Absolute Configuration of Carotenoids

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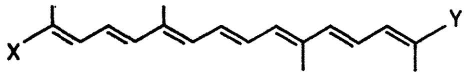
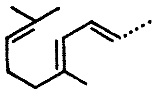
Summary *X*-Ray crystallographic analysis of a degradation product of fucoxanthin shows that zeaxanthin has the 3*R*,3′*R* configuration: the stereochemistry of other common xanthophylls is discussed in the light of this result.

FUCOXANTHIN (**1**),[1] neoxanthin (**2**),[2] and violaxanthin (**3**),[3,4] have been converted into zeaxanthin (**4**) by reactions which do not break the carbon–oxygen bonds at either C-3 or C-3′. All products have o.r.d. properties in good agreement with those of natural zeaxanthin.[4] The four major xanthophylls cited above therefore have the same absolute configurations at these two positions, which must themselves be identical.[4] O.r.d. measurements indicate that the "zeaxanthin end groups" in *β*-cryptoxanthin (**5**), α-cryptoxanthin (**6**), rubixanthin (**7**), gazaniaxanthin (*cis*-5′ isomer of **7**), *β*-citraurin (**8**), reticulatoxanthin (**9**), and capsanthin (**10**) have the same absolute configurations as those in zeaxanthin itself.[4] Furthermore the configurations at C-3 and C-3′ in the acetylenic carotenoids alloxanthin (**13**) and diatoxanthin (**14**) have been correlated with those of the corresponding positions in zeaxanthin.[4,5] We now report the key configuration of zeaxanthin (**4**).

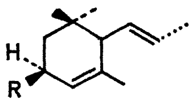
The allenic ketone (**18**), a degradation product of fucoxanthin (**1**),[1] has been converted into the *p*-bromobenzoate (**19**) by reactions which preserve the stereochemistry at all three asymmetric centres (reduction with $LiAlH_4$; re-oxidation of the allylic OH with MnO_2; esterification with *p*-BrC_6H_4·CO·Cl).[5] This derivative has now been shown by X-ray crystallography to have the absolute configuration (**19**). This result confirms the absolute configuration (*i* and *j*) suggested for the allenic end groups in fucoxanthin (**1**), neoxanthin (**2**), and related pigments.[5] Moreover, since the stereochemistry at C-3 is the same as that at C-3 and C-3′ in zeaxanthin, the end groups in the latter must have the R-configuration (*e*), as was proposed on biogenetic grounds.[6,7] The asymmetric centre at C-3 in the unsymmetrical carotenoids mentioned above with one "zeaxanthin end group" can also be represented as R, as can the corresponding positions in the acetylenic end groups (*g*) of alloxanthin (**13**) and diatoxanthin (**14**).



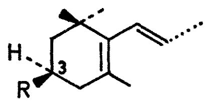
	X	Y		X	Y		X	Y
1	*h*	*j*	7	*e*	*a*	13	*g*	*g*
2	*f*	*i*	8	*e*	CHO	14	*e*	*g*
3	*f*	*f*	9	*e*	CH:CHAc	15	*e*	*c*
4	*e*	*e*	10	*e*	*k*	16	*f*	*c*
5	*e*	*d*	11	*k*	*k*	17	*d*	*b*
6	*e*	*b*	12	*d*	*k*			



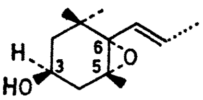
a



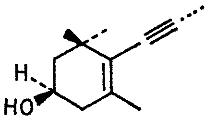
b, R = H
c, R = OH



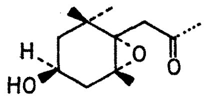
d, R = H
e, R = OH



f



g



h

The five-membered ring in capsanthin (**10**) has previously been shown to have the related $3S,5R$-configuration given in (*k*);[7] o.r.d. measurements reveal that the analogous end group in capsorubin (**11**) and cryptocapsin (**12**) have the same stereochemistry.[4,7] The configuration established for zeaxanthin is therefore consistent with the scheme suggested for the biogenesis of capsanthin and related pigments.[7]

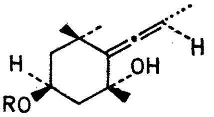
The epoxy end groups in neoxanthin (**2**) and violaxanthin (**3**) can now be written as (*f*) since the 5,6-epoxide is believed[2,4] to be *trans* to the 3-hydroxyl.† The 5,6-epoxide in fucoxanthin (**1**) is thought to have the same (*trans*) configuration,[1] but the evidence is less convincing; this final uncertainty concerning the stereochemistry of the most abundant natural carotenoid is receiving further study.

Experiments with etiolated maize seedlings and *Physalis alkekengi* have shown that it is the *pro*(R) hydrogen atom from C-5 of mevalonic acid that is lost in the introduction of the hydroxy-functions in lutein (**15**) and β-cryptoxanthin (**5**).[9] This indicates that the oxygen functions in lutein have the same stereochemistry as that, now assigned the R-configuration, in β-cryptoxanthin; moreover that the biological hydroxylation at C-3 in carotenoids, like many hydroxylations in di- and tri-terpenes, involves replacement of a hydrogen atom without inversion.

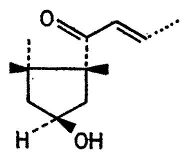
No conclusion can yet be drawn concerning the asymmetry at C-6′ in lutein and its derivatives, or the corresponding position in α-carotene (**17**)‡ and α-cryptoxanthin (**6**).

Crystals of the p-bromobenzoate (**19**) are orthorhombic, space group $P2_12_12_1$, with $a = 13{\cdot}61$, $b = 22{\cdot}35$, $c = 6{\cdot}56$ Å, $D_m = 1{\cdot}37$, $Z = 4$, $D_c = 1{\cdot}35$. The structure was solved by the heavy-atom method, and least-squares refinement has so far reduced R to 0·155 for 1253 independent reflections recorded with Mo-K_α radiation on a General Electric XRD6 diffractometer.

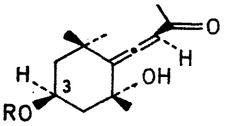
The absolute configuration was determined by the method of Bijvoet,[10] using 15 pairs of reflections on an *hkl* Weissenberg photograph, all of which gave a consistent result.



i, R = H
j, R = Ac



k



18, R = Ac
19, R = p-Br·C_6H_4·CO

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† Natural violaxanthin has o.r.d. properties which are different from those of the two main isomeric products obtained by epoxidation of zeaxanthin acetate with monoperphthalic acid, and subsequent hydrolysis.[4] Studies with simple models indicate that the *in vitro* process favours epoxidation *cis* to the C-3 oxygen function.[1,4,5,8]

‡ *Note added in proof.* A recent paper (C. H. Eugster, R. Buchecker, C. Tscharner, G. Uhde, and G. Ohloff, *Helv. Chim. Acta*, 1969, **52**, 1729) reports the absolute configuration of α-carotene.

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