

INSECT GROWTH REGULATORS—VIII SYNTHESIS OF A CYCLIC ANALOG OF JUVENILE HORMONE—II

C. WAWRZEŃCZYK and A. ZABŹA

Institute of Organic and Physical Chemistry Technical University of Wrocław, Poland

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Abstract—The "true" cyclic analog of JH-II was obtained in a six step synthesis from natural (+)-limonene as starting material.

Since 1966, when the active principle of paper factor-juvabion was isolated, purified and characterised,^{1,2} a large number of cyclic juvenile hormone analogs have been synthesised. The structures of these analogs differ from the structures of natural JH hormones in their carbon skeleton and, in addition, they usually contain other structural fragments, like alkoxy groups, additional heteroatoms (O, N, S) and very often aromatic rings.³ The main problem in the synthesis of these juvenoids has usually been to obtain the compounds with the highest hormone activity.

In this paper we describe the first synthesis of a "true" cyclic analog of JH-II in which the basic carbon skeleton is unchanged, and the cyclic ring arises by junction of C atoms C-8 and C-13 in the chain of the JH-II molecule (Fig. 1). This junction restricts to some extent the flexibility of the JH-II molecule, fixing the geometry of the C₉–C₁₀ and C₁₁–C₁₂ bonds as *s-cis* and the C₈–C₉ bond as *s-trans*.

Reactions were carried out as shown in Fig. 2. Natural (+)-limonene (1) with R chiral center at carbon C-4 was used as the starting material. Therefore, the by-products and the final JH-II cyclic analog are optically active.

9-Hydroxymethyl-1,8(10)-*p*-menthadiene (2) was obtained according to Blomquist *et al.*⁴ The oxidation of this compound with pyridinium chlorochromate gave a mixture of three aldehydes 4, 5 and 6 (54%, 16% and 30% respectively). Only aldehyde 4 was used as a substrate in the next step of the synthesis. Catalytic isomerisation of this mixture (in triethylamine-ethanol system) raised the concentration of 4 to 84%. Aldehyde 5 constitutes the remaining 16%. These aldehydes were isolated by column chromatography and their structures confirmed by PMR and IR spectroscopy. The PMR spectra of both stereoisomers are very similar (Experimental). A more distinct difference was observed for the chemical shift values of Me₃-protons in the vicinity of the aldehyde group. These protons in isomer 4 exhibit a signal which is shifted downfield as a result of the deshielding effect of the *cis*-situated aldehyde group ($\delta = 2.44$ ppm, doublet, $J = 1.5$ Hz), while those in isomer 5 exhibit a signal at 2.10 ppm (doublet, $J = 1.5$ Hz). Aldehyde 4 was treated

with NaBH₄ to give alcohol 7. This was converted into a bromide which was used as an alkylating agent in reaction with ethyl acetoacetate. The resulting product was decarboxylated to give ketone 8 in 64% yield. Condensation of 8 with trimethyl phosphonoacetate in the presence of NaH gave a mixture of unsaturated esters 9 and 10 (70% and 30% respectively). Pure stereoisomers were isolated by means of column chromatography. The geometry of the double bonds formed in isomers 9 and 10 was established by PMR spectra. The signal of Me-protons at the formed double bond in isomer 9 is shifted downfield due to the deshielding effect of the *cis*-oriented ester group ($\delta = 2.37$ ppm). The corresponding signal for ester 10 is at $\delta = 2.17$ ppm. Small differences in chemical shift values are also observed for olefinic protons at C-2: for isomer 10 $\delta = 6.00$ and isomer 9 $\delta = 5.88$ ppm.

The esters 9 and 10 were oxidised with *m*-chloroperoxybenzoic acid in methylene chloride. In this reaction a mixture of mono- and diepoxides was formed which were very difficult to separate. We could separate monoepoxide and diepoxide fractions only. A similar result was obtained when we used monoperphthalic acid as oxidising agent. Then we decided to synthesise monoepoxides 12 and 14 via bromohydrins 11 and 13 according to van Tamelen⁵ and Krimer.⁶ Thus, the esters 9 and 10 were treated with N-bromosuccinimide followed by sodium methoxide in methanol to give monoepoxides 12 and 14. Their structures were confirmed by means of IR and PMR spectroscopy. In the PMR spectrum of epoxide 12 (Fig. 3) signals of protons of Me groups at C-7 were found $\delta = 1.83$, C-3 $\delta = 2.43$, C-4' $\delta = 1.55$ and ester Me group $\delta = 3.92$ ppm, two signals of olefinic protons at $\delta = 5.87$ for H-2 and $\delta = 5.36$ for H-6, and a very characteristic one for proton H-3', deshielded by the epoxide ring at $\delta = 3.08$ ppm (doublet, $J = 4$ Hz). The shape of this signal is similar to that of the signal of the corresponding proton in the (+)-*trans*-epoxy-limonene molecule (Fig. 3).

Since (+)-limonene was used as starting material and substitution of the cyclohexane ring was *trans*, as evi-

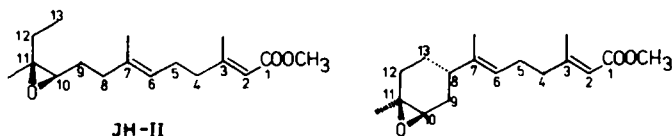


Fig. 1.

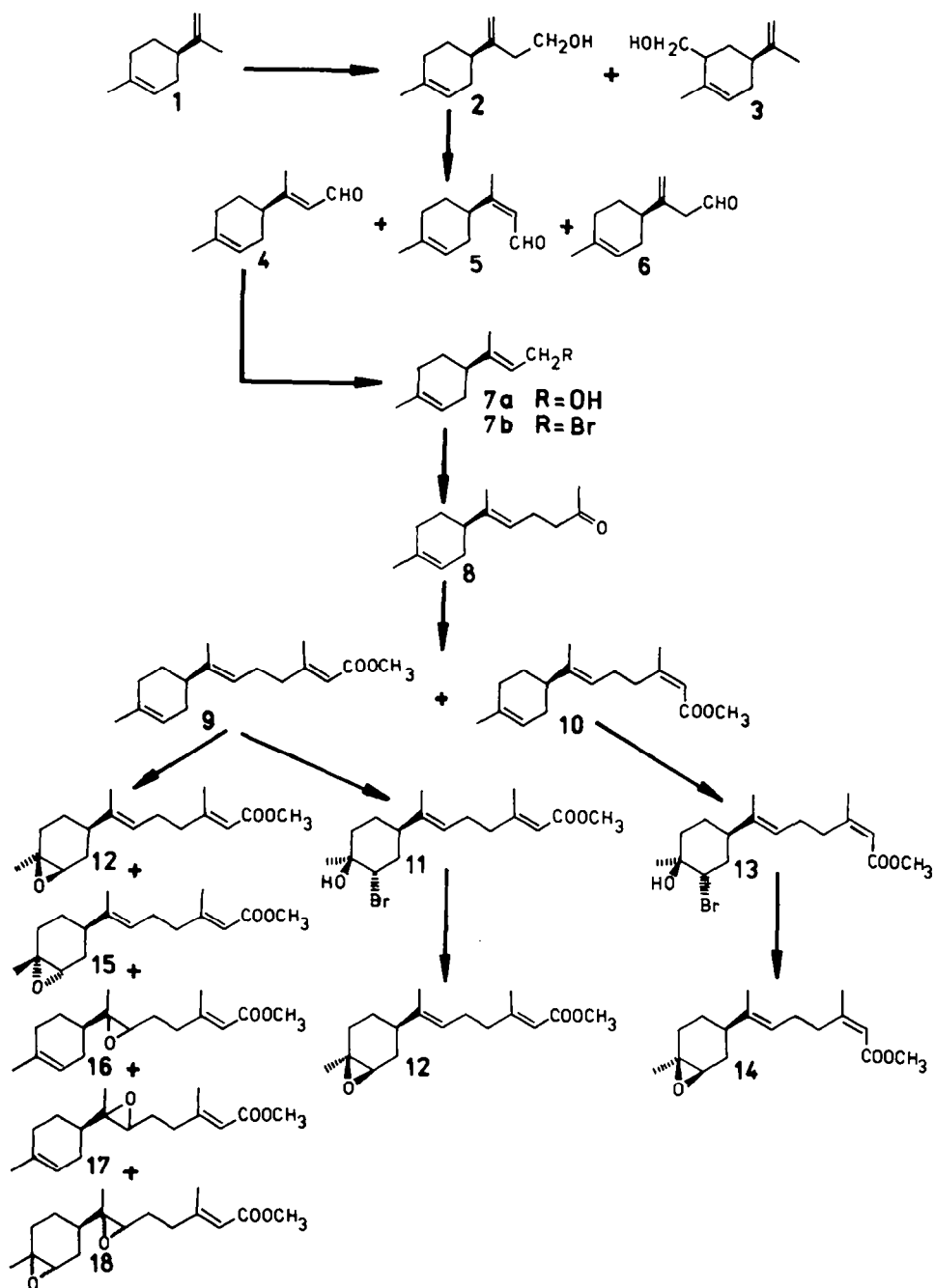


Fig. 2.

denced by PMR spectroscopy, the signs of chirality at carbon C-4' and carbon C-3' could be fixed as *S* and *R* respectively. The corresponding chiral atoms in natural JH-I⁷ have the same configuration. The PMR spectrum of isomeric epoxyster 14 was very similar to that reported for epoxyster 12. The main difference was observed for the chemical shift values of the Me group at C-3 and the protons in methylene group C-4 only. The signals of the methylene C-4 protons were shifted downfield ($\delta = 2.8$ – 3.0 ppm) as a result of the deshielding effect of the *cis*-situated ester group. On the other hand, the signal of the Me group protons at C-3 is observed at higher field ($\delta = 2.17$ ppm) due to a *trans* orientation with respect to the ester group.

The juvenile hormone activity of the two epoxysters 12 and 14 was tested on freshly moulted pupae of the yellow mealworm, *Tenebrio molitor* L. and *Dysdercus cingulatus*. Although both isomers are biologically active their activity did not reach the level of original juvenile hormone JH-II. The results of biological investigations will be discussed in separate paper.

EXPERIMENTAL

IR spectra were recorded on a Perkin-Elmer 621 Infracord spectrophotometer (film). PMR spectra were determined on a NMR Tesla 80 MHz BS 497 spectrometer with CCl_4 as solvent and HMDS as external reference. Glc analysis was carried out on a Chromatron instrument, model GCHF 18.3.4, equipped with

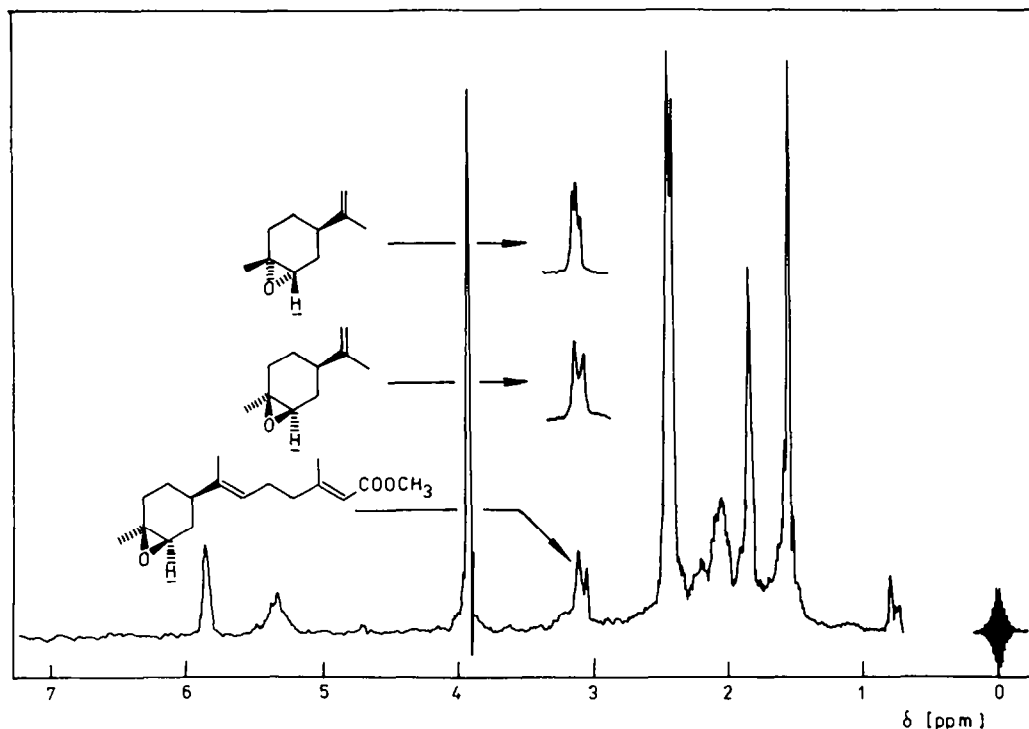


Fig. 3. PMR spectrum of methyl (1'R,3'R,4'S)-(2E,6E)-3,7-dimethyl-7-(3',4'-epoxy-4'-methyl-cyclohexyl)-heptadien-2,6-oate (12).

FID, using a steel column filled with: 5% XE-60 on Chromosorb G (1=2 m, 110°) for aldehydes, 20% Carbowax M-20 on Varaport-30 (1=3 m, 180°) for esters and ketones, 20% Carbowax M-20 on Chromosorb W (1=3 m, 200°) for alcohols. The starting (+)-limonene ($[\alpha]_D^{20} = +104.30^\circ$, $n_D^{20} = 1.4740$) was obtained from cummin oil by fractional distillation.

Reaction of (+)-limonene with paraformaldehyde. A soln of BF_3 -etherate (1.0 ml) in 60 ml anhydrous CH_2Cl_2 was added to a stirred mixture of (+)-limonene (68 g; 0.5 mole), PFA (7.5 g; 0.25 mole) and 250 ml anhydrous CH_2Cl_2 at room temp. under N_2 . This mixture was stirred for 1 hr, treated with NaHCO_3 aq (20 ml), and dried over MgSO_4 . After removal of solvent and unreacted (+)-limonene *in vacuo*, the residue was distilled and the following two fractions obtained: (1) 9 g, b.p. 97–99°/1 mm Hg containing 80% of alcohol 2 (glc analysis), (2) 11 g, b.p. 99–100°/1 mm Hg 97% of alcohol 2 (glc analysis), $n_D^{20} = 1.4984$, $[\alpha]_D^{20} = +48.20^\circ$. The IR spectrum showed characteristic absorptions at 3350 (s), 3095 (m), 3010 (m), 1640 (m), 1040 (s), 1180 (s), 890 (s), 800 (s) cm^{-1} . The PMR spectrum showed the following assigned values δ : 1.93 (s, $\text{CH}_3\text{C}=\text{CH}-$), 2.53 (t, $J = 7$ Hz, $-\text{CH}_2-\text{CH}_2\text{OH}$), 3.68 (s, $-\text{CH}_2\text{OH}$), 3.90 (t, $J = 7$ Hz, $-\text{CH}_2-\text{CH}_2-\text{OH}$), 5.05 (d, $J = 4$ Hz, $\text{CH}_2=\text{C}-$), 5.6 (m, $-\text{C}=\text{CH}-\text{CH}_2-$).

(1'R)-(2E)-3-Methyl-3-(4'-methylcyclohexen-3'-yl)-propen-2-ol-1(4) and (1'R)-(2Z)-3-Methyl-3-(4'-methylcyclohexene-3'-yl)-propen-2-ol-1(5). Pyridinium chlorochromate (32.3 g; 0.15 mole) and NaOAc (2.5 g; 0.03 mole) were suspended in anhyd. CH_2Cl_2 (250 ml), and alcohol 2 (16.6 g; 0.1 mole) was rapidly added at room temp. (according to Corey⁷). The mixture was stirred for 2 hr, the solvent removed and the residue washed with dry ether and the collected extracts filtered through Florisil. Solvent evaporation *in vacuo* gave 13.2 g (80% yield) of crude products a mixture of three aldehydes 4, 5 and 6 (54%, 16% and 30% respectively, glc). This mixture was added to a soln of 1 ml triethylamine in 150 ml abs EtOH and kept at room temp. for 24 hr. After solvent evaporation the residue (13.1 g) contained 84% of aldehyde 4 and 16% of aldehyde 5. Aldehyde 4 was purified via preparative column chromatography (silica gel,

eluent: petroleum-ethyl ether 19:1), and showed the following physical properties: b.p. 115–117°/1 mm Hg, $n_D^{20} = 1.5190$, $[\alpha]_D^{20} = +98.30^\circ$ (MeOH, c, 9.77). PMR: δ , 1.93 (s, $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 2.41 (d, $J = 1$, 5 Hz, $-\text{C}(\text{CH}_3)=\text{CH}-\text{CHO}$), 5.63 (m, $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 6.05 (m, $J = 8$ Hz, $J = 1$, 5 Hz, $-\text{C}(\text{CH}_3)=\text{CH}-\text{CHO}$), 10.2 (d, $J = 8$ Hz, $-\text{CH}-\text{CHO}$). IR: cm^{-1} , 3050 (w), 2725 (w), 1680 (s), 1630 (m), 795 (s), 850 (s). (Found: C, 80.29; H, 9.70. Calc. for $\text{C}_{11}\text{H}_{16}\text{O}$: C, 80.41; H, 9.82%). Aldehyde 5 showed the following physical properties: b.p. 110–112°/1 mm Hg, $n_D^{20} = 1.5135$, $[\alpha]_D^{20} = -9.70^\circ$ (MeOH, c, 6.77). PMR: δ , 1.93 (s, $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), (d, $J = 1$, 5 Hz, $-\text{C}(\text{CH}_3)=\text{CH}-\text{CHO}$), 5.62 (m, $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 6.03 (m, $J = 1$, 5 Hz, $J = 8$ Hz, $-\text{C}(\text{CH}_3)=\text{CH}-\text{CHO}$), 10.2 (d, $J = 8$ Hz, $-\text{CH}-\text{CHO}$). IR: cm^{-1} , 3020 (m), 3060 (m), 2730 (m), 1680 (s), 1620 (m), 850 (s).

(1'R)-(2E)-3-Methyl-3-(4'-methylcyclohexen-3'-yl)-propen-2-ol-1(7a). After dissolving 4 (2.35 g, 0.014 mole) in 25 ml MeOH a soln of NaBH_4 (0.2 g, 0.005 mole) in EtOH (10 ml) was added. Stirring was continued for 5 hr at room temp., the mixture was poured into brine and the product extracted with petroleum. The combined extracts were washed, dried (MgSO_4) and the solvent evaporated. The crude 7a was distilled: b.p. 120–123°/1 mm Hg, $n_D^{20} = 1.5045$, $[\alpha]_D^{20} = +88.3^\circ$ (MeOH, c, 9.32); PMR: δ , 1.93 (s, $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$ and $-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{OH}$), 3.5 (s, $-\text{CH}-\text{CH}_2-\text{OH}$), 4.34 (d, $J = 7$ Hz, $-\text{CH}-\text{CH}_2-\text{OH}$), 5.6 (m, $-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-\text{OH}$ and $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$). IR: cm^{-1} , 3320 (s), 3020 (m), 1670 (m), 1020 (s), 1370 (s), 825 (s). (Found: C, 79.45; H, 12.12. Calc. for $\text{C}_{11}\text{H}_{18}\text{O}$: C, 79.46; H, 10.91%).

(1'R)-(5E)-6-Methyl-6-(4'-methylcyclohexen-3'-yl)hexen-5-one-2(8). To a stirred soln of 7a (2.0 g, 0.0012 mole) in dry ethyl ether (35 ml) under N_2 at -2° , PBr_3 (2.0 g, 0.007 mole) in 5 ml of dry ethyl ether was added dropwise. The mixture was stirred for 6 hr at 0° , poured into ice-water and the whole extracted with ether. The ether soln was washed with water, sat NaHCO_3 aq and sat NaCl aq, dried (MgSO_4) and concentrated to give 2.8 g (95% yield) of crude 7b.

Ethyl acetoacetate (2.23 g, 0.017 mole) in 5 ml dry DMF was added dropwise with cooling (ice-water) to a stirred mixture of

[†]Short path distillation.

NaH (0.4 g, 0.016 mole) in 50 ml of DMF. To the Na derivative formed, bromide **7b** (2.8 g; 0.012 mole) in 10 ml dry DMF was added and the mixture stirred 24 hr at room temp. Thereafter the mixture was poured into ice and the product extracted with petroleum. After solvent evaporation, 50 ml of 5% NaOH aq was added dropwise to the residue and heated on a water bath for 6 hr. Thereafter the mixture was cooled and extracted with petroleum. The combined extracts were washed with brine, dried (MgSO_4) and concentrated *in vacuo* to give crude **8**, which was purified by column chromatography on silica gel "Nagel" 100-200 mesh with 19:1 petroleum-ether as eluent. 1.6 g (64% yield) pure **8** was obtained: b.p. 145-148°/3 mm Hg, $n_D^{20} = 1.4880$, $[\alpha]_D^{20} = +60.0$ (MeOH, *c* 8.27). PMR: δ , 1.86 (s, $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$ and $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 2.3 (s, $-\text{CH}_2-\text{CO}_2\text{CH}_3$), 5.31 (m, $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 5.56 (m, $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$). IR: cm^{-1} , 3050 (m), 1720 (s), 1670 (w), 910 (m). (Found: C, 81.23; H, 10.50. Calc. for $\text{C}_{14}\text{H}_{22}\text{O}_2$: C, 81.50; H, 10.75%).

Methyl (1'R)-(2E,6E)-3,7-dimethyl-7-(4'-methylcyclohexen-3'-yl)-heptadien-2,6-oate (9) and methyl(1'R)-(2Z,6E)-3,7-dimethyl-7-(4'-methylcyclohexen-3'-yl)-heptadien-2,6-oate (10). To a suspension of NaH (0.36 g; 0.015 mole) in 120 ml dry THF, trimethyl phosphonoacetate (2.8 g, 0.015 mole) in 10 ml dry THF was added dropwise under N_2 . Stirring was continued for 1 hr and after cooling **8** (1.55 g, 0.0075 mole) in 10 ml THF was added. The mixture was stirred for 24 hr at room temp. followed by 15 hr at 50-70°. The reaction course was checked by tlc. Thereafter the mixture was cooled, diluted with water and extracted with light petroleum. The combined extracts were washed with brine, dried (MgSO_4) and the soln was evaporated to give a mixture of 2E- and 2Z-isomers of esters **9** and **10** (70% and 30% respectively, glc). These isomers were separated via preparative column chromatography (silica gel, eluent: petroleum-ether, 19:1), thus 1.30 g of isomer 2E and 0.40 g of isomer 2Z there was obtained (86% yield). The esters showed the following physical properties: Ester **9**: b.p. 150-151°/1 mm Hg, $n_D^{20} = 1.5036$, $[\alpha]_D^{20} = +48.82^\circ$ (MeOH, *c* 8.3); PMR: δ , 1.88 (s, $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$ and $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 2.37 (d, $J = 2$ Hz, $-\text{C}(\text{CH}_3)=\text{CH}-\text{CO}_2\text{CH}_3$), 3.91 (s, $-\text{CO}_2\text{CH}_3$), 5.32 (m, $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 5.62 (m, $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 5.88 (m, $-\text{CH}-\text{CO}_2\text{CH}_3$). IR: cm^{-1} , 3030 (w), 1720 (s), 1650 (s), 1220 (s), 1150 (s), 860 (s). (Found: C, 77.55; H, 9.85. Calc. for $\text{C}_{17}\text{H}_{26}\text{O}_2$: C, 77.82; H, 9.99%). Ester **10**: b.p. 145-148°/1 mm Hg, $n_D^{20} = 1.5024$, $[\alpha]_D^{20} = +46.20^\circ$ (MeOH, *c* 8.74). PMR: δ , 1.94 (s, $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$ and $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 2.17 (s, $-\text{C}(\text{CH}_3)=\text{CH}-\text{CO}_2\text{CH}_3$), 4.0 (s, $-\text{CO}_2\text{CH}_3$), 5.57 (m, $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 5.74 (m, $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 6.00 (m, $-\text{CH}-\text{CO}_2\text{CH}_3$). IR: cm^{-1} , 3040 (w), 1720 (s), 1650 (s), 1150 (s), 855 (s).

Methyl (1'R)-(2E,6E)-3,7-dimethyl-7-(3'-bromo-4'-hydroxy-4'-methylcyclohexyl)-heptadien-2,6-oate (11) and methyl (1'R)-(2Z,6E)-3,7-dimethyl-7-(3'-bromo-4'-hydroxy-4'-methylcyclohexyl)-heptadien-2,6-oate (13). Ester **9** (0.43 g, 0.0016 mole) was dissolved in 20 ml THF-water (7:3) soln and N-bromosuccinimide (0.33 g; 0.0019 mole) was added portionwise. The mixture was stirred for 3 hr at room temp., poured into water and the product extracted with ether. The extracts were washed with brine, dried (MgSO_4) and the solvent evaporated to give crude **11**. Silica gel chromatography (elution with 50% petroleum in ether) gave 0.5 g (86% yield) of pure **11**: $n_D^{20} = 1.5230$, $[\alpha]_D^{20} = +14.90^\circ$ (MeOH, *c* 5.36); PMR: δ , 1.66 (s, $-\text{CH}_2-\text{C}(\text{OH})(\text{CH}_3)-\text{CHBr}-$), 1.90 (d, $J = 2$ Hz, $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 2.43 (d, $J = 2$ Hz, $-\text{C}(\text{CH}_3)=\text{CH}-\text{CO}_2\text{CH}_3$), 3.9 (s, $-\text{CO}_2\text{CH}_3$), 4.36 (m, $-\text{C}(\text{CH}_3)(\text{OH})-\text{CHBr}-\text{CH}_2-$), 5.40 (m, $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 5.83 (m, $-\text{CH}-\text{CO}_2\text{CH}_3$). IR: cm^{-1} , 3400 (s), 1720 (s), 1645 (s), 1480 (s), 1150 (s), 860 (m).

Compound **13** was prepared as described for **11** in 70% yield from ester **10**: $n_D^{20} = 1.5100$, $[\alpha]_D^{20} = +17.40^\circ$ (MeOH, *c* 3.44); PMR: δ , 1.68 (s, $-\text{C}(\text{CH}_3)(\text{OH})-\text{CHBr}-$), 1.93 (d, $J = 2$ Hz, $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 2.21 (d, $J = 2$ Hz, $-\text{C}(\text{CH}_3)=\text{CH}-\text{CO}_2\text{CH}_3$), 3.93 (s, $-\text{CO}_2\text{CH}_3$), 4.41 (m, $-\text{C}(\text{CH}_3)(\text{OH})-\text{CHBr}-$), 5.52 (m, $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 5.91 (m, $-\text{CH}-\text{CO}_2\text{CH}_3$). IR: cm^{-1} , 3420 (s), 1720 (s), 1650 (s), 1160 (s), 850 (s).

Methyl (1'R,3'R,4'S)-(2E,6E)-3,7-dimethyl-7-(3',4'-epoxy-4'-methylcyclohexyl)-heptadien-2,6-oate (12) and methyl (1'R,3'R,4'S)-(2Z,6E)-3,7-dimethyl-7-(3',4'-epoxy-4'-methylcyclohexyl)-heptadien-2,6-oate (14). To a cooled soln of **11** (0.32 g, 0.009 mole) in 15 ml anhyd MeOH, NaOMe (formed from reaction of 0.05 g of Na with 25 ml of MeOH, was added. After stirring for 3 hr at room temp., the solvent was removed and the residue was purified by column chromatography (silica gel, eluent: petroleum-ether (4:1) to give **12** (0.23 g; 93% yield); $n_D^{20} = 1.4995$, $[\alpha]_D^{20} = +30.0^\circ$ (MeOH, *c* 5.61). PMR: δ , 1.55 (s, $-\text{CH}-\text{C}(\text{CH}_3)=$), 1.83 (d, $J = 2$ Hz, $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-$), 2.43 (d, $J = 2$ Hz, $-\text{CH}_2-\text{C}(\text{CH}_3)=\text{CH}-\text{CO}_2\text{CH}_3$), 3.08 (d, $J = 4$ Hz, $-\text{CH}-\text{C}(\text{CH}_3)-$), 3.92 (s, $-\text{CO}_2\text{CH}_3$), 5.36 (m, $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 5.87 (m, $-\text{CH}-\text{CO}_2\text{CH}_3$). IR: cm^{-1} , 1720 (s), 1650 (s), 1140 (s), 840 (s). (Found: C, 73.08; H, 8.90. Calc. for $\text{C}_{17}\text{H}_{26}\text{O}_3$: C, 73.35; H, 9.41%).

Epoxyester 14 was prepared as described for **12** in 90% yield from **13**: $n_D^{20} = 1.4960$, $[\alpha]_D^{20} = +38.80^\circ$ (MeOH, *c* 4.02). PMR: δ , 1.53 (s, $-\text{CH}-\text{C}(\text{CH}_3)=$), 1.85 (d, $J = 2$ Hz, $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-$), 2.17 (d, $J = 2$ Hz, $-\text{C}(\text{CH}_3)=\text{CH}-\text{CO}_2\text{CH}_3$), 3.1 (d, $J = 4$ Hz, $-\text{CH}-\text{C}(\text{CH}_3)-$), 3.97 (s, $-\text{CO}_2\text{CH}_3$), 5.43 (m, $-\text{CH}-\text{C}(\text{CH}_3)=\text{CH}-\text{CH}_2-$), 5.88 (m, $-\text{CH}-\text{CO}_2\text{CH}_3$). IR: cm^{-1} , 1720 (s), 1650 (s), 1160 (s), 850 (s).

Epoxydation with m-chloroperbenzoic acid of ester 9. A soln of m-chloroperbenzoic acid (0.48 g, 0.0027 mole) in CH_2Cl_2 (10 ml) was added to a soln of **9** (0.65 g, 0.0025 mole) in CH_2Cl_2 (15 ml) at 0-5°. The mixture was set aside for 0.5 hr, diluted with a Na_2CO_3 aq containing a small amount of Na_2SO_3 and extracted with CH_2Cl_2 . The combined extracts were washed with brine, dried (Na_2SO_4) and the solvent was evaporated to give a crude oily epoxyester (0.55 g, 80% yield). Silica gel chromatography of the crude reaction product (elution with petroleum-acetone (14:1), gave 0.1 g of **18** and a fraction (0.4 g) containing a mixture of **12**, **15**, **16**, **17**, (determined by means of PMR spectroscopy, but not separated into pure fractions).

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