by a Wittig reaction with compound (VI); the structure of (XVIII) was confirmed from GLC data and its PMR spectrum. The PMR spectrum, as that of (XI), contains doublet pairs at 0.94 and 0.96 ppm (CH_3—C^6) corresponding to the Z- and E-isomers of (XVIII), and also doublet pairs at 0.92 and 0.90 ppm (CH_3—C^2) with the specified integral intensity ratio. The conversion of (XVIII) to the desired enantiomer (4R,8S)-(I) was carried out as described above, through intermediate stages involving alcohol (2R,6S)-(XII), bromide (2R,6S)-(XIII), and olefin (5R,9S)-(XV), with overall yields of 15 and 19% with respect to original compounds (II) and (IV), respectively.



The physicochemical characteristics of the synthesized pheromone (4R,8R)-(I) and its synergist (4R,8S)-(I), including $[\alpha]_D$, almost completely coincided with the published data [2, 3].

Thus the effective synthesis of optically pure (4R,8R)- and (4R,8S)-4,8-dimethyldecanals, meal worm attractants, was accomplished starting from the readily available acid (II) and alcohol (IV).

EXPERIMENTAL

IR spectra were obtained in $CHCl_3$ on a UR-20 instrument; UV spectra of alcoholic solutions were obtained on a Specord UV-VIS spectrometer. NMR spectra, relative to TMS, were measured on Varian DA 60-IL or Bruker WM-250 spectrometers. Mass spectra were obtained on Varian MAT CH-6 or LKB-2091 spectrometers at an ionizing voltage of 70 eV. GLC was carried out on a LKhM-80 instrument (column size, 3 m × 3 mm, with 15% Carbowax 20 M on Chromatone N-AW-HMDS). Optical rotation was measured on a Perkin—Elmer 141 polarimeter at 20 ± 2°C in $CHCl_3$.

Acetoxy Acid (II). This acid is a colorless liquid with a bp of 109-111°C (0.5 mm), n_D^{25} 1.4375, $[\alpha]_D$ +7.0° (c 20), [5]: bp 158-160°C (10 mm), n_D^{26} 1.4388, $[\alpha]_D$ +7.2° (c 20.7, $CHCl_3$), 97% optical purity.

(R)-2-Methylbut-3-enyl Acetate (III). A 60.8-g quantity (137 mmoles) of $Pb(OAc)_4$ was added in portions to a mixed suspension (at 75°C) containing 15 g (86 mmoles) of compound (II), 2 g (10 mmoles) $Cu(OAc)_2 \cdot H_2O$, and 5 ml Py in 150 ml benzene (Ar); the mixture was boiled at a uniform rate. After addition of $Pb(OAc)_4$, the mixture was boiled for 30 min, cooled to 25°C, diluted with 200 ml ether, and filtered through 70 g SiO_2. The filtrate was washed with saturated aqueous $NaHCO_3$ and NaCl, dried with $MgSO_4$, concentrated at atmospheric pressure, and distilled. A 6.6-g yield (60%) of compound (III) was obtained; bp 50°C (25 mm), n_D^{20} 1.4150, $[\alpha]_D$ +11.1° (c 10). IR spectrum (ν, cm^{-1}): 920, 1000, 1040, 1090, 1250, 1265, 1375, 1390, 1420, 1460, 1645, 1740, 2880, 2975, 3045, 3085. PMR spectrum (60 MHz, CCl_4, δ, ppm, J, Hz): 1.01 d (3H, CH_3, J = 7), 1.95 s (3H, CH_3CO), 2.46 m (1H, CH), 3.87 br. d (2H, CH_2O, J = 7) 4.8-6.0 m (3H, CH_2=CH). Mass spectrum m/z (%): 98(5), 73(11), 68(22), 67(5), 55(3), 53(3), 43(100), 41(4). Found: C 65.72; H 9.42%. $C_7H_{12}O$. Calculated: C 65.60; H 9.44%.

(R)-2-Methyl-4-hydroxbutyl Acetate (V). A solution containing 1.1 g (8.6 mmoles) of compound (III) in 5 ml THF was added after 15 min to a mixed suspension (at 10°C) containing 1.5 g (12 mmoles) BBN in 15 ml THF (Ar). After 1 h the mixture was cooled to 0°C and was treated first with 2.5 g (30.5 mmoles) AcONa in 6 ml H_2O and then (after 30 min) with 9 ml (87 mmoles) 30% H_2O_2. The mixture was stirred for 2 h at 25°C, diluted with 30 ml ether, washed with saturated aqueous NaCl, dried with $MgSO_4$, and concentrated. The residue was chromatographed on 60 g SiO_2. Gradient elution from hexane to ether (up to 45% of the

latter) yielded 1.24 g (99%) of compound (V); bp 65°C (0.5 mm), n_D^{20} 1.4351, $[\alpha]_D$ −1.4° (c 5). IR spectrum (ν, cm^{-1}): 915, 985, 1040, 1060, 1245, 1370, 1390, 1425, 1475, 1740, 2885, 2940, 2965, 3470, 3640. PMR spectrum (60 MHz, $CDCl_3$, δ, ppm, J, Hz): 0.95 d (3H, CH_3, J = 6.5), 1.3-1.8 m (3H, HC^2, HC^3), 2.03 s (3H, CH_3CO), 3.68 t (2H, HC^4, J = 6.5), 3.93 d (2H, HC^1, J = 6.5). Mass spectrum, m/z (%): 116(1), 115(1), 103(5), 86(6), 85(14), 73(6), 72(7), 71(5), 68(10), 61(16), 58(6), 57(8), 56(51), 55(15), 45(5), 44(7), 43(100), 41(25). Found: C 57.47; H 9.87%. $C_7H_{14}O_3$. Calculated: C 57.51; H 9.65%.

(R(-2-Methyl-4-oxobutyl Acetate (VI). A suspension containing 3.12 g (14.5 mmoles) of compound (XXII) and 1.38 g (9.5 mmoles) of compound (V) in 25 ml CH_2Cl_2 was mixed for 2 h at 25°C; it was then diluted with 30 ml ether and filtered through 10 g SiO_2. The fitrate was concentrated in a vacuum and distilled. A 1.02-g yield (75%) of compound (VI) was obtained; bp 51°C (0.7 mm), n_D^{20} 1.4258, $[\alpha]_D$ +7.5 (c 5). IR spectrum (ν, cm^{-1}): 910, 945, 990, 1045, 1250, 1370, 1380, 1470, 1725, 2730, 2885, 2970, 3035. PMR spectrum (250 MHz, $CDCl_3$, δ, ppm, J, Hz): 1.01 d (3H, CH_3, J = 6.5), 1.9 m (1H, HC^2); 2.0 s (3H, CH_3CO), 2.4 m (2H, HC^3), 3.95 m (2H, HC^1), 78 t (1H, CHO, J = 2). Mass spectrum, m/z (%): 101(13), 100(7) 84(8), 83(5), 73(5), 72(6), 71(5), 69(7), 61(13), 58(7), 57(8), 56(29), 55(16), 44(16), 43(100), 41(15). Found: C 58.39; H 8.40%. $C_{17}H_{12}O_3$. Calculated: C 58.32; H 8.39%.

(R)-2-Methylbut-3-en-1-ol (VII). A mixed emulsion containing 0.9 g (7 mmoles) of compound (III) in 3 ml ether and 1 g (18 mmoles) KOH in 4 ml H_2O–MeOH (1:1) was allowed to stand for 1 h at 25°C and then diluted with ether. The organic layer was separated, neutralized with 3% HCl, dried with $MgSO_4$, concentrated at atmospheric pressure, and distilled. A 0.59-g yield (98%) was obtained; bp 50°C (30 mm), n_D^{20} 1.4270, $[\alpha]_D$ +33.8° (c 5) (cf. [7], bp 128-129°C). PMR spectrum (60 MHz, $CDCl_3$, δ, ppm, J, Hz): 0.98 d (3H, CH_3, J = 7), 2.4 m (1H, CH), 3.43 d (2H, CH_2O, J = 6.5), 4.8-6.0 m (3H, CH_2=CH).

(R)-1-Tosyloxy-2-methylbut-3-ene (VIII) and (R)-4-Bromo-3-methylbut-1-ene (1X). A 1.5-M n-BuLi solution in hexane was added dropwise to a mixed solution (at −20°C) containing 4 g (46.5 mmoles) of compound (VII) and 5 mg triphenylmethane in 70 ml ether and 2 ml HMFA (Ar) until a stable rose color was obtained (30-35 ml, 45-50 mmoles). After 15 min, 10 g (52.5 mmoles) of TsCl was added at −30°C. The mixture was heated for 30 min to 25°C, diluted with 50 ml ether; washed with saturated NaCl solution, dried with $MgSO_4$, and concentrated in a vacuum. About 12 g of product was obtained, a part of which (about 0.3 g) was chromatographed on 10 g SiO_2. Gradient elution from hexane to ether (up to 30% of the latter) afforded an analytic sample of tosylate (VIII) in the form of an oil; $[\alpha]_D$ −4.8° (c 5). IR spectrum (ν, cm^{-1}): 820, 850, 930, 945, 970, 1020, 1100, 1180, 1190, 1245, 1290, 1310, 1360, 1420, 1460, 1500, 1600, 1645, 2885, 2940, 2986, 3040. UV spectrum (λ_{max}, nm (ε)): 225 (13 200)), 262(600). PMR spectrum (60 MHz, $CDCl_3$, δ, ppm, J, Hz): 0.99 d (3H, CH_3C^2, J = 7), 2.43 s (3H, CH_3), 2.5 m (1H, HC^2), 3.87 br. d (2H, CH_2O, J = 7), 4.8-6.0 m (3H, CH_2=CH, 7.32 br. d and 7.77 br. d (4H, C_6H_4, J = 8). Mass spectrum, m/z(%): 185(2), 173(7), 155(72), 91(100), 68(83), 65(33), 55(42), 44(89), 43(75), 40(100). Found: C 59.76; H 6.78; S 13.61%. $C_{12}H_{16}O_3S$. Calculated: C 59.97; H 6.71; S 13.35%.

The crude tosylate (VIII) suspension and 30 g (0.29 mmole) NaBr in 150 ml DMF were mixed for 2 h at 60-65°C, diluted with 100 ml H_2O, and extracted with pentane. The extract was dried with $MgSO_4$, filtered through 10 g SiO_2, concentrated at atmospheric pressure, and distilled. A 4.55-g yield (66%) of compound (IX) was obtained; bp 48°C (75 mm), n_D^{20} 1.4600, $[\alpha]_D$ +11.1° (c 5) [cf. [8], bp 111-114°C (760 mm]. PMR spectrum (60 MHz, $CDCl_3$, δ, ppm, J, Hz): 1.13 d (3H, CH_3, J = 6.5), 2.54 m (1H, CH), 3.32 d (2H, CH_2Br, J = 6.5). 4.9-6.1 m (3H, CH_2=CH).

(S)-1-Bromo-2-methylbutane (XVI). A 8.29-g portion (43.5 mmoles) of TsCl was added for 5 min to a solution containing 3.3 g (37.5 mmoles) technical-grade (IV) [TU 6-09-06-838-76, $[\alpha]_D$ −5.5° (without solvent), 91% optical purity] in 50 ml Py at 0°C. The mixture was kept for 3 h at 0°C, decanted into 300 ml glacial 10% HCl, and extracted with ether. The extract was washed with saturated NaCl, dried with $MgSO_4$, and concentrated in a vacuum. The residue (~9 g) was mixed with 24 g (0.23 mole) NaBr in 120 ml DMF. As described above, this yielded 4.5 g (80%) of compound (XVI); bp 55°C (80 mm), n_D^{20} 1.4450, $[\alpha]_D$, +4.3° (c 5); cf. [14], bp 119°C, $[\alpha]_D$ +3.92° (without solvent). PMR spectrum (250 MHz, $CDCl_3$, δ, ppm, J, Hz): 0.91 t (3H, CH_3, J = 7.5), 1.02 d (3H, CH_3, J = 6.5), 1.2-1.6 m (2H, CH_2), 1.73 m (1H, CH), 3.37 m (2H, CH_2Br).

2-Methylbut-2E/Z-en-1-yltriphenylphosphonium Bromide (Xa). A solution containing 0.7 g (4.7 mmoles) of compound (IX) and 1.45 g (5.5 mmoles) Ph_3P in 5 ml THF was heated at 120-130°C in a sealed glass ampul util precipitate formation ceased (about 10 h). The preci-

pitate was filtered and washed with ether. A 1.84-g yield (95%) of a product containing about 70% of compound (Xa) was obtained; mp 138-142°C. PMR spectrum (250 MHz, CD_3OD, δ, ppm, J, Hz): 1.32 br. s and 1.34 br. s (3H, CH_3C^2), 1.72 br. d (3H, CH_3, J = 6), 4.25 br. d and 4.30 br. d (2H, CH_2, J = 8), 5.18 br. q (1H, CH, J = 6), 7.8 m (15H, C_6H_5).

(R)-2-Methylbut-3-en-1-yltriphenylphosphonium Bromide (X). A mixture containing 1.15 g (7.7 mmoles) of compound (IX), 2.3 g (8.8 mmoles) PH_3P, and 1 ml THF was kept for 5 h in a Teflon ampul at 80°C and 14 kbar. The crystalline product that was formed was washed with ether and dried in a vacuum. A 3.08-g yield (97%) of compound (X) was obtained; mp 145-146°C, $[\alpha]_D$ −4.6° (c 10). IR spectrum (KBr, ν, cm^{-1}): 505, 535, 695, 730, 755, 1000, 1110, 1325, 1440, 1585, 1640, 2790, 2860, 2990, 3000, 3050. UV spectrum (λ_{max}, nm, (ε)): 227 (26 700) 268(310). PMR spectrum (250 MHz, CD_3OD, δ, ppm, J, Hz): 1.18 br. d (3H, CH_3, J = 7), 2.7 m (1H, CH), 3.6 m (2H, CH_2P), 4.8 m (2H, H_2C=C), 5.7 m (1H, HC=C), 7.8 m (15H, C_6H_5). Mass spectrum, m/z (%): 331(4), 263(6), 262(33), 202(5), 184(6), 183(26), 152(4), 108(13), 107(7), 91(5), 81(5), 69(17), 68(16), 67(21), 60(24), 56(22), 55(12), 53(19), 45(41), 44(100), 43(73), 41(45), 39(25). Found: C 67.06; H 5.64; Br 19.13; P 7.36%. $C_{23}H_{24}BrP$. Calculated: C 67.16; H 5.88; Br 19.42; P 7.53%.

(S)-2-Methylbutyltriphenylphosphonium Bromide (XVII). In a similar manner 2.25 g (70%) of compound (XVII) was obtained from 1.18 g (7.8 mmoles) of compound (XVI) and 2.3 g (8.8 mmoles) Ph_3P; mp 156-157°C, $[\alpha]_D$ +78° (c 5); cf. [15], mp 153-155°C. PMR spectrum (250 MHz, CD_3OD, δ, ppm, J, Hz): 0.78 t (3H, CH_3 J = 7), 0.87 d (3H, CH_3, J = 6.5), 1.37 m (2H, CH_2), 1.86 m (1H, CH), 3.2 m (2H, CH_2P), 7.8 m (15H, C_6H_5).

(2R,6R)-2,6-Dimethylocta-4E/Z,7-dien-1-yl Acetate (XI). A 9.5-ml portion of 1.35 M n-BuLi in hexane (12.8 mmoles) was added after 20 min to a mixed suspension (at −30°C) containing 5.28 g (12.8 mmoles) compound (X) in 25 ml THF (Ar). The mixture was allowed to stand for 30 min and, after 15 min at −30°C, was treated with 1.85 g (12.8 mmoles) of compound (VI) in 4 ml THF. After 20 min the mixture was heated to 25°C; after 1 h it was diluted with 20 ml hexane and filtered through 7 g SiO_2. The filtrate was washed with saturated NaCl, dried with $MgSO_4$, concentrated in a vacuum, and distilled. A 1.93-g yield (77%) of compound (XI) was obtained; bp 57-59°C (1 mm), n_D^{20} 1.4470, $[\alpha]_D$ +53.6° (c 10). IR spectrum (ν, cm^{-1}): 610, 670, 790, 920, 995, 1040, 1250, 1370, 1390, 1460, 1635, 1725, 2880, 2935, 2970, 3020, 3090. PMR spectrum (250 MHz, $CDCl_3$, δ, ppm, J, Hz): 0.92 d and 0.95 d (3H, CH_3C^2, J = 7), 1.06 d and 1.09 d (3H, CH_3C^6, J = 7), 1.7-2.2 m (3H, HC^2, HC^3), 2.07 s (3H, CH_3CO), 2.83 m and 3.15 m (1H, HC^6), 3.92 m (2H, HC^1), 4.9-5.9 m (5H, HC=CH). ^{13}C NMR spectrum (62.89 MHz, $CDCl_3$, δ, ppm) for Z-(XI): 16.7 ($\underline{C}H_3$–C^2), 20.5 ($\underline{C}H_3$–C^6), 20.7 ($\underline{C}H_3CO$), 31.1 (C^3), 33.1 (C^2), 35.5 (C^6), 68.8 (C^1), 112.3 (C^8), 126.1 (C^4), 135.1 (C^5), 142.7 (C^7), 170.9 (C=O); for E-(XI): 16.5 ($\underline{C}H_3$–C^2), 19.9 ($\underline{C}H_3$–C^6), 20.7 ($\underline{C}H_3CO$), 32.9 (C^2), 36.4 (C^3), 40.2 (C^6), 68.8 (C^1), 112.6 (C^8), 126.3 (C^4), 136.3 (C^5), 143.0 (C^7), 170.9 (C=O). Mass spectrum, m/z(%): 136(12), 121(12), 107(28), 93(43), 81(28), 79(43), 67(23), 55(31), 43(100), 41(32). Found: C 73.41; H 10.25%. $C_{12}H_{20}O_2$. Calculated: C 73.43; H 10.27%

(2R,6S)-2,6-Dimethyloct-4E/Z-en-1-yl Acetate (XVIII). In a similar manner 2.64 g (6.4 mmoles) of compound (XVII) and 0.92 g (6.4 mmoles) of compound (VI) yielded 1.03 g (81%) of compound (XVIII); bp 55-56°C (1 mm), n_D^{21} 1.4362, $[\alpha]_D$ +14.1° (c 2.7). IR spectrum (ν, cm^{-1}): 610, 645, 850, 920, 950, 990, 1040, 1260, 1370, 1390, 1460, 1660, 1730, 2880, 2930, 2970, 3015. PMR spectrum (250 MHz, $CDCl_3$, δ, ppm, J, Hz): 0.83 t (3H, HC^8, J = 7), 0.90 d and 0.92 d (3H, CH_3C^2, J = 7) 0.94 d and 0.96 d (3H, CH_3C^6, J = 7), 1.28 m (2H, HC^7), 1.8-2.2 m (3H, HC^2, HC^3), 2.07 s (3H, CH_3CO), 2.32 m (1H, HC^6), 3.92 m (2H, HC^1), 5.1-5.4 m (2H, HC=CH). Mass spectrum, m/z (%): 138(21), 135(14), 109(65), 96(31), 81(36), 69(28), 55 (43), 43(100), 41(47). Found: C 72.99; H 11.34%. $C_{12}H_{22}O_2$. Calculated: C 72.68; H 11.18%.

(2R,6R)- and (2R,6S)-2,6-Dimethyloctanols (XII). A solution containing 1.66 g (8.5 mmoles) of compound (XI) in 15 ml EtOH was hydrogenated over 0.15 g of 5% Pd/C under standard conditions until H_2 absorption ceased (about 3 h). The catalyst was filtered, and 0.5 g (9 mmoles) KOH in 5 ml water was added to the filtrate. The mixture was kept for 2 h at 25°C (GLC control). It was then diluted with 50 ml ether, neutralized with 3% HCl, washed with saturated NaCl, dried with $MgSO_4$, and concentrated in a vacuum; the residue was distilled. A 1.3-g yield (97%) of (2R,6R)-(XII) was obtained; bp 60°C (1 mm), n_D^{20} 1.4371, $[\alpha]_D$ +6.9° (c 5) (cf. [12]: n_D^{20} 1.4368). PMR spectrum (60 MHz, $CDCl_3$, δ, ppm, J, Hz): 0.8-1.0 m (9H, CH_3), 1.1-1.3 m (8H, CH_2), 1.4-1.8 m (2H, CH), 3.44 br. d (2H, CH_2O, J = 6.5).

In a similar manner 0.79 g of compound (XVIII) yielded 0.58 g (92%) of (2R,6S)-(XII); bp 60°C (1 mm), n_D^{20} 1.4375, $[\alpha]_D$ +15.7°C (c 3). PMR spectrum (250 MHz, $CDCl_3$, δ, ppm, J, Hz): 0.83 d (3H, CH_3C^6, J = 6.5), 0.86 t (3H, HC^8, J = 6.5) 0.91 d (3H, CH_3C^2, J = 7), 1.0-1.4 m (9H, CH_2, HC^6), 1.6 m (1H, HC^2), 3.45 m (2H, CH_2O).

(2R,6R)- and (2R,6S)-1-Bromo-2,6-dimethyloctanes (XIII). In a manner analogous to that described for bromide (IX), 1.1 g (7 mmoles) of (2R,6R)-(XII) in 15 ml ether, about 5 ml of 1.5 M n-BuLi in hexane (about 7.5 mmoles), 1.5 g (7.9 mmoles) TsCl, and 4 g (39 mmoles) NaBr in 25 ml DMF yielded 1.47 g (95%) of (2R,6R)-(XIII); bp 45°C (0.7 mm), n_D^{20} 1.4565, $[\alpha]_D$ −3.1° (c 5). IR spectrum (ν, cm^{-1}): 530, 620, 650, 730, 935, 1070, 1185, 1240, 1380, 1465, 2860, 2875, 2930, 2960, 3015. PMR spectrum (250 MHz, $CDCl_3$, δ, ppm, J, Hz): 0.85 d (3H, CH_3C^6, J = 7), 0.88 t (3H, HC^8, J = 7), 1.01 d (3H, CH_3C^2, J = 7) 1.1-1.5 m (9H, HC^3, HC^4, HC^5, HC^6, HC^7), 1.8 m (1H, HC^2), 3.37 m (2H, CH_2Br). Mass spectrum, m/z (%): 165(16), 163(18), 111(22), 84(55), 69(65), 66(45), 57(100), 55(61), 43(97), 41(90). Found: C 54.58; H 9,57; Br 35.94%. $C_{10}H_{21}Br$. Calculated: C 54.30; H 9.57; Br 36.12%.

In a similar manner 0.45 g of (2R,6S)-(XII) yielded 0.56 g (91%) of compound (2R,6S)-(XIII); bp 50°C (1 mm), n_D^{20} 1.4565, $[\alpha]_D$ +3.2° (c 2). PMR spectrum (250 MHz, $CDCl_3$, δ, ppm, J, Hz): 0.85 d (3H, CH_3C^6, J = 6.5) 0.87 t (3H, HC^8, J = 6.5), 1.02 d (3H, CH_3C^2, J = 7), 1.1-1.5 m (9H, CH_2, HC^6), 1.8 m (1H, HC^2), 3.37 m (2H, CH_2Br).

(4R,8R)-4,8-Dimethyldecanol (XIV). A solution containing 0.27 g (6.1 mmoles) ethylene oxide in 2 ml ether was added after 10 min to a mixed (at 0°C) Grignard reagent obtained from 1.24 g (5.6 mmoles) (2R,6R)-(XIII) and 0.15 g (6.2 mg·atom) Mg in 6 ml ether. The mixture was mixed for 3 h at 0°C and was then heated for 30 min to 25°C. After 2 h it was decomposed with saturated NH_4Cl and filtered. The filtrate was washed with water, dried with $MgSO_4$, and concentrated in a vacuum. The residue (1.3 g) was chromatographed on 50 g SiO_2. Gradient elution from hexane to ether (to 20% of the latter) yielded 0.32 g (about 30%) of compound (XIV); bp 80-83°C (1 mm), n_D^{26} 1.4378 $[\alpha]_D$ −1.0° (c 5) [cf. [13], bp 72-73°C (0.3 mm)]. PMR spectrum (60 MHz, CCl_4, δ, ppm, J, Hz): 0.9 m (9H, CH_3), 1.2 m (12H, CH_2), 1.5 m (2H, CH), 3.51 t (2H, CH_2O, J = 6).

Similarly, the use of a Li derivative, obtained from 1.21 g (5.5 mmoles) (2R,6R)-(XIII) and 0.11 g (15.7 mg-atom) Li in 10 ml hexane and 0.33 g (7.5 mmoles) ethylene oxide, afforded 0.25 g (24%) of compound (XIV).

(5R,9R)- and (5R-9S)-5,9-Dimethylundecenes (XV). An 80-mg portion (0.4 mmoles) of CuI was added to a mixed Grignard reagent (at −30°C) prepared from 0.91 g (4.1 mmoles) (2R,6R)-(XIII) and 0.1 g (4.2 mg·atom) Mg in 7 ml THF. The suspension was mixed for 30 min at −20°C and then treated for 10 min at −40°C with 0.84 g (6.9 mmoles) allyl bromide in 2 ml THF. The mixture was heated for 40 min to 25°C. After 30 min it was decomposed with saturated NH_4Cl and filtered. The filtrate was washed with water, dried with $MgSO_4$, and concentrated in a vacuum. The residue (about 1 g) was chromatographed on 30 g SiO_2. Elution with hexane yielded 0.51 g (68%) of (5R, 9R)-(XV); bp 50°C (1 mm), n_D^{20} 1.4345, $[\alpha]_D$ −2.0° (c 5). IR spectrum (ν, cm^{-1}): 560, 645, 915, 1000, 1370, 1380, 1465, 1640, 2880, 2970, 3085. PMR spectrum (250 MHz, $CDCl_3$, δ, ppm): 0.9 m (9H, CH_3), 1.0-1.5 m (12H, CH, CH_2), 2.07 m (2H, HC^3), 4.9-5.1 m (2H, HC^1), 5.83 m (1H, HC^2). Mass spectrum, m/z(%): M^+ 182(4), 140(10), 125(6), 111(8), 97(16), 85(23), 84(18), 83(39), 71(39), 70(42), 69(47), 57(93), 56(83), 55(83), 43(100), 41(92), 39(30). Found: C 85.65; H 14.22%. $C_{13}H_{26}$. Calculated: C 85.63; H 14.37%.

Similarly, 0.5 g of (2R,6S)-(XIII) afforded 0.27 g (65%) of (5R,9S)-(XV); bp 45°C (0.8 mm), n_D^{21} 1.4339, $[\alpha]_D$ +8.2° (c 1.7). PMR spectrum (250 MHz, $CDCl_3$, δ, ppm): 0.88 m (9H, CH_3), 1.0-1.5 m (12H, CH, CH_2), 2.08 m (2H, HC^3), 4.9-5.1 m (2H, HC^1), 5.82 m (1H, HC^2).

(4R,8R)- and (4R,8S)-4,8-Dimethyldecanals (I). An ozone–air mixture (about 1% O_3) was bubbled (at −70°C) through a solution containing 0.3 g (1.6 mmoles) (5R,9R)-(XV) in 30 ml CH_2Cl_2 containing 0.3 ml Py till the disappearance of the original olefin (25 min, TLC control). The mixture was decanted into 15 ml of 5% Me_2S in MeOH. After 3 h it was washed with 1% HCl and saturated aqueous $NaHCO_3$ and NaCl, dried with Na_2SO_4, and concentrated in a vacuum. The residue (0.3 g) was chromatographed on 15 g SiO_2. Gradient elution from hexane to ether (up to 10% of the latter) and distillation of the product yielded 0.23 g (78%) of compound (4R,8R)-(I); bp 60°C (1 mm), n_D^{22} 1.4334, $[\alpha]_D$ −7.0° (c 1) [cf. [2], bp 65°C (2.5 mm), n_D^{22} 1.4336, $[\alpha]_D^{22.5}$ −7.37° (c 2.04, $CHCl_3$). PMR spectrum (250 MHz, $CDCl_3$, δ, ppm): 0.85 m (9H, CH_3), 1.0-1.8 m (12H, CH, CH_2), 2.41 m (2H, HC^2), 9.78 t (1H, CHO, J = 1.8 Hz).

Similarly, 0.1 g of (5R,9S)-(XV) afforded 80 mg (79%) of compound (4R,8S)-(I); bp 65-70°C (1 mm) (bath), n_D^{19} 1.4370, $[\alpha]_D$ +10.9° (c 1) [cf. [3], bp 78-79°C (5 mm), n_D^{21} 1.4346, $[\alpha]_D^{21}$ +10.8° (c 2.39, $CHCl_3$)]. PMR spectrum (250 MHz, $CDCl_3$, δ, ppm): 0.85 m (9H, CH_3), 1.0-1.8 m (12H, CH, CH_2), 2.43 m (2H, HC^2), 9.79 t (1H, CHO, J = 1.8 Hz).

CONCLUSIONS

1. The effective synthesis of optically pure (4R,8R)-(−)-4,8-dimethyldecanal, the aggregational pheromone of meal worms, and of its synergist, (4R,8S)-(+)-4,8-dimethyldecanal, is described.

2. The readily available (R)-(+)-4-methyl-5-acetoxyvaleric acid was used for the first time as a chiral source for the synthesis of optically active natural compounds.

LITERATURE CITED

1. T. Suzuki, Agric. Biol. Chem., 45, 2641 (1981).
2. K. Mori, S. Kuwahara, and H. Ueda, Tetrahedron, 39, 2439 (1983).
3. K. Mori, M. Kato, and S. Kuwahara, Leibigs Ann. Chem., 861 (1985).
4. T. Suzuki, J. Kozaki, R. Sugawara, and K. Mori, Appl. Entomol. Zool., 19, 15 (1984).
5. R. Brettle and F. S. Holland, J. Chem. Soc., 4836 (1962).
6. R. A. Sheldon and J. K. Kochi, in: Organic Reactions, Vol. 19, Wiley, New York (1972), p. 279.
7. G. Piankatelli and A. Scettri, Gazz. Chim. Ital., 104, 343 (1974).
8. R. G. Almquist, J. Craze, C. Jennings-White, et al., J. Med. Chem., 25, 1292 (1982).
9. A. M. Moiseenkov, I. M. Zaks, and B. S. Él'yanov, Zh. Obshch. Khim., 53, 1260 (1983).
10. D. E. Dorman, M. Jautelat, and J. D. Roberts, J. Org. Chem., 36, 2757 (1971).
11. J. W. De Haan and I. J. M. Van de Ven, Org. Magn. Reson., 5, 147 (1973).
12. W. J. Houlihan, Perfum. Essent. Oil Record., 52, 781 (1962).
13. M. M. Martin and J. G. MacConnell, Tetrahedron, 26, 307 (1970).
14. K. Mori, Tetrahedron, 30, 3817 (1974).
15. M. Kobayashi, T. Minamizawa, and H. Mitsuhashi, Steroids, 29, 823 (1977).