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# NATURAL ACETYLENES OF SPECIAL BIOSYNTHETIC INTEREST

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**Abstract**—Acetylenic metabolites which probably do not evolve from oleate through stearolate or crepenynate are reviewed

## INTRODUCTION

OVER 600 natural acetylenes have been isolated within the last 20 yr [1] Many were obtained from fungi and plants, and in most structures a triple bond was conjugated with further unsaturation, as in matricaria ester (1) Their arrangement of unsaturation and functional

$$\mathrm{Me\ CH{=}CH{\cdot}[C{\equiv}C]_2\ CH{=}CH\ CO_2Me} \qquad (1)$$

$$\mathrm{Me\ [CH_2]_7\ CH\overset{c}{=}CH\ [CH_2]_7{\cdot}CO_2Me} \qquad (2)$$

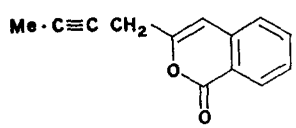
groups led to theories[2] that polyacetylenes evolved when oleate (2) was progressively dehydrogenated *via* stearolate (3) or crepenynate (4).

$$\mathrm{Me\ [CH_2]_7{\cdot}C{\equiv}C\ [CH_2]_7{\cdot}CO_2Me} \qquad (3)$$

$$\mathrm{Me{\cdot}[CH_2]_4{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}CH\overset{c}{=}CH{\cdot}[CH_2]_7\ CO_2Me.} \qquad (4)$$

This review concerns those acetylenes which are not easily accommodated by such theories An exception may comprise a compound with a branched carbon chain, or one which has a triple bond *sufficiently* removed from any unsaturated system which was derived from a polyyne fragment for the triyne (5) has been shown[3] to be a precursor

$$\mathrm{Me\ [C{\equiv}C]_3{\cdot}CH_2{\cdot}CH\overset{c}{=}CH\ [CH_2]_3{\cdot}OAc} \qquad (5)$$




(6)

of the monoacetylene capillarin (6). These biosynthetically unusual acetylenes are grouped conveniently into the following classes (i) Carotenoids, (ii) Other terpenoids; (iii) Miscellaneous acetylenes

[1] Recent reviews include SIR E R H JONES, *Chem Br* **2**, 6 (1966), F BOHLMANN, *Fortschr Chem Org. Naturstoffe*, **25**, 1 (1967)

[2] J D BU'LOCK, *Comparative Phytochemistry* (edited by T SWAIN), p 79 and references therein, Academic Press, London

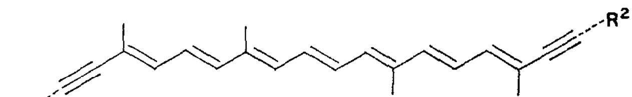
[3] F BOHLMANN, R JENTE, W LUCAS, J LASER and H SCHULTZ, *Chem Ber* **100**, 3183 (1967)

*Carotenoids*

Alloxanthin (7, $R^1=R^2=a$, Table 1) was the first acetylenic carotenoid to be fully characterized[4] Since 1967 algae and marine organisms have yielded seven further carotenoids[5] in which the acetylene bond always appears in the 7,8 position (Table 1) The all-*trans* polyene counterpart for each acetylene has also been isolated from natural sources. This prompts the hypothesis that, say, alloxanthin ($7, R^1=R^2=a$) and diatoxanthin ($8, R^1=R^2=a$) could be derived by stepwise dehydrogenation of zeaxanthin ($9, R^1=R^2=a$).

Modern spectroscopic techniques indicated that several well-known xanthophylls[5] like neoxanthin (10, $R=c$, $X=H$), in fact contained an allene group in the 6,8 position Allenic

TABLE 1 ACETYLENIC CAROTENOIDS



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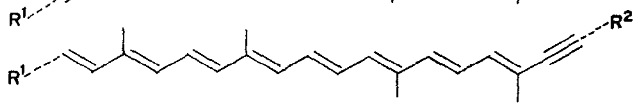

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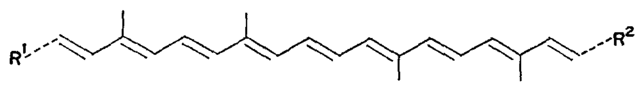
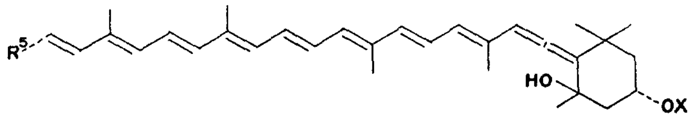
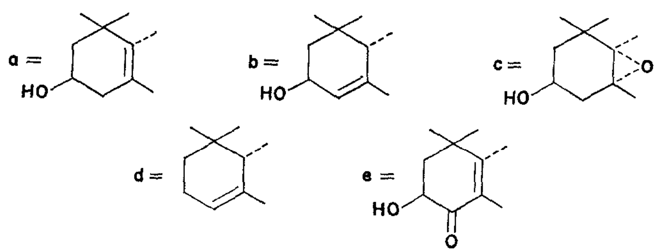


(9)



(10)

X=H or Ac



| Acetylenic carotenoid | Structure | $R^1$ | $R^2$ | Reference | Polyene analogue (based on 9) |
|---|---|---|---|---|---|
| Alloxanthin | 7 | a | a | 4, 6, 8 | Zeaxanthin |
| Diatoxanthin | 8 | a | a | 4, 9 | Zeaxanthin |
| Crocoxanthin | 8 | d | a | 4 | Zeinoxanthin |
| Monoadoxanthin | 8 | b | a | 4 | Lutein |
| Pectenolone | 8 | e | a | 6 | Adonixanthin |
| Diadinoxanthin | 8 | c | a | 8, 9 | Antheraxanthin |
| Asterinic acid | 7 | e | e | 7 | Astaxanthin |
| | 8 | e | e | | |

[4] A K Mallams, E S Waight, B C L Weedon, D T Chapman, F T Haxo, T W Goodwin and D M Thomas, *Chem Commun* 301 (1967) and later work

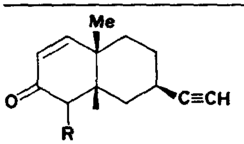
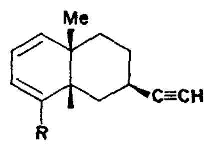
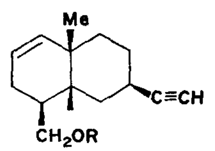
[5] B C L Weedon, Lecture read to the Royal Australian Chemical Institute, Sydney (August 1968), *Rev Pure Appl Chem* **202,** 51 (1970)

carotenoids are widely distributed in the higher plants and algae, and their discovery aroused interest in possible biological interconversion with acetylenic carotenoids All these carotenoids have the dihydroxy or hydroxyacetoxy end group as in (10), and significantly no diallenic or acetylen-allenic carotenoid has yet been recorded. Accordingly the allenic end-group has been transformed *in vitro* into an acetylenic end-group[10] and vice versa[11]

*Other Terpenoids*

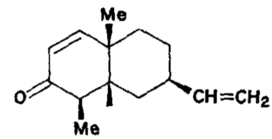
Several norsesquiterpenoids with an ethynyl substituent at C(7) were isolated (Table 2) by Nozoe[12,14] from the Benihi tree *Chamaecyparis formosensis* Matsum (Cupressaceae); the vinyl analogue (11) was also present Hortmann[15] has speculated on the ring biosynthesis of these noreudesmanes

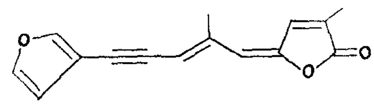
TABLE 2 ETHYNYL TERPENES FOUND IN BENIHI TREE[12–14]

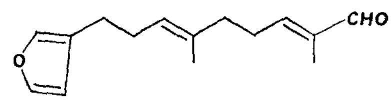
| | | |
|---|---|---|
|  | R = α-Me<br>R = β-Me<br>R = α-OH | Isochamaecynone<br>Chamaecynone<br>Hydroxyisochamaecynone |
|  | R = $CH_2OH$<br>R = CHO | Dehydrochamaecynenol<br>Dehydrochamaecynenol |
|  | R = H<br>R = Ac | Chamaecynenol<br>Chamaecynenol acetate |

Massy-Westropp[16] characterized "freelingyne" (12) amongst "related" sesquiterpenes in the wood oil of the Angiosperm *Eremophila freelingii* (Myoporaceae) The skeleton was partially established on biosynthetic grounds, and clearly was thought to be an oxidation product of a diolefin like torreyal (13), rather than a cyclization product of a diacetylenic intermediate (14). Torreyal has been isolated[17] from the wood oil of the Gymnosperm, *Torreya nucifera* Sieb et Zucc (Taxaceae).

[6] S A CAMPBELL, A K MALLAMS, E S WAIGHT, B C L WEEDON, M BARBIER, E LEDERER and A SALAQUE, *Chem Commun* 941 (1967)
[7] N A SORENSEN, S L JENSEN, B BORDALEN, A HAUG, C ANZELL and G FRANCIS, *Acta Chem Scand* **22**, 344 (1968)
[8] K AITZETMULLER, W A SVEC, T J KATZ and H H STRAIN, *Chem Commun* 32 (1968)
[9] K EGGER, H NITSCHE and H KLEINIG, *Phytochem* **8**, 1583 (1969)
[10] H NITSCHE, *Tetrahedron Letters* 3343 (1970), H NITSCHE, K EGGER and A D DABBAGH, *Tetrahedron Letters* 2999 (1969), see also K EGGER, A D DABBAGH and H NITSCHE, *Tetrahedron Letters* 2995 (1969)
[11] S W RUSSELL and B C. L WEEDON, *Chem Commun* 85 (1969)
[12] T NOZOE, Y S CHENG and T TODA, *Tetrahedron Letters* 3663 (1966)
[13] T ASAO, S IBE, K TAKASE, Y S CHENG and T NOZOE, *Tetrahedron Letters* 3639 (1968)
[14] K TAKASE, S IBE, T ASAO, T NOZOE, H SHIMANOUCHI and Y SASADA, *Chem & Ind* 1638 (1968)
[15] A G HORTMANN, *Tetrahedron Letters* 5785 (1968)
[16] R A MASSY-WESTROPP, G D REYNOLDS and T M SPOTSWOOD, *Tetrahedron Letters* 1939 (1966)
[17] T SAKAI, K NISHIMURA and Y. HIROSE, *Bull Chem Soc Japan* **38**, 381 (1965)


(11)


(12)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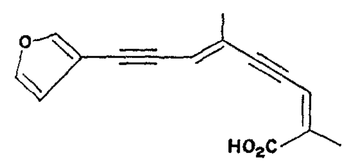
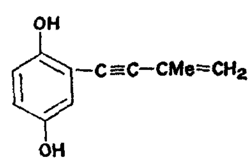

(14)

*Miscellaneous Acetylenes*

Only two types have branched carbon skeletons. Siccayne (15) has been extracted[18] from one of the fungi imperfecti, *Helminthosporium siccans* g-207. The amino acids


(15)

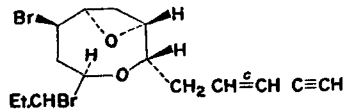
(16–18) have been discovered[19] in the seed oil *Euphoria longan* (Sapindaceae) and homoisoleucine was suggested as the precursor of the acetylene (16).

$$HC{\equiv}C\ CH(CH_2R)\ CH_2{\cdot}CH_2(NH_2){\cdot}CO_2H \qquad \begin{array}{ll}(16) & R{=}H\\ (17) & R{=}OH\end{array}$$

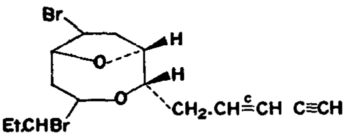
$$HC{\equiv}C{\cdot}CH(OH)\ CH_2\ CH(NH_2){\cdot}CO_2H \qquad (18)$$

Ethynyl metabolites isolated from red algae (Rhodomelaceae) include laureatin (19), isolaureatin (20) (*Laurencia nipponica* Yamada)[20, 21] and laurencin (21) (*Laurencia glandulifera* Kutzing)[22] These acetylenes all contain bromine and oxygen atoms attached to

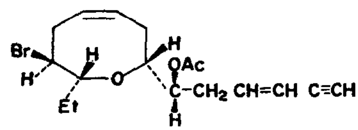
[18] K Ishibashi, K Nose, T Shindo, M Arai and H Mishina, *Ann Report Sankyo Res Lab* **20**, 76 (1968)
[19] M L Sung, L Fowden, D S Millington and R C Sheppard, *Phytochem* **8**, 1227 (1969)
[20] T Irie, M Izawa and E Kurosawa, *Tetrahedron Letters* 2091 (1968)
[21] T Irie, M Izawa and E Kurosawa, *Tetrahedron Letters* 2735 (1968), T Irie, M Izawa and E Kurosawa, *Tetrahedron* **26**, 851 (1970)
[22] T Irie, M Suzuki and T Masamune, *Tetrahedron* **24**, 4193 (1968)




(19)




(20)




(21)

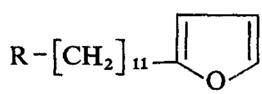
adjacent carbon atoms. Different positions of a $C_{15}$ chain are linked by an oxygen bridge in the *trans* enyne (21) than in the *cis* enynes (19) and (20) to engender the eight membered ring. Bu'Lock[2] has suggested that hexadeca-4,7,10,13-tetraenoate, which has been detected[23] in Chlorophyta (Scenedesmus), is epoxidized, then cyclizes and undergoes transannular reactions.

From the essential oil of the tree *Litsea oderifera* Valeton (Lauraceae), Matthews[24] obtained the methoxyacetylene homologues (22; n = 7,9).

$$Me \cdot CH(OMe) \cdot [CH_2]_n \cdot C \equiv CH \qquad (22)$$

Recently Lifshitz[25] isolated eight related vinyl and ethynyl $C_{17}$ compounds (Table 3) from the seed of the avocado pear (variety Nabal or Effinger; *Persea gratissima* Gaertn.; Lauraceae)

Table 3. Metabolites isolated from avocado pear




$R \cdot [CH_2]_{11}$ CO $CH_2$ CH(OH) $CH_2OAc$
$R \cdot [CH_2]_{11}$ CH(OH) $CH_2$ CH(OH) $CH_2OAc$
R $[CH_2]_{11} \cdot CH(OH) \cdot CH_2 \cdot CH(OH)$ $CH_2OH$

R = $CH_2{=}CH{-}$ or $HC{\equiv}C{-}$

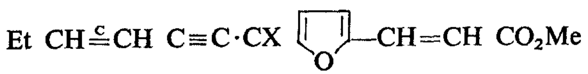
Various microorganisms have been reported to produce monoacetylenes (Table 4); however, recent work[26] has indicated that culture conditions are difficult to reproduce

[23] E Klenk and W Knipprath, *Z Physiol Chem* **317**, 243 (1959)
[24] W S Matthews, G. B Pickering and A T Umoh, *Chem & Ind* 122 (1963)
[25] Y Kashman, I Neeman and A Lifshitz, *Tetrahedron* **25**, 4617 (1969)
[26] J K Jenkins, Sir E R H Jones, V Thaller and J L Turner, unpublished work.

TABLE 4 MONOACETYLENES AND RELATED COMPOUNDS FOUND IN MICROORGANISMS

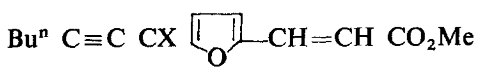
| Microorganism | Metabolite | Reference |
|---|---|---|
| *Escherichia Coli* (Bacteria) | $HC{\equiv}C\ CO_2H$ | 27 |
| *Streptomyces griseus* | $H_2N\ CO\ C{\equiv}C\ CO\ NH_2$ | 28 |
| (Actinomycetates) | $H_2N{\cdot}CO{\cdot}C(OEt){=}CH{\cdot}CO{\cdot}NH_2$ | 29 |
| *Rhodotorula glutinus* | $HC{\equiv}C\ [CH_2]_8\ CO_2H$ | 30 |
| var lusitanica | $H_2C{=}CH\ [CH_2]_8\ CO_2H$ | |
| (Yeast) | | |

The broad bean, *Vicia faba* L (Papilionaceae), produces[31, 32] wyerone (23), wyerol (24) and the dihydro derivatives dihydrowyerone (25) and dihydrowyerol (26) The free acid from wyerone has recently been detected[33] in tissues of broad bean infected by the parasites



(23) X=O

(24) X=H(OH)



(25) X=O

(26) X=H(OH)

*Botrytis cinerea* and *B fabae* Carbon-14 labelled acetate has been incorporated into these metabolites,[32] but the roles of oleate and other fatty acid esters in their biogenesis[32, 34] have not yet been precisely established The presence of a terminal *cis*-butenyl rather than *cis*-propenyl prompted Jones[31] to suggest that linolenate (27) was an intermediate instead of stearolate (3) or crepenynate (4)

The Santalaceae and Olacaceae[1,35] have long been known to contain unbranched $C_{18}$ acetylenic acids which presumably originate *via* stearolate or crepenynate, their unsaturation starts in the 9,10 position and extends progressively into the distal half, as in (28)[36]

$$Et{\cdot}CH\overset{c}{=}CH\ CH_2\ CH\overset{c}{=}CH\ CH_2\ CH\overset{c}{=}CH\ [CH_2]_7\ CO_2Me \quad (27)$$

$$Me\ [CH_2]_5\ CH{=}CH\ C{\equiv}C\ CHX\ [CH_2]_6\ CO_2H \quad (28)\ X{=}H;\ (29)\ X{=}OH$$

$$H_2C{=}CH\ [CH_2]_4\ CH{=}CH{\cdot}C{\equiv}C\ [CH_2]_7\ CO_2H \quad (30)$$

[27] W F LANGE, *Proc Soc Exptl Biol Med* **29**, 1134 (1931–32)
[28] S SUZUKI, G NAKAMARA, K OKUMA, Y TOMIYAMA, *J Antibiotics (Japan)* **11A**, 81 (1958), H TANIYAMA, S TAKEMURA, K KAGEYAMA and M FUNAKI, *J Pharm Soc Japan* **79**, 1510 (1959)
[29] Y SEKIZAWA, *J Biochem (Japan)* **45**, 73 (1958)
[30] L N PRISTA, *Anais Fac Farm Porto* **14**, 19 (1954)
[31] C H FAWCETT, D M SPENCER, R L WAIN, A G FALLIS, Sir E R H JONES, M LE QUAN, C B PAGE, V THALLER, D C SHUBROOK and P M WHITHAM, *J Chem Soc* **C**, 2455 (1968)
[32] R A M ROSS, D Phil Thesis, Oxford (1970)
[33] R M LETCHER, D A WIDDOWSON, B J DEVERALL and J W MANSFIELD, *Phytochem* **9**, 249 (1970)
[34] A G FALLIS, Sir E R H JONES, M G PELLATT and V THALLER, unpublished work
[35] F D GUNSTONE, *Progr Org Chem* **4**, 1 (1958), I A WOLFF, *Science* **154**, 1140 (1966)
[36] S P LIGTHELM and H M SCHWARTZ, *J Am Chem Soc* **72**, 1868 (1950) and later work

Terminal unsaturation is prevalent, e g. (30), as well as allylic hydroxylation at C-8, as in (29). Lately $C_{17}$ counterparts have[37] been characterized; these can be thought to be derived from heptadec-8-enoate in place of oleate Some oddities are known· sterculynic acid (31) (*Sterculia alata* Roxb ),[38] isanolic acid[39] (32) (Oliniaceae); and tariric acid (33) an analogue of petroselenic acid, which has only been found[40] in Genus *Picramnia* (Simaroubeaceae)

$$HC{\equiv}C\cdot[CH_2]_7\ \underset{\diagdown\ \diagup \atop CH_2}{C{=}C}\ [CH_2]_6\ CO_2H \qquad (31)$$

$$Pr^n\cdot CH{=}CH\cdot C{\equiv}C\cdot C{\equiv}C\cdot CH_2\cdot CH(OH)\ [CH_2]_6\ CO_2H \qquad (32)$$

$$Me\ [CH_2]_{10}\ C{\equiv}C\ [CH_2]_4\ CO_2H \qquad (33)$$

*Future Work*

Many of these acetylenes have been characterized by the aid of modern separation, analytical and spectroscopic techniques However, they appear more widespread than the typical polyacetylene and within 20 years the polyacetylene group may well become the smaller group of acetylene metabolites. Some of the natural products described are also suitable models with which to study the *in vivo* formation of the triple bond.

*Acknowledgements*—This review was collated during a tenure of a Science Research Council Studentship at the Dyson Perrins Laboratory, Oxford The author thanks Professor Sir Ewart Jones and Dr V Thaller for encouragement, and J W Keeping for help in nomenclature

[37] G N Smith and J D Bu'Lock, *Chem & Ind* 1840 (1965), R G Powell, C R Smith, Jr , C A Glass and I A Wolff, *J Org Chem* , **31**, 528 (1966)
[38] A W Jevans and C Y Hopkins, *Tetrahedron Letters* 2167, (1968)
[39] H P Kaufmann, J Baltes and H Herminghaus, *Fette Seifen*, **53**, 537 (1951), A Seher, *Liebigs Ann Chem* **589**, 222 (1954)
[40] A Steger and J Van Loon, *Rec Trav Chem Pays Bas*, **52**, 593 (1933) and references therein.

*Key Word Index*—Acetylenes, crepenynin acid, stearolic acid, biosynthesis, acetylenic carotenoids, acetylenic terpenes