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CONFIGURATION OF CAROTENOID EPOXIDES

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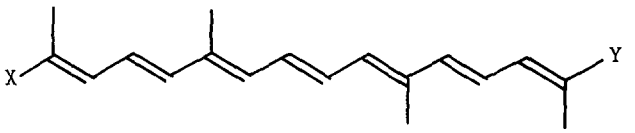
The 3S,5R,6S configuration (a) has been proposed for the epoxide end groups in violaxanthin (1), lutein epoxide (2),[1] and neoxanthin (3),[2] and the 3S,5S,6R configuration (b) for the principal semi-synthetic end group obtained by epoxidation of zeaxanthin and lutein (acetates) in vitro.[1] The configuration at 3 was established by direct correlation with a compound of known absolute stereochemistry[3] but that at 5,6 rests on the preferred cis epoxidation observed with simple cyclohex-3-enols and their acetates.[1,4] Examination of the n.m.r. spectra of the furanoid oxides, which are formed from the carotenoid epoxides in the presence of traces of acids,[5] confirms these assignments.

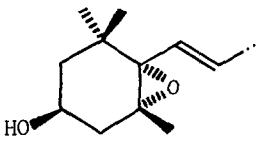
Table. Characteristic n.m.r. bands of furanoid oxides.

	(δ, $CDCl_3$, 100 MHz)				
End Group	1-Me (equatorial)	1-Me (axial)	5-Me	9-Me	7-H, and 8-H[§]
f	1.15	1.30	1.58	1.69	5.12 5.21
g	1.17	1.32	1.52	1.78	5.04 5.27 (J = 2 Hz)
h	1.20	1.14	1.45	1.74	5.17 5.25
i	1.21	1.13	1.46	1.78	5.08 5.33 (J = 2 Hz)
j	1.16	1.11	1.43	1.75	5.16
k	1.18	1.11	1.46	1.80	5.23 5.06 (J = 2 Hz)

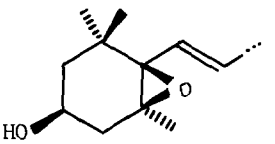
[§] Comparison of the observed coupling constants with those of appropriate models suggests that in the end groups g, i, and k the polyene chain at 8 is trans to the methyl group at 5, whereas in end groups f, h, and j it is cis.



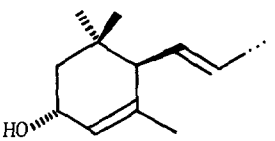
(1) X = Y = a
(2) X = a, Y = c
(3) X = a, Y = d
(4) X = m, Y = e
(5) X = f, Y = c
(6) X = g, Y = c
(7) X = h, Y = c
(8) X = i, Y = c
(9) X = Y = f
(10) X = f, Y = g
(11) X = Y = j
(12) X = j, Y = k



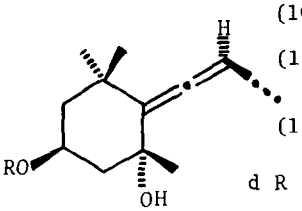
a



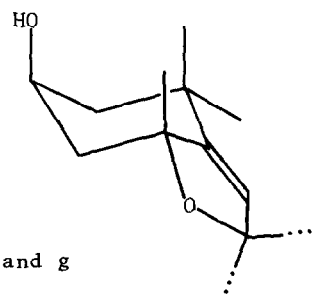
b



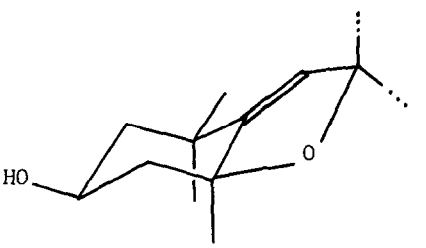
c



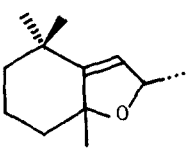
d R = H
e R = Ac



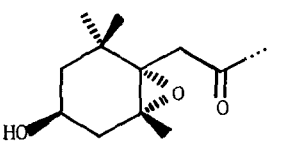
f and g



h and i



j and k



m

The end group (a) rearranges to give two furanoid oxide end groups (f and g), whilst (b) gives two different end groups (h and i).* The four end groups can be distinguished by their n.m.r. features (Table). Comparison of these results with those for the two aurochrome* end groups (j and k) show that in the natural series (f and g) there is an axial hydroxyl at 3 which deshields the axial methyls at 1 and 5 by about 0.2 p.p.m. (cf. steroid models,[6] triterpenoid models,[7] and loliolide[8]), i.e. the oxygen functions at 3 and 5 are trans. In contrast the equatorial hydroxyl in the semi-synthetic series (h and i) only shows a small effect.

Since each end group gives only two furanoid oxides, differing at 8, the stereochemistry is preserved at 5 during the isomerisation.† This confirms the configuration (a) and (b) respectively for the natural and semi-synthetic 5,6-epoxide end groups.

The n.m.r. spectrum[2] of the mixture of furanoid oxides from neoxanthin (3) shows the presence of the two end groups (f) and (g). This confirms that the epoxide end group in neoxanthin is identical with those in violaxanthin. Reduction of fucoxanthin (4), and treatment of the resulting fucoxanthols with $HCl/CHCl_3$, gives a similar mixture of furanoid oxides. Its n.m.r. spectrum[9] again reveals the presence of the two end groups (f) and (g). This supports the 3S,5R,6S configuration for the end group (m) in fucoxanthin since the conversion probably involves allylic dehydration followed by isomerisation. An alternative mechanism is for the 8-hydroxyl to open the epoxide ring (with inversion of configuration at 5) to give a 6-hydroxy compound, followed by dehydration. However this seems unlikely since dehydration of related compounds needs much more vigorous conditions.[10]

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*Lutein epoxide gave chrysanthemaxanthin (5) and flavoxanthin (6) whilst semi-synthetic lutein epoxide gave (7) and (8). Two auroxanthins (9) and (10) were obtained from violaxanthin (1) and two aurochromes (11) and (12) were obtained from the bis-epoxide of β-carotene. The two isomers in each pair of furanoid oxides were separated by chromatography on $CaCO_3$. Four isomers have been prepared in the mutatoxanthin series.

†Inversion at 5 due to initial solvolysis is excluded since related 5,6-dihydroxy compounds are unchanged under the conditions used.

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