Synthesis of Sesquiterpenes, Occidentalol, Chamaecynone and Related Compounds Characterised by a *cis*-Eudesmane Structure

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In continuation of our synthetic work for constructing the *cis*-decalin skeleton by a double Michael annulation using 3-methyl-4-methylenecyclohex-2-enone and its congeners with dimethyl 3-oxoglutarate, the sesquiterpenes, occidentalol, chamaecynone, and related compounds have been synthesised in a stereoselective manner.

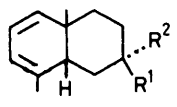
There have been several reports [1] describing the total synthesis of the sesquiterpenes, occidentalol (1) and chamaecynone (4) characterised by having a *cis*-eudesmane structure. We report here a new synthesis of these terpenes and related compounds as an extension of our synthetic work [2] concerned with a new annulation reaction for constructing *cis*-decalin by reaction of 3,5-dimethyl-4-methylenecyclohex-2-enone with dimethyl 3-oxoglutarate in dimethyl sulphoxide in the presence of potassium fluoride.

As reported previously [3] we investigated the isomerisation of the diketo-diester (11) into the *trans*-diketo-diester (17) under the same conditions as used for the double Michael annulation in the expection that, provided the second Michael addition was reversible, isomerisation of the diketo-diester (11) to the thermodynamically more stable *trans*-isomer (17) might take place; the attempt, however, was unsuccessful. Nevertheless, with the same purpose in mind, the diketo-diester (11) was treated with potassium t-butoxide in t-butyl alcohol under reflux for two days, to give the diketo-ester (12) as the sole product in 70% yield; this was a result of a retro-Claisen fragmentation. The isomeric diketo-diester (18) [2] gave an inseparable mixture under the same conditions. The structure of the diketo-ester (12) was incidentally disclosed by an attempt to reduce the ketone group of the β-keto-ester functionality in (12) into a methylene group by Coates' procedure.[4] Thus, treatment of compound (12) with chloromethyl methyl ether in the presence of sodium hydride in hexamethylphosphoric triamide gave the methoxymethyl ether (13), which was subjected to reduction with lithium in liquid ammonia. Separation of the reduction products gave the diol (19) as the only identifiable product in low yield. Its ^{1}H n.m.r. spectrum showed a signal at δ 4.72, as a singlet assigned to an olefinic proton of the enol ether group, suggesting, in turn, the structure of the diketo-ester (12).

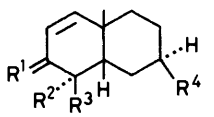
Acetalisation of the diketo-ester (12) with ethylene glycol and boron trifluoride-diethyl ether in tetrahydrofuran gave the mono-acetal (14) in 80% yield. Reduction of (14) with sodium borohydride in aqueous tetrahydrofuran gave a mixture of the stereoisomeric acetal alcohols (20) and (21), both of which were isolated in pure form after column chromatography on silica gel in chloroform in 55 and 12% isolated yield, respectively. Although the stereostructures of (20) and (21) have not been established with certainty, in their n.m.r. spectra, the former (20) exhibited a broad signal ($W_{\frac{1}{2}}$ 8.0 Hz) at δ 4.33 assigned to an equatorial proton on the carbon bearing a hydroxy-group, while the latter (21) showed a broad signal ($W_{\frac{1}{2}}$ 20 Hz) at δ 4.00 assigned to an axial proton.

Treatment of the acetal-alcohol (20) with thionyl chloride in pyridine gave the conjugated ester (15) and the chlorothio-ester (22) in 74 and 10% yield, respectively. Although the mass spectrum (EI) of the latter showed no molecular ion peak (expected at *m/z* 380), the presence of a remarkable peak at *m/z* 297 (corresponding to *m/z* 380—SOCl), suggested that the latter compound was not a chloride but, rather, the chlorothioester (22). On treatment with 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) in benzene the chlorothio-ester (22) gave the conjugated ester (15) in good yield. Therefore,the mixture obtained by the dehydration reaction of the acetal-alcohol (20) was, without purification, treated with DBU, to give the conjugated ester (15) from (20) in 50% yield. Attempts to reduce the double bond in (15) using several catalysts were unsuccessful, no up-take of hydrogen being observed. Hydrolysis of the acetal moiety of the ester (15) with hydrochloric acid and acetic acid in aqueous tetrahydrofuran with cooling gave the keto-ester (16). Hydrogenation of the keto-ester (16) with a platinum catalyst in ethanol for one week gave a mixture consisting of five products (revealed by thin layer chromatography), from which the hydroxy-ester (23) was isolated as a major product in 66% isolated yield. A ^{1}H n.m.r. spectrum of (23) showed the signal at δ 4.12 as a quintet (*J* 3.0 Hz) assigned to an equatorial proton on C-2 and the configuration of the methoxycarbonyl group on C-6 was ultimately disclosed by the fact that the ester (23) was transformed to the known diene-ester (2). Separation and purification of the mixture obtained by the hydrogenation with repeated column chromatography gave two hydroxy-esters (24) and (25) and two keto-esters (26) and (27). Oxidation of the hydroxy-ester (23) with Jones' reagent gave the keto-ester (26) and reduction of this sodium borohydride yielded the hydroxy-esters (23) and (24). These facts indicate that (23) and (24) are stereoisomeric with respect to the configuration of the C-2 hydroxy-group. Oxidation of the hydroxy-ester (25) with the same reagent gave the keto-ester (27) different from the keto-ester (26). The configuration of the hydroxy-group of (25) was assigned as axial, since the shape of the signal of the C-2 proton (carbinyl proton) in its ^{1}H n.m.r. spectrum is similar to that of the hydroxy-ester (24).

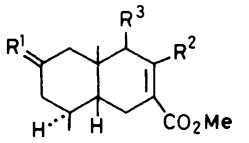
Treatment of the hydroxy-ester (23) with phosphoryl chloride in pyridine afforded the ester (28) as the sole product in 90% yield; this on bromination in chloroform gave the dibromide (30) the ^{1}H n.m.r. spectrum of which exhibited a signal (δ 4.50) as a doublet (*J* 3.5 Hz) assigned to the C-1 proton, confirming, in turn, the structure of the ester (28). Treatment of the ester (28) with *N*-bromosuccinimide in carbon tetrachloride yielded the bromide (29). Since this was rather unstable on storage, it was, without further purification, submitted to dehydrobromination with DBU in benzene, to give the diene-ester (2) in 27% isolated yield. The i.r. (neat) and ^{1}H n.m.r. spectra of (2) were identical with those of an authentic sample.[1a] Since the diene-ester (2) had already been



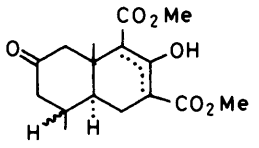
(1) R^1 = H; R^2 = 
(2) R^1 = CO_2Me; R^2 = H
(3) R^1 = H; R^2 = CO_2Me



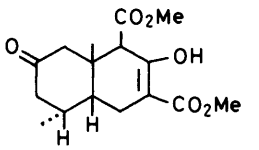
(4) R^1 = O; R^2 = Me; R^3 = H; R^4 = C≡CH
(5) R^1 = H_2; R^2 = H; R^3 = Me; R^4 = CH_2OH
(6) R^1 = H_2; R^2 = H; R^3 = Me; R^4 = CHO
(7) R^1 = H_2; R^2 = H; R^3 = Me; R^4 = $CH{=}CBr_2$
(8) R^1 = H_2; R^2 = H; R^3 = Me; R^4 = C≡CH
(9) R^1 = O; R^2 = H; R^3 = Me; R^4 = C≡CH
(10) R^1 = O; R^2 = OH; R^3 = Me; R^4 = C≡CH



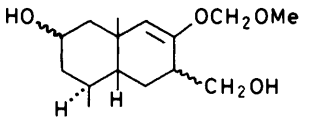
(11) R^1 = O; R^2 = OH; R^3 = CO_2Me
(12) R^1 = O; R^2 = OH; R^3 = H
(13) R^1 = O; R^2 = OCH_2OMe; R^3 = H
(14) R^1 =  ; R^2 = OH; R^3 = H
(15) R^1 =  ; R^2 = R^3 = H
(16) R^1 = O; R^2 = R^3 = H



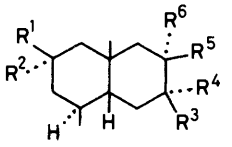
(17)



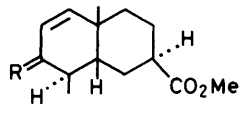
(18)



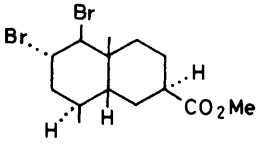
(19)



(20) R^1, R^2 =  ; R^3 = CO_2Me; R^4 = R^6 = H; R^5 = OH
(21) R^1, R^2 =  ; R^3 = CO_2Me; R^4 = R^5 = H; R^6 = OH
(22) R^1, R^2 =  ; R^3 = CO_2Me; R^4 = R^6 = H; R^5 = OSOCl
(23) R^1 = R^4 = R^5 = R^6 = H; R^2 = OH; R^3 = CO_2Me
(24) R^1 = OH; R^2 = R^4 = R^5 = R^6 = H; R^3 = CO_2Me
(25) R^1 = OH; R^2 = R^3 = R^5 = R^6 = H; R^4 = CO_2Me
(26) R^1, R^2 = O; R^3 = CO_2Me; R^4 = R^5 = R^6 = H
(27) R^1, R^2 = O; R^3 = R^5 = R^6 = H; R^4 = CO_2Me



(28) R = H_2
(29) R = 



(30)

transformed into occidentalol (1), we slightly modified the transformation. Thus the diene-ester (2) was smoothly converted into the epimeric diene-ester (3) with sodium methoxide in methanol in much better yield (85%) than with potassium t-butoxide.[1a,e] The spectroscopic properties of the epimeric diene-ester (3) were also identical with those of the authentic sample.[1a] Reaction of (3) with methyl-lithium furnished (±)-occidentalol (1), m.p. 72—73 °C, the i.r. (CCl_4) and ^1H n.m.r. spectra of which were identical with those of occidentalol; thus the stereoselective synthesis of this sesquiterpene was completed.

Next, we focused our attention on the synthesis of chamaecynone (4) and related compounds. Lithium aluminium hydride reduction of the ester (28) gave the alcohol (5), oxidation of which with Collins' reagent in methylene chloride afforded the aldehyde (6). The aldehyde was not so stable. Therefore, the aldehyde (6) obtained by the oxidation was immediately submitted to treatment with carbon tetrabromide and triphenylphosphine in methylene chloride,[5] to give the dibromide (7) as an oil in 85% yield. Subsequent treatment of (7) with n-butyl-lithium in tetrahydrofuran followed by water [5] furnished the acetylene (8) in 75% yield.

Attempted oxidation of the allylic position in the A-ring of (8) with chromium trioxide-pyridine complex in the standard manner [6] led to recovery of starting material. Eventually the oxidation was accomplished with the same reagent by refluxing the reaction mixture for 48 h and adding freshly prepared reagent [in total a 32 : 1 molar ratio of the reagent: (8) was added] at intervals of several hours. Work-up gave (±)-isochamaecynone (9) (m.p. 96—97 °C) in 48% isolated yield along with 5% of recovery of the starting material (8). The synthetic (±)-isochamaecynone showed identical spectroscopic properties (i.r. and ^1H n.m.r.) with natural isochamaecynone.[7,*]

Treatment of (±)-isochamaecynone with 2.3% ethanolic potassium hydroxide gave a mixture consisting of (±)-isochamaecynone (9) and (±)-chamaecynone (4) in a ratio of 3 : 7 (revealed by gas chromatography). (±)-Chamaecynone was isolated from the mixture in 50% isolated yield (m.p. 94—95 °C, purified by sublimation). On the other hand, treatment of (±)-isochamaecynone with potassium t-butoxide in the air gave (±)-hydroxyisochamaecynone (10) in 45% yield, the i.r. and ^1H n.m.r. spectra of which were identical with those of hydroxyisochamaecynone.[1j,k] (±)-Chamaecynone also

* The synthetic racemic isochamaecynone exhibited in the i.r. spectrum in KBr bands identical with those of isochamaecynone from natural sources. The fact suggested (±)-isochamaecynone may form racemic mixture (congromerate) rather than a racemic compound.

gave (±)-hydroxyisochamaecynone under the same conditions in 30% yield.

Experimental

M.p.s were determined with a Yanagimoto hot-stage apparatus and are uncorrected. I.r. spectra were recorded on Hitachi 215 Grating Infrared Spectrophotometer. ^{1}H N.m.r spectra were recorded using a Varian HA-100D, a Varian A-60, and a JEOL JNM-PMR 60 Spectrometer in deuteriochloroform with tetramethylsilane as an internal standard unless otherwise stated. Mass spectra were recorded with a JEOL JMS-O1SG-2 on direct-inlet system.

Treatment of the Diketo-diester (11) *with Potassium t-Butoxide in t-Butyl Alcohol.*—A solution of the diketo-diester (11) (7.4 g) and potassium t-butoxide (5.3 g) in t-butyl alcohol (150 ml) was refluxed with stirring under argon for 2 d; it was then concentrated under reduced pressure to leave a residue which was dissolved in cold water. The aqueous solution was acidified with hydrochloric acid and extracted with ether. The extract was washed with aqueous sodium carbonate and water, dried, and concentrated to dryness to give the diketo-ester (12) (4.22 g) as crystals, m.p. 114—116 °C, $\nu_{max.}$ (Nujol), 1 710, 1 690, 1 645, and 1 610 cm^{-1}; δ 1.03 (3 H, d, *J* 6.0 Hz), 1.08 (3 H, s), 3.78 (3 H, s), 12.03 (1 H, s) (Found: C, 66.9; H, 8.1. $C_{14}H_{20}O_4$ requires C, 66.6; H, 8.0%).

The Methoxymethyl Ether (13) *of the Diketo-ester* (12).—A mixture of the diketo-ester (12) (100 mg), sodium hydride (19 mg as 50% oil dispersion), and hexamethylphosphoric triamide (7 ml) was stirred for 1 h. To the mixture was dropwise added chloromethyl methyl ether (1 ml) with stirring and ice cooling. The whole was stirred at room temperature for 4 h, and then diluted with aqueous sodium hydrogen carbonate, and extracted with ether. The extract was washed with 1% sodium hydroxide and brine, dried, and concentrated to dryness to leave the methoxymethyl ether (7) (100 mg) as an oil, $\nu_{max.}$ (neat), 1 700 and 1 630 cm^{-1}; δ 1.06 (3 H, d, *J* 5.5 Hz), 1.10 (3 H, s), 3.44 (3 H, s), 3.75 (3 H, s), and 4.96 (2 H, s), which was, without further purification, subjected to the reduction, since column chromatographic purification of the methoxymethyl ether with silica gel resulted in cleavage of the methoxymethyl ether group.

Reduction of the Methoxymethyl Ether (13) *with Lithium in Liquid Ammonia.*—A solution of the ether (13) (125 mg) in ether (5 ml) was dropwise added to a solution of lithium (50 mg) in liquid ammonia (*ca.* 10 ml) at −78 °C; the whole was then stirred at the same temperature for 1 h. Ammonium chloride was added to the solution and the ammonia was evaporated off. The residue was extracted with ether. The extract was washed with dilute hydrochloric acid and brine, and dried. Removal of the solvent gave a residue (77 mg) which was subjected to preparative thin layer chromatography on a silica gel plate using chloroform–ethanol (8 : 1) as developing solvent. The diol (19) (15 mg) was obtained as a major product, m.p. 94—96 °C, $\nu_{max.}$ ($CHCl_3$), 3 550 and 1 660 cm^{-1}; δ 0.94 (3 H, d, *J* 6.0 Hz), 1.07 (3 H, s), 3.41 (3 H, s), 4.72 (1 H, broad s), and 4.95 (2 H, s); M^+ 270 corresponding to $C_{15}H_{26}O_4$.

Acetalisation of the Diketo-ester (12).—A mixture of the diketo-ester (12) (7.2 g), ethylene glycol (2.4 ml), boron trifluoride–diethyl ether (20 drops), and tetrahydrofuran (100 ml) was set aside at room temperature for one week; the mixture was then diluted with aqueous sodium carbonate and extracted with ether. The extract was washed with brine and dried. Removal of the solvent gave the mono-acetal (14) (6.8 g) which crystallised from n-hexane, m.p. 85—87 °C, $\nu_{max.}$ (Nujol), 1 660 and 1 605 cm^{-1}; δ 0.91 (3 H, d, *J* 6.0 Hz), 0.97 (3 H, s), 3.75 (3 H, s), 3.90 (4 H, broad s), and 12.06 (1 H, s) (Found: C, 64.6; H, 8.2. $C_{16}H_{24}O_5$ requires C, 64.8; H, 8.2%).

Sodium Borohydride Reduction of the Mono-acetal (14).—A solution of sodium borohydride (120 mg) in water (2 ml) was dropwise added to a solution of the mono-acetal (14) (500 mg) in tetrahydrofuran (10 ml) with stirring at room temperature. After the mixture had been stirred for 3 h, the whole was diluted with water and extracted with ether. The extract was washed with brine, dried, and concentrated to dryness to leave an oily residue which was chromatographed on silica gel in chloroform. Elution with chloroform gave a mixture consisting of two products. Separation of the mixture by preparative thin layer chromatography on a silica gel plate using chloroform–acetone (15 : 1) gave the acetal-alcohol (20) (300 mg) as crystals, m.p. 95—97 °C, $\nu_{max.}$ (KBr), 3 485 and 1 715 cm^{-1}; δ 0.96 (3 H, d, *J* 6.0 Hz), 1.24 (3 H, s), 3.71 (3 H, s), 3.91 (4 H, broad s), and 4.33 (1 H, m) (Found: C, 64.3; H, 8.8. $C_{16}H_{26}O_5$ requires C, 64.4; H, 8.8%) and the stereoisomeric acetal-alcohol (11) (60 mg) as an oil, $\nu_{max.}$ ($CHCl_3$), 3 560 and 1 718 cm^{-1}; δ 0.93 (3 H, d, *J* 6.0 Hz), 1.02 (3 H, s), 3.70 (3 H, s), 3.88 (4 H, broad s), and 4.00 (1 H, m); M^+ 298 corresponding to $C_{16}H_{26}O_5$.

Dehydration of the Acetal-alcohol (20).—Thionyl chloride (3 drops) was added with stirring to a solution of the acetal-alcohol (20) (45 mg) in pyridine (2 ml) at −78 °C. The mixture was stirred at room temperature overnight, diluted with aqueous sodium carbonate, and extracted with ether. The extract was washed with dilute hydrochloric acid and brine, dried, and concentrated to leave an oil which was chromatographed on silica gel in chloroform. Elution with chloroform gave the ester (15) (31 mg) which crystallised from n-hexane m.p. 74—76 °C, $\nu_{max.}$ (Nujol), 1 700 and 1 640 cm^{-1}; δ 0.91 (3 H, d, *J* 5.5 Hz), 0.92 (3 H, s), 3.73 (3 H, s), 3.92 (4 H, broad s), and 6.92 (1 H, m). Subsequent elution with the same solvent gave the chlorothio-ester (22) (6 mg) as an oil, $\nu_{max.}$ ($CHCl_3$) 1 715 cm^{-1}; δ 0.93 (3 H, d, *J* 5.5 Hz), 1.19 (3 H, s), 3.70 (3 H, s), 3.89 (4 H, broad s), and 5.05 (1 H, m), which gave the ester (15) by treatment with DBU in benzene. The ester (15) was prepared from the mono-acetal (14) by sequential treatment as follows. Reduction of the mono-acetal (14) (1.5 g) was carried out in the same manner as mentioned above to give the mixture (1.5 g) of the acetal-alcohols (20) and (21). The mixture, without purification, treated with thionyl chloride (1 ml) in pyridine (40 ml) in the same way. The resulting mixture (1.5 g) was treated with DBU (*ca.* 1 ml) in benzene (20 ml) to give a product which was chromatographed on silica gel in chloroform. Elution with chloroform gave the ester (15) (709 mg). Treatment of the ester (15) (1.5 g) with concentrated hydrochloric acid (4 ml) and acetic acid (4 ml) in tetrahydrofuran (40 ml), and water (20 ml) gave the keto-ester (16) (1.27 g) as an oil after work-up, $\nu_{max.}$ ($CHCl_3$), 1 695 and 1 645 cm^{-1}; δ 1.03 (3 H, d, *J* 5.8 Hz), 1.04 (3 H, s), 3.75 (3 H, s), and 6.87 (1 H, m); M^+ 236 corresponding to $C_{14}H_{20}O_3$.

Hydrogenation of the Keto-ester (16).—The keto-ester (16) (909 mg) was hydrogenated with Adams' catalyst (150 mg) in ethanol (25 ml) under an atmospheric pressure of hydrogen for 1 week. Work-up gave a mixture which was chromatographed on silica gel in n-hexane. Elution with 6% acetone in n-hexane gave a mixture (A) consisting of the keto-ester (26) and (27). Subsequent elution with the same solvent gave the hydroxy-ester (23) (610 mg) as an oil, $\nu_{max.}$ ($CHCl_3$) 3 580 and 1 718 cm^{-1}; δ 0.93 (3 H, d, *J* 7.0 Hz), 0.99 (3 H, s), 3.67 (3 H,

s), and 4.12 (1 H, quintet, J 3.0 Hz); M^+ 240 corresponding to $C_{14}H_{24}O_3$. Elution with chloroform gave a mixture (B) of the hydroxy-esters (24) and (25). Re-chromatography of the mixture (A) on silica gel in n-hexane graduated with acetone gave the keto-ester (26) (30 mg) as an oil, $\nu_{max.}$ ($CHCl_3$), 1 715 cm^{-1}; δ 1.04 (3 H, d, J 5.5 Hz), 1.14 (3 H, s), and 3.65 (3 H, s); M^+ 238 corresponding to $C_{14}H_{22}O_3$. Further elution with the same solvent system gave the keto-ester (27) (25 mg) as an oil, $\nu_{max.}$ ($CHCl_3$) 1 718 cm^{-1}; δ 1.08 (3 H, s), 1.11 (3 H, d, J 6.0 Hz), and 3.67 (3 H, s); M^+, 238. Re-chromatography of the mixture (B) on silica gel in n-hexane–acetone gave the hydroxy-ester (24) (25 mg) as crystals, m.p. 68—69 °C (from n-hexane); $\nu_{max.}$ (Nujol) 3 200 and 1 723 cm^{-1}; δ 0.94 (3 H, (3 H, d, J 6.0 Hz), 1.05 (3 H, s), 3.65 (3 H, s), and 3.72 (1 H, m) (Found: C, 69.9; H, 10.3. $C_{14}H_{24}O_3$ requires C, 70.0; H, 10.1%). Elution with the same solvent gave the hydroxy-ester (25) (35 mg) as crystals, m.p. 54—56 °C (from n-hexane), $\nu_{max.}$ (Nujol) 3 250 and 1 735 cm^{-1}; δ 1.06 (3 H, s), 1.16 (3 H, d, J 7.0 Hz), 3.66 (3 H, s), and 4.04 (1 H, m) (Found: C, 69.5; H, 10.2. $C_{14}H_{24}O_3$ requires C, 70.0; H, 10.1%), M^+ 240. Oxidation of the hydroxy-ester (23) (31 mg) with Jones' reagent in the usual manner gave the keto-ester (26) (28 mg). Oxidation of the hydroxy-ester (25) with the same way gave the keto-ester (27). Reduction of the keto-ester (26) (100 mg) with sodium borohydride in aqueous tetrahydrofuran gave the hydroxy-ester (23) (60 mg) and (24) (30 mg).

4,r-9-*Dimethyl*-6-*methoxycarbonyl*-3,t-4,5,t-6,7,8,9,c-10-*octahydronaphthalene* (28).—Phosphoryl chloride (15 drops) was added to a solution of the hydroxy-ester (23) (182 mg) in pyridine (14 ml) with stirring at −78 °C; the whole was then allowed to rise to room temperature, after which it was stirred for 2 h, and finally concentrated under reduced pressure to *ca.* 3 ml. The resulting solution was diluted with water and extracted with ether. The extract was washed with aqueous sodium carbonate, dilute hydrochloric acid, and water, dried, and concentrated to dryness to give the ester (28) (153 mg) as an oil, $\nu_{max.}$ ($CHCl_3$) 1 720 and 1 650 cm^{-1}, δ 0.93 (3 H, d, J 6.0 Hz), 1.06 (3 H, s), 3.67 (3 H, s), 5.34 (1 H, diffused d, J 10.0 Hz), and 5.58 (1 H, diffused d, J 10.0 Hz), M^+ 222 corresponding to $C_{14}H_{22}O_2$. The ester (28) (45 mg) gave the dibromide (30) (66 mg) by treatment with bromine (33 mg) in chloroform (10 ml), $\nu_{max.}$ (neat) 1 725 cm^{-1}; δ 1.03 (3 H, d, J 6.0 Hz), 1.22 (3 H, s), 3.67 (3 H, s), 4.50 (1 H, d, J 3.5 Hz), and 4.92 (1 H, q, J 3.5 Hz); M^+ 380, 382, and 384 (*ca.* 1 : 2 : 1).

4,r-9-*Dimethyl*-6-*methoxycarbonyl*-5,t-6,7,8,9,c-10-*hexahydronaphthalene* (2).—A solution of the ester (28) (300 mg), *N*-bromosuccinimide (241 mg), and azobis(isobutyronitrile) (catalytic amount) in carbon tetrachloride (30 ml) was refluxed under argon for 1 h and then filtered. The filtrate was concentrated to dryness to leave an oil which was treated with DBU (0.5 ml) in benzene (15 ml) under reflux overnight. The solution was diluted with benzene and washed with dilute hydrochloric acid, aqueous sodium carbonate, and water, dried, and concentrated to dryness to leave an oily residue, which was chromatographed on silica gel in n-hexane. Elution with n-hexane–chloroform (1 : 1) gave the diene-ester (2) (80 mg) as an oil, $\nu_{max.}$ (neat) 1 730 cm^{-1}; δ (CCl_4), 0.86 (3 H, s), 1.80 (3 H, d, J 1.0 Hz), 2.48 (1 H, m), 3.65 (3 H, s), 5.22 (1 H, d, J 9.5 Hz), 5.52 (1 H, m), and 5.76 (1 H, dd, J 9.5 and 5.5 Hz); M^+ 220 corresponding to $C_{14}H_{20}O_2$. The i.r. spectrum of the diene-ester (2) was identical with that of authentic sample.[1a]

Epimerisation of the Diene-ester (2).—A solution of sodium (0.2 g) and the diene-ester (2) (75 mg) in methanol (15 ml) was refluxed under argon for 16 h and then concentrated under reduced pressure to leave a residue which was taken up in water. The aqueous solution was acidified with dilute hydrochloric acid and extracted with ether. The extract was treated with ethereal diazomethane. Work-up gave a residue which was chromatographed on silica gel in n-hexane. Elution with n-hexane–chloroform (95 : 5) gave the epimeric diene-ester (3) (64 mg) as an oil, $\nu_{max.}$ (neat) 1 735 cm^{-1}; δ (CCl_4), 0.86 (3 H, s), 1.80 (3 H, d, J 1.0 Hz), 3.58 (3 H, s), 5.28 (1 H, d, J 9.0 Hz), 5.55 (1 H, m), and 5.82 (1 H, dd, J 9.0 and 5.0 Hz); M^+ 220 corresponding to $C_{14}H_{20}O_2$. The i.r. spectrum of the epimeric diene (3) was identical with that of authentic sample.[1a]

(±)-*Occidentalol* (1).—A solution of the diene (3) (72 mg) in ether (5 ml) was treated with methyl-lithium in the conventional way. Work-up gave (±)-occidentalol (purified by a column chromatography on silica gel in benzene followed by sublimation), m.p. 72—73 °C. The i.r. (CCl_4) and ^1H n.m.r. spectra of (±)-occidentalol were identical with those of authentic sample.[1a]

4,r-9-*Dimethyl*-6-*hydroxymethyl*-3,t-4,5,t-6,7,8,9,c-10-*octahydronaphthalene* (5).—The ester (28) (812 mg) was treated to an excess of lithium aluminium hydride in ether to give the alcohol (5) (710 mg) as an oil, $\nu_{max.}$ (neat), 3 300 cm^{-1}; δ 0.92 (3 H, d, J 5.5 Hz), 1.03 (3 H, s), 5.33 (1 H, diffused d, J 10.0 Hz), and 5.53 (1 H, diffused d, J 10.0 Hz); M^+ 194 corresponding to $C_{13}H_{22}O$.

4,r-9-*Dimethyl*-6-*formyl*-3,t-4,5,t-6,7,8,9,c-10-*octahydronaphthalene* (6).—To a stirred mixture of Collins' reagent (800 mg) and the alcohol (5) (204 mg) in methylene chloride (15 ml) at room temperature, was added Collins' reagent (400 mg); additional reagent was added at 15 min intervals (5 × 400 mg; total 2 g) after which the whole was stirred for 100 min and then filtered. The filtrate was diluted with methylene chloride and the solution washed with 5% aqueous sodium hydrogen carbonate, dilute hydrochloric acid, and brine, and then dried. Removal of the solvent gave a residue which was chromatographed on silica gel in methylene chloride. Elution with the same solvent gave the aldehyde (6) (158 mg) as an oil, $\nu_{max.}$ ($CHCl_3$) 2 700 and 1 715 cm^{-1}; δ 0.95 (3 H, d, J 5.5 Hz), 1.05 (3 H, s), 5.37 (1 H, diffuse d, J 10.0 Hz), 5.57 (1 H, diffuse d, J 10.0 Hz), and 9.67 (1 H, d, J 1.2 Hz). Since the aldehyde (6) was not so stable, it was used without further purification.

4,r-9-*Dimethyl*-6-(2′,2′-*dibromovinyl*)3-,t-4,5,t-6,7,8,9,c-10-*octahydronaphthalene* (7).—A solution of triphenylphosphine (4.6 g) in methylene chloride (5 ml) was added dropwise to a solution of carbon tetrabromide (2.9 g) in methylene chloride (5 ml) under argon at 0 °C and the whole was stirred for 5 min. To the solution was added dropwise a solution of the aldehyde (6) (245 mg) in methylene chloride (4 ml) with stirring at 0 °C. The whole was stirred for 10 min, diluted with water, and extracted with methylene chloride. The extract was dried and concentrated to dryness to leave a residue which was chromatographed on silica gel in n-hexane. Elution with the same solvent gave the dibromide (27) (375 mg) as an oil, $\nu_{max.}$ ($CHCl_3$) 1 650w and 1 620 cm^{-1}; δ 0.97 (3 H, d, J 5.5 Hz), 1.04 (3 H, s), 5.37 (1 H, diffuse d, J 10.0 Hz), 5.55 (1 H, diffuse d, J 10.0 Hz), and 6.23 (1 H, d, J 9.0 Hz); M^+ 346, 348, and 350 corresponding to $C_{14}H_{20}Br_2$.

4,r-9-*Dimethyl*-6-*ethynyl*-3,t-4,5,t-6,7,8,9,c-10-*octahydronaphthalene* (8).—A solution of n-butyl-lithium (1.5 ml; 1.6M solution in n-hexane) was added dropwise to a solution of the

dibromide (7) (375 mg) in tetrahydrofuran (6 ml) with stirring at −78 °C under argon. The whole was stirred at −78 °C for 1 h and at 25 °C for 1 h, quenched with water, and extracted with n-pentane. The extract was washed with dilute hydrochloric acid and brine and then dried. Removal of the solvent gave a residue which was chromatographed on silica gel in n-hexane. Elution with the same solvent gave the ethynylnaphthalene (8) (151 mg) as a colourless oil, $\nu_{max.}$ ($CHCl_3$) 3 285 and 2 105 cm^{-1}; δ 0.93 (3 H, d, *J* 6.0 Hz), 1.06 (3 H, s), 2.03 (1 H, d, *J* 2.0 Hz), 5.34 (1 H, diffuse d, *J* 10.0 Hz), and 5.54 (1 H, diffuse d, *J* 10.0 Hz); M^+ 188 corresponding to $C_{14}H_{20}$.

(±)-*Isochamaecynone* (9).—A mixture of chromium trioxide–pyridine complex (CrO_3–2py) (1 g), the ethynylnaphthalene (8) (68 mg), and methylene chloride (20 ml) was heated under reflux with stirring. Freshly prepared chromium trioxide–pyridine complex (0.5 g) was added to the mixture and then a second portion after 2 h. The whole was heated under reflux overnight, diluted with methylene chloride, and filtered. The filtrate was washed with 5% aqueous sodium hydrogen carbonate, dilute hydrochloric acid, and water, and then dried and concentrated to dryness to leave an oil; this was subjected to preparative thin layer chromatography on a silica gel plate with chloroform as eluant. The major product collected was re-chromatographed on silica gel by development (×4) with n-hexane–acetone (10 : 1). (±)-Isochamaecynone (9) (35 mg) was isolated as the major product, m.p. 96—98 °C (purified by sublimation). Its i.r. and ^1H n.m.r. spectra were identical with those of authentic sample.[7]

Treatment of (±)-*Isochamaecynone* (9) *with Potassium Hydroxide in Ethanol.*—A solution of (±)-isochamaecynone (9) (30 mg) in 2.3% ethanolic potassium hydroxide (4.7 ml) was stirred under argon at room temperature overnight and then diluted with dilute hydrochloric acid and extracted with ether. The extract was washed with brine, dried, and concentrated to dryness to leave a residue which was subjected to preparative thin layer chromatography on a silica gel plate with n-hexane–acetone (10 : 1) as developing solvent. Crystalline (±)-chamaecynone (4) (15 mg) was isolated, m.p. 94—95 °C (purified by sublimation), the spectroscopic properties [i.r. and ^1H n.m.r. (in CCl_4)] of which were identical with those of an authentic sample of (±)-chamaecynone.[1h,i]

(±)-*Hydroxyisochamaecynone* (10).—A solution of (±)-isochamaecynone (9) (20 mg), potassium t-butoxide (35 mg), and triethyl phosphite (32 mg) in t-butyl alcohol (2.5 ml) was stirred in the air at room temperature for 5 h; the mixture was then diluted with dilute hydrochloric acid and extracted with ether. The extract was washed with brine and dried. Removal of the solvent gave a residue (15 mg) which crystallised from ether–light petroleum (b.p. 35—45 °C) to afford (±)-hydroxyisochamaecynone (10) (5 mg). The i.r. and ^1H n.m.r. spectra were identical with those of hydroxyisochamaecynone isolated from natural sources.[1j,k] (±)-Chamaecynone (4) (9 mg) was treated in the same manner to give (±)-hydroxyisochamaecynone (10) (2 mg).

Acknowledgements

We thank Professors K. Takase and T. Toda (Tohoku University) for the copies of the spectra of the diene-esters (2) and (3), occidentalol, isochamaecynone, and hydroxyisochamaecynone, and Dr. T. Harayama (Kyoto University) for the copies of spectra of (±)-chamaecynone. We also thank the Ministry of Education, Japanese Government for financial support of this research (Grant-in aid, No. 56570726).

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Received 24th February 1982; *Paper* 2/340