Carotenoids and Related Compounds. Part 37.[1] Stereochemistry and Synthesis of Capsorubin

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The two oxygen substituents in the end groups of capsorubin were shown to be *trans* to one another by synthesis of optically inactive forms of the carotenoid, and of the isomers which have the corresponding *cis*-structure. The 3*S*,5*R*,3'*S*,5'*R* configuration thus established for the natural carotenoid was confirmed by synthesis of this stereoisomer from (+)-camphor.

Cryptocapsin has the 3'*S*,5'*R* configuration, and the racemic form has been synthesised.

Capsanthin has the 3*R*,3'*S*,5'*R* configuration.

Capsorubin (1), capsanthin (2), and cryptocapsin (3) constitute a group of related pigments which occurs principally in red peppers (*Capsicum annuum*).[2-6] N.m.r. studies in the elucidation of their gross structures revealed that the two end groups in capsorubin, and one of the end groups in both capsanthin and cryptocapsin, all have the same relative stereochemistry.[4,6] Subsequent o.r.d. studies indicated that these end groups also have the same absolute configuration.[7]

Cholnoky and Szabolcs [8] found that oxidative degradation of capsorubin yielded a mixture of acids which included camphoronic acid (9). Faigle and Karrer [9] showed that the camphoronic acid formed in a similar degradation of capsanthin has the same optical rotation as that reported earlier for a sample prepared by degradation of (+)-camphor (10). As the stereochemistry of the latter was known, and has since been confirmed by *X*-ray crystallographic analysis of (+)-3-bromocamphor,[10] these results established an *R* configuration at the acylated carbon atoms (C-5 and/or C-5') in the cyclopentane end groups of the red pepper pigments.† We consider next the hydroxylated carbon atoms (C-3 and/or C-3').

Our i.r. studies favoured a *trans*-configuration (a) for the two oxygen substituents in the cyclopentane end groups.[4] However, Faigle and Karrer [9,11] proposed a *cis*-configuration (b) since ozonolysis of both capsanthin acetate and capsorubin acetate gave an optically active hydroxycamphonanic acid at first regarded as (11) because it formed a γ-lactone (14) when sublimed at 250 °C.[9]

Confirmation of the *trans*-configuration in the end groups was then provided by our synthesis of optically inactive forms of capsorubin in which both end groups were either *cis* [*e.g.* (4)] or *trans* [*e.g.* (1)].[12] In showing that capsorubin has the *trans* arrangement of oxygen substituents in both end groups, and hence the 3*S*,5*R*,3'*S*,5'*R* configuration (1),† these results provided the first elucidation of the absolute stereochemistry of a natural chiral carotenoid.[13] The o.r.d. studies mentioned earlier, showed that cryptocapsin has the corresponding 3'*S*,5'*R* configuration (3), and indicated that in capsanthin the 3-hydroxycyclohexene end group has the same absolute configuration as those in zeaxanthin (5). Since capsorubin is believed to be formed in nature from violaxanthin (6),[14] the diepoxide of zeaxanthin (5), by rearrangements of the pinacollic type [4,5] which do not involve the oxygen substituents at C-3 and C-3', the determination of the stereochemistry of capsorubin indicated that zeaxanthin has the 3*R*,3'*R* configuration.[7,12] This assignment has now been confirmed independently,[15] and hence capsanthin has the 3*R*,3'*S*,5'*R* configuration. The relative configuration of the three chiral centres has also been confirmed by *X*-ray crystallographic analysis of the bis-*p*-bromobenzoate.[16]

Final confirmation of the basic conclusions summarised above was obtained by a stereochemically controlled synthesis of (3*S*,3*R*,3'*S*,3'*R*)-capsorubin (1).[17] This provided the first synthesis of a chiral xanthophyll with the natural configuration.

Details of these and related synthetic studies in both the optically inactive and optically active series are given in this paper.

Optically Inactive Series.‡—The readily available β-diketone (18) [18] was converted into the enol ether (19) which was reduced with lithium aluminium hydride. Treatment of the product with acid yielded the crystalline cyclohexenone (20) which was hydrogenated catalytically to give a mixture of the required cyclohexanone (22) and the cyclic ether (21). The latter on treatment with dilute acid was converted almost quantitatively into the cyclohexanone (22), which was oxidised with chromic acid to give the keto-acid (23). This was stable to heat, thus excluding the β-keto-acid structure that would have been obtained had the initial reaction with the β-diketone (18) given the isomeric enol ether (29).

Autoxidation of the keto-acid (23) in the presence of potassium t-butoxide gave the diosphenol (24). This on treatment with dilute alkali, underwent the expected benzylic acid type of rearrangement with ring contraction. The resulting α-hydroxy-acids (25) were not isolated, but oxidised directly to the keto-acid (26). No camphononic acid (30) was detected, indicating that autoxidation of (23) had occurred at C-6 and not at C-2. Confirmation of the carbon skeleton of (26) was obtained by Huang-Minlon reduction to camphonanic acid (28).

Reduction of the keto-acid (26) with potassium borohydride gave the γ-lactone (14), which was hydrolysed to the *cis*-hydroxy-acid (11), and the *trans*-hydroxy-acid (15). The latter sublimed unchanged at 100 °C under reduced pressure, but sublimation at 230 °C gave the γ-lactone (14) of the *cis*-hydroxy-acid with inversion of configuration at C-1. This

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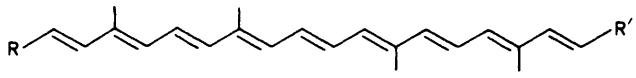
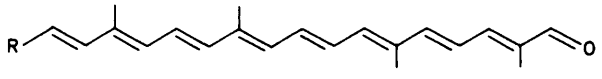
† The numbering of carbon atoms in carotenoids is in accordance with the recommendations of the IUPAC-IUB Commission on Biochemical Nomenclature, and may therefore differ from that of the corresponding positions in the precursors.

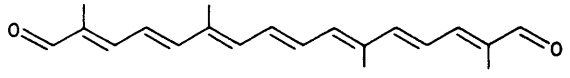
‡ In this section, unless otherwise indicated, formula numbers relate to optically inactive compounds; any stereochemistry implied by the formulae then relates to relative configuration between centres.



(1) R = R′ = a
(2) R = a, R′ = c
(3) R = a, R′ = d
(4) R = R′ = b
(5) R = R′ = c
(6) R = R′ = e



(7) R = d



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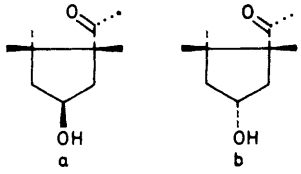
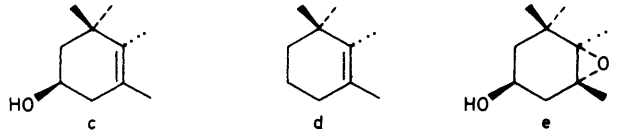
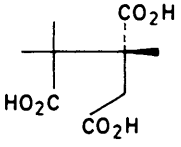


a b



c d e



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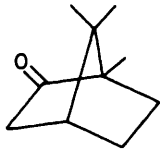

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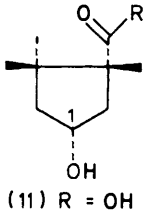
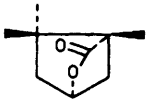


(11) R = OH
(12) R = OMe
(13) R = Me



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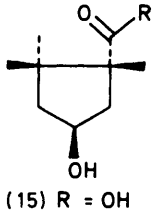
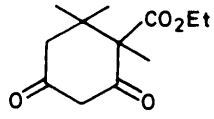


(15) R = OH
(16) R = OMe
(17) R = Me



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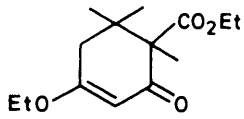

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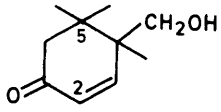

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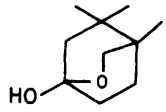

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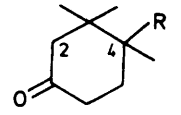
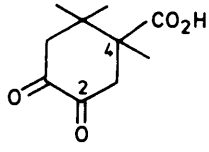


(22) R = CH_2OH
(23) R = CO_2H



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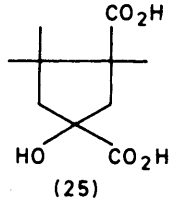

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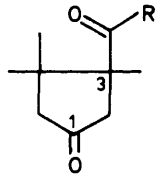
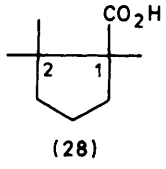


(26) R = OH
(27) R = OMe



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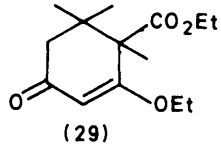

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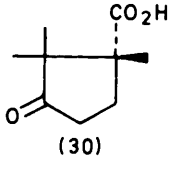


(30)

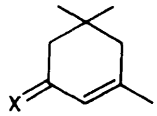
explained the results of Faigle and Karrer [9] with the hydroxy-camphonanic acid from capsorubin and capsanthin, and is in agreement with the later results of the Swiss authors.[19]

The *cis*- and *trans*-hydroxy-acids were separately treated with methyl-lithium to give the corresponding *cis*- (13) and *trans*- (17) hydroxy-ketones. These were condensed with crocetindial (8) [20] in the presence of potassium hydroxide to give the 'all-*trans*' carotenoids (4) and (1) respectively as mixtures of DL- and *meso*-isomers. That from the *cis*-hydroxy-ketone (13) had n.m.r. and chromatographic properties which were clearly different from those of capsorubin. That from the *trans*-hydroxy-ketone (17) had the same light absorption and n.m.r. properties as natural capsorubin, and did not separate from it on thin-layer chromatography. The end groups in the natural carotenoid must therefore have the *trans*-configuration (a). A similar condensation of the *trans*-hydroxy-ketone with β-apo-8′-carotenal (7) [21] gave (±)-cryptocapsin (3) with n.m.r. and chromatographic properties in good agreement with those of natural cryptocapsin.[6]

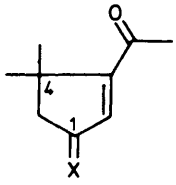
Alternative routes to the key intermediates (26) and (15) were examined. Methylation of (35) and its derivatives, readily obtained from isophorone (31), did not give significant amounts of the desired products. The known hydroxy-acid (37) [22,23] was converted into the chloromethyl ketone (38). Treatment with sodium methoxide (Favorskii rearrangement) gave the hydroxy-esters (12) and (16), mainly the former, in a combined overall yield of *ca.* 20%. A similar rearrangement of the chloromethyl ketone (40) from (39) [24,25] gave (27) in <10% overall yield.

*Optically Active Series.**—During studies on the mould

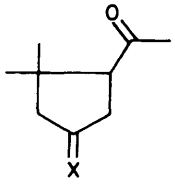
* In this section, unless otherwise indicated, formula numbers signify the unique stereoisomer shown by the formula.



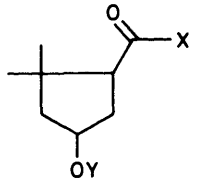
(31) X = O
(32) X = NH_2CONHN



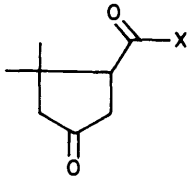
(33) X = O
(34) X = NH_2CONHN



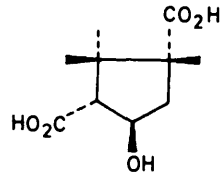
(35) X = O
(36) X = NH_2CONHN



(37) X = OH, Y = H
(38) X = CH_2Cl, Y = Ac



(39) X = OH
(40) X = CH_2Cl



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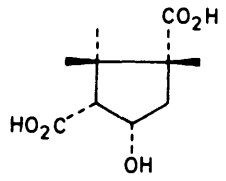

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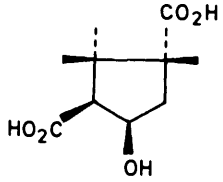

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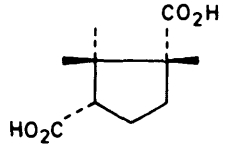

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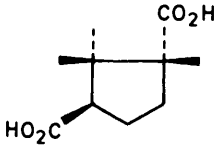

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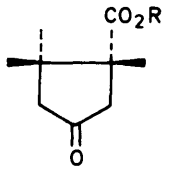


(46) R = H
(47) R = Me

metabolite lagopodine A, Marquet *et al.*[26] prepared the 3*R*-isomer (46) of the keto-acid (26) by a lengthy series of reactions starting with (+)-camphor (10). This involved a carefully controlled oxidation of the dimethyl ester of the hydroxycamphoric acid (41), and decarboxylation of the β-keto-acid obtained on hydrolysis of the initial product. Since the overall yield from (+)-camphor was only *ca.* 0.03%, the route was not judged suitable for the synthesis of capsorubin. Attention was therefore directed to the stereoisomeric hydroxycamphoric (42) and hydroxyisocamphoric (43) acids * which Bredt prepared from bromocamphoric and bromoisocamphoric acids * in his classical studies on camphor.[27] Bredt established the relative configuration of the carboxy groups in the two bromo-acids by reduction to camphoric (44) and isocamphoric (45) acid respectively. His further observation that the hydroxycamphoric acid yields a γ-lactone, allows the configuration (42) to be assigned to this acid, and the configuration (43) to the isomeric hydroxyisocamphoric acid. Using the technique developed by Marquet *et al.*[26] for (41), both (42) and (43) were converted into (46), giving a combined overall yield of *ca.* 0.4% from camphor. Reduction of (46) with potassium borohydride gave, as expected, both the γ-lactone (14) and the *trans*-hydroxy-acid (15). The latter was identical with a sample prepared by ozonolysis of capsanthin.[13] A superior route to this key intermediate (15) was subsequently developed.

Methyl ω-camphanate (48),[27,28] also prepared from (+)-camphor, was reduced with lithium aluminium hydride to give the triol (49). Fission of the α-glycol function with periodic acid gave the keto-alcohol (50), the structure of which was confirmed by chromic acid oxidation to camphononic acid (30). The keto-alcohol (50) was then submitted to the series of reactions developed in the steroid field to achieve ketone 1,2-transposition.[29,30]

* Different trivial names were used by Bredt but are less meaningful in the present context.

Condensation of the keto-alcohol with benzaldehyde gave the benzylidene derivative (51), which was reduced with sodium borohydride, and the resulting mixture of diols was acetylated. Ozonolysis of the diacetates gave the keto-diacetates (52) which were reduced with zinc and acetic acid to give the keto-acetate (54). Hydrolysis, and chromic acid oxidation of the resulting alcohol (53), gave the required 3*R*-keto-acid (46) in *ca.* 15% overall yield from camphor.

The keto-acid (46) was converted, as described previously, into the 1*S*,3*R* *trans*-hydroxy-acid (15) which, on treatment with methyl-lithium gave the corresponding hydroxy-ketone (17). The latter was condensed with crocetindial (8) [20] to give (3*S*,5*R*,3′*S*,5′*R*)-capsorubin (1) which was identical with a sample of the natural pigment. The c.d. curves of the natural and synthetic samples were in excellent agreement.[17] Subsequently an alternative synthesis of the keto-acid (46) from camphor has been described,[31] and a new route to the key-intermediate (17) outlined.[32,33]

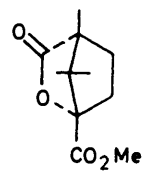
Experimental

Unless indicated to the contrary, the following general points apply.

All operations involving polyenes were carried out in an atmosphere of nitrogen, and polyene solutions were evaporated under reduced pressure. Light petroleum refers to the fraction, b.p. 60—80 °C.

Alumina for chromatography was graded according to Brockmann and Schodder.[34] Thin layer chromatograms (t.l.c.) were performed on Merck Kieselgel with the eluants indicated in parentheses, and gas liquid chromatograms (g.l.c.) on polyethylene glycol adipate supported on Celite.

N.m.r. spectra were determined on dilute solutions in deuteriochloroform using tetramethylsilane as an internal reference. The results are quoted as δ values; singlets are indicated by s, doublets by d, quartets by q, multiplets by m, and a broad signal by b. Coupling constants (*J*) are given in Hz, and the numbers of hydrogens, *e.g.* 3 H, refer to the relative numbers of protons represented by the band in question. Selected bands only are cited for i.r. light absorption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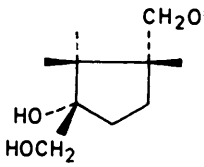
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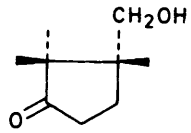
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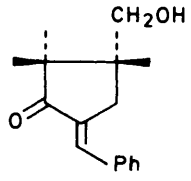
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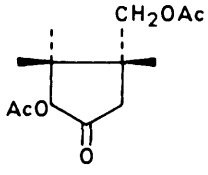
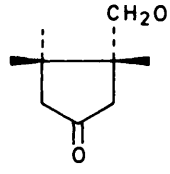
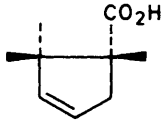

(52)


(53) R = H
(54) R = Ac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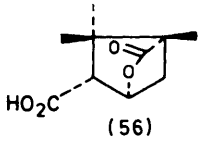
(56)

spectra, and for mass spectra; percentages refer to the intensity of the mass spectral line relative to the base peak.

Melting points are uncorrected.

Optically Inactive Series *

6-*Ethoxycarbonyl*-3-*ethoxy*-5,5,6-*trimethylcyclohex*-2-*en*-1-*one* (19).—A solution of 4-ethoxycarbonyl-4,5,5-trimethylcyclohexa-1,3-dione [18] (18) (190 g) and toluene-*p*-sulphonic acid (4.5 g) in ethanol (1.5 l) and benzene (900 ml) was heated under reflux under a Dean-Stark separator for 4 days. At intervals the condensate in the separator was run off, and the solvent in the reaction mixture was replenished. The mixture was cooled, evaporated under reduced pressure, diluted with light petroleum (b.p. 40—60 °C), washed with saturated sodium hydrogen carbonate, dried ($MgSO_4$), and evaporated. Distillation of the residue gave the *enol ether* (176 g) as a colourless oil, b.p. 118 °C/0.35 mmHg, n_D^{24} 1.4878; $\lambda_{max.}$ (EtOH) 256 nm (ε 5 700); $\nu_{max.}$ (liq. film) 1 721, 1 653, and 1 608 cm^{-1} (Found: C, 66.0; H, 8.8. $C_{14}H_{22}O_4$ requires C, 66.1; H, 8.7%).

4-*Hydroxymethyl*-4,5,5-*trimethylcyclohex*-2-*en*-1-*one* (20).—A solution of the above enol ether (10.0 g) in ether (50 ml) was added to lithium aluminium hydride (2.0 g) in ether (150 ml). The mixture was heated under reflux for 20 h, then cooled and treated with saturated ammonium chloride (15 ml).

Isolation of the crude product with ether gave an oil which was dissolved in methanol (100 ml) and 0.01N-sulphuric acid (1 ml) was added. The solution was stirred for 30 min, then poured into water, and the product isolated with ether. Chromatography (alumina, 1% EtOH in C_6H_6) gave the *cyclohexenone* (4.4 g) which crystallised from light petroleum (b.p. 40—60 °C) and had m.p. 151 °C; $\lambda_{max.}$ (EtOH) 230 nm (ε 7 800); $\nu_{max.}$ (CCl_4) 3 680, 1 672, and 1 600 cm^{-1} (Found: C, 71.2; H, 9.75. $C_{10}H_{16}O_2$ requires C, 71.4; H, 9.6%). The n.m.r. spectrum exhibited an AB quartet (δ 5.86 and 6.54, *J* 10.7) attributable to the two olefinic protons. The 2,4-*dinitrophenylhydrazone* had m.p. 178 °C; $\lambda_{max.}$ (EtOH) 373 nm (ε 26 000) (Found: C, 54.8; H, 5.7; N, 16.3. $C_{16}H_{20}N_4O_5$ requires C, 55.15; H, 5.8; N, 16.1%).

4-*Hydroxymethyl*-3,3,4-*trimethylcyclohexan*-1-*one* (22).—The preceding cyclohexenone (21.0 g) in ethanol (50 ml) was shaken in hydrogen in the presence of palladised charcoal (10% Pd, 3.0 g) until absorption was complete (1.1 mol). Removal of catalyst and solvent gave a crude product which upon evaporation under reduced pressure separated into a volatile oil (11 g) and a non-volatile solid (10 g). Crystallisation of the latter from light petroleum gave the *hydroxycyclohexanone*, m.p. 170 °C; $\nu_{max.}$ (CCl_4) 3 636 and 1 715 cm^{-1} (Found: C, 70.3; H, 10.7. $C_{10}H_{18}O_2$ requires C, 70.55; H, 10.65%). The 2,4-*dinitrophenylhydrazone* crystallised from methanol as yellow needles, m.p. 131 °C (Found: C, 54.6; H, 6.05; N, 16.05. $C_{16}H_{22}N_4O_5$ requires C, 54.85; H, 6.35; N, 16.0%).

The volatile oil, $\nu_{max.}$ (CCl_4) 3 448 cm^{-1} (no i.r. light absorption in the carbonyl region), was formulated as the cyclic ether (21). With Brady's reagent it gave the 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 131 °C, just described, in good yield. The oil (10 g) was dissolved in methanol (500 ml) and 0.1N-sulphuric acid (50 ml) was added. The solution was heated under reflux for 30 min, then cooled and poured into water. Isolation of the product with ether gave the hydroxycyclohexanone (9.0 g), m.p. and mixed m.p. with the sample described above, 170 °C (total yield from the cyclohexenone, 90%).

4-*Carboxy*-3,3,4-*trimethylcyclohexan*-1-*one* (23).—A solution of chromic acid, prepared by dissolving chromium trioxide (25 g) in 2N-sulphuric acid (70 ml) was added slowly to one of the preceding hydroxycyclohexanone (12.0 g) in acetone (150 ml). The mixture was stirred at 20 °C for 2 h, and then poured into water. Extraction with ether, isolation of the acidic product (extraction with $NaHCO_3$), and from this of the ketonic material (bisulphite complex), and crystallisation from a mixture of ethyl acetate and light petroleum, gave the *keto-acid* (4.5 g) as prisms, m.p. 188 °C; $\nu_{max.}$ ($CHCl_3$) 1 706 cm^{-1} (Found: C, 65.2; H, 9.0. $C_{10}H_{16}O_3$ requires C, 65.2; H, 8.75%). It did not decarboxylate when heated to 210 °C, thus excluding the alternative β-keto-acid structure. The 2,4-*dinitrophenylhydrazone* crystallised from methanol as yellow plates, m.p. 193 °C; $\lambda_{max.}$ (EtOH) 355 nm (ε 17 500) (Found: C, 52.35; H, 5.85; N, 15.15. $C_{16}H_{20}N_4O_6$ requires C, 52.75; H, 5.55; N, 15.4%).

Starting from the enol ether (19) (400 g), and treating the whole of the crude product from the catalytic reduction stage with dilute sulphuric acid, gave the keto-acid (45 g) in 16% overall yield.

4-*Carboxy*-4,5,5-*trimethylcyclohexane*-1,2-*dione* (24).—A solution of the preceding keto-acid (4.4 g) in N-potassium t-butoxide in t-butyl alcohol (200 ml) was shaken in oxygen until absorption was complete (1.05 mol). The solution was poured into water and the mixture acidified with 10% hydrochloric acid. Isolation of the product (4.5 g) with chloroform, and crystallisation from aqueous alcohol, gave the 1,2-*dione*

* See footnote ‡, p. 1465.

(4.0 g), m.p. 136—137 °C which existed largely in the diosphenol form; $\nu_{max.}$ ($CHCl_3$) 1 695 and 1 672 cm^{-1}; $\lambda_{max.}$ (EtOH) 268 nm, (ε 6 500); $\lambda_{max.}$ (aq.KOH) 312 nm (ε 5 200) (Found: C, 60.65; H, 7.05. $C_{10}H_{14}O_4$ requires C, 60.6; H, 7.1%). Reaction with *o*-phenylenediamine gave the *phenazine* derivative which crystallised from aqueous alcohol as yellow rhombs, m.p. 210 °C; $\nu_{max.}$ ($CHCl_3$) 1 706 cm^{-1} (Found: C, 71.05, H, 6.8; N, 10.25. $C_{16}H_{18}N_2O_2$ requires C, 71.1; H, 6.7; N, 10.35%).

3-*Carboxy*-3,4,4-*trimethylcyclopentan*-1-*one* (26).—A solution of the preceding 1,2-dione (4.2 g) in 5% aqueous potassium hydroxide (100 ml) was boiled under reflux until it no longer exhibited light absorption at 312 nm (20 h). The solution was then cooled, and neutralised with 0.1N-hydrochloric acid. Orthophosphoric acid (H_3PO_4) (9.0 g) was added, and then sodium bismuthate (9.0 g). After the mixture had been stirred overnight, the product was isolated by thorough extraction with ether to give the *keto-acid* (3.5 g) which crystallised from ethyl acetate–light petroleum as rhombs, m.p. (sealed tube) 224 °C [depressed to 207 °C on admixture with an authentic sample of the isomeric camphononic acid (30), m.p. 226 °C]; $\nu_{max.}$ ($CHCl_3$) 1 736 and 1 701 cm^{-1} (Found: C, 63.35; H, 8.4. $C_9H_{14}O_3$ requires C, 63.5; H, 8.3%). The 2,4-*dinitrophenylhydrazone* crystallised from methanol as yellow needles, m.p. 223 °C (Found: C, 52.0; H, 5.3. $C_{15}H_{18}N_4O_6$ requires C, 51.4; H, 5.2%).

Treatment of the keto-acid with diazomethane gave the corresponding methyl ester (27) which readily separated from methyl campononate on mixed g.l.c.

1-*Carboxy*-1,2,2-*trimethylcyclopentane* (28).—A solution of the preceding keto-acid (350 mg), sodium hydroxide (300 mg), and hydrazine hydrate (100%, 0.4 ml) in diethylene glycol (5 ml) was heated under reflux for 1 h, and then at 200 °C for 3 h. Isolation of the product in the usual way gave the (±)-acid which crystallised from aqueous ethanol as rhombs, m.p. 195—196 °C (lit.,[35] m.p. 193—194 °C); $\nu_{max.}$ ($CHCl_3$) 1 700 cm^{-1}. Its methyl ester did not separate from an authentic sample of methyl (+)-camphanate on mixed g.l.c.

cis- *and* trans-3-*Carboxy*-3,4,4-*trimethylcyclopentan*-1-*ol* (11) *and* (15).—(*a*) Potassium borohydride (400 mg) was added slowly to a warm solution of sodium hydroxide (350 mg) and the keto-acid (26) (900 mg) in water (13 ml). The resulting mixture was heated at 100 °C for 16 h, and then cooled. Sulphuric acid (1.5 ml) in water (7 ml) was added, and the mixture was heated for 1 h, then cooled and extracted thoroughly with ether. The ethereal extracts were washed with saturated sodium hydrogen carbonate. The alkaline extracts were acidified with 2N-hydrochloric acid to give the trans-*hydroxy-acid* (100 mg) which crystallised from ethyl acetate–light petroleum as prisms, m.p. 221.5 °C; $\nu_{max.}$ ($CHCl_3$) 1 698 cm^{-1} (Found: C, 63.0; H, 9.55. $C_9H_{16}O_3$ requires C, 62.75; H, 9.4%). The *trans*-hydroxy-acid sublimed unchanged at 100 °C/10^{-3} mmHg, but when sublimed at 230 °C/760 mmHg the product consisted of the γ-lactone (14) of the *cis*-hydroxy-acid.

The neutral ether solution from which the *trans*-hydroxy-acid had been extracted was evaporated to give a *lactone* (14) (450 mg) which sublimed at 100 °C/0.1 mmHg, and had m.p. 181 °C; $\nu_{max.}$ ($CHCl_3$) 1 760 cm^{-1} (Found: C, 69.8; H, 9.25. $C_9H_{14}O_2$ requires C, 70.1; H, 9.15%).

The lactone (1.0 g) was dissolved in warm 10% aqueous sodium hydroxide (20 ml). The solution was cooled and then acidified to pH 4 with 0.1N-hydrochloric acid. Isolation of the product with ether gave the cis-*hydroxy-acid* (0.9 g) which crystallised from ethyl acetate–light petroleum as needles, m.p. 201 °C; $\nu_{max.}$ ($CHCl_3$) 1 698 cm^{-1} (Found: C, 62.5; H, 9.35. $C_9H_{16}O_2$ requires C, 62.75; H, 9.4%). Sublimation of the *cis*-hydroxy-acid at 100 °C/0.2 mmHg gave the γ-lactone, m.p. and mixed m.p. 181 °C.

Treatment of the two hydroxy-acids with diazomethane gave the corresponding methyl esters (12) and (16) which separated readily on mixed g.l.c.; the C–Me bands of the *cis*-hydroxy-ester ($CHCl_3$, 60 MHz) were found at δ 0.96 (s, 6 H) and 1.12 (s, 3 H), whereas those for the *trans*-isomer occurred at δ 0.86 (s, 3 H), 1.14 (s, 3 H), and 1.28 (s, 3 H).

(*b*) A solution of 3-carboxy-4,4-dimethylcyclopentan-1-ol [22,23] (37) (720 mg, m.p. 113 °C) and acetic anhydride (2 ml) in pyridine (4 ml) was kept at 20 °C for 2 days. The mixture was poured into water and the product isolated with ether. A mixture of the resulting acetate and oxalyl chloride (3 ml) was kept at 20 °C for 2 h, and the excess of reagent was then removed under reduced pressure. The residual oil, in ether (5 ml), was treated with an excess of diazomethane, and hydrogen chloride was then bubbled through the solution until the latter was no longer yellow. The solution was then washed with water, dried, and evaporated to give the chloromethyl ketone (38) as a pale yellow lachrymatory oil (450 mg).

The ketone was added to sodium methoxide (from 0.3 g of Na) in methanol (10 ml). After 2.5 h, the mixture was poured into water and the product isolated with ether. The resulting oil was shown by g.l.c., and mixed g.l.c. with authentic samples, to contain *cis*- (40%) and *trans*- (20%) 3-methoxycarbonyl-3,4,4-trimethylcyclopentan-1-ol, (12) and (16) respectively. The *cis*-hydroxy-ester was isolated by g.l.c. (100 °C) and hydrolysed with 2N-sodium hydroxide to give the *cis*-hydroxy-acid (11), m.p. and mixed m.p. with a sample from (*a*), 201 °C. Chromic acid oxidation of the mixture of *cis*- and *trans*-hydroxy-esters, and hydrolysis of the product, gave 3-carboxy-3,4,4-trimethylcyclopentan-1-one (26), m.p. 224 °C, undepressed on admixture with the sample described previously, in an overall yield from (37) of *ca.* 20%. A similar series of reactions starting with 3-carboxy-4,4-dimethylcyclopentan-1-one [24,25] (39) also gave the same trimethyl keto-ester (27) but in only 8% overall yield.

trans-3-*Acetyl*-3,4,4-*trimethylcyclopentan*-1-*ol* (17).—A solution of the preceding *trans*-hydroxy-acid (2.0 g) in ether (20 ml) was added to one of methyl-lithium (from 15 g methyl iodide) in ether. The solution was boiled under reflux for 24 h and then cooled. Water was added cautiously, and the product isolated with ether to give the trans-*hydroxy-ketone* (1.4 g), as a colourless oil, b.p. 87—90 °C/0.8 mmHg; $\nu_{max.}$ ($CHCl_3$) 3 650 and 1 695 cm^{-1} (Found: C, 70.4; H, 10.5. $C_{10}H_{18}O_2$ requires C, 70.55; H, 10.65%). The 2,4-dinitrophenylhydrazone crystallised from ethyl acetate–light petroleum as plates, m.p. 129 °C.

cis-3-*Acetyl*-3,4,4-*trimethylcyclopentan*-1-*ol* (13).—Reaction of methyl-lithium with the *cis*-hydroxy-acid (0.8 g), as described for the *trans*-isomer, gave the cis-*hydroxy-ketone* (0.6 g), b.p. 65—70 °C/1 mmHg; $\nu_{max.}$ ($CHCl_3$) 3 450 and 1 695 cm^{-1} (Found: C, 70.45; H, 10.4. $C_{10}H_{18}O_2$ requires C, 70.55; H, 10.65%). The 2,4-dinitrophenylhydrazone crystallised from methanol as needles, m.p. 123 °C.

The 3,3′-*Dihydroxy*-κ,κ-*carotene*-6,6′-*diones* ('*Optically Inactive Capsorubins*') (1).—(*a*) A solution of the *trans*-hydroxy-ketone (17) (1.4 g), crocetindial [20] (140 mg), and potassium hydroxide (400 mg) in ethanol (8 ml) was warmed for 5 min, and then kept in the dark for 24 h. Benzene was added and the benzene solution was washed with water and then evaporated. Chromatography of the residue (grade IV

alumina, 1% ethanol in benzene) collection of the main band, and crystallisation from a mixture of benzene and light petroleum, gave the mixture of DL- and *meso*-isomers of the all-*trans* carotenoid with *trans* hydroxy-keto end groups (70 mg), m.p. (evac. cap.) 144—145 °C; $\lambda_{max.}$ (C_6H_6) 519 (ε 101 000), 486 (ε 120 000) and (inflexion) 455 nm; $\nu_{max.}$ ($CHCl_3$) 3 650, 1 664, 1 582, 1 542, 1 006, 980, and 970 cm^{-1}; δ (60 MHz) 0.85 (s, 6 H), 1.20 (s, 6 H), 1.38 (s, 6 H), and 1.98 (s, 12 H) (Found: C, 79.6; H, 9.3; O, 10.55. $C_{40}H_{56}O_4$ requires C, 79.95; H, 9.4; O, 10.65%). No separation of the DL- and *meso*-forms was observed on t.l.c. (1 : 1 acetone and light petroleum), and there was no separation on mixed t.l.c. from an authentic sample of natural capsorubin, m.p. 201 °C, which had the same light absorption (visible and i.r.) and n.m.r. properties as the synthetic product.

(*b*) A similar condensation of crocetindial [20] (75 mg) with the *cis*-hydroxy-ketone (13) (0.7 g) gave the all-*trans* carotenoid (4) with two *cis*-hydroxy-keto end groups (11 mg); $\lambda_{max.}$ (C_6H_6) 522 (ε 100 000), 488 (ε 121 000) and (inflexion) 457 nm; $\nu_{max.}$ ($CHCl_3$) 3 600, 3 460, 1 650, 1 582, 1 541, 1 006, 980, and 970 cm^{-1}; δ (60 MHz) 0.97 (s, 12 H), 1.15 (s, 6 H), and 2.00 (s, 12 H) (Found: C, 79.65; H, 9.2; O, 10.55. $C_{40}H_{56}O_4$ requires C, 79.95; H, 9.4; O, 10.65%). No separation of the DL- and *meso*-forms was observed on t.l.c., but the sample was more readily eluted than either the product from (*a*) or natural capsorubin under the conditions described above.

3′-*Hydroxy*-β,κ-*caroten*-6′-*one* ('*Optically Inactive Cryptocapsin*') (3).—A solution of the *trans*-hydroxy-ketone (17) (1.0 g), β-apo-8′-carotenal [21] (7) (400 mg), and potassium hydroxide (500 mg) in ethanol (10 ml) was warmed for 5 min and then kept at 20 °C in the dark for 36 h. Isolation of the product in the manner described for the crocetindial condensation, and crystallisation from benzene–light petroleum, gave the (±)-all-*trans* carotenoid with the *trans*-hydroxy-keto end group (60 mg), m.p. (evac. cap.) 131—132 °C; $\lambda_{max.}$ (C_6H_6) 520 and 486 nm (ε 93 700 and 115 000 respectively); $\nu_{max.}$ ($CHCl_3$) 3 650, 1 660, 1 585, 1 006, 985, and 970 cm^{-1}; δ (60 MHz) 0.85 (s, 3 H), 1.03 (s, 6 H), 1.20 (s, 3 H), 1.37 (s, 3 H), 1.72 (s, 3 H), and 1.98 (s, 12 H) (Found: C, 83.95; H, 9.45; O, 5.5. $C_{40}H_{56}O_2$ requires C, 84.45; H, 9.9; O, 5.65%). There was no separation on mixed t.l.c. from an authentic sample of natural cryptocapsin, m.p. 160—161 °C, which had light absorption (visible and i.r.) and n.m.r. properties in good agreement with those of the synthetic product.

3-*Acetyl*-4,4-*dimethylcyclopent*-2-*en*-1-*one* (33).—Ozonised oxygen (*ca.* 3% O_3) was bubbled through a solution of isophorone semicarbazone (32) (15.0 g) until reaction was complete. Sodium iodide (18.0 g) and acetic acid (15.0 g) were added, and the solution was decolourised by addition of saturated sodium thiosulphate. The mixture was poured into water and the product isolated with dichloromethane. Crystallisation from ethanol gave 1-*formyl*-4,4-*dimethyl*-2-*semicarbazonoheptan*-6-*one* (7.7 g), m.p. 115—116 °C; $\lambda_{max.}$ (EtOH) 273 nm (ε 18 000); $\nu_{max.}$ (Nujol) 3 380, 3 300, 3 200, 1 710, 1 690, and 1 590 cm^{-1}; δ (CF_3CO_2H; 60 Mz) 1.12 (s, 6 H), 2.62 (s, 3 H), 2.79 (s, 2 H), and 9.55 (s, 1 H) (Found: C, 52.7; H, 7.3; N, 18.3. $C_{10}H_{17}N_3O_3$ requires C, 52.85; H, 7.55; N, 18.5%).

2N-Sodium hydroxide (10 ml) was added to a solution of the keto-aldehyde (4.2 g) in methanol (25 ml). The mixture was kept overnight and then poured into water. Isolation of the product with ether, and crystallisation from methanol, gave the diketone *mono-semicarbazone* (34) (2.5 g), m.p. 216—217 °C; $\lambda_{max.}$ (MeOH) 309 nm (ε 29 000); $\nu_{max.}$ (Nujol) 3 400, 3 250, 3 180, 1 690, 1 650, and 1 580 cm^{-1}; δ (60 MHz) 1.33 (s, 6 H), 2.35 (s, 3 H), 2.44 (s, 2 H), 5.7 (b, 2 H), 6.78 (s, 1 H), and 8.62 (b 1 H) (Found: C, 57.5; H, 7.3; N, 20.3. $C_{10}H_{15}N_3O_2$ requires C, 57.4; H, 7.25; N, 20.1%).

A suspension of the mono-semicarbazone (4.0 g) in 2N-hydrochloric acid (400 ml) was boiled under reflux overnight and then cooled. Isolation of the product with ether and crystallisation from hexane, gave the *diketone* (1.2 g) as plates, m.p. 60—61 °C; $\lambda_{max.}$ (MeOH) 243 nm (ε 14 500); $\nu_{max.}$ (Nujol) 1 720, 1 690, 1 600, and 1 210 cm^{-1}; δ (60 MHz) 1.40 (s, 6 H), 2.41 (s, 2 H), 2.48 (s, 3 H), and 6.54 (s, 1 H) (Found: C, 70.75; H, 7.95. $C_9H_{12}O_2$ requires C, 71.0; H, 7.95%). The *bis-semicarbazone* had m.p. 262—263 °C; $\lambda_{max.}$ (MeOH) 314 nm (ε 30 000) (Found: C, 49.5; H, 6.8. $C_{11}H_{18}N_6O_2$ requires C, 49.6; H, 6.8%).

3-*Acetyl*-4,4-*dimethylcyclopentan*-1-*one* (35).—A mixture of zinc dust (20 g) and a solution of the mono-semicarbazone (34) (20.0 g) in acetic acid (150 ml) was heated under reflux for 2 min and then cooled rapidly. Filtration, addition of an excess of 50% sodium hydroxide, isolation of the product with chloroform, and crystallisation from 5% methanol in benzene, gave the *saturated mono-semicarbazone* (36) (14.0 g), m.p. 194 °C; $\lambda_{max.}$ (MeOH) 223 nm (ε 16 500); $\nu_{max.}$ (Nujol) 3 450, 3 320, 3 180, 1 705, 1 690, 1 660, and 1 570 cm^{-1}; δ (60 MHz) 0.94 (s, 3 H), 1.28 (s, 3 H), 2.20 (s, 3 H), 2.33 (s, 2 H), 5.6 (b, 2 H), and 8.3 (b, 1 H) (Found: C, 57.0; H, 8.1; N, 20.0. $C_{10}H_{17}N_3O_2$ requires C, 56.85; H, 8.1; N, 19.9%).

Sodium nitrite (15.0 g) in water (50 ml) was added slowly to a well stirred, cold (0 °C) solution of the saturated mono-semicarbazone (9.1 g) in acetic acid (75 ml). The mixture was stirred at 0 °C for 4 h, and then overnight at 20 °C. Addition of water, and isolation of the product with ether, gave the *saturated diketone* (5.6 g), b.p. 62—64 °C/0.06 mmHg; n_D^{15} 1.4688; $\nu_{max.}$ (film) 1 740, 1 710, and 1 205 cm^{-1}; δ (60 MHz) 1.00 (s, 3 H), 1.33 (s, 3 H), 2.06 (s, 2 H), 2.20 (s, 3 H), 2.40 (m, 2 H), and 3.10 (bq, 1 H) (Found: C, 69.95; H, 9.3. $C_9H_{14}O_2$ requires C, 70.1; H, 9.15%). The *bis-semicarbazone* had m.p. 249 °C (decomp.); $\lambda_{max.}$ (MeOH) 229 nm (ε 30 000) (Found: C, 49.0; H, 7.8. $C_{11}H_{20}N_6O_2$ requires C, 49.2; H, 7.5%).

The mono-semicarbazone (36) was converted quantitatively into a *benzylidene derivative* which crystallised from methanol and had m.p. 199—200 °C; $\lambda_{max.}$ (MeOH) 295, 229, and (inflexion) 223 nm (ε 23 000, 20 000, and 18 500 respectively) (Found: C, 68.2; H, 7.1; N, 13.9. $C_{17}H_{21}N_3O_2$ requires C, 68.2; H, 7.05; N, 14.05%). Treatment with nitrous acid in acetic acid, and ozonolysis of the product in chloroform, gave 3-carboxy-4,4-dimethylcyclopentan-1-one (39) which was isolated as the methyl ester, m.p., and mixed m.p. with an authentic specimen, 38 °C (lit.,[25] m.p. 39 °C).

Optically Active Series *

(+)-*Camphoric Acid* (44).—This starting material was obtained commercially, or by oxidation of (+)-camphor with nitric acid in the presence of mercuric acetate. It had m.p. 185 °C (lit.,[36] m.p. 187 °C); $\nu_{max.}$ (Nujol) 1 690 cm^{-1}; δ [$(CD_3)_2CO$] 0.89 (s, 3 H), 1.25 (s, 3 H), 1.32 (s, 3 H), 1.4—2.7 (m, 4 H), 2.88 (dd, J_1 10, J_2 8, 3 H), and 8.5 (b, 2 H).

Hydroxycamphoric (42) *and Hydroxyisocamphoric Acid* (43).—Camphoric acid (44) was converted into dehydrocamphoric acid (55) by the method of Bredt.[27] Reaction with hydrobromic acid in the presence of lithium bromide at 100 °C, and fractional crystallisation of the product (40%), gave (i) bromocamphoric acid, m.p. 158 °C (lit.,[27] m.p. 158—160 °C); $\nu_{max.}$ (Nujol) 1 700 cm^{-1}; δ [$(CD_3)_2CO$; 60 MHz] 0.88 (s, 3 H), 1.34

* See footnote *, p. 1466.

(s, 3 H), 1.46 (s, 3 H), 1.8—2.2 (m, 2 H), 3.28 (d, *J* 8, 1 H), 4.7 (m, 1 H), and 2.20 (b, 2 H); (ii) bromoisocamphoric acid, m.p. 227 °C (lit.,[27] m.p. 232 °C); $\nu_{max.}$ (Nujol) 1 695 cm^{-1}; δ [$(CD_3)_2CO$; 60 MHz] 0.97 (s, 3 H), 1.20 (s, 6 H), 3.38 (d, *J* 8, 1 H), 4.69 (q, *J* 8, 1 H), and 9.43 (bs, 2 H).

Treatment of the low melting bromocamphoric acid with hot aqueous sodium carbonate gave the γ-lactone (56) (85%), m.p. 231—232 °C (lit.,[27] m.p. 228 °C); $\nu_{max.}$ (ether) 1 780 cm^{-1}; δ [$(CD_3)_2CO$; 60 MHz] 1.00 (s, 3 H), 1.15 (s, 3 H), 1.25 (s, 3 H), 1.9—2.2 (m, 2 H), 2.96 (d, *J* 1.5, 1 H), 4.98 (bs, 1 H), and 5.4 (b, 1 H). The γ-lactone (1.8 g) and 2N-sodium hydroxide (25 ml) were heated under reflux for 1 h. The mixture was cooled (0 °C), acidified with 2N-sulphuric acid, and the product isolated with ether to give the *hydroxycamphoric acid* (42) (1.65 g) which crystallised from a mixture of ethyl acetate and light petroleum, and had m.p. 154—155 °C; $\nu_{max.}$ (Nujol) 3 450 and 1 695 cm^{-1}; δ [$(CD_3)_2CO$; 60 MHz] 1.15 (s, 3 H), 1.22 (s, 3 H), 1.29 (s, 3 H), 2.89 (d, *J* 7, 1 H), 4.55 (m, 1 H), and 7.2 (b, 2 H) (Found: C, 55.6; H, 7.7; O, 36.8. $C_{10}H_{16}O_5$ requires C, 55.55; H, 7.45; O, 37.0%).

Treatment of the high melting bromoisocamphoric acid with hot aqueous sodium carbonate, and isolation of the product in the usual way gave the hydroxyisocamphoric acid (43) (55%) which crystallised from a mixture of ethyl acetate and light petroleum, and had m.p. 179—180 °C (lit.,[27] m.p. 194 °C); $\nu_{max.}$ (Nujol) 1 672 cm^{-1} (Found: C, 55.7; H, 7.45. Calc. for $C_{10}H_{16}O_5$: C, 55.55; H, 7.45%).

(3R)-3-*Methoxycarbonyl*-3,4,4-*trimethylcyclopentan*-1-*one* (47).—(*a*) A slight excess of diazomethane in ether was added to a solution of the hydroxycamphoric acid (42) (4.8 g) in ether (5 ml). When the reaction was complete, the solution was washed with water, dried ($MgSO_4$), and evaporated. The resulting diester was dissolved in ether (100 ml), and a solution of potassium dichromate (9.02 g) and concentrated sulphuric acid (7 ml) in water (37 ml) was added dropwise with stirring during 1.5 h. The mixture was stirred for a further 2.5 h and the ethereal layer was then separated, washed with water, dried, and evaporated. To the residual oil was added a solution of acetic acid (57 ml) and hydrochloric acid (36 ml) in water (7 ml). The mixture was then boiled under reflux for 7 h, cooled, and poured into water. Isolation of the product with ether, and preparative g.l.c. (125 °C), gave the ester (300 mg, 8%), m.p. 33—34 °C; $\nu_{max.}$ (CCl_4) 1 745 and 1 735 cm^{-1}; δ [$(CD_3)_2CO$; 60 MHz] 1.00 (s, 3 H), 1.17 (s, 3 H), 1.28 (s, 3 H), 2.18 (d, *J* 19, 1 H), 2.21 (s, 2 H), 2.80 (d, *J* 19, 1 H), and 3.68 (s, 3 H). The n.m.r. and i.r. data were in good agreement with those reported by Marquet *et al.*[26] On mixed g.l.c. the ester did not separate from a sample of its enantiomer (kindly provided by Professor D. Arigoni) or from one of the racemate (see above).

(*b*) Similar treatment of the hydroxyisocamphoric acid (43) (4.6 g) gave the required keto-ester (360 mg, 14%), m.p. 33—34 °C, undepressed on admixture with a sample from (*a*).

Methyl ω-*Camphanate* (48).—Reaction of camphoric acid with phosphorus pentachloride gave α-chlorocamphoric acid dichloride (83%), b.p. 140—150 °C/14 mmHg (lit.,[27] b.p. 148—149 °C/12 mmHg); $\nu_{max.}$ (film) 1 785 cm^{-1}; δ 1.25 (s, 3 H), 1.61 (s, 3 H), 1.66 (s, 3 H), and 1.8—3.0 (m, 4 H). A solution of the latter in dimethylformamide when added to ice and water yielded α-chlorocamphoric anhydride (85%), m.p. 236 °C (lit.[37] m.p. 233—235 °C); $\nu_{max.}$ (Nujol) 1 817 and 1 768 cm^{-1}; δ 1.07 (s, 3 H), 1.14 (s, 3 H), 1.35 (s, 3 H), and 1.9—2.7 (m, 4 H). Treatment of the anhydride with boiling 0.1N-sulphuric acid led to ω-camphanic acid (87%), m.p. 201—202 °C (lit.,[38] m.p. 199 °C); $\nu_{max.}$ (Nujol) 1 765 and 1 740 cm^{-1}; $\nu_{max.}$ ($CHCl_3$) 1 780 and 1 720 cm^{-1}; δ 1.03 (s, 3 H), 1.11 (s, 3 H), 1.14 (s, 3 H), 1.4—2.7 (m, 4 H), and 10.17 (s, 1 H); *m/z* 198 ($M^{+\cdot}$; $C_{10}H_{14}O_4$ requires *m/z* 198). Esterification with methanol in the presence of sulphuric acid produced methanol ω-camphanate (91%), m.p. 107—108 °C (lit.,[27] m.p. 109 °C); $\nu_{max.}$ (Nujol) 1 782 and 1 728 cm^{-1}; δ 0.96 (s, 3 H), 1.06 (s, 3 H), 1.12 (s, 3 H), 1.6—2.7 (m, 4 H), and 3.84 (s, 3 H).

1,3-*Bishydroxymethyl*-2,2,3-*trimethylcyclopentan*-1-*ol* (49).—Lithium aluminium hydride (6.0 g) was added slowly to methyl ω-camphanate (25.0 g) in ether (500 ml). The solution was boiled under reflux for 18 h and then cooled (0 °C). The complex was decomposed by the addition of an excess of a saturated aqueous solution of sodium potassium tartrate. Isolation of the product (continuous ether extraction) gave a waxy solid (20.0 g, 90%). Recrystallisation of a small portion from a mixture of ether and light petroleum gave the *triol* as prisms, m.p. 164.5 °C; $\nu_{max.}$ (Nujol) 3 170 cm^{-1}; δ 0.82 (s, 3 H), 0.87 (s, 3 H), 0.98 (s, 3 H), 1.4—2.2 (m, 4 H), 3.21 (d, *J* 11, 1 H), 3.60 (bs, 2 H), 3.61 (d, *J* 11, 1 H) and 5.27 (b, 3 H); *m/z* 188.141 ($M^{+\cdot}$, $C_{10}H_{20}O_3$ requires *m/z* 188.141, 3%), 170 (M − 18, 10%), 157 (M − 31, 20%), 109 (M − 79, 100%).

3-*Hydroxymethyl*-2,2,3-*trimethylcyclopentan*-1-*one* (50).—The preceding triol (20.0 g) in water (250 ml) was added to periodic acid (32.5 g) in water (125 ml) and the mixture was kept at 20 °C for 1 h. Isolation of the product with ether gave a waxy solid (14 g, 85%), m.p. 193—196 °C. Recrystallisation of a sample from a mixture of ether and light petroleum gave the *keto-alcohol* as needles, m.p. 197—198 °C; $\nu_{max.}$ (Nujol) 3 435 and 1 732 cm^{-1}; δ 0.97 (s, 9 H), 1.7—2.5 (m, 4 H), 2.1 (bs, 1 H), and 3.49 (s, 2 H); δ (C_6D_6) 0.66 (s, 3 H), 0.81 (s, 3 H), 0.87 (s, 3 H), 1.15 (s, 1 H), 1.25—2.30 (m, 4 H), and 3.13 (s, 2 H); *m/z* 156.115 ($M^{+\cdot}$, $C_9H_{16}O_2$ requires *m/z* 156.115, 20%), 141 (M − 15, 5%), 138 (M − 18, 2%), 125 (M − 31, 6%), 123 (M − 33, 3%), 96 (M − 60, 24%), 83 (M − 73, 100%) and 55 (M − 100, 23%) (Found: C, 68.95; H, 10.3. $C_9H_{16}O_2$ requires C, 69.2; H, 10.3%). The 2,4-*dinitrophenylhydrazone* crystallised from a mixture of benzene and light petroleum as orange needles, m.p. 161—162 °C; $\lambda_{max.}$ (EtOH) 365, 270 (shoulder) and 230 nm; δ 0.99 (s, 3 H), 1.17 (s, 6 H), 1.53 (s, 1 H), 1.5—2.8 (m, 4 H), 3.55 (s, 2 H), 7.31 (bs, 1 H), 7.95 (d, *J* 10.5, 1 H), and 8.31 (d, *J* 10.5, 1 H) (Found: C, 53.6; H, 6.2; N, 16.8. $C_{15}H_{20}N_4O_5$ requires C, 53.55; H, 6.0; N, 16.65%). The p-*tosylhydrazone* (70%) crystallised from ether–chloroform–light petroleum and had m.p. 114—115 °C; $\lambda_{max.}$ (EtOH) 231 nm; $\nu_{max.}$ (Nujol) 3 220 and 1 600 cm^{-1}; δ 0.83 (s, 3 H), 0.92 (s, 6 H), 1.57 (bs, 1 H), 1.3—2.3 (m, 4 H), 2.40 (s, 3 H), 3.25 (d, *J* 11, 1 H), 3.33 (d, *J* 11, 1 H), 7.26 (d, *J* 9, 2 H), 7.42 (bs, 1 H) and 7.81 (d, *J* 9, 2 H); *m/z* 324.150 ($M^{+\cdot}$, $C_{16}H_{24}NO_3S$ requires *m/z* 324.150).

Oxidation of the keto-alcohol with chromic acid, as described below for the isomer (53), gave the known keto-acid (camphononic acid) (30) (95%) as colourless prisms, m.p. and mixed m.p. 226 °C (lit.,[39] m.p. 228 °C); $\nu_{max.}$ (Nujol) 1 730 and 1 710 cm^{-1}; δ 1.02 (s, 3 H), 1.07 (s, 3 H), 1.25 (s, 3 H), 1.7—2.7 (m, 4 H) and 10.04 (b, 1 H); δ [$(CD_3)_2CO$] 0.96 (s, 3 H), 1.01 (s, 3 H), 1.23 (s, 3 H), 1.2—2.5 (m, 4 H), and 7.8 (b, 1 H); *m/z* 170 ($M^{+\cdot}$, $C_9H_{14}O_3$ requires *m/z* 170, 75%), 142 (M − 28, 58%) and 83 (M − 87, 100%). The *benzylidene derivative* (55% yield) crystallised from aqueous ethanol as yellow plates, m.p. 155—157 °C; $\lambda_{max.}$ (EtOH) 296 nm (ε 21 700); $\nu_{max.}$ ($CHCl_3$) 1 712 and 1 631 cm^{-1} (Found: C, 74.15; H, 6.95. $C_{16}H_{18}O_3$ requires C, 74.4; H, 7.0%).

5-*Benzylidene*-3-*hydroxymethyl*-2,2,3-*trimethylcyclopentan*-1-*one* (51).—The preceding keto-alcohol (18.5 g) and benzaldehyde (18.5 ml) were dissolved in a solution of potassium hydroxide (7.5 g) in ethanol (515 ml) and water (5 ml). The

mixture was boiled under reflux for 30 min and then kept at 20 °C for 18 h. Dilution with water, extraction with ether, and crystallisation of the crude product from benzene–light petroleum gave the *benzylidene derivative* (23.6 g, 82%) as prisms, m.p. 152.5—153.5 °C; $\lambda_{max.}$ (EtOH) 297 nm (ε 22 500); $\nu_{max.}$ (Nujol) 3 413, 1 710, and 1 630 cm^{-1}; δ 1.02 (s, 3 H), 1.06 (s, 6 H), 1.47 (bs, 1 H), 2.61 (dd, J_1 17, J_2 3, 1 H), 3.01 (dd, J_1 17, J_2 3, 1 H), 3.50 (s, 2 H) and 7.40 (m, 6 H); *m/z* 244.146 ($M^{+\cdot}$, $C_{16}H_{20}O_2$ requires *m/z* 244.146, 65%), 229 (M − 15, 8%), 226 (M − 18, 6%), 214 (M − 30, 17%; *m** 187.7, $214^2/244$ = 187.7), 213 (M − 31, 17%), 211 (M − 18 − 15, 18%; *m** 196.9, $211^2/226$ = 197.0), 183 (M − 61, 17%), 116 (M − 128, 100%), 91 (M − 153, 28%), and 83 (M − 161, 55%) (Found: C, 78.6; H, 8.15. $C_{16}H_{20}O_2$ requires C, 78.65; H, 8.25%). The *trimethylsilyl ether* (78%) had b.p. 145—150 °C/0.1 mmHg; m.p. 38 °C; $\lambda_{max.}$ (EtOH) 295.5 nm (ε 24 000); $\nu_{max.}$ (film) 1 720 and 1 635 cm^{-1}; δ 0.03 (s, 9 H), 1.03 (s, 3 H), 1.06 (s, 3 H), 1.11 (s, 3 H), 2.64 (dd, J_1 17, J_2 3, 1 H), 2.93 (dd, J_1 17, J_2 3, 1 H), 3.44 (s, 2 H), and 7.3—7.7 (m, 6 H); *m/z* 316.185 ($M^{+\cdot}$, $C_{19}H_{28}O_2Si$ requires *m/z* 316.186, 17%), 301 (M − 15, 10%), 226 (M − 90, 100%), 213 (M − 103, 12%), 211 (M − 90 − 15, 42%; *m** 196.8, $211^2/226$ = 197.0), 198 (M − 118, 25%), and 183 (M − 118 − 15, 50%; *m** 169.1, $183^2/198$ = 169.1).

3-*Acetoxymethyl*-3,4,4-*trimethylcyclopentan*-1-*one* (54).—A solution of sodium borohydride (16.0 g) and sodium hydroxide (3.0 g) in water (30 ml) was added slowly to one of the benzylidene derivative (53) (20.0 g) in methanol (800 ml), and the mixture was stirred at 20 °C for 24 h. The bulk of the solvent was then evaporated under reduced pressure, the residue diluted with water, and the product isolated with ether giving a mixture of *diols* (19.0 g, 95%) as a glass; $\lambda_{max.}$ (EtOH) 258 nm (ε 18 000); $\nu_{max.}$ (film) 3 400, 2 990, 1 600, and 1 500 cm^{-1}; δ 0.78 (s), 0.91 (s), 0.97 (s), 100 (s) (total 9 H), 1.5—2.4 (bm, 2 H), 2.5—2.8 (m, 2 H), 3.5 (m, 2 H), 4.1—4.7 (m, 1 H), 6.6 (m, 1 H) and 7.30 (m, 5 H); *m/z* 246 ($M^{+\cdot}$, $C_{16}H_{22}O_2$ requires *m/z* 246).

Acetic anhydride (80 ml) was added slowly to the preceding diols in pyridine (80 ml) and the mixture was kept at 20 °C for 18 h. Water (200 ml) was then added slowly to the cooled mixture, and the product isolated with ether to give a mixture of *diacetates* (25.0 g, 98%) as a colourless oil; $\lambda_{max.}$ (EtOH) 258 nm (ε 16 000); $\nu_{max.}$ (film) 1 733, 1 603, and 1 502 cm^{-1}; δ 0.88 (s), 0.91 (s), 0.98 (s), 1.02 (s) (total 6 H), 1.08 (s, 3 H), 2.05 (s, 3 H), 2.15 (s, 3 H), 2.4—2.9 (m, 2 H), 3.97 (m, 0.9 H), 4.04 (s, 1.1 H), 5.65 (m, 1 H), 6.33 (m, 1 H), and 7.1—7.4 (m, 5 H); *m/z* 330 ($M^{+\cdot}$, $C_{20}H_{26}O_4$ requires *m/z* 330, 8%), 288 (M − 42, 44%), 270 (M − 60, 35%), 245 (M − 85, 6%), and 91 (100%).

Ozonised oxygen (*ca.* 3% O_3) was bubbled through a solution of the above diacetates (2.0 g) in methanol (30 ml) and ethyl acetate (12 ml) at −70 °C for 80 min. The solution was flushed with nitrogen, and then acetic acid (38 ml) was added. The mixture was warmed to 0 °C and zinc dust (6 g) was added gradually. The mixture was filtered and the filtrate diluted with water. Isolation of the crude product with ether, and chromatography on silica gel, furnished the *keto-diacetates* (52) (1.15 g, 75%) as a colourless oil; $\nu_{max.}$ (film) 1 756 and 1 740 cm^{-1}; δ 0.93 (s, 3 H), 1.10 (s, 3 H), 1.16 (s, 1.5 H), 1.29 (s, 1.5 H), 2.08 (s, 3 H), 2.17 (s, 3 H), 2.24 (m, 2 H), 4.09 (bs, 2 H), 5.36 (s, 0.5 H) and 5.60 (bs, 0.5 H); *m/z* 256 ($M^{+\cdot}$, $C_{13}H_{20}O_5$ requires *m/z* 256).

Activated zinc dust (36 g) was added to the above keto-diacetates (0.5 g) in glacial acetic acid (40 ml). The mixture was boiled under reflux for 18 h, then cooled and filtered. The filtrate was diluted with water and the product isolated with ether to give the required *keto-acetate* (54) (0.34 g, 85%) as a colourless oil, b.p. 138—142 °C/21 mmHg; $\nu_{max.}$ (film) 1 747 cm^{-1}; δ 1.10 (bs, 9 H), 2.06 (s, 3 H), 2.26 (m, 4 H), and 4.05 (s, 2 H); *m/z* 198.125 ($M^{+\cdot}$, $C_{11}H_{18}O_3$ requires *m/z* 198.126, 50%), 183 (M − 15, 10%), 180 (M − 18, 6%), 156 (M − 42, 8%), 138 (M − 60, 30%), 125 (M − 73, 84%), and 72 (M − 126, 100%). For preparative purposes the purification of the intermediate keto-diacetate was omitted.

3-*Hydroxymethyl*-3,4,4-*trimethylcyclopentan*-1-*one* (53).—A mixture of the preceding keto-acetate (5.0 g) and potassium hydroxide (10 g) in methanol (200 ml) was kept at 20 °C for 18 h, and then diluted with water. Isolation of the product with ether, and crystallisation from a mixture of ether and light petroleum, gave the *keto-alcohol* (3.41 g, 86%) as needles, m.p. 184—185 °C; $\nu_{max.}$ (Nujol) 1 713 cm^{-1}; δ 1.03 (s, 3 H), 1.07 (s, 3 H), 1.09 (s, 3 H), 2.0—2.5 (2dd, *J ca.* 18, 4 H), 2.43 (bs, 1 H), 3.53 (d, *J* 9, 1 H), and 3.61 (d, *J* 9, 1 H); *m/z* 156.115 ($M^{+\cdot}$, $C_9H_{16}O_2$ requires *m/z* 156.115, 23%), 141 (M − 15, 5%; *m** 127.5, $141^2/156$ = 127.4), 138 (M − 18, 3%; *m** 122.1; $138^2/156$ = 122.1), 125 (M − 31, 4%), 124 (M − 32, 2%), 123 (M − 15 − 18, 2%; *m** 109.7, $123^2/138$ = 109.6; *m** 107.4, $123^2/141$ = 107.3), 110 (M − 46, 8%), 100 (M − 56, 30%), 83 (M − 73, 55%), 72 (M − 84, 45%), and 56 (M − 100, 100%) (Found: C, 68.9; H, 10.25. $C_9H_{16}O_2$ requires C, 69.2; H, 10.3%).

(3R)-3-*Carboxy*-3,4,4-*trimethylcyclopentan*-1-*one* (46).—(*a*) Chromic acid [15 ml of a solution prepared by dissolving chromium trioxide (15 g) in water (33 ml) and sulphuric acid (11.5 ml)] was added slowly to the preceding keto-alcohol (52) (3.0 g) in acetone (90 ml), and the mixture was kept at 20 °C for 30 min. Excess of alcohol was added to quench the reaction, after which the mixture was diluted with water and the product isolated with ether. Crystallisation gave the *keto-acid* (3.4 g, 97%) as needles, m.p. 222 °C (lit.,[26] m.p. 221 °C); $\nu_{max.}$ (Nujol) 1 730 and 1 685 cm^{-1}; δ 1.14 (s, 3 H), 1.22 (s, 3 H), 1.35 (s, 3 H), 2.19 (d, *J* 19, 1 H), 2.35 (bs, 2 H), and 3.00 (d, *J* 19, 1 H); *m/z* 170 ($M^{+\cdot}$, $C_9H_{14}O_3$ requires *m/z* 170, 37%), 155 (M − 15, 12%), 152 (M − 18, 15%), 125 (M − 45, 15%), and 86 (M − 84, 100%); c.d. [2.940 mg in methanol (3 ml); Δε with $\lambda_{max.}$ in nm in parentheses] −0.92 (216), 0.00 (246), +0.49 (276), +0.60 (286), +0.53 (294), +0.25 (304), −0.07 (311), and −0.10 (322).

(*b*) A mixture of the keto-ester (47) (620 mg) and 2N-sodium hydroxide (20 ml) was heated under reflux for 1.5 h, and then cooled and extracted with ether. Acidification of the aqueous layer with 2N-hydrochloric acid, isolation of the product with ether, and crystallisation of the product from ethyl acetate, gave the acid (560 mg, 95%), m.p. 222 °C; $\nu_{max.}$ (CH_2Cl_2) 1 745 and 1 700 cm^{-1}; δ [$(CD_3)_2CO$, 60 MHz] 1.08 (s, 3 H), 1.18 (s, 3 H), 1.30 (s, 3 H), 2.20 (d, *J* 19, 1 H), 2.24 (s, 2 H), 2.80 (d, *J* 19, 1 H), and 6.30 (b, 1 H).

(1R,3R)- *and* (1S,3R)-3-*Methoxycarbonyl*-3,4,4-*trimethylcyclopentan*-1-*ol*, (12) *and* (16).—(*a*) A mixture of platinum dioxide (40 mg) and the preceding keto-acid (50 mg) in 0.5N-hydrochloric acid (AnalaR, 8 ml) and glacial acetic acid (2 ml) was shaken in an atmosphere of hydrogen at 20 °C and atmospheric pressure until 1 mol equiv. of hydrogen had been absorbed (30 h). Removal of catalyst, and isolation of the product with ether gave a semisolid (31 mg) which was treated with an excess of ethereal diazomethane. The resulting esters were separated by g.l.c. (200 °C) giving: (i) the 1R,3R (cis-) *hydroxy-ester* (24 mg) as a colourless oil; $\nu_{max.}$ ($CHCl_3$) 3 450 and 1 716 cm^{-1}; δ 0.96 (bs, 6 H), 1.13 (s, 3 H), 1.3—2.3 (m, 2 H), 3.64 (bs, 1 H), 3.71 (s, 3 H), and 4.2 (m, 1 H); *m/z* 169 (M − OH, $C_{10}H_{17}O_2$ requires *m/z* 169).

(ii) The 1S,3R (trans-) *hydroxy-ester* (9 mg) as a colourless

oil; $\nu_{max.}$ ($CHCl_3$) 3 630 and 1 716 cm^{-1}; δ [$(CD_3)_2CO$] 0.82 (s, 3 H), 1.10 (s, 3 H), 1.26 (s, 3 H), 1.3—2.2 (m, 3 H), 2.76 (dd, J_1 8, J_2 14, 1 H), 3.5 (bs, 1 H), 3.60 (s, 3 H), and 4.35 (m, 1 H); δ (C-Me bands only) 0.85, 1.13, and 1.29; *m/z* 169.123 (*M* − OH, $C_{10}H_{17}O_2$ requires *m/z* 169.123).

(*b*) A solution of the keto-acid (50 mg) in 0.5N-sodium hydroxide (8 ml) was shaken with a ruthenium catalyst (5% Ru on carbon, 50 mg) in an atmosphere of hydrogen at 20 °C and atmospheric pressure for 65 h. The mixture was filtered, the filtrate acidified with dilute sulphuric acid, and the product isolated with ether to give a mixture of hydroxy-acids (52 mg) as a colourless solid. Its n.m.r. spectrum indicated the presence of equal amounts of the 1*S*,3*R* (*trans*-) hydroxy-acid described above, and of the 1*R*,3*R* (*cis*-) hydroxy-acid. Esterification of the mixture with diazomethane, and g.l.c., gave the two isomeric esters described above (*a*).

(*c*) The keto-acid (50 mg) in isopropyl alcohol (5 ml) was added slowly to sodium shot (1.0 g) in boiling toluene (20 ml). The mixture was boiled under reflux for 1.5 h, and then cooled. An excess of ethanol was added and the mixture poured onto ice and acidified with concentrated hydrochloric acid. Isolation of the product with ether gave a solid (50 mg) which was shown by n.m.r. spectroscopy to contain *ca.* 70% of the *cis* and *ca.* 30% of the *trans*-hydroxy-acid. Esterification of the mixture with diazomethane, and g.l.c., gave the two isomeric esters described above in (*a*).

(1R,3R)- *and* (1S,3R)-3-*Carboxy*-3,4,4-*trimethylcyclopentan*-1-*ol*, (11) *and* (15).—Potassium borohydride (985 mg) was added slowly to a well stirred solution of the corresponding keto-acid (2.75 g) in 2N-sodium hydroxide (25 ml). The mixture was boiled under reflux for 17 h and then cooled. Concentrated sulphuric acid (5 ml) in water (25 ml) was added and the mixture boiled under reflux for 1 h and then cooled. A sublimate (1.2 g, 40%) which had collected in the condenser was collected giving the γ-lactone (14), m.p. 181—182 °C (Faigle *et al.*[9] give m.p. 181 °C for a sample obtained by degradation of capsanthin); $\nu_{max.}$ (Nujol) 1 790 cm^{-1}; δ 1.01 (s, 3 H), 1.09 (s, 3 H), 1.17 (s, 3 H), 1.76 (m, 2 H), 1.97 (m, 2 H), and 4.70 (m, 1 H). On mixed g.l.c. (75 °C), the lactone did not separate from the racemic sample described above.

A suspension of the γ-lactone (45 mg) in 2N-sodium hydroxide (10 ml) was heated under reflux for 5 min. The resulting solution was cooled (0 °C) and acidified to pH 4 by dropwise addition of 2N-hydrochloric acid. Isolation of the product with ether, and crystallisation from ethyl acetate–light petroleum gave the 1*R*,3*R* (*cis*-) hydroxy-acid (27 mg), m.p. 200—201 °C (Faigle *et al.*[9] give m.p. 200 °C for a sample derived from capsanthin); $\nu_{max.}$ 3 500 and 1 705 cm^{-1}; δ (60 MHz, main bands only) 0.96 (s, 3 H), 1.06 (s, 3 H), 1.14 (s, 3 H), 4.4 (m, 1 H), and 5.5 (b, 1 H).

The aqueous mixture from which the γ-lactone had been sublimed was extracted with ether. The ethereal extracts were washed with water, dried, and evaporated. Crystallisation of the residue from ethyl acetate–light petroleum gave the 1*S*,3*R* (*trans*-) hydroxy-acid (1.30 g) as needles, m.p. 216—217 °C (Faigle *et al.*[9,11] give m.p. 217 °C for the degradation product of capsanthin); $\nu_{max.}$ (Nujol) 3 460 and 1 698 cm^{-1}; δ [$(CD_3)_2CO$] 0.92 (s, 3 H), 1.14 (s, 3 H), 1.29 (s, 3 H), 1.3—2.2 (m, 3 H), 2.79 (dd, J_1 8.5, J_2 14.5, 1 H), and 4.2—4.8 (bm, 2 H); δ 0.94 (s, 3 H), 1.14 (s, 3 H), 1.32 (s, 3 H), 1.4—2.2 (m, 5 H), 2.8 (dd, J_1 8.5, J_2 14.5, 1 H), 4.4 (m, 1 H) and 6.6 (b, 2 H).

(1S,3R)-3-*Acetyl*-3,4,4-*trimethylcyclopentan*-1-*ol* (17).—A solution of the *trans*-hydroxy-acid (1.26 g) in ether (55 ml) was added slowly to ethereal methyl-lithium (1M; 100 ml). The mixture was boiled under reflux for 18 h and then cooled. Ice and water were added cautiously and the product isolated with ether to give the 1S,3R-*hydroxy-ketone* as a colourless oil (670 mg, 55%), b.p. 89—93 °C/0.9 mmHg which solidified on storage and had m.p. 27—28 °C; $\nu_{max.}$ ($CHCl_3$) 3 640 and 1 695 cm^{-1}; δ 0.85 (s, 3 H), 1.14 (s, 3 H), 1.30 (s, 3 H), 1.5—1.9 (m, 3 H), 2.10 (s, 3 H), 2.8 (dd, J_1 14, J_2 8, 1 H), and 4.5 (m, 1 H); δ [$(CD_3)_2CO$] 0.83 (s, 3 H), 1.14 (s, 3 H), 1.27 (s, 3 H), 1.5—1.9 (m, 3 H), 2.06 (s, 3 H), 2.7 (bs, 1 H), and 2.74 (dd, J_1 14, J_2 8, 1 H) (Found: C, 70.5; H, 10.8. $C_{10}H_{18}O_2$ requires C, 70.55; H, 10.65%). On mixed g.l.c. (150 °C) the hydroxy-ketone did not separate from the racemic sample described above.

(3S,5R,3'S,5'R)-*Capsorubin* (1).—The preceding hydroxy-ketone (600 mg) and crocetindial[20] (65 mg) were added to a solution of potassium hydroxide (175 mg) in ethanol (3.5 ml). The mixture was warmed to *ca.* 40 °C for 5 min, and then stirred in the dark for 68 h. The mixture was then diluted with benzene, and the benzene layer was washed with water, dried, and evaporated. Preparative t.l.c. of the residue (35% acetone in light petroleum) gave all-*trans*-(3*S*,5*R*,3'*S*,5'*R*)-capsorubin (15 mg) which crystallised from benzene–chloroform–light petroleum and had m.p. (evac. capillary) 216—217 °C; $\lambda_{max.}$ (C_6H_6) 530 (ε 102 000), 486 (ε 124 000) and (inflexion) 459 nm; $\nu_{max.}$ (KBr disc) 3 420, 1 664, 1 584, 1 546, and 980 cm^{-1}; δ 0.84 (s, 6 H), 1.21 (s, 6 H), 1.37 (s, 6 H), 1.5—2.2 (*ca.* 8 H), 1.95 (s, 6 H), 1.98 (s, 6 H), 2.93 (dd, J_1 8, J_2 14, 2 H), 6.2—6.8 (m, 12 H), and 7.31 (d, *J* 15, 2 H); *m/z* 600.418 ($M^{+\cdot}$, $C_{40}H_{56}O_4$ requires *m/z* 600.418, 4%), 494 (*M* − 106, 6%), 445 (*M* − 155, 4%), 127 (100%), and 109 (100%); c.d. [1.086 mg in dioxan (5 ml); Δε with $\lambda_{max.}$ in nm in parentheses] +2.21 (220), −1.10 (254), +6.09 (300), and −1.80 (372).

The synthetic carotenoid did not separate from an authentic sample of natural capsorubin on mixed thin layer chromatography on either silica gel (35% acetone in light petroleum) or basic magnesium carbonate (10% acetone in light petroleum, or 3% acetone in benzene), and the m.p. was undepressed on admixture. The n.m.r., u.v., and i.r. spectra of the natural and synthetic spectra were superimposable. The c.d. spectra were in good agreement.[17]

Ozonolysis of Capsanthin (2).—Ozonised oxygen (*ca.* 3% O_3) was bubbled through a solution of capsanthin (500 mg) in carbon tetrachloride (50 ml) and acetic acid (50 ml) until the solution was colourless. Hydrogen peroxide (30%; 15 ml) and water (100 ml) were added, and the mixture was heated under reflux for 2 h and then cooled (0 °C). Saturated aqueous sodium sulphite was added slowly until no further reaction occurred, after which the mixture was acidified with 2N-sulphuric acid. Isolation of the crude product (350 mg) with ether, reaction in ether at 0 °C with an excess of ethereal diazomethane, and preparative g.l.c. (200 °C) gave (1*S*,3*R*)-3-methoxycarbonyl-3,4,4-trimethylcyclopentan-1-ol (22 mg, 15%), *m/z* 169.123 (*M* − OH, $C_{10}H_{17}O_2$ requires *m/z* 169.123). On mixed g.l.c. the degradation product did not separate from the synthetic material described above. The two samples had identical mass spectra, and o.r.d. studies confirmed that they had the same abolute configuration.

A mixture of the hydroxy-ester (16 mg) from capsanthin and 2N-sodium hydroxide (5 ml) was heated under reflux for 2 h, after which it was cooled and acidified with 2N-hydrochloric acid. Isolation of the product with ether, and crystallisation from ethyl acetate–light petroleum gave (1*S*,3*R*)-3-carboxy-3,4,4-trimethylcyclopentan-1-ol (7 mg), m.p. 216—217 °C; *m/z* 154.099 (*M* − 18, $C_9H_{14}O_2$ requires *m/z* 154.099). There was no depression of m.p. on admixture with the synthetic material described above. The two samples had identical n.m.r. and mass spectra, and o.r.d. studies confirmed that they had the same absolute configuration.

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References

1 Part 36, P. E. Ellis, A. E. Faruk, G. P. Moss, and B. C. L. Weedon, *Helv. Chim. Acta*, 1981, **64**, 1092.
2 L. Zechmeister and L. Cholnoky, *Liebigs Ann. Chem.*, 1934, **509**, 269; 1935, **516**, 30.
3 L. Cholnoky, K. Györgyfy, E. Nagy, and M. Pánczél, *Acta Chim. Acad. Sci. Hung.*, 1955, **6**, 143; *Nature* (*London*), 1957, **178**, 410.
4 M. S. Barber, L. M. Jackman, C. K. Warren, and B. C. L. Weedon, *Proc. Chem. Soc.*, 1960, 19; *J. Chem. Soc.*, 1961, 4019.
5 R. Entschel and P. Karrer, *Helv. Chim. Acta*, 1960, **43**, 89.
6 L. Cholnoky, J. Szabolcs, R. D. G. Cooper, and B. C. L. Weedon, *Tetrahedron Lett.*, 1963, 1257.
7 L. Bartlett, W. Klyne, W. P. Mose, P. M. Scopes, G. Galasko, A. K. Mallams, B. C. L. Weedon, J. Szabolcs, and Gy. Tóth, *J. Chem. Soc. C*, 1969, 2527.
8 L. Cholnoky and J. Szabolcs, *Experientia*, 1960, **16**, 483.
9 H. Faigle and P. Karrer, *Helv. Chim. Acta*, 1961, **44**, 1904.
10 F. H. Allen and D. Rogers, *Chem. Commun.*, 1966, 837; *J. Chem. Soc. B*, 1971, 632.
11 H. Faigle and P. Karrer, *Helv. Chim. Acta*, 1961, **44**, 1257.
12 R. D. G. Cooper, L. M. Jackman, and B. C. L. Weedon, *Proc. Chem. Soc.*, 1962, 215.
13 B. C. L. Weedon in 'Carotenoids,' ed. O. Isler, Birkhäuser, Basel, 1971.
14 D. Goodfellow, G. P. Moss, J. Szabolcs, Gy. Tóth, and B. C. L. Weedon, *Tetrahedron Lett.*, 1973, **40**, 3925.
15 J. R. Hlubucek, J. Hora, S. W. Russell, T. P. Toube, and B. C. L. Weedon, *J. Chem. Soc., Perkin Trans. I*, 1974, 848.
16 I. Ueda and W. Nowacki, *Z. Krist.*, 1974, **140**, 190.
17 B. C. L. Weedon, *Pure Appl. Chem.*, 1973, **35**, 113.
18 A. W. Crossley, *J. Chem. Soc.*, 1901, 138.
19 J. W. Faigle, H. Müller, W. von Philipsborn, and P. Karrer, *Helv. Chim. Acta*, 1964, **47**, 741.
20 O. Isler, H. Gutmann, H. Lindlar, M. Montavon, R. Rüegg, G. Ryser, and P. Zeller, *Helv. Chim. Acta*, 1956, **39**, 463.
21 R. Rüegg, M. Montavon, G. Ryser, G. Saucy, U. Schwieter, and O. Isler, *Helv. Chim. Acta*, 1959, **42**, 854.
22 W. H. Perkin and J. F. Thorpe, *J. Chem. Soc.*, 1899, **75**, 52.
23 L. Crombie and D. A. Mitchard, *J. Chem. Soc.*, 1964, 5640.
24 W. H. Perkin and J. F. Thorpe, *J. Chem. Soc.*, 1901, 729.
25 N. J. Toivonen, *Acta Sci. Fennicae* I, 1922, **26**, 1.
26 A. Marquet, M. Dvolaitzky, and D. Arigoni, *Bull. Soc. Chim. Fr.*, 1966, 2956.
27 J. Bredt, *Liebigs Ann. Chem.*, 1913, **395**, 26, 39.
28 O. Aschan, *Ber.*, 1895, **28**, 922.
29 M. Fétizon, J.-C. Gramain, and I. Hanna, *C. R. Acad. Sci.*, 1967, **265**, 929.
30 J. E. Bridgeman, C. E. Butchers, E. R. H. Jones, A. Kasal, G. D. Meakins, and P. D. Woodgate, *J. Chem. Soc. C*, 1970, 244.
31 J. Goldman, N. Jacobsen, and K. Torssell, *Acta Chem. Scand., Ser. B*, 1974, **28**, 492.
32 A. K. Chopra, G. P. Moss, and B. C. L. Weedon, *J. Chem. Soc., Chem. Commun.*, 1977, 467.
33 A. Rüttimann in 'Carotenoid Chemistry and Biochemistry,' eds. G. Britton and T. W. Goodwin, Pergamon Press, Oxford, 1982, p. 71.
34 H. Brockmann and H. Schodder, *Ber.*, 1941, **74**, 73.
35 K. Hancock and H. L. Lochte, *J. Am. Chem. Soc.*, 1939, **61**, 2448.
36 O. Aschan, *Ber.*, 1894, **27**, 2001.
37 J. E. Marsh and J. A. Gardner, *J. Chem. Soc.*, 1896, **69**, 81.
38 O. Aschan, *Liebigs Ann. Chem.*, 1913, **290**, 187.
39 A. Lapworth and W. H. Lenton, *J. Chem. Soc.*, 1901, **79**, 1286.

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