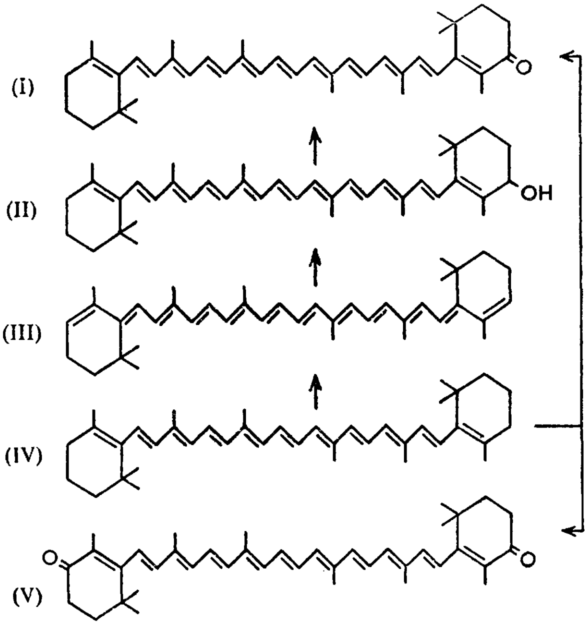
804. *Carotenoids and Related Compounds. Part VII.* Synthesis of Canthaxanthin and Echinenone.*

By C. K. Warren and B. C. L. Weedon.

A method has been developed for the introduction of the 2 : 6 : 6-trimethyl-3-oxo*cyclo*hex-1-enyl group into polyenes, and used to synthesise canthaxanthin and echinenone from crocetin-dial and β-*apo*-2-carotenal respectively.

Echinenone was first isolated from the gonads of the sea urchin *Paracentrotus* (*Strongylocentrotus*) *lividus* by Lederer who suggested that it was a keto-derivative of β-carotene.[1] Goodwin and Taha[2] later formulated echinenone as 4-oxo-β-carotene (I), and advanced arguments for its identity with both myxoxanthin[3] and aphanin[4] from the blue algæ *Oscillatoria rubescens* and *Aphanizomenon flos-aquae* respectively.



By hydrolysis of the boron trifluoride complex of dehydro-β-carotene (III) Wallcave and Zechmeister[5] obtained "*iso*cryptoxanthin" for which they deduced the structure (II). Oppenauer oxidation of this compound by Ganguly, Krinsky, and Pinckard[6] gave

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* Part VI, preceding paper.

[1] Lederer, *Compt. rend.*, 1935, **201**, 300; Lederer and Moore, *Nature*, 1936, **137**, 996.

[2] Goodwin and Taha, *Biochem. J.*, 1950, **47**, 244; 1951, **48**, 513; cf. Goodwin, *ibid.*, 1956, **63**, 481.

[3] Heilbron and Lythgoe, *J.*, 1936, 1376; Karrer and Rutschmann, *Helv. Chim. Acta*, 1944, **27**, 1691.

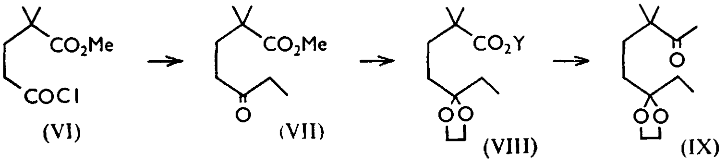
[4] Tischer, *Z. physiol. Chem.*, 1938, **251**, 109; 1939, **260**, 257.

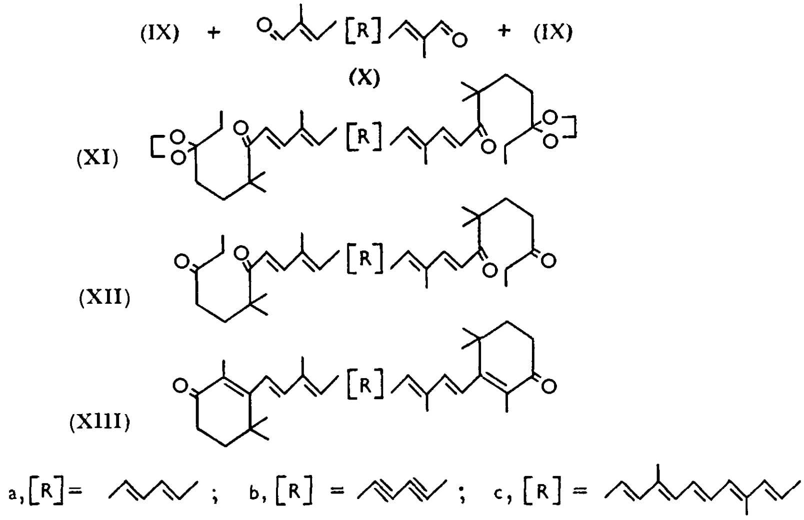
[5] Wallcave and Zechmeister, *J. Amer. Chem. Soc.*, 1953, **75**, 4495; cf. *ibid.*, 1956, **78**, 3188.

[6] Ganguly, Krinsky, and Pinckard, *Arch. Biochem. Biophys.*, 1956, **60**, 345.

a product which was not isolated, but was claimed as echinenone from its spectral and chromatographic properties. From the complex mixture of substances formed on treatment of β-carotene with *N*-bromosuccinimide in chloroform containing 1% of alcohol, Petracek and Zechmeister[7] isolated mono- and di-oxo-derivatives in 5 and 1% yield respectively. They presented convincing evidence for the formulation of these products as (I) and (V). The monoketone they identified with echinenone and the diketone with canthaxanthin, a pigment first isolated by Haxo[8] from the edible mushroom *Cantharellus cinnabarinus* and subsequently found in some mutant strains of the bacterium *Corynebacterium michiganense*.[9] In this paper we report unambiguous rational syntheses of both carotenoids. A different approach to canthaxanthin has been briefly outlined by Isler *et al.*[10]

Reaction of the half-ester acid chloride (VI) of αα-dimethylglutaric acid with ethylcadmium furnished the keto-ester (VII). This readily exchanged the ethylenedioxy-group with 2-ethylenedioxybutane, to give the ester (VIII; Y = Me) which was hydrolysed to the corresponding acid (VIII; Y = H). Treatment of the latter with methyl-lithium gave the methyl ketone (IX), which was characterised by the formation of a mono-semicarbazone and, after initial hydrolysis, a bis-2 : 4-dinitrophenylhydrazone.





To establish the validity of the method envisaged for the introduction of the trimethyl*cyclo*hexenone ring system into polyenes, the following synthesis was carried out. Condensation of the tetraenedial[11] (Xa) with the methyl ketone (IX) in the presence of aluminium

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[7] Petracek and Zechmeister, *J. Amer. Chem. Soc.*, 1956, **78**, 1427; *Arch. Biochem. Biophys.*, 1956, **61**, 137; cf. Entschel and Karrer, *Helv. Chim. Acta*, 1958, **41**, 402.

[8] Haxo, *Botan. Gaz.*, 1950, **112**, 228.

[9] Saperstein and Starr, *Biochem. J.*, 1954, **57**, 273.

[10] Isler, Montavon, Rüegg, Saucy, and Zeller, *Verh. Naturforsch. Ges. Basel*, 1956, **67**, 379; Isler, Guex, Lindlar, Montavon, Rüegg, Ryser, Saucy, and Schwieter, *Chimia* (*Switz.*), 1958 **12**, 89.

[11] Warren and Weedon, preceding paper.

tert.-butoxide gave the diketone (XIa) which was hydrolysed to the tetraketone (XIIa). [The diacetylenic analogue (XIIb) was similarly prepared from (Xb).[12]] On treatment with methanolic potassium hydroxide the tetraketone (XIIa) underwent the expected cyclisation to give the octaenedione (XIIIa).

The methyl ketone (IX) was then condensed with crocetin-dial[13] (Xc) in the presence of potassium hydroxide, and gave the nonaenedione (XIc) in 62% yield. Removal of the protecting groups by treatment with acetone and toluene-*p*-sulphonic acid afforded the tetraketone (XIIc), in 72% yield, which was cyclised with alkali to give canthaxanthin (XIIIc = V) in 33% yield.

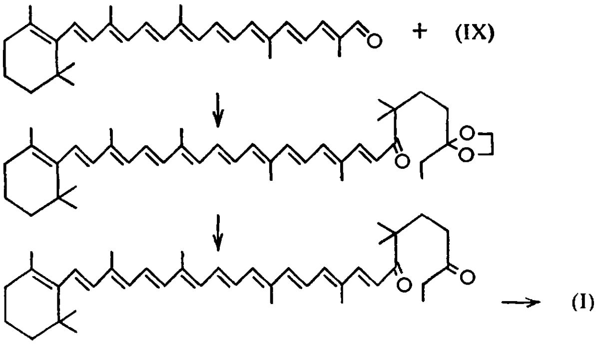
Similarly condensation of β-*apo*-2-carotenal[14] (XIV) with the methyl ketone (IX) gave (32%) the decaene ketone (XV) which was hydrolysed to the diketone (XVI) in 46% yield. Cyclisation with alkali occurred readily and furnished echinenone (I) in 83% yield. In a mixed chromatogram the product did not separate from the main carotenoid of the blue alga *Anabaena cylindrica*.

TABLE 1. *Light absorption of polyene-ketones in benzene.*

(Max. in mμ; ε × 10^{-3} in parentheses.)

XIa	449 (78)	428 (85)	XV	484 (120)
XIIa	450 (87)	423 (89)	XVI	483 (121)
XIIIa	—	425 (71)	I	472 (115)
			Natural echinenone [2]	466—468
XIc	518 (116)	485 (128)	,, aphanin [4]	472
XIIc	520 (121)	485 (130)		
XIIIc = V	—	480 (118)		
Natural canthaxanthin [7]	—	480 (118)		

The visible-light absorption properties of the polyene ketones mentioned above are summarised in Table 1. It is noteworthy that the fine structure typical of the spectra of the majority of carotenoids, and present in those of the acyclic ketones, is lacking in the spectra of the natural and the synthetic *cyclo*hexenones.



Some important features of the infrared spectra of the polyene ketones are indicated in Table 2. There are significant differences between the bands due to the conjugated carbonyl group in the *cyclo*hexenones and in the related acyclic ketones. In the former, which perforce have an *s-trans*-configuration about the bond joining the carbonyl group and the polyene chain, absorption is at lower frequencies and of much greater intensity (per C=O group) than in the latter. This lends considerable support to the suggestion made in the previous paper that polyene ketones with a bulky terminal group adopt an *s-cis*-configuration.

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[12] Ahmad and Weedon, *J.*, 1953, 3286.
[13] Isler, Gutman, Lindlar, Montavon, Rüegg, Ryser, and Zeller, *Helv. Chim. Acta*, 1956, **39**, 463.
[14] Karrer and Solmssen, *ibid.*, 1937, **20**, 682; Karrer, Solmssen, and Gugelmann, *ibid.*, p. 1020.

TABLE 2. *Infrared light absorption of polyene ketones* (KBr *discs or, where indicated,* $CHCl_3$ *solutions*).

(Frequencies in cm.$^{-1}$; relative intensity in parentheses.)

	Unconjug. C=O stretching	Conjug. C=O stretching	Conjug. C=C stretching region				CH out-of-plane deformation region of conjug. *trans*-CH=CH		
XIa		1668s	1603m	1569vs	1535m		1004m	989s	
XIc		1672s		1584s	1546vs		1006ms	983s	968s
		1674 (387) *							
XV		1669s		1574vs	1550vs	1512s	1003s	985s	964vs
XIIa	1709s	1669s	1607m	1566vs	1538m		1004m	988s	
XIIb	1706s	1671s		1586vs			1001m	986s	970w
XIIc	1708s	1671s		1582s	1547vs		1004ms	980s	968s
	1715 (~660) *	1672 (~395) *							
XVI	1709m	1667m	1600w	1575s	1550s	1506s	1003m		966s
XIIIa		1652vs	1610m	1563s	1538w			991vs	966w
V		1658vs	1608w	1581m	1555s		998m		966s
		1651 (940) *							
I		1657s			1550m		1003m		966vs
		1655 (440) *							

* In $CHCl_3$; vs, very strong; s, strong; ms, medium strong; m, medium; w, weak.

EXPERIMENTAL

(See notes preceding the Experimental section to Part VI.)

4-Cyano-2 : 2-dimethylbutanal[15] (with N. F. HOLYER).—A styrene-type quaternary ammonium anion-exchange resin [Amberlite resin, IRA-400 (OH), Rohm and Haas Co., Phil., U.S.A., B.D.H., Poole, Eng.] was steeped overnight in 5% aqueous sodium hydroxide, then washed with water and finally with acetone.

Acrylonitrile (150 g.) was added slowly to a well-stirred and cooled (ice) mixture of *iso*butyraldehyde (200 g.) and the pre-treated ion-exchange resin (54 g.). By regulating the rate of addition the temperature of the mixture was kept at 50—55°. After the addition of the acrylonitrile, the mixture was warmed to 70° for 150 min. The mixture was then cooled and filtered. The filtrate was dried (Na_2SO_4) and distilled to give the cyano-aldehyde (200 g.), b. p. 79—81·5°/0·4 mm., n_{D}^{22} 1·4381 (Tschudi and Schinz[16] give b. p. 70—75°/0·1 mm., n_{D}^{20} 1·4349).

αα-Dimethylglutaric Acid.—The above cyano-aldehyde (200 g.) was slowly added to a mixture of 65% nitric acid (330 ml.) and concentrated sulphuric acid (50 ml.) at 60°. By adjustment of the rate of addition, and occasional cooling in ice, the temperature of the mixture was kept at 70—75°. When the addition of the cyano-aldehyde was complete (3 hr.), the solution was kept at 70—75° for a further hour. The mixture was cooled and diluted with ice-water (200 g.), and the precipitated product filtered off. Recrystallisation from water gave αα-dimethylglutaric acid (120 g.), m. p. 80—82° (Tiemann[17] gives m. p. 85°; Wendt[18] gives m. p. 78°).

Dimethyl αα-Dimethylglutarate.—A solution of αα-dimethylglutaric acid (160 g.) and concentrated sulphuric acid (8 ml.) in methanol (2 l.) was refluxed for 16 hr., then cooled. Excess of solid sodium hydrogen carbonate was added and the methanol was distilled off. The residual oil in ether (600 ml.) was washed with water and dried (Na_2SO_4). Distillation gave dimethyl αα-dimethylglutarate (120 g.), b. p. 117—119°/20 mm., n_{D}^{23} 1·4281 (Blaise[19] gives b. p. 215°).

Methyl Hydrogen αα-Dimethylglutarate.—A solution of dimethyl αα-dimethylglutarate (106 g.) and potassium hydroxide (35 g.) in methanol (650 ml.) was kept at 20° for 16 hr. The mixture was refluxed for 2 hr., then cooled and evaporated to dryness under reduced pressure. The solid residue was treated with the theoretical quantity of 2N-hydrochloric acid, and the liberated half-ester was extracted with ether. The ethereal extracts were washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. Distillation of the residue from a

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[15] Cf. Howk and Langkammerer, U.S.P. 2,579,580.
[16] Tschudi and Schinz, *Helv. Chim. Acta*, 1950, **33**, 1865.
[17] Tiemann, *Ber.*, 1900, **33**, 2942.
[18] Wendt, *Ber.*, 1941, **74**, 1242.
[19] Blaise, *Bull. Soc. chim. France*, 1899, **21**, 626.

Kon flask gave an oil (b. p. 98—99°/0·05 mm., n_D^{22} 1·4391) which readily crystallised. Recrystallisation from light petroleum gave *methyl hydrogen αα-dimethylglutarate* (76 g.) as needles, m. p. 43·5—45·0° (Found: C, 54·75; H, 8·15. $C_8H_{14}O_4$ requires C, 55·15; H, 8·1%).

Methyl 2 : 2-*Dimethyl*-5-*oxoheptanoate* (VII).—The preceding methyl half-ester (76 g.) was dissolved in thionyl chloride (120 ml.), and the solution kept at 20° for 3 days. After removal of excess of thionyl chloride at reduced pressure, the residual acid chloride, in benzene (300 ml.), was slowly added to a stirred solution of ethylcadmium (from 100 g. of ethyl bromide) in benzene (1 l.). The mixture was refluxed for 50 min., then cooled. Ice and 2N-sulphuric acid (250 ml.) were added. Isolation of the product with benzene in the usual way and fractional distillation (Stedman column, 15 × 2 cm.; partial take-off head) gave the above *keto-ester* (52 g.), b. p. 74—75°/0·7 mm., n_D^{21} 1·4352 (Found: C, 64·35; H, 9·8. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·75%). A solution of the keto-ester (200 mg.), semicarbazide hydrochloride (300 mg.), and crystalline sodium acetate (0·5 g.) in aqueous ethanol (1 : 1; 4 ml.) was kept at 0° for 14 days. Water (2 ml.) was added and the mixture was kept at 0° for 1 hr. Collection of the solid and recrystallisation from aqueous methanol gave the *semicarbazone* (240 mg.) as plates, m. p. 123—124° (Found: C, 54·4; H, 8·55. $C_{11}H_{21}O_3N_3$ requires C, 54·3; H, 8·7%).

2 : 2-*Dimethyl*-5-*oxoheptanoic Acid*.—Methyl 2 : 2-dimethyl-5-oxoheptanoate (1·0 g.), 5N-sodium hydroxide (1·2 ml.), and methanol (1·5 ml.) were refluxed together for 30 min. Water (1·0 ml.) was added and refluxing was continued for 60 min. The mixture was cooled and evaporated almost to dryness. Water (1·0 ml.) was added and the evaporation was repeated. A solution of the wet residue in water (5 ml.) was acidified with 2N-hydrochloric acid, and the liberated organic acid was isolated with ether. Crystallisation from pentane, containing a trace of ether, gave the keto-acid (0·6 g.), m. p. 24—26·5°. The 2 : 4-*dinitrophenylhydrazone*, crystallised from aqueous methanol, had m. p. 112—126° (Found: C, 50·85; H, 5·8. $C_{15}H_{20}O_6N_4$ requires C, 51·15; H, 5·7%). The *benzylammonium salt* crystallised from ethyl acetate–light petroleum (9 : 1) as needles, m. p. 75° (Found: C, 68·55; H, 9·0. $C_{16}H_{25}O_3N$ requires C, 68·8; H, 9·0%). When kept at 10^{-6} mm. the salt lost benzylamine.

Methyl 5-*Ethylenedioxy*-2 : 2-*dimethylheptanoate* (VIII; Y = Me).—A mixture of methyl 2 : 2-dimethyl-5-oxoheptanoate (42 g.), 2-ethylenedioxybutane (110 g.), and toluene-*p*-sulphonic acid (0·2 g.) was refluxed through a fractionating column (Stedman, 15 × 2 cm.) under a partial take-off head. At intervals during 7 hr. small portions of the distillate were withdrawn until a total of 37 ml. had been collected. The mixture was cooled, washed with saturated aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and distilled through the same fractionating column, to give the *ethylenedioxy-ester* (32 g.), b. p. 90—92°/1·0 mm., n_D^{21} 1·4438 (Found: C, 63·25; H, 9·8. $C_{12}H_{22}O_4$ requires C, 62·6; H, 9·65%).

5-*Ethylenedioxy*-2 : 2-*dimethylheptanoic Acid* (VIII; Y = H). The above ethylenedioxy-ester (32 g.), 5N-sodium hydroxide (28·0 ml.), and methanol (35 ml.) were refluxed together for 30 min. Water (22 ml.) was added and the mixture was refluxed for 1 hr. The mixture was cooled and evaporated almost to dryness. Water (15 ml.) was added, and most of the solvent was again evaporated. A solution of the residue in water (100 ml.) was cooled to 0° and shaken with ether (250 ml.) whilst 2N-hydrochloric acid was added until the mixture was almost neutral. The organic layer was separated, and the aqueous phase was extracted with ether (50 ml. × 3). The combined ethereal solutions were dried ($MgSO_4$) and evaporated. Crystallisation of the residual oil from pentane, containing a trace of ether, gave the ethylenedioxy-acid (28 g.) as prisms, m. p. 15—17°, mixed m. p. with the keto-acid described above, 0—15°.

Treatment of the ethylenedioxy-acid with Brady's reagent gave the 2 : 4-dinitrophenylhydrazone of the corresponding keto-acid, m. p. and mixed m. p. 111—126°.

Addition of benzylamine (0·5 ml.) in benzene (0·5 ml.) to the ethylenedioxy-acid (0·5 g.) gave a pale yellow solid. Recrystallisation from ethyl acetate–light petroleum (9 : 1) gave the *benzylammonium salt* (0·4 g.), m. p. 88—88·5°, mixed m. p. with the corresponding derivative of the keto-acid 66—68° (Found: C, 66·85; H, 9·35. $C_{18}H_{29}O_4N$ requires C, 66·85; H, 9·05%).

6-*Ethylenedioxy*-3 : 3-*dimethyloctan*-2-*one* (IX).—5-Ethylenedioxy-2 : 2-dimethylheptanoic acid (27 g.) in ether (100 ml.) was slowly added to a vigorously stirred solution of methyllithium (6·1 g.) in ether (250 ml.). The mixture was refluxed for 90 min., then cooled to 0°. Cold water (100 ml.) was added. Isolation of the product with ether in the usual way and distillation gave the *ethylenedioxy-ketone* (22 g.), b. p. 78—84°/0·5 mm., n_D^{21} 1·4508 (Found:

C, 67·55; H, 10·9. $C_{12}H_{22}O_3$ requires C, 67·25; H, 10·35%). The *semicarbazone* (92% yield) crystallised from aqueous methanol as plates, m. p. 119·5° (Found: C, 57·35; H, 9·3. $C_{13}H_{25}O_3N_3$ requires C, 57·55; H, 9·3%). Treatment of the ethylenedioxy-ketone with Brady's reagent gave the derivative of the corresponding diketone in 89% yield. Crystallisation from dioxan–methanol–water (1 : 1 : 1) gave 3 : 3-*dimethyloctane*-2 : 6-*dione* 2 : 4-*dinitrophenylhydrazone* as orange needles, m. p. 179—185° (Found: C, 49·9; H, 5·15. $C_{22}H_{26}O_8N_8$ requires C, 49·8; H, 4·95%).

3 : 24-*Di*(*ethylenedioxy*)-6 : 6 : 10 : 17 : 21 : 21-*hexamethylhexacosa*-8 : 10 : 12 : 14 : 16 : 18-*hexaene*-7 : 20-*dione* (XIa).—A mixture of 2 : 9-dimethyldeca-2 : 4 : 6 : 8-tetraenedial (206 mg.), 6-ethylenedioxy-3 : 3-dimethyloctan-2-one (5·0 g.) and aluminium *tert.*-butoxide (1·0 g.) in benzene (10 ml.) was heated under reflux for 20 hr., then cooled and diluted with benzene (100 ml.). The solution was washed successively with 0·05N-sulphuric acid, saturated sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and evaporated. Excess of 6-ethylenedioxy-3 : 3-dimethyloctan-2-one was distilled off at 60° (bath-temp.)/10^{-6} mm. Chromatography of the residue in benzene on alumina, isolation of the main yellow band, and crystallisation from benzene–light petroleum gave the hexaenedione (162 mg.) as yellow needles, m. p. 143—146°.

6 : 6 : 10 : 17 : 21 : 21-*Hexamethylhexacosa*-8 : 10 : 12 : 14 : 16 : 18-*hexaene*-3 : 7 : 20 : 24-*tetraone* (XIIa).—A solution of the preceding hexaenedione (136 mg.) in acetone (60 ml.) containing toluene-*p*-sulphonic acid (20 mg.) was refluxed for 90 min. The mixture was cooled, diluted with benzene (100 ml.), washed with saturated sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and evaporated. Recrystallisation of the residue from benzene–light petroleum gave the *tetraone* (105 mg.) as yellow needles, m. p. 105—107° (Found: C, 78·0; H, 9·4. $C_{32}H_{46}O_4$ requires C, 77·7; H, 9·35%).

3 : 10-*Dimethyl*-1 : 12-*di*-(2 : 6 : 6-*trimethyl*-3-*oxo*cyclo*hex*-1-*enyl*)*dodeca*-1 : 3 : 5 : 7 : 9 : 11-*hexaene* (XIIIa).—A solution of the above hexaenetetraone (36 mg.) in 10% methanolic potassium hydroxide (50 ml.) and benzene (5 ml.) was refluxed for 2½ hr. The mixture was cooled, diluted with benzene (100 ml.), washed successively with water, 0·5N-sulphuric acid, saturated sodium hydrogen carbonate solution, and water, dried (Na_2SO_4), and evaporated. Chromatography of the residue from benzene on alumina gave two bands, A and B, which were eluted with benzene. The solution from the more readily eluted band A was evaporated, and the residue was crystallised from light petroleum, to give the *dione* (10·5 mg.) as orange-yellow needles, m. p. 203° (Found: C, 83·3; H, 9·5. $C_{32}H_{42}O_2$ requires C, 83·8; H, 9·25%). The solution from band B was evaporated, and the residue was recycled to give a further 3 mg. of the required dione (total yield 13·5 mg., 40%).

3 : 24-*Di*(*ethylenedioxy*)-6 : 6 : 10 : 17 : 21 : 21-*hexamethylhexacosa*-8 : 10 : 16 : 18-*tetraene*-12 : 14-*diyne*-7 : 20-*dione* (XIb).—A solution of 2 : 9-dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-dial [12] (100 mg.), 6-ethylenedioxy-3 : 3-dimethyloctan-2-one (2 ml.), and aluminium *tert.*-butoxide (1·0 g.) in benzene (10 ml.) was boiled for 20 hr. and then cooled. Isolation of the product in the usual way gave the *dione*, which crystallised from benzene–light petroleum in yellow prisms (56 mg.), 114—115° (Found: C, 74·8; H, 8·9. $C_{36}H_{50}O_6$ requires C, 74·7; H, 8·7%), $\lambda_{max.}$ (in *n*-hexane) 403, 373, 347, and 254 mμ ($\varepsilon \times 10^{-3}$, 50·4, 51·9, 42·1, and 16·7 respectively).

6 : 6 : 10 : 17 : 21 : 21-*Hexamethylhexacosa*-8 : 10 : 16 : 18-*tetraene*-2 : 14-*diyne*-3 : 7 : 20 : 24-*tetraone* (XIIb).—A solution of the preceding dione (42 mg.) and toluene-*p*-sulphonic acid (20 mg.) in acetone (24 ml.) was boiled for 90 min. Isolation of the product in the usual way gave the *tetraone* which crystallised from benzene–light petroleum as yellow prisms (8 mg.), m. p. 127—128° (Found: C, 78·45; H, 8·2. $C_{32}H_{42}O_4$ requires C, 78·35; H, 8·65%), $\lambda_{max.}$ (in *n*-hexane) 402, 372, 346, and 254 mμ ($\varepsilon \times 10^{-3}$, 45·0, 46·0, 37·6, and 14·9 respectively).

3 : 30-*Di*(*ethylenedioxy*)-6 : 6 : 10 : 14 : 19 : 23 : 27 : 27-*octamethyldotriaconta*-8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24-*nonaene*-7 : 26-*dione* (XIc).—A suspension of crocetindial [20] (253 mg.) in a mixture of 6-ethylenedioxy-3 : 3-dimethyloctan-2-one (4·2 ml.) and 5% ethanolic potassium hydroxide (6·0 ml.) was kept at 20°, and shaken occasionally, for 4 hr. The mixture was then refluxed for 15 min., cooled, diluted with benzene (100 ml.), washed successively with water, 0·05N-sulphuric acid, saturated sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and evaporated. The oily residue, consisting mainly of excess of the initial methyl ketone, was diluted with light petroleum (40 ml.) and kept overnight at 0°.

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[20] Isler, Gutmann, Lindlar, Montavon, Rüegg, Ryser, and Zeller, *Helv. Chim. Acta*, 1956, **39**, 463.

The deep-red leaflets (362 mg.), m. p. 170—172°, which had separated were collected and recrystallised from benzene–light petroleum to give the *nonaenedione* as deep-red leaflets, m. p. 174° (Found: C, 76·5; H, 9·85. $C_{44}H_{64}O_6$ requires C, 76·7; H, 9·35%).

6 : 6 : 10 : 14 : 19 : 23 : 27 : 27-*Octamethyldotriaconta*-8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24-*nonaene*-3 : 7 : 26 : 30-*tetraone* (XIIc).—A solution of the preceding nonaenedione (310 mg.) in acetone (50 ml.) containing toluene-*p*-sulphonic acid (20 mg.) was refluxed for 60 min., then cooled, diluted with benzene (150 ml.), washed with saturated sodium hydrogen carbonate solution and water, and dried (Na_2SO_4). Evaporation, and crystallisation of the residue from benzene–light petroleum, gave the *nonaenetetraone* (174 mg.) as deep-red plates, m. p. 174° (Found: O, 10·5. $C_{40}H_{56}O_4$ requires O, 10·65%). The mother-liquors from the above crystallisations were evaporated to dryness and the residue dissolved in acetone (25 ml.) containing toluene-*p*-sulphonic acid (10 mg.). In 3 days at 0°, the solution deposited deep-red crystals which recrystallised from benzene–light petroleum to give a further 23 mg. of the nonaenetetraone (total yield 197 mg., 72%).

Canthaxanthin (V).—A suspension of the preceding nonaenetetraone (100 mg.) in 10% methanolic potassium hydroxide (150 ml.) and benzene (20 ml.) was refluxed for 2 hr. (A homogeneous solution was obtained after 30 min.) The mixture was cooled, diluted with benzene (250 ml.), washed successively with water, 2N-sulphuric acid, saturated sodium hydrogen carbonate solution, and water, dried (Na_2SO_4), and evaporated. Chromatography of the residue from benzene solution on grade III alumina gave two red bands, A and B, which were eluted with benzene. The solution from the more readily eluted band A was evaporated to dryness and the residue crystallised from benzene–light petroleum to give canthaxanthin (23 mg.) as red prisms, m. p. 215° (Found: O, 5·7. $C_{40}H_{52}O_2$ requires O, 5·65%). The solution from band B was evaporated to dryness and the residue recycled to give a further 8 mg. of canthaxanthin (total yield 31 mg., 33%). No study was made of the optimum conditions for the cyclisation. (For natural canthaxanthin, Petracek and Zechmeister [7] give m. p. 213°.)

3-*Ethylenedioxy*-6 : 6 : 10 : 14 : 19 : 23-*hexamethyl*-25-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*enyl*)-*pentacosa*-8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24-*nonaen*-7-*one* (XV).—A suspension of β-*apo*-2-carotenal (102 mg.) in a mixture of 6-ethylenedioxy-3 : 3-dimethyloctan-2-one (4·2 ml.) and 5% ethanolic potassium hydroxide (4·2 ml.) was kept at 20°, and shaken occasionally, for 6½ hr. The mixture was then refluxed for 15 min., cooled, diluted with benzene (60 ml.), washed successively with water, 0·05N-sulphuric acid, saturated sodium hydrogen carbonate solution, and water, dried (Na_2SO_4), and evaporated. The excess of the initial methyl ketone was distilled off at 60° (bath-temp.)/10^{-6} mm. Chromatography of the residue from light petroleum on grade III alumina gave one main red band which was eluted with benzene–light petroleum (1 : 1). Evaporation and crystallisation of the glass-like residue from light petroleum gave the *nonaenone* (47·5 mg.) as violet needles, m. p. 124—125° (Found: O, 7·9. $C_{42}H_{60}O_3$ requires O, 7·85%).

6 : 6 : 10 : 14 : 19 : 23-*Hexamethyl*-25-(2 : 6 : 6-*trimethyl*cyclo*hex*-1-*enyl*)*pentacosa*-8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24-*nonaene*-3 : 7-*dione* (XVI).—A solution of the preceding nonaenone (86 mg.) in acetone (50 ml.) containing toluene-*p*-sulphonic acid (10 mg.) was kept overnight at 20°. The mixture was then refluxed for 30 min., cooled, diluted with benzene (60 ml.), washed successively with saturated sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. Crystallisation of the residue from methanol–light petroleum gave the *nonaenedione* (27 mg.) as dull red prisms, m. p. 124° (Found: O, 6·0. $C_{40}H_{56}O_2$ requires O, 5·65%). The mother-liquors from the above crystallisations were combined and evaporated. Chromatography of the residue from light petroleum on grade III alumina gave one main red band which was developed with benzene–light petroleum (b. p. 60—80°) and eluted with benzene. Evaporation and crystallisation of the resdue from light petroleum gave a further 10·5 mg. of the nonaenedione (total yield 37 mg., 46%).

Echinenone (I).—A solution of the preceding nonaenedione (28 mg.) in 10% methanolic potassium hydroxide (35 ml.), containing benzene (5 ml.), was refluxed for 150 min. The product crystallised out from the hot mixture as violet plates, m. p. 186—187°. Recrystallisation from benzene–methanol gave echinenone (23 mg.) as violet plates, m. p. 187° (Found: C, 87·25; H, 10·05. $C_{40}H_{54}O$ requires C, 87·2; H, 9·9%). (For natural echinenone, Lederer [1] gives m. p. 178—179° and 192°; for synthetic echinenone Petracek and Zechmeister [7] give m. p. 175—178°.)

Dried *Anabaena cylindrica* (1·9 g.) was extracted at 20° with methanol (25 ml.) for 4 days, then with ether (25 ml.) for 5 hr., and again with ether (30 ml.) for 16 hr. The extracts were combined and evaporated. Chromatography of the residue on alumina (grade IV) first from benzene and then from light petroleum (b. p. 40—60°) gave a reddish-brown band, $\lambda_{max.}$ 472 mμ (492 mμ in CS_2). In a mixed chromatogram this band did not separate from synthetic echinenone.

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