Pure & Appl. Chem., Vol. 47, pp. 161–171. Pergamon Press, 1976. Printed in Great Britain.

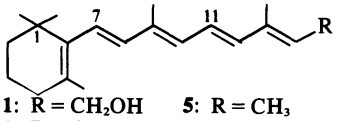
SYNTHESIS OF CAROTENOIDS AND RELATED POLYENES

B. C. L. WEEDON
Department of Chemistry, Queen Mary College, Mile End Road, London E1 4NS, UK

Abstract—Syntheses reported over the last 5 yr in the vitamin A and carotenoid fields are reviewed. Some previously unpublished work is described. This includes new routes to zeaxanthin and rhodoxanthin, the synthesis of optically inactive forms of the structures proposed for tunaxanthin, lutein and calthaxanthin, and the preparation of various polyene β-diketones, including the structure assigned to trikentriorhodin.

1. INTRODUCTION

The wide variety of natural carotenoids presents the chemist with a fascinating range of challenges to his ingenuity in synthesis. Increasingly synthesis is being invoked not just to confirm a structure for which there is already convincing evidence, but to elucidate some doubtful feature. Moreover the value of some carotenoids as colouring matters for human and animal food, and the nutritional importance of vitamin A (1), ensures that a search is maintained for new and better methods of polyene synthesis. It is therefore scarcely surprising that substantial progress has been made since a comprehensive review was published by Mayer and Isler[1] in 1971.



1: R = CH_2OH **5**: R = CH_3
2: R = CH_2OAc **6**: R = $CH{=}PPh_3$
3: R = CHO **7**: R = CH_2NC
4: R = CO_2H

2. CAROTENOID TRANSFORMATIONS

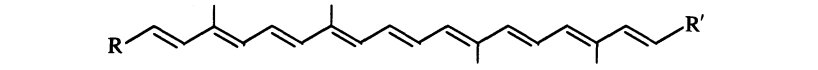
Before dealing with the development of new total syntheses, transformations that have been achieved with various natural and synthetic carotenoids deserve mention.

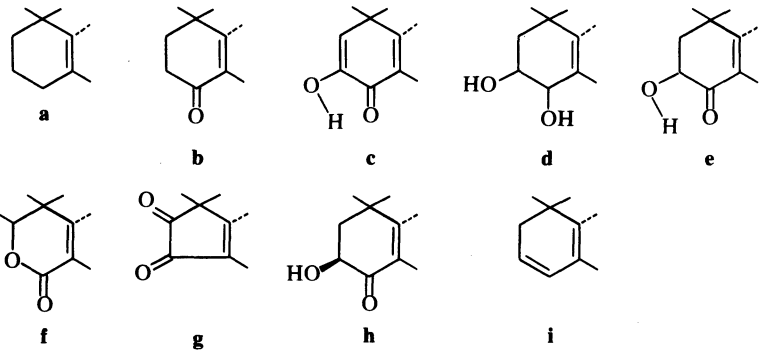
3,4,3′,4′-*Oxygenated β,β-carotenes*

The autoxidation of canthaxanthin (9) in the presence of potassium *tert.*-butoxide to give astacene (10) has been improved[3] and is now capable of giving yields of *ca.*95%. On further reaction under the same conditions, astacene is slowly converted into the lactols (11) and (12), with loss of one and two carbon atoms respectively.[4] These are the first oxa-carotenoids to be reported. Oxidation of astacene (10), and related diosphenols, with manganese dioxide gives nor-carotenoids with carbocyclic rings. This reaction was used to synthesise violerythrin (13) from astacene (10),[5] and subsequently the unsymmetrical intermediate (14) was isolated and identified with roserythrin.[6,7]

Hydride reduction of astacene gives a mixture of tetraols (15) which on controlled oxidation with dichlorodicyano-*p*-benzoquinone gives low yields of astaxanthin (16).[3,8] Recently a 30% yield of the unsymmetrical intermediate (17), idoxanthin, was obtained by treatment with chromium trioxide on graphite.[9] Base promoted hydrogen transfer between the tetraols and astacene also gives idoxanthin (17) in *ca.*30% yield.[4]

Bodea *et al.*[10] reported that the mixture of tetraols (15) could be separated by chromatography on magnesium oxide into its constituents, one of which appeared to be an optically inactive form of crustaxanthin. Though other workers have experienced difficulties in carrying out this separation,[11,12] t.l.c. on silicagel using a mixture (10:2:1)





8: R = R′ = **a**
9: R = R′ = **b**
10: R = R′ = **c**
11: R = **f**, R′ = **c**
12: R = R′ = **f**
13: R = R′ = **g**
14: R = **g**, R′ = **c**
15: R = R′ = **d**
16: R = R′ = **e**
17: R = **e**, R′ = **d**
18: R = R′ = **g**
19: R = R′ = **i**

of benzene, ethyl acetate and ethanol as eluent, has enabled us[4] to confirm the original claim and estimate the proportions of the three isomers (in order of decreasing polarity) as 20:5:1. On the basis of NMR studies these bis-α-glycols are assigned the threo, threo, the threo-erythro, and the erythro, erythro configurations respectively. In the light of this result, we have also repeated the hydride reduction of natural astaxanthin and separated the optically active forms of the three isomers which, by this route, are formed in the proportions 10:10:1. The three products exhibited closely similar c.d. curves, showing that the configuration of the 4- and 4'-hydroxyls have little influence on the chiroptical properties of the tetraol, which must therefore be largely determined by the configuration at C-3 and C-3'. This provides direct justification of the basic assumption made by Andrewes *et al.* in their assignment of the 3S,3'S-configuration (18) to natural astaxanthin.[12]

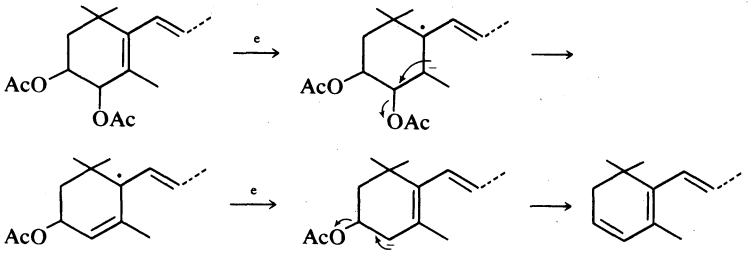
Treatment of the tetraols with acetic anhydride in pyridine gives the corresponding mixture of tetra-acetates.[13] Cathodic reduction at mercury of these esters in acetonitrile, with tetra-*n*-butylammonium perchlorate as supporting electrolyte gives 3,4,3',4'-tetradehydro-β,β-carotene (19) in good yield.[14] This elimination of the oxygen functions can be rationalised as shown in Scheme 1.

It is consistent with this mechanism that vitamin A acetate (2), under similar conditions, gives axerophthene (5) almost quantitatively; in this instance the allylic carbanion formed initially is rapidly protonated.[15]

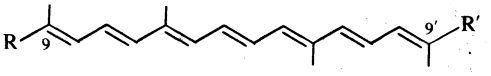
Carotenoid epoxides

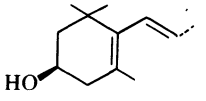
The epoxidation of lutein (20), preferably as the acetate, gives two epoxides. The minor product is identical with natural lutein epoxide (21), and on isomerisation in the presence of acids gives chrysanthemaxanthin and flavoxanthin (22) which differ in configuration at C-8 but retain the original configuration at C-5. The major synthetic 5,6-epoxide gives a similar mixture of furanoid oxides with the opposite configuration at C-5. The NMR properties of these and related semi-synthetic products establish that the epoxide group in such natural carotenoids as lutein epoxide (21), violaxanthin (23), and neoxanthin (24), is *trans* to the hydroxyl at C-3, i.e. that the common 3-hydroxy-5,6-epoxy end group has the 3S,5R,6S-configuration (c).[16] Degradation studies by Eugster *et al.* lead to the same conclusion.[17]

Lithium aluminium hydride reduction of fucoxanthin (25) gives a mixture of fucoxanthols (26) differing in configuration at C-8. These may be separated chromatographically and both, on mild acid treatment, are converted (but at different rates) into two isomers of

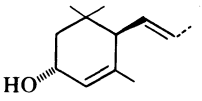


Scheme 1. Cathodic reduction of 3,4,3',4'-tetraacetoxy-β,β-carotene (Utley *et al.*[14]).

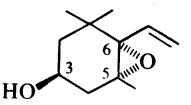




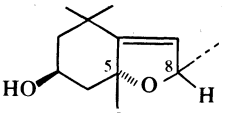
a



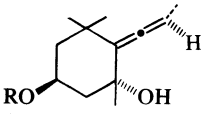
b



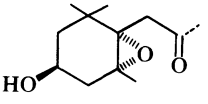
c



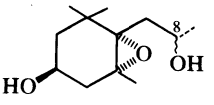
d



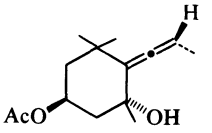
e: R = H
f: R = Ac



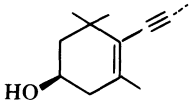
g



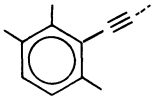
h



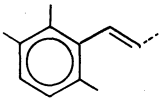
i



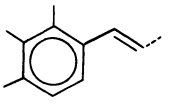
j



k



l



m

20: R = **a**, R' = **b**
21: R = **c**, R' = **b**
22: R = **d**, R' = **b**
23: R = R' = **c**
24: R = **c**, R' = **e**
25: R = **g**, R' = **f**
26: R = **h**, R' = **e**

27: R = **d**, R' = **e**
28: R = **g**, R' = **i**
29: R = R' = **c**
30: R = R' = **j**
31: R = **k**, R' = **l**
32: R = **k**, R' = **m**

fucochrome (27) differing only in configuration at C-8.[18] This reveals that in the formation of the fucochromes from the fucoxanthols the configuration is lost at C-8 but retained at C-5. It is therefore concluded that in fucoxanthin the hydroxyl at C-3 must also be *trans* to the 5,6-epoxide. This removes the remaining uncertainty concerning the 3S,5R,6S,3'S,5'R,6'R-configuration assigned to this major carotenoid.[19]

Stereomutation

Iodine catalysed stereomutation of fucoxanthin (25) gives various isomers, one of which (28) is formed by a switch of configuration about the allene group from R to S. This product, which is readily converted back to the common "all-*trans* form", has been detected in fresh seaweed, and may play an important rôle in the biosynthesis of fucoxanthin.[20]

Stereomutation of violaxanthin (29) gives the 9-*cis* isomer, violeoxanthin, the transformation being reversible. A similar stereomutation occurs readily about the 9,10-double bond of neoxanthin (24).[21] Under similar conditions, alloxanthin (30) is converted rapidly and irreversibly into the 9,9'-di*cis* isomer, manixanthin, which is presumably the thermodynamically most stable isomer.[22–24] The aromatic acetylenic carotenoids, 7,8-dehydroisorenieratene (31) and 7,8-dehydrorenieratene (32) behave analogously.[24]

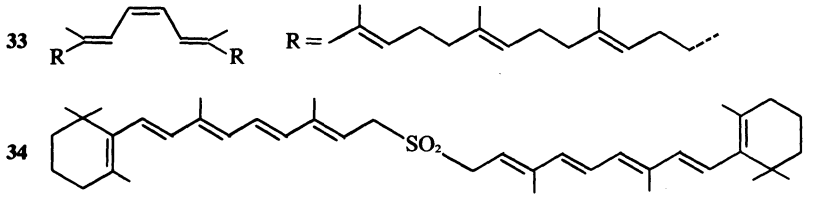
3. METHODS FOR ELABORATION OF POLYENE CHAINS

The vinyl ether synthesis, acetylenic routes, and reactions of the Wittig type retain their importance as the principle methods for building up the carbon skeleton of carotenoids and related polyenes.[1,28] Nevertheless a good deal of attention has been paid to new or improved methods of olefination.

Bestman *et al.* [29] have given details of the formation of β-carotene (8) in 35% yield by autoxidation of the phosphoran (6) derived from vitamin A. Treatment of the corresponding phosphonium periodate with lithium ethoxide gives a similar yield of β-carotene directly.[29]

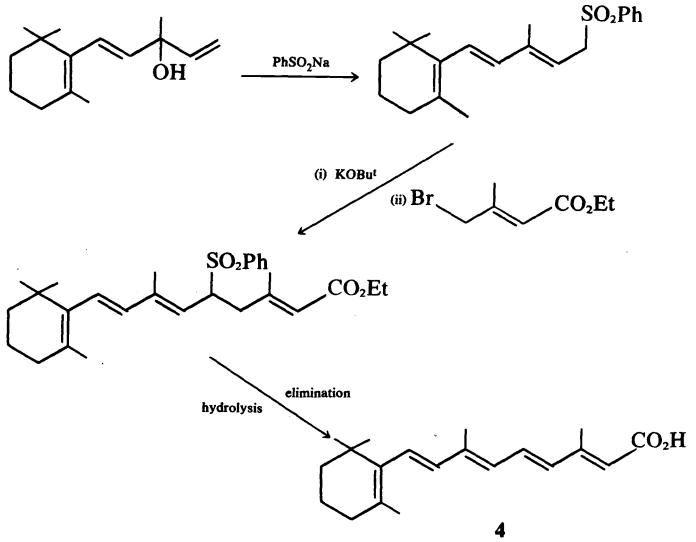
Buddrus[30] has exemplified his method of carrying out Wittig reactions in ethylene oxide by syntheses of both vitamin A (1) and β-carotene (6). Similar condensations in 1,2-epoxybutane have been used in the synthesis of phytoene (33) and related compounds.[31,32] Some Wittig condensations are conveniently carried out at low temperature by treating the phosphonium salt with potassium hydroxide in isopropanol in the presence of the aldehyde.[33] Conventional Wittig reactions have been used extensively to synthesise deuterium or tritium labelled carotenoids; the label may either be incorporated into one of the precursors, or introduced into the phosphoran by base promoted exchange.[29,34–36] The Wittig reaction has also been used to prepare polyene β-diketone.[37,38]

The condensation of retinyl isocyanide (7) with retinal



A series of papers by Liu and his collaborators have described the "one way sensitised photochemical isomerisation" of β-ionone and many of its derivatives. Their work has made available for the first time many of the highly hindered 7-*cis* isomers in the β-ionone and β-ionylidene series, including the 7-*cis*, 7,9-*dicis*, and 7,9,13-tri*cis* isomers of retinal (3).[25–27]

(3), in the presence of butyl lithium, to give β-carotene (8) illustrates an alternative type of olefination to the Wittig reaction.[39] Much attention has also been paid to the synthetic application of sulphones. Thus Julia *et al.*[40] have prepared vitamin A acid (4) in good yield by the route illustrated in Scheme 2, and this approach has been extended recently by Fischli and Mayer to the synthesis

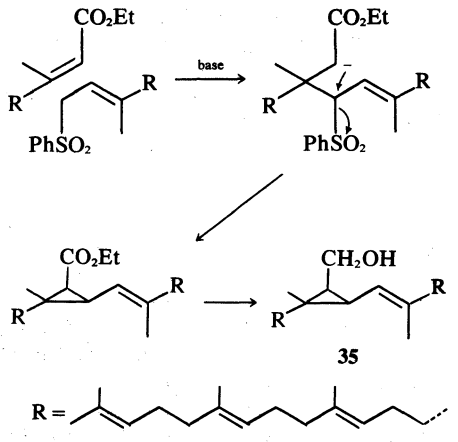


Scheme 2. Sulphone synthesis of vitamin A acid (Julia *et al.*[40]).

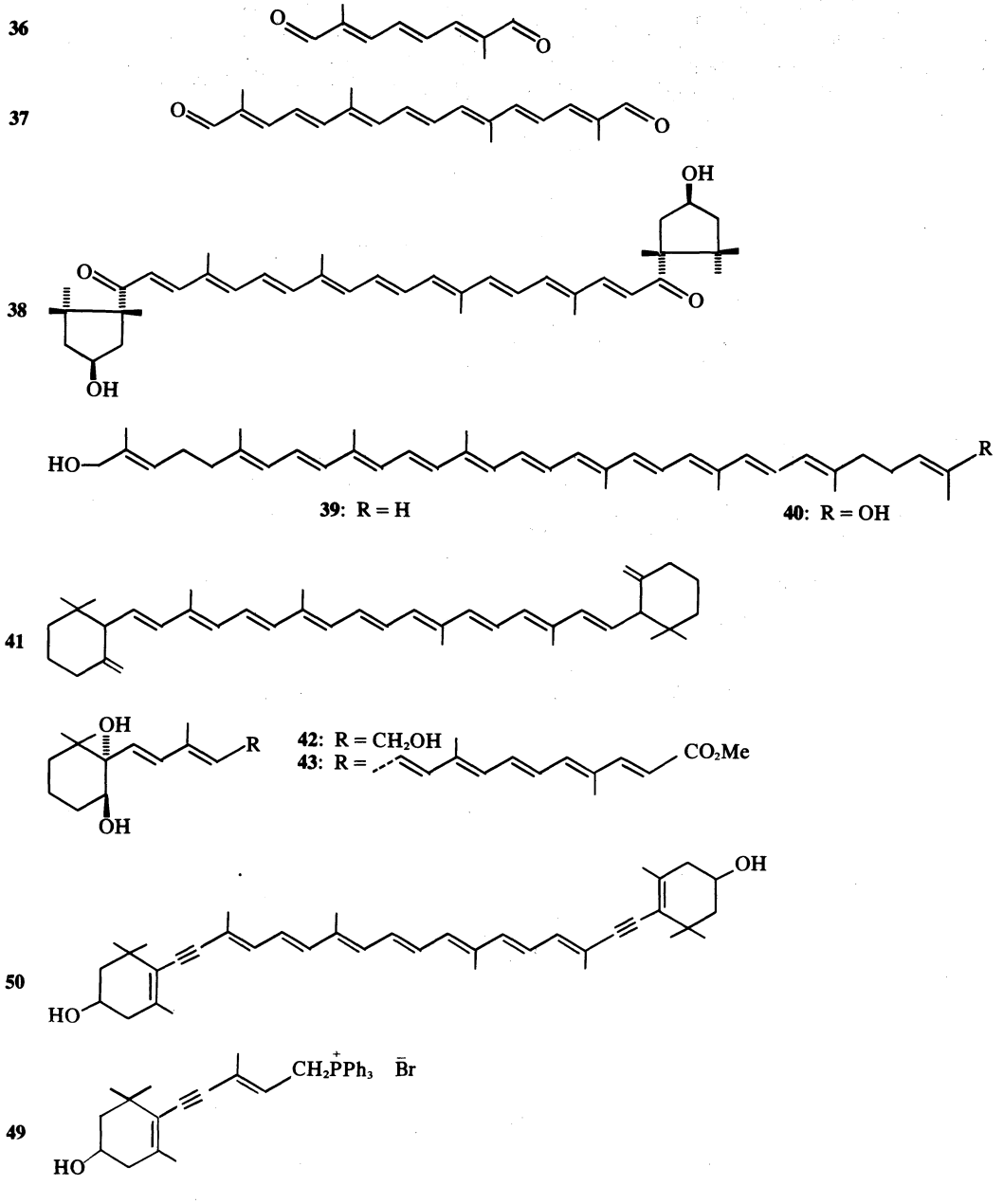
of apocarotenoids and torularhodin ethyl ester.[41] Büchi and Freidinger[42] have prepared retinyl sulphone (34) from vitamin A (1) and diphthalimido sulphide, and converted the sulphone into β-carotene (8) by treatment first with butyl lithium, and then with iodine. The synthesis of pre-phytoene alcohol (35) by Crombie *et al.*[43] also deserves mention (Scheme 3) (an alternative synthesis of this important compound has been reported by Rilling *et al.*[44]).

Treatment of retinal (3) with a lithium aluminium hydride–titanium chloride reagent gives β-carotene in *ca.*85% yield.[45] The reaction is believed to proceed via the pinacol which has previously been converted into β-carotene.[46] The pinacol can also be prepared by cathodic reduction of retinal; α- and β-ionone under similar conditions give the corresponding pinacols almost quantitatively.[47]

Polyene aldehydes and dialdehydes on treatment with butylamine in ethyl acetate in the presence of iso-butyl



Scheme 3. Synthesis of pre-phytoene alcohol (Crombie *et al.*[43]).



borate are readily converted into the mono- or di-imines. These condense with methyl ketones to give the "aldol" condensation products, or with the boric anhydride complex[48] of acetylacetone to give polyene β-diketones.[37] Alternative routes to the latter structures are described later.

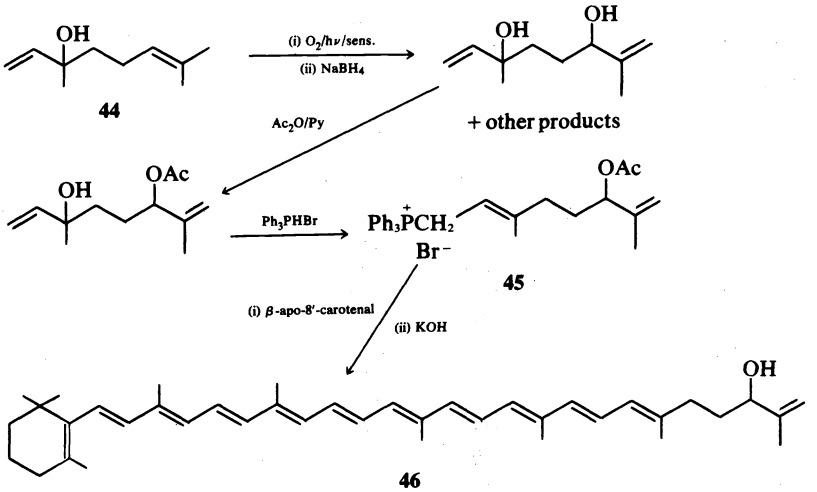
4. CAROTENOID SYNTHESES

New routes to vitamin A and β-carotene have been mentioned in the previous sections. Most syntheses of other carotenoids that have been reported in the last few years are based on one of the well known polyene aldehydes or dialdehydes, in particular (36) and (37), and the novelty in the syntheses consists largely in the preparation of the two end groups.

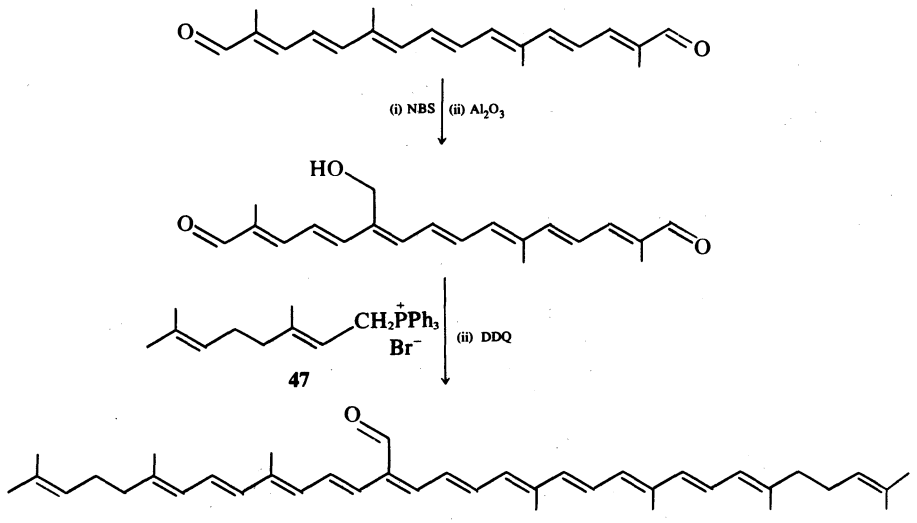
As reported at the 1972 Symposium, the first synthesis of an optically active xanthophyll possessing the correct natural configuration, 3S,5R,3'S,5'R-capsorubin (38), has been achieved by an aldol condensation of the C_{20}-dial (37) with the appropriate methyl ketone.[31] Both lycoxanthin (39) and lycoxanthophyll (40) were obtained from the same starting material and the appropriate Wittig reagents.[6,49] Wittig condensations with the C_{10}-dial (36) have been used to prepare β,γ-carotene and γ,γ-carotene (41).[6,50] An X-ray crystallographic study of the triol (42) used in the synthesis of (±)-azafrin methyl ester (43) from the C_{10}-dial (36) has now established conclusively the threo configuration of the α-glycol system in natural azafrin.

Kjøsen and Liaaen-Jensen[51] have recently confirmed the structure of aleuriaxanthin (46) by synthesis of the racemate. Photosensitised autoxidation of linalool (44) was a key step in the preparation of the necessary Wittig reagent (45) (Scheme 4). The Trondheim group have also found that reaction of the C_{20}-dial (37) with N-bromosuccinimide (NBS), and hydrolysis of the allylic bromide first formed, gives the hydroxy-dial (47), and have used this compound in a Wittig condensation to confirm the structure of lycopen-20-al (48) (Scheme 5); a mixture of rhodopin-20-al and rhodopin-20'-al was also obtained.[52]

Wittig condensations with the C_{20}-dial (37) have been used in a new synthesis of 3,3'-dihyroxyisorenieratene,[53] and in the preparation of various unnatural aromatic carotenoids.[54-56] Yamaguchi *et al.*[24] have reported the synthesis of the aromatic acetylenic carotenoids, 7,8-didehydroisorenieratene (31) and 7,8-didehydrorenieratene (32) from the C_{10}-dial (36) (cf.



Scheme 4. Synthesis of (±)-aleuriaxanthin (Kjøsen and Liaaen-Jensen[49]).



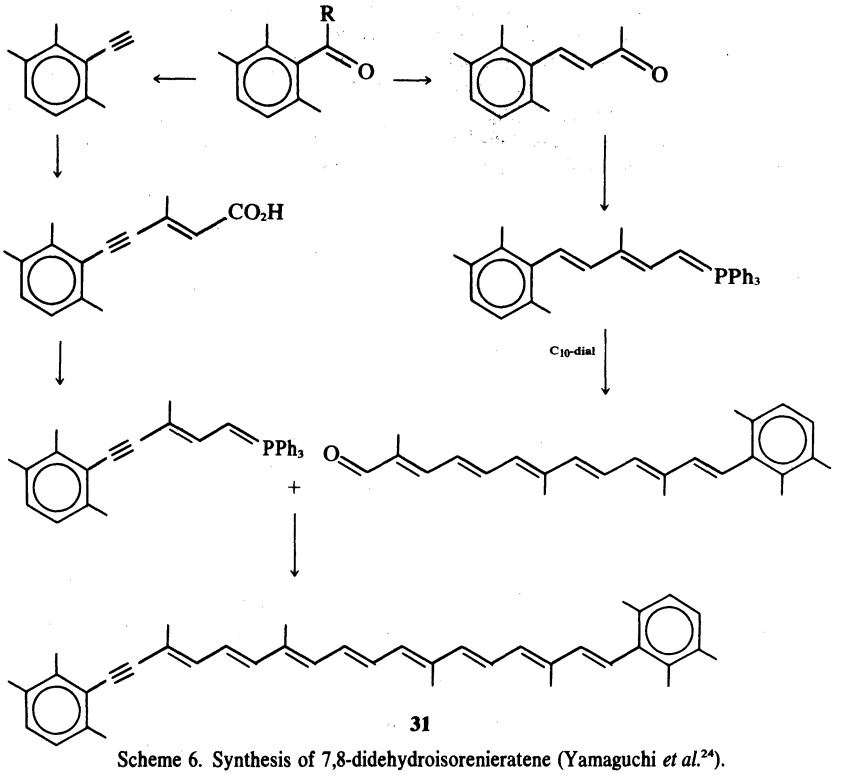
Scheme 5. Synthesis of lycopen-20-al (Puntervold and Liaaen-Jensen[52]).

Scheme 6). By carrying out the final Wittig condensation at low temperature, low yields were obtained of the all-*trans* isomers identical with the minor natural pigments in *Reniera japonica*; under most conditions the more stable 9-*cis* isomers were formed. Using the low temperature KOH/i-PrOH method, the all-*trans* isomer of alloxanthin (50) has been prepared from the C_{10}-dial and the *trans*-phosphonium salt (49).[54] Wittig condensations based on the $C_{15}+C_{10}+C_{15}\rightarrow C_{40}$ approaches have also been used in the synthesis of (optically inactive) β,β-carotene-2,2'-diol (51) (Scheme 7),[57] and of 2R,2'R-dimethyl-β,β-carotene from the corresponding irone.[58]

The same general approach was used earlier to synthesise (optically inactive) zeaxanthin (55) from the C_{10}-dial and the Wittig salt (54).[59] The latter intermediate was prepared by a lengthy route from isophorone, but can now be prepared more readily from α-ionone (52) (Scheme 8).[60] Condensation of the phosphonium salt (54) with apo-8'-lycopenal, gave (±)-rubixanthin (56).[61] The total synthesis of 3R,3'R-zeaxanthin, identical with the natural pigment, is reported at this meeting.[62]

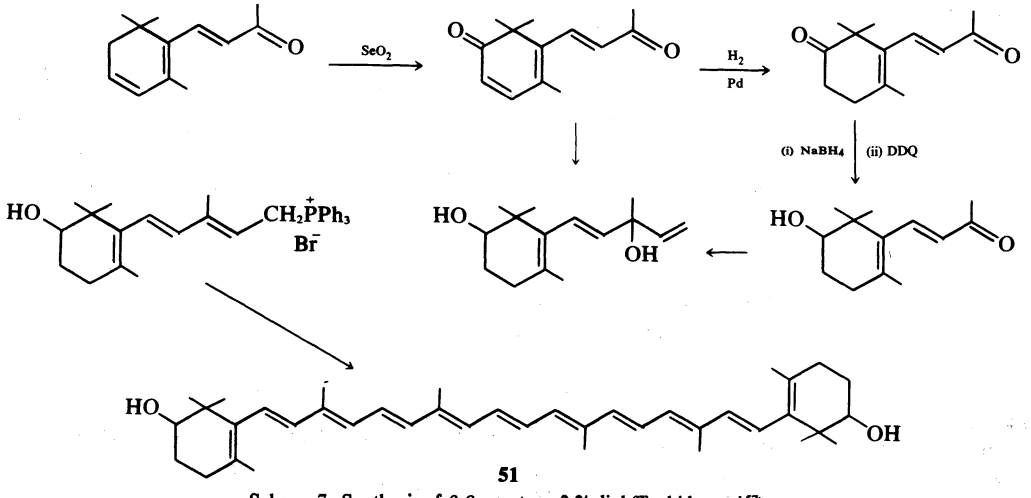
The dioxolanation procedure for converting the α- into the β-series has also been applied[60] (Scheme 9) to prepare (59), a key intermediate in the Surmatis route for the synthesis of rhodoxanthin (60).[63]

Tunaxanthin, a pigment in many fish, has been formulated as an ϵ,ϵ-carotene-3,3'-diol.[64] The two (optically inactive) carotenoids (62) and (63), differing in the relative configuration of the two substituents at C-3 and C-6 in the end groups, have now been synthesised



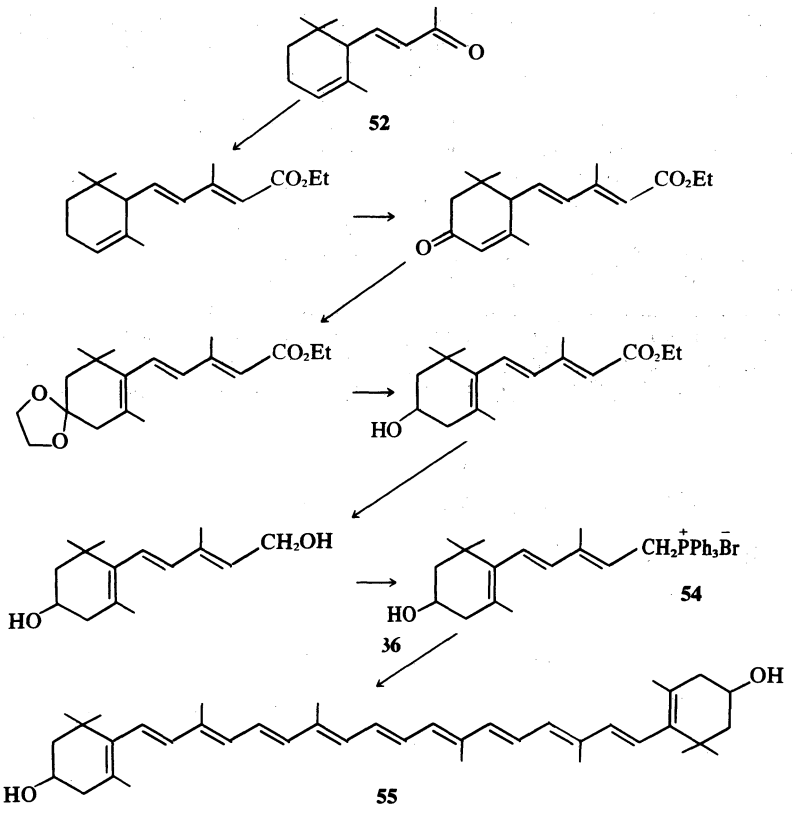
31

Scheme 6. Synthesis of 7,8-didehydroisorenieratene (Yamaguchi *et al.*[24]).

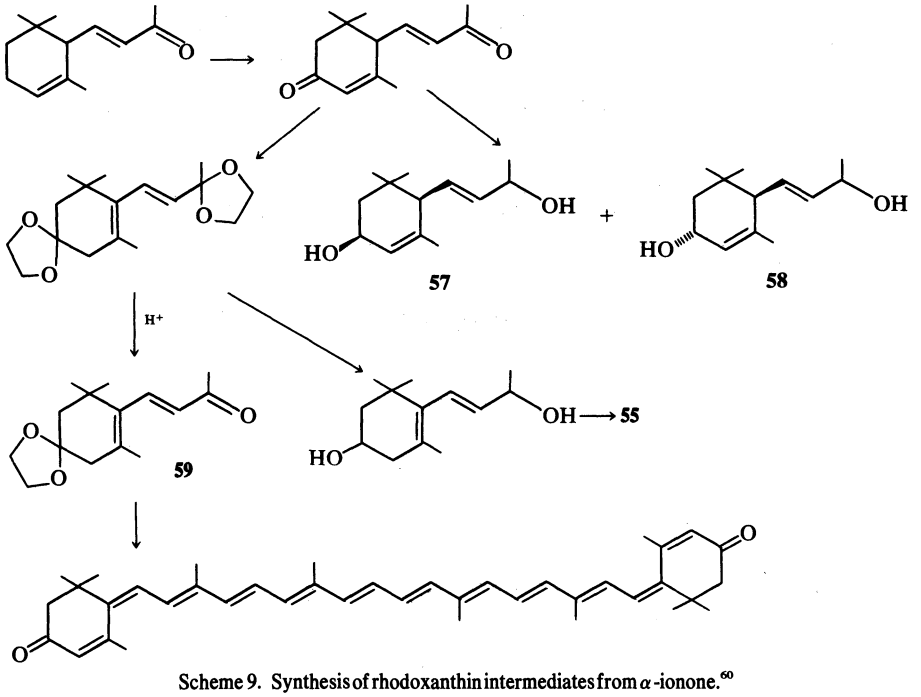


51

Scheme 7. Synthesis of β,β-carotene-2,2'-diol (Tsukida *et al.*[57]).



Scheme 8. Synthesis of zeaxanthin from α-ionone.[60]

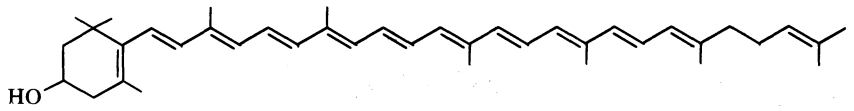


Scheme 9. Synthesis of rhodoxanthin intermediates from α-ionone.[60]

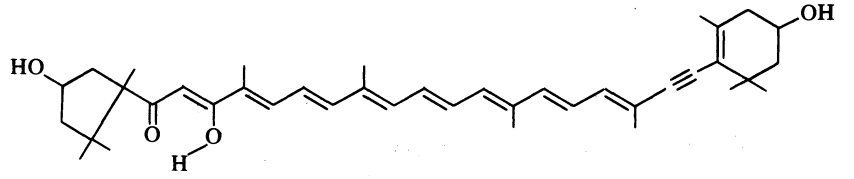
(Scheme 10).[60] The assignment of the relative configuration to the end groups in the two series was made unambiguously by X-ray crystallographic analysis of the 3,6-*cis*-acetoxy-aldehyde (61).[65] The two products differ noticeably in their NMR and chromatographic properties. Preliminary TLC comparisons with a concentrate of natural tunaxanthin shows that the latter resembles (63).

Another reason for undertaking the syntheses of (62) and (63) relates to the absolute configuration of lutein (20). The latter has three asymmetric centres, and was shown

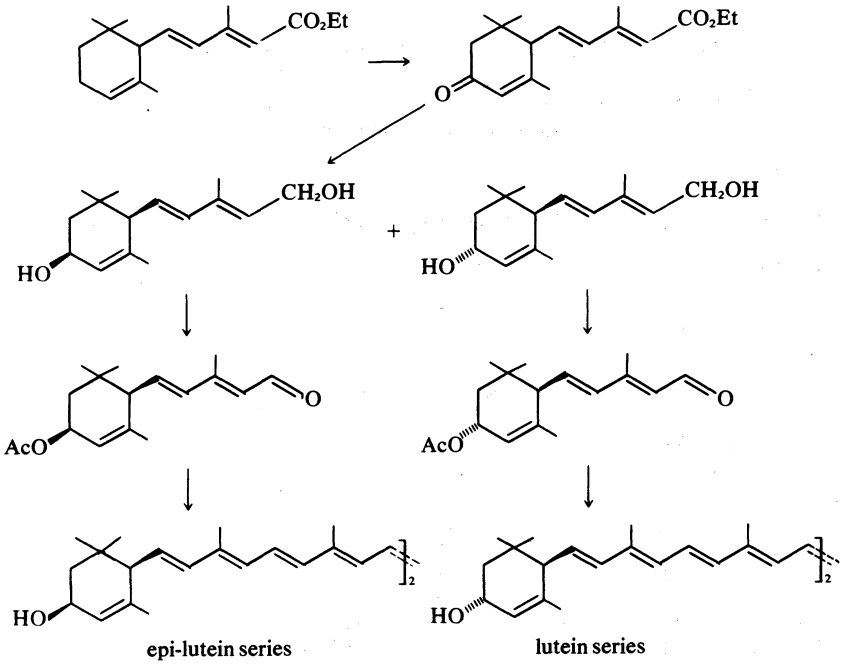
56



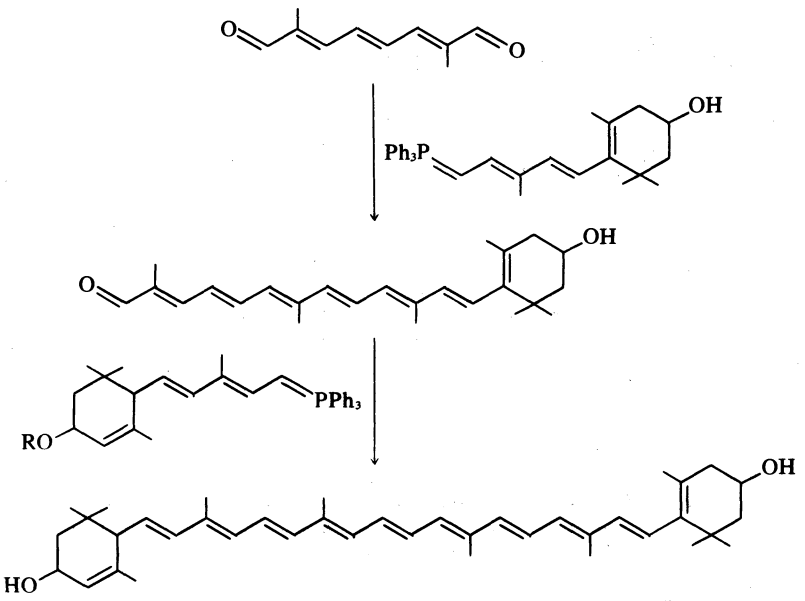
64



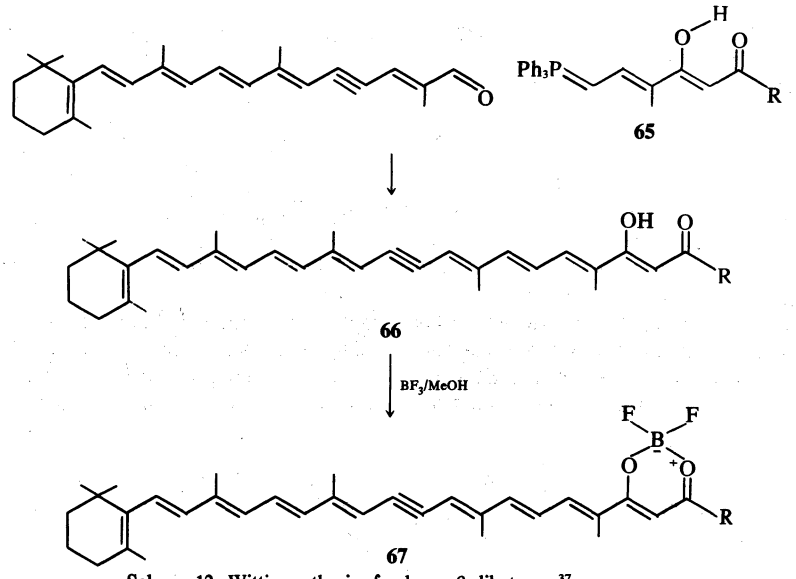
to have a 3R,6'R configuration.[66] We originally took reports of biosynthetic studies[67] to indicate that the remaining centre at C-3' has the S configuration. However Eugster *et al.*[68] came to the opposite conclusion from studies on products obtained from lutein after O-methylation. Our ^{1}H and ^{13}C studies on lutein, and the two models (57) and (58), led to the same conclusion,[69] and recently Andrewes *et al.*[70] have succeeded in obtaining



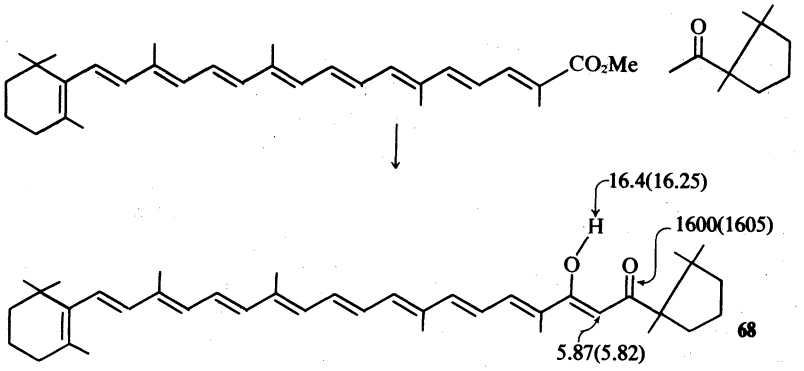
Scheme 10. Synthesis of ε,ε-carotene-3,3'-diols.[60]



Scheme 11. Synthesis of (optically inactive) lutein and its 3'-epimer.[60]

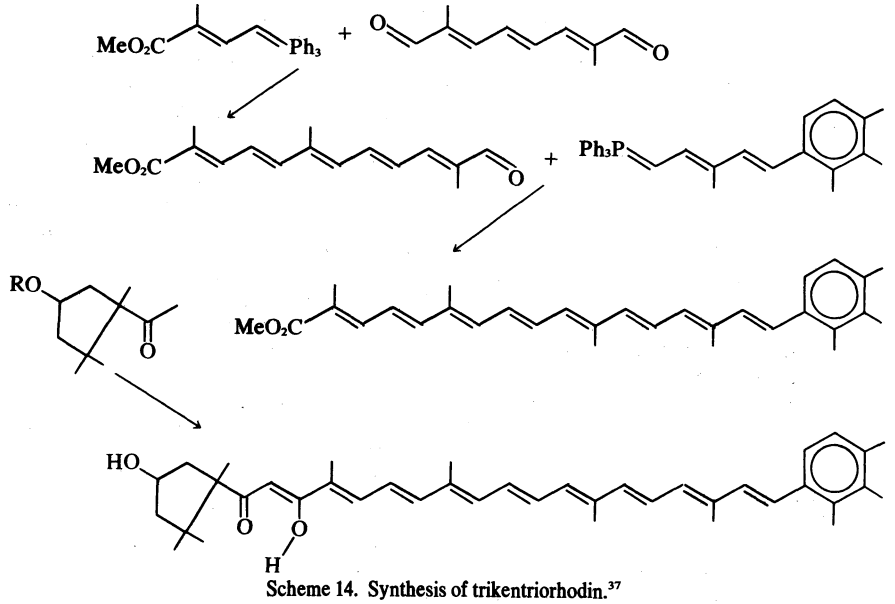


Scheme 12. Wittig synthesis of polyene β-diketones.[37]



	Methyl bands (δ)		
β-diketone(68)	0.88	1.09	1.18
deshydroxy-capsorubin	0.85	1.11	1.19
capsorubin(38)	0.85	1.20	1.38
mytiloxanthin(64)	0.85	1.19	1.34

Scheme 13. Claisen type synthesis of polyene β-diketones.[37] Key NMR and i.r. bands are given in 68 and (in parentheses) the corresponding bands for mytiloxanthin (64). The table compares the NMR bands due to the three methyls on the five-membered ring in the synthetic β-diketone 68 with the corresponding bands in deshydroxy-capsorubin, capsorubin (38) and mytiloxanthin (74).



Scheme 14. Synthesis of trikentriorhodin.[37]

meso-zeaxanthin from lutein by prototropic rearrangement. Any remaining doubts are resolved by comparison of the NMR properties of lutein with those of (62) and (63). The α-end group of lutein clearly relates to those in (63) which are known to have the 3,6-*trans* configuration from the X-ray studies on (61). The configuration of lutein must therefore by 3R,3'R,6'R. The explanation of the biosynthetic results remains obscure; there is as yet no evidence from the synthetic compounds that a 3,6-*cis* end group flips configuration readily to give the 3,6-*trans* end group, which might be expected to be the more stable. Using Wittig reagents derived from intermediates in the synthesis of (62) and (63), optically inactive forms have been prepared of both lutein and its 3'-epimer (Scheme 11).[60] The latter has the relative configuration recently assigned to calthaxanthin.[71]

Finally I should like to indicate the progress made in developing routes for the synthesis of polyene β-diketones, a class of natural pigments which was reported for the first time at the 1972 Symposium,[31] and which includes the carotenoids mytiloxanthin (64) from the edible mussel *Mytilus edulis*,[72] and trikentriorhodin (69) from the marine sponge *Trikentrion helium*.[73] Condensation of a phosphonium salt such as (65) (prepared by hydration of the corresponding acetylenic ketone) with polyene aldehydes or dialdehydes gives the required structures (e.g. 66, Scheme 12).[37] It is interesting to note that these polyene β-diketones combine readily with boron trifluoride to give a new class of carotenoid derivatives, the difluoroborates (e.g. 67). Alternatively the polyene β-diketones can be prepared by a Claisen type condensation between a polyene carboxylate and a methyl ketone.[37] In this way (68) has been synthesised (Scheme 13). The NMR bands associated with its cyclopentane end group resemble those of the same end group in deshydroxy-capsorubin (cf. 38). In other words the chemical shifts of the five-membered ring methyl groups are very similar in the polyene ketone and the corresponding β-diketone. This justifies one of the assumptions made in the structural assignment of both mytiloxanthin and trikentriorhodin. The synthesis of the structure (69) assigned to trikentriorhodin was recently accomplished on a small scale using the route outlined in Scheme 14.[37]

Acknowledgements—I should like to express my warm appreciation to all my collaborators, both past and present, at Queen Mary College on whose results I have drawn freely to illustrate various points in this review and progress report. Our polyene group at present consists of Drs. G. P. Moss, T. P. Toube, M. Hodler, and M. Ito, Miss E. A. H. Hall, and Messrs. A. Chopra, P. R. Ellis, E. Faruk, and J. F. Hagel.

REFERENCES

[1]H. Mayer and O. Isler, *Carotenoids* (editor O. Isler), Chap. 6, Birkhäuser, Basle (1971).
[2]J. B. Davis and B. C. L. Weedon. *Proc. Chem. Soc.* 182 (1960).
[3]R. D. G. Cooper, J. B. Davis, A. P. Leftwick, C. Price and B. C. L. Weedon. *J. C. S. Perkin I* 2195 (1975).
[4]M. Hodler, G. P. Moss and B. C. L. Weedon, Unpublished results.
[5]R. Holzel, A. Leftwick and B. C. L. Weedon. *Chem. Commun.* 128 (1969).
[6]S. Liaaen-Jensen. *Pure Appl. Chem.* **35**, 81 (1973).
[7]G. W. Francis, S. Hertzberg, R. R. Upadhyay and S. Liaasen-Jensen. *Acta Chem. Scand.* **23**, 1097 (1972).
[8]A. P. Leftwick and B. C. L. Weedon *Chem. Commun.* 49 (1967).
[9]M. Hodler, H. Thommen, and H. Mayer. *Chimia* **28**, 723 (1974).
[10]E. Nicoară, G. Illyes, M. Şuteu and C. Bodea. *Rev. Roum. Chim.* **12**, 547 (1967).
[11]F.-C. Czygan. *Flora A* **59**, 339 (1968); *Z. Naturforsch.* **B23**, 1367 (1968).
[12]A. G. Andrewes, G. Borch, S. Liaaen-Jensen and G. Snatzke. *Acta Chem. Scand.* **B28**, 730 (1974).
[13]F. Kienzle and M. Hodler. *Helv. Chim. Acta* **58**, 198 (1975).
[14]M. Hodler, B. Terem, J. H. P. Utley and B. C. L. Weedon, Unpublished results.
[15]J.-G. Gourcy, B. Terem, J. H. P. Utley and B. C. L. Weedon, Unpublished results.
[16]G. Goodfellow, G. P. Moss, J. Szabolcs, Gy. Tóth and B. C. L. Weedon. *Tetrahedron Lett.* 3925 (1973).
[17]H. Cadosch and C. H. Eugster. *Helv. Chim. Acta* **57**, 1472 (1974).
[18]K. Bernhard, G. P. Moss, Gy. Tóth and B. C. L. Weedon, *Tetrahedron Lett.* 115 (1976).
[19]B. C. L. Weedon, *Carotenoids* (editor O. Isler), Chap. 5. Birkhäuser, Basle (1971).
[20]K. Bernhard, G. P. Moss. Gy. Tóth and B. C. L. Weedon *Tetrahedron Lett.* 3899 (1974).
[21]G. P. Moss, J. Szabolcs, Gy. Tóth and B. C. L. Weedon. *Acta Chem. Hung.* In press.
[22]B. C. L. Weedon, *Rev. Pure Appl. Chem.* (*Australia*) **20**, 51 (1970).
[23]J. Y. Cheng, M. Don-Paul and R. J. Antia, *J. Protozool.* **21**, 761 (1974).
[24]T. Ike, J. Inanago, A. Nakano, N. Okukado and M. Yamaguchi. *Bull. Chem. Soc. Jap.* **47**, 350 (1974).
[25]V. Ramamurthy, G. Tustin, C. C. Yau and R. S. H. Liu, *Tetrahedron* **31**, 193 (1975).
[26]V. Ramamurthy and R. S. H. Liu, *Tetrahedron* **31**, 201 (1975).
[27]A. E. Asato and R. S. H. Liu, *J. Am. chem. Soc.* In press.
[28]O. A. Malchenko, S. K. Seit-Ablaeva, N. V. Zotchik and Z. A. Rubtsov, *Khim.-Farm. Zh.* **7**, (2), 18 (1973).
[29]H. J. Bestman, O. Kratzer, R. Armsen and E. Maekawa, *Liebig's Annalen* 760 (1973).
[30]J. Buddrus, *Chem. Ber.* **107**, 2050 (1974).
[31]B. C. L. Weedon, *Pure Appl. Chem.* **35**, 113 (1973).
[32]N. Khatoon, D. E. Loeber, T. P. Toube and B. C. L. Weedon, *J. C. S. Perkin I* 1457 (1975); *Chem. Commun.* 996 (1972).
[33]Brit. Patent 877351.
[34]Å. Eidem and S. Liaaen-Jensen. *Acta Chem. Scand.* **B28**, 273 (1974).
[35]J. E. Johansen and S. Liaaen-Jensen. *Acta Chem. Scand.* **B28**, 301, 349 (1974).
[36]H. Brzezinka, B. Johannsen and H. Budzikiewicz, *Z. Naturforsch.* **B29**, 429 (1974).
[37]A. Chopra, G. P. Moss and B. C. L. Weedon, Unpublished results.
[38]H.-J. Bestmann and R. W. Saalfrank. *Angew. Chem. Internat. Edit.* **9**, 367 (1970).
[39]F. Kienzle, *Helv. Chim. Acta* **56**, 1662, 1671 (1973).
[40]M. Julia and D. Arnould, *Bull. Soc. Chim. France* 747 (1973).
[41]A. Fischli and H. Mayer, *Helv. Chim. Acta* **58**, 1492 (1975).
[42]G. Büchi and R. M. Freidinger, *J. Am. chem. Soc.* **96**, 3332 (1974).
[43]L. Crombie, D. A. R. Findley and D. A. Whiting, *Chem. Commun.* 1045 (1972); R. V. M. Campbell, L. Crombie, D. A. R. Findley, R. W. King, G. Pattenden and D. A. Whiting. *J. C. S. Perkin I* 897 (1975).
[44]L. J. Altman, L. Ash, R. C. Kowerski, W. W. Epstein, B. R. Larsen, H. C. Rilling, F. Muscio and D. E. Gregonis, *J. Am. chem. Soc.* **94**, 3257 (1972).
[45]J. E. McMurry and M. C. Fleming. *J. Am. chem. Soc.* **96**, 4708 (1974).
[46]Eastman Kodak Co., Brit. Pat. 1097497 (1968).
[47]R. Sioda, B. Terem, J. H. P. Utley and B. C. L. Weedon, Unpublished results.
[48]H. J. J. Pabon, *Rec. Trav. Chim.* **83**, 379 (1964).
[49]H. Kjøsen and S. Liaaen-Jensen, *Acta Chem. Scand.* **25**, 1500 (1971).
[50]A. G. Andrewes and S. Liaaen-Jensen, *Acta Chem. Scand.* **27**, 1401 (1973).

[51]H. Kjøsen and S. Liaaen-Jensen, *Acta Chem. Scand.* **27**, 2493 (1973).
[52]O. Puntervold and S. Liaaen-Jensen, *Acta Chem. Scand.* **B28**, 1096 (1974).
[53]N. Okukado, T. Kimura and M. Yamaguchi, *Mem. Fac. Sci., Kyushu Univ. Ser. C.* **9**, 139 (1974); *Chem. Abstr.* **81**, 152447.
[54]A. Khare, G. P. Moss and B. C. L. Weedon, Unpublished results.
[55]G. W. Francis, *Acta Chem. Scand.* **26**, 2969 (1972).
[56]N. Okukado, *Bull. Chem. Soc. Jap.* **47**, 2345 (1974).
[57]K. Tsukida, K. Saiki, M. Ito, I. Tomofugi and M. Ogawa, *J. Nutr. Sci. Vitaminol.* **21**, 147 (1975).
[58]A. G. Andrewes, S. Liaaen-Jensen and G. Borch. *Acta Chem. Scand.* **B28**, 737 (1974).
[59]D. E. Loeber, S. W. Russell, T. P. Toube, B. C. L. Weedon and J. Diment, *J. Chem. Soc. C.* 404 (1971).
[60]E. Faruk, G. P. Moss and B. C. L. Weedon, Unpublished results.
[61]N. Khatoon, T. P. Toube and B. C. L. Weedon, Unpublished results.
[62]H. Mayer, W. Boguth, H. G. W. Leuenberger, E. Widmer and R. Zell, *Abstr. Fourth Internat. Symp. Carotenoids* 43 (1975); *cf.* Swiss Patent Appl. No. 11437/74.
[63]J. D. Surmatis, A. Walser, J. Gibas, U. Schwieter and R. Thommen, *Helv. Chim. Acta* **53**, 974 (1970).
[64]G. F. Crozier and D. W. Wilkie, *Comp. Biochem. Physiol.* **18**, 801 (1966).
[65]H. W. Dias and M. B. Hursthouse, Unpublished results.
[66]D. Goodfellow, G. P. Moss and B. C. L. Weedon, *Chem. Commun.* 1578 (1970).
[67]T. J. Walton, G. Britton and T. W. Goodwin, *Biochem. J.* **112**, 383 (1969).
[68]R. Buchecker, P. Hamm and C. H. Eugster, *Helv. Chim. Acta* **57**, 631 (1974).
[69]D. Goodfellow, G. P. Moss, P. Pregosin and B. C. L. Weedon, Unpublished results.
[70]A. G. Andrewes, G. Borch and S. Liaaen-Jensen, *Acta Chem. Scand.* **B28** 139 (1974).
[71]A. G. Dabbagh and K. Egger, *Z. Pflanzenphysiol.* **72**, 177 (1974).
[72]A. Khare, G. P. Moss and B. C. L. Weedon, *Tetrahedron Lett.* 3921 (1973).
[73]M. Aguilar-Martinez and S. Liaaen-Jensen, *Acta Chem. Scand.* **B28**, 1247 (1974).