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STEREOCONTROLLED SYNTHESIS OF THE DI-CIS-PENTAENE CHROMOPHORE FOUND IN PHYTOFLUENE FROM TANGERINE TOMATO FRUITS

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Summary The di-*cis*-pentaene chromophore found in natural phytofluene (2) from Tangerine tomatoes has been synthesised by judicious choice of phosphine oxide anion intermediates and conditions for their reactions with unsaturated aldehydes.

We have recently described the stereostructures of the intriguing poly-*cis*-carotenoid pigments found in Tangerine tomato fruits,[1] which together are responsible for the striking colour variation of this fruit compared to the common red variety. Our results support the view that *cis*-carotenoids are more widely involved in general carotenoid biosynthesis than hitherto imagined, and significantly, they suggest that phytoene (1) is the clear branch point for poly-*cis*-carotenoid formation in tomato fruits. Phytoene (1) from the Tangerine tomato, like that from standard red tomatoes, has the C-15-mono-*cis*-stereochemistry.[2] By contrast, phytofluene, which is present as the labile C-15-mono-*cis*-isomer in red tomatoes, was shown to have the C-15, C-9'-di-*cis*-stereochemistry in Tangerine tomato fruits. Thus during the 'desaturation' of phytoene to phytofluene in the Tangerine tomato, at the same time as the C-11'-*trans*-double bond is introduced, the C-9' double bond undergoes specific *trans*-to-*cis* isomerisation; this is a sequence of considerable mechanistic and enzymatic interest. Di-*cis*-phytofluene (2) is the first authentic poly-*cis*-compound to be identified in carotenoid biosynthesis. In view of its special importance and significance to current theories of biogenetic transformations of acyclic carotenoids,[3] we have sought to confirm its stereochemistry by unambiguous synthesis of the di-*cis* pentaene chromophore found within its structure.

Our recent investigations of the controlled synthesis of poly-*cis* polyene isoprenoids,[4] suggested that appropriate phosphine oxide anion intermediates could be used to introduce the necessary *cis*- and *trans*-double bonds of the pentaene chromophore in (2). This was found to be the case.

Metallation of the *cis*(*Z*)-phosphine oxide (3)[2,4] at -78° using *n*-BuLi, followed by reaction with the *trans*(*E*)-aldehyde (4),[5] and warming to 25° led in one step to the C-6 mono-*cis*(*Z*)-tetraenoate (5) (35%) showing complete preservation of the *cis*(*Z*)-and *trans*(*E*)-double bonds in the starting materials, and with > 98% *trans*(*E*)-olefination. Successive treatment of the ester (5) with lithium aluminium hydride and activated manganese dioxide then led to the C-6 mono-*cis*(*Z*)-trienal (6) without loss of stereochemical integrity of the original *cis*(*Z*)-and *trans*(*E*)-double bonds in (5).

A Horner condensation between the phosphine oxide (7), m.p. 79 - 80°, derived from *trans*(*E*),*trans*(*E*)-farnesyl chloride, and the trienal (6) (*n*-BuLi; -60°, 5 mins.) followed by quenching with water at -60° led (74%) to a 3:4 mixture of *erythro*-and *threo*-β-hydroxyphosphine oxide intermediates which was separated by chromatography (silica gel; 1:1 ethyl acetate: *n*-hexane). Treatment of the *erythro*-intermediate (8) with sodium hydride in dimethylformamide in the dark under nitrogen, followed by rapid work-up and chromatography (silica gel; 1:40 acetone:*n*-hexane) then led to the di-*cis*(*Z*)-octaene (2,R=H) (35%), $\lambda_{max.}$(*n*-hexane) 318 inf.,332, 349 and 367 nm, $\nu_{max.}$(film) 960, 885, 775 cm.$^{-1}$, τ8.09(C-13'-Me), 8.18(C-9'-Me), 8.20(C-13-Me), 8.38(C-9-Me); δ12.4(C-13'-Me), 16.0(C-9-Me), 16.6(C-13-Me), 24.1(C-9'-Me), 26.8(C-7), 32.8(C-8'), 39.8(C-8), 40.5(C-12) p.p.m. displaying spectral data closely similar to those found in natural C-15, C-9'-di-*cis*-phytofluene, $\lambda_{max.}$(*n*-hexane) 318 inf.,331, 348 and 367 nm, $\nu_{max.}$ (film) 960, 885, 775 cm.$^{-1}$, τ8.09(C-13'-Me), 8.17(C-9'-Me), 8.19(C-13-Me), 8.37(C-9-Me); δ12.4(C-13'-Me), 16.0(C-9-Me), 16.6(C-13-Me), 24.1(C-9'-Me), 26.7(C-7), 32.8(C-8'), 39.7(C-8), 40.5(C-12) p.p.m. from Tangerine tomato fruits.[6]

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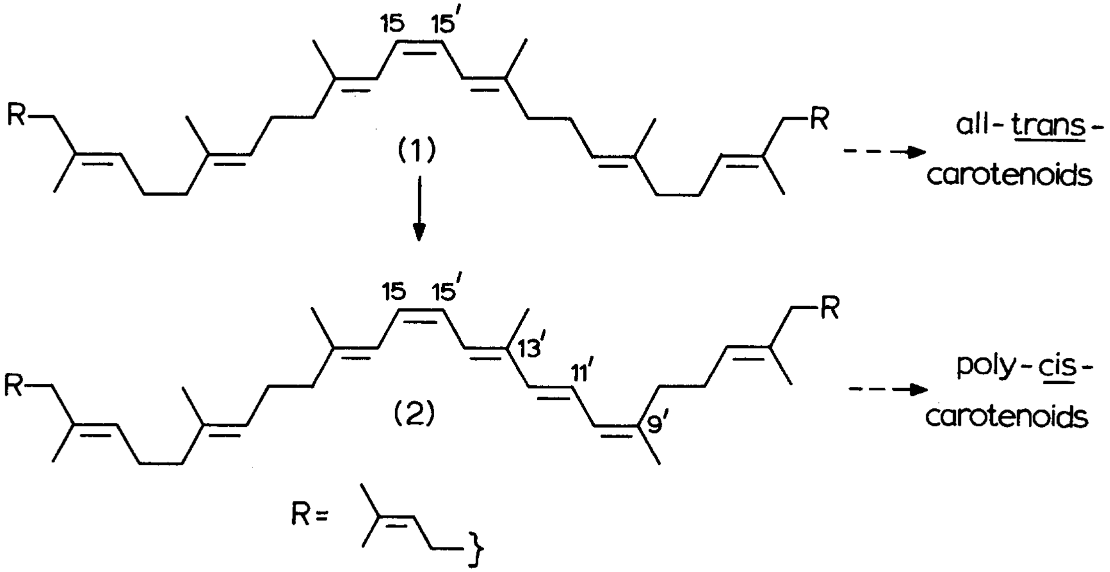
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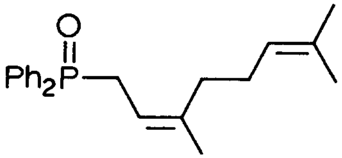
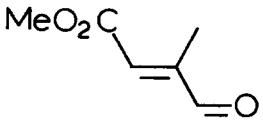


(3)



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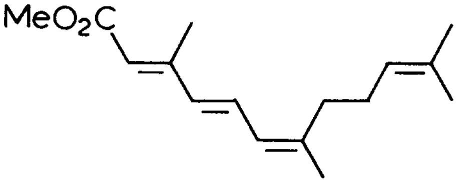

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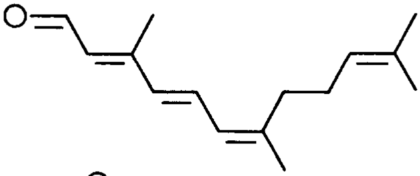

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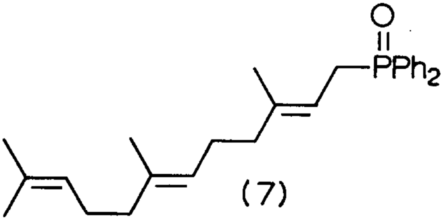
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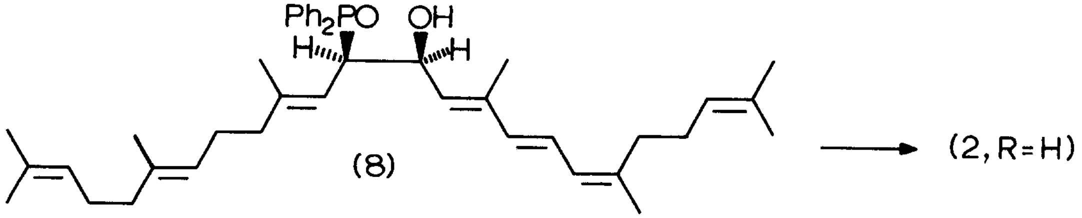
Ph2PO
OH
H
H
(8)
(2, R=H)

References

1. J.M. Clough and G. Pattenden, *J.C.S. Chem. Comm.*, 616 (1979). *cf*. G. Englert, B.O. Brown, G.P. Moss, B.C.L. Weedon, G. Britton, T.W. Goodwin, K.L. Simpson, and R.J.H. Williams, *ibid*., 545 (1979).
2. In this Letter, Carotenoid nomenclature is used for numbering the hydrocarbon chains, and stereoisomerism is designated by the configurational descriptors *cis* and *trans*; where appropriate, the systematic *Z*-*E* nomenclature is also given, in parenthesis.
3. see: B.H. Davies and R.F. Taylor, *Pure Appl. Chem.*, *47*, 211 (1976).
4. J.M. Clough and G. Pattenden, *Tetrahedron Letters*, 4159 (1978).
5. G. Pattenden and B.C.L. Weeden, *J. Chem. Soc. (C)*, 1984 (1968).
6. The corresponding *threo*-intermediate (*cf*. 8) led to the C-9-mono-*cis*(*Z*)-octaene, λ_{max} 317 inf., 331, 348, 367 nm, $\nu_{max.}$ (film) 960, 880 cm.$^{-1}$, τ8.08, 8.19 (C-9'-Me and C-13-Me), 8.38; δ12.7, 16.0, 16.9, 24.1, 26.8, 32.8, 39.8, 40.3 p.p.m.

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