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PRODUCTS ACTIVE ON ARTHROPOD—III†

INSECT JUVENILE HORMONE MIMICS (PART 3): CYCLONONANE ANALOGUE OF CECROPIA JUVENILE HORMONE‡

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Abstract—Synthesis of cyclononane analogue of Cecropia juvenile hormone-I is described. The analogue is only moderately active against *Dysdercus cingulatus*.

Opening of cyclic or closing of acyclic structures has often been exploited, sometimes with gratifying results, in the molecular modification of biologically active compounds.[1] The approach is essentially based on the hypothesis that such transformations may lead to compounds with comparable shapes and other physical characteristics, and thus, may retain, in a modified form, the biological activity. Though, several compounds based on Cecropia juvenile hormone-I (JH-I; 1), JH-II (2), and JH-III (3)[2] containing 3-,[3] 5-[4,6] and 6-membered[4,5,7] carbocycles have been synthesised, invariably additional C atoms have also been incorporated. Many of these compounds were found to be effective growth regulators, though on different insect species. The present investigation was undertaken to see how by closing a part-structure of JH-I (1), the JH activity would be affected. Of the very large number of structures that can be generated from such an exercise, we have restricted our effort to those schematically shown in Fig. 1. The synthesis of 4 is described in the present communication, while the preparation of 5 and 6 will form the subject matter of a subsequent publication. It is realised that in going to structures such as 4, 5, 6 there will be some distortion in the shape of the original molecule (1), but this is not significant, as verified from molecular models, the overall essentially linear disposition of the functionality being maintained.

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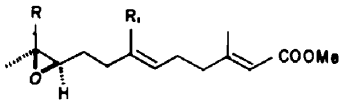

1 : R = R₁ = Et
2 : R = Et, R₁ = Me
3 : R = R₁ = Me

5-Methyl-cyclonon-4(Z)-en-1-one

For the synthesis of 4, 5-methyl-cyclonon-4(*Z*)-en-1-one (8) appeared to be a logical and convenient starting point. The preparation of 8 has, apparently, not been described. Suitably constituted 1,3-glycols can be made to fragment generating olefinic ketones, in which the ethylenic linkage is formed in a stereospecific manner.[8] This reaction (Fig. 2) appeared most suitable for the synthesis of 8. The required diol 15 was prepared from the known[9,10] bicyclic keto alcohol 9, along the lines indicated in Fig. 3. The ketol 9 was converted to the olefinic alcohol 11 *via* the thioketal (10), either by desulphurization with Raney Ni[11] or with sodium-liquid ammonia.[12] The olefin 11 on exposure to perbenzoic acid in dichloromethane, furnished the desired epoxy derivative, in which the oxirane function is considered to be β-oriented (12), in view of the known[13] assistance from an OH function in directing the peracid attack in a non-polar solvent. Refluxing of 12 with LAH in THF yielded, in excellent yield, a crystalline diol, which from its PMR spectrum was clearly the required 13, as anticipated.[14]

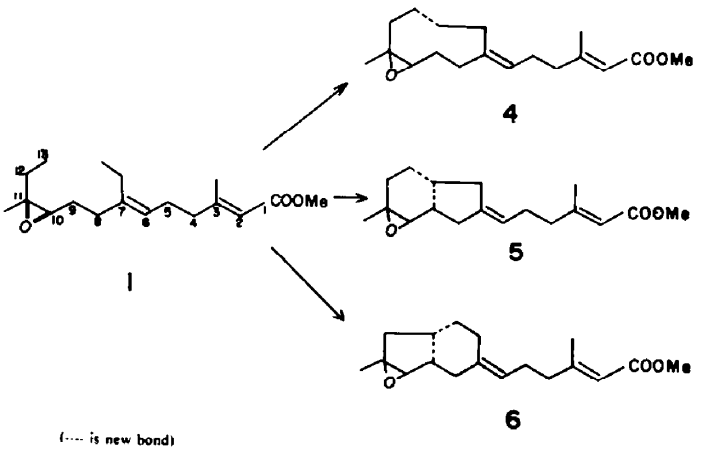

Fig. 1. Some modes of ring-incorporation in JH-I.

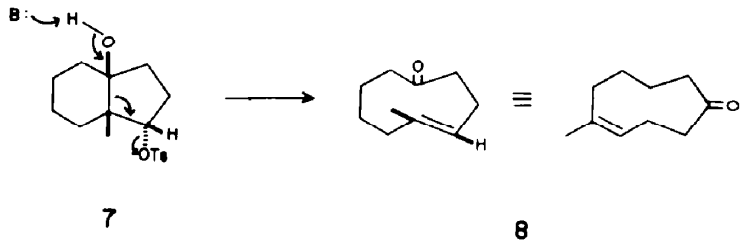

Fig. 2.

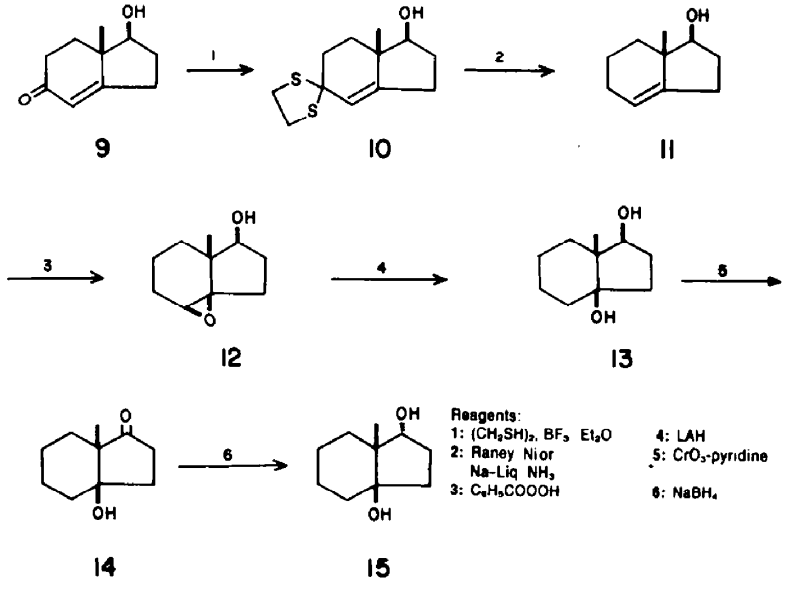

Fig. 3. Synthesis of 4, 5, 6, 7, 8, 9-hexahydro-8β-methylindane-1α, 9β-diol.

Pyridine-chromic acid[15] oxidation of **13** furnished ketol **14**. Hydride reduction of **14** was expected to occur from the convex face of the molecule, possibly further assisted[16] by the 9β-OH, to give essentially **15**. In practice, $NaBH_4$-MeOH reduction of **14** afforded a single crystalline diol, which was distinct from **13** (m.p., IR, PMR)[17] and is thus clearly the required **15**. The secondary hydroxyl in **15** was readily esterified with *p*-toluenesulphonyl chloride and pyridine to give **7**. This mono-tosylate (**7**) on treatment with NaH in tetrahydrofuran (35°, 24 hr) smoothly underwent the expected cleavage (Fig. 2) to furnish the anticipated 5 - methyl - cyclonon - 4(*Z*) - en - -1 - one (**8**. Mass: *m/e* 152. IR: C=O 1705 cm^{-1} PMR: Me–C=CH, 1.63 ppm, s; Me–C=CH–CH_2, 1 H, 5.50 ppm, b sig., W'_H = 14 Hz), the *Z* geometry of the olefinic linkage arising[8] from the *anti*-configuration of the Me and the leaving group in **7**.

Since, the configuration of the tertiary OH in **7** is not relevant for fragmentation to **8**, attempts were made in the initial stages of this investigation for inversion of the OH configuration in **11** by several methods,[18] but without much success.

Methyl cis - 10, 11 - *epoxy* - 7", 13 - *cyclo* - 7 - *ethyl* - 3, 11 - *dimethyl* - *trideca* - 2 (E), 6(ξ) - *dienoate* (**20**)

5-Methyl-cyclononenone (**8**) obtained as above, was next successfully elaborated into the required JH-I analogue **20**, along the lines depicted in Fig. 4. Condensation of **8** with the ylide from the much exploited[19] acetal phosphonium salt (**16**), followed by acid hydrolysis, afforded the expected dienone (**17**). The product appears to be stereo-chemically homogeneous from its behaviour on two different GLC columns (Carbowax, SE-30) and from its PMR spectrum, though this conclusion could be misleading;[20] the stereochemistry of the product also remains obscure.[21] The dienone (**17**) was next exposed[22] to dimethyl methoxycarbonylmethyl - phosphonate in presence of base to furnish finally a mixture 2:1 of the triene esters (**18**, **19**), which were readily separated by inverted - dry - column - chromatography (IDCC).[23] As expected,[22] the major product was the *E*-isomer (**18**), which was readily recognized[24] from its PMR Spectrum.

Epoxidation of the *E*-isomer (**18**) with *m*-chloroperbenzoic acid led to a mixture of the desired monoepoxide (**20**) and the diepoxide (6, 7: 10, 11-diepoxy), which were separated by preparative - layer - chromatography and recognized from their spectral characteristics.

Juvenile hormone activity

The targeted compound **20** was evaluated[25] against three insects: *Dysdercus cingulatus* F. (5th instar larvae), *Graphosoma italicum* Mull (5th instar larvae), and *Tenebrio molitor* L. (pupae). The inhibition dose-50 (ID-50)[26] was found to be 8.0, > 500 and > 500 respectively for the three insects; the corresponding values[27] for JH-I being 0.5, 1.0 and 1.0. Thus compound **20** has only moderate activity[28] against Pyrrhocorid bugs and is completely inactive against the other two insect types.

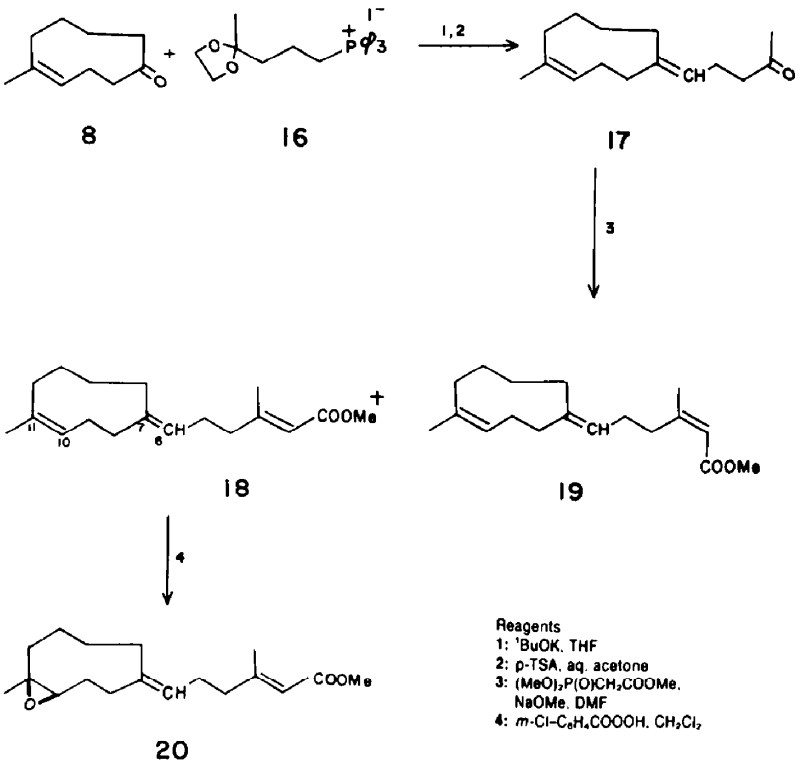

Fig. 4. Synthesis of cyclononane analogue of JH-I.

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 (anhyd 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 (A1 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 (δ); 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 hr and standardised.[29] Tlc was carried out on SiO_2-gel layers (0.25 mm) containing 15% gypsum and activated 110–115° (2 hr).

8β-Methylhydrind-4(9)-en-1β-ol (11)

To a soln of **9** (16.6 g; 0.01 mole), and ethanedithiol (14.1 g; 0.15 mole) in dry MeOH (120 ml), BF_3–etherate (14 ml) was added at 0–5° (10 min) and the mixture left aside overnight (14 hr) and allowed to reach room temp (25–28°). The resulting yellow soln was poured into ice-cold 10% NaOH aq (250 ml), extracted with $CHCl_3$ (75 ml × 4), washed with H_2O (100 ml × 2), dried and freed of solvent to furnish **10** as a crystalline solid (21.79; 90%), m.p. 105–106°. IR ($CHCl_3$): 3420, 2910, 1660, 1425, 1270, 1060, 865 cm^{-1}. PMR ($CDCl_3$): Me.C (3H, s, 0.97 ppm), SCH_2CH_2S (4H, q, 3.33 ppm, $J_1 = 7$ Hz, $J_2 = 4$ Hz), CHOH (1H, t, 3.65 ppm, J = 8 Hz). Mass: *m/e* 242 (M^+; 85%), 214 (55%), 182 (54%), 149 (27%), 138 (42%), 131 (53%), 118 (68%), 105 (100%), 91 (38%), 61 (42%), 60 (30%).

This product was suitable for desulphurization to **11** by either of the following two methods.

(i) *With Raney* Ni. A mixture of the above thioketal (2 g, 0.0083 mole), Raney Ni-W_2[30] (10 g) and EtOH (150 ml) was refluxed (20 hr, N_2), after which it was filtered and the solid and filtrate transferred to appropriate places in a Soxhlet extraction set-up. After the Raney Ni had been continuously extracted for 24 hr, the soln was freed of EtOH to get a yellowish solid, which was taken up in benzene–EtOAc (9:1) (1.5 ml) and filtered through a column of silica gel/II (30 cm × 1.4 cm), which was washed with the same solvent (250 ml). Removal of solvent furnished a solid which was purified by distillation: b.p. 90–95° (bath)/0.05 mm, m.p. 51–52°. IR (CCl_4):OH 3360, 1055 cm^{-1}; C=C 1630, 852 cm^{-1}. PMR: Me.C (3H, s, 0.88 ppm), CHOH (1H, t, 3.52 ppm, J = 8 Hz), CH=C (1H, bm, 5.23 ppm, $W_H = 9$ Hz). Mass: *m/e* 152 (M^+; 73%), 134 (41%), 119 (35%), 109 (65%), 97 (48%), 95 (40%), 93 (100%), 91 (51%), 81 (40%), 79 (52%), 67 (35%). (Found: C, 78.60; H, 10.30. $C_{10}H_{16}O$ requires: C, 78.89; H, 10.59%).

(ii) *With sodium-liq. ammonia.* The thioketal (12 g; 0.05 mole) in dry ether (500 ml) was added to liq. NH_3 (~ 1500 ml) and to this sodium (12 g, 0.52 g atom), cut in small pieces, was added (10 min) with continuous stirring. After another 15 min, the blue color of the reaction mixture was discharged by cautions addition of EtOH (25 ml). Ammonia was allowed to evaporate and the residue worked up with ether in the usual manner to finally furnish the required compound (**11**), m.p. 51–52° (6 g; 79%).

4,9-Epoxy-8β-methylhydrindan-1β-ol (12)

To a stirred soln of **11** (6.08 g; 0.04 mole) in CH_2Cl_2 (50 ml), a CH_2Cl_2 soln of PBA (0.7246 N, 55.7 ml; 0.04 mole) was added at 0–5° (30 min) and then left aside at the same temp for another 2 hr. To the mixture, water (100 ml) was added, the ether layer separated and the aq. part extracted with CH_2Cl_2 (50 ml × 3). Usual work-up furnished **12** as a colorless oil (5.8 g; 87%). IR ($CHCl_3$): 3460, 2950, 1468, 1040, 912 cm^{-1}. PMR: Me.C (3H, s, 0.97 ppm), epoxy-H (1H, m, 3.03–3.33 ppm), CHOH (1H, m, 3.7–4.1 ppm). Mass: *m/e* 168 (M^+, 24%), 124 (100%), 111 (32%), 109 (39%), 97 (55%), 95 (35%), 93 (37%), 81 (40%), 79 (39%), 66 (44%), 55 (39%). (Found: C, 71.6; H, 9.7. $C_{10}H_{16}O_2$ requires: C, 71.43; H, 9.52%).

8β-Methylhydrindan-1β, 9β-diol (13)

To a stirred slurry of LAH (1.1 g; 0.03 mole) in THF (40 ml), was added a soln of the above alcohol (5 g; 0.03 mole) in THF (10 ml) during 20 min at room temp (25–30°) and refluxed (6 hr). The reaction mixture was decomposed with cold water and worked-up in the usual manner to get the diol **13** as a white solid (4.59 g; 90%) which was crystallized from ether: light petroleum/1:2 to get the pure diol (4 g), m.p. 114–115°. IR ($CHCl_3$): 3430, 2960, 2884, 1462, 1012, 886 cm^{-1}. PMR ($CDCl_3$): Me.C (3H, s, 1.06 ppm), CHOH (1H, t, 3.70 ppm, J = 6 Hz), OH (1H, bs, 2.9 ppm). Mass: *m/e* 152 ($M^+ - 18$; 100%), 137 (78%), 134 (52%), 123 (51%), 109 (99%), 108 (85%), 107 (50%), 105 (69%), 104 (43%), 103 (55%), 81 (48%). (Found: C, 70.8; H, 10.8. $C_{10}H_{18}O_2$ requires: C, 70.59; H, 10.59%).

8β-Methyl-9β-hydroxyhydrindan-1-one (14)

CrO_3 (18 g; 0.18 mole) was added to a stirred soln of pyridine (28.4 g; 0.36 mole) in CH_2Cl_2 (450 ml) and the deep burgandy soln was stirred (15 min) at room temp. (25–30°). The diol **13** (5.1 g; 0.03 mole) in CH_2Cl_2 (10 ml) was added in one portion with stirring. A tarry black deposit separated immediately. After stirring (15 min) at room temp, the soln decanted from the residue and the residue washed with Et_2O (100 ml × 3). The mixed organic soln was washed successively with 10% NaOH aq (100 ml × 3), 10% HCl aq (100 ml × 1), 10% $NaHCO_3$ aq (100 ml × 1), brine and dried. Solvent was removed and the residue was taken up in Et_2O (200 ml), filtered, washed with brine, dried and freed of solvent to furnish **14** as a white solid which was distilled, b.p. 95–100°/0.05 mm, m.p. 89–90°, yield 3.49 g (69%). IR ($CHCl_3$): 3460, 2940, 2870, 1740, 1455, 1218, 1090, 960 cm^{-1}. PMR ($CDCl_3$): Me.C (3H, s, 1.02 ppm). Mass: *m/e* 168 (M^+; 83%), 150 (28%), 121 (23%), 112 47%), 111 (25%), 109 (38%), 108 (100%), 97 (45%), 95 (58%), 93 (39%), 67 (25%), 55 (31%). (Found: C, 71.2; H, 9.8. $C_{10}H_{16}O_2$ requires: C, 71.43; H, 9.52%).

8β-Methylhydrindan-1α, 9β-diol (15)

To a stirred soln **14** (3.36 g; 0.02 mole) in CH_3OH (30 ml) was added $NaBH_4$ (0.756 g; 0.02 mole) in small portions (15 min) followed by additional stirring at room temp (15 hr). Cold saturated aq soln of tartaric acid was added with ice-cooling until the white precipitate redissolved. Almost all of the Me_3OH was removed under reduced pressure and the resulting aq soln was extracted with Et_2O (50 ml × 4), the extract worked up in the usual manner to get **15** as a white solid which was crystallized from ether: light petroleum/1:2 to furnish pure diol (2.97 g; 87%), m.p. 122–123°. IR ($CHCl_3$): 3470, 2950, 1480, 1470, 1070, 900 cm^{-1}. PMR ($CDCl_3$): Me.C (3H, s, 1.02 ppm), CHOH (1H, t, 4.22 ppm, J = 7 Hz). Mass: *m/e* 152 ($M^+ - 18$, 94%), 137 (88%), 112 (56%), 109 (100%), 108 (73%), 97 (78%), 95 (100%), 93 (63%), 85 (59%), 83 (56%), 81 (72%), 67 (78%), 55 (72%). (Found: C, 71; H, 10.3. $C_{10}H_{18}O_2$ requires: C, 70.59; H, 10.59%).

5-Methyl-cyclonon-4(Z)-en-1-one (8)

To a soln of **15** (2.5 g; 0.015 mole) in dry pyridine (40 ml) was added *p*-toluenesulfonyl chloride (3.5 g; 0.018 mole) at 0° and left overnight at 10–15°. The mixture was then diluted with cold H_2O (250 ml), extracted with Et_2O (30 ml × 3), washed with H_2O (30 ml × 1), 15% HCl aq (30 ml × 2) and further worked up to yield **7** as a pale yellow oil (4.48 g; 97%) which was satisfactory for the next step.

The above tosylate (3.24 g; 0.01 mole) in THF (5 ml) was added to a stirred suspension of freshly prepared $KOBu^t$ (3.36 g; 0.03 mole) in THF (30 ml) at room temp (25–30°) under N_2. After stirring (20 hr) at room temp, the resulting yellow soln was diluted with H_2O (50 ml) and brine (50 ml) and the product taken up in Et_2O (40 ml × 3). The organic layer was worked up in the usual manner to give a yellow oil which was taken up in light petroleum (2 ml) and filtered through a silica gel/II column (15 cm × 1 cm), which was further washed with light petroleum: C_6H_6/1:1 (500 ml). The eluate was freed of solvent to get **8** as a colourless liquid (1.17 g; 77%), b.p. 115–120° (bath)/4 mm, n_D^{26} 1.4869, (glc purity, 96%; 10% Carbowax 20 M; 170°). IR (CCl_4): 2936, 1705, 1470, 1450, 1375, 1335, 1235, 1148, 1115, 1042, 980, 860, 830 cm^{-1} PMR: Me.C=CH (3H, bs. 1.63 ppm), Me.C=CH (1H, bm, 5.50 ppm, W_H = 14 Hz). Mass: *m/e* 152 (M^+, 33%), 150 (34%), 108 (41%), 95 (47%), 93 (100%), 91 (43%), 81 (49%), 80 (51%), 79 (79%), 77 (46%), 66 (76%), 55 (71%), 53 (51%). (Found: C, 79.2; H, 10.6. $C_{10}H_{16}O$ requires: C, 78.95; H, 10.53%).

6″, 12-Cyclo-10-methyl-6-ethyl-dodeca-5(ξ), 9Z)-dien-2-one (17)

To a stirred suspension of freshly prepared $KOBu^t$ (1.85 g; 0.017 mole) in THF (30 ml) **16** (7.79 g; 0.015 mole) was added and the mixture stirred for another 0.5 hr at room temp (25–30°). To the resulting orange phosphorane a soln of **8** (1.52 g; 0.01 mole) in THF (3 ml) was added (5 min) with stirring and the stirring continued for another 2 hr (N_2) at room temp and then for 12 hr at 50°. THF was distilled off and the residue treated with light petroleum (100 ml), filtered and the filtrate washed with brine, and dried and concentrated to ~ 50 ml. The resulting soln was chilled to − 10 to − 15° (3 hr) and filtered to remove triphenylphosphine oxide. The filtrate was freed of solvent to furnish a 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 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 a yellow oil which was taken up in light petroleum (3 ml) and filtered through a column of silica gel/II (20 cm × 2 cm). The column was washed with light petroleum: C_6H_6/1:1 (800 ml) and the eluate worked up to give **17** as a colorless liquid (1.46 g; 73%), b.p. 125–130° (bath)/0.01 mm, n_D^{26} 1.4983. (glc purity, 98%; 5% Carbowax 20 M, 190°, 10% SE-30; 200°). IR (CCl_4): 2916, 1720, 1662, 1445, 1352, 1268, 1155, 1022, 980, 945, 855 cm^{-1}. PMR: Me.C=CH (3H, bs, 1.60 ppm), COMe (3H, s, 2.04 ppm), CH=C (1H, t, 5.18 ppm, J = 6 Hz), Me.C=CH (1H, bm, 5.46 ppm, W_H = 15 Hz). Mass: *m/e* 220 (M^+; 27%), 162 (66%), 146 (43%), 135 (53%), 107 (33%), 95 (43%), 94 (73%), 93 (41%), 81 (41%), 79 (100%), 66 (44%), 55 (41%). (Found: C, 82; H, 11.2. $C_{15}H_{24}O$ C, 81.82; H, 10.92%).

Methyl)(E, ξ, Z- and Z, ξ, Z-7″, 13-cyclo-7-ethyl-3, 11-dimethyl-trideca-2, c, 10-trienoate (18 *and* 19)

To a stirred suspension of NaOMe (0.552 g; 0.1 mole) in DMF (15 ml) was added trimethylphosphonoacetate (1.8 g; 0.01 mole) at 25° and stirred for 30 min under N_2. To the clear soln of phosphonate carbanion, thus obtained was added a soln of **17** (1.12 g; 0.005 mole) in DMF (2 ml) at 20° and stirred (24 hr) at room temp (25–30°). The resulting yellow soln was then decomposed with H_2O (35 ml), extracted with Et_2O (25 ml × 4), washed with brine, dried and freed of solvent to get a mixture of **18** and **19** (0.98 g; 72%), b.p. 155–160°/0.01 mm. (glc purity, 96%; 5% Carbowax 20 M; 220°; **19**:**18**/34:66).

The above mixture (750 mg) was separated by Inverted-dry-column-chromatography[23] (silica gel, 24 cm × 4.6 cm; light petroleum: C_6H_6/60:40) to get pure **18** and **19**.

Compound **18** (340 mg): b.p. 155–160°/0.01 mm, n_D^{26} 1.5081. (glc purity, 95%; 5% Carbowax 20 M; 220°.) IR (CCl_4): 2918, 2864, 1726, 1652, 1440, 1366, 1230, 1158, 1064, 930, 870 cm^{-1}. PMR: Me.C=CH (3H, s, bs, 1.60 ppm), *Z*-Me.C=C.COOMe (3H, s, 2.13 ppm), COOMe (3H, s, 3.62 ppm), CH=C (1H, bm, 5.12 ppm, W_H = 12 Hz), Me.C=CH (1H, bm, 5.48 ppm, W_H = 14 Hz), C=CH·COOMe (1H, bs, 5.58 ppm). Mass; *m/e* 276 (M^+; 15%), 163 (42%), 135 (47%), 114 (52%), 107 (60%), 103 (55%), 101 (53%), 95 (67%), 82 (64%), 81 (95%), 79 (91%), 67 (80%), 55 (100%), 53 (56%). (Found: C, 78.4; H, 10.2. $C_{18}H_{28}O_2$ requires: C, 78.26; H, 10.15%).

Compound **19** (160 mg): b.p. 155–160°/0.01 mm, n_D^{26} 1.5067. (glc purity, 94%; 5% Carbowax 20 M; 220°.) IR (CCl_4): 2930, 2860, 1735, 1648, 1448, 1380, 1244, 1228, 1064, 926, 860 cm^{-1}. PMR: Me.C=CH (3H, bs, 1.60 ppm), *E*-Me.C=CH.COOMe (3H, d, 1.88 ppm, J = 2 Hz), COOMe(3H, s, 3.62 ppm, W_H = 14 Hz), 5.22 ppm, J = 7 Hz), Me.C=CH (1H, bm, 5.48 ppm, W_H = 14 Hz), C = CH.COOMe (1H, bs, 5.58 ppm). Mass: *m/e* 276 (M^+, 44%), 163 (58%), 135 (75%), 114 (57%), 107 (90%), 95 (69%), 93 (53%), 81 (100%), 79 (90%), 67 (74%), 55 (67%). (Found: C, 78.6; H, 10.5. $C_{18}H_{28}O_2$ requires: C, 78.26; H, 10.15%).

Methyl)cis - 10, 11 - epoxy - 7', 13 - cyclo - 7 - ethyl - 3, 11 - dimethyl - trideca - 2 (E), 6 (ξ) - dienoate (**20**)

A soln of m-Cl-$PhCO_3H$ (0.232 g; 65%) in CH_2Cl_2 (10 ml) was added to a soln of **18** (0.276 g; 0.001 mole) in CH_2Cl_2 (10 ml) at 0°. The mixture was then left aside overnight at 0°. The usual work-up furnished a colorless oil (0.254 g) which was purified by preparative-later-chromatography (silica gel, 20 cm × 20 cm × 0.5 mm; light petroleum: EtOAc/18:2) to get the required analogue **20** (70 mg; R_f 0.52). IR (CCl_4): 2930, 2860, 1720, 1645, 1432, 1378, 1356, 1220, 1145, 1035, 862 cm^{-1}. PMR: Epoxy-Me (3H, s, 1.20 ppm), Me.C=C.COOMe (3H, ss, 2.13 ppm), COOMe (3H, s, 3.62 ppm), CH=C (1H, bm, 5.12 ppm, J = 12 Hz), C = CH.COOMe (1H, bs, 5.58 ppm). Mass; *m/e* 292 (M^+, 4%), 161 (92%) 135 (64%), 121 (53%), 114 (60%), 107 (60%), 95 (89%), 93 (79%), 80 (100%), 78 (70%), 67 (77%), 55 (72%). (Found: C, 74.2; H, 9.7. $C_{18}H_{28}O_3$ requires: C, 73.97; H, 9.59%.)

REFERENCES AND NOTES

[1]See e.g.: A. Burger, *Medicinal Chemistry* (Edited by A. Burger), Part I, pp. 78–80. Wiley-Interscience, New York (1970).

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[25]The authors are grateful to Prof. K. Slama for the assay, which was carried out by topical application of the compound in acetone on insects 0–20 hr after ecdysis.

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