A Simple Synthesis of Methyl 10,11-Oxido-3,7,11-trimethyldodeca-2,4,6-trienoate, an Analog of the *Cecropia* Juvenile Hormone^{†1}

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Dehydro derivatives of juvenile hormones such as I or II have been reported to be biologically active.^{1,2)} Their syntheses, however, were carried out in somewhat complicated manner employing either a very carefully selected condition¹⁾ or a lengthy route.²⁾ Herein we describe a simple synthesis of methyl 10,11-oxido-3,7,11-trimethyldodeca-2,4,6-trienoate (II).

Citral (III) was condensed with ethyl senecioate (IV) in the presence of potassium amide in liquid ammonia to give a crude acid (Va) after alkaline hydrolysis. This type of condensation was known to give an all-*trans* trienoic acid.³⁾ The crude acid was treated with diazomethane and chromatographed over silicic acid to give an ester (Vb) in 34% yield from III. GLC analysis revealed this to be of 97% purity. Thus the reaction proceeded stereoselectively. The large coupling constant ($J_{4,5}=15\text{Hz}$) shown by the C-4 proton together with a strong IR absorption at 962 cm^{-1} indicated the *trans*-geometry of the double bond at C-4,5. Oxidation of the methyl ester (Vb) with *m*-chloroperbenzoic acid gave a mixture of the mono epoxide (II) and the diepoxide (VI) which could be separated by preparative TLC.

The mono epoxide (II) was reported to exhibit a specific activity on three Hemiptera species, namely, *Pyrrhocoris apterus*, *Dysdercus intermedius*, and *Graphosoma italicum*, and a very low activity on the beetles *Tenebrio*. In our hands it was almost inactive (score⁴⁾ 0.2 at $10\text{ }\mu\text{g}$ per insect) on *Tenebrio molitor* and inactive on *Bombyx mori*.

^{†1} Synthesis of Compounds with Juvenile Hormone Activity. Part XIX. Part XVIII, Y. Ozawa, K. Mori and M. Matsui, *Agr. Biol. Chem.*, **38**, 1383 (1974).

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FIG. 1.

EXPERIMENTAL

Methyl 3,7,11-trimethyldodeca-2,4,6,10-all-trans-tetraenoate (Vb). A solution of citral (III, 17 g) and ethyl senecioate (IV, 19 g) in dry ether (250 ml) was slowly added to a suspension of KNH_2 (from 14 g of K) in liquid NH_3 (400 ml) at $-50 \sim -60^\circ\text{C}$ with stirring. The stirring was continued for 10 hr at $-50 \sim 60^\circ\text{C}$. Then NH_3 was allowed to evaporate at room temp. The residue was dissolved in MeOH (150 ml) and H_2O (200 ml). The resulting solution was stirred for 1.5 days at room temp and then concentrated *in vacuo*. The residual alkaline aqueous solution was extracted with ether to remove neutral impurities. The aqueous layer was acidified with dil. H_2SO_4 and extracted with ether. This ethereal solution was washed with salt NaCl solution, dried (MgSO_4) and concentrated to give 18.0 g of a crude oil. This was esterified with CH_2N_2 to give the corresponding methyl ester (Vb). Purification by silica gel chromatography afforded 9.2 g (34% from III) of pure Vb, bp $136 \sim 140^\circ\text{C}$ (0.3 mmHg); $n_D^{18.5}$ 1.5255; IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 2850, 1705, 1598, 1420, 1230, 1123, 962; NMR δ (60 MHz, CCl_4): 1.60 (3H, s), 1.68 (3H, s), 1.82 (3H, s), 2.01 (3H, s), 2.08~2.25 (4H), 3.60 (3H, s), 5.03 (1H, br. s), 5.49 (1H, s), 6.13 (1H, d, $J=10.5\text{ Hz}$), 6.68 [6.62 (0.6H, d, $J=15\text{ Hz}$), 6.80 (0.4H, d, $J=15\text{ Hz}$)], 7.54 (1H, d, $J=15\text{ Hz}$); MS: m/e 248 (M^+), 179, 147, 125, 119, 95, 69; GLC: Column, LAC-2R 446 at 200°C ; Carrier gas, N_2 , 1.7 kg/cm²; Rt 14.6 min (*trans*, 96.7%), 11.5 min (*cis*, 3.3%). Anal. Found: C, 77.81; H, 9.91. Calcd. for $\text{C}_{16}\text{H}_{24}\text{O}_2$: C, 77.37; H, 9.74%.

Methyl 10,11-oxido-3,7,11-trimethyldodeca-2,4,6-all-trans-trienoate (II). A solution of *m*-chloroperbenzoic acid (1.14 g) in CH_2Cl_2 (10 ml) was slowly added to a stirred and ice-cooled solution of Vb (1 g) in CH_2Cl_2 (10 ml) and the mixture was left to stand overnight in a refrigerator. It was diluted with CH_2Cl_2 (100 ml) and washed with 2% Na_2CO_3 and water, dried (MgSO_4) and concentrated *in vacuo* to give 780 mg of crude epoxides. A portion (150 mg) of it was purified by preparative TLC (SiO_2 , C_6H_6 -EtOAc 5: 1) to give 55 mg of I (*Rf* 0.65) and 46 mg of VI (*Rf* 0.45). The mono epoxide (I) showed the following properties; n_D^{19} 1.5205; IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 2850; 1705, 1598, 1420, 1230, 1123, 962; NMR δ (60 MHz, CCl_4) 1.24 (3H, s), 1.27 (3H, s), 1.65~1.70 (2H), 1.87 (3H, s), 2.06 (3H, s), 2.19~2.69 (3H), 3.68 (3H, s), 5.59 (1H, s), 6.15 (1H, d, $J=10.5$ Hz), 6.81 [6.69 (0.6H, d, $J=15$ Hz), 6.87 (0.4H, d, $J=15$ Hz)], 7.71 (1H, d, $J=15$ Hz); UV $\lambda_{\text{max}}^{\text{EtOH}}$: 265 nm (ϵ 10900) MS: m/e 264 (M^+), 232, 178, 161, 133, 125, 95, 84. *Anal.* Found: C, 72.25; H, 9.32. Calcd. for $\text{C}_{16}\text{H}_{24}\text{O}_3$: C, 72.69; H, 9.15%. The diepoxide (VI) showed the following properties: n_D^{19} 1.5186; IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 2850, 1705, 1598, 1420, 1230, 962; NMR δ (60 MHz, CCl_4)

1.25 (3H, s), 1.27 (3H, s), 1.29 (3H, s), 1.60~1.68 (4H), 2.03 (3H, s), 2.57 (1H, br. s), 3.33 (1H, d, $J=7.8$ Hz), 3.68 (3H, s), 5.80 [5.72 (0.6H, d, $J=10$ Hz), 5.92 (0.4H, d, $J=15$ Hz)], 7.92 (1H, d, $J=15$ Hz). *Anal.* Found: C, 68.70; H, 8.76. Calcd. for $\text{C}_{16}\text{H}_{14}\text{O}_4$: C, 68.54; H, 8.63%.

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