Note

Synthesis of the Enantiomers of 14-Methyl-1-octadecene, the Sex Pheromone of the Peach Leafminer Moth†

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The peach leafminer moth (Lyonetia clerkella L.) is one of the serious pests in peach orchards in Japan. In 1984, Sugie et al. identified its sex pheromone as 14-methyl-1-octadecene 1.1) Their synthetic (+)-1 was as active as a crude extract from virgin females of L. clerkella under field conditions.1) Another synthesis of (+)-1 was reported recently.2) Nothing is known, however, about the absolute configuration at C-14 of the natural pheromone 1. Herein we describe a short synthesis of both the enantiomers of 1.

As our chiral starting materials we used the enantiomers of methyl β-hydroxyisobutyrate 2. Both the enantiomers of β-hydroxyisobutyric acid recently became available by microbial oxidation of isobutyric acid employing Candida rugosa IFO 0750 and IFO 1542, respectively.3)

As shown in the scheme, our synthesis was simple and straightforward. Conversion of (R)-2 into (R)-3 was carried out as reported previously.4) Treatment of (R)-3 with n-propylmagnesium bromide in the presence of dilithium tetrachlorocuprate5,6) was followed by removal of the tetrahydropyranyl group with acid to give (S)-4a. The corresponding tosylate (S)-4b was treated with 11-dodecenylmagnesium bromide in the presence of dilithium tetrachlorocuprate to furnish crude (S)-1. This was repeatedly chromatographed over silica gel impregnated with silver nitrate to give pure (S)-1, [α]D21 +1.21° (n-hexane). The repeated chromatography at this stage caused a loss of the material and the overall yield of (S)-1 from (R)-2 was 6.5%. The optical purity of (S)-1 was thought to be ≥95%, since we started from (R)-2 of 95.8% e.e. as estimated by an HPLC analysis of the (R)-α-methoxy-α-trifluoromethylphenylacetate [(R)-MTPA ester] of (R)-2.4) In the same manner, (R)-1, [α]D21 1.06° (n-hexane) was prepared from (S)-2 in a 9.4% overall yield. The optical purity of (R)-1 was also thought to be ≥95%, considering the high enantiomeric excess (97.8%) of (S)-2 as determined by an HPLC analysis of the corresponding (R)-MTPA ester.4) It should be added that, in the present synthesis, we used no reaction which might cause racemization at the chiral center.

In summary, we prepared both the enantiomers of 14-methyl-1-octadecene 1. A biological study will reveal the stereochemistry-activity relationship in the perception of this sex pheromone.

EXPERIMENTAL

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

(S)-(-)-2-Methyl-1-hexanol (S)-4a. A solution of n-PrMgBr in THF was prepared from n-PrBr (62.4g, 507mmol) and Mg (12.3g, 506mg atom) in dry THF (400ml). A solution of Li2CuCl4 in THF (0.1 m, 68ml, 6.8mmol) was added dropwise to the stirred and ice-cooled suspension of n-PrMgBr under Ar to give a grayish purple suspension, to which was added dropwise a solution of (R)-3 (5.56g, 16.9mmol) in dry THF (30ml) at 0°C. After stirring overnight at 0°C, the mixture was poured into an ice and saturated NH4Cl solution, and then extracted with ether. The ether solution was worked up as usual, and the residual oil was dissolved in MeOH (120ml) containing p-TsOH (0.15 g). The solution was stirred and heated under reflux for 2 hr. It was then neutralized with K2CO3 (0.2g). A usual work-up of the mixture was followed by distillation of the crude product to give 1.41 g (71.9%) of (S)-4a, bp 93°C/50mmHg, nD21 1.4212; [α]D -13.5° (c=21.6, ether); IR ν̂ cm-1: 3350 (s), 1040 (s); NMR (CDCl3) δ: 0.89 (3H, t, /=6Hz), 0.90 (3H, d, J=6Hz), 0.90 (8H, dd, J1=5.4Hz, J2=6.6Hz); GLC: column, 3% SE-30, 2m x 4mm at 60°C; N2 at 1.1 kg/cm2; tR 6.6 min (single peak).


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(R)-(+)−2-Methyl-1-hexanol (R)-4a. In the same manner as already described, (S)-3 (7.39 g) gave 906 mg (67.8%) of (R)-4a as a colorless oil, bp 99°C/25mmHg, \( n_\text{D}^0 \) 1.4211; \( [\alpha]_D^0 +13.6^\circ \) (c=21.5, ether) \[lit.7] for optically impure (fl)-4a: \( [\alpha]_D^0 +2.47^\circ \) (c=21.9, ether). Anal. Found: C, 72.32; H, 13.79. Calcd. for C\(_7\)H\(_{16}\)O: C, 72.35; H, 13.88%.

The IR and NMR spectra of (R)-4a were identical with those of (S)-4a. (R)-4a was gas-chromatographically pure.

(S)-2-Methylhexyl tosylate (S)-4b. a-TsCl (1.4g, 7.3mmol) was added to a stirred and ice-cooled solution of (S)-4a (580mg, 5.0mmol) in dry pyridine (3ml). The mixture was stirred for 6hr at 0°C. Subsequent work-up gave 1.33g (98.2%) of (S)-4b as a colorless oil, IR \( v \) cm\(^{-1}\): 1360 (s), 1190 (s), 1180 (s). This was employed in the next step without further purification.

(R)-2-Methylhexyl tosylate (R)-4b. In the same manner as already described. (R)-4a (355mg) yielded (R)-4b (807mg, 97.3%) as an oil.

(S)-{+)-14-Methyl-l-octadecene (S)-1. A solution of 5 in THF was prepared from 11-dodecenyl bromide (2.9g, 11.7mmol) and Mg (0.27g, 11.1mg atom) in dry THF (25ml), employing a few drops of 1,2-dibromoethane as the initiator. To a stirred and cooled solution of (S)-4b (1.00g, 3.69mmol) in dry THF (6ml) at -70°C under Ar was added dropwise the solution of 5, followed by a solution of Li\(_2\)CuCl\(_4\) (0.1 m, 1.8ml, 0.18mmol). The resulting mixture was allowed to warm to room temperature during 2hr and the stirring was continued overnight. It was then poured into an ice and saturated NH\(_4\)Cl solution and extracted with \( \theta \)-hexane. The \( \theta \)-hexane solution was washed with saturated NH\(_4\)Cl solution and brine, dried over MgSO\(_4\) and concentrated in vacuo. The residue was chromatographed several times over silica gel (c, 600 g in total) impregnated with 10% AgNO\(_3\) (elution with \( \theta \)-hexane-benzene) or 10% AgNO\(_3\) (n-hexane). Subsequent distillation gave 90mg (9.2%) of (S)-1 as a colorless oil, bp 130°C (bath temperature)/0.4mmHg, \( n_\text{D}^2 \) 1.4426; \( [\alpha]_D^2 +1.21^\circ \) (c=3.3, n-hexane); IR \( v \) max cm\(^{-1}\): 3090 (w), 2980 (s), 2940 (s), 2870 (s), 1820 (w), 1640 (w), 1460 (m), 1375 (m), 990 (w), 910 (m), 720 (w); NMR (CC\(_4\)) \( \delta \): 0.75-1.00 (6H, m), 1.10-1.70 (16H, br. s), 1.70-2.20 (2H, m), 3.34 (2H, t, J=6Hz), 4.55-4.90 (2H, m), 5.20-5.70 (1H, m); MS m/z: 226 (M\(^+\)); GLC: column, 3% SE-30, 2m x4mm at 190°C; N\(_2\) at 1.5kg/cm\(^2\); t\( _R \) 4.19 min (99.4%). Anal. Found: C, 85.69; H, 14.60. Calcd. for C\(_{19}\)H\(_{38}\): C, 85.63; H, 14.37%.

(R)-(−)-14-Methyl-1-octadecene (R)-1. This was prepared from (R)-4b (631 mg) in the same manner as already described. The crude product was chromatographed four times over silica gel (c, 80 g in total) impregnated with 10% AgNO\(_3\) (elution with n-hexane). The residue was distilled to give 108 mg (17.4%) of (R)-1 as a colorless oil, bp 120°C (bath temperature)/0.2mmHg, \( n_\text{D}^1 \) 1.4432; \( [\alpha]_D^1 -1.06^\circ \) (c=3.15, n-hexane); MS m/z: 226 (M\(^+\)); (R)-1 was 99.5% pure as estimated by GLC analysis. The IR and NMR spectra were identical with those of (S)-1. Anal. Found: C, 85.98; H, 11.49. Calcd. for C\(_{19}\)H\(_{38}\): C, 85.63; H, 14.37%.

11-Dodecenyl bromide. 11-Dodecencol was prepared from 10-undecenoic acid by one-carbon elongation via 11-dodecenenitrile.\(^{10}\) 11-Dodecenenitrile was hydrolysed with 20% KOH in 60% EtOH aq. to give 11-dodecanedioic acid, bp 132−139°C/0.25mmHg, \( n_\text{D}^2 \) 1.4455, in a 94.3% yield. The acid was reduced with LiAlH\(_4\) in ether to give 11-dodecencol, bp 100°C/0.35mmHg, \( n_\text{D}^0 \) 1.4480, in a 96.4% yield. The alcohol was treated with p-TsCl in pyridine to give the corresponding tosylate in a 92.3% yield. Treatment of the tosylate with LiBr in acetone gave the bromide in a 94.9% yield as a colorless oil. The bromide showed the following properties: bp 95−97°C/1.1mmHg, \( n_\text{D}^2 \) 1.4649; IR \( v \) max cm\(^{-1}\): 3090 (w), 1640 (m), 990 (m), 910 (m): NMR (CC\(_4\)) \( \delta \): 1.20−1.70 (16H, br. s), 1.70−2.20 (2H, m), 3.34 (2H, t, J=6Hz), 4.55−4.90 (2H, m), 5.20−5.70 (1H, m); MS m/z: 226 (M\(^+\)); (R)-1 was 99.5% pure as estimated by GLC analysis. The IR and NMR spectra were identical with those of (S)-1.

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