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RETRO CAROTENOIDS WITH SUBSTITUTED 2,5-OXA-BICYCLOHEPTANE END GROUPS

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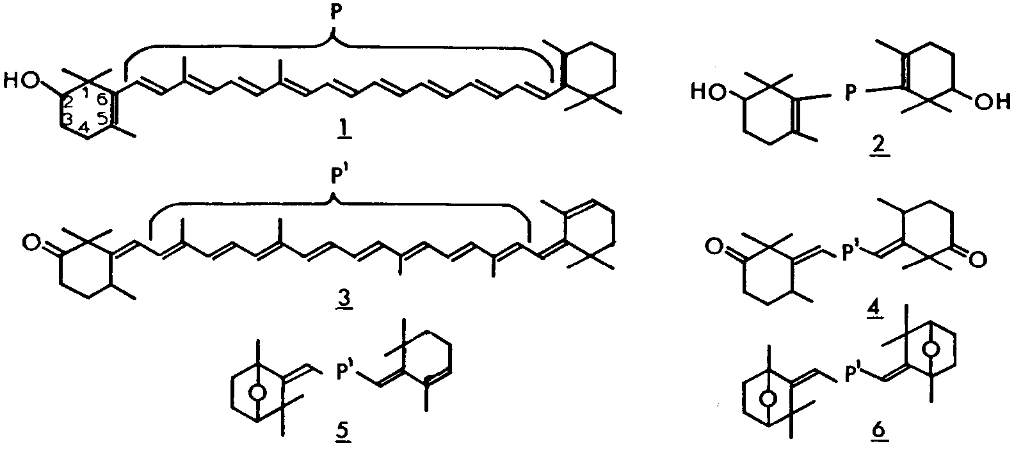
BF_3-mediated formation of a 2,5-oxygen bridge from carotenoids with 2-hydroxy β-type end groups accompanied by dehydrogenation and retro shift of the polyene system is reported. The configuration of the Δ6,6' double bonds are established by ^1H NMR.

It has been reported[1] that treatment of β,β-caroten-2-ol (1) and β,β-carotene 2,2'-diol (2) with BF_3-etherate caused dehydrogenation with concomitant retro-rearrangement of the polyene chain. Initially it was assumed that the 2-hydroxy function had been oxidized to provide the corresponding ketones 3 and 4[1], a mechanistically obscure reaction.

During a recent reinvestigation the products were shown to be the 2,5-bicyclic oxides 5 and 6, Scheme 1.

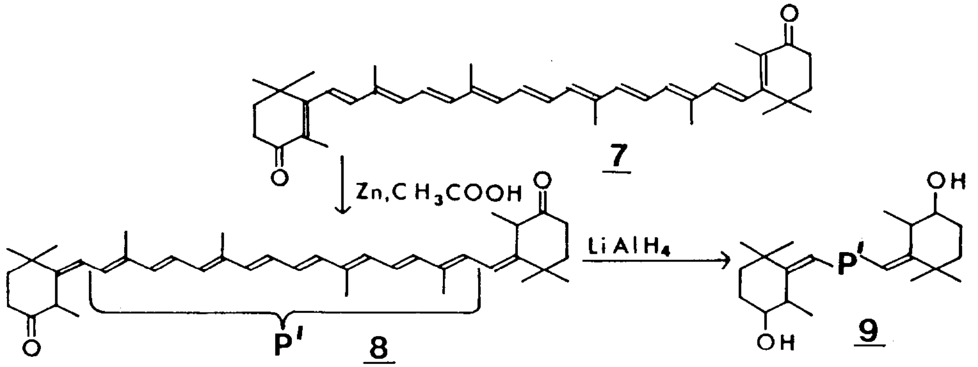


Scheme 1

Treatment of (2R)-β,β-caroten-2-ol (1a) *ex Trentepohlia iolithus*[2] in several portions (total 6.2 mg) with a 2.5% solution of BF_3-etherate in ethanol-free $CHCl_3$ (total 16 ml) provided 5a as the major product in 20-60% yield. Product 5a, available 1.4 mg, exhibited λ_{max} (acetone) 432, 456 and 483 nm as previously reported[1] and could not be separated chromatographically (TLC, SiO_2, 5% ether in CH_2Cl_2) from the BF_3-product earlier obtained[1] from 1.

Similarly treatment of (2R,2'R)-β,β-carotene-2,2'-diol (2a, 1.8 mg) *ex Trentepohlia iolithus*[2] yielded 6a (0.9 mg, 50%). Product 6a exhibited identical R_F upon co-chromatography and the same vis. spectrum as the BF_3-product previously obtained from the diol 2[1] with λ_{max} (ether) 418, 442 and 470 nm.

For comparison of chromophores 6,5'-retro-5,6-dihydro-β,β-carotene-4,4'-diol (9) and 6,5'-retro-5,6-dihydro-β,β-carotene-4,4'-dione (8) were prepared from canthaxanthin (7) by ω,ω'-reduction with Zn-CH_3COOH in dry pyridine[3], followed by reduction of the keto groups with $LiAlH_4$, Scheme 2.



Scheme 2

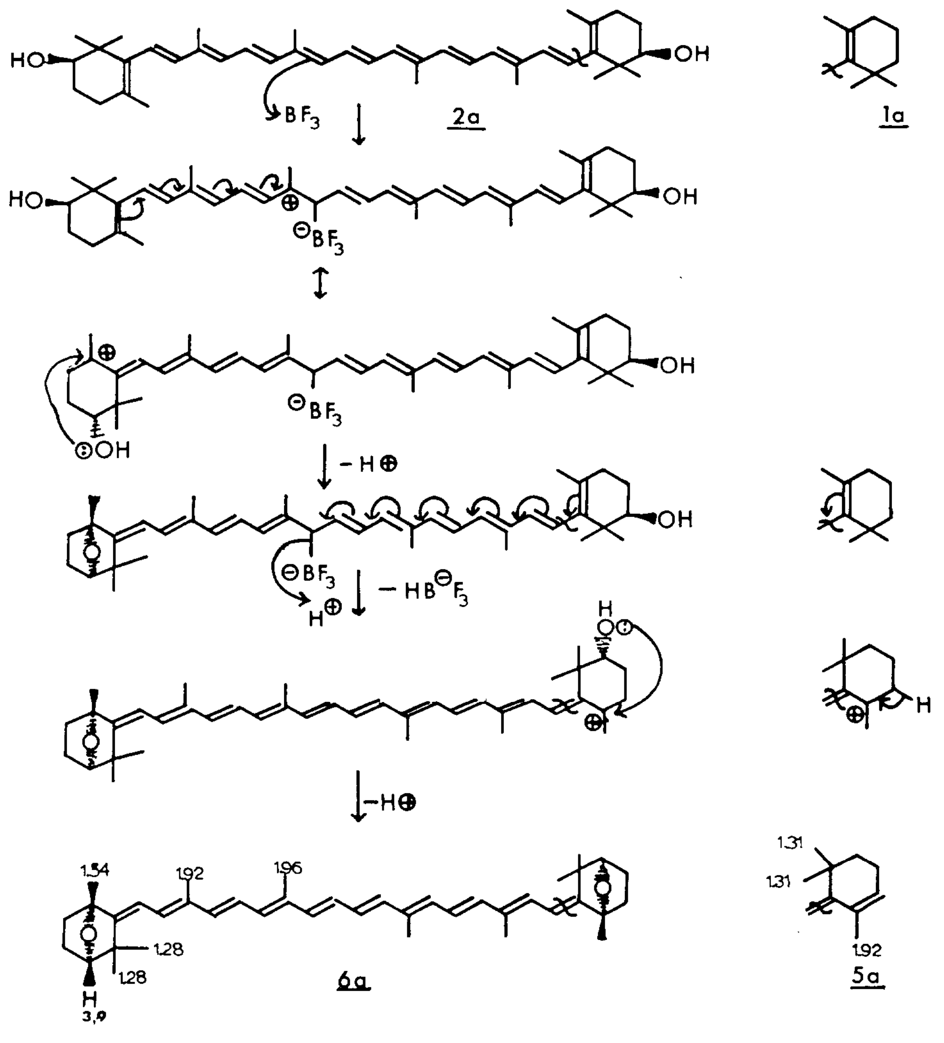
Products 8 and 9 were characterized by vis. IR, ^1H NMR and ^{13}C NMR spectra. They exhibited λ_{max} (ether) 418, 442 and 470 nm consistent with their decaene retro chromophore[4].

Structure 6a (Scheme 3) for the BF_3-product of (2R,2'R)-β,β-caroten-2,2'-diol (2a) is based on the following evidence: The vis. spectrum supports identical chromophores for 6a and the models 8 and 9. The mass spectrum showed m/e 566 (M, consistent with $C_{40}H_{54}O_2$), M-92 and M-106. IR spectra (KBr) of 6a (and 5a) had ν_{max} 3040 (w), 2960, 2930, 2860 (s), 1460 (s), 1320, 1120 (s, C-O stretch), 950 and 970 (s, retro[5]) cm^{-1}. A variable to absent carbonyl absorption at 1735 cm^{-1} [1] is ascribed to a contaminant. ^1H NMR data are given in Scheme 3 and Table 1 in comparison with data for 2,5-epoxy-megastigma-6(E), 8(E)-diene (10) and its 6(Z) isomer (11). The ^{13}C NMR spectrum showed no signal for C=O and a δ 86 signal assigned to C-2; the sp^2 C region was very similar for 6a and the models 8 and 9. As previously reported[1] neither 6a nor 5a gave any reduced products upon treatment with $LiAlH_4$, consistent with their tetrahydrofurane structures.

Structure 5a (Scheme 3) for the BF_3-product of (2R)-β,β-caroten-2-ol (1a) follows from the corresponding evidence: The vis. spectrum is consistent with a retro undecaene chromophore, the mass spectrum had diagnostic peaks at m/e 550 (M, consistent with $C_{40}H_{54}O$), M-92 and M-106, ^1H NMR (Scheme 3, Table 1) and ^{13}C NMR and IR as cited above.

By analogy with the previously discussed mechanism for BF_3-mediated dehydrogenation of carotenoids[7] the formation of these novel carotenoids is rationalized in Scheme 3.

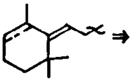
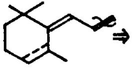
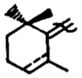
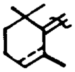
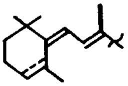
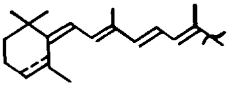
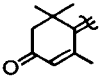
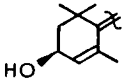
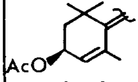
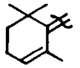
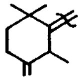
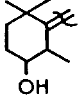
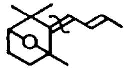
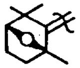
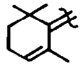
Regarding the stereochemistry of the Δ6,6' double bonds in the products 5a and 6a, comparison with the ^{1}H NMR data for relevant retro carotenoids[8] and for the models 10 and 11[6], 8 and 9 prove 6(E),6'(E)-configuration for 6a and 6(E),6'(Z)-configuration for 5a as given in Scheme 3.



Scheme 3

The 2,5-oxa-bicycloheptane derivatives 5a and 6a are the first synthetically prepared carotenoids with a 2,5-oxygen bridge. Recently a natural carotenoid, eutreptiellanone, with a 3,6-oxygen bridge has been encountered in an algae[9]. These synthetic and natural carotenoids with an oxygen bridge locking the boat conformation represent stable tetrahydrofurane derivatives.

Table 1. ^{1}H NMR ($CDCl_3$) signals for the methyl groups of <u>retro</u> compounds.

END GROUP		 ⇒ trans  ⇒ cis	 1,1-Dimethyl	 5-Methyl	 9-Methyl	 13-Methyl	Ref.
		trans=Z	1,38;1,38	2,15	2,03-1,98		8
		cis=E	1,25;1,25	2,31			
		trans=Z	1,44;1,24	1,97	1,97	1,97	8
		cis=E	1,10;1,24	2,12			
		trans=Z	1,44;1,30	1,95	1,97	1,97	8
		cis=E	1,14?				
		trans=Z	1,31	1,92	1,96	1,97	8
		cis=E	1,12	2,09			
		"trans"=Z			1,96	1,96	
	8	"cis"=E	1,21 ;1,24	1,36			
		"trans"=Z			1,96	1,96	
	9	"cis"=E	1,14	1,23			
	10	"trans"=E	1,28	1,50	1,78	-	
	11	"cis"=Z	1,04;1,13	1,75	1,78	-	6
	5a,6a	"trans"=E	1,28	1,54	1,92	1,96	
		"cis"=Z					
		trans=Z	1,31;1,38	1,92	1,96	1,96	

References

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