(*E*/*Z*)-Isomerization of (all-*E*)-5,6-Diepikarpoxanthin

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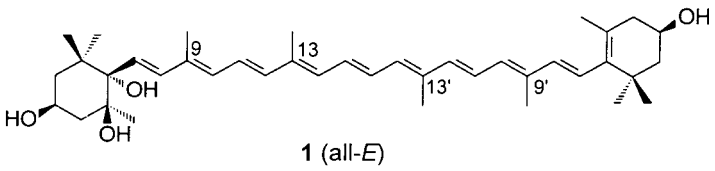
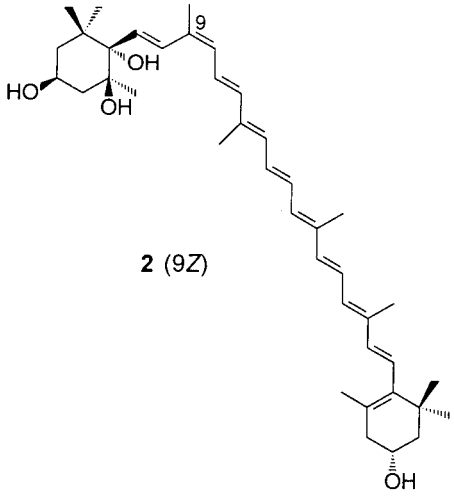
(all-*E*)-5,6-Diepikarpoxanthin (=(all-*E*,3*S*,5*S*,6*S*,3′*R*)-5,6-dihydro-*β*,*β*-carotene-3,5,6,3′-tetrol; **1**) was submitted to thermal isomerization and I_2-catalyzed photoisomerization. The structures of the main products, *i.e.* (9*Z*)- (**2**), (9′*Z*)- (**3**), (13*Z*)- (**4**), (13′*Z*)- (**5**), and (15*Z*)-5,6-diepikarpoxanthin (**6**), were determined by their UV/VIS, CD, ^{1}H-NMR, and mass spectra. In addition, (9*Z*,13′*Z*)- or (13*Z*,9′*Z*)- (**7**), (9*Z*,9′*Z*)- (**8**), and (9*Z*,13*Z*)- or (9′*Z*,13′*Z*)-5,6-diepikarpoxanthin (**9**) were tentatively identified as minor products of the I_2-catalyzed photoisomerization.

Introduction. – (all-*E*)-5,6-Diepikarpoxanthin ((all-*E*,3*S*,5*S*,6*S*,3′*R*)-5,6-dihydro-*β*,*β*-carotene-3,5,6,3′-tetrol; **1**), a naturally occurring carotenoid containing a 3,5,6-trihydroxy-5,6-dihydro-*β*-end group and a 3-hydroxy-*β*-end group, was recently isolated from the red spice paprika (*Capsicum annuum*) and from petals of *Lilium tigrinum* [1][2]. In continuation of our investigations of (*E*/*Z*)-isomerization of carotenoids [3–6], we now report investigations of the thermal isomerization and the I_2-catalyzed photoisomerization of (all-*E*)-5,6-diepikarpoxanthin (**1**). The resulting five main (mono-*Z*)-isomers, *i.e.*, (9*Z*)- (**2**), (9′*Z*)- (**3**), (13*Z*)- (**4**), (13′-*Z*)- (**5**), and (15*Z*)-5,6-diepikarpoxanthin (**6**) were characterized by their UV/VIS, CD, ^{1}H-NMR, and mass spectra. On the one hand, the (*Z*)-isomers **2**–**6** were prepared in view of their use as reference compounds for the identification of new naturally occurring (*Z*)-carotenoids. On the other hand, the comparison of the (*E*/*Z*)-isomerization (structures of products, composition of the equilibrium mixtures, interconversion rate) of carotenoids with different end groups may give an indication of the structures of the naturally occurring (*Z*)-isomers. During our earlier research, the (*E*/*Z*)-isomerization of violaxanthin, antheraxanthin, lutein epoxide, cycloviolaxanthin, cucurbitaxanthin A, each containing a 5,6-dihydro-*β*-end group, have been investigated [3–8].

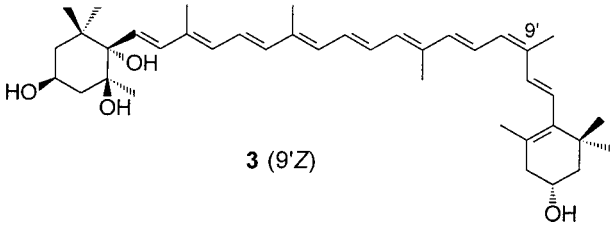
Results. – *Thermal Isomerization*. The thermal isomerization of **1** (benzene, 80°, 2 h) gave, in agreement with the pioneering studies of *Zechmeister* [9] and with our recent results [4–7], three (mono-*Z*)-isomers, *i.e.*, (13*Z*)- (**4**), (13′*Z*)- (**5**), and (15*Z*)-5,6-diepikarpoxanthin (**6**), and, in very small quantities, two isomers **A** and **B**, which presumably correspond to a (di-*Z*)- and a (poly-*Z*)-isomer, and which were not identified. When the time of the isomerization was increased, decomposition of all isomers and an increase in the amount of (di-*Z*)-isomers was observed [4][7]. The composition of the equilibrium mixture obtained by thermal isomerization as determined by HPLC [1] (*Fig. 1,a*) and column chromatography (CC; see *Exper. Part*) and characteristic UV/VIS data (λ_{max} and $\%A_{cis\text{-peak}}/A_{max}$) are presented in *Table 1*. The



1 (all-*E*)



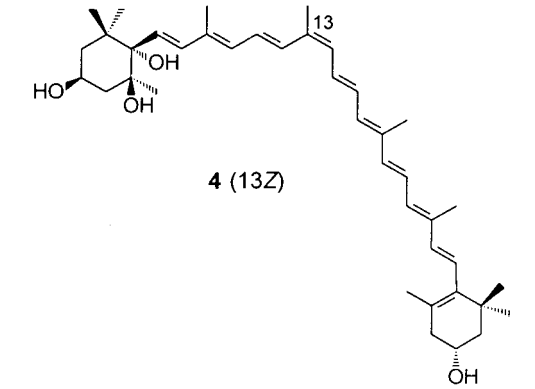
2 (9*Z*)



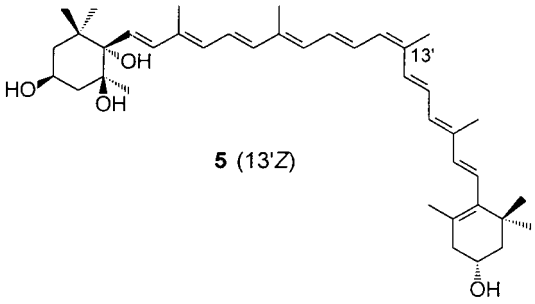
3 (9'*Z*)

preparative separation was achieved by CC (see *Exper. Part*), and the fractions of the corresponding isomers were crystallized from benzene/hexane 1:4 to give 3.0 mg of **4** ((13*Z*)), 3.0 mg of **5** ((13′*Z*)), and 0.6 mg of **6** ((15*Z*)).

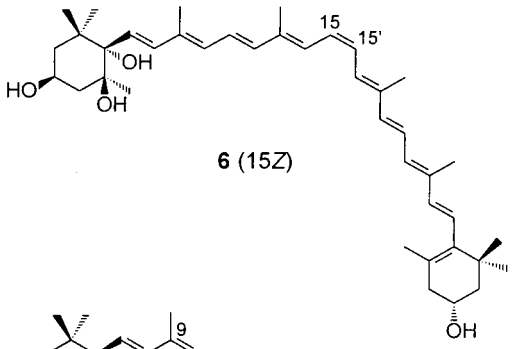
Iodine-Catalyzed Photoisomerization. In agreement with previous results for other carotenoids [7–11], the I_2-catalyzed photoisomerization (recently considered to result in a thermodynamic equilibrium [11]) of **1** gave the five (mono-*Z*)-isomers (9*Z*)- (**2**), (9′*Z*)- (**3**), (13*Z*)- (**4**), (13′*Z*)- (**5**), and (15*Z*)-5,6-diepikarpoxanthin (**6**). In addition, the thermodynamic equilibrium mixture contained, in minor amounts, three (di-*Z*)-isomers **7**–**9**, which were tentatively identified from their UV/VIS spectra as the (9*Z*,13′*Z*)- or (13*Z*,9′*Z*)- (**7**), the (9*Z*,9′*Z*)- (**8**), and the (9*Z*,13*Z*)- or (9′*Z*,13′*Z*)-5,6-diepikarpoxanthin (**9**). Furthermore, three additional tentatively identified isomers **C**–**E**, were observed. The composition determined by HPLC [1] (*Fig. 1,b*) and CC (see *Exper. Part*) and the characteristic UV/VIS data (λ_{max} and $\%A_{cis\text{-peak}}/A_{max}$) are shown in



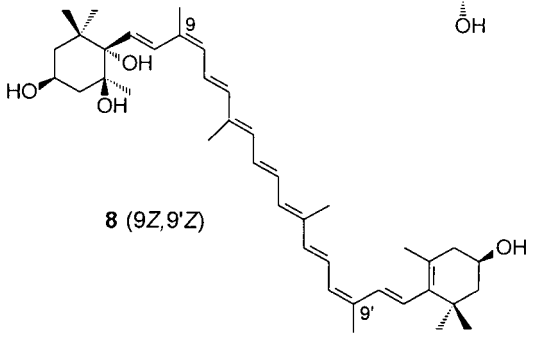
4 (13*Z*)



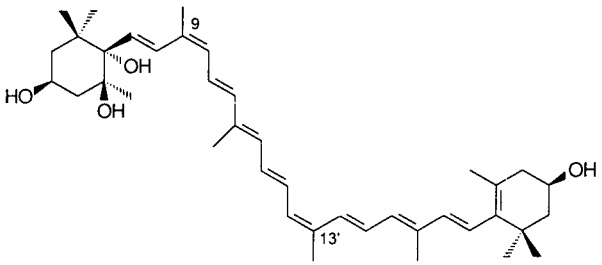
5 (13'*Z*)



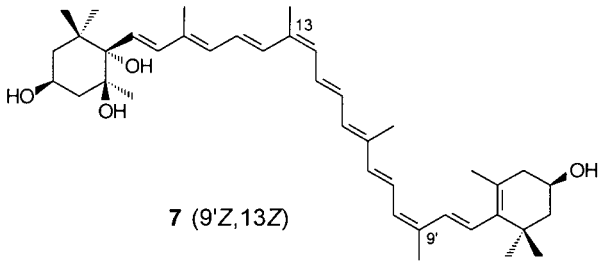
6 (15*Z*)



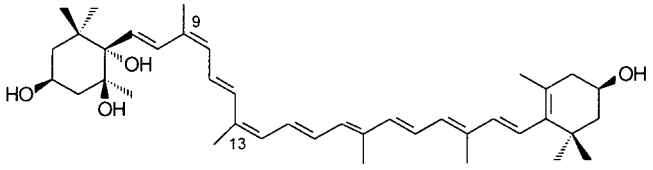
8 (9*Z*,9'*Z*)



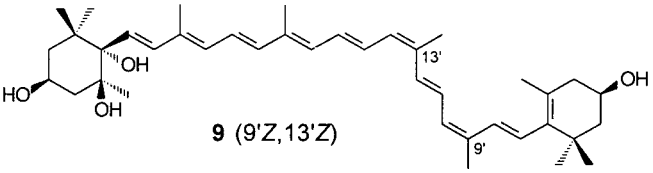
7 (9Z,13'Z)



7 (9'Z,13Z)



9 (9Z,13Z)



9 (9'Z,13'Z)

Table 1. The preparative separation was achieved by repeated CC (see *Exper. Part*), and afterwards, the carotenoids were crystallized from benzene/hexane 1:4 to give 3.3 mg of **2** ((9*Z*)), 3.3 mg of **3** ((9′*Z*)), 1.0 mg of **4** ((13*Z*)), 0.8 mg of **5** ((13′*Z*)), 0.3 mg of **6** ((15*Z*)), 0.3 mg of **7** ((9*Z*,13′*Z*) or (13*Z*,9′*Z*)), 0.9 mg of **8** ((9*Z*,9′*Z*)), and 3.5 mg of **9** ((9*Z*,13*Z*) or (9′*Z*,13′*Z*)).

Spectroscopic Characterization. The UV/VIS spectra of all geometric 5,6-di-epikarpoxanthin isomers **1**–**9** with the main absorption maximum between 442–458 nm (in benzene) are in agreement with a decaene chromophore. The occurrence of a weak

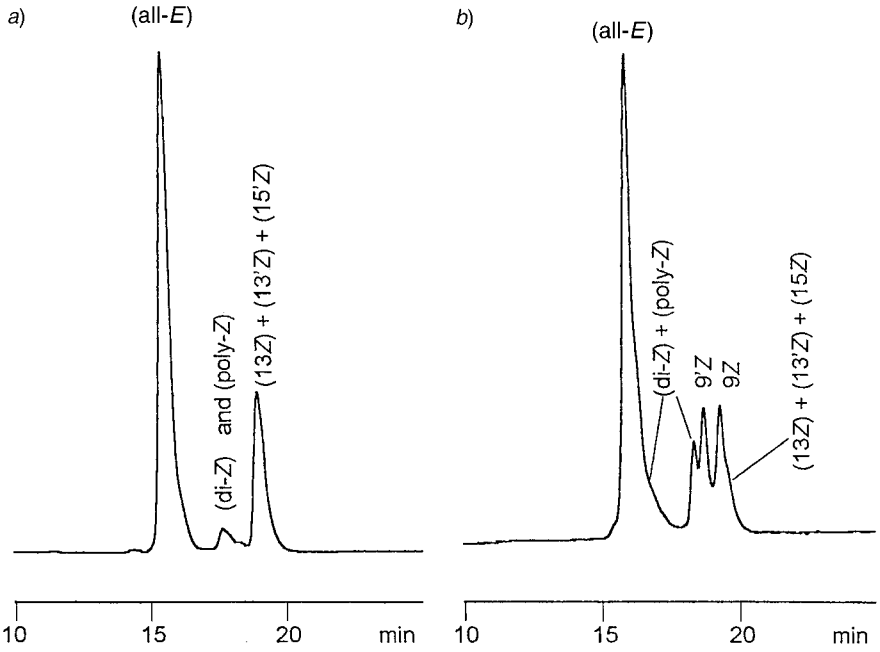


Fig. 1. *HPLC Separation of the equilibrium mixtures obtained* a) *by thermal isomerization and* b) *by I_2-catalyzed photoisomerization of (all-*E*)-5,6-diepikarpoxanthin* (**1**)

cis-peak and the small hypsochromic shift of λ_{max} ($\Delta\lambda_{max} = 5-6$ nm) is characteristic for **2** and **3** (*Table 1* and *Fig. 2,a*) and is in agreement with geometric isomers containing a double bond in a peripheral position. Both **4** and **5** exhibit strong *cis*-peaks at *ca.* 339 nm and considerable $\Delta\lambda_{max}$ values ($\Delta\lambda_{max} = 7-8$ nm; *Table 1* and *Fig. 2,b*), characteristic for an isomer with a (*Z*)-double bond in a more central position of the polyene chain [7]. The small hypsochromic-shift values of 3–4 nm, accompanied by a prominent *cis*-peak (*Table 1* and *Fig. 2,b*), suggest the (15*Z*)-configuration for **6** [4][8][9][13]. The considerable hypsochromic shift $\Delta\lambda_{max}$ of 12–14 nm, together with a weak *cis*-peak (*Table 1*), indicate the (9*Z*,9′*Z*)-configuration for **8** [4][8][12][14]. The considerable $\Delta\lambda_{max}$ values (10–11 nm and 12–14 nm, resp.), together with a moderate *cis*-peak, suggest either the (9*Z*,13′*Z*)- or the (9′*Z*,13*Z*)-configuration for **7** and the (9*Z*,13*Z*)- or the (9′*Z*,13′*Z*)-configuration for **9**, in accordance with our previous results [3][4][12][14].

The configuration of the double bonds of the polyene chain in **2**–**6** was determined by ^{1}H-NMR spectroscopy, by application of ^{1}H,^{1}H-COSY and ^{1}H,^{1}H-T-ROESY techniques [15][16]. The data given in the *Exper. Part*, especially the isomerization shift data (*Table 2*), are in agreement with the data in [16] and confirm the structures **2**–**6**.

In the CD spectrum at $-180°$, the (all-*E*)-isomer **1** exhibits prominent maxima at 220 (negative), 250 (positive), and 285 nm (negative) and weaker maxima between 300 and 350 nm (*Fig. 3*). In the spectra of the (mono-*Z*)-isomers **2**–**6** (*Figs. 3* and *4*), the signs are reversed below 300 nm, and in addition, the (13*Z*)-, (13′*Z*)-, and (15*Z*)-

Table 1. *Composition of the Equilibrium Mixtures Obtained by Thermal Isomerization and by I_2-Catalyzed Photoisomerization of (*all-E*)-5,6-Diepikarpoxanthin* (**1**), *with the λ_{max} and $\%A_{cis\text{-}peak}/A_{max}$ of the Isomers.* Isomers are listed in the order of their decreasing adsorption affinity on the $CaCO_3$ column.

Isomer	Percentage of isomer	λ_{max} [nm] in C_6H_6	$\%A_{cis\text{-}peak}/A_{max}$
Thermal isomerization:			
A (di-*Z*)-I[a])	< 1	479, 451, 427, 340	67
5 (13′*Z*)	13	479, 451, 428, 339	47
6 (15*Z*)	3	483, 454, 433, 338	47
B (poly-*Z*)-I[a])	2	468, 443, 420, 338	18
4 (13*Z*)	12	479, 451, 428, 339	34
1 (all-*E*)	69	487, 458, 434	–
unidentified	< 1	–	–
I_2-Catalyzed photoisomerization:			
C (di-*Z*)-II[a])	< 1	475, 447, 425, 338	43
7 (di-*Z*)-III	2	476, 447, 425, 338	27
5 (13′*Z*)	9	479, 451, 428, 339	47
3 (9′*Z*)	11	481, 452, 427, 339	9
8 (di-*Z*-IV)	3	473, 446, 423, 337	10
D (poly-*Z*)-II[a])	< 1	469, 444, 420, 338	24
E (poly-*Z*)-III[a])	< 1	472, 442, 418, 342	12
6 (15*Z*)	< 1	483, 454, 433, 338	47
4 (13*Z*)	6	479, 450, 428, 339	34
1 (*all-E*)	55	487, 458, 434	–
2 (9*Z*)	10	481, 453, 430, 338	8
9 (di-*Z*)-V	2	473, 446, 424, 336	19
unidentified	1	–	–

[a]) These isomers were not prepared in a crystalline state, and they were characterized by their λ_{max} and $\%A_{cis\text{-}peak}/A_{max}$.

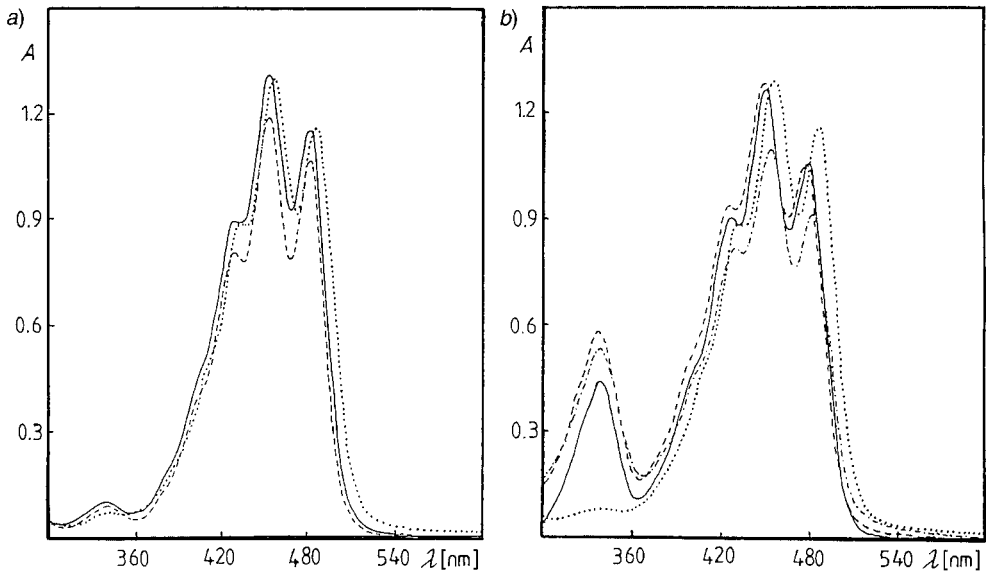


Fig. 2. *UV/VIS Spectra* a) *of (9*Z*)-5,6-diepikarpoxanthin* (**2**; —), *(9′*Z*)-5,6-diepikarpoxanthin* (**3**; -----), *and (all-*E*)-5,6-diepikarpoxanthin (**1**;* .....), *and* b) *of (13*Z*)-5,6-diepikarpoxanthin* (**4**; —, *(13′*Z*)-5,6-diepikarpoxanthin* (**5**; -----), *(15*Z*)-5,6-diepikarpoxanthin* (**6**; -·-·-·-), *and (all-*E*)-5,6-diepikarpoxanthin* (**1**; .....) *in benzene*

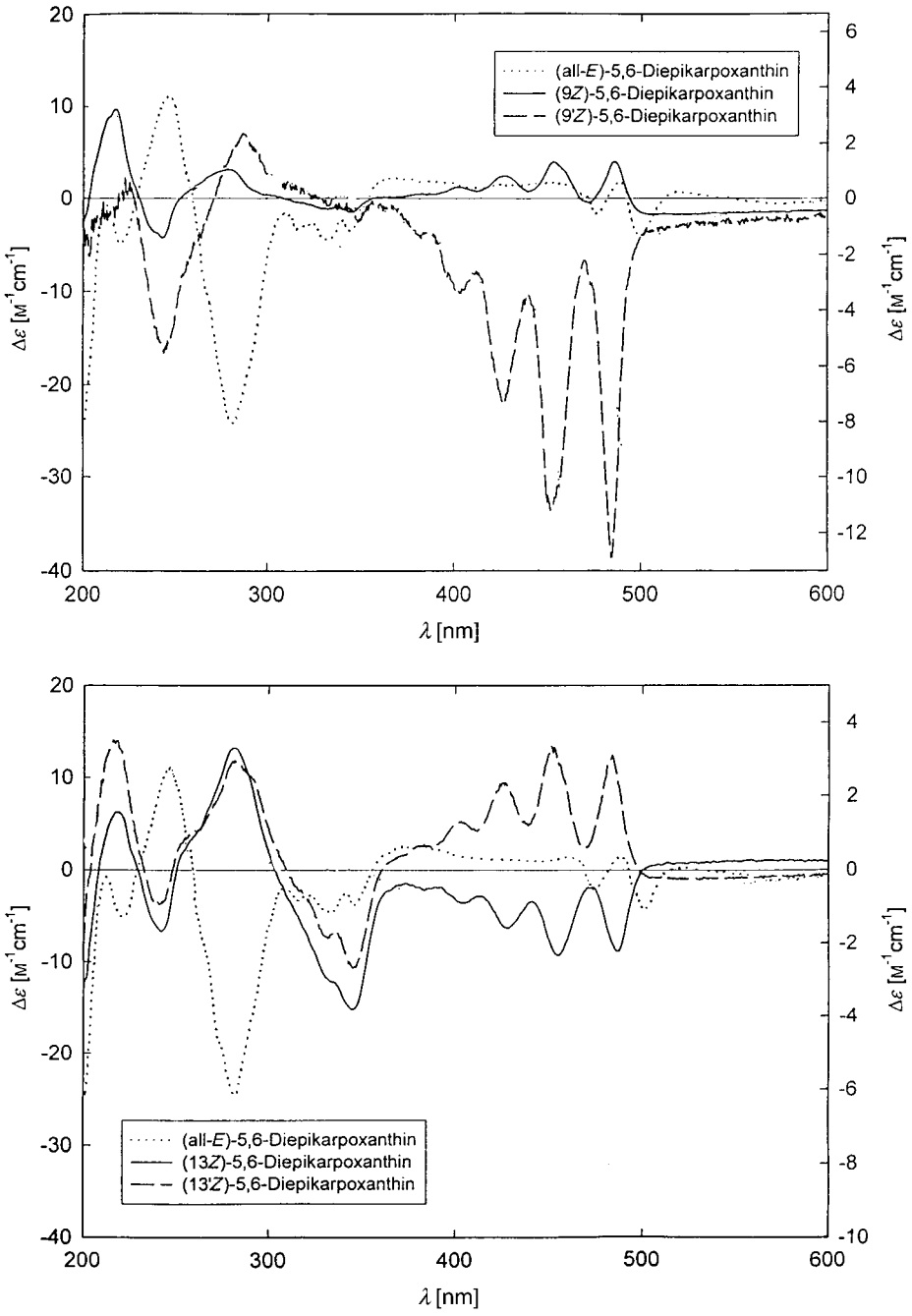


Fig. 3. *CD Spectra of (9Z)-, (13Z)-, (13'Z)-, and (all-E)-5,6-diepikarpoxanthin* (**2**–**5**, and **1**, resp.) *in* Et_2O/*isopentane/EtOH 5 : 5 : 2 at* $-180°$

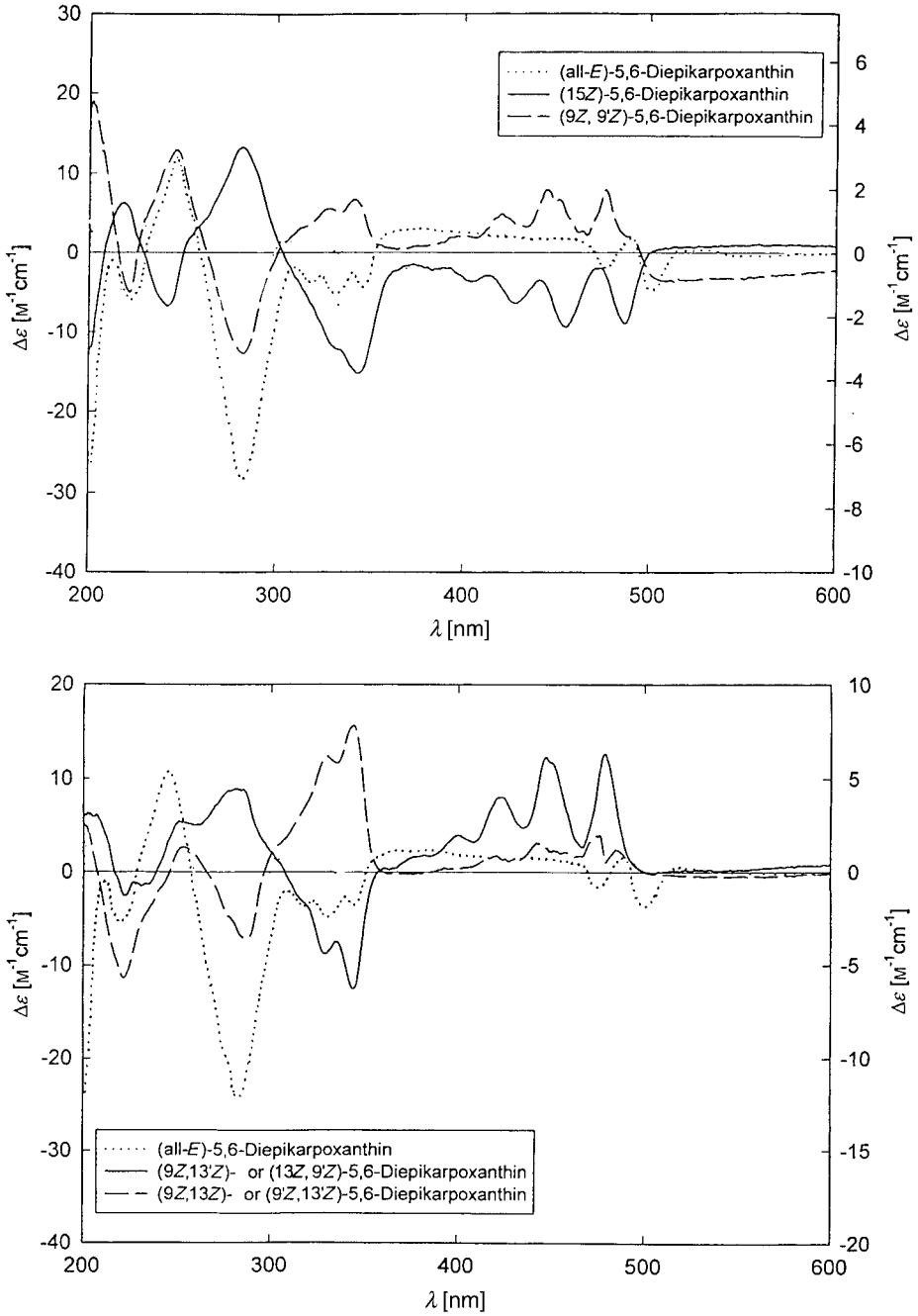


Fig. 4. *CD Spectra of (15Z)-5,6-diepikarpoxanthin* (**6**), *(di-Z)-5,6-diepikarpoxanthins* **7**–**9**, *and (all-*E*)-5,6-diepikarpoxanthin* (**1**) *in* Et_2O*/isopentane/EtOH 5 : 5 : 2 at* −180°

Table 2. *Isomerization Shifts* ($\Delta\delta = \delta(Z) - \delta(\text{all-}E)$) *of 5,6-Diepikarpoxanthin Isomers* **2**–**6**

	$\Delta\delta = \delta(9Z) - \delta(\text{all-}E)$		$\Delta\delta = \delta(9'Z) - \delta(\text{all-}E)$	
	measured	[16]	measured	[16]
H–C(8)	+0.56	+0.54		
H–C(10)	−0.12	−0.09		
H–C(11)	+0.16	+0.10		
H–C(12)	−0.05	−0.06		
H–C(8′)			+0.56	+0.54
H–C(10′)			−0.07	−0.09
H–C(11′)			+0.10	+0.10
H–C(12′)			−0.06	−0.06
	$\Delta\delta = \delta(13Z) - \delta(\text{all-}E)$		$\Delta\delta = \delta(13'Z) - \delta(\text{all-}E)$	
	measured	[16]	measured	[16]
H–C(10)	+0.06	+0.05		
H–C(12)	+0.54	+0.52		
H–C(14)	−0.13	−0.13		
H–C(15)	+0.17	+0.16		
H–C(15′)	−0.06	−0.08		
H–C(10′)			+0.06	+0.05
H–C(12′)			+0.54	+0.52
H–C(14′)			−0.14	−0.13
H–C(15′)			+0.18	+0.16
H–C(15)			−0.06	−0.08
	$\Delta\delta = \delta(15Z) - \delta(\text{all-}E)$			
	measured	[16]		
H–C(11)	+0.05	+0.04		
H–C(12)	+0.08	+0.07		
H–C(14)	+0.42	+0.41		
H–C(15)	−0.22	−0.23		
H–C(11′)	+0.05	+0.04		
H–C(12′)	+0.08	+0.07		
H–C(14′)	+0.42	+0.41		
H–C(15′)	−0.22	−0.23		

isomers **4**–**6**, respectively, exhibit a prominent maximum in the region of 345 nm. For the (di-*Z*)-isomers **7**–**9**, the signs of the maxima at short wavelengths are the same as for the (all-*E*)-isomer **1** (*Figs. 3* and *4*). However, it must be pointed out that these compounds have not been fully characterized.

The mass spectra of all the isomers **1**–**9** showed the corresponding molecular-ion peak at *m*/*z* 602, and, in addition, signals at 584 ($[M - H_2O]^+$), 566 ($[M - 2\,H_2O]^+$), 510 ($[M - \text{toluene}]^+$), 504, 221, 181, 145, 119, and 91 were observed [17][18].

Discussion. – The I_2-catalyzed isomerization of (all-*E*)-5,6-diepikarpoxanthin (**1**) gave a complex mixture of (*Z*)-isomers, which was demanding to separate. As main products, the (9′*Z*)- (**3**), (9*Z*)- (**2**), (13′*Z*)- (**5**), and (13*Z*)-5,6-diepikarpoxanthin (**4**) were isolated. In contrast, in the thermal isomerization, mainly the (13*Z*)- and the (13′*Z*)-isomers **4** and **5**, respectively, were formed in significant amounts. Therefore, the thermal isomerization of **1** is a suitable method for the preparation of **4** and **5**. The

isolated (mono-*Z*)-isomers **2**–**6** may be helpful in the search for naturally occurring (*Z*)-isomers of **1**.

The structures of the main products of the (*E*/*Z*)-isomerization of 5,6-diepikarpoxanthin (**1**) correspond to the products of the (*E*/*Z*)-isomerization of other carotenoids with the 5,6-dihydro-*β*-end group with the same chromophore. Also, the composition of the equilibrium mixtures were very similar for all compounds with the 5,6-dihydro-*β*-end group, independent of the structure of the second end group (*β*-, 3-hydroxy-*β*-, 5,6-epoxy-5,6-dihydro-3-hydroxy-*β*-, 3,6-epoxy-5,6-dihydro-*β*-, and *ε*-end groups) investigated before. The rate of the (*E*/*Z*)-isomerization of (all-*E*)-5,6-diepikarpoxanthin (**1**) was of the same order as the rate of the (*E*/*Z*)-isomerization of other carotenoids with a 5,6-dihydro-*β*-end group. The equilibrium was reached by thermal isomerization within 120 min and by I_2-catalyzed photoisomerization within 40 min [3–9].

It is well-established that carotenoids with saturated cyclic end groups containing two or three OH groups generate nonconservative CD spectra. Therefore, no correlation can be made between the CD spectra and the chirality at a specific center [19]. This is examplified by the spectra of karpoxanthin and 6-epikarpoxanthin, which exhibit a similar shapes. Also, the case of (*Z*)-isomers of these carotenoids is poorly understood, due to the lack of literature data. The CD spectra of the (*E*/*Z*)-isomers of 5,6-diepikarpoxanthin are similar to those of (all-*E*)-, (5*Z*)-, and (7*Z*)-1,2-epoxy-1,2-dihydrolycopene and the (all-*E*)- and (7′*Z*)-isomers of 1′,2′-epoxy-1′,2′-dihydro-*β*,*ψ*-carotene. Especially at low temperature, these compounds show 'conservative-like' CD spectra, which invert sign upon isomerization, but only in the UV part of the spectra [20]. This has been explained by the enhanced flexibility of the end groups, in comparison with the *β*-end group.

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Experimental Part

1. *General*. See [1].

2. *HPLC*. See [1].

3. *Thermal Isomerization*. A soln. of 40 mg of (all-*E*)-5,6-diepikarpoxanthin (**1**; m.p. 150°; purity (HPLC) > 95%) in 400 ml of benzene was refluxed during 2 h under N_2 in the dark [4][7][9], and, after the usual workup [21], the equilibrium mixture was submitted to CC.

4. *Iodine-Catalyzed Photoisomerization*. A soln. of 100 mg of (all-*E*)-5,6-diepikarpoxanthin (**1**) in 1000 ml of benzene was isomerized under N_2 in scattered daylight in the presence of 2 mg of I_2 (2% rel. to the carotenoid) [4][8][9]. The isomerization was monitored by UV/VIS [7], and when the thermodynamic equilibrium was reached (*ca.* 40 min), the soln. was washed free of I_2 with 5% $Na_2S_2O_3$ soln. After the usual workup [21], the mixture was submitted to CC.

5. *Isolation*. The reaction mixtures were separated by CC (6 × 30 cm columns, 4 columns for thermal isomerization, 12 columns for photoisomerization) with $CaCO_3$ and 0.5% acetone in benzene. Typical picture after development of the thermal-isomerization mixture: 3 mm pale brownish yellow (unidentified); 2 mm of intermediate zone; 3 mm yellow (*Zone 1*; **A**); 5 mm of intermediate zone; 15 mm yellow (*Zone 2*; **5**); 2 mm of intermediate zone; 5 mm pale yellow (*Zone 3*; **6**); 4 mm of intermediate zone; 3 mm pale yellow (*Zone 4*; **B**); 8 mm of intermediate zone; 15 mm yellow (*Zone 5*; **4**); 12 mm of intermediate zone; 40 mm yellow (*Zone 6*; **1**). Picture after development of the photoisomerization mixture: 4 mm brownish yellow (unidentified); 2 mm of intermediate zone; 3 mm pale yellow (*Zone 1*; **C**); 3 mm of intermediate zone; 5 mm pale yellow (*Zone 2*; **7**);

5 mm of intermediate zone; 6 mm yellow (*Zone 3*; **5**); 3 mm of intermediate zone; 8 mm yellow (*Zone 4*; **3**); 6 mm of intermediate zone; 6 mm pale yellow (*Zone 5*; **8**); 3 mm of intermediate zone; 3 mm pale yellow (*Zone 6*; **D**); 4 mm of intermediate zone; 3 mm pale yellow (*Zone 7*; **E**); 5 mm of intermediate zone; 5 mm pale yellow (*Zone 8*; **6**); 10 mm of intermediate zone; 12 mm yellow (*Zone 9*; **4**); 6 mm of intermediate zone; 25 mm yellow (*Zone 10*; **1**); 3 mm of intermediate zone; 20 mm pale yellow (*Zone 11*; **2**); 4 mm of intermediate zone; 8 mm pale yellow (*Zone 12*; **9**). For further purification, the fractions were submitted to repeated CC in the same system, and, after development and the usual workup [21], the carotenoids were crystallized from benzene/hexane 1:4 to give, from the thermal-isomerization mixture, 5 mg of **1**, 3.0 mg of **4**, 3.0 mg of **5**, and 0.6 mg of **6**. From the photoisomerization mixture, 10 mg of **1**, 3.3 mg of **2**, 3.3 mg of **3**, 1.0 mg of **4**, 0.8 mg of **5**, 0.3 mg of **6**, 0.3 mg of **7**, 0.9 mg of **8**, and 0.5 mg of **9** were obtained.

6. *(all-*E*)-5,6-Diepikarpoxanthin* (=*(all-*E*,3*S*,5*S*,6*S*,3′*R*)-5,6-Dihydro-β,β-carotene-3,5,6,3′-tetrol*; **1**). M.p. 158–160°. UV/VIS (benzene): 487, 458, 434 (*Fig. 2*). CD (EPA, −180°): 212 (−0.23), 220 (−1.32), 247 (+3.06), 281 (−6.89), 311 (−0.73), 332 (−1.19). NMR and MS: see [1].

7. *(9*Z*)-5,6-Diepikarpoxanthin* (**2**). M.p. 108–110°. Purity (HPLC): 95%. UV/VIS (benzene): *Table 1*, *Fig. 2,a*. CD (EPA, r.t.): 194.0 (+0.05), 195.5 (+0.16), 198.5 (−1.03), 205.0 (−0.12), 216.5 (+0.53), 243.0 (−0.44), 278.0 (+0.07), 330.0 (−0.16). CD (EPA, −180°): 190.0 (+1.01), 198.0 (−1.20), 217.5 (+3.27), 243.0 (−1.41), 297.0 (+1.04), 330.0 (−0.38), 344.0 (−0.49), 380.0 (+0.16) (*Fig. 3*). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.94 (*s*, Me(16)); 1.08 (*s*, Me(16′)); 1.08 (*s*, Me(17′)); 1.16 (*s*, Me(18)); 1.33 (*s*, Me(17)); 1.49 ($J_{gem} \approx J(2'ax,3') = 12.0$, H_{ax}–C(2′)); 1.67 (*ddd*, $J_{gem} = 14.8$, $J(2ax,3) = 3.3$, $J(2ax,4ax) = 2.1$, H_{ax}–C(2)); 1.74 (*s*, Me(18′)); 1.78 (*ddd*, $J_{gem} = 12.0$, $J(2'eq,3') = 3.6$, $J(2'eq,4'eq) = 2.1$, H_{eq}–C(2′)); 1.86 (*ddd*, $J_{gem} = 14.5$, $J(4ax,3) = 2.8$, $J(4ax,2ax) = 2.1$, H_{ax}–C(4)); 1.92 (*dd*, $J_{gem} = 14.8$, $J(2eq,3) = 3.2$, H_{eq}–C(2)); 1.98 (*s*, Me(19′)); 1.98 (*s*, Me(20′)); 1.99 (*s*, Me(19)); 1.99 (*s*, Me(20)); 2.05 (*dd*, $J_{gem} = 16.8$, $J(4'ax,3') = 9.7$, H_{ax}–C(4′)); 2.12 (*dd*, $J_{gem} = 14.5$, $J(4eq,3) = 3.3$, H_{eq}–C(4)); 2.40 (*ddd*, $J_{gem} = 16.8$, $J(4'eq,3') = 5.5$, $J(4'eq,2'eq) = 2.1$, H_{eq}–C(4′)); 4.01 (*m*, H–C(3′)); 4.29 (*m*, H–C(3)); 6.10 (*d*, $J(10,11) = 11.7$, H–C(10)); 6.12 (*m*, H–C(7′)); 6.12 (*m*, H–C(8′)); 6.16 (*d*, $J(10',11') = 11.6$, H–C(10′)); 6.26 (*m*, H–C(14)); 6.26 (*m*, H–C(14′)); 6.32 (*d*, $J(12,11) = 14.9$, H–C(12)); 6.37 (*d*, $J(12',11') = 14.3$, H–C(12′)); 6.40 (*dd*, $J(7,8) = 15.7$, H–C(7)); 6.64 (*d*, H–C(15)); 6.64 (*m*, H–C(15′)); 6.65 (*dd*, $J(11',10') = 11.6$, $J(11',12') = 14.3$, H–C(11′)); 6.79 (*dd*, $J(11,10) = 11.7$, $J(11,12) = 14.9$, H–C(11)); 6.91 (*d*, $J(8,7) = 15.7$, H–C(8)). EI-MS: 602 (32, M^+), 584 (5, $[M - H_2O]^+$), 510 (6, $[M$ − toluene$]^+$), 351 (6), 221 (8), 181 (8), 145 (9), 119 (8), 91 (15), 32 (49), 28 (100).

8. *(9′*Z*)-5,6-Diepikarpoxanthin* (**3**). M.p. 100–102°. Purity (HPLC): 96%. UV/VIS (benzene): *Table 1*, *Fig. 2,a*. CD (EPA, r.t.): 195.0 (0.00), 196.5 (−9.33), 198.5 (−0.85), 205.0 (−1.30), 228.0 (+0.78), 248.0 (−0.89), 284.0 (+1.09), 347.0 (+0.16), 370.0 (+0.36). CD (EPA, −180°): 203.5 (−2.07), 214.0 (−0.65), 224.5 (+0.44), 244.0 (−5.53), 287.0 (+2.36), 348.0 (−0.78), 382.0 (−1.39), 386.0 (−1.22) (*Fig. 3*). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.90 (*s*, Me(16)); 1.09 (*s*, Me(16′)); 1.10 (*s*, Me(17′)); 1.13 (*s*, Me(18)); 1.32 (*s*, Me(17)); 1.48 ($J_{gem} \approx J(2'ax,3') = 11.8$, H_{ax}–C(2′)); 1.66 (*ddd*, $J_{gem} = 14.5$, $J(2ax,3) = 3.3$, $J(2ax,4ax) = 2.1$, H_{ax}–C(2)); 1.78 (*s*, Me(18′)); 1.79 (*ddd*, $J_{gem} = 11.8$, $J(2'eq,3') = 3.5$, $J(2'eq,4'eq) = 2.1$, H_{eq}–C(2′)); 1.85 (*ddd*, $J_{gem} = 14.6$, $J(4ax,3) = 2.8$, $J(4ax,2ax) = 2.1$, H_{ax}–C(4)); 1.91 (*dd*, $J_{gem} = 14.5$, $J(2eq,3) = 3.3$, H_{eq}–C(2)); 1.97 (*s*, Me(19′)); 1.98 (*s*, Me(20)); 1.98 (*s*, Me(20′)); 1.99 (*s*, Me(19)); 2.04 (*dd*, $J_{gem} = 16.7$, $J(4'ax,3') = 9.8$, H_{ax}–C(4′)); 2.11 (*dd*, $J_{gem} = 14.6$, $J(4eq,3) = 3.3$, H_{eq}–C(4)); 2.42 (*ddd*, $J_{gem} = 16.7$, $J(4'eq,3') = 5.4$, $J(4'eq,2'eq) = 2.1$, H_{eq}–C(4′)); 4.03 (*m*, H–C(3′)); 4.28 (*m*, H–C(3)); 6.08 (*d*, $J(10',11') = 11.5$, H–C(10′)); 6.13 (*d*, $J(7',8') = 15.1$, H–C(7′)); 6.23 (*d*, $J(10,11) = 11.3$, H–C(10)); 6.27 (*m*, H–C(14)); 6.27 (*m*, H–C(14′)); 6.30 (*d*, $J(12',11') = 15.2$, H–C(12′)); 6.36 (*m*, H–C(7)); 6.36 (*m*, H–C(8)); 6.38 (*d*, $J(12,11) = 15.0$, H–C(12)); 6.64 (*m*, H–C(15)); 6.64 (*m*, H–C(15′)); 6.65 (*dd*, $J(11,10) = 11.3$, $J(11,12) = 15.0$, H–C(11)); 6.67 (*d*, $J(8',7') = 15.1$, H–C(8′)); 6.74 (*dd*, $J(11',10') = 11.5$, $J(11',12') = 15.2$, H–C(11′)). EI-MS: 602 (37, M^+), 584 (6, $[M - H_2O]^+$), 510 (7, $[M$ − toluene$]^+$), 351 (4), 221 (6), 181 (6), 145 (6), 119 (7), 91 (15), 32 (77), 28 (100).

9. *(13*Z*)-5,6-Diepikarpoxanthin* (**4**). M.p. 99–100°. Purity (HPLC): 92%. UV/VIS (benzene): *Table 1*, *Fig. 2,b*. CD (EPA, r.t.): 194.0 (−0.40), 196.0 (+0.23), 198.0 (−1.30), 201.0 (−0.74), 220.5 (+0.52), 244.5 (−1.00), 280.5 (+1.46), 333.5 (−1.11). CD (EPA, −180°): 195.0 (−2.14), 218.5 (+1.85), 244.0 (−4.86), 280.5 (+5.69), 330.5 (−4.07), 345.5 (−5.41), 400.0 (+0.17) (*Fig. 3*). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.91 (*s*, Me(16)); 1.08 (*s*, Me(16′)); 1.08 (*s*, Me(17′)); 1.14 (*s*, Me(18)); 1.33 (*s*, Me(17)); 1.49 ($J_{gem} \approx J(2'ax,3') = 12.0$, H_{ax}–C(2′)); 1.66 (*ddd*, $J_{gem} = 14.8$, $J(2ax,3) = 3.3$, $J(2ax,4ax) = 2.1$, H_{ax}–C(2)); 1.75 (*s*, Me(18′)); 1.78 (*ddd*, $J_{gem} = 12.0$, $J(2'eq,3') = 3.6$, $J(2'eq,4'eq) = 2.1$, H_{eq}–C(2′)); 1.86 (*ddd*, $J_{gem} = 14.5$, $J(4ax,3) = 2.8$, $J(4ax,2ax) = 2.1$, H_{ax}–C(4)); 1.92 (*dd*, $J_{gem} = 14.8$, $J(2eq,3) = 3.1$, H_{eq}–C(2)); 1.97 (*s*, Me(19′)); 1.97 (*s*, Me(20′)); 2.00 (*s*, Me(19)); 2.00 (*s*, Me(20)); 2.05 (*dd*, $J_{gem} = 16.8$, $J(4'ax,3') = 9.9$, H_{ax}–C(4′)); 2.12 (*dd*, $J_{gem} = 14.5$, $J(4eq,3) = 3.2$, H_{eq}–C(4)); 2.40 (*ddd*, $J_{gem} = 16.8$, $J(4'eq,3') = 5.6$, $J(4'eq,2'eq) = 2.1$, H_{eq}–C(4′)); 4.01 (*m*, H–C(3′)); 4.29 (*m*, H–C(3)); 6.13 (*d*, $J(14,15) \approx 12$, H–C(14)); 6.13 (*m*, H–C(7′)); 6.13 (*m*, H–C(8′));

6.17 (*d*, *J*(10′,11′) = 11.6, H–C(10′)); 6.25 (*d*, *J*(14′,15′) = 11.6, H–C(14′)); 6.28 (*d*, *J*(10,11) = 11.6, H–C(10)); 6.38 (*m*, H–C(7)); 6.38 (*m*, H–C(8)); 6.38 (*d*, *J*(12′,11′) = 14.6, H–C(12′)); 6.57 (*dd*, *J*(15′,14′) ≈ 12, *J*(15′,15) ≈ 14, H–C(15′)); 6.65 (*dd*, *J*(11,10) = 11.6, *J*(11,12) = 14.7, H–C(11)); 6.65 (*dd*, *J*(11′,10′) = 11.6, *J*(11′,12′) = 14.6, H–C(11′)); 6.80 (*dd*, *J*(15,14) ≈ 12, *J*(15,15′) ≈ 14, H–C(15)); 6.91 (*d*, *J*(12,11) = 14.7, H–C(12)). EI-MS: 602 (8, M^+), 584 (2, $[M-H_2O]^+$), 510 (2, $[M-\text{toluene}]^+$), 221 (3), 181 (4), 91 (11), 32 (78), 28 (100).

10. *(13′Z)-5,6-Diepikarpoxanthin* (**5**). M.p. 98–99°. Purity (HPLC): 90%. UV/VIS (benzene): *Table 1*, *Fig. 2,b*. CD (EPA, r.t.): 192.5 (–0.12), 195 (+0.51), 198 (–1.31), 212.5 (+0.46), 218.0 (+0.73), 219.5 (+0.75), 243.5 (–0.46), 283.5 (+0.48), 334.5 (–0.65), 341 (–0.59). CD (EPA, –180°): 195.0 (–0.82), 197.0 (–1.67), 199.0 (–2.50), 216.0 (+3.52), 241.5 (–0.92), 281.5 (+2.98), 293.0 (+2.46), 331.0 (–1.84), 344.5 (–2.66), 380.0 (+0.63) (*Fig. 3*). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.90 (*s*, Me(16)); 1.09 (*s*, Me(16′)); 1.09 (*s*, Me(17′)); 1.13 (*s*, Me(18)); 1.32 (*s*, Me(17)); 1.49 ($J_{gem} \approx J$(2′ax,3′) = 12.0, H_{ax}–C(2′)); 1.66 (*ddd*, J_{gem} = 14.6, *J*(2ax,3) = 3.3, *J*(2ax,4ax) = 2.2, H_{ax}–C(2)); 1.75 (*s*, Me(18′)); 1.79 (*ddd*, J_{gem} = 12.0, *J*(2′eq,3′) = 3.4, *J*(2′eq,4′eq) = 2.0, H_{eq}–C(2′)); 1.85 (*ddd*, J_{gem} = 14.4, *J*(4ax,3) = 2.9, *J*(4ax,2ax) = 2.2, H_{ax}–C(4)); 1.91 (*dd*, J_{gem} = 14.6, *J*(2eq,3) = 3.2, H_{eq}–C(2)); 1.97 (*s*, Me(20)); 1.98 (*s*, Me(19′)); 1.99 (*s*, Me(19)); 2.00 (*s*, Me(20′)); 2.06 (*dd*, J_{gem} = 16.9, *J*(4′ax,3′) = 9.5, H_{ax}–C(4′)); 2.11 (*dd*, J_{gem} = 14.4, *J*(4eq,3) = 3.3, H_{eq}–C(4)); 2.40 (*ddd*, J_{gem} = 16.9, *J*(4′eq,3′) = 5.6, *J*(4′eq,2′eq) = 2.0, H_{eq}–C(4′)); 4.02 (*m*, H–C(3′)); 4.28 (*m*, H–C(3)); 6.12 (*d*, *J*(14′,15′) ≈ 12, H–C(14′)); 6.14 (*m*, H–C(7′)); 6.14 (*m*, H–C(8′)); 6.21 (*d*, *J*(10′,11′) = 11.6, H–C(10′)); 6.23 (*d*, *J*(10,11) = 11.6, H–C(10)); 6.25 (*d*, *J*(14,15) ≈ 12, H–C(14′)); 6.36 (*m*, H–C(7)); 6.36 (*m*, H–C(8)); 6.38 (*d*, *J*(12,11) = 15.0, H–C(12)); 6.57 (*dd*, *J*(15,14) ≈ 12, *J*(15,15′) ≈ 14, H–C(15)); 6.63 (*dd*, *J*(11,10) = 11.6, *J*(11,12) = 15.0, H–C(11)); 6.66 (*dd*, *J*(11′,10′) = 11.6, *J*(11′,12′) = 14.8, H–C(11′)); 6.81 (*dd*, *J*(15′,14′) ≈ 12, *J*(15′,15) ≈ 14, H–C(15′)); 6.90 (*d*, *J*(12′,11′) = 14.8, H–C(12′)). EI-MS: 602 (19, M^+), 584 (3, $[M-H_2O]^+$), 510 (3, $[M-\text{toluene}]^+$), 351 (4), 221 (3), 181 (5), 119 (6), 115 (5), 91 (16), 32 (100), 28 (100).

11. *(15Z)-5,6-Diepikarpoxanthin* (**6**). M.p. 85–87°. Purity (HPLC): 90%. UV/VIS (benzene): *Table 1*, *Fig. 2,b*. CD (EPA, r.t.): 194.0 (+0.28), 196.0 (–1.35), 198.0 (+0.71), 201.5 (–0.75), 204.5 (–0.34), 215.0 (+0.21), 243.0 (–0.83), 282.5 (+0.71), 331 (–0.96), 390.0 (+0.02). CD (EPA, –180°): 190.0 (–3.16), 195.5 (–5.79), 199.5 (–3.33), 218.0 (+1.56), 242.0 (–1.66), 282.0 (+3.30), 332.5 (–2.94), 344.0 (–3.80), 373.0 (–0.36), 383.5 (–0.54), 395.0 (–0.48) (*Fig. 4*). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.91 (*s*, Me(16)); 1.09 (*s*, Me(16′)); 1.09 (*s*, Me(17′)); 1.18 (*s*, Me(18)); 1.32 (*s*, Me(17)); 1.49 ($J_{gem} \approx J$(2′ax,3′) = 11.9, H_{ax}–C(2′)); 1.66 (*ddd*, J_{gem} = 14.7, *J*(2ax,3) = 3.3, *J*(2ax,4ax) = 2.1, H_{ax}–C(2)); 1.75 (*s*, Me(18′)); 1.78 (*ddd*, J_{gem} = 11.9, *J*(2′eq,3′) = 3.5, *J*(2′eq,4′eq) = 2.1, H_{eq}–C(2′)); 1.86 (*ddd*, J_{gem} = 14.8, *J*(4ax,3) = 2.8, *J*(4ax,2ax) = 2.1, H_{ax}–C(4)); 1.91 (*dd*, J_{gem} = 14.7, *J*(2eq,3) = 3.1, H_{eq}–C(2)); 1.98 (*s*, Me(20)); 1.98 (*s*, Me(19′)); 1.98 (*s*, Me(20′)); 2.00 (*s*, Me(19)); 2.04 (*dd*, J_{gem} = 16.9, *J*(4′ax,3′) = 9.8, H_{ax}–C(4′)); 2.11 (*dd*, J_{gem} = 14.8, *J*(4eq,3) = 3.3, H_{eq}–C(4)); 2.40 (*ddd*, J_{gem} = 16.9, *J*(4′eq,3′) = 5.5, *J*(4′eq,2′eq) = 2.1, H_{eq}–C(4′)); 4.01 (*m*, H–C(3′)); 4.29 (*m*, H–C(3)); 6.12 (*m*, H–C(8′)); 6.13 (*m*, H–C(7′)); 6.17 (*d*, *J*(10′,11′) = 11.4, H–C(10′)); 6.24 (*d*, *J*(10,11)) = 11.4, H–C(10)); 6.37 (*m*, H–C(7)); 6.37 (*m*, H–C(8)); 6.41 (*m*, H–C(15)); 6.41 (*m*, H–C(15′)); 6.44 (*d*, *J*(12′,11′) = 14.9, H–C(12′)); 6.45 (*d*, *J*(12,11) = 15.3, H–C(12)); 6.68 (*dd*, *J*(11,10) = 11.4, *J*(11,12) = 15.3, H–C(11)); 6.68 (*m*, H–C(14)); 6.68 (*m*, H–C(14′)); 6.69 (*dd*, *J*(11′,10′) = 11.4, *J*(11′,12′) = 14.9, H–C(11′)). EI-MS: 602 (8, M^+), 584 (2, $[M-H_2O]^+$), 510 (2, $[M-\text{toluene}]^+$), 221 (2), 181 (3), 145 (3), 119 (3), 91 (4), 32 (80), 28 (100).

12. *Additional (Z)-Isomers of 5,6-Diepikarpoxanthin* (**1**). *(9Z,13′Z)- or (13Z,9′Z)-5,6-Diepikarpoxanthin* (**7**): M.p. 98°. UV/VIS (benzene): *Table 1*. CD (EPA, r.t.): 194.5 (+0.60), 197.0 (–4.95), 200.0 (+0.14), 207.5 (+1.90), 213.5 (+1.68), 234.5 (–1.03), 255.0 (+1.15), 274.0 (+3.03), 330.0 (–3.85). CD (EPA, –180°): 198.0 (+4.98), 222.0 (–2.55), 234.5 (1.28), 252.0 (+0.54), 259.5 (+5.04), 281.5 (+8.92), 329.0 (–8.70), 343.5 (–12.47), 360.0 (+0.40), 380.0 (+17), 400.0 (+0.39) (*Fig. 4*). EI-MS: 602 (14, M^+).

(9Z,9′Z)-5,6-Diepikarpoxanthin (**8**): UV/VIS: *Table 1*. CD (EPA, r.t.): 194.0 (–0.11), 196.0 (+2.68), 198.0 (+0.85), 201.0 (+1.50), 204.0 (+4.68), 223.5 (–0.02), 249.5 (+3.32), 283.0 (–2.24), 331.0 (+1.54), 358.0 (+0.90). CD (EPA, –180°): 190 (+17.47), 196.0 (+29.88), 198.5 (+16.09), 203.0 (+19.13), 222.0 (–4.93), 246.5 (+12.91), 282.5 (–12.67), 313.0 (+3.20), 327.0 (+5.50), 341.5 (+6.72), 397.0 (+2.00) (*Fig. 4*). EI-MS: 602 (33, M^+), 584 (5, $[M-H_2O]^+$), 510 (6, $[M-\text{toluene}]^+$), 351 (5), 221 (6), 181 (6), 145 (7), 119 (7), 91 (11), 32 (100), 28 (96).

(9Z,13Z)- or (9′Z,13′Z)-5,6-Diepikarpoxanthin (**9**): M.p. 108–110°. UV/VIS: *Table 1*. CD (EPA, r.t.): 220.0 (–1.84), 255.0 (–0.12), 287.0 (–1.00), 330.5 (+2.37), 395.0 (–0.16), 423.0 (0.00), 435.0 (–0.09), 470.0 (+0.36), 356.0 (+0.13). CD (EPA, –180°): 190.0 (+2.55), 195.0 (+4.09), 198.0 (+2.48), 221.5 (–5.69), 253.5 (+1.37), 286.0 (–3.54), 330.0 (+6.23), 344.0 (+7.81), 370.0 (–0.09) (*Fig. 4*). EI-MS: 602 (14, M^+).

(Di-Z)- and (Poly-Z)-Isomers **A**–**E**: UV/VIS: *Table 1*.

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