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CLAIMED 6*R*/6*S* ALLENE ISOMERIZATION IN CAROTENOIDS IS GEOMETRICAL 9-*TRANS*/9-*CIS* ISOMERIZATION

Terje Bjørnland[a], Gerhard Englert[b], Kurt Bernhard[c] and Synnøve Liaaen-Jensen*[a]

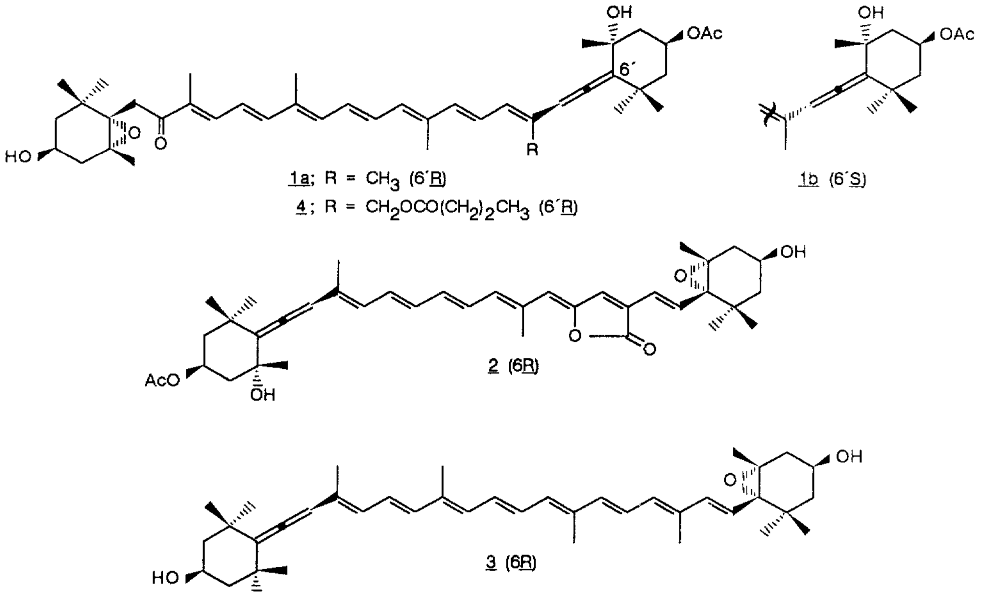
[a]Organic Chemistry Laboratories, Norwegian Institute of Technology,
University of Trondheim, N-7034 Trondheim-NTH, Norway

[b]Central Research Units and [c]Department of Vitamin and Nutritional Research,
F. Hoffmann-La Roche & Co., Ltd CH-4002 Basel, Switzerland

Summary. Previously claimed isolations of (*S*) allene isomers of natural carotenoids have been disproved. Detailed ^{1}H NMR have demonstrated that these isomers are geometrical isomers with the *cis*-bond adjacent to the allenic bond.

From their results on photosensitized oxygenation of hydroxy-β-ionol, providing an allene of established relative configuration, Isoe *et al.*[1] in 1971 suggested that the biosynthesis of allenic carotenoids might proceed by a similar mechanism. A subsequent *S* → *R* isomerization of the allenic bond would then be required in order to account for the chirality of natural allenic carotenoids.

The isolation of a minor presumed (6'*S*) allenic isomer (1b) of (6'*R*)-fucoxanthin (1a, Scheme 1), was later claimed[2] i) from an iodine catalyzed stereomutation mixture of 1a and ii) from the brown alga *Fucus serratus*. The main diagnostic feature for the presumed 6'*S* isomer was a pronounced downfield shift in the ^{1}H NMR spectrum of the allenic proton from 6.05 ppm for 1a to 6.55 ppm for 1b.



Scheme 1

Subsequently we isolated a similar stereoisomer of peridin (2) and of neoxanthin (3), both with shifted allenic proton NMR signal, from their iodine catalyzed quasiequilibrium mixtures in *ca* 10% yield^{3}.

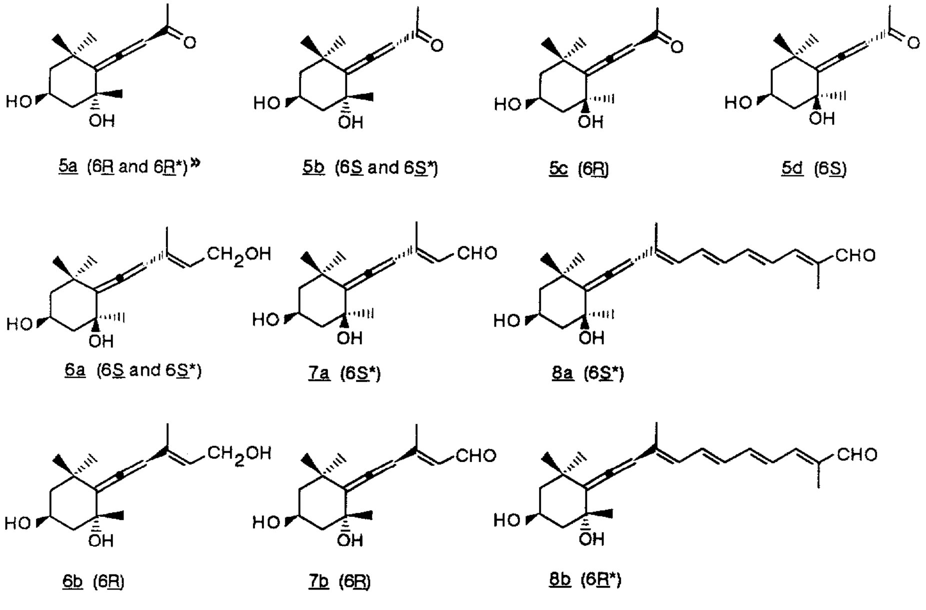
However, it has been shown^{4} that 0.5 ppm downfield shifts are compatible with *cis*-configurated carotenoids. Therefore an alternative interpretation could be (6'*R*)-9'-*cis* (or (6*R*)-9-*cis*) instead of (6'*S*) (or 6*S*).

We have now used 19'-butanoyloxyfucoxanthin (4)^{5} as a model, since it is known that substituted in-chain methyl groups promote *cis*-isomerization of the adjacent double bond^{6}. The 9'-*cis* isomer was consequently expected as a major component of the iodine catalyzed stereoisomerization mixture. Indeed a 6.534 ppm isomer, isolated by column chromatography on $CaCO_3$ using 8% acetone in benzene as an eluent, represented as much as 45% of total.

Detailed ^{1}H NMR studies of all-*trans* 4 (4a) and the 9'-*cis* isomer (4b), including 400 MHz TOCSY-1D, TOCSY-2D and particularly 500 MHz CAMELSPIN or ROESY (rotating frame NOE) have demonstrated 9'-*cis* configuration for the 6.534 ppm isomer (4b)^{7}.

4a exhibited an essentially conservative^{8} CD spectrum, and the 6.534 ppm isomer a mirror-image Cotton effect, compatible with the 9'-*cis* configuration (4b)^{7}.

No other isomers isolated from the iodine catalyzed mixtures of 2, 3 and 4a exhibited a shifted allenic proton in ^{1}H NMR, and a concomitant 6'*R* → 6'*S* and 9'-*trans* → 9'-*cis* isomerization is disregarded.



»R* and S* indicate relative configuration, *i.e.* racemates of these structures

Scheme 2

Subsequently, the ^{1}H NMR data of a number of allenic model compounds (Scheme 2) were analyzed. For the syntheses of optically active 5a-d, see ref. 11.

The downfield ^{1}H NMR shift of the allenic proton of 5a (6R* by carotenoid numbering) versus 5b (6S*) reported to be 0.17 ppm only[1], were in our experiments (400 MHz) with more recently prepared synthons[11] 5a (6R) and 5b (6S) confirmed as 0.11 ppm in $CDCl_3$ and 0.07 ppm in DMSO (Table 1).

^{1}H NMR data for the C-5 epimeric allenic ketones 5c (6R) and 5d (6S) now prepared[11] have a chemical shift difference of 0.02 ppm in $CDCl_3$ and of 0.10 ppm in DMSO and the two 6R isomers (5a and 5c, 5.75 ppm and 5.72 ppm) and two 6S isomers (5b and 5d, 5.82 ppm) have closely similar chemical shifts for the allenic proton within the 6R-series and 6S-series.

Aditionally, the difference between the chemical shift of the allenic protons in 6a and 6b, 7a and 7b and 8a and 8b, respectively, are ≤ 0.17 ppm. Consequently the configuration at C-5 appears to have little influence on the chemical shift of the allenic proton.

The available synthetic models of 6S allenic isomers which are C-5 epimeric in relation to 1-4, namely the triol 6a prepared here (6S)[12] and by Ito *et al.*(6S*)[9] and their aldehydes 7a (6S*)[9,12] and 8a (6S*)[9] all have chemical shifts of the allenic proton at values ≤ 6.20 ppm (Table 1).

Table 1. ^{1}H NMR signals of the allenic H (δ-values).

	$CDCl_3$		DMSO	
1,2,3,4a	6.03 - 6.06	Δ~0.50		
4b (9'-*cis*-4)	6.53			
5a	5.83[1], 5.86	Δ=0.11	5.75	Δ=0.07
5b	6.00[1], 5.97		5.82	
5c	5.91	Δ=0.02	5.72	Δ=0.10
5d	5.93		5.82	
6a	6.09[9], 6.10	Δ=0.15	6.02	Δ=0.12
6b	5.95		5.90	
7a	6.17[9]	Δ=0.09		
7b	6.08			
8a	6.20[9]	Δ=0.17		
8b	6.03[9]			

We therefore conclude that the presumed 6S (6'S) allenic isomers of 1, 2 and 3 (3 occurring as a natural 9'-*cis* isomer in green photosynthetic tissues[10]) represent 9'-*cis*-1, 9-*cis*-2 and 9-*cis*-3 isomers, respectively, and that R,S isomerization of the allenic bond in carotenoids is a less favoured process than *trans*/*cis* isomerization of other double bonds.

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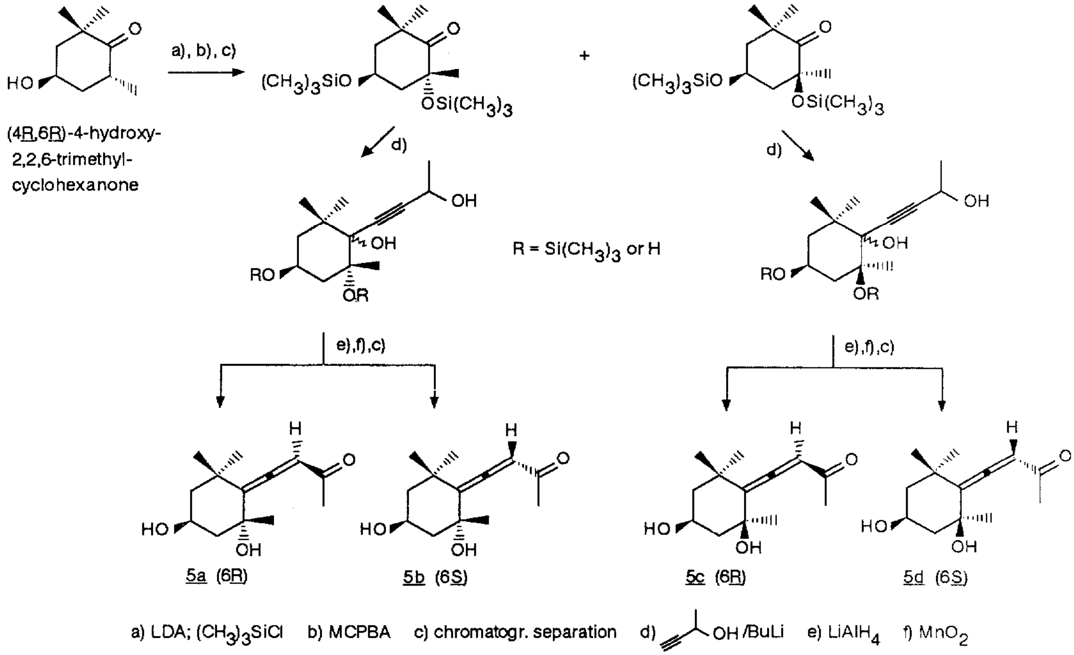

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