Note

Simple Synthesis of a Mixture of (*E*)- and (*Z*)-5-Undecenoic Acid, Sex Pheromone of the Varied Carpet Beetle[†]

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In 1985, Kuwahara and Nakamura identified a mixture of (*E*)- and (*Z*)-5-undecenoic acids (**1**) as the female-produced sex pheromone of the varied carpet beetle, *Anthrenus verbasci* L.¹⁾ This insect causes severe damage to dry proteinous materials such as museum specimens, woolen and silk fabrics, fur products and other stored materials.

Although Kuwahara and Nakamura have already reported a synthesis of **1** (*E*:*Z*=25:75) starting from 5-acetoxypentanal,¹⁾ there is a strong need to develop a simpler and more efficient synthesis of **1** to test the practicality of using **1** for pest control. This note describes such a new synthesis of **1** as shown in the scheme.

Commercially available 2,3-dihydropyran was hydrated by an *Organic Syntheses* procedure to give 2-hydroxytetrahydropyran (**2**) in an 83% yield.²⁾ Wittig reaction between **2** and the phosphorane **3** furnished a mixture of (*E*)- and (*Z*)-5-Undecen-1-ol (**4**) in a 90% yield. Oxidation of **4** with Jones reagent gave the desired acid **1** in a 69% yield. Inspection of the ¹³C NMR spectrum of **1** revealed its major component to be the (*Z*)-isomer, because the signals due to the allylic carbons (7C and 4C) of the (*Z*)-isomer, which appeared in higher fields (δ 29.42 and 31.59) than those of the (*E*)-isomer (δ 31.88 and 32.58) were more

intense.^{3~5)}

The *E*:*Z* ratio of our **1** was estimated to be 18:82 by a GLC analysis of its methyl ester. Almost the same result was obtained by examining the 400 MHz ¹H NMR spectrum of a mixture of the epoxides derived by acetylating and epoxidizing **4**. The (*E*)-epoxide originating from (*E*)-**4**

showed signals due to the epoxy protons ($\text{R}-\overset{\text{H}}{\underset{\text{O}}{\text{C}}}-\overset{\text{H}}{\text{C}}-\text{R}'$) at

δ =2.65~2.71, while the (*Z*)-epoxide exhibited them at δ =2.88~2.96 in the ratio of *E*:*Z*=17:83. The natural pheromone **1** consists of a mixture of (*E*)- and (*Z*)-**1** in a ratio of 15:85.¹⁾ Accordingly, our synthetic **1** possessed an isomeric ratio similar to that of natural **1**.

In summary, the sex pheromone **1** was synthesized from 2,3-dihydropyran in a 51.5% overall yield in three steps.

Experimental

5-Undecen-1-ol 4. To a stirred suspension of *n*-hexyltriphenylphosphonium bromide (34.57 g, 81 mmol; 2.5 eq.) in dry tetrahydrofuran (200 ml) cooled at -17°C under argon was added dropwisely over 20 min a solution of *n*-butyllithium in *n*-hexane (1.59 M, 50.94 ml, 81 mmol). Stirring was continued for 40 min after the addition at the same temperature to complete the formation of **3**. A solution of **2** (3.30 g, 32 mmol) in dry tetrahydrofuran (30 ml) was then added dropwisely over 15 min to the stirred and cooled Wittig reagent, keeping the temperature below 10°C. The mixture was stirred for 1.5 hr at the same temperature. Subsequently, it was poured into saturated ammonium chloride solution (400 ml), and extracted with ether and dichloromethane. The extract was dried with magnesium sulfate, filtered and concentrated *in vacuo*. The residue was triturated with *n*-hexane, and filtered to remove triphenylphosphine oxide. The filtrate was concentrated *in vacuo*, and distilled to give 4.64 g (90.0%) of **4**, bp 77~80°C (2.5 mmHg), n_D^{25} 1.4462; IR ν_{max} , cm⁻¹ (film): 3350 (O-H), 1650 (C=C), 1060 (C-O); NMR (100 MHz, CDCl₃) δ : 0.90 (3H, deformed t, *J*=7 Hz, CH₃), 1.10~1.80 (10H, m, CH₂), 1.47 (1H, s, OH), 1.85~2.20 (4H, m, CH₂C=CCH₂), 3.66 (2H, t, *J*=7 Hz, CH₂O), 5.30~5.50 (2H, m, CH=CH); GLC (column, OV-101, 50 m $\times$ 0.25 mm; temperature rate, 100°C + 1°C/min; carrier gas, nitrogen, 1.0 kg/cm²) t_R : 44.4 min (single peak). Anal. Found: C, 77.39; H, 12.83. Calcd. for C₁₁H₂₂O: C, 77.58; H, 13.02%.

5-Undecenoic acid 1. To a stirred and ice-cooled solution of **4** (3.40 g, 21.3 mmol) in acetone (40 ml) was added dropwisely Jones reagent (8 N CrO₃, 12.5 ml) at 5~10°C. Stirring was continued for 1 hr, before the excess chromic acid was destroyed by adding 2-propanol (4 ml). The

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mixture was diluted with water, concentrated *in vacuo* to remove acetone, and extracted with ether. The ether solution was washed with brine, dried with magnesium sulfate, and concentrated *in vacuo*. The residue was distilled to give 2.59 g (69.3%) of **1**, bp 106~114°C (1.2 mmHg), n_D^{25} 1.4436; IR $\nu_{\max}$ cm⁻¹ (film): 3600~2400 (CO₂H), 1710 (CO₂H), 930 (CO₂H); ¹H NMR (100 MHz CDCl₃) δ : 0.90 (3H, t, $J=6$ Hz, CH₃), 1.10~1.15 (6H, m, CH₂ at C-8,9 and 10), 1.50~1.86 (2H, m, CH₂ at C-3), 1.86~2.20 (4H, m, CH₂ at C-4 and 7), 2.38 (2H, t, $J=7.5$ Hz), 5.35 (0.8H, dt, $J=11$, 6 Hz, olefinic H at C-6 of (Z)-**1**), 5.43 (0.8H, dt, $J=11$, 6 Hz, olefinic H at C-5 of (Z)-**1**), 5.26~5.63 (0.4H, m, olefinic 2H of (E)-**1**), 8.0~10.0 (1H, br, COOH); ¹³C NMR (25 MHz, CDCl₃) δ : 14.1 (11C), 22.6, 24.7, 26.5, 27.3, 29.4 [7C of (Z)-**1**], 31.6 [4C of (Z)-**1**], 31.9 [7C of (E)-**1**], 32.6 [4C of (E)-**1**], 33.5, 128.2 [6C of (Z)-**1**], 128.7 [6C of (E)-**1**], 131.4 [5C of (Z)-**1**], 132.0 [5C of (E)-**1**], 180.0 (1C). The ratio of intensity of the signals due to (Z)-**1** and (E)-**1** was 81~85:15~19. GLC (column, PEG-20M, 2 m $\times$ 4 mm; temperature rate, 100°C + 3°C/min; carrier gas, nitrogen, 1.0 kg/cm²) t_R : 37.1 min (96.8%). *Anal.* Found: C, 71.48; H, 10.93. Calcd. for C₁₁H₂₀O₂: C, 71.69; H, 10.94%.

GLC analysis of the methyl ester of 1. The methyl ester was prepared in the usual manner by treating **1** with diazometane. GLC (column, OV-1, 60 m $\times$ 0.25 mm; temperature rate, 70°C + 3°C/min; carrier gas, nitrogen, 1.5 kg/cm²) t_R : 35.27 min [82%, (Z)-isomer], 35.57 min [18%, (E)-isomer].

¹H-NMR analysis of the epoxyacetates derived from **4**.

Acetylation of **4** (100 mg) with acetic anhydride (0.5 ml) and pyridine (1 ml) was followed by epoxidation with *m*-chloroperbenzoic acid (161 mg) in dichloromethane (5 ml) to give the epoxyacetates (100 mg). NMR (400 MHz, CDCl₃) δ : 0.90 (3H, t, $J=7$ Hz, CH₃ at C-11), 1.24~1.42 (4H, m), 1.42~1.64 (6H, m), 1.64~1.80 (2H, m), 2.05 (3H, s, COCH₃), 2.65~2.71 (0.34H, m, R- $\overset{\text{H}}{\underset{\text{O}}{\text{C}}}$ -R' of the (E)-epoxide), 2.88~2.96 (1.66H, m, R- $\overset{\text{H}}{\underset{\text{O}}{\text{C}}}$ -R' of the (Z)-epoxide), 4.08 (2H, t, $J=7$ Hz, CH₂OAc). The *E*:*Z* ratio of **4** was therefore estimated to be 17:83.

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