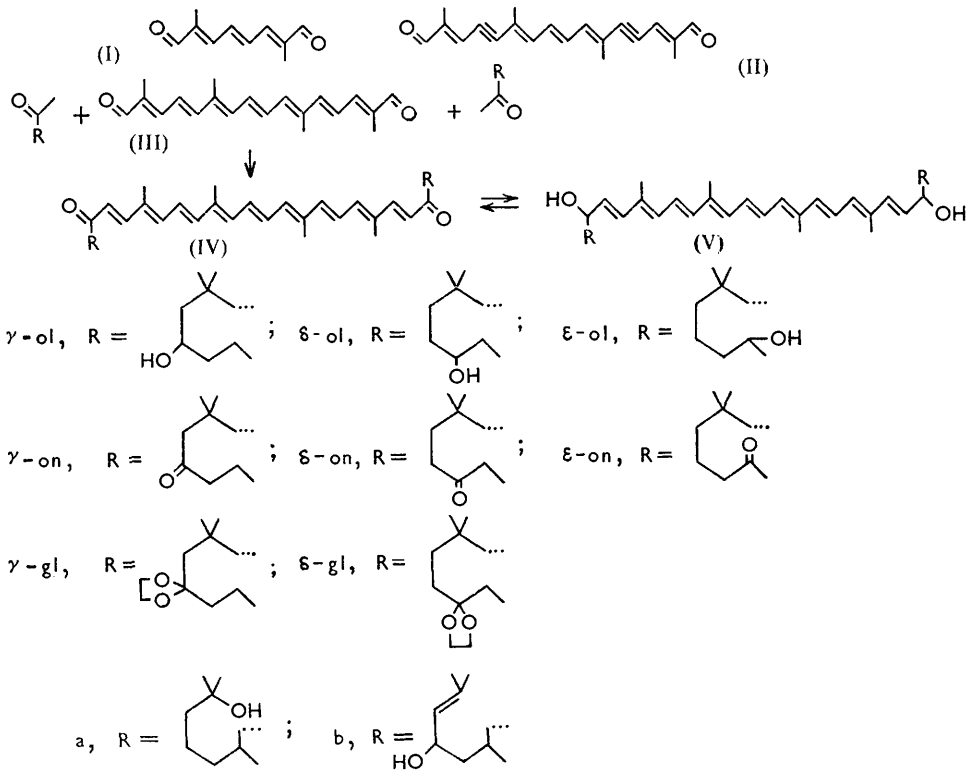
803. *Carotenoids and Related Compounds. Part VI.* Some Conjugated Polyene Diketones, and their Comparison with Capsorubin.*

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

The formulation of capsorubin as a conjugated nona-unsaturated dione has been confirmed, and four such structures have been excluded by synthetical means.

Capsorubin, a pigment found in small amounts in red peppers (*Capsicum annuum*), contains four oxygen atoms of which two are present in hydroxyl groups. To account for the remaining oxygen atoms, the results of microhydrogenation, and the similarity in the visible spectrum with those of β-carotenone and bixin-dial, Zechmeister and Cholnoky [1] proposed for capsorubin a partial structure of type (IV). No carbonyl reactions were reported, but ketones of the type envisaged are known to be rather inert.



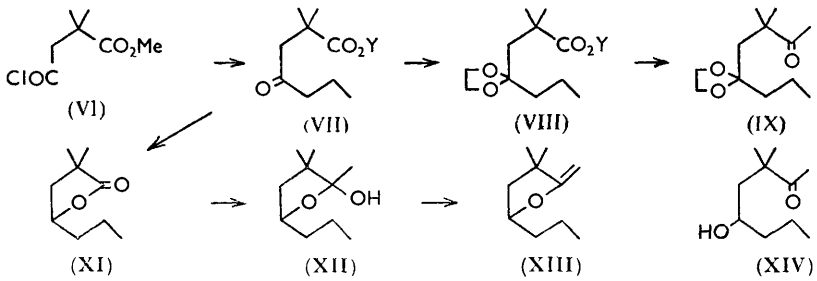
Support for the partial structure (IV) has previously been provided by the synthesis from both the C_{10} dial [2] (I) and the C_{20} dial [3] (II) of the nonaenedione (IV; R = Bu^t) which also resembled capsorubin closely in its visible-light absorption. Further confirmation of the chromophore has now been obtained in three independent ways. (i) Examination of the infrared spectrum of capsorubin revealed a band also present in the spectra of authentic compounds of the type (IV), and attributable to conjugated

* Part V, *J.*, 1954, 4168.

[1] Zechmeister and Cholnoky, *Annalen*, 1934, **509**, 269; 1935, **516**, 30; 1940, **543**, 248.
[2] Ahmad and Weedon, *J.*, 1953, 3815.
[3] *Idem*, *J.*, 1953, 3286.

carbonyl groups. (ii) Treatment of capsorubin with potassium borohydride resulted in shifts in the visible-light absorption maxima consistent with selective reduction of two terminal carbonyl groups to give a nonaene chromophore. That no further transformation had occurred was shown by regeneration of capsorubin on oxidation (see below). Similar reduction of capsanthin with potassium borohydride gave capsanthol, which has previously been prepared by the Ponndorf method.[4] (iii) Alkaline degradation of capsorubin furnished crocetin-dial (III). The reaction, which is analogous to the conversion of capsanthin into β-citraurin,[5] may be regarded as a fission of the double bonds αβ to the carbonyl groups.

The structural problem with capsorubin is therefore largely confined to the nature of the two end groups (R in IV). Zechmeister and Cholnoky [1] favoured the "γ-hydroxy-ketone structure" (IV; γ-ol), and more recently Karrer and his colleagues [6] suggested the "ε-hydroxy-ketone structure" (IV; ε-ol). In view of the scarcity of capsorubin, it seemed that these and related structures could be most readily checked by synthetical means. During our work along these lines Isler *et al.*[7] developed a route to crocetin-dial (III) which made this compound more readily available than the diacetylenic analogue (II) and greatly facilitated our investigations.



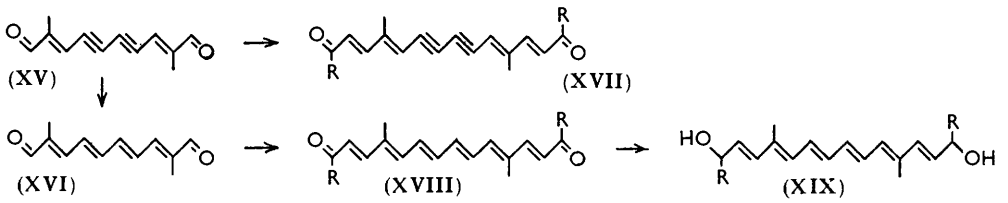
Reaction of the half-ester acid chloride (VI) of αα-dimethylsuccinic acid with di-*n*-propylcadmium gave the keto-ester (VII; Y = Me). Hydrolysis and catalytic reduction of the resulting acid (VII; Y = H), yielded the γ-lactone (XI). This reacted with methylmagnesium bromide to give the unsaturated ether (XIII), dehydration of the initial product (XII) occurring on distillation. With Brady's reagent the ether (XIII) readily gave a derivative of the corresponding hydroxy-ketone (XIV), but attempts to hydrolyse the ether and condense the product with aldehydes were unsuccessful, doubtless owing to the ease of cyclisation of the hydroxy-ketone (XIV). Attention was therefore directed to a related methyl ketone with a suitably protected oxygen group at position 5.

Exchange of ethylenedioxy-group [8] between the γ-keto-ester (VII; Y = Me) and 2-ethylenedioxybutane could not be achieved, presumably for steric reasons as the required reaction occurred readily with the isomeric δ-keto-ester [9] and with ethyl lævulate. However, reaction of the γ-keto-ester (VII; Y = Me) with ethylene glycol under carefully controlled conditions gave the dioxolan (VIII; Y = Me); glycol esters of the acid (VII; Y = H) formed simultaneously were converted into the starting material and re-cycled with unchanged keto-ester. Alkaline hydrolysis then gave the corresponding acid (VIII; Y = H) which on treatment with methyl-lithium furnished the required methyl ketone (IX). This formed a monosemicarbazone but, owing to hydrolysis of the protecting group, a bis-2 : 4-dinitrophenylhydrazone.

In previous condensations of polyene-dials with methyl ketones the latter were used

[4] Karrer and Hübner, *Helv. Chim. Acta*, 1936, **19**, 474; cf. Goodwin, Land, and Sissins, *Biochem. J.*, 1956, **64**, 486.
[5] Zechmeister and Cholnoky, *Annalen*, 1937, **530**, 291.
[6] Entschel, Eugster, and Karrer, *Helv. Chim. Acta*, 1956, **39**, 1263.
[7] Isler, Gutmann, Lindlar, Montavon, Rüegg, Ryser, and Zeller, *ibid.*, 1956, **39**, 463.
[8] Dauben, Löken, and Ringold, *J. Amer. Chem. Soc.*, 1954, **76**, 1359.
[9] Warren and Weedon, following paper.

in large excess (*ca.* 500 mol.). To develop methods more suitable for use with our ketone (IX) and with related ketones, various condensations were carried out with simple methyl ketones and crocetin-dial (III) to give the nonaenediones (IV; R = Me, Pr^i, and Bu^t); also between acetone, pinacolone, and ketone (IX) with both the dienediynedial [2] (XV) and the tetraenedial (XVI) to give the derived diketones (XVII and XVIII, R = Me, and Bu^t; XVII, γ-gl; and XVIII, γ-gl). The tetraenedial (XVI) was obtained by partial reduction



(γ-ol and other suffixes have the values assigned above.)

of the dienediynedial (XV); the initial product gave a higher-melting form on irradiation. The spectral properties of the two isomers indicated that they were the " central di-*cis* "- and the " all-*trans* "-form respectively. Both on condensation with pinacolone gave the same product, stereomutation of the " di-*cis* "-structure occurring during the reaction.

Condensation of crocetin-dial (III) with the ketone (IX) was next studied; the yield of the dione (IV; γ-gl) ranged from 0 to 48% depending on the precise conditions used. Removal of the protecting groups by treatment with acetone and toluene-*p*-sulphonic acid gave the tetraone (IV; γ-on) in 55% yield. The isomeric tetraone (IV; δ-on) was prepared similarly (see following paper), and β-carotenone (IV; ε-on) by oxidation of β-carotene.[10] An attempt to oxidise capsorubin to a tetraketone for comparison with the three synthetic materials unfortunately failed. The possibility of converting the latter into dihydroxy-diketones, by reduction of the four carbonyl groups and subsequent selective oxidation of the two allylic hydroxyl groups, was therefore examined.

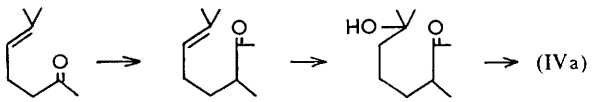
After model experiments with the hexaenes (XVIII, R = Bu^t; XVIII, γ-on and δ-on), the tetraketones (IV; γ-on, δ-on, and ε-on) were reduced with potassium borohydride to the corresponding tetraols (V). Selective methods for the regeneration of the polyene-diketone chromophore were studied on the hexaenediol (XIX; R = Bu^t). Oxidation with manganese dioxide, surprisingly, failed. Treatment with *N*-bromosuccinimide in chloroform [11] gave the hexaenedione (XVIII; R = CMe_3) in 9% yield. Oxidation with *o*-chloranil, a reagent recently developed by Braude, Linstead, *et al.*,[12] destroyed the polyene system, but substitution of *p*-chloranil for the *o*-quinone gave the hexaenedione in 20% yield. Application of the latter method to the hydroxy-compounds formed on reduction of capsanthin and capsorubin with potassium borohydride regenerated the two carotenoids. However, no nonaene diketone was obtained on treatment of the tetraol (V; γ-ol) with *p*-chloranil, and therefore the γ-hydroxy-ketone structure (IV; γ-ol) cannot represent capsorubin. Oxidation of the two isomeric tetraols (V; δ-ol and ε-ol) gave the dihydroxy-diketones (IV; δ-ol and ε-ol) in 9 and 6% overall yields from the tetraones (IV; δ-on and ε-on). These results, and those of small-scale experiments with the hexaenetetraols (XIX; γ-ol and δ-ol), suggested that hydroxyl substituents in the γ-position interfere with the oxidation of polyene glycols by *p*-chloranil, possibly owing to a cyclic attack on an intermediate carbonium ion.

Both the dihydroxy-diketones (IV; δ-ol and ε-ol) had visible-light absorption properties which resembled those of capsorubin very closely. The infrared spectra exhibited many similar characteristics but there were a number of significant differences, notably in the 1000—1100 $cm.^{-1}$ region. Further, the synthetic materials differed from the natural

[10] Kuhn and Brockmann, *Ber.*, 1932, **65**, 894; 1934, **67**, 885; *Annalen*, 1935, **516**, 123.
[11] Cf. Petracek and Zechmeister, *J. Amer. Chem. Soc.*, 1956, **78**, 1427.
[12] Braude, Linstead, and Wooldridge, *J.*, 1956, 3070.

in melting point and chromatographic behaviour. There seems little doubt, in view of their mode of formation, that the synthetic compounds have an " all-*trans* "-structure. Since stereomutation of capsorubin gives no isomers with visible-light absorption at longer wavelengths,[1] the natural carotenoid must also be " all-*trans*." The differences in properties between the natural and the synthetic compounds seem greater than can be attributed to stereoisomerism involving the hydroxy-substituents [cf. similarity of the (±)- and the (−)-form of zeaxanthin [13,14]] and it is therefore concluded that capsorubin has neither of the structures (IV; δ-ol and ε-ol).

Consideration of the infrared absorption of capsorubin and synthetic nonaene diketones at 1000—1100 cm.$^{-1}$ led at one stage to the view that the natural carotenoid might possess a structure of the lycopene type. One such possibility was (IVa), but this too was excluded in the following way. A Darzens reaction between methylheptenone (XX) and ethyl α-chloropropionate yielded the ketone (XXI), which was hydrated with sulphuric acid to give the hydroxy-ketone (XXII). This on condensation with crocetin-dial (III) gave (11%) the dihydroxy-diketone (IVa), which also differed from capsorubin.



(XX) (XXI) (XXII)

The visible-light absorption properties of the polyene diketones mentioned above are summarised in Table 1. The nonaene diketones have spectra very similar to that of capsorubin, though greater fine structure is observed with the dimethyl and the di*iso*propyl diketone (IV; R = Me and Pr^{i}).

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

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

	Hexaenes				*Nonaenes*			
(XVIII; R = Me)	441 (67·7)	416 (68·1)			(IV; R = Me)	515 (93)	482 (104)	456 (69)
(XVIII; R = Bu^{t})	445 (75)	420 (76)	398 (47·5)		(IV; R = Pr^{i})	518 (103)	483 (115)	458 (78)
(XVIII; γ-gl)	449 (79)	424 (86)			(IV; R = Bu^{t})	518 (114)	483 (124)	
(XVIII; γ-on)	450 (84)	424 (86)			(IV; γ-gl)	518 (112)	484 (127)	
(XVIII; δ-gl) [9]	449 (78)	424 (85)			(IV; γ-on)	520 (117)	486 (123)	
(XVIII; δ-on) [9]	450 (87)	423 (89)			(IV; δ-gl) [9]	518 (116)	485 (128)	
(XVIII; δ-ol)	450 (83·5)	424 (85·5)			(IV; δ-on) [9]	520 (121)	485 (130)	
					(IV; δ-ol)	520 (123)	485 (130)	
					(IV; ε-on)	520 (113)	485 (131)	
					(IV; ε-ol)	520 (120)	485 (129)	
					(IVa)	519 (121)	485 (131)	
					Capsorubin	523 (115)	489 (132)	

Some salient features of the infrared spectra of the natural and synthetic ketones are recorded in Table 2. The conjugated carbonyl stretching frequencies of most of the synthetic ketones occur within the 1660—1672 cm.$^{-1}$ range. Both capsorubin and capsanthin exhibit a well-defined maximum in this region, the intensity of the band for capsorubin being twice that for capsanthin. Moreover there is satisfactory agreement between the intensity of the band for capsorubin and those of the synthetic nonaene diketones with large *tert.*-alkyl end groups. This provides good support for the view that capsorubin and capsanthin contain two and one conjugated carbonyl group respectively. The ε values of all these compounds are, however, considerably lower than those of the dimethyl diketones and of the *cyclo*hexenones reported in the following paper. These differences may well be due to an *s-cis*-conformation's being preferred in those acyclic polyene diketones with bulky end groups (see a discussion by Erskine and Waight [15]).

[13] Karrer and Solmssen, *Helv. Chim. Acta*, 1935, **18**, 477.
[14] Isler, Lindlar, Montavon, Rüegg, Saucy, and Zeller, *ibid.*, 1956, **39**, 2041.
[15] Erskine and Waight, Chem. Soc. Symposium on " Steric Effects in Conjugated Systems," Butterworths, 1958.

Sterically hindered *s-trans*-conformations seem unlikely in view of the visible-light absorption characteristics. The possibility that the double bonds formed in the condensation of the polyene dialdehydes with methyl ketones have a (hindered-)*cis*-configuration also seems to be excluded by the visible spectra.

The polyene ketones all show much stronger absorption in the C=C stretching region than related polyenes, such as β-carotene, without carbonyl conjugation. The three tetraenediynediones examined exhibited a single strong band in the neighbourhood of 1587 cm.$^{-1}$. Most of the related hexaenediones had a strong band at slightly lower frequencies flanked by two bands of lower intensity. Most of the nonaenediones were characterised by two strong bands, at *ca.* 1584 and 1544 cm.$^{-1}$. The diketones possessing terminal methyl and *sec.*-alkyl groups had additional bands in the 1625—1660 cm.$^{-1}$ region.

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

(Frequencies in cm.$^{-1}$; also ε, or an indication of relative intensity.)

	Unconjug. C=O stretching	Conjug. C=O stretching		Conjug. C=C stretching region			CH out-of-plane deformation region of conjug. *trans*-CH=CH		
Tetraenediynediones									
XVII; γ-gl		1675s			1589vs		1001m	982m	965m
XVII; γ-on	1706s	1676s			1587vs		1003m	986w	966w
XVII; δ-on [a]	1706s	1671s			1586vs		1001m	986s	970w
Hexaenediones									
XVIII; R = Me		1658s 1668 (~615) †	1631s	1613w*	1585vs	1569w*		930s	978m
XVIII; R = Bu^t		1678s 1677 (384) †		1610m	1574vs	1541m	1006s	989s	
XVIII; γ-gl		1675s		1607m	1562vs	1538w*	1003m	989s	970m
XVIII; γ-on	1706s	1667s		1605m	1563vs	1536m	1001w	993s	979m
XVIII; δ-gl [a]		1668s		1603m	1569vs	1535m	1004w	989s	
XVIII; δ-on [a]	1709s	1669s		1607m	1566vs	1538m	1004m	988s	
Nonaenediones									
IV; R = Me		1664s 1669 (~650) †	1626s		1598s	1555s	1009s	976s*	966s
IV; R = Pr^i		1675s 1675 (~250) †	1658m 1656 ‡		1585s	1545vs	1007ms	980s	970s
IV; R = Bu^t		1669s			1587s	1543vs	1004s	979s	969s
IV; γ-gl		1667s			1585s	1543vs	1007m	977s	970s
IV; γ-on	1708s	1672s			1585s	1546vs	1003ms	977s	969s
IV; δ-gl [a]		1672s 1674 (387) †			1584s	1546vs	1006ms	983s	968s
IV; δ-on [a]	1708s 1715 (~660) †	1671s 1672 (~395) †			1582s	1547vs	1004ms	980s	968s
IV; ε-on	1706s	1667s			1584s	1543vs	1003m	982s	970s
IV; ε-ol		1668s 1664 (350) †			1587s 1586s	1548vs 1543vs	1007m 1004s	982m 982s	969m 970s
IV; δ-ol †		1664 (348)			1585s	1542vs	1003s	982s	969s
IVa †		1667m 1669 (~250) †	1639s		1584s	1542vs	1005s	982s	972s
Natural carotenoids									
Capsorubin †		1664 (387)			1582s	1542vs	1007s	982s	969s
Capsanthin † §		1661 (195)			1575s	1550vs	1006s	977s	966vs

* Shoulder. † In $CHCl_3$. ‡ Also 1645. § Also 1600m and 1506s. vs, very strong; s, strong; ms, medium-strong; m, medium; w, weak. [a] See following paper.

An outstanding feature of the spectra of " all-*trans* "-polyenes is a strong band at 964 cm.$^{-1}$ which is assigned to the CH out-of-plane deformation of the CH=CH groupings.[16,17] In all the polyene ketones now studied this band is apparently split;

[16] Lunde and Zechmeister, *J. Amer. Chem. Soc.*, 1955, **77**, 1647.
[17] *Idem, Acta Chem. Scand.*, 1954, **8**, 1421.

thus the nonaenediones exhibit a clearly discerned triplet with maxima at *ca.* 1004, 980, and 969 cm.$^{-1}$.

On the basis of thirty-seven analyses of capsorubin and its esters, dried under considerably more vigorous conditions than are normally employed, Cholnoky *et al.*[18] have recently concluded that capsorubin contains four hydrogen atoms fewer than formerly believed. This suggests several further structures for investigation. However, the formula (IVb) proposed by the Czech workers is difficult to reconcile with the infrared spectral differences discussed above, and, as a γ-hydroxy-ketone, with the regeneration of capsorubin by chloranil oxidation of the potassium borohydride reduction product.

Experimental

M. p.s were determined on samples in evacuated sealed capillary tubes.

As far as possible, operations involving unsaturated compounds were carried out in an inert atmosphere, usually of nitrogen. Solutions of polyenes were evaporated under reduced pressure. Unless stated otherwise, alumina for chromatography was pretreated as described by Cheeseman *et al.*,[19] and was Grade III on the Brockmann and Schodder activity scale.[20] Light petroleum normally refers to the fraction of b. p. 60—80°.

Except where indicated to the contrary, visible- and ultraviolet-light absorption measurements were made on benzene solutions, and infrared absorption measurements were determined on potassium bromide discs; most of the relevant spectral data are summarised in the Tables.

Oxygen analyses were carried out by Oliver's modification [21] of Unterzaucher's method.[22]

Dimethyl αα-Dimethylsuccinate.—A mixture of ethyl cyanoacetate (298 g.), acetone (184 g.), glacial acetic acid (50 g.), benzene (250 ml.), and *p*-aminophenol (1·4 g.) was refluxed under a Dean–Stark phase-separator until 55 ml. of water had been collected (cf. Prout [23]). Distillation gave ethyl α-cyano-β-methylcrotonate (318 g., 79%), b. p. 116—120°/18 mm., m. p. 27°. Recrystallisation of a specimen from light petroleum gave the cyano-ester as needles, m. p. 33° (Vogel [24] gives m. p. 33°).

A solution of potassium cyanide (330 g.) in water (600 ml.) was added to one of the cyano-ester (317 g.) in ethanol (1·5 l.), and the mixture was kept at 20° for 40 hr. (cf. Vogel [24]). Most of the solvent was distilled off and concentrated hydrochloric acid (3 l.) was cautiously added to the residue (copious evolution of hydrogen cyanide). The mixture was refluxed for 3 hr., then cooled and extracted with ether in a continuous-extractor for 3 days. Evaporation of the extract and crystallisation of the residue from concentrated hydrochloric acid gave αα-dimethylsuccinic acid (215 g.), m. p. 141—142° (Vogel [24] gives m. p. 141°).

The acid was boiled with methanol (2·2 l.) and concentrated sulphuric acid (10 ml.) for 16 hr. Excess of solid sodium hydrogen carbonate was added and the mixture was evaporated. Isolation of the product in the usual way gave the diester (214 g.), b. p. 95—97°/21 mm., n_D^{25} 1·4212 (Bone, Sudborough, and Sprankling [25] gave b. p. 201—202°).

α-Methyl β-Hydrogen αα-Dimethylsuccinate.—A solution of dimethyl αα-dimethylsuccinate (237 g.) and potassium hydroxide (85 g.) in methanol (1·5 l.) was kept at 20° for 16 hr. The mixture was refluxed for 2 hr., then evaporated to dryness. The residue was treated with the theoretical quantity of 2N-hydrochloric acid. Isolation of the product with ether, and distillation through a fractionating column (Dufton; 20 × 2 cm.), gave an oil (160·5 g.), b. p. 104°/1·5 mm., which readily crystallised. Recrystallisation from light petroleum gave α-methyl β-hydrogen αα-dimethylsuccinate (104 g., 48%), m. p. 37—41° (Bone, Sudborough, and Sprankling [25] give m. p. 40·5—41°). The forerun from the distillation was recycled and the crude product was combined with the oil from the mother-liquors of the above crystallisation. Distillation and recrystallisation of the distillate from light petroleum, gave a further 51 g. of the half-ester, m. p. 37—41°. The total yield was 155 g. (71%).

[18] Cholnoky, Szabo, and Szabolcs, *Annalen*, 1957, **606**, 194.
[19] Cheeseman, Heilbron, Jones, and Weedon, *J.*, 1949, 3120.
[20] Brockmann and Schodder, *Ber.*, 1941, **74**, 73.
[21] Oliver, *Analyst*, 1955, **80**, 593.
[22] Unterzaucher, *Ber.*, 1940, **73**, 391.
[23] Prout, *J. Org. Chem.*, 1953, **18**, 928.
[24] Vogel, *J.*, 1928, 2010.
[25] Bone, Sudborough, and Sprankling, *J.*, 1904, 534.

Methyl 2 : 2-*Dimethyl*-4-*oxoheptanoate* (VII; Y = Me).—A solution of the preceding half-ester (103 g.) in thionyl chloride (160 ml.) was kept for 3 days at 20°. Excess of thionyl chloride was removed under reduced pressure and the residual acid chloride in benzene (250 ml.) was slowly added to a vigorously stirred solution of di-*n*-propylcadmium (from 170 g. of *n*-propyl bromide) in benzene (1 l.). The mixture was refluxed for 1 hr., then cooled and treated with ice and 2N-sulphuric acid. The organic layer was separated, washed with saturated sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. Distillation of the residue through a fractionating column (Stedman; 30 × 2 cm.) under a partial take-off head, gave *methyl* 2 : 2-*dimethyl*-4-*oxoheptanoate* (89 g.), b. p. 118·5°/23 mm., n_D^{18} 1·4388 (Found: C, 64·0; H, 9·85. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·75%). The 2 : 4-*dinitrophenylhydrazone* crystallised from methanol as yellow needles, m. p. 109—110° (Found: N, 15·15. $C_{16}H_{22}O_6N_4$ requires N, 15·3%).

2 : 2-*Dimethyl*-4-*oxoheptanoic Acid* (VII; Y = H).—A solution of the preceding keto-ester (10 g.) in 10% methanolic potassium hydroxide (75 ml.) was refluxed for 2 hr., then evaporated to dryness, and the residue was treated with an excess of 2N-hydrochloric acid. Isolation of the product with ether gave the *keto-acid* (3·8 g.) which crystallised from light petroleum as prisms, m. p. 72—73° (Found: C, 62·8; H, 9·45. $C_9H_{16}O_3$ requires C, 62·75; H, 9·35%). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate as yellow prisms, m. p. 210—218° (Found: N, 15·8. $C_{15}H_{20}O_6N_4$ requires N, 15·9%).

4-*Hydroxy*-2 : 2-*dimethylheptanoic Lactone* (XI).—A solution of the preceding keto-acid (20·5 g.) in methanol (75 ml.) was shaken with Raney nickel in hydrogen at 175°/100 atm. until absorption was complete. Removal of catalyst and solvent, and distillation of the residue, gave an oil (13·5 g.), b. p. 120—125°/20 mm., and the keto-acid (3·5 g.), m. p. 70—72°. The oil, in ether, was shaken once with dilute ammonium hydrogen carbonate solution to remove traces of starting material. Isolation of the product and distillation gave the *lactone* (12·5 g.), b. p. 106—108°/15 mm., n_D^{22} 1·4355, m. p. 28—29° (unchanged on crystallisation from pentane; needles) (Found: C, 69·05; H, 10·05. $C_9H_{16}O_2$ requires C, 69·2; H, 10·3%).

Tetrahydro-3 : 3-*dimethyl*-2-*methylene*-5-*propylfuran* (XIII).—An ethereal solution (20 ml.) of methylmagnesium bromide (from 1·1 g. of magnesium) was added slowly to the preceding lactone (6·3 g.) in ether (50 ml.) at 0°. The mixture was stirred at 20° for 12 hr., boiled for 5 min., and cooled. Addition of saturated ammonium chloride and isolation of the product gave (i) the *tetrahydrofuran* (2·2 g.), b. p. 87—90°/35 mm., n_D^{21} 1·4421 (Found: C, 78·25; H, 11·95. $C_{10}H_{18}O$ requires C, 77·85; H, 11·75%), and (ii) the lactone (3·0 g.), b. p. 105—110°/17 mm., m. p. 28—29°.

Treatment of the tetrahydrofuran with Brady's reagent gave the 2 : 4-*dinitrophenylhydrazone* of 5-hydroxy-3 : 3-dimethyloctan-2-one. It crystallised from ethanol in needles, m. p. 129° (Found: N, 16·1. $C_{16}H_{24}O_5N_4$ requires N, 15·9%).

Methyl 4-*Ethylenedioxy*-2 : 2-*dimethylheptanoate* (VIII; Y = Me).—A mixture of methyl 2 : 2-dimethylheptan-4-onoate (40 g.), ethylene glycol (16·2 g.), toluene-*p*-sulphonic acid (0·1 g.), and benzene (50 ml.) was refluxed with vigorous stirring for 7 hr. under a Dean–Stark phase separator. The mixture was cooled, then washed successively with water, saturated sodium hydrogen carbonate, and water. The benzene solution was dried (Na_2SO_4) and evaporated. Distillation of the residue through a fractionating column (Stedman, 15 × 2 cm.) under a partial take-off head gave *methyl* 4-*ethylenedioxy*-2 : 2-*dimethylheptanoate* (10 g.), b. p. 144—146°/29 mm., n_D^{19} 1·4448 (Found: C, 62·3; H, 9·7. $C_{12}H_{22}O_4$ requires C, 62·6; H, 9·65%). The residue (10 g.) from the distillation consisted of a mixture of glycol esters which was converted into the original methyl ester by treatment overnight with boiling 1% (w/v) methanolic sulphuric acid (250 ml.). By combining the product with the forerun (20 g., b. p. 112—144°/29 mm.) from the preceding distillation, and recycling the material, a further quantity of the protected methyl ester was obtained. A total of three recyclisations raised the overall yield to 23·8 g. (48%) of methyl 4-ethylenedioxy-2 : 2-dimethylheptanoate.

From an attempted exchange of ethylenedioxy-group to the keto-ester from 2-ethylenedioxybutane the starting materials were recovered. A further experiment in which a small amount of ethylene glycol was added to the reaction mixture was also unsuccessful.

4-*Ethylenedioxy*-2 : 2-*dimethylheptanoic Acid* (VIII; Y = H).—Methyl 4-ethylenedioxy-2 : 2-dimethylheptanoate (8·4 g.), 5N-sodium hydroxide (7·5 ml.), and methanol (8 ml.) were refluxed together for 30 min. Water (4 ml.) was added and the mixture was refluxed for 60 min. The mixture was evaporated almost to dryness under reduced pressure; water (5 ml.)

was added and the evaporation repeated. A solution of the product in water (40 ml.) was cooled to 0° and shaken with ether (100 ml.) whilst 2N-hydrochloric acid was added until the mixture was almost neutral. Isolation of the acid product with ether yielded a gum which crystallised from pentane to give *4-ethylenedioxy-2 : 2-dimethylheptanoic acid* (6·4 g.) as prisms, m. p. 47·5—48·5° (Found: C, 61·05; H, 9·5%; equiv., 222. $C_{11}H_{20}O_4$ requires C, 61·1; H, 9·3%; equiv., 216). On admixture with 2 : 2-dimethyl-4-oxoheptanoic acid the m. p. was strongly depressed. Treatment of the protected acid with Brady's reagent gave 2 : 2-dimethyl-4-oxoheptanoic acid 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 210—218°.

5-Ethylenedioxy-3 : 3-dimethyloctan-2-one (IX).—4-Ethylenedioxy-2 : 2-dimethylheptanoic acid (11·0 g.) in ether (100 ml.) was slowly added to a vigorously stirred ethereal solution of methyl-lithium (2·35 g. in 100 ml.). The mixture was refluxed for 90 min., then cooled to 0° and treated with cold water (40 ml.). The ethereal layer was separated and the aqueous phase was extracted with ether (2 × 25 ml.). The combined ethereal solutions were washed with water, dried (Na_2SO_4–$MgSO_4$), and evaporated. Distillation of the residue gave *5-ethylenedioxy-3 : 3-dimethyloctan-2-one* (8·1 g.), b. p. 66·5—68·5°/0·6 mm., n_D^{25} 1·4502 (Found: C, 67·35; H, 10·45. $C_{12}H_{22}O_3$ requires C, 67·25; H, 10·35%). The *semicarbazone* crystallised from aqueous methanol as needles (95%), m. p. 181·5—182° (Found: C, 57·25; H, 9·2. $C_{13}H_{25}O_3N_3$ requires C, 57·55; H, 9·3%). Treatment of the ketone with Brady's reagent gave *3 : 3-dimethyloctane-2 : 5-dione bis-2 : 4-dinitrophenylhydrazone* in 93% yield. It crystallised from aqueous dioxan as yellow needles, m. p. 178·5—179·5° (Found: C, 49·65; H, 4·95. $C_{22}H_{26}O_8N_8$ requires C, 49·8; H, 4·95%).

Ethyl 4-Ethylenedioxypentanoate.—A mixture of ethyl lævulate (30·0 g.), 2-ethylenedioxybutane (106 g.), and toluene-*p*-sulphonic acid (0·1 g.) was refluxed through a fractionating column (Stedman, 15 × 2 cm.) under a partial take-off head. At regular intervals during 12 hr., a few drops of the distillate were drawn off until a total of 27·5 ml. was collected. Solid anhydrous sodium carbonate (0·1 g.) was added and the excess of 2-ethylenedioxybutane was distilled off. Distillation of the residue from a Kon flask gave the crude product (35·0 g.), b. p. 102—115°/15 mm., n_D^{15} 1·4330. Redistillation gave ethyl γ-ethylenedioxy-*n*-valerate (26·6 g.), b. p. 107°/12 mm., n_D^{20} 1·4340 (Found: C, 57·6; H, 8·7. Calc. for $C_9H_{16}O_4$: C, 57·45; H, 8·55%). (Kuhn [26] gives b. p. 110—112°/15 mm.)

Ethyl lævulate with ethylene glycol (cf. Kuhn [26]) gave a mixture of starting materials, the required product, and the corresponding acid.

4-Ethylenedioxypentanoic Acid.—Hydrolysis of the preceding ester (24·2 g.) in methanol (26 ml.) with 5N-sodium hydroxide (26·7 ml.), and isolation of the product as described for (VIII; Y = H), gave *4-ethylenedioxypentanoic acid* which crystallised from light petroleum as prisms (17·3 g.), m. p. 35·5—37·0° (Found: C, 52·3; H, 7·7%; equiv. wt., 160. $C_7H_{12}O_4$ requires C, 52·5; H, 7·55%; equiv., 160).

5-Ethylenedioxyhexan-2-one.—Reaction of the preceding acid (7·3 g.) in ether (100 ml.) with methyl-lithium (2·3 g.) in ether (100 ml.), and isolation of the product in the usual way, gave the *ketone* (4·4 g.), b. p. 101·5—102°/12 mm., n_D^{22} 1·4411 (Found: C, 60·55; H, 9·25. $C_8H_{14}O_3$ requires C, 60·75; H, 8·9%). The *semicarbazone* (75% yield) crystallised from water as plates, m. p. 141° (Found: C, 50·6; H, 7·9. $C_9H_{17}O_3N_3$ requires C, 50·2; H, 7·95%). Treatment of the ketone with Brady's reagent gave acetonylacetone bis-2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 270° (Found: C, 46·0; H, 4·05. Calc. for $C_{18}H_{18}O_8N_8$: C, 45·6; H, 3·85%).

2 : 9-Dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-dial (XV).—A solution of 2 : 9-dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-diol (5·5 g.) in acetone (550 ml.) was shaken with manganese dioxide (110 g.; commercial, undried) for 7 hr. Isolation of the product and crystallisation from aqueous methanol gave the dial (5·2 g.), m. p. 116—117° (Ahmad and Weedon [2] give m. p. 116—117°).

Yields of only 10—52% of dial were obtained when the manganese dioxide had been dried in a vacuum over phosphoric oxide for 8 weeks.

2 : 9-Dimethyldeca-2 : 4 : 6 : 8-tetraene-1 : 10-dial (XVI).—(i) A solution of 2 : 9-dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-dial (900 mg.) in ethyl acetate (50 ml.) was shaken in an atmosphere of hydrogen, in the presence of Lindlar's lead-poisoned palladium catalyst (300 mg.),[27] until 2 mol. of hydrogen had been absorbed. Benzene was added to dissolve the

[26] Kuhn, *J. prakt. Chem.*, 1940, **156**, 103.
[27] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.

precipitated product, and the solution was filtered and evaporated. The residue in benzene (100 ml.) was poured on a short column of alumina. Development of the chromatogram with benzene gave a main yellow band which was eluted with the same solvent (500 ml.). A small crystal of iodine was added to the solution, and the mixture was irradiated with a 200 w lamp for 12 hr., and with diffuse daylight for 30 hr. The solution was washed with 5% aqueous sodium thiosulphate and water, dried (Na_2SO_4), and evaporated. Recrystallisation of the residue from benzene–light petroleum gave the " *all*-trans "-*tetraene-dial* (470 mg.) as long orange needles, m. p. 181—182° (Found: C, 75·7; H, 7·6. $C_{12}H_{14}O_2$ requires C, 75·75; H, 7·4%), $\lambda_{max.}$ 380 and 361 mμ ($\varepsilon \times 10^{-3}$, 62·6 and 63·9 respectively), $\nu_{max.}$ 1658 (CH=O) and 9851 cm.$^{-1}$ (conjug. *trans*-CH=CH).

(ii) Partial reduction of the dienediynedial (2·18 g.) in the manner described above, removal of catalyst and solvent, and crystallisation of the residue from benzene gave a " di-*cis* "-isomer of the tetraenedial (800 mg.) as yellow needles, m. p. 176—177°, depressed to 161—164° on admixture with the " all-*trans* "-isomer. This had $\lambda_{max.}$ 380 and 361 mμ ($\varepsilon \times 10^{-3}$, 61·3 and 63·1 respectively) and $\nu_{max.}$ 1658 (C=O), 1424 and 7752 cm.$^{-1}$ (*cis*-CH=CH). Chromatography of the mother-liquors from the crystallisation afforded the " all-*trans* "-tetraenedial (314 mg.), m. p. and mixed m. p. 180—182°.

(iii) A solution of the " di-*cis* "-dial (12 mg.) in benzene (10 ml.) containing a trace of iodine, was irradiated under a 200 w lamp for 2 hr., during which the temperature of the solution rose to 50—60°. The mixture was washed with 5% sodium thiosulphate solution and water, dried (Na_2SO_4), and evaporated. Recrystallisation of the residue from benzene gave the " all-*trans* "-dial (9 mg.) as long orange needles, m. p. 180—181 (mixed m. p. with an authentic sample, 180—182°; mixed m. p. with the " di-*cis* "-dial 162—165°).

Unless stated otherwise the " all-*trans* "-tetraenedial was used in subsequent reactions.

5 : 12-*Dimethylhexadeca*-3 : 5 : 11 : 13-*tetraene*-7 : 9-*diyne*-2 : 15-*dione* (XVII; R = Me).—A solution of 2 : 9-dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-dial (100 mg.) and aluminium *tert.*-butoxide (1·5 g.) in acetone (15 ml.) and benzene (15 ml.) was refluxed for 16 hr., then cooled and poured into 2N-sulphuric acid (20 ml.). The mixture was extracted with ether. The ethereal extracts were washed with saturated sodium hydrogen carbonate and water, dried, (Na_2SO_4), and evaporated. Chromatography of the residue from benzene on alumina gave a main yellow band which was eluted. Evaporation of the solution, and crystallisation of the residue from benzene–light petroleum, gave the dione (40 mg.) as yellow prisms, m. p. 149—151° (Ahmad and Weedon [3] give m. p. 149—151°).

2 : 2 : 6 : 13 : 17 : 17 - *Hexamethyloctadeca*-4 : 6 : 12 : 14 - *tetraene* - 8 : 10 - *diyne* - 3 : 16 - *dione* (XVII; R = Bu^t).—A solution of 2 : 9-dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-dial (100 mg.) and aluminium *tert.*-butoxide (1·5 g.) in pinacolone (1·0 ml.) and benzene (15 ml.) was refluxed for 16 hr., then cooled and poured into 2N-sulphuric acid. Isolation of the product as in the preceding experiment gave the *dione* which crystallised from benzene–light petroleum in yellow needles (70 mg.), m. p. 153—155° (Found: C, 81·6; H, 8·7. $C_{24}H_{30}O_2$ requires C, 82·25; H, 8·65%), $\lambda_{max.}$ in ethanol, 402, 372, 345, and 255 mμ ($\varepsilon \times 10^{-3}$, 42·3, 44·2, 35·2, and 14·4 respectively).

4 : 23 - *Di*(*ethylenedioxy*) - 6 : 6 : 10 : 17 : 21 : 21 - *hexamethylhexacosa* - 8 : 10 : 16 : 18 - *tetraene* - 12 : 14-*diyne*-7 : 20-*dione* (XVII; γ-gl).—A solution of 2 : 9-dimethyldeca-2 : 8-diene-4 : 6-diyne-1 : 10-dial (200 mg.) and aluminium *tert.*-butoxide (2·0 g.) in 5-ethylenedioxy-3 : 3-dimethyloctan-2-one (2·5 ml.) and benzene (10 ml.) was refluxed for 20 hr., then cooled and poured into 0·5N-sulphuric acid (100 ml.). The mixture was extracted with ether. The ethereal extracts were washed with saturated aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. The excess of ethylenedioxydimethyloctanone was distilled off at 60° (bath temp.)/10^{-6} mm. Chromatography of the residue in benzene (25 ml.) on alumina and isolation of the main yellow band yielded a solid (140 mg.). Crystallisation from benzene–light petroleum gave the *dione* (109 mg.) as yellow needles, m. p. 104—105° (Found: C, 74·95; H, 8·85. $C_{36}H_{50}O_6$ requires C, 74·7; H, 8·7%), $\lambda_{max.}$ in *n*-hexane 401, 371, 346, and 254 mμ ($\varepsilon \times 10^{-3}$, 45·2, 50·0, 42·1, and 18·3 respectively).

6 : 6 : 10 : 17 : 21 : 21-*Hexamethylhexacosa*-8 : 10 : 16 : 18-*tetraene*-12 : 14-*diyne*-4 : 7 : 20 : 23-*tetraone* (XVII; γ-on).—A solution of the preceding dione (95 mg.) in acetone (25 ml.) containing toluene-*p*-sulphonic acid (20 mg.) was refluxed for 2 hr. The mixture was cooled, diluted with ether (100 ml.), washed with saturated sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. Chromatography of the residue from benzene on alumina,

isolation of the main yellow band, evaporation, and crystallisation of the residue from benzene–light petroleum gave the tetraone (26 mg.) as yellow prisms, m. p. 94—95°, $\lambda_{max.}$ in *n*-hexane 402, 372, 346, and 254 mμ ($\varepsilon \times 10^{-3}$, 42·4, 46·8, 39·7, and 17·2 respectively).

5 : 12-*Dimethylhexadeca*-3 : 5 : 7 : 9 : 11 : 13-*hexaene*-2 : 15-*dione* (XVIII; R = Me).—5% Ethanolic potassium hydroxide (2 ml.) was added to 2 : 9-dimethyl-2 : 4 : 6 : 8-tetraene-1 : 10-dial (78 mg.) in acetone (7·0 ml.), and the solution was kept for 20° for 30 min. Benzene (100 ml.) was added, and the solution was washed with 2N-sulphuric acid, saturated sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. Chromatography of the residue in benzene on alumina, isolation of the main yellow band, evaporation, and crystallisation of the residue from benzene–light petroleum gave the *dione* (38 mg.) as orange plates, m. p. 171—172° (Found: O, 12·0. $C_{18}H_{22}O_2$ requires O, 11·85%).

2 : 2 : 6 : 13 : 17 : 17-*Hexamethyloctadeca*-4 : 6 : 8 : 10 : 12 : 14-*hexaene*-3 : 16-*dione* (XVIII; R = Bu^t).—(i) A solution of 2 : 9-dimethyldeca-2 : 4 : 6 : 8-tetraene-1 : 10-dial (128 mg.) and aluminium *tert.*-butoxide (1·0 g.) in pinacolone (2 ml.) and benzene (10 ml.) was refluxed for 16 hr., then cooled and poured into 2N-sulphuric acid (20 ml.). Extraction with benzene and isolation of the product as in the preceding experiment gave the *dione* which crystallised from benzene–light petroleum in yellow needles (153 mg.), m. p. 206—207° (Found: C, 81·5; H, 9·6. $C_{24}H_{34}O_2$ requires C, 81·3; H, 9·65%). Condensation of the " di-*cis* "-tetraenedial with pinacolone gave the same product.

Potassium borohydride (150 mg.) was added during 1 hr. to a boiling solution of the dione (196 mg.) in methanol (10 ml.). The solution was cooled, and 0·05N-sulphuric acid (40 ml.) was added. Isolation of the product with ether and crystallisation from aqueous ethanol gave the diol (173 mg.) as an unstable, microcrystalline, yellow solid, m. p. 152—156°, $\lambda_{max.}$ 399 and 376 mμ ($\varepsilon \times 10^{-3}$, 65·7 and 63·4 respectively), $\nu_{max.}$ 3390 cm.$^{-1}$ (no absorption in the carbonyl region).

(ii) A solution of the preceding diol (10 mg.) and chloranil (15 mg.) in benzene (1·5 ml.) was kept at 20° for 18 hr., then poured on a column of alumina, and the chromatogram was developed with benzene. The main yellow band yielded the hexaenedione (2 mg.), m. p. 202—204°, mixed m. p. with a sample from (i), 202—205°, $\lambda_{max.}$ 445 and 420 mμ.

Oxidation of the diol (10 mg.) in benzene (1·5 ml.) with tetrachloro-*o*-benzoquinone (15 mg.) (cf. Braude, Linstead, and Wooldridge [12]) at 80° for 30 min., or 20° for 16 hr., gave none of the required dione. Treatment of the diol (8 mg.) in acetone (1 ml.) with manganese dioxide (240 mg.) at 20° for 65 hr., and finally under reflux for 3·5 hr., yielded no dione; the diol (2 mg.; estimated spectroscopically) was recovered.

(iii) A solution of *N*-bromosuccinimide (14 mg.) in chloroform (10 ml.; free from ethanol and hydrochloric acid) was added to the diol (14 mg.) in the same solvent (10 ml.). One minute later, powdered *N*-phenylmorpholine (14 mg.) was added with stirring. After being refluxed for 30 min., the mixture was cooled and washed with 2N-hydrochloric acid, aqueous sodium hydrogen carbonate, and water. The chloroform solution was dried (Na_2SO_4) and evaporated. Chromatography of the residue from benzene on alumina, isolation of the main yellow band, evaporation, and crystallisation of the residue from light petroleum gave the hexaenedione (1·2 mg.) as yellow needles, m. p. and mixed m. p. 206—207°, $\lambda_{max.}$ 445 and 420 mμ.

4 : 23-*Di*(*ethylenedioxy*)-6 : 6 : 10 : 17 : 21 : 21-*hexamethylhexacosa*-8 : 10 : 12 : 14 : 16 : 18-*hexaene*-7 : 20-*dione* (XVIII; γ-gl).—A solution of 2 : 9-dimethyldeca-2 : 4 : 6 : 8-tetraene-1 : 10-dial (200 mg.), aluminium *tert.*-butoxide (1·0 g.), and 5-ethylenedioxy-3 : 3-dimethyloctan-2-one (2·0 g.) in benzene (10 ml.) was refluxed for 20 hr., then cooled and diluted with benzene (100 ml.). The solution was washed with 0·05N-sulphuric acid, then with saturated sodium hydrogen carbonate solution, dried (Na_2SO_4), and evaporated. The excess of ethylenedioxydimethyloctanone was distilled off at 60° (bath temp.)/10^{-6} mm. Chromatography of the residue in benzene (25 ml.) on alumina, isolation of the main yellow band, evaporation, and crystallisation of the residue from benzene–light petroleum gave the dione (56 mg.) as yellow needles, m. p. 124—126·5°.

6 : 6 : 10 : 17 : 21 : 21-*Hexamethylhexacosa*-8 : 10 : 12 : 14 : 16 : 18-*hexaene*-4 : 7 : 20 : 23-*tetraone* (XVIII; γ-on).—(i) A solution of the preceding dione (40 mg.) and toluene-*p*-sulphonic acid (10 mg.) in acetone (25 ml.) was refluxed for 90 min., then cooled and diluted with benzene (50 ml.). The solution was washed with saturated aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. Isolation of the product by chromatography from

benzene on alumina and crystallisation from benzene–light petroleum gave the *tetraone* (16 mg.) as yellow needles, m. p. 119—124° (Found: C, 77·6; H, 9·55. $C_{32}H_{46}O_4$ requires C, 77·7; H, 9·35%).

(ii) Condensation of 2 : 9-dimethyldeca-2 : 4 : 6 : 8-tetraene-1 : 10-dial (152 mg.) with 5-ethylenedioxy-3 : 3-dimethyloctan-2-one (2·0 g.), in the manner described above, and hydrolysis of the crude product, gave the tetraone (35 mg.), m. p. 119—124°.

(iii) A solution of 6 : 6 : 10 : 17 : 21 : 21-hexamethylhexacosa-8 : 10 : 16 : 18-tetraene-12 : 14-diyne-4 : 7 : 20 : 23-tetraone (25 mg.) in ethyl acetate (4 ml.) was shaken in hydrogen in the presence of Lindlar's catalyst [27] until 2 mol. of hydrogen had been absorbed. The catalyst and solvent were removed and the residue in benzene (*ca.* 10 ml.), containing a trace of iodine, was exposed to diffuse daylight for 8 hr. The solution was washed with 5% aqueous sodium thiosulphate, dried, and evaporated. Chromatography of the residue from benzene on alumina furnished the hexaenetetraone (2 mg.), m. p. and mixed m. p. 119—123°, $\lambda_{max.}$ 449 and 424 mμ.

6 : 6 : 10 : 17 : 21 : 21 - *Hexamethylhexacosa* - 8 : 10 : 12 : 14 : 16 : 18 - *hexaene* - 4 : 7 : 20 : 23 - *tetraol* (XIX; γ-ol).—Potassium borohydride (20 mg.) was added during 15 min. to a boiling solution of the preceding tetraone (23 mg.) in methanol (15 ml.). 2N-Sodium hydroxide (1·0 ml.) was added, and the solution was refluxed for 15 min., cooled, diluted with ether (50 ml.), washed with water, dried (Na_2SO_4), and evaporated. The residual unstable oil exhibited visible light absorption maxima at 400 and 377 mμ, and (in CCl_4) an infrared absorption maximum at 3360 cm.$^{-1}$, but no absorption in the carbonyl region. The tetraol content was estimated spectrally as 5 mg. Oxidation with chloranil (15 mg.) in benzene (1 ml.) at 20° for 16 hr., and chromatography, gave no product with a hexaenedione chromophore.

Reduction of the tetraone, and treatment of the crude reaction mixture with 0·05N-sulphuric acid, gave a product with $\lambda_{max.}$ 400 and 377 mμ, but no infrared absorption maximum in the hydroxyl or carbonyl region; presumably cyclisation of the initial product had occurred to give a bistetrahydrofuran derivative.

6 : 6 : 10 : 17 : 21 : 21-*Hexamethylhexacosa*-8 : 10 : 12 : 14 : 16 : 18-*hexaene*-3 : 7 : 20 : 24-*tetraol* (XIX; δ-ol) *and the* 3 : 24-*Dihydroxy*-7 : 20-*dione* (XVIII; δ-ol).—Potassium borohydride (50 mg.) was added during 15 min. to a boiling solution of 6 : 6 : 10 : 17 : 21 : 21-hexamethylhexacosa-8 : 10 : 12 : 14 : 16 : 18-hexaene-3 : 7 : 20 : 24-tetraone [9] (40 mg.) in methanol (5 ml.). 2N-Sodium hydroxide (1·0 ml.) was then added, and the solution was refluxed for 15 min., cooled, and diluted with water (20 ml.). The product was isolated with ether and crystallised from benzene–light petroleum to give the tetraol (9·4 mg.) as an unstable, microcrystalline yellow solid, m. p. 110—120°, $\lambda_{max.}$ 399 and 376 mμ (ε × 10^{-3}, 64·7 and 66·5 respectively), $\nu_{max.}$ 3370 cm.$^{-1}$ (no absorption in the carbonyl region).

A solution of the tetraol (6·5 mg.) and chloranil (7·5 mg.) in benzene (2 ml.) was kept at 20° for 65 hr., then poured on a column of alumina. The chromatogram was developed with benzene–chloroform (2 : 1). Isolation of the main band, and crystallisation from benzene–light petroleum, gave the hydroxy-dione (0·7 mg.) as orange-yellow prisms, m. p. 107—110°.

5 : 9 : 14 : 18-*Tetramethyldocosa*-3 : 5 : 7 : 9 : 11 : 13 : 15 : 17 : 19-*nonaene*-2 : 21-*dione* (IV; R = Me).—A mixture of crocetin-dial (106 mg.), acetone (7 ml.), and 5% ethanolic potassium hydroxide (2 ml.) was shaken at frequent intervals and kept at 20° for 45 min. Benzene (60 ml.) was added and the mixture was washed with water, 2N-sulphuric acid, saturated sodium hydrogen carbonate solution, and water. The solution was dried (Na_2SO_4) and evaporated. Chromatography of the residue in benzene on alumina, and crystallisation from benzene–light petroleum, gave the dione (70 mg.) as deep-red plates, m. p. 179—181° (Found: O, 8·8. $C_{26}H_{32}O_2$ requires O, 8·5%).

2 : 6 : 10 : 15 : 19 : 23-*Hexamethyltetracosa*-4 : 6 : 8 : 10 : 12 : 14 : 16 : 18 : 20-*nonaene*-3 : 22-*dione* (IV; R = Pr^i).—A mixture of crocetin-dial (49 mg.), 3-methylbutan-2-one (4 ml.) and 5% ethanolic potassium hydroxide was shaken occasionally and kept at 20° for 24 hr. Isolation of the crude product, as in the previous experiment, and crystallisation from benzene–light petroleum gave the *dione* (46·5 mg.) as purple plates, m. p. 187° (Found: O, 7·6. $C_{30}H_{40}O_2$ requires O, 7·4%).

2 : 2 : 6 : 10 : 15 : 19 : 23 : 23-*Octamethyltetracosa*-4 : 6 : 8 : 10 : 12 : 14 : 16 : 18 : 20-*nonaene*-3 : 22-*dione* (IV; R = Bu^t).—(i) A mixture of crocetin-dial (30 mg.), pinacolone (2 ml.), aluminium *tert.*-butoxide, and benzene (10 ml.) was refluxed for 16 hr., then cooled, diluted with benzene (50 ml.), and washed with 2N-sulphuric acid, saturated sodium hydrogen carbonate

solution, and water. The benzene solution was dried (Na_2SO_4) and evaporated. Crystallisation of the residue from benzene–light petroleum gave the *dione* (11 mg.) as purple plates, m. p. 221—222° (Found: C, 82·75; H, 9·45. $C_{32}H_{44}O_2$ requires C, 83·4; H, 9·65%). Ahmad and Weedon [2] give m. p. 220—221° (Kofler block). Chromatography of the mother-liquors on alumina gave a main red band which was eluted with benzene. Evaporation of the resultant solution, and crystallisation of the residue from benzene–light petroleum, gave a further 11 mg. of the dione (total yield 22 mg., 49%).

(ii) A mixture of crocetin-dial (44 mg.), pinacolone (3 ml.), and 5% methanolic potassium hydroxide (3 ml.) was warmed to effect complete dissolution of the dial, and was then kept at 20° for 20 hr. After addition of 2½% methanolic potassium hydroxide (15 ml.), the solution was kept at 20° for a further 50 hr. The crystalline precipitate was filtered off and recrystallised from benzene–light petroleum, to give the dione (10 mg.), m. p. and mixed m. p. 221—222°. After being diluted with chloroform (50 ml.), the filtrate from the reaction mixture was washed successively with water, 2N-sulphuric acid, saturated aqueous sodium hydrogen carbonate, and water. The chloroform solution was dried (Na_2SO_4) and evaporated. Chromatography of the residue from benzene on alumina gave a further 5 mg. of the dione (total yield 15 mg., 23%).

4 : 29-*Di*(*ethylenedioxy*)-6 : 6 : 10 : 14 : 19 : 23 : 27 : 27-*octamethyldotriaconta*-8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24-*nonaene*-7 : 26-*dione* (IV; γ-gl).—A mixture of crocetindial (240 mg.), 5-ethylenedioxy-3 : 3-dimethyloctan-2-one (7·0 g.), and 5% ethanolic potassium hydroxide (9·0 ml.) was refluxed for 30 min., then cooled rapidly, diluted with benzene (100 ml.), and washed successively with water, 0·05N-sulphuric acid, saturated sodium hydrogen carbonate solution, and water. The benzene solution was dried (Na_2SO_4) and evaporated. The oily residue was diluted with light petroleum (50 ml.). When kept overnight at 0°, the solution deposited deep-red leaflets (265 mg., 48%), m. p. 178—180°. Recrystallisation from benzene–light petroleum gave the *dione* as deep red leaflets, m. p. 182—183° (Found: C, 77·05; H, 9·55. $C_{44}H_{64}O_6$ requires C, 76·7; H, 9·35%).

Evaporation of the crude reaction product at 60°/10^{-6} mm., and chromatography of the residue, gave the dione in 22% yield. Longer reaction resulted in destruction of the dione.

Attempts to condense crocetin-dial with the methyl ketone by means of 5% methanolic potassium hydroxide at 20°, boiling 5% potassium hydroxide in ethyl cellosolve, or aluminium *tert.*-butoxide in boiling benzene gave none of the required product.

6 : 6 : 10 : 14 : 19 : 23 : 27 : 27 - *Octamethyldotriaconta* - 8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24 - *nonaene*-4 : 7 : 26 : 29-*tetraone* (IV; γ-on).—A solution of the preceding nonaenedione (260 mg.) and toluene-*p*-sulphonic acid (25 mg.) in acetone (50 ml.) was refluxed for 1 hr., cooled, diluted with benzene (150 ml.), and washed with saturated aqueous sodium hydrogen carbonate and water. The benzene solution was dried (Na_2SO_4) and evaporated. Crystallisation of the residue from benzene–light petroleum gave the *tetraone* (123 mg.) as purple leaflets, m. p. 159° (Found: C, 80·35; H, 9·9. $C_{40}H_{56}O_4$ requires C, 79·95; H, 9·4%).

Chromatography of the crude product did not raise the yield.

6 : 6 : 10 : 14 : 19 : 23 : 27 : 27 - *Octamethyldotriaconta* - 8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24 - *nonaene*-4 : 7 : 26 : 29-*tetraol* (V; γ-ol).—Potassium borohydride (100 mg.) was added during 30 min. to a boiling solution of the preceding tetraone (98 mg.) in methanol (15 ml.). 2N-Sodium hydroxide (2 ml.) was added, and the solution was refluxed for 15 min. and then cooled. Benzene (100 ml.) was added and the solution was washed with water, dried (Na_2SO_4), and evaporated. Crystallisation of the residue from benzene–light petroleum gave the tetraol (15·5 mg.) as an unstable, microcrystalline, red solid, m. p. 174—180° (sintered at 155°), $\lambda_{max.}$ 480, 450, and 426 mμ (ε × 10^{-3}, 93, 105, and 81 respectively), $\nu_{max.}$ 3380 $cm.^{-1}$ (no absorption in the carbonyl region).

Oxidation of the tetraol (14 mg.) with chloranil (13 mg.) in benzene–ethanol (9 : 1; 5 ml.) at 20° for 16 hr. gave no product with a nonaenedione chromophore. Another experiment was followed spectroscopically for 8 days, but gave no indication of nonaenedione formation. Oxidation of the tetraol in chloroform with *N*-bromosuccinimide, or in acetone with manganese dioxide, also gave no nonaenedione.

3 : 30 - *Dihydroxy* - 6 : 6 : 10 : 14 : 19 : 23 : 27 : 27 - *octamethyltriaconta* - 8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24 - *nonaene*-7 : 26 - *dione* (IV; δ-ol).—Potassium borohydride (60 mg.) was added during 10 min. to a boiling solution of 6 : 6 : 10 : 14 : 19 : 23 : 27 : 27 - octamethyldotriaconta - 8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24 - nonaene-3 : 7 : 26 : 30-tetraone [9] (50 mg.) in

methanol (10 ml.). Isolation of the crude product as in the previous experiment, chromatography from benzene on alumina, and elution of the main yellow band with 1% ethanol in benzene, gave a solution of the nonaene tetraol (38 mg., estimated spectroscopically), $\lambda_{max.}$ 476, 446, and 422 mμ. Evaporation gave a yellow oil which was dissolved in benzene–ethanol (19 : 1; 30 ml.). Chloranil (42 mg.) was added, and the solution kept at 20° and examined spectrographically at intervals. After 22 hr. the reaction had ceased. Addition of further chloranil (10, 10, 10, and 80 mg.) periodically produced only a small increase in the proportion of the required chromophore. After 144 hr. the reaction mixture was evaporated. Chromatography of the residue from benzene on alumina, elution of the main red band with 1—2% of ethanol in benzene, and crystallisation from benzene–light petroleum gave the *dihydroxy-dione* (4·5 mg.) as purple leaflets, m. p. 170—171° (Found: O, 10·6. $C_{40}H_{60}O_4$ requires O, 10·6%), $\nu_{max.}$ 3620, 3400, and 1664 cm.$^{-1}$. In a mixed chromatogram on alumina the dihydroxy-dione was less strongly adsorbed than capsorubin.

6 : 6 : 10 : 14 : 19 : 23 : 27 : 27 - *Octamethyldotriaconta* - 8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24 - *nonaene*-2 : 7 : 26 : 31-*tetraol* (V; ε-ol) *and the* 2 : 31-*Dihydroxy*-7 : 26-*dione* (IV; ε-ol).—Oxidation of β-carotene by the method of Kuhn and Brockmann [10] gave β-carotenone as purple leaflets, m. p. 171—172° [Kuhn *et al.*[10] give m. p. 174—175° (corr.)].

Reduction of β-carotenone (39 mg.) in boiling methanol (7 ml.) with potassium borohydride (42 mg.), and purification of the product as in the preparation of the isomeric 4 : 7 : 26 : 29-tetraol, gave the 2 : 7 : 26 : 31-tetraol (19 mg.) as an unstable, microcrystalline red solid, m. p. 180—185° (sintered at 160°), $\lambda_{max.}$ 480, 450, and 425 mμ (ε × 10^{-3}, 103, 106, and 73·5 respectively) $\nu_{max.}$ 3380 cm.$^{-1}$.

A solution of the tetraol (40 mg.) and chloranil (36 mg.) in benzene (9 ml.) and ethanol (1 ml.) was kept at 20° for 20 hr. and then evaporated. Chromatography of the residue from benzene–chloroform on alumina, isolation of the main band, and crystallisation from benzene–light petroleum gave the *dihydroxy-dione* (8 mg.) as purple prisms, m. p. 166° (Found: C, 79·05; H, 10·85. $C_{40}H_{60}O_4$ requires C, 79·4; H, 10·0%). In a mixed chromatogram on alumina with 0·5% ethanol in benzene as the eluent, the dihydroxy-dione was less strongly adsorbed than capsorubin.

Reduction and Regeneration of Capsanthin.—Capsanthin was isolated from *Capsicum annuum* as red needles, m. p. 181—182°, $\lambda_{max.}$ 483 mμ, inflexion 518 mμ (ε × 10^{-3}, 121 and 95 respectively).

Potassium borohydride (40 mg.) was added during 45 min. to a boiling solution of capsanthin (30·5 mg.) in methanol (10 ml.). 2N-Sodium hydroxide (1·0 ml.) was then added and the mixture was refluxed for 15 min. Isolation of the crude product in the usual way, and crystallisation from benzene–light petroleum, gave capsanthol (14 mg.) as dark red prisms, m. p. 180—182°, depressed to 170—176° on admixture with capsanthin. It had absorption maxima at 483 and 455 mμ (ε × 10^{-3}, 90 and 95 respectively), and at 3370 cm.$^{-1}$. (For the product of Ponndorf reduction, Karrer and Hubner [4] give m. p. 175—176°, $\lambda_{max.}$ 492 and 462 mμ.)

A solution of capsanthol (7·5 mg.) and chloranil (8 mg.) in benzene–ethanol (19 : 1; 5 ml.) was kept at 20° for 22 hr., then evaporated. Chromatography of the residue on alumina, elution of the main red band with 1% of ethanol in benzene, evaporation, and crystallisation from benzene–light petroleum gave capsanthin (2 mg.) as red needles, m. p. and mixed m. p. 181°. The visible and infrared spectra were identical with those of natural capsanthin. No separation was observed in a mixed chromatogram.

Reduction and Regeneration of Capsorubin.—Potassium borohydride (11 mg.) was added during 100 min. to a boiling solution of capsorubin (1·1 mg.) in methanol (3 ml.). 2N-Sodium hydroxide (0·5 ml.) was added and the mixture was refluxed for 10 min. Isolation of the product in the usual way and chromatography from benzene on alumina gave a yellow band which was eluted with 1% of ethanol in benzene. The resulting solution of the tetraol (40% spectroscopic yield) had $\lambda_{max.}$ 476 and 447 mμ.

The solution of the tetraol was evaporated and the residue was dissolved in benzene–ethanol (19 : 1; 2 ml.). Chloranil (0·5 mg.) was added and the solution kept at 20° for 92 hr. (a further 0·1 mg. of chloranil was added after 13 hr.). The course of the reaction was followed spectroscopically, and a smooth regeneration of the capsorubin spectrum was observed. Evaporation of the reaction mixture, and chromatography of the residue from benzene on alumina, gave a main red band which was eluted with 1·5% of ethanol in benzene. Its visible-light absorption spectrum was identical with that of capsorubin, and no separation was observed in a mixed chromatogram with the natural carotenoid.

Alkaline Fission of Capsorubin.—(i) A solution of capsorubin (0·6 mg.) in benzene (0·5 ml.) and 10% ethanolic potassium hydroxide (2 ml.) was refluxed for 2 hr. The mixture was cooled, diluted with benzene (20 ml.), washed 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 three bands: A (most strongly adsorbed), $\lambda_{max.}$ 521 and 489 mμ (cf. capsorubin, $\lambda_{max.}$ 523 and 489); B, $\lambda_{max.}$ 499 and 469 mμ; and C, $\lambda_{max.}$ 474 and 446 mμ (cf. crocetin-dial, $\lambda_{max.}$ 474 and 446 mμ). Band C (spectroscopic yield 0·06 mg., 20%) did not separate from crocetin-dial in a mixed chromatogram.

(ii) Hydrolysis of capsorubin (17 mg.) in the above manner, evaporation of band C, and crystallisation of the residue from benzene–light petroleum, gave crocetin-dial (0·2 mg.) as needles, m. p. 189° (undepressed on admixture with an authentic specimen, m. p. 190°), $\lambda_{max.}$ 474 and 446 mμ.

3 : 7-*Dimethyloct*-6-*en*-2-*one* (XXI).—Powdered sodium methoxide (80 g.) was added during 40 min. to a stirred and cooled (ice–salt) mixture of ethyl α-chloropropionate (14·3 g.) and 6-methylhept-5-en-2-one (111 g.). The mixture was stirred at 20° for 4 hr., then again cooled (ice) and 15% methanolic potassium hydroxide (550 ml.) was added. The mixture was stirred at 20° for 2 hr., then diluted with water (1 l.) and extracted with ether. The aqueous layer was acidified with concentrated hydrochloric acid and extracted with ether. The ethereal extract was dried ($MgSO_4$) and evaporated. The residue was heated at 140° for 1½ hr., cooled, and dissolved in benzene–ether (1 : 1). The solution was washed with 2N-sodium carbonate and water, dried ($MgSO_4$), and evaporated. Distillation of the residue gave 3 : 7-*dimethyloct*-6-*en*-2-*one* (24·8 g.), b. p. 192—197°, 88—90°/14 mm., n_D^{20} 1·4434 (Found: C, 77·5; H, 11·95. $C_{10}H_{18}O$ requires C, 77·85; H, 11·75%), $\nu_{max.}$ (liquid film) 1706 cm.$^{-1}$. The *semicarbazone* (80% yield) crystallised from aqueous ethanol in prisms, m. p. 61—64° (Found: C, 62·65; H, 10·0. $C_{11}H_{21}ON_3$ requires C, 62·5; H, 10·0%).

7-*Hydroxy*-3 : 7-*dimethyloctan*-2-*one* (XXII).—3 : 7-Dimethyloct-6-en-2-one (10·0 g.) was shaken with 35% (w/v) sulphuric acid (200 ml.) for 5½ hr. The mixture was extracted with ether, cooled at −40°, and stirred vigorously whilst 40% aqueous sodium hydroxide was added cautiously until the mixture was alkaline. The mixture was warmed to 20°, sufficient water was added to dissolve the inorganic salts, and the solution was extracted continuously with ether for 16 hr. The extract was dried ($MgSO_4$) and evaporated, and the residue was distilled to give the *hydroxy-ketone* (2·9 g.), b. p. 64°/0·1 mm., n_D^{26} 1·4444 (Found: C, 69·8; H, 11·8. $C_{10}H_{20}O_2$ requires C, 69·7; H, 11·7%), $\nu_{max.}$ (liquid film) 3360 and 1705 cm.$^{-1}$.

Similar treatment of 6-methylhept-5-en-2-one (10·0 g.) gave 6-hydroxy-6-methylheptan-2-one (6·3 g.), b. p. 72°/0·2 mm., n_D^{20} 1·4445 (Found: C, 66·4; H, 11·3. Calc. for $C_8H_{16}O_2$: C, 66·6; H, 11·2%) (Rupe and Schlochoff [28] give b. p. 106°/9 mm.), $\nu_{max.}$ (liquid film) 3360 and 1708 cm.$^{-1}$.

2 : 31 - *Dihydroxy* - 2 : 6 : 10 : 14 : 19 : 23 : 27 : 31 - *octamethyldotriaconta* - 8 : 10 : 12 : 14 : 16 : 18 : 20 : 22 : 24 - *nonaene* - 7 : 26 - *dione* (IVa).—A mixture of crocetin - dial (64 mg.), 7-hydroxy - 3 : 7 - dimethyloctan - 2 - one (0·9 g.) and 5% ethanolic potassium hydroxide (3 ml.) was shaken occasionally and kept at 20° for 3½ hr., then refluxed for 30 min., cooled, and diluted with benzene (50 ml.), washed with water, 0·05N-sulphuric acid, saturated aqueous sodium hydrogen carbonate, and water, dried (Na_2SO_4), and evaporated, finally at 60° (bath temp.)/10^{-6} mm. The residue in benzene–chloroform (17 : 3; 50 ml.) was poured on a column of alumina, and the chromatogram was developed with 1% of ethanol in benzene. Isolation of the main red band, evaporation, and crystallisation from benzene–light petroleum gave the *dihydroxy-dione* (12·5 mg.), m. p. 133—134° (Found: O, 10·4. $C_{40}H_{60}O_4$ requires O, 10·6%), $\nu_{max.}$ 3530, 3390, 1667, and 1639 cm.$^{-1}$. A further 2 mg. of product were obtained by chromatography of the mother-liquors. In a mixed chromatogram on alumina the dihydroxy-dione was less strongly adsorbed than capsorubin.

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[28] Rupe and Schlochoff, *Ber.*, 1905, **38**, 1503.

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