

Carotenoids of Higher Plants

6.* Total Synthesis of Lycoxanthin and Lycophyll

HELGE KJØSEN and SYNNØVE LIAAEN-JENSEN

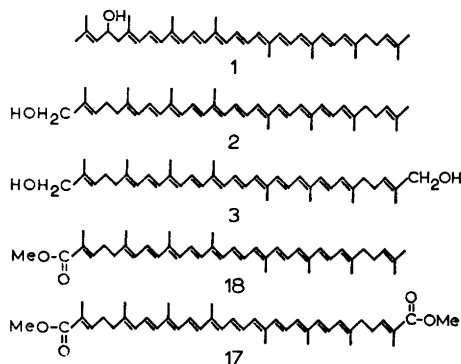
Organic Chemistry Laboratories, Norwegian Institute of Technology, University of Trondheim, Trondheim, Norway

The total synthesis of lycoxanthin (Ψ,Ψ -caroten-16-ol, 2) and lycophyll (Ψ,Ψ -caroten-16,16'-diol, 3) is reported. The identity of natural and synthetic lycoxanthin and lycophyll has been unambiguously demonstrated. Physical properties of intermediates and products are given.

The intermediate methyl carotenates 17 and 18 are new C_{40} -carotenoids not described previously.

Lycoxanthin and lycophyll occur naturally, together with lycopene, in ripe berries of bittersweet (*Solanum dulcamara* L.).¹ The structure of lycoxanthin was first considered to be 1 (Ψ,Ψ -caroten-3-ol)¹ but has later been revised to 2 (Ψ,Ψ -caroten-16-ol).²⁻⁴ Lycoxanthin has been claimed to be present in a number of other organisms (see Ref. 2) but so far *S. dulcamara* is the only substantiated source.

In a previous communication⁵ we have reported the first successful total synthesis of lycoxanthin and lycophyll and we now present full details.



* No. 5. *Acta Chem. Scand.* 25 (1971) 1500.

RESULTS AND DISCUSSION

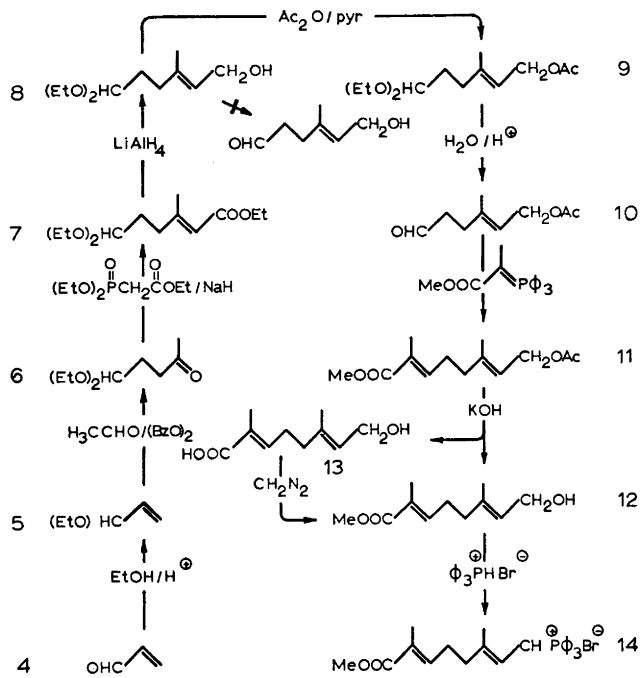
The synthesis of lycoxanthin (2) and lycophyll (3) was effected according to Schemes 1 and 2; (7-carbomethoxy-3-methylocta-2,6-dienyl) triphenylphosphonium bromide (14) being a key intermediate.

The synthesis was based on the availability of crocetinial (15) and geranyltriphenylphosphonium bromide. In previous unsuccessful attempts with Kelly⁶ to synthesize lycoxanthin (2) the potential 16-hydroxy function of lycoxanthin (2) was protected as a tetrahydropyranyl ether at an early stage of the synthesis. However, under the acidic conditions necessary for hydrolysis of the acetal the carotenoid degraded. This led to the conclusion that the potential hydroxy group of lycoxanthin (2) ought to be present as a function which could be converted to the free alcohol (2) under neutral or alkaline conditions. In the present approach the hydroxy function of lycoxanthin (2) was introduced as a carbomethoxy group (11) and reduced with lithium aluminium hydride to the corresponding alcohol on the carotenoid level (Scheme 2).

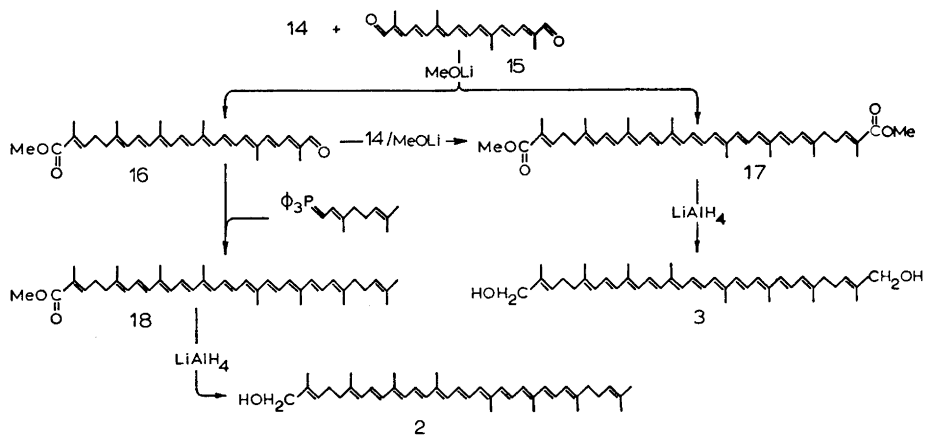
Acrolein (4) was converted to the diethyl acetal 5 with ethanol and catalytic amounts of *p*-toluene sulphonic acid.⁷ The acetal 5 was then reacted with acetaldehyde under pressure in the presence of perbenzoate to give levulaldehyde diethyl acetal (6)⁸ which was condensed with ethyl diethylphosphonoacetate in a Horner reaction⁹ to give the α,β -unsaturated ester 7 in quantitative yield (*cis*+*trans*). This ester was reduced quantitatively with lithium aluminium hydride to the allylic alcohol 8. Hydrolysis of the acetal at this stage failed presumably due to extensive rearrangements and/or cyclization. The alcohol 8 was therefore acetylated with acetic anhydride in pyridine and the resulting acetate 9 was readily hydrolysed to give the free aldehyde 10 in 68 % yield. The aldehyde 10 was then condensed with α -carbomethoxyethylidetriphenylphosphorane in a Wittig reaction to give the α,β -unsaturated ester 11 in 67 % yield (*cis*+*trans*). Attempted partial saponification of the acetoxy function gave a mixture of the desired product 12 and the free carboxylic acid 13. The carboxylic acid 13 was esterified with diazomethane to give an additional amount of 12. Reaction of 12 with excess triphenylphosphonium bromide in methylene chloride solution gave the Wittig salt 14 (84 % yield) as a viscous oil.

The Wittig salt 14 was condensed with crocetin dialdehyde (15) in a Wittig reaction to give a mixture of the C_{30} -monoaldehyde 16 (32 % yield) and the C_{40} -diester 17 (2 %), which were separated by chromatography. The C_{30} -monoaldehyde 16 was condensed with geranyl triphenylphosphorane, prepared *in situ* from the Wittig salt, to give the C_{40} -monoester 18 in quantitative yield. Reduction of 18 with lithium aluminium hydride gave lycoxanthin (2) in 79 % yield. The diester 17 was further obtained (60 % yield) from condensation of the C_{30} -aldehyde 16 with excess phosphorane of 14. Reduction of the diester 17 with lithium aluminium hydride gave crude lycophyll (3) in 76 % yield, crystallized without prior column chromatography to avoid destruction (see below).

Direct comparison showed that synthetic lycoxanthin (2) and lycophyll (3) had identical physical, including chromatographic (Table 1), properties



Scheme 1.



Scheme 2.

with the carotenoids of natural origin (see Experimental Part and the previous communication ⁵). Spectral curves are not included here since they are available elsewhere. ^{2,10,11}

Table 1. R_F -values.

| System | Compound | | | | | | |
|----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| | 16 | 17 | 18 | 2 | Nat. 2 | 3 | Nat. 3 |
| SS 287 | 0.64 ^a | 0.63 ^a | 0.66 ^a | 0.60 ^b | 0.60 ^b | 0.62 ^c | 0.62 ^c |
| SS 288 | 0.55 ^a | 0.61 ^a | 0.70 ^a | 0.42 ^b | 0.42 ^b | 0.40 ^c | 0.40 ^c |
| AH 81 | 0.58 ^a | 0.72 ^a | 0.78 ^a | 0.62 ^b | 0.62 ^b | — | — |
| SG 81 | 0.48 ^a | 0.50 ^a | 0.60 ^a | 0.42 ^b | 0.42 ^b | 0.46 ^c | 0.46 ^c |
| SiO ₂ TLC | 0.74 ^d | — | 0.50 ^d | 0.07 ^d | 0.07 ^d | 0.40 ^f | 0.40 ^f |
| | 0.68 ^e | — | 0.74 ^e | 0.45 ^e | 0.35 ^e | | |

^a 5 % acetone in petroleum ether. ^b 10 % acetone in petroleum ether. ^c 20 % acetone in petroleum ether. ^d Benzene. ^e Chloroform. ^f 10 % methanol in chloroform.

The 16,16'-dioxxygenated system was in our hands unstable compared to most carotenoids. The amount of the symmetrical diester 17 obtained in the synthesis of the C₃₀-monoaldehyde 16 was only 7.5 % relative to the monoaldehyde after column chromatography, whereas considerably higher yield would be expected from this type of reaction. Low yields of the dimethyl ester 17 and lycophyll (3) in various experiments is primarily ascribed to low recoveries on column chromatography (alumina) for these particular carotenoids.

We have already reported ⁵ that only the 1,2-*trans* and 1,2,1',2'-*ditrans* isomers of lycoxanthin (2) and lycophyll (3) were isolated in the final steps. It is of interest to consider the amount of corresponding *cis* isomers of some of the intermediates. Judged from the NMR spectra (olefinic proton β to carbonyl) the intermediates 11, 12, and 13 contained 17 %, 10 %, and 13 % *cis* isomers, respectively. The other intermediates could not be checked since the β -hydrogen signals were obscured by other signals, and the isomers could not be separated by chromatography. One possible explanation to the fact that only all *trans* lycoxanthin (2) and lycophyll (3) were isolated is preferential crystallization of these isomers.

The monocyclic C₄₀ methyl carotenoate torularhodin methyl ester is naturally occurring.¹² However, aliphatic methyl carotenoates such as 17 and 18 have not yet been encountered in nature. Since these carotenoids are described for the first time in this study their NMR-spectra are included (Fig. 1) together with that of the new apo-carotenoid 16.

EXPERIMENTAL

General. For synthetic purposes normal laboratory grade chemicals and solvents were used.

Column chromatography was carried out on silica or alumina activity grade ¹³ 2 (3 % H₂O) and 3 (6 % H₂O) and analytical grade solvents were employed.

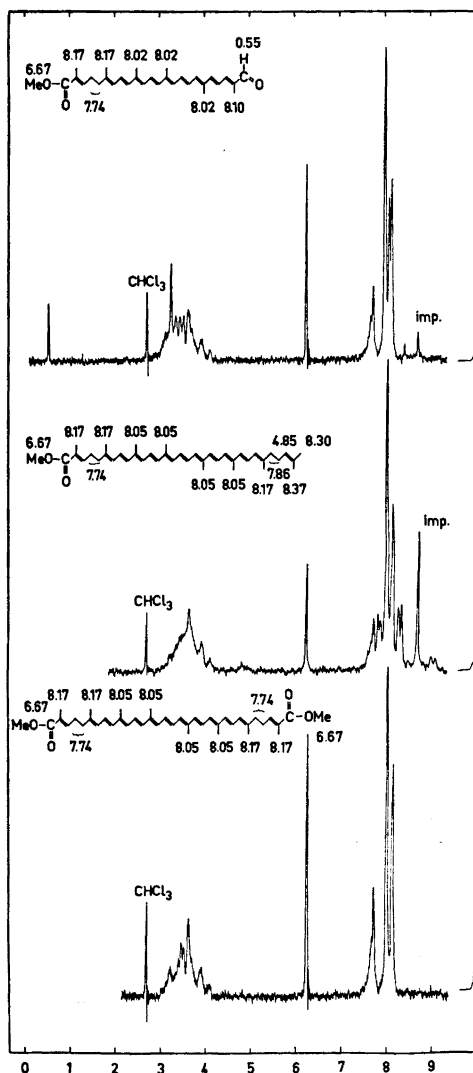


Fig. 1. Proton magnetic resonance spectra in deuteriochloroform of methyl 8'-oxo-apo-8'- Ψ,Ψ -caroten-16-oate (16), methyl Ψ,Ψ -caroten-16-oate (18), and dimethyl Ψ,Ψ -carotene-16,16'-dioate (17).

Paper chromatography was carried out on Schleicher & Schüll Nos. 287 (kieselguhr containing, SS 287) and 288 (alumina containing, SS 288) and Whatman AH 81 (aluminium hydroxide containing, AH 81) and SG 81 (silica containing, SG 81) circular papers. Acetone-petroleum ether (b.p. 40–65°C) mixtures were employed as developers.

Thin layer chromatography was carried out on silica plates (Merck, Silica G) using analytical grade benzene, chloroform, or methanol in chloroform for development.

Melting points were determined on an Electrothermal melting point apparatus in sealed evacuated tubes and are uncorrected.

Visible light absorption spectra were recorded on a Coleman Hitachi 124 spectrophotometer, IR spectra on a Perkin Elmer 257 spectrometer and NMR spectra on a Varian

A-60 A instrument in deuteriochloroform solution with tetramethylsilane as internal standard. Mass spectra were registered with an AEI MS902 instrument with a bombardment energy of 70 eV and an ion source temperature of 190–230°C.

1,1-Diethoxy-2-propene (acrolein diethyl acetal, 5) was synthesized from acrolein (4, 354 g) and absolute ethanol (552 g) using *p*-toluenesulphonic acid (21 mg) as catalyst according to the method of Weisblat *et al.*,⁷ yield 377 g (48 %); b.p. 120–122°C; $n_D^{22} = 1.4011$; ν_{\max} (liq.) 3100–2820 and 1480–1320 (CH), 1125, 1060, 990 (C–O), 935 (H₂C=) and 840 cm⁻¹; τ (CDCl₃) 4.14 td (1H, $J_{1,3} = 4.5$ Hz, $J_{2,3} = 17.5$ Hz (*trans*), $J_{2,3'} = 10$ Hz (*cis*), H-2), 4.69 dd (1 H, $J_{2,3} = 17.5$ Hz, $J_{3,3'} = 3$ Hz, H-3), 4.80 dd (1 H, $J_{2,3'} = 10$ Hz, $J_{3,3'} = 3$ Hz, H-3'), 5.15 d (1 H, $J_{1,2} = 4.5$ Hz, H-1), 6.42 q and 6.49 q (4 H, $J = 7.5$ Hz, OCH₂), 8.88 t (6 H, $J = 7.5$ Hz, CH₂CH₃).

1,1-Diethoxypentan-4-one (levulaldehyde diethyl acetal, 6) was prepared as described by Mondon.⁸ Acrolein acetal (5, 130 g), acetaldehyde (240 g) and benzoylperoxide (7 g) were heated in an autoclave at 80°C for 53 h, cooled, and excess acetaldehyde was removed by distillation. The residue was fractionated under reduced pressure, the fraction distilling at 77–108°C/15 mm was collected, redistilled, and the fraction boiling at 85–89°C/15 mm (68 g, 39 %) was collected; $n_D^{22} = 1.4224$; ν_{\max} (liq.) 3000–2820 (CH), 1720 (C=O), 1460–1330 (CH), 1165, 1130 and 1070 (C–O) cm⁻¹; τ (CDCl₃) 5.53 t (1 H, $J = 5.5$ Hz, H-1), 6.43 q and 6.48 q (4 H, $J = 7$ Hz, OCH₂), 7.50 t (2 H, $J = 7$ Hz, CH₂-3), 7.88 s (3 H, CH₃-5), 8.15 dt (2 H, $J_{1,2} = 5.5$ Hz, $J_{2,3} = 7$ Hz, CH₂-2), 8.83 t (6 H, $J = 7$ Hz, CH₂CH₃).

Ethyl 6,6-diethoxy-3-methylhex-2-enoate (7). Sodium hydride (50 % in mineral oil, 5.28 g) was washed repeatedly with petroleum ether and suspended in dry tetrahydrofuran (50 ml). Ethyl diethyl phosphonoacetate^{9,14} (24.6 g) was added and the mixture stirred until H₂-evolution had ceased (*ca.* 1 h). Levulaldehyde diethyl acetal (6, 17.4 g) in dry tetrahydrofuran (50 ml) was added and the reaction mixture stirred at room temperature for 31 h and finally refluxed for 2 h. The mixture was cooled, saturated sodium bicarbonate solution added and the product extracted with ether. The combined extracts were washed with water until neutral, dried over anhydrous sodium sulfate and evaporated to dryness; yield 24.34 g (99.7 %) crude 7; $n_D^{21} = 1.4514$; ν_{\max} (liq.) 3010–2820 (CH), 1715 (C=O), 1650 (conj. C=C), 1445, 1375, 1350 (CH), 1225 (ester C–O), 1150 and 1065 (ether C–O) cm⁻¹; τ (CDCl₃) 4.50 q (1 H, $J = 1.5$ Hz, H-2), 5.55 t (1 H, $J = 5$ Hz, H-6), 5.87 q (2 H, $J = 7$ Hz, CH₂CH₃ ester), 6.42 q and 6.46 q (4 H, $J = 7$ Hz, CH₂CH₃ ether), 7.83 d (3 H, $J = 1.5$ Hz, CH₃-3), *ca.* 7.80 (2 H, CH₂-4), *ca.* 8.20 m (2 H, CH₂-5), 8.74 t (3 H, $J = 7$ Hz, CH₂CH₃ ester), 8.82 t (6 H, $J = 7$ Hz, CH₂CH₃ ether).

6,6-Diethoxy-3-methylhex-2-en-1-ol (8). 7 (12.2 g) was reduced with lithium aluminium hydride (1.43 g) in dry ether (100 ml) at 0°C and the reaction continued at room temperature for 20 h. Ammonium chloride (1.8 g) in water (6 ml) was added, the mixture stirred for 1/2 h and filtered. Evaporation of the solvent gave 9.54 g (94.5 %) crude 8; $n_D^{20} = 1.4552$; ν_{\max} (liq.) 3600–3200 (OH), 3000–2820 (CH), 1665 (C=C), 1445, 1375, 1345 (CH), 1125, 1060 (C–O) and 1005 (OH) cm⁻¹; τ (CDCl₃) 4.50 t (1 H, $J = 7$ Hz, H-2), 5.55 t (1 H, $J = 5$ Hz, H-6), 5.92 d (2 H, $J = 7$ Hz, CH₂-1), 6.43 q and 6.48 q (4 H, $J = 7$ Hz, CH₂CH₃ ether), *ca.* 8.13 m (2 H, CH₂-4), *ca.* 8.28 m (2 H, CH₂-5), 8.33 s (3 H, CH₃-3), 8.80 t (6 H, $J = 7$ Hz, CH₂CH₃ ether).

6,6-Diethoxy-3-methylhex-2-enyl acetate (9). 8 (18.86 g) and acetic anhydride (20.4 g) in dry pyridine (20 ml) was stirred at room temperature for 20 h. The mixture was neutralized with saturated sodium bicarbonate solution and extracted with ether. The combined extracts were washed with water until neutral and evaporated with benzene to dryness; yield 24.83 g (100 %) crude 9; $n_D^{20} = 1.4489$; ν_{\max} (liq.) 3040–2820 (CH), 1740 (C=O), 1670, 1650 (C=C), 1445, 1375, 1345 (CH), 1235 (C–O acetate), 1180, 1065 and 1025 (C–O ether) cm⁻¹; τ (CDCl₃) 4.65 t (1 H, $J = 7$ Hz, H-2), 5.45 d (2 H, $J = 7$ Hz, CH₂-1), 5.56 t (1 H, $J = 5$ Hz, H-6), 6.44 q and 6.50 q (4 H, $J = 7$ Hz, CH₂CH₃), *ca.* 7.92 m (2 H, CH₂-4), 8.05 s (3 H, CH₃ acetate), *ca.* 8.25 m (2 H, CH₂-5), 8.30 s (3 H, CH₃-3), 8.75 t (6 H, $J = 7$ Hz, CH₂CH₃).

6-Oxo-3-methylhex-2-enyl acetate (10). Hydrolysis of the acetal was affected as described by Surmatis *et al.*¹⁵ 9 (12.2 g) and sodium acetate (20 g) in water (15 ml) and glacial acetic acid (100 ml) were heated at 90°C for 3 h. Water was added and the mixture extracted with ether. The combined extracts were washed with sodium bicarbonate solution and water until neutral and evaporated with benzene to dryness; yield 5.8 g (68 %)

crude; 10; $n_D^{20} = 1.4714$; ν_{\max} (liq.) 3040–2820 (CH), 2730 (–CH=O), 1735 (C=O acetate and aldehyde), 1445, 1385, 1370 (CH), 1235 (C–O acetate), 1030, 960 and 795 cm^{-1} ; τ (CDCl_3) 0.27 t (1 H, $J = 1.5$ Hz, H-6), 4.61 t (1 H, $J = 7$ Hz, H-2), 5.42 d (2 H, $J = 7$ Hz, CH_2 -1), 7.52 m (4 H, CH_2 -4, CH_2 -5), 8.00 s (3 H, CH_3 acetate), 8.28 s (3 H, CH_3 -3).

7-Carbomethoxy-3-methylocta-2,6-dienyl acetate (11). α -Carbomethoxyethylidene-triphenylphosphorane (18 g) and 10 (6.35 g) in dry benzene (100 ml) were refluxed for 36 h. The solvent was evaporated and the residue chromatographed twice on silica. Triphenylphosphine oxide was eluted with benzene and 11 with chloroform. 11 (6 g, 67.5 %) had $R_F = 0.55$ on silica plates using chloroform as developer; ν_{\max} (liq.) 3060–2820 (CH), 1740 (C=O, acetate), 1715 (C=O, methyl ester), 1650 (conj. C=C), 1440, 1385, 1370 (CH), 1270 (C–O, methyl ester), 1235 (C–O, acetate), 1185, 1130, 1105, 1085, 1025 (C–O), 960 and 750 cm^{-1} ; τ (CDCl_3) 3.28 t (0.83 H, $J = 8$ Hz, H-6, *trans*), 4.09 t (0.17 H, $J = 8$ Hz, H-6, *cis*), 4.60 t (1 H, $J = 7$ Hz, H-2), 5.42 d (2 H, $J = 7$ Hz, CH_2 -1) 6.32 s (3 H, OCH_3), 7.75 m (4 H, CH_2 -4, CH_2 -5), 8.00 s (3 H, CH_3 acetate), 8.15 s (3 H, CH_3 -8), 8.25 s (3 H, CH_3 -3).

7-Carbomethoxy-3-methylocta-2,6-dien-1-ol (12). 11 (4.24 g) was saponified with 10 % methanolic potassium hydroxide (100 ml) in ether (100 ml) at room temperature for 2 h. Water was added and the mixture extracted with ether. The combined extracts were washed with water until neutral and evaporated with benzene to dryness; yield 2.0 g (57.5 %). Some free acid 13 was transferred into ether by acidification of the water phase. The ether extracts were washed with water until neutral and evaporated with benzene to dryness; yield 1.0 g (31 %) 13. The acid 13 was reacted with excess diazomethane in ether to give an additional 1.08 g (100 %) 12. Combined yield 3.08 g (88.5 %) 12; ν_{\max} (liq.) 3600–3200 (OH), 3040–2800 (CH), 1715 (C=O), 1440, 1390 (CH), 1275 (C–O), 1200, 1130, 1090, 1010 (OH), 790 and 750 cm^{-1} ; τ (CDCl_3) 3.27 t (0.9 H, $J = 8$ Hz, H-6 *trans*), 4.09 t (0.1 H, $J = 8$ Hz, H-6 *cis*), 4.75 t (1 H, $J = 7$ Hz, H-2), 5.89 d (2 H, $J = 7$ Hz, CH_2 -1), 6.30 s (3 H, OCH_3), 7.75 m (5 H, CH_2 -4, CH_2 -5, OH), 8.17 s (3 H, CH_3 -8), 8.32 s (3 H, CH_3 -3).

7-Carboxy-3-methylocta-2,6-dien-1-ol (13) had the following characteristics: $n_D^{20} = 1.5062$; ν_{\max} (liq.) 3600–2500 (OH), 3010–2700 (CH), 1690 (C=O), 1645 (conj. C=C), 1420, 1390 (CH), 1285 (C–O), 1135, 1085, 995 (OH), and 760 cm^{-1} ; τ (CDCl_3) 2.20 s (2 H, OH), 3.17 t (0.87 H, $J = 8$ Hz, H-6 *trans*), 3.97 t (0.13 H, $J = 8$ Hz, H-6 *cis*), 4.75 t (1 H, $J = 7$ Hz, H-2), 5.85 d (2 H, $J = 7$ Hz, CH_2 -1), 7.78 m (4 H, CH_2 -4, CH_2 -5), 8.17 s (3 H, CH_3 -8), 8.32 s (3 H, CH_3 -3).

(7-Carbomethoxy-3-methylocta-2,6-dienyl) triphenylphosphonium bromide (14). 12 (2.05 g) and triphenylphosphonium bromide (10 g) in methylene chloride (100 ml) were refluxed for 72 h. The reaction mixture was cooled and water added followed by extraction with methylene chloride. The solvent was evaporated and methanol added. Triphenylphosphine (identified by cochromatography and mixed melting point) crystallized and was removed by filtration. The crude product was chromatographed on silica. Triphenylphosphine was eluted with chloroform and the Wittig salt 14 with methanol. Several attempts at crystallization failed and 14 (4.62 g, 84 %) was obtained as a viscous oil.

Methyl 8'-oxo- α -apo-8'- Ψ - Ψ -carotene-16-oate (16). To crocetin dialdehyde (15, 296 mg) in benzene (20 ml) were added 14 (0.1 g) in methanol (1 ml) and 0.2 M butyl lithium in ether (1 ml) in portions. The mixture was kept at reflux under a blanket of nitrogen until 1.8 g of 14 had been added. Water was added and the mixture extracted with ether. The extracts were washed with water until neutral and the solvent was evaporated. The residual pigments were dried by evaporation with benzene and chromatographed twice on alumina. 16 (147 mg, 32 %, spectrophotometrically estimated) was eluted with 50 % benzene in petroleum ether. Crystallization from acetone–petroleum ether afforded 47.2 mg crystalline 16; m.p. 131–132°C; λ_{\max} (acetone) 468 [E(1 %, 1 cm) = 2820] and (487) nm, λ_{\max} (petroleum ether) (444), 466.5 and 495.5 nm; ν_{\max} (KBr) 3030 (CH olefinic), 3000–2800 (CH), 1715 (C=O, ester), 1675 (C=O, aldehyde), 1650 (C=C, conj. ester), 1610 (C=C, conj. aldehyde), 1585, 1560, 1515 (C=C), 1435, 1400–1370, 1355 (CH), 1260 (C–O, ester), 1180, 1160, 1120, 1088 (C–O), 1003, 955 (*trans* –CH=CH–), 825 (>C=CH–) and 745 cm^{-1} ; τ (CDCl_3) 0.55 s (1 H, H-8'), 3.0–4.3 (14 H, olefinic), 6.67 s (3 H, OCH_3) 7.74 (4 H, CH_2 -3, CH_2 -4), 8.02 s (9 H, CH_3 at C-9, C-13 and C-13'), 8.10 s (3 H, CH_3 at C-9'), 8.17 s (6 H, CH_3 at C-1 and C-5); m/e 460 (M), 445 (M–15), 429 (M–31), 401 (M–59), 381 (M–79), 368 (M–92), 354 (M–106), 347 (M–113), 311 (M–92–57), 299 (M–69), 277.

A small amount (11 mg, 1.75 %) of the symmetrical diester *17* was also eluted with 50 % benzene in petroleum ether, but was slightly less polar than *16*. Preparation and properties of *17* is described below.

Methyl Ψ,Ψ-caroten-16-oate (18). Geranylidenetriphenylphosphorane was prepared from geranyltriphenylphosphonium bromide (200 mg) and an equivalent amount of 0.2 M butyl lithium in dry ether. The resultant dark red solution was stirred for approximately 1 min and *16* (85 mg) in methylene chloride (20 ml) was added. The mixture was stirred at reflux under nitrogen. Additional amounts of phosphorane prepared from the Wittig salt (100 mg) and equivalent amount of base, as described above, were added in portions until 800 mg of Wittig salt had been used (ca. 50 min). Water was added and the water phase extracted with ether. The extracts were washed with water, evaporated with benzene to dryness and the pigments chromatographed twice on alumina activity grade 3 (6 % H₂O). *18* (113 mg, 100 %) was eluted with 20 % benzene in petroleum ether. Crystallization from carbon disulphide-methanol and recrystallization from acetone afforded *18* (7.25 mg) of m.p. 145–148°C; λ_{\max} (acetone) (425), 448, 474 [$E(1\%$, 1 cm) = 2880] and 505 nm; ν_{\max} (KBr) 3030 (CH, olefinic), 3000–2800 (CH), 1715 (C=O), 1650 (conj. C=C), 1626, 1550 (C=C), 1435, 1400–1350 (CH), 1260 (C–O), 1235, 1190, 1170, 1115, 1080, 960 (*trans* –CH=CH–), 825 (>C=CH–) and 745 cm⁻¹; τ (CDCl₃) 3.0–4.3 (17 H, olefinic), 4.85 m (1 H, H-2'), 6.67 s (3 H, OCH₃), 7.74 (4 H, CH₂-3, CH₂-4), 7.83 and 7.90 (4 H, CH₂-3' and CH₂-4'), 8.04 s (12 H, in-chain CH₃), 8.17 s (9 H, CH₃ at C-1, C-5 and C-5'), 8.30 s and 8.37 s (3 + 3 H, CH₃ at C-1') 8.73 (imp.); *m/e* 580 (M), 565 (M-15), 549 (M-31), 511 (M-69), 501 (M-79), 488 (M-92), 474 (M-106), 467 (M-113), 443 (M-106-31), 422 (M-158), 419 (M-92-69), 405 (M-106-69), 382 (M-106-92).

Lycoxanthin (Ψ,Ψ-caroten-16-ol, 2). *18* (100 mg) in 20 mg portions were each reduced at room temperature with a dilute suspension of lithium aluminium hydride in dry ether (2.5 ml). The reactions were quenched after ca. 10 sec by addition of moist ether. Water was added and the pigments were extracted with ether, washed with water and evaporated with benzene to dryness. *18* (10 mg) was recovered after chromatography on alumina (activity grade 3).

Lycoxanthin (67 mg, 79 % based on reacted *18*) was eluted with 10 % ether in benzene. Crystallization from acetone-petroleum ether and recrystallization from acetone gave 10 mg *2* of m.p. 173–174°C undepressed on admixture with natural lycoxanthin of m.p. 173–174°C. Natural and synthetic lycoxanthin could not be separated by chromatography (Table 1). Synthetic *2* had the following spectral characteristics: λ_{\max} (acetone) 448, 474 [$E(1\%$, 1 cm) = 3080] and 505 nm, λ_{\max} (petroleum ether) 443, 469 and 500 nm; ν_{\max} (KBr) 3550–3150 (OH), 3030 (CH, olefinic), 3000–2800 (CH), 1625, 1550 (C=C), 1440, 1400–1350 (CH), 1005 (OH), 960 (*trans* –CH=CH–), 880, 825 (>C=CH–) cm⁻¹; τ (CDCl₃) 3.0–4.3 (16 H, olefinic), ca. 4.60 m (1 H, H-2), ca. 4.83 m (1 H, H-2'), 6.00 s (2 H, CH₂-16), 7.85 (8 H, CH₂-3, 4, 3' and 4'), 8.05 s (12 H, in-chain CH₃), 8.19 s (6 H, CH₃ at C-5 and C-5'), 8.31 s (6 H, CH₃ at C-1 and C-1'), 8.33 s (3 H, CH₃ at C-1'); *m/e* 552 (M), 536 (M-16), 534 (M-18), 483 (M-69), 467 (M-85), 460 (M-92), 446 (M-106), 428 (M-106-18), 399 (M-153), 394 (M-158), 368 (M-92-92).

Dimethyl Ψ,Ψ-carotene-16,16'-dioate (17). To *16* (41.6 mg) in benzene (5 ml) were added in portions *14* (50 mg) in methanol (0.5 ml) and 0.2 M butyl lithium in dry ether (0.5 ml) until 500 mg of *14* was added (ca. 3 h). The reaction mixture was treated as described for *18* above. The pigments (53 mg) were chromatographed on a silica column. *17* (29.2 mg, 60.5 % based on reacted *16*) was eluted with benzene and some unreacted *16* (6 mg) with chloroform. The combined products from several experiments (50 mg of *17*) were rechromatographed on silica and eluted with 5 % ethyl acetate in benzene. Crystallization from acetone-petroleum ether afforded *17* (6.7 mg); m.p. 148–148.5°C; λ_{\max} (acetone) (425), 446, 473 [$E(1\%$, 1 cm) = 2650] and 505 nm; ν_{\max} (KBr) 3030 (CH, olefinic), 3000–2800 (CH), 1712 (C=O), 1650 (conj. C=C), 1435, 1400–1350 (CH), 1270 (C–O), 1240, 1190, 1115, 1080, 960 (*trans* –CH=CH–), 825 (>C=CH–) and 745 cm⁻¹; τ (CDCl₃) 3.0–4.3 (18 H, olefinic), 6.67 s (6 H, OCH₃), 7.74 (8 H, CH₂-3, 4, 3' and 4'), 8.05 s (12 H, in-chain CH₃), 8.17 s (12 H, CH₃ at C-1, 1', 5 and 5'); *m/e* 624 (M), 609 (M-15), 589 (M-31), 565 (M-59), 545 (M-79), 532 (M-92), 518 (M-106), 511 (M-113), 501 (M-92-31), 487 (M-106-31), 466 (M-158), 443 (M-181).

Lycophyll (Ψ,Ψ-carotene-16,16'-diol, 3). *17* (29.2 mg) was reduced in portions (ca. 10 mg in tetrahydrofuran (5 ml)) with excess lithium aluminium hydride in tetrahydro-

furan solution at 0°C for ca. 30 min. The reaction was followed by TLC on silica and the reaction was quenched by addition of ethyl acetate and water. The reaction mixture was extracted with ether and the combined extracts were washed with water until neutral and evaporated with benzene to dryness. Combined yield of 3 from three experiments was 20.4 mg (76.6 %). Crystallization from acetone-petroleum ether gave 5.86 mg impure (lipid) 3; λ_{\max} (acetone) (420), 447, 473.5 [$E(1\%, 1\text{ cm})=1640$] and 504.5 nm; ν_{\max} (KBr) 3600-3100 (OH), 3050-2800 (CH), 1630 (C=C), 1440, 1390-1360 (CH), 1005 (OH), 960 (*trans* -CH=CH-), and 825 (>C=CH-) cm^{-1} ; $\tau(\text{CDCl}_3)$ 3.0-4.3 (16 H, olefinic), ca. 4.60 m (2 H, H-2, 2'), 6.00 s (4 H, CH₂-16, 16'), 7.84 (8 H, CH₂-3, 4, 3', and 4'), 8.05 s (12 H, in-chain CH₂), 8.17 s (6 H, end-of-chain CH₂), 8.31 s (6 H, CH₂ at C-1, 1'), 8.73 (imp.), 9.08 (imp.); *m/e* 568 (M), 551 (M-17), 550 (M-18), 483 (M-85), 476 (M-92), 462 (M-106), 410 (M-158).

Acknowledgements. The experience gained by our colleague Dr. M. Kelly in earlier attempts to synthesize lycoxanthin was of great value in planning this work. H.K. was supported by a grant from the *Norwegian Research Council of Science and Humanities* to S. L. J.

REFERENCES

1. Zechmeister, L. and Cholnoky, L. v. *Ber.* **69** (1936) 422.
2. Markham, M. C. and Liaaen-Jensen, S. *Phytochemistry* **7** (1968) 839.
3. Cholnoky, L., Szabolcs, J. and Waight, E. S. *Tetrahedron Letters* **1968** 1931.
4. Kelly, M., Authén Andresen, S. and Liaaen-Jensen, S. *Acta Chem. Scand.* **25** (1971) 1607.
5. Kjösen, H. and Liaaen-Jensen, S. *Acta Chem. Scand.* **25** (1971) 1500.
6. Liaaen-Jensen, S. *Pure Appl. Chem.* **20** (1969) 421.
7. Weisblat, D. I., Magerlein, B. J., Myers, D. R., Hanze, A. R., Fairburn, E. I. and Rolfson, S. T. *J. Am. Chem. Soc.* **75** (1953) 5893.
8. Mondon, A. *Angew. Chem.* **64** (1952) 224.
9. Wadsworth, W. S. and Emmonds, W. D. *J. Am. Chem. Soc.* **83** (1961) 1733.
10. Enzell, C. R., Francis, G. W. and Liaaen-Jensen, S. *Acta Chem. Scand.* **23** (1969) 727.
11. Kjösen, H. *Thesis*, University of Trondheim 1972.
12. Arpin, N. and Liaaen-Jensen, S. *C. R. H. Acad. Sci. Ser. D* **265** (1967) 1083.
13. Brockmann, H. and Schodder, H. *Ber.* **74** (1941) 73.
14. Speziale, A. J. and Freeman, R. C. *J. Org. Chem.* **23** (1958) 1883.
15. Surmatis, J. D., Walser, A., Gibas, J., Schwieter, U. and Thommen, R. *Helv. Chim. Acta* **53** (1970) 974.

Received May 16, 1972.