New Stereoselective Synthesis of 9-Methyl-*cis*-decalin Derivatives by Double Michael Reaction of 3-Methyl-4-methylenecyclohex-2-enone and its Congeners with Dimethyl 3-Oxoglutarate

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Double Michael reaction of 3-methyl-, 2,3-dimethyl-, and 3,5-dimethyl-4-methylenecyclohex-2-enone with dimethyl 3-oxoglutarate in dimethyl sulphoxide in the presence of potassium fluoride gave stereoselectively 9-methyl-, 1,9-dimethyl-, and 4,9-dimethyl-6,8-dimethoxycarbonyl-*cis*-decahydronaphthalene-2,7-dione, respectively, and starting from these annulation products some sesquiterpenes having the *cis*-decahydronaphthalene skeleton were formally synthesised.

A NUMBER of methods for constructing the decalin (decahydronaphthalene) system, a common constituent of the skeleton of sesquiterpenes, have been used so far, Robinson annulation being the most widely applied method. The first stage of this annulation involves cyclohexanone derivatives as Michael donors and methyl vinyl ketone or its equivalent as the Michael acceptor. Here we report a new type of annulation in which cyclic ketones are the Michael acceptors and the open-chain compound is the Michael donor.

RESULTS AND DISCUSSION

The principal feature of the new annulation is the condensation of a 4-methylenecyclohex-2-enone with dimethyl 3-oxoglutarate. The first stage of the reaction is the 1,6-Michael addition of the glutarate to the dienone, and the second stage is the stereoselective intramolecular 1,4-Michael addition, completing the construction of a *cis*-decalin skeleton in one operation.

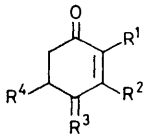
3-Methyl-4-methylenecyclohex-2-enone (1),[1] easily prepared from Hagemann's ester, was first selected as a Michael acceptor, since Deslongchamps indicated that the methyl homologue (2) could be used as a Michael acceptor for 1,6-addition reactions with diethyl malonate.[2] Dimethyl 3-oxoglutarate was adopted as a Michael donor, which had a symmetric structure and an active methylene suitable to form a six-membered ring in the second stage. Treatment of the dienone (1) with dimethyl 3-oxoglutarate in dimethyl sulphoxide in the presence of potassium fluoride as catalyst at 55—60 °C for two days gave a mixture of the stereoisomeric diketo-diesters (3) and (4) in 40 and 1% yields, respectively (indicated as the enol forms). Both gave the same diketone (5) on hydrolysis with sodium chloride in dimethyl sulphoxide–water.[3] The result indicated that they were stereoisomeric at C-8. At an early stage in our investigation on the double Michael annulation, the reaction was carried out under air. An attempt to convert the *cis*-diketo-diester (3) to the *trans*-diketo-diester (6) under the same conditions as the double Michael reaction, in the expectation that the second stage of the annulation reaction might be reversible and the *cis*-diketo-diester (3) might be partly converted to the *trans*-one (6) (thought to be thermodynamically more stable), led to a low yield of the air oxidation product (7), along with recovery of the starting material (3).[4] This suggested that the reaction should be carried out in the absence of oxygen, and when the annulation was carried out under argon atmosphere, the yield of the diketo-diester (3) was improved (60% isolated yield).

Treatment of the diketone (5) with ethane-1,2-dithiol and boron trifluoride–ether in tetrahydrofuran gave the dithioacetal (8) which was smoothly transformed to 9-methyl-*cis*-decahydronaphthalene (9) on reduction with Raney nickel in ether. The ^{13}C n.m.r. and i.r. spectra of the decalin (9) were identical with those reported in the literature,[5] confirming the *cis*-ring junction of the annulation product (3).

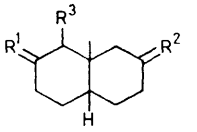
The double Michael reaction on the dimethylcyclohexenone (2) under argon similarly gave two products (10) and (11) in 34 and 20% isolated yield, respectively. The structures of these compounds were confirmed by *X*-ray crystallography.[6] [Since compound (11) did not form suitable crystals, it was converted into the methyl ether (12) with diazomethane in the usual manner, which formed a single crystal suitable for *X*-ray analysis.] The results obtained by *X*-ray crystallography on the diketo-diester (10) and the methyl ether (12) indicated that both have the *cis*-ring junction as expected; (10) adopts a steroid conformation and (12) a distorted non-steroid conformation.

In repeated runs of this annulation, we realised that the volume of dimethyl sulphoxide used as a solvent affected the ratio of the products (10) and (11). When the annulation was carried out in a large volume of dimethyl sulphoxide, the diketo-diester (10) was isolated as a major product as mentioned above, while in a small volume of the solvent, the ratio of the products was nearly equal or sometimes reversed (see Experimental section). We have had no plausible explanation for this result at present.

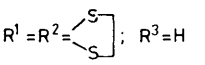
In order to extend the applicability of the new annulation reaction to construction of the *cis*-decalin system, the dienone (13) was prepared. The dimethylcyclohexenone ester (14) has been prepared from Hagemann's ester by Ananthanarayan and Sorensen.[7] However, the



(1) $R^1 = R^4 = H$; $R^2 = Me$; $R^3 = CH_2$
(2) $R^1 = H$; $R^2 = R^4 = Me$; $R^3 = CH_2$
(13) $R^1 = R^2 = Me$; $R^4 = H$; $R^3 = CH_2$
(14) $R^1 = R^2 = Me$; $R^4 = H$; $R^3 = CHCO_2Et$
(27) $R^1 = Me$; $R^2 = H$; $R^3 = CHCO_2Et$; $R^4 = CHMe_2$
(29) $R^1 = Me$; $R^2 = H$; $R^3 = CHCH_2OH$; $R^4 = CHMe_2$
(30) $R^1 = Me$; $R^2 = H$; $R^3 = CH_2$; $R^4 = CHMe_2$
(31) $R^1 = Me$; $R^2 = H$; $R^3 = CHCH_2OTs$; $R^4 = CHMe_2$
(32) $R^1 = Me$; $R^2 = H$; $R^3 = CHCH\ Cl$; $R^4 = CHMe_2$

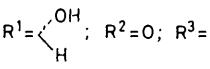


(5) $R^1 = R^2 = O$; $R^3 = H$

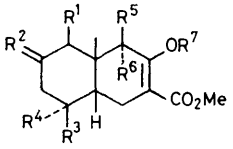


(8) $R^1 = R^2 =$; $R^3 = H$

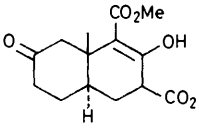
(9) $R^1 = R^2 = H_2$; $R^3 = H$
(20) $R^1 = H_2$; $R^2 = O$; $R^3 = Me$



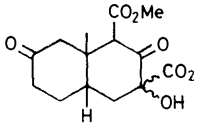
(23) $R^1 =$; $R^2 = O$; $R^3 = Me$



(3) $R^1 = R^3 = R^4 = R^6 = R^7 = H$; $R^2 = O$; $R^5 = CO_2Me$
(4) $R^1 = R^3 = R^4 = R^5 = R^7 = H$; $R^2 = O$; $R^6 = CO_2Me$
(10) $R^1 = R^4 = R^6 = R^7 = H$; $R^2 = O$; $R^3 = Me$; $R^5 = CO_2Me$
(11) $R^1 = R^3 = R^6 = R^7 = H$; $R^2 = O$; $R^4 = Me$; $R^5 = CO_2Me$
(12) $R^1 = R^3 = R^6 = H$; $R^2 = O$; $R^4 = R^7 = Me$; $R^5 = CO_2Me$
(17) $R^1 = Me$; $R^2 = O$; $R^3 = R^4 = R^6 = R^7 = H$; $R^5 = CO_2Me$



(6)

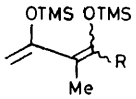


(7)

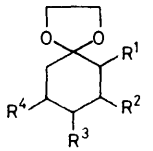
(18) $R^1 = Me$; $R^2 =$; $R^3 = R^4 = R^6 = R^7 = H$; $R^5 = CO_2Me$

(19) $R^1 = Me$; $R^2 = H_2$; $R^3 = R^4 = R^6 = R^7 = H$; $R^5 = CO_2Me$
(21) $R^1 = Me$; $R^2 = O$; $R^3 = R^4 = R^6 = H$; $R^5 = CO_2Me$; $R^7 = Ac$

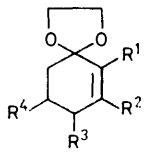
(22) $R^1 = Me$; $R^2 =$; $R^3 = R^4 = R^6 = H$; $R^5 = CO_2Me$; $R^7 = Ac$



(15) R = Me
(25) R = H [(*E*)-form]

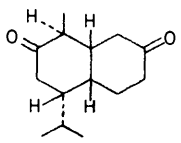


(a)



(b)

(16) $R^1 = R^2 = Me$; $R^3 = CO_2Et$; $R^4 = H$
(28) $R^1 = Me$; $R^2 = H$; $R^3 = CO_2Et$; $R^4 = CHMe_2$



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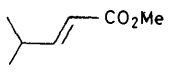
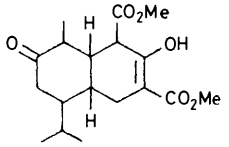


(26)



(33)

methylation of Hagemann's ester with methyl iodide and sodium hydride gave a mixture consisting of four compounds (by g.l.c.) even after spinning-band distillation. Thus an alternative synthesis of the ester (14) was undertaken. Treatment of 3-acetylbutan-2-one with trimethylsilyl chloride, zinc chloride, and triethylamine in benzene and ether gave the disilyl ether (15). The silyl-ether was subjected to a Diels–Alder cycloaddition with ethyl acrylate in xylene in a sealed tube at 170—180 °C (bath temperature) for four days. The resulting mixture was, without further purification, treated with dilute hydrochloric acid to yield the dimethyl cyclohexenone ester (14) in 22% yield after repeated distillation.

Acetalisation of the ester (14) with ethylene glycol in benzene in the presence of toluene-*p*-sulphonic acid with azeotropic removal of water gave a mixture of the acetals (16) (isomeric with respect to the position of the double bond, revealed by gas chromatography–mass spectroscopy). Reduction of the mixture with lithium aluminium hydride in ether, followed by acid hydrolysis with dilute hydrochloric acid, furnished the dienone (13) in 40% yield from the cyclohexenone ester (14) as a result of hydrolysis of the acetal group and concomitant dehydration of the primary alcohol group.

Double Michael reaction of the dienone (13) in a similar manner gave the diketo-diester (17) in 20% yield. Thioacetalisation of the diketo-diester (17) gave the monothioacetal (18) in good yield, which, on reduction with Raney nickel, gave the keto-diester (19). Hydrolysis of the keto-ester with sodium chloride in dimethyl sulphoxide–water furnished the ketone (20), the n.m.r. and i.r. spectra of which were identical with those of an authentic sample,* confirming the *cis*-ring junction in the Michael product (17). The ketone (20) is a key intermediate of the synthesis of (±)-eremophilenolide,[9] (±)-furanoeremophilane,[8] and (±)-fukinone.[9]

Acetylation of the diketo-diester (17) gave the acetate (21). Reduction of the acetate with sodium borohydride in aqueous tetrahydrofuran gave the alcohol (22) in 75% yield. The configuration of the hydroxy-group of this alcohol was ultimately confirmed by the synthesis of the hydroxy-ketone (23). Thus, hydrolysis of the alcohol (22) with dilute hydrochloric acid in acetic acid gave the hydroxy-ketone (23), which was identical with an authentic sample * by i.r. and n.m.r. spectral comparison, and since the hydroxy-ketone (23) has been transformed into (±)-3α-hydroxyeremophilenolide,[10] the synthesis of this hydroxy-ketone represents an alternative formal synthesis of the sesquiterpene.

A further example of this stereoselective double Michael annulation was provided by the synthesis of 4-isopropyl-1-methyl-2,7-dioxo-*cis*-decalin (24) (6-demethylamorphane [11]). The Diels–Alder cycloaddition of the diene (25) [12] and methyl 4-methylpent-2-enoate (26) [13] afforded a cycloaddition product, which, on hydrolysis with dilute hydrochloric acid, gave the keto-ester (27) in 59% yield. Regioselectivity of the cycloaddition rested on the investigation of Ibuka and his co-workers.[12] Acetalisation of the keto-ester (27) gave the acetal (28), which was submitted to reduction with lithium aluminium hydride in ether followed by hydrolysis with dilute hydrochloric acid in acetic acid to give a mixture of the keto-alcohol (29) and the dienone (30) in 60 and 35% yield, respectively, both being separable in pure form by column chromatography with silica gel in chloroform. Attempts to convert the alcohol (29) into the dienone (30) with several kinds of acids and under forcing conditions was unsuccessful, in contrast to the preparation of dienones (1), (2), and (13). Tosylation of the alcohol (29) in the usual manner gave the tosylate (31) and the chloride (32) in 60 and 21% yield, respectively. Treatment of the tosylate and the chloride with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in benzene furnished the dienone (30) in good yield. However, the double Michael annulation of the dienone in the same manner as above was unsuccessful. Eventually, we found that when the dienone (30) was treated with dimethyl 3-oxoglutarate in *t*-butyl alcohol in the presence of DBU and triethylamine, a mixture consisting of stereoisomers of the diketo-diester (33) was obtained in low yield. Although attempts to separate the isomers were unsuccessful, hydrolysis of the mixture with hydrochloric acid in acetic acid gave a crystalline diketone (24) as one of the products. The structure of the diketone (24) was confirmed by *X*-ray crystallography. Crystal data for (24); $C_{14}H_{22}O_2$, monoclinic prisms, m.p. 158—160 °C (from n-hexane–benzene), space group $C2/c$, $a = 20.91$, $b = 7.31$, $c = 19.57$ Å, $\beta = 119.6°$, $D_m = 1.142$ g cm^{-3} $Z = 8$, $D_C = 1.136$ g cm^{-3}. Determination of the cell parameters and collection of the intensity data were performed on a Rigaku AFC-5 diffractometer using Mo-K_α radiation ($\lambda = 0.709\,26$ Å). The structure was solved by direct methods and refined by full-matrix least-squares to an *R*-factor of 7.6% for 1 237 reflections. The result obtained from *X*-ray crystallography designated the stereoselective mode of the new double Michael annulation.†

EXPERIMENTAL

M.p.s were determined with a Yanagimoto hot-stage apparatus and are uncorrected. I.r. spectra were recorded on a Hitachi 215 in Nujol unless otherwise stated. ^{1}H N.m.r. spectra were recorded using Varian HA-100D, Varian A-60, and JEOL JNM-PMR 60 instruments in deuteriochloroform with tetramethylsilane as internal standard; ^{13}C n.m.r. spectra were recorded on a Varian CFT-20. Mass spectra were recorded with a JEOL JMS-01SG-2 on a direct-inlet system.

Double Michael Annulation of 4-Methylene-3-methylcyclohex-2-enone (1) *with Dimethyl 3-Oxoglutarate.*—A mixture of the dienone (1) (10 g), dimethyl 3-oxoglutarate (15g), potassium fluoride (9.5 g), and dimethyl sulphoxide

* The i.r. and ^{1}H n.m.r. spectra of the ketone (20) and the hydroxy-ketone (23) were provided by Dr. T. Kato (Tohoku University).

† The observed and calculated structure factors, anisotropic thermal parameters, and atomic co-ordinates are deposited as Supplementary Publication No. SUP 23165 (15 pp.). For details see Notice to Authors No. 7, *J. Chem. Soc., Perkin Trans. 1*, 1980, Index issue.

(5 m) was stirred under argon at 60—70 °C for two days, then concentrated under reduced pressure to give a residue. After addition of water to the residue, the gummy precipitate was thoroughly extracted with ether. The ethereal extract was washed with aqueous sodium carbonate and 1% aqueous sodium hydroxide. The sodium hydroxide washing was acidified with concentrated hydrochloric acid and extracted with ether. The combined extracts were washed with brine and dried. Removal of the solvent gave a residue which crystallised from ether to give the *diketo-diester* (3) (6 g). The mother-liquor was concentrated and the residue was chromatographed over silica gel in chloroform. Elution with the same solvent gave an additional crop of (3) (8.5 g), m.p. 133 °C; $\nu_{max.}$ 1 720, 1 690, 1 650, and 1 610 cm^{-1}; δ 1.03 (3 H, s), 3.02 (1 H, t, *J* 1.2 Hz, 8-H), 3.74 and 3.79 (each 3 H, s), and 12.00 (1 H, s) (Found: C, 60.6; H, 6.7. $C_{15}H_{20}O_6$ requires C, 60.8; H, 6.8%). Repeated column chromatography of the residue from the above crystallisation gave the isomeric *diketo-diester* (4) (0.58 g), m.p. 108—109 °C; $\nu_{max.}$, 1 720, 1 700, 1 645, and 1 620 cm^{-1}; δ 1.13 (3 H, s), 3.34 (1 H, t, *J* 1.8 Hz, 8-H), 3.72, and 3.80 (each 3 H, s), and 12.10 (1 H, s) (Found: C, 60.6; H, 7.0. $C_{15}H_{20}O_6$ requires C, 60.8; H, 6.8%).

9-*Methyl*-cis-*decahydronaphthalen*-2,7-*dione* (5).—A solution of the diketo-diester (3) (3.0 g) and sodium chloride (0.7 g) in dimethyl sulphoxide (30 ml) and water (0.6 ml) was refluxed overnight and concentrated to dryness under reduced pressure to leave a residue which was distributed between water and ether, and the ether layer was washed with dilute hydrochloric acid, aqueous sodium carbonate, and water, dried, and concentrated to give the *diketone* (5) (1 g), which crystallised from n-hexane–ether, m.p. 121—123 °C; $\nu_{max.}$ 1 697 cm^{-1}; δ 1.06 (3 H, s) (Found: C, 73.3; H, 8.9. $C_{11}H_{16}O_2$ requires C, 73.3; H, 9.0%). The isomeric diketo-diester (4) gave the same diketone (5) in the same manner in a similar yield.

Thioacetalisation of the Diketone (5).—A mixture of the diketone (5) (290 mg), ethane-1,2-dithiol (1 g), and boron trifluoride–ether (4 drops) was allowed to stand overnight and diluted with chloroform. The chloroform solution was washed with aqueous sodium carbonate and water, dried, and concentrated to dryness to give the *dithioacetal* (8) (480 mg) which crystallised from ether, m.p. 167—169 °C δ 1.18 (3 H, s) and 3.28 (8 H, s) (Found: C, 54.0; H, 7.4. $C_{15}H_{24}S_4$ requires C, 54.2; H, 7.3%).

Reduction of the Dithioacetal (8).—The dithioacetal (8) (500 mg) was treated with Raney nickel [prepared from Raney alloy (25 g)] in ether under reflux for 10 h. Usual work-up gave 9-methyl-*cis*-decahydronaphthalene (9) (200 mg), which showed identical spectroscopic properties with those reported in the literature.[5]

The Double Michael Annulation of 4-*Methylene*-3,5-*dimethylcyclohex*-2-*enone* (2) *with Dimethyl* 3-*Oxoglutarate*.—(*a*) A mixture of the dienone (2) (16.8 g), dimethyl 3-oxoglutarate (32.5 g), potassium fluoride (14.5 g), and dimethyl sulphoxide (150 ml) was stirred at 55—60 °C under argon for 3 days and after removal of the solvent under reduced pressure, the resulting residue was distributed between a small amount of water and a large amount of ether. The ether layer was worked up in the same manner as the case of the double Michael annulation of the dienone (1). The product obtained from the 1% sodium hydroxide-soluble portion was fractionally recrystallised from ether to give the *diketo-diester* (10) (7g), m.p. 146—147 °C; $\nu_{max.}$ 1 730, 1 710, 1 655, and 1 618 cm^{-1}; δ 1.02 (3 H, d, *J* 5.5 Hz), 1.14 (3 H, s), 3.22 (1 H, t, *J* 1.5 Hz), 3.77 and 3.81 (each 3 H, s), and 12.14 (1 H, s) (Found: C, 62.1; H, 7.3. $C_{16}H_{22}O_6$ requires C, 61.9; H, 7.2%). The mother-liquors from the recrystallisation were concentrated and the residue was chromatographed on silica gel in chloroform. Elution with chloroform gave the *diketo-diester* (11) (7.7 g) which crystallised from ether, m.p. 154—157 °C; $\nu_{max.}$ 1 730, 1 698, 1 655, and 1 618 cm^{-1}; δ 0.99 (3 H, s), 1.07 (3 H, d, *J* 5.5 Hz), 2.93 (1 H, s), 3.74 and 3.82 (each 3 H, s), and 11.98 (1 H, s) (Found: C, 61.9; H, 7.3. $C_{16}H_{22}O_6$ requires C, 61.9; H, 7.2%). Subsequent elution with the same solvent gave additional crops of the diketo-diester (10) (6 g).

(*b*) The dienone (2) (10 g) was treated in the same manner in dimethyl sulphoxide (10 ml) to give a mixture (18 g) as a product soluble in 1% sodium hydroxide, from which the diketo-diester (11) (5 g) was obtained on the first crystallisation from ether. The mother-liquors were concentrated and the residue was chromatographed on silica gel in chloroform. The first elution with chloroform gave an additional crop of the diketo-diester (11) (2.5 g). The second elution with the same solvent gave the diketo-diester (10) (3.5 g). The diketo-diester (11) gave the *methyl ether* (12) by treatment with diazomethane–ether in the usual way, m.p. 113—115 °C (from ether); $\nu_{max.}$ 1 720, 1 695, and 1 660 cm^{-1}; δ 0.98 (3 H, s), 1.06 (3 H, d, *J* 5.5 Hz), 2.98 (1 H, br s), 3.65, 3.73, and 3.78 (each 3 H, s) (Found: C, 62.8; H, 7.5. $C_{17}H_{24}O_6$ requires C, 63.0; H, 7.5%).

Trimethylsilylation of 3-*Methylpentane*-2,4-*dione*.—Dry zinc chloride (2g) was added to triethylamine (117 ml) and the mixture was stirred for 10 min. To the mixture a solution of 3-methylpentane-2,4-dione (27.4 g) in ether (100 ml) and benzene (100 ml) was added with cooling and to the cold solution trimethylsilyl chloride (80 g) was added dropwise with stirring and the whole was refluxed for 2 days. The reaction mixture was quickly filtered with suction and the filtrate was concentrated under reduced pressure to leave an oil which was subjected to distillation. The distillate (b.p. 77—85 °C/7 mmHg) was collected and redistillation of the distillate gave the disilyl ether (15) (19 g), b.p. 82—84 °C/7 mmHg, as a mixture of geometrical isomers.

Diels–Alder Cycloaddition of the Disilyl Ether (15) *and Ethyl Acrylate*.—A solution of the disilyl ether (15) (19 g) and ethyl acrylate (10 g) in xylene (16 ml) was heated in a sealed tube at 170—180 °C for four days and concentrated to dryness to leave an oil which was treated with a mixture of 10% hydrochloric acid (6 ml) and tetrahydrofuran (20 ml) with stirring at room temperature for 1 h. The solution was diluted with water and extracted with ether. The extract was washed with aqueous sodium carbonate and water, dried, and concentrated to dryness to give the dimethylcyclohexenone ester (14) (3.5 g), b.p. 133 °C/7 mmHg; $\nu_{max.}$ (neat), 1 715 and 1 655 cm^{-1}; δ 1.28 (3 H, t, *J* 7.0 Hz), 1.81 (3 H, m, *J* 1.0 Hz), 1.97 (3 H, m, *J* 1.0 Hz), 3.28 (1 H, m), and 4.21 (2 H, q, *J* 7.0 Hz).

4-*Methylene*-2,3-*dimethylcyclohex*-2-*enone* (13).—A solution of the foregoing dimethylcyclohexenone ester (14) (50 g), ethylene glycol (31.6 g), and toluene-*p*-sulphonic acid (0.2 g) in benzene was refluxed for 72 h while water was removed with a Dean and Stark apparatus, poured onto aqueous sodium carbonate, and extracted with benzene. The benzene extract was washed with water, dried, and concentrated under pressure to leave a mixture of the acetals (16a and b) (49 g), b.p. 130—132 °C/5 mmHg. A solution of the mixture (49 g) in ether (200 ml) was added dropwise to a

suspension of lithium aluminium hydride (8 g) in ether (500 ml) cooled in ice–water with stirring, and the whole refluxed for 2 h. After decomposing the excess of reagent with water, the ether solution was dried with potassium carbonate and filtered. The filtrate was concentrated to an oil (42 g) which was treated with 3% hydrochloric acid (100 ml) and acetic acid (60 ml) with stirring at room temperature for 2 h. The mixture was diluted with water and extracted with ether. The extract was washed with aqueous sodium carbonate and water, dried, and concentrated to dryness to leave an oil (20 g) which gave the dienone (13) (11 g) by fractional distillation, b.p. 71—75 °C/10 mmHg; $\nu_{max.}$ (neat), 1 720 and 1 650 cm^{-1}; δ 1.89 (3 H, br s), 2.05 (3 H, d, *J* 1.0 Hz), 5.23 (1 H, br s), and 5.30 (1 H, br s).

The Double Michael Annulation of the Dienone (13).—The foregoing dienone (13) (10 g) was treated with dimethyl 3-oxoglutarate (13 g) in the same manner as the dienone (1) and (2) mentioned above to yield the *diketo-diester* (17) (4.5 g) which crystallised from ether, m.p. 139—143 °C, $\nu_{max.}$ 1 725, 1 692, 1 655, and 1 618 cm^{-1}; δ 0.88 (3 H, s), 1.01 (3 H, d, *J* 6.5 Hz), 3.32 (1 H, s), 3.73 and 3.80 (each 3 H, s), and 11.93 (1 H, s) (Found: C, 61.8; H, 7.3. $C_{16}H_{22}O_6$ requires C, 61.9; H, 7.2%).

Thioacetalisation of the Diketo-diester (17).—The diketo-diester (17) (350 mg) was treated with ethane-1,2-dithiol (2 g) and boron trifluoride–ether (5 drops) at room temperature for 40 h. The mixture was concentrated under reduced pressure to leave an oil which was taken up in chloroform. The chloroform solution was washed with aqueous sodium carbonate and water and dried. Removal of the solvent gave the thioacetal (18) (350 mg) which crystallised from ether, m.p. 147—150 °C; $\nu_{max.}$ 1 720, 1 660, and 1 620 cm^{-1}; δ 1.07 (3 H, s), 1.20 (3 H, d, *J* 6.3 Hz), 3.23 (4 H, s), 3.48 (1 H, s), 3.70 and 3.79 (each 3 H, s), and 11.87 (1 H, s); *m/e* 386 (M^+).

Desulphurisation of the Thioacetal (18).—A solution of the thioacetal (18) (342 mg) and Raney nickel (prepared from 20 g of alloy) in ethanol (80 ml) was refluxed for 8 h and filtered. The filtrate was concentrated to an oil which was taken up in chloroform. The chloroform solution was washed with brine, dried, and concentrated. Chromatography of the resulting residue on silica gel eluting with chloroform gave the keto-diester (19) (85 mg) as an oil; $\nu_{max.}$ (neat), 1 725, 1 655, and 1 620 cm^{-1}; δ 0.87 (3 H, d, *J* 6.0 Hz), 0.93 (3 H, s), 3.55 (1 H, br s), 3.70 and 3.77 (each 3 H, s), and 11.95 (1 H, s); *m/e* 296 (M^+).

1,9-*Dimethyl*-cis-*decahydronaphthalen*-7-*one* (20).—A mixture of the keto-diester (19) (80 mg), sodium chloride (60 mg), dimethyl sulphoxide (2 ml), and three drops of water was refluxed for 18 h, diluted with water, and extracted with ether. The ethereal extract was washed with aqueous sodium carbonate and water, and solvent removed to give 1,9-dimethyl-*cis*-decahydronaphthalen-7-one (20) (30 mg) as an oil; $\nu_{max.}$ 1 710 cm^{-1}; δ(CCl_4), 0.84 (3 H, d, *J* 6.0 Hz) and 0.94 (3 H, s); *m/e* 180 (M^+); it showed identical spectroscopic data with those of authentic sample.

Acetylation of the Diketo-diester (17).—The diketo-diester (17) (1.5 g) was acetylated with acetic anhydride (3 ml) in pyridine (30 ml) in the usual manner to give the *acetate* (21) (1.6 g) which crystallised from ether, m.p. 103—105 °C; $\nu_{max.}$, 1 750, 1 730, and 1 700 cm^{-1}; δ 0.86 (3 H, s), 1.01 (3 H, d, *J* 6.8 Hz), 2.18 (3 H, s), 3.29 (1 H, br s), 3.72, and 3.74 (each 3 H, s) (Found: C, 61.1; H, 7.0. $C_{18}H_{24}O_7$ requires C, 61.4; H, 6.9%).

Sodium Borohydride Reduction of the Acetate (21).—A solution of sodium borohydride (100 mg) in water (1 ml) was dropwise added to a solution of the acetate (21) (400 mg) in tetrahydrofuran (10 ml) with vigorous stirring at room temperature and the whole was stirred for 10 min, diluted with water, and extracted with ether. The extract was washed with brine, dried, and concentrated to give the *alcohol* (22) (300 mg) which crystallised from n-hexane–ether, m.p. 125—127 °C; $\nu_{max.}$ 3 425, 1 750, 1 720, 1 700, and 1 660 cm^{-1}; δ 0.94 (3 H, d, *J* 7.0 Hz), 1.03 (3 H, s), 2.15 (3 H, s), 3.47 (1 H, s), 3.71 (6 H, s), and 4.15 (1 H, m, $W_{1/2}$ 20 Hz) (Found: C, 60.8; H, 7.5. $C_{18}H_{26}O_7$ requires C, 61.0; H, 7.4%).

2-*Hydroxy*-1,9-*dimethyl*-cis-*decahydronaphthalen*-7-*one* (23).—A solution of the alcohol (22) (254 mg) in acetic acid (1 ml), water (19 ml), and concentrated hydrochloric acid (3 ml) was refluxed overnight, diluted with water, and extracted with ether. The extract was washed with aqueous sodium carbonate and water, dried, and concentrated to dryness to leave an oil which was chromatographed on silica gel in chloroform. Elution with 1% acetone–chloroform gave the hydroxy-ketone (23) (50 mg) as an oil; $\nu_{max.}$ (neat), 3 420 and 1 700 cm^{-1}; δ 0.97 (3 H, d, *J* 6.4 Hz), 0.98 (3 H, s), and 3.49 (1 H, td, *J* 9.5 and 5.0 Hz); *m/e* 196 (M^+); the i.r. and ^{1}H-n.m.r. spectra were identical with those of authentic sample. The hydroxy-ketone (23) gave the benzoate with benzoyl chloride in pyridine in the usual manner, m.p. 98—100 °C, $\nu_{max.}$ 1 700 cm^{-1}; δ(CCl_4), 0.93 (3 H, d, *J* 6.5 Hz), 1.10 (3 H, s), 4.92 (1 H, m), and 7.23—7.60 and 7.85—8.10 (3 H and 2 H, m, Ar-H); these spectral data were identical with those of the authentic sample.[10]

5-*Isopropyl*-2-*methyl*-4-*methoxycarbonylcyclohex*-2-*enone* (27).—A solution of (*E*)-2-methyl-1,3-bis(trimethylsilyloxy)-buta-1,3-diene (25) (13 g) and methyl 4-methylpent-2-enoate (26) (10.3 g) in xylene (15 ml) was heated in a sealed glass tube under argon at 170—180 °C for 40 h, then concentrated to an oil. The oily residue was treated with 10% hydrochloric acid (6 ml) in tetrahydrofuran (20 ml) with stirring at room temperature for 30 min, then the whole was diluted with water and extracted with ether. The extract was washed with aqueous sodium carbonate and water, dried, and concentrated to an oil, chromatography of which on silica gel eluting with chloroform gave 5-isopropyl-2-methyl-4-methoxycarbonylcyclohex-2-enone (27) (6.6 g); $\nu_{max.}$ (neat) 1 725 and 1 665 cm^{-1}; δ 0.88 (3 H, d, *J* 6.7 Hz), 0.93 (3 H, d, *J* 6.7 Hz), 1.81 (3 H, d, *J* 1.5 Hz), 3.35 (1 H, m, $W_{1/2}$ 13 Hz), 3.75 (3 H, s), and 6.52 (1 H, dq, *J* 3.0 and 1.5 Hz).

5-*Isopropyl*-4-*methylene*-2-*methylcyclohex*-2-*enone* (30).—The keto-ester (27) (3.4 g) was heated in benzene with ethylene glycol (2 ml) and toluene-*p*-sulphonic acid (50 mg), with removal of water by a Dean and Stark apparatus for 24 h. Usual work-up gave a mixture of the acetal esters (28a and b) (3.8 g); $\nu_{max.}$ (neat) 1 730 and 1 705 cm^{-1} (assigned to an ester CO and a conjugated ester CO), which was, without further purification, reduced with lithium aluminium hydride (2 g) in ether (400 ml) under reflux for 2 h. After the excess of reagent was decomposed by adding water, the mixture was dried with potassium carbonate and filtered. The filtrate was concentrated to dryness to give the alcohol, which was treated with concentrated hydrochloric acid (5 ml) in acetic acid (10 ml) and water (10 ml) with stirring for 2 h. The reaction mixture was diluted with water, basified with potassium carbonate, and extracted with ether. The extract was washed with brine, dried, and concentrated to dryness to leave an oil which was

chromatographed on silica gel in chloroform. The first elution with chloroform gave the dienone (30) (820 mg); $\nu_{max.}$ (neat) 1 660 cm^{-1}; δ, 0.87 (3 H, d, *J* 6.5 Hz), 0.89 (3 H, d, *J* 6.5 Hz), 1.82 (3 H, d, *J* 0.7 Hz), 5.16 and 5.25 (each 1 H, br s), and 6.86 (1 H, br s); *m/e* 164 (M^+). Subsequent elution with the same solvent gave the hydroxy-ketone (29) (1.55 g) as an oil; $\nu_{max.}$ (neat), 3 370 and 1 650 cm^{-1}; δ 0.86 (3 H, d, *J* 6.5 Hz), 0.93 (3 H, d, *J* 6.5 Hz), 1.78 (3 H, t, *J* 1.5 Hz), 3.65 (1 H, dd, *J* 11.0 and 5.5 Hz), 3.92 (1 H, dd, *J* 11.0 and 5.0 Hz), and 6.78 (1 H, dq, *J* 3.0 and 1.5 Hz); *m/e* 182 (M^+). Attempts to convert the hydroxy-ketone (29) to the dienone (30) by treatment with several kinds of acid gave no dienone.

Tosylation of the Hydroxy-ketone (29).—A mixture of the hydroxy-ketone (29) (1 g), toluene-*p*-sulphonyl chloride (1.57 g), and pyridine (20 ml) was allowed to stand at room temperature overnight, then concentrated under reduced pressure to give a residue which was taken up in chloroform. The chloroform solution was washed with dilute hydrochloric acid, sodium carbonate, and water, dried, and concentrated to give a residue, chromatography of which on silica gel eluting with chloroform gave the *toluene-p-sulphonate* (31) (1.1 g) which crystallised from n-hexane–ether, m.p. 104—106 °C; $\nu_{max.}$ 1 665 cm^{-1}; δ 0.78 (3 H, d, *J* 6.5 Hz), 0.85 (3 H, d, *J* 6.5 Hz), 1.73 (3 H, t, *J* 1.5 Hz), 2.46 (3 H, s), 4.02 (1 H, dd, *J* 9.8 and 5.0 Hz), 4.24 (1 H, dd, *J* 9.8 and 5.0 Hz), 6.43 (1 H, dq, *J* 3.0 and 1.5 Hz), 7.36 (2 H, d, *J* 8.5 Hz), and 7.80 (2 H, d, *J* 8.5 Hz) (Found: C, 64.1; H, 7.3. $C_{18}H_{24}O_4S$ requires C, 64.3; H, 7.2%). Further elution with the same solvent gave the chloride (32) (230 mg) as an oil; $\nu_{max.}$ ($CHCl_3$) 1 665 cm^{-1}; δ, 0.86 (3 H, d, *J* 6.5 Hz), 0.95 (3 H, d, *J* 6.5 Hz), 1.80 (3 H, t, *J* 1.8 Hz), 2.72 (1 H, m, $W_{1/2}$ 16 Hz), 3.58 (1 H, dd, *J* 11.0 and 5.0 Hz), 3.81 (1 H, dd, *J* 11.0 and 5.0 Hz), and 6.63 (1 H, dq, *J* 3.0 and 1.5 Hz); *m/e* 200 (M^+). Both *toluene-p-sulphonate* (31) and chloride (32) gave the dienone (30) by treatment with DBU: a solution of (31) (500 mg) and DBU (452 mg) in benzene (10 ml) was heated with stirring at 60 °C for 6.5 h, washed with dilute hydrochloric acid, aqueous sodium hydrogencarbonate, and brine, and dried; removal of the solvent gave the dienone (30) (236 mg).

Double Michael Annulation of the Dienone (30).—A solution of the dienone (30) (147 mg) DBU (0.2 ml), and triethylamine (0.15 ml) in t-butyl alcohol (5 ml) was heated at 50—60 °C with stirring under argon for 3 days and concentrated to dryness; the residue was taken up in ether, then washed with dilute hydrochloric acid, aqueous sodium carbonate, and 1% aqueous sodium hydroxide. The sodium hydroxide washings were acidified with concentrated hydrochloric acid and extracted with ether. The organic layer was washed with brine and dried. Removal of the solvent gave an oil, chromatography of which on silica gel eluting with chloroform gave a mixture consisting of four compounds (revealed by the ^1H n.m.r. spectrum, which showed the protons of an enolic hydroxy-group at δ 12.13, 12.17, 12.18, and 12.48 as singlets, ratio 1 : 9 : 10 : 1). The mixture was subjected to the hydrolysis and decarboxylation reaction with concentrated hydrochloric acid (3 ml), acetic acid (5 ml), and water (2 ml). After heating on a water-bath for 4 h, the mixture was diluted with water, basified with potassium carbonate, and extracted with ether. The ethereal extract was washed with water, dried, and concentrated to dryness to leave a residue which crystallised from ether to give 4-*isopropyl*-1-*methyl*-cis-*decahydronaphthalen*-7-*one* (24) (20 mg), m.p. 158—160 °C; $\nu_{max.}$ 1 685 cm^{-1}; δ 0.92 (3 H, d, *J* 6.0 Hz), 1.00 (3 H, d, *J* 6.0 Hz), and 1.05 (3 H, d, *J* 6.0 Hz) (Found: C, 75.6; H, 10.1. $C_{14}H_{22}O_2$ requires C, 75.6; H, 10.0%). The structure of (24) was confirmed by *X*-ray crystallography.

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