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# PRODUCTS ACTIVE ON ARTHROPOD—IV[a]

## INSECT JUVENILE HORMONE MIMICS—4: HYDRINDANE ANALOGUES OF *CECROPIA* JUVENILE HORMONE[b]

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**Abstract**—Synthesis of cis-hydrindane analogues (**2**, **3**) of *Cecropia* juvenile hormone-I from common intermediate *cis*-hydrindane-2, 5-dione is presented. The analogues are only moderately active against *Dysdercus cingulatus*.

In continuation of our work[1] on the synthesis of novel juvenile hormone mimics based on closing a part-structure of *Cecropia* juvenile hormone-I (**1**), we wish to report the synthesis of hydrindane analogues of type **2** and **3** (Fig. 1).

*Cis-Hydrindane-2, 5-dione* (**8**). For the synthesis of **2** and **3**, *cis*-hydrindane-2, 5-dione (**8**) appeared to be an appropriate starting material. Apparently, this compound has not been prepared so far. However, the known[2] 2,5-diacetoxyindane (**5**) could be readily converted into the required dione (**8**) by catalytic hydrogenation[3] of the derived phenol alcohol (**6**) over Raney Ni in presence of alkali, followed by Jones' oxidation (Fig. 2). For the Baeyer–Villiger oxidation of **4** to **5** a more convenient procedure using $H_2O_2$ and HCOOH was developed. In view of the fact that Ni hydrogenation of indanes[4] and more specifically their hydroxy derivatives,[5] leads to *cis*-hydrindanes, the dione obtained by the sequences shown in Fig. 2 is assigned *cis* stereochemistry.

*Methyl cis*-10, 11-*epoxy*-7″, 9:7″, 13-*cis*-*cyclo*-7-*ethyl*-3, 11-*dimethyltrideca*-2(*E*), 6(ξ)-*dienoate* (**15**). Hydrindane analogue **15** was elaborated from the diketone **8**, following sequence of reactions depicted in Fig. 3.

Selective Wittig reaction of the diketone (**8**; IR: C=O 1725, 1755 $cm^{-1}$) with methylenetriphenylphosphorane furnished the desired olefin **9** (IR: C=O 1745 $cm^{-1}$). Conditions for this selective six-membered carbonyl olefination were critical but the process became efficient when carefully executed (strictly anhydrous conditions, inverse addition[6] of one equivalent of the reagent, and temp in the range 0–3°). Refluxing of **9** with p-TSA in benzene afforded essentially a single product (GLC, TLC, PMR) which, from its PMR spectrum (Me.C=CH, 3 H, *bs*, 1.68 ppm; Me.C=CH, 1 H, *bs*, 5.36 ppm, $W_H = 7.5$ Hz) was clearly **10**, rather than the $\Delta^{5:6}$-isomer. Exposure of **10** to the phosphorane from the Wittig salt **11**[7], followed by acid hydrolysis, furnished the desired dienone **12**. This product appears to be stereochemically homogeneous from its behaviour on two different GLC columns (Carbowax, SE-30) and from its PMR data (single Me–C=CH signal *bs*, 1.65 ppm), though this conclusion could be misleading;[8] stereochemistry of the product also remains abscure.[9] Condensation of the dienone **12** with methyl diethylphosphonoacetate in presence of base yielded a 3:1 (GLC) mixture of the triene esters (**13**, **14**) readily separated by inverted-dry-column-chromatography (DCC).[10] As anticipated,[11] the major product was the E-isomer (**13**), which was readily recognized[12] from its PMR spectrum.

Epoxidation of the E-isomer (**13**) with m-chloroperbenzoic acid in methylene dichloride led to the targeted monoepoxide (**15**) with some con-

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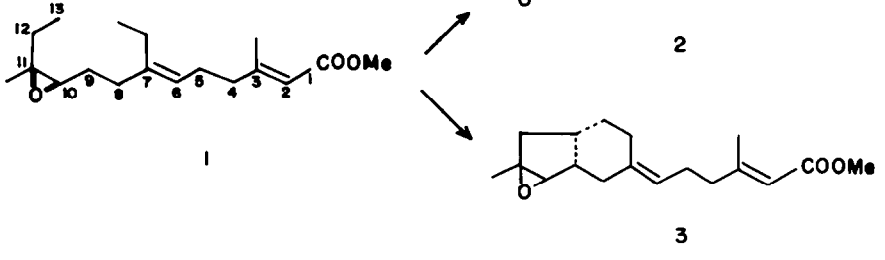



1 2 3

Fig. 1. Some modes of ring-closure in JH-I.

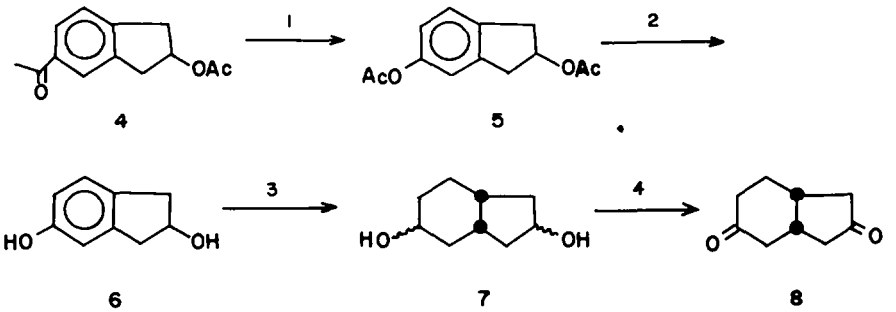



Fig. 2. Synthesis of cis-hydrindane-2, 5-dione. Reagents: 1, HCOOH, $H_2O_2$; 2, 8% KOH-MeOH; 3, Raney Ni, $H_2$, 10% NaOH aq. EtOH; 4, Jones' reagent.

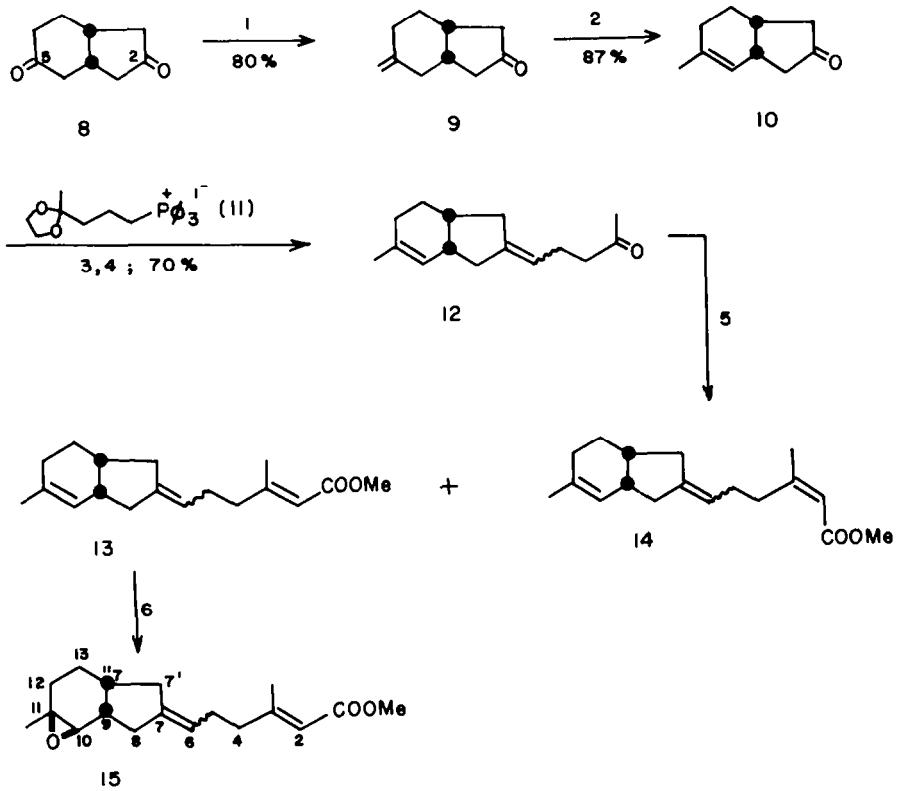



Fig. 3. Synthesis of hydrindane analogue 14 of JH-I. Reagents: 1, $MeP^+\phi_3I^-$, $KOBu^t$, THF; 2, p-TSA, $C_6H_6$; 3, $KOBu^t$, THF; 4, *p*-TSA, aq. acetone; 5, $(EtO)_2P(O)CH_2COOMe$, 6, *m*-Cl-$C_6H_4COOOH$, $CH_2Cl_2$. NaOMe, DMF.

tamination from the isomeric 6, 7-epoxide and the 6, 7:10, 11-diepoxide. Preparative-layer-chromatography furnished somewhat pure **15**. For **15**, stereochemistry shown is preferred, as the peracid attack should preferably occur from the convex face of the substrate **13**.

*Methyl cis*-10, 11-*epoxy*-7″, 13:9, 13-*cis*-*cyclo*-7-*ethyl*-3, 11-*dimethyltrideca*-2(*E*), 6(ξ)-*dienoate* (**24**). Synthetic scheme depicted in Fig. 4 was utilized to prepare the title compound **24** from the same diketone **8**. Sodium borohydide reduction of **8** furnished in good yield the anticipated hydroxyketone **16** (IR: OH 3460, 1060 $cm^{-1}$; C=O 1740 $cm^{-1}$); cyclohexanones are known[13] to react faster than cyclopentanones when exposed to hydride reduction conditions. Treatment of **16** with excess[14] (5 mole equiv) of methyltriphenylphosphonium iodide in presence of base furnished the expected hydroxyolefin **17** (IR: OH 3340, 1060 $cm^{-1}$; $C=CH_2$ 3070, 1660, 880 $cm^{-1}$. PMR: $C=CH_2$, 2 H, s, 4.83 ppm). Pyridinium chromate-on-silica gel[15] oxidation of **17**, afforded, in good yield, the required olefinic ketone **18** (IR: C=O 1720 $cm^{-1}$; $C=CH_2$ 3060, 1655, 882 $cm^{-1}$). This compound, on being refluxed in $C_6H_6$ in presence of p-TSA, led to a 65:35 (GLC) mixture of isomerised olefins (**19, 20**). The mixture was separated by preparative GLC and products identified on the basis of their PMR spectral data. Irradiation of olefinic H at 5.13 ppm (x or x′; **19a**, **20a**) led to the identification of the vicinal methine proton (y/y′,

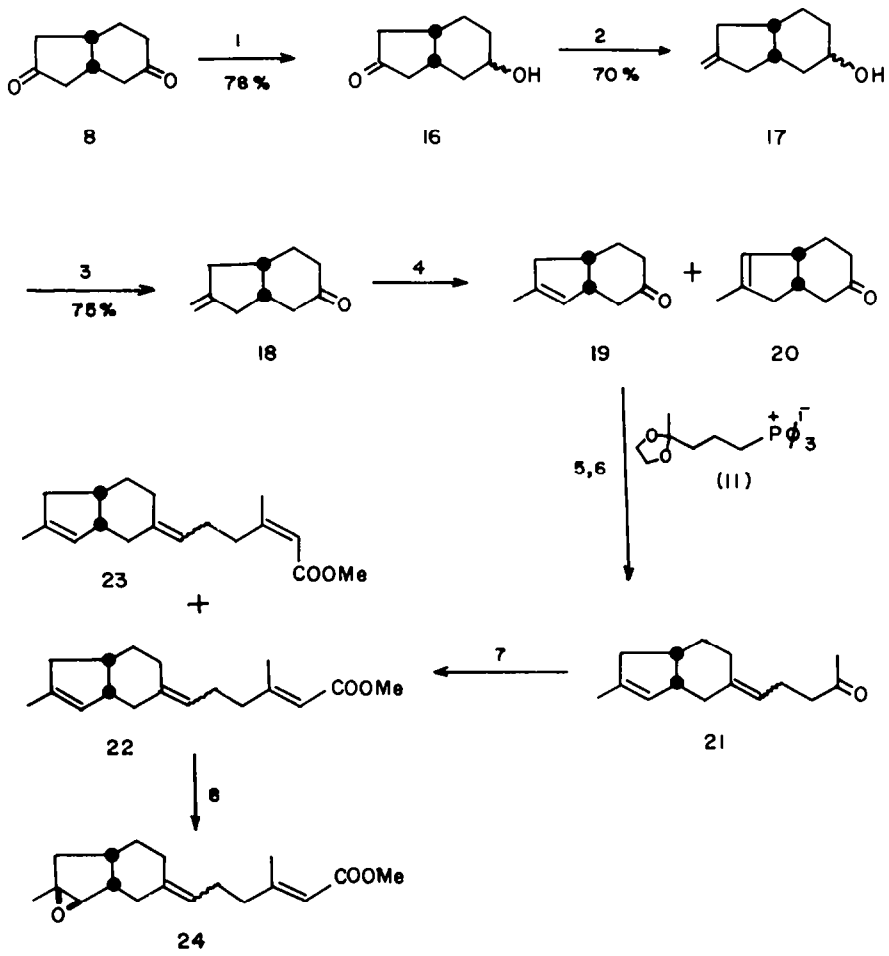
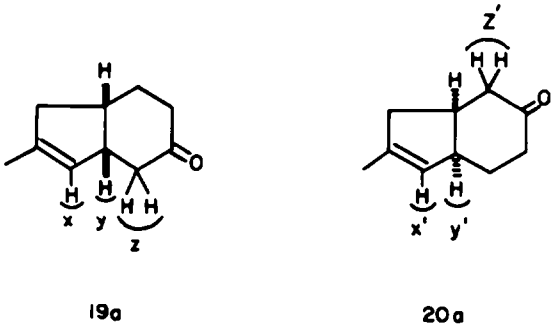



Fig. 4. Synthesis of hydrindane analogue **24** of JH-I Reagents: 1, $NaBH_4$, EtOH; 2, $MeP^+\phi_3I^-$, KOBu$^t$, THF; 3, $CrO_3$–pyr–$SiO_2$ gel; 4, p-TSA, $C_6H_6$; 5, KOBu$^t$, THF; 6, p-TSA, aq. acetone; 7, $(MeO)_2P(O)CH_2COOMe$, NaOMe, DMF; 8, m-Cl-$C_6H_4COOOH$, $CH_2Cl_2$.

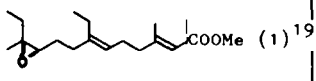
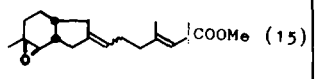
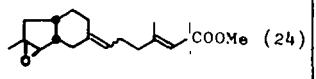
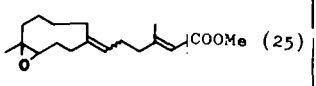



~ 2.88 ppm); irradiation at 2.88 ppm led to collapse of a split signal at 2.08 ppm, assignable to $CH_2CO$ (z/z') in the case of only one compound, which then must be assigned structure **19**. Interaction of **19** with the phosphonium salt **11** in presence of KOBu$^t$ in THF, followed by acid hydrolysis furnished the dienone **21**, which from its PMR spectrum and GLC behaviour (single peak on two different columns; Carbowax, SE30) appears to be a single isomer (*cf* **12**). Horner–Wittig reaction[11] of **21** with trimethylphosphonoacetete in presence of sodium methoxide in DMF yielded an approx. 2:1 (GLC) mixture of triene esters **22**, **23**; which were separated by IDCC; structures were readily assigned[12] on the basis of their PMR spectra.

Epoxidation of the E-isomer (**22**) with m-chloroperbenzoic acid furnished the desired **24** as the main product, which could be partially purified by preparative-layer-chromatography. Based on reasons already considered in the case of **15**, this epoxide (**24**) is also assigned the stereochemistry shown.

*Juvenile hormone activity.* The two hydrindane analogues **15** and **24** were evaluated[16] against three insects: *Dysdercus cingulatus* F., *Graphosoma italicum* Mull. and *Tenebrio molitor* L. Results, in terms of inhibition dose-50 (IR-50),[17] are given in Table 1. For comparison, data have also been included for JH-1 (**1**) and the cyclononane analogue (**25**) described earlier.[1] Compounds 15, 24 and 25 have only moderate[18] activity against Pyrrhocorid bugs and are completely inactive against the other two insect types. Thus, these compounds belong to the class of selective juvenoids. This selectivity may be ascribed to decreased flexibility of the molecule, resulting in incompatability with certain receptor sites.

Table 1. Insect juvenile hormone activity

| Compound | Inhibition dose-50 (ID-50) | | |
|---|---|---|---|
| | $D_5E$ | $G_5E$ | TpE |
|  COOMe (1)[19] | 0.5 | 1 | 1 |
|  COOMe (15) | 1.0 | in | in |
|  COOMe (24) | 5.0 | in | in |
|  COOMe (25) | 8.0 | in | in |

ID-50 : represents amounts in μg per specimen which will cause exactly half-larval or half-pupal adultoids

$D_5E$ : Dysdercus cingulatus F., 5th instar larvae, external application.

$G_5E$ : Graphosoma italicum Mull., 5th instar larvae, external application.

TpE : Tenebrio molitor L., pupae, external application

in : inactive upto 500 μg/spec.

## EXPERIMENTAL

All m.ps and b.ps are uncorrected. Light petroleum refers to the fraction b.p. 60–80°. All solvent extracts were finally washed with brine and dried (anhydrous $Na_2SO_4$).

The following instruments were used for spectral/analytical data: Perkin–Elmer infrared spectrophotometer, model 267; Perkin–Elmer model R32 (90 MHz), NMR spectrometer; Varian Mat. CH-7 Mass spectrometer (70 eV, direct inlet system); Hewlett–Packard 5712A and 7624A gas chromatographs (Al columns, 180 cm × 0.6 cm; support 60–80 mesh Chromosorb W; carrier gas, $H_2$). All PMR spectra were recorded with 15–20% soln in $CCl_4$ (unless otherwise stated) with TMS as internal reference; signals are reported in ppm($\delta$); while citing PMR data the following abbreviations have been used; *s*, singlet; *d*, doublet; *t* triplet; *q*, quartet; *m*, multiplet; *b*, broad. While summarising mass spectral data, besides the molecular ion, ten most abundant ions (*m/e*) are reported with their relative intensities.

Silica gel for column chromatography (−100, +200 mesh) was washed with hot water till sulphate-free, dried at 125–130° for 6–8 hrs and standardised.[20] TLC was carried out on $SiO_2$-gel layers (0.25 mm) containing 15% gypsum and activated at 110–115° (2 hr).

### 2, 5-*Diacetoxyindane* (5)

To a stirred soln of HCOOH (60 ml, 85%) and $H_2O_2$ (14 ml, 30%) ketone **4** (10.9 g, 0.05 mole) was added during 15 min at room temp (25–30°) and further stirred at the same temp for 22 hr. Removal of HCOOH under reduced pressure at 35–40° gave a reddish product (diol formate–acetate) which was mixed with KOH (7.0 g), $H_2O$ (5 ml), $CH_3OH$ (50 ml) and refluxed (5 hr). Methanol was removed under reduced pressure and the residue diluted with $H_2O$ (100 ml), acidified with dil HCl (1:1), extracted with EtOAc and worked up in the usual manner to furnish a product which was acetylated (12 hr) with $Ac_2O$ (30 ml) and pyridine (5 ml) at room temp. Usual work-up of the product with EtOAc (75 ml × 3) and distillation afforded **5** as a white solid (8.9 g, 76%), b.p. 180° (bath)/1 mm, m.p. 70–71° (lit[2]: m.p. 72–73°).

### *Indane*-2, 5-*diol* (6)

The above diacetate (10.0 g, 0.043 mole) in MeOH (60 ml) was mixed with KOH (6 g), $H_2O$ (15 ml) and refluxed (5 hr). Removal of $CH_3OH$ under reduced pressure and usual work-up of the residue gave **6** as a white solid (4.2 g, 66%), b.p. 215–220° (bath) 1 mm, m.p. 112–113°. IR(KBr): 3380, 3140, 1605, 1474, 1428, 1330, 1280, 1250, 1235, 1132, 1045, 940, 882, 750 $cm^{-1}$. Mass: *m/e* 150 ($M^+$, 68%), 121 (27%), 108(28%), 107(61%), 94(26%), 93(100%), 92(42%), 91(43%), 80(54%), 78(39%), 54(27%). (Found: C, 72.22; H, 6.90. $C_9H_{10}O_2$ requires: C, 71.98; H, 6.71%.

### *cis-Hydindane*-2, 5-*diol* (7)

The diol **6** (13.9 g, 0.093 mole) in EtOH (300 ml) was hydrogenated in a Parr apparatus with Raney Ni-$W_2$ (2.0 g) and 10% NaOH aq (10 ml) at a pressure of ~1600 psi at 155–160° for 8 hr. The reaction mixture was cooled, and filtered. Ethanol was removed under reduced pressure and the residue diluted with $H_2O$ (50 ml), neutralized with 15% HCl aq, extracted with EtOAc (75 ml × 3), washed, dried and freed of solvent to furnish a colourless thick liquid (13.9 g) which was chromatographed on a silica gel/II column (30 cm × 4.5 cm) with TLC monitoring (50% EtOAc in $C_6H_6$). The column was eluted with $C_6H_6$–EtOAc/1:1 (1000 ml), to give hydrogenolysed product (4.0 g); further elution with EtOAc (1250 ml) furnished the desired saturated diol **7** as a colorless thick liquid (9.8 g, 68%) which was pure enough for the next step.

### *cis-Hydrindane*-2, 5-*dione* (8)

To a stirred soln of above diol **7** (7.7 g, 0.05 mole) in acetone (40 ml) was added Jones' reagent[21] (17 ml) at 5–8°

during 6 hrs. The product was isolated with $CHCl_3$. Distillation gave **8** as a colorless liquid (7.3 g, 96%), b.p. 150–155° (bath)/0.1 mm, $n_D^{26}$ 1.4981. (GLC purity 96%; 5% Carbowax 20 M, 190°). IR ($CCl_4$): 3030, 2950, 1755, 1725, 1420, 1240, 1215, 1170, 1150 $cm^{-1}$. Mass: *m/e* 152($M^+$, 100%), 123(22%), 111(33%), 96(30%), 83(21%), 70(33%), 69(96%), 68(26%), 56(84%), 55(35%), 54(21%). (Found: C, 71.32; H, 7.40. $C_9H_{12}O_2$ requires: C, 71.02; H, 7.95%.

*5-Methylene-cis-hydrindan-2-one* (**9**)

To a stirred suspension of freshly prepared KOBu$^t$ (2.7 g, 0.024 mole) in $C_6H_6$ (130 ml) was added methyl triphenylphosphonium iodide (8.88 g; 0.022 mole) and the mixture stirred for another 0.5 hr at room temp (25–30°). The resulting yellow phosphorane soln was transferred with $N_2$ to the addition funnel and added (1 hr) dropwise to a stirred soln of the diketone **8** (3.08 g, 0.02 mole) in $C_6H_6$ (10 ml) at 0–3° and further stirred for 2 hr at the same temp. After additional stirring (5 hr) at room temp, the brownish reaction mixture was diluted with $H_2O$ (50 ml), $C_6H_6$ layer separated and aq layer extracted with light petroleum (75 ml × 3). The organic layer was worked up in the usual manner to give a semi-solid which was treated with light petroleum (50 ml), digested (10 min), and filtered. The resulting soln was chilled to −10 to −15° (3.5 hr) and filtered to remove triphenylphosphine oxide. The filtrate was freed of solvent to furnish an yellowish oil which was taken up in light petroleum (3 ml) and filtered through a column of silica gel/II (15 cm × 2.5 cm). The column was washed with light petroleum–$C_6H_6$/1:1 (600 ml) and the eluate worked up to give **9** as a colorless liquid (2.4 g, 80%), b.p. 90–92° (bath)/0.1 mm, $n_D^{26}$ 1.5066 (GLC purity 95%; 5% Carbowax 20 M, 180°). IR ($CCl_4$): 2920, 1745, 1410, 1150, 900 $cm^{-1}$. PMR: $C{=}CH_2$ (24, *d*, 4.70, 4.76 ppm). Mass: *m/e* 150 ($M^+$, 100%), 108 (35%), 107 (40%), 95(80%), 94(33%), 93(100%), 92(33%), 91(33), 81(55%), 80(80%), 68(33%). (Found: C, 79.50; H, 9.30. $C_{10}H_{14}O$ requires: C, 79.95; H, 9.39%.

*5-Methyl-cis-hydrind-4-en-2-one* (**10**)

A mixture of the olefin **9** (3.0 g, 0.02 mole), p-TSA-$H_2O$ (0.3 g) in $C_6H_6$ (50 ml) was heated at reflux (10 hr). The cooled reddish mixture was diluted with $H_2O$ (40 ml) and neutralized (solid $NaHCO_3$). The $C_6H_6$ layer was separated and aq layer extracted with $C_6H_6$ (50 ml × 3) and worked up in the usual manner to give **10** as a colorless liquid (2.6 g, 87%), b.p. 90–92° (bath)/0.1 mm, $n_D^{26}$ 1.4988 (GLC purity 97%; 5% Carbowax 20 M, 180°). IR($CCl_4$): 3010, 2922, 1745, 1458, 1442, 1410, 1220, 1155 $cm^{-1}$. PMR: Me. C=C (3 H, bs, 1.68 ppm), CH=C (1H, bs, 5.36 ppm, $W_H$ = 7.5 Hz). Mass: *m/e* 150 ($M^+$, 40%), 122(14%), 107(41%), 91(100%), 93(27%), 92(33%), 82(14%), 80(41%), 78(28%), 59(20%), 54(25%). (Found: C, 79.50; H, 9.30. $C_{10}H_{14}O$ requires: C, 79.95; H, 9.39%).

*6″, 8:6″, 12-cis-Cyclo-10-methyl-6-ethyldodeca-5* (ξ), *9* (*Z*)*-dien-2-one* (**12**)

To a stirred suspension of freshly prepared KOBu$^t$ (2.46 g, 0.0219 mole) in THF (40 ml) was added the acetal phosphonium iodide (**11**; 10.36 g, 0.02 mole) and the mixture stirred (30 min) at room temp (25–30°). To the resulting orange phosphorane soln, a soln of olefinic ketone **10** (1.5 g, 0.01 mole) in THF (3 ml) was added (5 min) with stirring and the stirring continued for another 1 hr ($N_2$) at room temp and then for 3 hr at 45–50°. THF was distilled off and the residue diluted with $H_2O$ (35 ml), extracted with light petroleum (40 ml × 4), dried and concentrated to 50 ml. This material was chilled to −10 to −15° (3.5) (3.5 hr) and filtered to remove triphenylphosphine oxide. The filtrate was freed of solvent to furnish an yellowish oil which was mixed with acetone (20 ml), $H_2O$ (5 ml), p-toluene sulfonic acid (0.1 g) and stirred (12 hr) at room temp to effect deketalization. Acetone was distilled off, the residue was diluted with $H_2O$ (25 ml), neutralized with solid $K_2CO_3$ (0.15 g) and extracted with light petroleum (30 ml × 4). The extract was worked up in the usual manner to furnish an yellow oil which was taken up in light petroleum (3 ml) and filtered through a column of silica gel/II (20 cm × 2). The column was washed with light petroleum–$C_6H_6$/1:1 (600 ml) and the eluate worked up to give **12** as a colorless liquid (1.40 g, 70%), b.p. 150 (bath)/0.1 mm, $n_D^{26}$ 1.5032 (GLC purity, 97%; 5% Carbowax 20 M, 200°). IR ($CCl_4$): 3008, 2920, 1720, 1440, 1370, 1235, 1170 $cm^{-1}$. PMR: Me.C=CH (3 H, bs, 1.65 ppm), COMe (3 H, *s*, 2.16 ppm), Me.C=CH, C=CH (2 H, bm, 5.0–5.5 ppm). Mass: *m/e* 218 ($M^+$, 81%), 162(61%), 148(56%), 135(69%), 107(72%), 106(33%), 95(100%), 94(82%), 93(63%), 80(46%), 78(41%), 72(26%). (Found: C, 82.80; H, 10.31. $C_{15}H_{22}O$ requires: C, 82.51; H, 10.16%.)

*Methyl E, ξ, Z- and Z, ξ, Z-7″, 9:7″, 13-cis-Cyclo-7-ethyl-3, 11-dimethyltrideca-2, 6, 10-trienoate* (**13** *and* **14**).

To a stirred suspension of NaOMe (1.74 g, 0.0322 mole) in DMF (15 ml) was added methyl diethylphosphonoacetate (5.78 g, 0.0275 mole) at 20–25° and stirred for 30 min under $N_2$. To this clear soln of phosphonate carbanion was added a soln of the ketone **12** (1.5 g, 0.0068 mole) in DMF (3 ml) at 20° and stirred (24 hr) at room temp (25–30°). The resulting dark brown soln was diluted with $H_2O$ (35 ml) and extracted with light petroleum (25 ml × 5). The combined extracts was worked up in the usual manner to furnish a yellowish oil (1.6 g, 89%) which was chromatographed on $SiO_2$/II column (13 cm × 2 cm). Light petroleum—$C_6H_6$/1:1 (850 ml) eluted a mixture of **13** and **14** (0.86 g), **12, 13** and **14** (0.265 g) and **13** (0.273 g).

The above mixture of **13** and **14** (1.0 g) was separated by IDCC (silica gel, 24 cm × 4.6 cm; light petroleum—$C_6H_6$/60:40) to get pure **13** and **14**.

E-Ester **13** (470 mg): b.p. 170 (bath)/0.05 mm, $n_D^{26}$ 1.5122 (GLC purity, 94%; 5% Carbowax 20 M, 190°). IR ($CCl_4$): 2905, 1720, 1644, 1430, 1372, 1352, 1320, 1272, 1220, 1142, 1045, 915 $cm^{-1}$. PMR: Me.C=CH (3 H, bs, 1.64 ppm), Me.C=C.COOMe (3 H, *s*, 2.15 ppm), COOMe (3 H, *s*, 3.61 ppm), C=CH two 1 H signals, *m*, 5.10 ppm, $W_H$ = 15 Hz, and 5.28 ppm, $W_H$ = 12 Hz), C=CH.COOMe (1 H, bs, 5.55 ppm). Mass: *m/e* 274 ($M^+$, 44%), 161 (100%), 133(50%), 119(25%), 114(60%), 105(73%), 93(72%), 91(58%), 81(55%), 79(50%), 77(38%). (Found: C, 79.11; H, 9.12. $C_{18}H_{26}O_2$ requires: C, 78.79; H, 9.55%.)

Z-Ester **14** (120 mg): b.p. 170° (bath)/0.05 mm, $n_D^{26}$ 1.5097. (GLC purity, 94%; 5% Carbowax 20 M, 190°). IR ($CCl_4$): 2920, 1718, 1640, 1430, 1372, 1232, 1145, 1050, 915, 850 $cm^{-1}$. PMR: Me.C=C (3 H, bs, 1.64 ppm), Me.C=COOMe (3 H, *s*, 1.88 ppm), COOMe (3, *s*, 3.62 ppm), C=CH (1 H, *m*, 5.16 ppm, $W_H$ = 14 Hz; 1 H, *m*, $W_H$ = 12 Hz), C=CHOOMe (1 H, bs, 5.55 ppm). Mass: *m/e* 274 ($M^+$, 55%), 161(100%), 160(32%), 159(34%), 133(85%), 114(60%), 105(78%), 93(72%), 91(47%), 81(47%), 79(39%). (Found: C, 79.20; H, 9.15. $C_{18}H_{26}O_2$ requires: C, 78.79; H, 9.55%.)

*Methyl cis-10, 11-epoxy-7″, 9:7″, 13-cis-cyclo-7-ethyl-3, 11-dimethyltrideca-2(E), 6(ξ)-dienoate* (**15**)

A soln of m-Cl-$PhCO_3H$ (131.6 mg, 65.5%) in $CH_2Cl_2$ (8 ml) was added to a soln of **13** (137 mg, 0.005 mole) in $CH_2Cl_2$ (5 ml) at 0°. The mixture was then left aside overnight at 0°. The usual work-up furnished a colorless oil (127 mg) which was purified by preparative-layer-chromatography (silica gel, 20 cm × 20 cm × 0.5 mm; light petroleum–EtOAc/18:2) to get the required JH-analogue **15** (41 mg; $R_f$ 0.5) still slightly contaminated with the 6, 7-epoxy derivative (PMR). IR ($CCl_4$): 2920, 1720, 1648, 1432, 1378, 1360, 1222, 1148, 860 $cm^{-1}$. PMR: Me (3 H, *s*, 1.26 ppm), Me.C=COOMe (3 H, *s*, 2.16 ppm), COOMe (3 H, *s*, 3.62 ppm), CH=C (1 H, *m*, 5.28 ppm), C=CH.COOMe (1 H, bs, 5.58 ppm). Mass: *m/e* 290 ($M^+$, 12%), 159(68%), 133(100%), 114(56%), 105(56%), 93(88%), 91(65%), 81(94%), 79(76%), 57(75%), 55(64%). (Found: C, 74.71; H, 9.20. $C_{18}H_{26}O_3$ requires: C, 74.44; H, 9.03%.)

*cis-Hydrindane-5-ol-2-one* (**16**)

To a stirred soln of the diketone **8** (6.08 g, 0.04 mole) in EtOH (100 ml) was added a soln of $NaBH_4$ (0.38 g, 0.01 mole) in EtOH (15 ml) at 0° during 20 min and further stirred at the same temp for 2 hr. After removal of the EtOH, the product (5.5 g) was isolated with $CHCl_3$, and chromatographed on a column of silica gel/II (60 cm × 2.5 cm). The column was eluted with $C_6H_6$ (100 ml), 10% EtOAc in $C_6H_6$ (50 ml × 2), 20% EtOAc in $C_6H_6$ (50 ml × 2), 30% EtOAc in $C_6H_6$ (50 ml × 4), 40% EtOAc in $C_6H_6$ (50 ml × 6), 50% EtOAc in $C_6H_6$ (50 ml × 2) and the eluates worked up to give starting dione **8** (0.405 g), required hydroxyketone **16** (4.8 g, 77.9%) and diol (0.376 g). Hydroxyketone (**16**): b.p. 160–3° (bath/0.1 mm. IR ($CCl_4$): 3460, 2990, 2940, 1740, 1460, 1412, 1375, 1170, 1060, 968 $cm^{-1}$. PMR: CHOH (1 H, *m*, 3.70 ppm): Mass: *m/e* 154 ($M^+$, 75%), 136(68%), 108(97%), 95(66%), 94(100%), 93(42%), 82(41%), 79(62%), 70(37%), 67(60%), 55(37%). (Found: C, 70.80; H, 9.41. $C_9H_{14}O_2$ requires: C, 70.10; H, 9.15%.)

2-*Methylene-cis-hydrindan-5-ol* (**17**)

To a stirred suspension of freshly prepared KOBu$^t$ (7.1 g) in THF (70 ml) was added methyl triphenylphosphonium iodide (24.0 g, 0.06 mole) and the mixture stirred for 0.5 hr ($N_2$) at room temp (25–30°). To the resulting intense yellow phosphorane, a soln of hydroxyketone **16** (1.8 g, 0.012 mole) in THF (3 ml) was added (5 min) with stirring and the stirring continued for another 5 hr ($N_2$) at room temp and then left overnight. THF was distilled off and the residue treated with $H_2O$ (25 ml), extracted with light petroleum (50 ml × 4), dried, and concentrated to 50 ml. The resulting soln was chilled to −10 to −15° (2 hr) and filtered to remove triphenylphosphine oxide. The filtrate was freed of solvent to furnish a yellow oil which was passed through a column of silica gel/II (10 cm × 2 cm). The column was washed with light petroleum–$C_6H_6$/1:1 (700 ml) and the eluate worked up to give **17** as a colorless liquid (1.28 g, 70%), b.p. 110° (bath)/0.1 mm, $n_D^{26}$ 1.5051. IR ($CCl_4$): 3340, 3070, 2920, 1660, 1452, 1432, 1368, 1240, 1162, 1060, 1010, 985, 880 $cm^{-1}$. PMR: CHOH (1 H, *m*, 3.3–4.0 ppm), C=$CH_2$ (2 H, *s*, 4.83 ppm). Mass: *m/e* 152 ($M^+$; 24%), 134(100%), 119(44%), 106(42%), 105(28%), 94(30%), 93(100%), 92(63%), 91(47%), 79(51%), 78(58%). (Found: C, 78.90; H, 10.12. $C_{10}H_{16}O$ requires: C, 78.89; H, 10.59%.)

2-*Methylene-cis-hydrindan-5-one* (**18**)

To a soln of olefinic alcohol **17** (1.5 g, 0.01 mole) in $CH_2Cl_2$ (60 ml) was added $CrO_3$-pyridine complex supported on silica gel[15] (28.6 g; 2.8 g reagent contained 400 mg of $CrO_3$) and shaken at room temp (25–30°) for 20 hr. The spent reagent was filtered off and washed with $CH_2Cl_2$ (20 ml × 3). The combined organic layers were washed with dil HCl (1:1, 25 ml × 1), $H_2O$ (25 ml × 2) and worked up in the usual manner to give **18** as a colorless liquid (1.1 g, 75%), b.p. 90° (bath)/0.1 mm, $n_D^{26}$ 1.4966 (GLC purity, 98%; 10% SE-30, 170°). IR ($CCl_4$): 3060, 2930, 1720, 1655, 1430, 1230, 1142, 882 $cm^{-1}$. PMR: C=$CH_2$ (2H, *d*, 4.84, 4.86 ppm). Mass: *m/e* 150 ($M^+$; 36%), 107(12%), 95(13%), 94(12%), 93(45%), 92(100%), 91(10%), 80(26%), 79(24%), 77(8%), 55(8%). (Found: C, 80.20; H, 9.59. $C_{10}H_{14}O$ requires: C, 79.95; H, 9.39%.)

2-*Methyl-cis-hydrind-2-en-5-one* (**19**) *and* 2-*Methyl-cis-hydrind-1-en-5-one* (**20**)

This product was prepared from **18** (3.0 g, 0.02 mole) in 85% yield in the same manner as described for **10**: b.p. 90 (bath)/0.1 mm (GLC purity, 96%; 5% Carbowax 20 M, 130°; 19:20/65:35).

The above mixture was separated by preparative gas chromatography (20% Carbowax 20 M on Chromosorb W, 45–60 mesh; 12 ft × $\frac{1}{8}$ in. Al Column; 160°; 100 ml/min). The compound **19** showed the following properties: b.p. 90–92°/0.1 mm, $n_D^{26}$ 1.4919. IR ($CCl_4$): 2918, 1710, 1438, 1372, 1330, 1315, 1220, 1120 $cm^{-1}$. PMR: Me.C=CH (3 H, *d*, 1.72 ppm, J = 1 Hz), Me.C=CH (1 H, bs, 5.13 ppm). Mass: *m/e* 150 ($M^+$; 19%), 107(20%), 95(12%), 94(21%), 93(96%), 92(32%), 91(36%), 80(100%), 79(75%), 77(43%), 57(17%). (Found: C, 80.30; H, 10.0. $C_{10}H_{14}O$ requires: C, 79.95; H, 9.39%.)

The compound **20** showed the following physical properties: b.p. 90–92° (bath)/0.1 mm, $n_D^{26}$ 1.4950. IR ($CCl_4$): 2916, 1710, 1440, 1224 $cm^{-1}$. PMR: Me.C=CH (3 H, bs, 1.70 ppm), Me.C=CH (1 H, bs 5.12 ppm). Mass: *m/e* 150 ($M^+$, 67%), 135(16%), 107(56%), 95(26%), 94(25%), 93(100%), 92(31%), 91(24%), 80(13%), 79(20%), 77(14%), 65(14%). (Found: C, 80.10; H, 9.80. $C_{10}H_{14}O$ requires: C, 79.95; H, 9.39%.)

6″,12:8, 12-*cis-Cyclo*-10-*methyl*-6-*ethyldodeca*-5 (ξ), 9 (*Z*)-*dien*-2-*one* (**21**)

This compound was prepared in 74% yield from **19** (0.75 g, 0.05 mole) in the same manner as described for **12**: b.p. 150–155° (bath)/0.1 mm; $n_D^{26}$ 1.4990 (GLC purity, 98%; 5% Carbowax 20 M, 190°). IR ($CCl_4$): 2940, 2870, 1730, 1450, 1365, 1166 $cm^{-1}$. PMR: Me.C=CH (3 H, bs, 1.70 ppm), COMe (3 H, *s*, 2.05 ppm), two C=CH (2H, bm, 5.0–5.20 ppm). Mass; *M/e* 218 ($M^+$, 73%), 200(19%), 160(36%), 145(26%), 133(59%), 105(17%), 94(15%), 93(97%), 92(18%), 81(20%), 80(100%). (Found: C, 82.61; H, 10.20; $C_{15}H_{22}O$ requires: C, 82.51; H, 10.16%.)

*Methyl E, Z- and Z, Z-7″*, 13:9, 13-*cis-cyclo*-7-*ethyl*-3, 11-*dimethyltrideca*-2, 6, 10-*trienoate* (**22** *and* **23**)

Trimethylphosphonoacetate (1.16 g, 0.0064 mole) was added (5 min) to a stirred suspension of NaOMe (0.347 g, 0.0064 mole) in DMF (6 ml), under $N_2$ and further stirred (30 min) at room temp (30°). To the resulting clear soln was added (5 min) a soln of ketone **21** (0.7 g, 0.0032 mole) in DMF (2 ml) at 20° and further stirred (24 hr) at room temp. This was then diluted with $H_2O$ (20 ml), extracted with $Et_2O$ (20 ml × 4) and worked up in the usual manner to furnish a mixture of **22** and **23** as a colorless liquid (0.624 g, 71%), b.p. 170°/0.05 mm (GLC purity 96%; 5% Carbowax 20 M, 190°; **22**:**23**/2:1).

The above mixture (600 mg) was separated by IDCC (silica gel, 24 cm × 4.6 cm, light petroleum—$C_6H_6$/60:40) to get pure **22** (273 mg) and **23** (130 mg).

The E-isomer **22** showed the following physical properties: b.p. 170° (bath)/0.05 mm, $n_D^{26}$ 1.5084. IR ($CCl_4$): 2960, 2880, 2860, 1735, 1660, 1450, 1262, 1240, 1162, 872 $cm^{-1}$. PMR: Me.C=CH (3 H, bs, 1.70 ppm), Me.C=C.COOMe (3 H, *s*, 2.13 ppm), COOMe (3 H, *s*, 3.62 ppm), two C=CH (2 H, bm, 5.11 ppm, $W_H$ = 17 Hz), C=CH.COOMe (1 H, bs, 5.57 ppm). Mass: *m/e* 274 ($M^+$; 98%), 161 (100%), 160 (22%), 145 (18%), 133 (51%), 119 (18%), 114 (39%), 105 (27%), 93 (64%), 81 (22%), 80 (40%). (Found: C, 78.50; H, 10.11. $C_{18}H_{26}O_2$ requires: C, 78.79; H, 9.55%.)

The Z-isomer **23** showed the following physical properties: b.p. 170° (bath)/0.05 mm, $n_D^{26}$ 1.5080. IR ($CCl_4$): 2930, 2860, 2840, 1730, 1652, 1450, 1440, 1365, 1325, 1240, 1196, 1165, 926, 870 $cm^{-1}$. PMR: Me.C=C (3 H, bs, 1.70 ppm), Me.C=C.COOMe (3 H, *s*, 1.88 ppm), COOMe (3 H, *s*, 3.62 ppm), two C=CH (2 H, bm, 5.11 ppm, $W_H$ = 13 Hz), C=CH.COOMe (1 H, bs, 5.57 ppm). Mass: *m/e* 274 ($M^+$; 90%), 161(100%), 160(21%), 133(65%), 132(18%), 119(24%), 114(44%), 105(40%), 93(87%), 91(20%), 81(40%), 80(80%). (Found: C, 78.80; H, 9.50. $C_{18}H_{26}O_2$ requires: C, 78.79; H, 9.55%.)

*Methyl cis*-10,11-*epoxy*-7″, 13:9,13-*cis-cyclo*-7-*ethyl*-3, 11-*dimethyltrideca*-2(*E*), 6(ξ)-*dienoate* (**24**)

Epoxidation of **22** (137 mg, 0.005 mole) with m-Cl-$C_6H_4COOOH$ in $CH_2Cl_2$ was carried out exactly as described for **15** to get a product still contaminated (PMR) with the 6, 7-epoxide. Data reported is after correction for the impurity. PMR: Me (3 H, *s*, 1.35 ppm), Me.C=C.COOMe (3 H, bs, 2.14 ppm), COOMe (3 H, *s*,

3.62 ppm), C=CH (1 H, bs, 5.2 ppm), C=CH.COOMe (1 H, bs, 5.61 ppm). Mass: *m/e* 290 ($M^+$, 15%), 177(40%), 133(43%), 119(61%), 114(46%), 105(41%), 93(100%), 92(71%), 91(71%), 81(72%), 80(54%), 79(66%). (Found: C, 74.30; H, 8.90. $C_{18}H_{26}O_3$ requires: C, 74.44; H, 9.03%.)

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[8]Mixtures of isomers have been reported from condensation of other ketones with the same phosphorane under essentially similar reaction conditions.[7d] However, it may be noted that the product derived from this material in the next step appeared to consist of only two compounds (**13**, **14**) both by GLC and PMR. Exactly parallel results were earlier[1] obtained while synthesising a cyclononane analogue of JH-I.

[9]It has not been possible to deduce the stereochemistry of the product from the PMR data or from analysis of similar cases.[7]

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