

## SYNTHESIS OF THE (R)(-)-ENANTIOMERS OF THE PHEROMONE COMPONENTS OF SEVERAL SPECIES OF TROGODERMA [COLEOPTERA: DERMESTIDAE]

R. ROSSI,\* P. A. SALVADORI, A. CARPITA,

Istituto di chimica Organica, Università di Pisa, Via Risorgimento 35, 56100-Pisa, Italy

and

A. NICCOLI

Istituto Sperimentale per la Zoologia Agraria, 50125-Cascine del Riccio, Firenze, Italy

(Received in UK 15 January 1979)

**Abstract**—The chemically pure (R)(-)-enantiomers of (Z)- and (E)-14-methyl-8-hexadecen-1-ol and of (Z)- and (E)-14-methyl-8-hexadecenal, which are sex pheromone components of several species of female dermestid beetles, were synthesised in fairly good overall yield and in rather high optical purity starting from (S)(-)-citronellol. A mixture of (R)(Z)- and (R)(E)-14-methyl-8-hexadecenal in the 92:8 ratio was 10<sup>7</sup> time less active than a mixture of the corresponding (S)-enantiomers when tested on male Khapra beetles, *Trogoderma granarium*.

The sex pheromones of several species in the dermestid genus *Trogoderma* are essentially constituted of (Z)- and/or (E)-14-methyl-8-hexadecenal, 1 and 2, respectively.<sup>1-3</sup> Both compounds have been found in the airborne pheromone released by calling female Khapra beetles, *T. granarium*, in the 92:8 ratio, respectively.<sup>1,2</sup> On the other hand, (Z)- and/or (E)-14-methyl-8-hexadecen-1-ol, 3 and 4, respectively, together with other compounds are secondary components of the pheromones extracted from females of *T. inclusum*, *T. granarium*, *T. simplex* and *T. variabile*.<sup>3</sup>

Recently, the biological response of the male Khapra

beetle to synthetic samples of the (S)-enantiomers (92.5% optically pure)<sup>4</sup> of a mixture of 1 and 2 in the 92:8 ratio, of (S)-2, of (S)(Z)- and (S)(E)-14-methyl-8-hexadecen-1-ol, (S)-3 and (S)-4, respectively, has been evaluated.<sup>5,6</sup> Among the compounds tested, the mixture of (S)-1 and (S)-2 showed the highest activity in eliciting both attraction (50% response level at 10<sup>-8</sup> ~ 10<sup>-9</sup> μg) and attempted mating and was 10 times more active than (S)-2.<sup>5,6</sup>

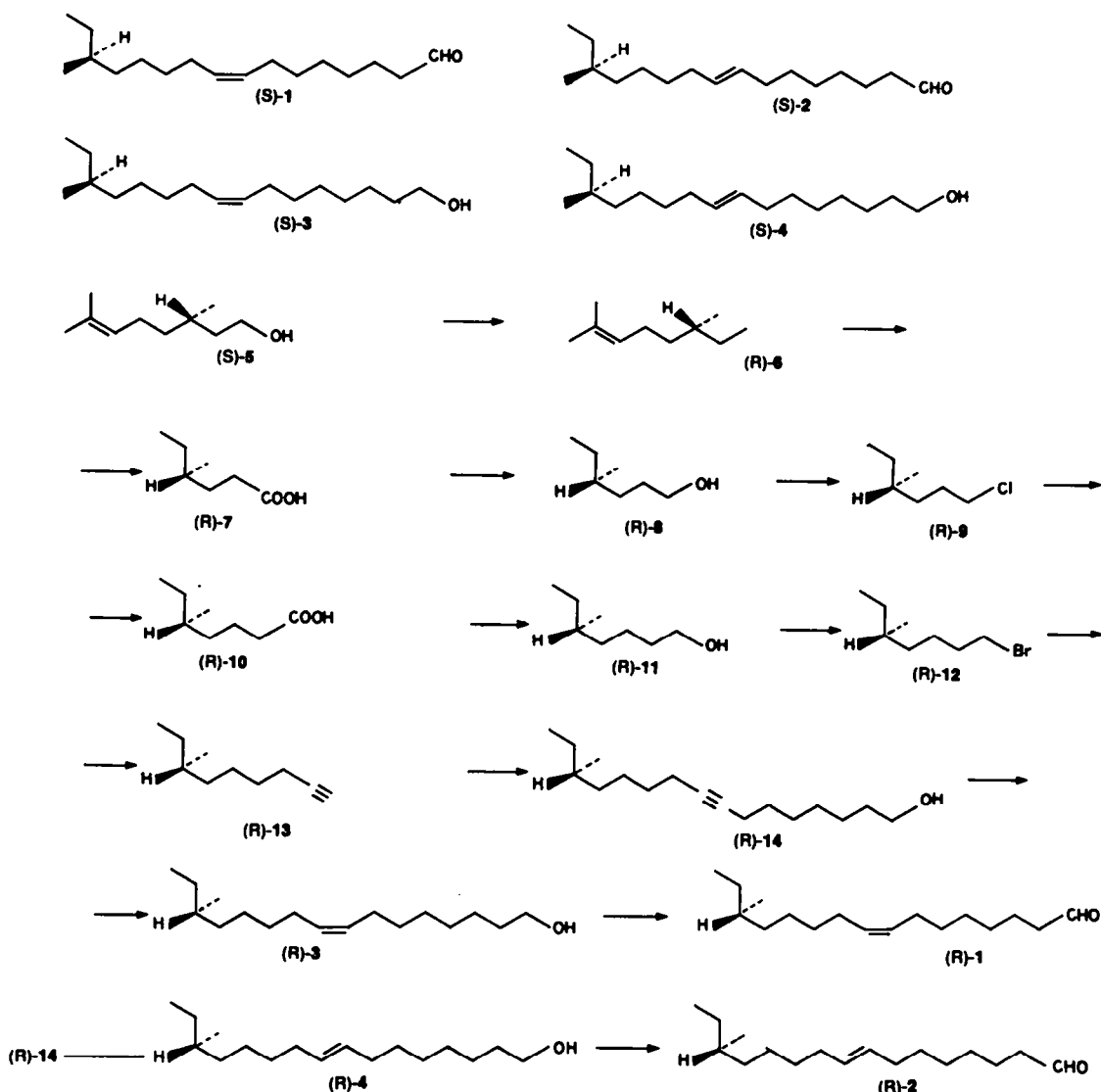
In order to elucidate the influence of the chiral quality of 1 and 2 on their biological activity for the male Khapra beetle, we have also synthesized the (R)-enantiomers of such compounds.

In this paper we wish to describe such synthesis<sup>a</sup> and to report the biological evaluation of our synthetic materials. The synthetic scheme we have followed to prepare (R)-1 and (R)-2 employes (-)-citronellol, (S)-5, as the starting material, and differs substantially from that very recently described by Mori *et al.*<sup>7</sup> for the preparation of both enantiomers of 1. Moreover, our reactions sequence, on the contrary to that used by Mori *et al.* affords in fairly good yield chemically pure compounds having well established optical purity (*ca* 84%).<sup>b</sup>

The mesylate deriving from 99% pure (S)-5 was converted in 70.7% yield into pure (R)-2,6-dimethyl-2-octene (6) by reduction with LAH. Periodic oxidation of the diol derived from (R)-6 gave crude (R)-4-methylhexanal which was directly oxidized with silver (I) oxide to afford (R)-4-methylhexanoic acid (R)-7, [ $\alpha$ ]<sub>D</sub><sup>25</sup> - 10.20 (neat) (85.9% o.p.),<sup>8</sup> in 63% overall yield. Reduction of (R)-7 with LAH gave pure (R)-4-methyl-1-hexanol, (R)-8, [ $\alpha$ ]<sub>D</sub><sup>25</sup> - 6.99 (neat), (85.6% o.p.)<sup>9</sup> in 92.4% yield. Treatment of (R)-8 with thionyl chloride and pyridine gave (R)-9 (90% yield) which was converted into the corresponding Grignard reagent and subsequently reacted with solid carbon dioxide to give (R)-5-methyl heptanoic acid, 10, [ $\alpha$ ]<sub>D</sub><sup>25</sup> - 7.42 (neat) (84.7% o.p.),<sup>9</sup> in 81.3% yield. This was reduced to the corresponding alcohol, (R)-11, which was reacted with phosphorous tribromide to give the bromide (R)-12 in 86% overall yield. Treatment of (R)-12 with a DMSO solution of lithium acetylide-ethylene diamine complex gave pure (R)-13, [ $\alpha$ ]<sub>D</sub><sup>25</sup> - 8.59 (83.9% o.p.)<sup>10</sup> in 57% yield. According to a procedure previously employed,<sup>4</sup> (R)-13 was converted into the corresponding alkynyllithium and coupled with 1-chloro-7-tetrahydropyranolxyheptane.

<sup>a</sup>One of us (R.R.) orally reported the synthesis of (R)(Z)-14-methyl-8-hexadecenal starting from (S)-citronellol at the EUACHEM Conference on Mono- and Sesquiterpenoids Varenna, Lake Como, on 27 August 1977.

<sup>b</sup>Mori *et al.*<sup>7</sup> employed (R)-citronellol as the common starting material for the preparation of (S)(Z)- and (R)(Z)-14-methyl-8-hexadecen-1-ol and of the corresponding aldehydes in a highly optically pure state (>95%). However, it must be noted that the optical purity of several compounds prepared by such Authors is very doubtful. They used in fact apparently pure (S)-4-methyl-1-hexanol having [ $\alpha$ ]<sub>D</sub><sup>25</sup> + 6.67 to prepare (S)(Z)-14-methyl-8-hexadecenal, (S)-1, having an optical purity higher than 92.5%. However, the rotatory power of this sample of 4-methyl-1-hexanol corresponds to a rather lower optical purity (81.2%). Optically pure (S)-4-methyl-1-hexanol has in fact [ $\alpha$ ]<sub>D</sub><sup>25</sup> + 8.16 [L. Lardicci and P. Pino, *Gazz. Chim. Ital.* 91, 441 (1961)]. Moreover, pure (R)-3-methyl-1-pentanol prepared by Mori *et al.* to synthesize (R)-1 in "a highly optically pure state" had [ $\alpha$ ]<sub>D</sub><sup>25</sup> - 5.42. Since the maximum rotatory power for such alcohol is [ $\alpha$ ]<sub>D</sub><sup>25</sup> + 8.77 [P. Pino, L. Lardicci as L. Centoni, *J. Org. Chem.* 24, 1399 (1959)], it is possible to establish that the alcohol used by Mori *et al.* had 63% optical purity. Similar inconsistencies may be pointed out in the paper of Mori *et al.* for several other compounds such as (R)-7-methyl-1-nonene, (S)- and (R)-7-methyl-1-nonyne, which on the basis of the reported rotatory powers have really 48, 86.6 and 52% optical purity, respectively. The maximum rotatory power for (S)-7-methyl-1-nonene is in fact [ $\alpha$ ]<sub>D</sub><sup>25</sup> + 10.3,<sup>1</sup> while that for (S)-7-methyl-1-nonyne is [ $\alpha$ ]<sub>D</sub><sup>25</sup> + 10.24 [L. Lardicci, C. Botteghi and E. Benedetti, *J. Org. Chem.* 31, 1534 (1966)]. On these basis, taking also into account that some impurities were present in the final products, (S)-1 and (R)-1, prepared by Mori *et al.*,<sup>7</sup> it is possible to infer that any conclusion of these Authors on the evaluation of the optical purity of the compounds from them synthesized, is very probably erroneous.



The crude product was treated with *p*-TsOH in MeOH to give (R)-14-methyl-8-hexadecyn-1-ol, (R)-14,  $[\alpha]_D^{25} - 4.93$  ( $c = 3.044$ ,  $\text{CHCl}_3$ ), in 50% yield. Semi-hydrogenation of (R)-14 at  $-10^\circ$  in pentane solution over Lindlar catalyst containing quinoline gave crude (R)-3 (95% yield) which was purified by column chromatography over  $\text{SiO}_2\text{-AgNO}_3$ . Oxidation by this alcohol according to Corey and Suggs<sup>11</sup> gave pure (R)-1,  $[\alpha]_D^{25} - 5.90$  ( $c = 4.570$ , ether), in 70% yield. The NMR, IR and mass spectra of such aldehyde were identical either to those of (S)-1 previously synthesized by us,<sup>4</sup> or to those reported for 1 isolated from natural sources.<sup>1</sup>

Pure (R)(E)-14-methyl-8-hexadecen-1-ol, (R)-4, was obtained in 85% yield from (R)-14 by reaction with LAH in diglyme<sup>12</sup> followed by purification by column chromatography over  $\text{SiO}_2\text{-AgNO}_3$ . Oxidation of (R)-4 with  $\text{CrO}_3\text{C}_2\text{H}_5\text{NHCl}^{11}$  gave in 50% yield pure (R)-2,  $[\alpha]_D^{25} - 5.04$  ( $c = 4.776$ , ether). The spectral properties of this compound were identical to those previously reported for (S)-2.<sup>4</sup>

Taking into account that no racemization could be occurred at any synthetic step later than (R)-13, and that

the optical purity of this compound was *ca.* 84%, the final products, (R)-1 and (R)-2 were estimated to be 84% optically pure.

The biological response of the male Khapra beetle *T. granarium* to a mixture of (R)-1 and (R)-2, in the 92:8 ratio, was also evaluated. The bioactivity was determined according to Levinson and Bar-Ilan<sup>13</sup> by establishing dose-response curves in an olfactometer providing concentric odor gradients. Responses of 120 male insects were recorded for a period of 15 min per dose. Four males (4–5 days postemergence) were employed in each run. The 50% response threshold dose resulted to be  $2 \times 10^{-1} \mu\text{g}$ , namely much higher than that of the corresponding mixture of the (S)-enantiomers ( $10^{-8}$ – $10^{-9} \mu\text{g}$ ).<sup>5,6</sup> This means that *T. granarium*, like several other insects,<sup>14,16</sup> has the ability to discriminate between the enantiomers of its pheromone. These results may also suggest that the compounds 1 and 2 isolated from *T. granarium*<sup>4</sup> are optically active with (S)-configuration. It is worth mentioning that, on the contrary, such compounds isolated from *T. inclusum* have (R)-configuration.<sup>17</sup>

## EXPERIMENTAL

All b.ps were uncorrected. IR spectra refer to films and were determined on a Perkin-Elmer Mod. 225 spectrometer. NMR spectra were recorded as  $\text{CCl}_4$  solns at 60 MHz with TMS as an internal standard on a Varian T-60 spectrometer. Mass spectra were recorded on a Varian MAT CH 7 spectrometer. Optical rotations were measured on a Schmidt-Haensch polarimeter. Gc analysis was performed on a DANI 3900 capillary columns dedicated gas chromatograph and on a C. Erba Fractovap GT gas chromatograph.

(R)-2,6-Dimethyl-2-octene (6). Methanesulfonyl chloride (40.2 g, 0.352 mol) was added in 45 min to a cooled ( $-10^\circ$ ) and stirred mixture of 99% pure (S)-(-)-citronellol (Fluka) (50.0 g, 0.320 mol) and triethylamine (48.6 g, 0.480 mol) in methylene chloride (1.5 l). Stirring at  $-10^\circ$  to  $0^\circ$  was continued for 2.5 hr. The mixture was washed repeatedly with ice-cold water, 5% HCl, water, and dried over  $\text{Na}_2\text{SO}_4$ . Evaporation of the solvent at 20 torr and room temp. leaved on oil (79.6 g) which was employed in the following step without further purification. The oil was diluted with dry ether (300 ml) and the resulting soln was slowly added to a stirred suspension of LAH (18.5 g, 0.486 mol) in ether (300 ml). The mixture was refluxed for 12 hr. After cooling, the mixture was hydrolysed with ice-cold water-dil. HCl and extracted with ether. The ether soln was dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The residue was fractionally distilled *in vacuo* to give (R)-6 (31.7 g, 70.7% yield): b.p.  $90^\circ/70$  torr;  $n_D^{25}$  1.4272;  $[\alpha]_D^{25}$  -8.88 (neat);  $\delta$  0.91 (6 H, m); 1.0-1.5 (5 H, bm); 1.60 (3 H, s); 1.70 (3 H, s); 1.97 (2 H, bq) and 5.06 ppm (1 H, m);  $\nu_{\text{max}}$  3060, 1635, 1380, 1370, 1150, 830, 765 and 730  $\text{cm}^{-1}$ ; MS: *m/e* 140 ( $M^+$ ). Lit.<sup>18</sup> b.p.  $162^\circ$ ;  $n_D^{25}$  1.4252;  $[\alpha]_D^{25}$  -9.33 (neat). Gc analysis (25 m Carbowax 20 M, capillary column) showed that (R)-6 was isomerically pure.

(R)-4-Methylhexanoic acid (7). 36%  $\text{H}_2\text{O}_2$  (24.5 ml) was dropwise added during 1.5 hr at room temp. to a stirred soln of (R)-6 (31.7 g, 0.226 mol) in anhydrous formic acid (103 ml). The temp. was then raised to  $45^\circ$  and the mixture was stirred overnight. The excess of formic acid was removed *in vacuo* at  $40^\circ$ . The residue was mixed with a 3 N ethanol soln of NaOH (130 ml) and the mixture was refluxed for 3 hr. The EtOH was removed *in vacuo* and later (300 ml) was added to the residue dissolved in ether (400 ml). Organic layer was separated and the aqueous layer was extracted with ether. The combined organic soln was washed repeatedly with water until neutrality, dried over  $\text{Na}_2\text{SO}_4$  and concentrated *in vacuo* at room temp. The residue (37.8 g) which was constituted of a crude diastereomeric mixture of 2,6-dimethyl-octan-2,3-diol, was dissolved in deareated ether (200 ml) and dropwise added at  $0^\circ$  under  $\text{N}_2$  to a stirred soln of  $\text{H}_2\text{JO}_6 \cdot 2\text{H}_2\text{O}$  (49.8 g, 0.217 mol) in THF (300 ml). The mixture was stirred for 1.5 hr at room temp. and then diluted with water. The organic layer was separated and the aqueous layer was extracted with ether. The combined ether soln was washed with water,  $\text{NaHCO}_3$  aq. and sat. NaCl soln, dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The residue was dropwise added at  $0^\circ$  in 45 min to an aqueous suspension of  $\text{Ag}_2\text{O}$  prepared from  $\text{AgNO}_3$  (95 g, 0.507 mol), NaOH (45.3 g, 1.13 mol) and water (200 ml). After stirring for 12 hr at room temp. and 3 hr at  $40^\circ$  the mixture was filtered. The aqueous soln was repeatedly extracted with ether, acidified with dil.  $\text{H}_2\text{SO}_4$  and extracted with ether (4  $\times$  100 ml). The ethereal acid extract was dried, concentrated and refluxed for 1.5 hr at 20 torr over  $\text{FeSO}_4$  (10 g) in order to eliminate  $\text{HNO}_3$ . Fractional distillation afforded pure (R)-7 (18.3 g, 62.3% yield): b.p.  $114^\circ/15$  torr;  $n_D^{25}$  1.4232;  $[\alpha]_D^{25}$  -10.20 (neat). Lit.<sup>24</sup> b.p.  $115-117^\circ/17$  torr;  $n_D^{25}$  1.4232;  $[\alpha]_D^{25}$  +11.87 (neat).

(R)-4-Methyl-1-hexanol (8). A soln of (R)-7 (97.5 g, 0.75 mol) in dry ether (400 ml) was slowly added under  $\text{N}_2$  to a stirred suspension of LAH (29.64 g, 0.78 mol) in dry ether (400 ml). The mixture was stirred for 6 hr under reflux and for 12 hr at room temp. Then water was added dropwise to the stirred and ice-cooled mixture to destroy the excess of LAH. The mixture was poured into ice-dil. HCl and extracted with ether. The ether soln

was washed with water,  $\text{NaHCO}_3$  aq. and brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The residue was fractionally distilled to give pure (R)-8 (80.4 g, 92.4% yield): b.p.  $82-83^\circ/16$  torr;  $n_D^{25}$  1.4240;  $[\alpha]_D^{25}$  -6.99 (neat). Lit.<sup>24</sup> b.p.  $82^\circ/16$  torr;  $n_D^{25}$  1.4241;  $[\alpha]_D^{25}$  +8.16 (neat). IR (neat):  $\nu_{\text{max}}$  3320 (s), 2960 (s), 2940 (s), 1460 (m), 1380 (m), 1050 (s). Gc analysis (2 m  $\times$  0.29 cm Carbowax 20 M on Chromosorb W 80-100 mesh) showed that (R)-8 was higher than 99% pure. Mori *et al.* reported  $n_D^{25}$  1.4278 and  $[\alpha]_D^{25}$  +6.63 (neat) for (S)-8. The optical purity of this alcohol, in case it was chemically pure, should be therefore 81.2%, namely rather lower than that (92.5%) Mori *et al.*<sup>7</sup> attribute to (S)-14-methyl-8-hexadecenal prepared from such alcohol.

(R)-1-Chloro-4-methylhexane (9). Thionyl chloride (75.2 ml) was dropwise added during 3 hr to a mixture of (R)-8 (80.4 g, 0.69 mol) and pyridine (55.2 ml) cooled at  $-10^\circ$ . The mixture was left overnight, then heated at  $100^\circ$  for 24 hr. Two layers formed during heating. Upper layer was separated, treated with ice-water,  $\text{NaHCO}_3$  aq. and water and dried over  $\text{Na}_2\text{SO}_4$ . Fractional distillation afforded pure (R)-9 (83.5 g, 90% yield): b.p.  $92.5-93^\circ/105$  torr;  $n_D^{25}$  1.4249;  $[\alpha]_D^{25}$  -9.49 (neat). Lit.<sup>9</sup>  $n_D^{25}$  1.4249;  $[\alpha]_D^{25}$  +10.5 (neat).

(R)-5-Methylheptanoic acid (10). The Grignard reagent prepared from (R)-9 (83.5 g, 0.62 mol) and Mg (15.8 g) in dry ether (800 ml) was added dropwise to a large excess of solid  $\text{CO}_2$  (3 kg). After 12 hr the mixture was poured into ice-dil.  $\text{H}_2\text{SO}_4$  and repeatedly extracted with ether. The extract was concentrated and the residue was treated at  $0^\circ$  with a large excess of 4 N NaOH aq. (250 ml). The resulting soln was extracted with ether (4  $\times$  100 ml), then acidified with dil.  $\text{H}_2\text{SO}_4$  and extracted again with ether (4  $\times$  100 ml). The acid extract was dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The residue was fractionally distilled to give pure (R)-10 (72.6 g, 81.3% yield): b.p.  $127.5^\circ/16$  torr;  $n_D^{25}$  1.4270;  $[\alpha]_D^{25}$  -7.42 (neat). (Found: C, 66.75; H, 11.41.  $\text{C}_9\text{H}_{18}\text{O}_2$  requires: C, 66.62; H, 11.18%). Lit.<sup>9</sup>  $n_D^{25}$  1.4275;  $[\alpha]_D^{25}$  +8.76.

(R)-5-Methyl-1-heptanol (11). According to the procedure employed to prepare (R)-8 from (R)-7, compound (R)-10 (72.0 g, 0.5 mol) was reduced with LAH (22.8 g) in dry ether (500 ml) to give pure (R)-11 (63.9 g, 98.4% yield): b.p.  $90^\circ/18$  torr;  $n_D^{25}$  1.4290;  $[\alpha]_D^{25}$  -7.80 (neat). Lit.<sup>19c</sup> b.p.  $87^\circ/20$  torr;  $n_D^{25}$  1.4290;  $[\alpha]_D^{25}$  +9.20. Gc analysis (2 m  $\times$  0.29 cm Carbowax 20 M on Chromosorb W 80-100 mesh) showed that the purity of (R)-11 was higher than 99%.

(R)-1-Bromo-5-methylheptane (12).  $\text{PBr}_3$  (36.5 ml) was added dropwise to compound (R)-11 (63.7 g, 0.49 mol). The mixture was stirred, heated at  $100^\circ$  for 3.5 hr, then cooled at room temp. After pouring into ice-water, the mixture was extracted with ether. The ether soln was dried and concentrated. The residue, cooled at  $0^\circ$  was extracted with conc.  $\text{H}_2\text{SO}_4$ . The organic layer was dissolved in ether, washed with water,  $\text{NaHCO}_3$  aq. and brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The residue was fractionally distilled to give pure (R)-12 (83.2 g, 88% yield): b.p.  $78-79^\circ/16$  torr;  $n_D^{25}$  +8.05.

(R)-7-Methyl-1-nonyne (13). A degassed soln of  $\text{LiC}\equiv\text{CH}$ -EDA (Ventron-Alfa) (22.9 g, 0.248 mol) in dry DMSO (150 ml) was added under  $\text{N}_2$  to a stirred mixture of (R)-12 (42.1 g, 0.218 mol) in dry DMSO (300 ml) cooled at  $<5^\circ$ . The mixture was stirred for 24 hr at room temp., then water (300 ml) was added. The resulting mixture was diluted with excess of water (1 l) and extracted with pentane. The extract was washed with sat. NaCl aq. dried and concentrated. The residue was fractionally distilled to give pure (R)-13 (17.1 g; 57% yield): b.p.  $112^\circ/150$  torr;  $n_D^{25}$  1.4256;  $[\alpha]_D^{25}$  -8.59 (neat);  $\delta$  0.89 (6 H, deformed t); 1.36 (9 H, br); 1.77 (1 H, t);  $\sim 2.17$  ppm (2 H, br). Lit.<sup>4</sup> d b.p.  $166-167^\circ$ ;  $n_D^{25}$  1.4255;  $[\alpha]_D^{25}$  +9.55.

(R)-14-Methyl-8-hexadecyn-1-ol (14). An hexane soln of BuLi (104 ml, 0.229 mol) was added under  $\text{N}_2$  to a stirred soln of (R)-13 (31.6 g, 0.229 mol) in anhyd HMPA (120 ml), cooled at  $0^\circ$ . The mixture was stirred for 30 min at  $0^\circ$  then hexane was evaporated at 20 torr. Subsequently, a soln of 1-chloro-7-tetrahydro-pyranloxy heptane<sup>20</sup> was slowly added at  $0^\circ$  under  $\text{N}_2$ . The mixture was stirred (49.2 g; 0.21 mol) for 12 hr at room temp., then it was poured into a large excess of ice-water and extracted repeatedly with hexane. The hexane soln was washed with sat. NaCl aq. dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The residue was dissolved in MeOH (450 ml) containing *p*-TsOH (2 g) and the

<sup>c</sup>These data are referred to a sample of (R)-6 containing ca 2% of 2,6-dimethyl-1-octene.

<sup>d</sup>Values referred to the (S)-enantiomer.

resulting soln was refluxed for 2 hr, concentrated *in vacuo*, diluted with water and extracted with hexane. Distillation of the dried extract gave (R)-14 (28.8 g, 50% yield): b.p. 133°/0.1 torr;  $n_D^{25}$  1.4648;  $[\alpha]_D^{25}$  -4.93 ( $c = 3.044$ ,  $\text{CHCl}_3$ ). MS *m/e* 252 ( $M^+$ );  $\nu_{\max}$  3300, 2930, 2850, 1450, 1050, 760 and 720  $\text{cm}^{-1}$ ;  $\delta$  0.92 (6 H, br), 1.40 (19 H, br), 2.13 (4H, br), 2.13 ppm (1 H, s) and 3.60 ppm (2 H, t). Lit.<sup>4</sup> d b.p. 133-134°/0.15 torr;  $n_D^{25}$  1.4645;  $[\alpha]_D^{25}$  +5.34 ( $\text{CHCl}_3$ ).

(Z)(R)-14-Methyl-8-hexadecen-1-ol (3). Compound (R)-14 (10.0 g, 0.039 mol) was hydrogenated at  $-10^\circ$  over Lindlar catalyst (1.3 g) in pentane (200 ml) containing quinoline (0.1 ml). Absorption of  $\text{H}_2$  ceased after 1 hr. The catalyst was filtered off and the filtrate was concentrated *in vacuo* to give crude (R)-3. This was chromatographed over  $\text{SiO}_2\text{-AgNO}_3$  (prepared from 200 g of Merck 70-230 mesh extra pure silica gel and 25.8 g of  $\text{AgNO}_3$  in 200 ml of acetonitrile), in hexane. Elution with hexane-ether (80:20) gave (R)-3 (8.3, 83.8% yield); b.p. 125-126°/0.1 torr;  $n_D^{25}$  1.4580;  $[\alpha]_D^{25}$  -5.27 ( $c = 4.738$ ,  $\text{CHCl}_3$ );  $\delta$  0.9 (6 H, br); 1.34 (19 H, br); 2.0 (4 H, br); 2.68 (1 H, s); 3.54 (2 H, t); and 5.28 ppm (2 H, m, seemingly t,  $J = 5$  Hz). MS *m/e* 254 ( $M^+$ ), 236 ( $M^+ - \text{H}_2\text{O}$ );  $\nu_{\max}$  3320, 3010, 2960, 2020, 2855, 1470, 1055 and 720  $\text{cm}^{-1}$ . Lit.<sup>4</sup> d b.p. 132-133° 0.2 torr;  $n_D^{25}$  1.4580;  $[\alpha]_D^{25}$  +5.33 ( $\text{CHCl}_3$ ). The spectral properties (IR, MS) of (R)-3 were identical with those previously reported by us<sup>4</sup> for (S)-3.

(R)(Z)-14-Methyl-8-hexadecenal (1). A soln of (R)-3 (6.5 g; 0.025 mol) in  $\text{CH}_2\text{Cl}_2$  (7 ml) was added in one portion under  $\text{N}_2$  to a stirred suspension of pyridinium chlorochromate (8.05 g, 0.037 mol) in anhyd  $\text{CH}_2\text{Cl}_2$  (70 ml). After 1.5 hr dry ether (150 ml) was added and the supernatant decanted from the black gum. The insoluble residue was washed thoroughly with anhyd ether ( $3 \times 50$  ml). The combined extracts were filtered through a short column of florisil and the solvent was removed at 20 torr. Fractional distillation of the residue afforded pure (R)-1 (4.41 g, 70% yield): b.p. 116-117°/0.15 torr;  $n_D^{25}$  1.4541;  $[\alpha]_D^{25}$  -5.90 ( $c = 4.570$ , ether);  $\delta$  0.87 (6 H, br); 1.33 (17 H, br); 2.00 (4 H, br); 2.37 (2 H, br); 5.30 (2 H, m,  $J = 5$  Hz); and 9.71 ppm (1 H, t); MS *m/e* 252 ( $M^+$ ), 223 ( $M^+ - \text{C}_2\text{H}_5$ , or  $M^+ - \text{CHO}$ ); 208 ( $M^+ - 44$ ) 44 ( $\text{H}-\text{O} = \text{CH}-\text{CH}_2$ ), 29 ( $\text{CHO}^+$  or  $\text{C}_2\text{H}_5^+$ );  $\nu_{\max}$  3010, 2940, 2910, 2840, 2720, 1725 and 1650  $\text{cm}^{-1}$ . Lit.<sup>4c</sup> b.p. 138-139°/1 torr;  $n_D^{25}$  1.4540;  $[\alpha]_D^{25}$  +6.05 (ether). Gic analysis (25 m Carbowax 20 M capillary column) showed that (R)-1 was chemically and isomerically pure.

(R)(E)-14-Methyl-8-hexadecen-1-ol (4). A soln of (R)-14 (8.0 g, 0.031 mol) in diglyme (25 ml) was added under  $\text{N}_2$  to a stirred suspension of LAH (5 g, 0.131 mol) in diglyme (100 ml) cooled at  $10^\circ$ . After keeping the temp. at  $140^\circ$  for 48 hr, the mixture was cooled and slowly hydrolysed under  $\text{N}_2$  with degassed ice-cold water. The aqueous slurry was neutralized with dil HCl and extracted with pentane (300 ml in 5 portions). The pentane extracts were concentrated *in vacuo* to give crude (R)-4. This was chromatographed over  $\text{SiO}_2\text{-AgNO}_3$  to give pure (R)-4 (6.69 g, 85% yield): b.p. 118-119°/0.07 torr;  $n_D^{25}$  1.4584;  $[\alpha]_D^{25}$  -5.45 ( $c = 2.858$ ,  $\text{CHCl}_3$ );  $\delta$  0.88 (6 H, br), 1.33 (19 H, br), 1.97 (4 H,

m), 3.24 (1 H, s), 3.50 (2 H, t), and 5.16 ppm (2 H, m);  $\nu_{\max}$  3320, 2960, 2920, 2850, 1460, 1370, 1055, 965 and 725  $\text{cm}^{-1}$ . MS *m/e* 254 ( $M^+$ ), 236 ( $M^+ - \text{H}_2\text{O}$ ). Lit.<sup>4c</sup> b.p. 108-109°/0.03 torr;  $n_D^{25}$  1.4584;  $[\alpha]_D^{25}$  +5.11 ( $\text{CHCl}_3$ ).

(R)(E)-14-Methyl-8-hexadecenal (2). According to the procedure described for the preparation of (R)-1, compound (R)-4 (5.0 g, 0.019 mol) was oxidized to give pure (R)-2 (2.39 g, 50% yield): b.p. 127°/0.45 torr;  $n_D^{25}$  1.4532;  $[\alpha]_D^{25}$  -5.04 ( $c = 4.776$ , ether); 0.87 (6 H, br), 1.33 (17 H, br), 2.00 (4 H, br), 2.37 (2 H, br), 5.30 (2 H, m), and 9.70 ppm (1 H, t);  $\nu_{\max}$  3010, 2940, 2910, 2840, 2710, 1730, 1460, 965 and 720  $\text{cm}^{-1}$ ; MS *m/e* 252 ( $M^+$ ), 223 ( $M^+ - \text{C}_2\text{H}_5$ , or  $M^+ - \text{CHO}$ ). Lit.<sup>4</sup> d b.p. 127-129°/0.5 torr;  $n_D^{25}$  1.4534;  $[\alpha]_D^{25}$  +5.62 (ether) Gic analysis (25 m Carbowax 20 M capillary column) showed that (R)-2 had chemical and isomer purity higher than 99%.

**Acknowledgements**—We thank the National Council of Researches (Rome) for financial support. Thanks are also due to Prof. R. Zocchi and Prof. G. A. Penili, Istituto Sperimentale per la Zoologia Agraria, Florence, for useful discussions.

#### REFERENCES

- J. H. Cross, R. C. Byler, R. F. Cassidy, Jr., R. M. Silverstein, R. E. Greenblatt, W. E. Burkholder, A. R. Levinson and H. Z. Levinson, *J. Chem. Ecol.* **2**, 457 (1976).
- A. R. Levinson, H. Z. Levinson, H. Schwainger, R. F. Cassidy, Jr. and R. M. Silverstein, *Ibid.* **4**, 95 (1978).
- R. E. Greenblatt, W. E. Burkholder, J. H. Cross, R. C. Byler and R. M. Silverstein, *Ibid.* **2**, 285 (1976).
- R. Rossi and A. Carpita, *Tetrahedron* **33**, 2447 (1977).
- R. Rossi and A. Niccoli, *Naturwissenschaften* **65**, 259 (1978).
- R. Rossi and A. Niccoli, *Redia* **LX**, 525 (1977).
- K. Mori, T. Suguro and M. Uchida, *Tetrahedron* **34**, 3119 (1978).
- L. Lardicci and P. Pino, *Gazz. Chim. Ital.* **91**, 441 (1961).
- L. Lardicci and L. Conti, *Ibid.* **92**, 428 (1962).
- L. Lardicci, C. Botteghi and E. Benedetti, *J. Org. Chem.* **31**, 1534 (1966).
- E. J. Corey and J. W. Suggs, *Tetrahedron Letters* 2647 (1975).
- R. Rossi and A. Carpita, *Synthesis* 561 (1977).
- H. Z. Levinson and A. R. Bar-Ilan, *J. Insect Physiol.* **16**, 561 (1970).
- R. G. Riley, R. M. Silverstein, J. C. Moser, *Ibid.* **20**, 1629 (1974).
- D. Klimetzek, G. Loskant, J. R. Vitè and K. Mori, *Naturwissenschaften* **63**, 581 (1976).
- Review: R. Rossi, *Synthesis* 413 (1978).
- K. Mori, *Tetrahedron* **30**, 3817 (1974).
- C. Carlini, D. Pini, O. Bonsignori and P. Neuenchwander, *Gazz. Chim. Ital.* **103**, 1297 (1976).
- L. Lardicci, P. Salvadori and P. Pino, *Ann. Chim.* **52**, 652 (1962).
- R. Rossi and C. Conti, *Chim. Ind. Milan* **57**, 581 (1975).