Note

Synthesis of Optically Active Forms of (*E*)-14-Methyl-8-hexadecenal (Trogodermal)[†]

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Trogoderma species of insects are notorious pests of stored products. Their sex pheromones were extensively studied by Burkholder, Levinson, Silverstein and their respective co-workers.¹⁾ They isolated the pheromones by aeration of the female beetles, identified them as (*Z*)-14-methyl-8-hexadecenal **1** and its (*E*)-isomer **2** and named them "trogodermal."²⁾ However, the absolute configuration at C-14 of **1** remained unknown until we synthesized the both (*R*)- and (*S*)-enantiomers (**1** and **1'**) in optically pure state starting from (*R*)-(+)-citronellol **3**.³⁾ The (*R*)-enantiomer **1** was biologically active on *Trogoderma inclusum* and *T. variable*, while its antipode **1'** was almost inactive.⁴⁾ This made us to believe that the natural pheromone was (*R*, *Z*)-trogodermal. In continuation of our work, here we record the synthesis of the highly optically pure enantiomers of (*E*)-trogodermal **2** which is the pheromone isolated from *Trogoderma glabrum* and *T. granarium* (Khapra beetle).²⁾

The known acetylenic alcohol **4** or **4'**³⁾ was reduced with lithium aluminum hydride in diglyme⁵⁾ to give an olefinic alcohol **5** or **5'**. This was oxidized with pyridinium chlorochromate ($\text{CrO}_3 \cdot \text{C}_5\text{H}_5\text{N} \cdot \text{HCl}$)⁶⁾ to give (*R*, *E*)-(-)-14-methyl-8-hexadecenal **2**, $[\alpha]_{\text{D}}^{21} - 5.99^\circ$ (ether) or its (*S*, *E*)-isomer **2'**, $[\alpha]_{\text{D}}^{25} + 6.18^\circ$ (ether). A synthesis of the (*S*, *E*)-isomer **2'**, $[\alpha]_{\text{D}}^{25} + 5.62^\circ$ (ether), was previously reported by Rossi and Carpita starting from (*S*)-(-)-2-methyl-1-butanol.⁷⁾ The physical properties of our products were in good accord with those reported by them.

Professor W. Burkholder and Dr. T. Shapas, the University of Wisconsin, kindly carried out a preliminary bioassay of these enantiomers revealing that (*R*)-**2** was ten to one hundred times more active than the (*S*)-isomer **2'** on *Trogoderma glabrum*, *T. inclusum*

and *T. variable*.⁸⁾ It is therefore evident that chirality plays an important role in pheromone perception of *Trogoderma* species. A small portion of our synthetic samples was further purified by preparative GLC (PEG 20M column). The EAG studies of our purified (*R*, *E*)- and (*S*, *E*)-trogodermals will be reported in due course by Professor H. Z. Levinson, Max-Planck-Institut für Verhaltensphysiologie.

EXPERIMENTAL

All bps were uncorrected. IR spectra (determined on a JASCO IRA-1 spectrometer) refer to films. NMR (recorded on a Hitachi R-24A spectrometer) spectra were recorded at 60 MHz in CCl_4 with TMS as an internal standard.

(S, E)-14-Methyl-8-hexadecen-1-ol (**5'**)

A solution of lithium aluminum hydride in diglyme was prepared by adding lithium aluminum hydride (1 g) in THF (2 ml) and diglyme (12 ml). The mixture was stirred and heated under N_2 to remove low bp fractions. To this was added a solution of **4'** (1.8 g) in diglyme (3 ml) with stirring at $0 \sim 5^\circ\text{C}$. After the addition the mixture was heated at 140°C for 48 hr. The excess lithium aluminum hydride was destroyed by the addition of water under ice-cooling. The mixture was poured into ice-dil HCl and extracted with *n*-hexane. The *n*-hexane solution was washed with water, sodium bicarbonate solution and brine, dried (MgSO_4) and concentrated *in vacuo*. The residue was distilled to give 1.28 g (71%) of **5'**, bp $132 \sim 133^\circ\text{C}$ (0.7 mmHg); $n_{\text{D}}^{21} 1.4574$ (lit.⁷⁾ $n_{\text{D}}^{25} 1.4584$; $[\alpha]_{\text{D}}^{21} + 5.52 \pm 0.02^\circ$ ($c = 4.598$, CHCl_3) [lit.⁷⁾ $[\alpha]_{\text{D}}^{25} + 5.11 \pm 0.23^\circ$ ($c = 2.823$, CHCl_3); IR ν_{max} cm^{-1} : 3350 (m), 2950 (s), 2875 (s), 1470 (m), 1440 (w), 1390 (w), 1060 (m), 970 (m), 775 (w), 730 (w); NMR δ 0.88 (6H, m), 1.30 (~19H, br), 1.88 (~5H, br), 3.49 (2H, t, $J = 6$ Hz), 5.26 (2H, m); MS: m/e 254 (M^+); GLC (Column, 5% FFAP, $1.5 \text{ m} \times 2 \text{ mm}$ at 180°C , Carrier gas, N_2 , 1.6 kg/cm^2); t_R 7.75 min. (single peak). Anal. Found: C,

[†] Pheromone Synthesis XXVII. Part XXVI, K. Mori, S. Tamada and P. A. Hedin, *Naturwissenschaften*, **65**, 653 (1978).

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80.03; H, 13.39. Calcd. for $C_{17}H_{34}O$: C, 80.24; H, 13.47%.

(R, E)-14-Methyl-8-hexadecen-1-ol (5)

This was prepared from 4 in the same manner as described above in 71% yield (1.29 g), bp 142~143°C (0.8 mmHg); n_D^{21} 1.4575; $[\alpha]_D^{21} -5.48 \pm 0.02^\circ$ ($c=4.615$, $CHCl_3$); GLC (Column, 5% FFAP, 1.5 m $\times$ 2 mm at 180°C; Carrier gas, N_2 , 1.6 kg/cm²): t_R 7.75 min (93%) with a major impurity at 4.9 min. Anal. Found: C, 79.97; H, 13.47. Calcd. for $C_{17}H_{34}O$: C, 80.24; H, 13.47%. The IR, NMR and mass spectra were identical with those of 5'.

(S, E)-14-Methyl-8-hexadecenal (2')

A solution of 5' (1 g) in CH_2Cl_2 (10 ml) was added dropwise to a stirred and ice-cooled suspension of pyridinium chlorochromate (6 g) and sodium acetate (0.5 g) in CH_2Cl_2 (40 ml). After the addition, the mixture was stirred for 2 hr at 0~5°C. The organic solution was separated from the tarry residue by decantation and the black residue was washed twice with CH_2Cl_2 . The organic solution was combined and filtered through a florisil column. The column was washed with ether. The organic solution was concentrated *in vacuo*. The residue was distilled to give 0.605 g (61%) of 2', bp 131~133°C (1.0 mmHg); n_D^{22} 1.4519 (lit.⁷⁾ n_D^{25} 1.4354); $[\alpha]_D^{22} +6.18 \pm 0.03^\circ$ ($c=4.20$, ether) [lit.⁷⁾ $[\alpha]_D^{25} +5.62 \pm 0.23^\circ$ ($c=3.553$, ether)]; IR ν_{max} cm⁻¹: 3020 (w), 2940 (s), 2870 (s), 2720 (w), 1740 (s), 1470 (m), 1420 (w), 1385 (w), 970 (m); NMR δ (100 MHz) 0.88 (6H, m), 1.30 (~17H, br), 1.95 (4H, br), 2.32 (2H, t, $J=6.5$ Hz), 5.26 (2H, m), 9.58 (1H, t, $J=2$ Hz); GLC (Column, 5% FFAP, 1.5 m $\times$ 2 mm at 160°C; Carrier gas, N_2 , 1.4 kg/cm²): t_R 6.25 min (97%), impurities at 4.0 and 8.2 min; TLC (40% $AgNO_3$ -Silica gel G; *n*-hexane-ether 3:2): R_f 0.75 (cf. R_f of 1 or 1': 0.66). Anal. Found: C, 80.62; H, 12.83. Calcd. for $C_{17}H_{32}O$: C, 80.89; H, 12.78%. A portion of this sample was further purified by GLC (PEG 20M, 2 m $\times$ 8 mm at 200°C) to show a single peak (t_R 3.2 min) on an LAC-2R-446 column (1.5 m $\times$ 3 mm at 180°C).

(R, E)-14-Methyl-8-hexadecenal (2)

This was prepared from 5 in the same manner as described above in 66% yield (0.65 g), bp 125~128°C (0.9 mmHg); n_D^{21} 1.4523; $[\alpha]_D^{21} -5.99 \pm 0.04^\circ$ ($c=5.08$, $CHCl_3$); GLC (Column, 5% FFAP, 1.5 m $\times$ 2 mm at 160°C; Carrier gas, N_2 , 1.4 kg/cm²): t_R 6.25 min (92%), impurities at 4.1 and 8.2 min. Anal. Found: C, 80.39; H, 12.90. Calcd. for $C_{17}H_{32}O$: C, 80.89; H, 12.78%. The IR, NMR, and TLC data were identical with those of 2'. This was also purified by GLC as described above for 2'.

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