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Bacterial Carotenoids. LII. C_{50}-Carotenoids. 18.* Synthesis of the Model Compounds (2*R*,6*S*,2′*R*,6′*S*)-2,2′-Dimethyl-γ,γ-carotene and (2*R*,2′*R*,6′*S*)-2,2′-Dimethyl-β,γ-carotene

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The title compounds were synthesized from (+)−(2*S*,6*R*)-*cis*-γ-irone(*1*). The physical properties of the C_{42}-carotenes *5* and *6* and intermediates are reported for future stereochemical correlation of naturally occurring carotenoids with γ-end-groups.

We have reported earlier on the syntheses and chiroptical properties of the C_{42}-carotenes (2*R*,2′*R*)-2,2′-dimethyl-β,β-carotene,[1] (2*R*,6*S*,2′*R*,6′*S*)-2,2′-dimethyl-ε,ε-carotene and (2*R*,6*R*,2′*R*,6′*R*)-2,2′-dimethyl-ε,ε-carotene.[2] The chiroptical and ^{1}H NMR properties of these synthetic, optically active carotenes were decisive in assigning the absolute configuration in relation to the naturally occurring C_{50}-carotenoids *C.p.* 450 [(2*R*,2′*R*)-2-(4-hydroxy-3-hydroxymethyl-2-butenyl)-2′-(3-methyl-2-butenyl)-β,β-carotene] [1] and decaprenoxanthin [(2*R*,6*R*,2′*R*,6′*R*)-bis(4-hydroxy-3-methyl-2-butenyl)-ε,ε-carotene].[2]

Carotenes in the C_{40}-series and carotenoids in the C_{50}-series featuring the γ-end-group with an exocyclic double bond have been reported to occur naturally, namely β,γ-carotene [4,5] (optically active,[6] stereochemistry unknown); γ,γ-carotene [5] (*7*, assumed optically active) and sarcinaxanthin (optically active).[7,8]

The availability of (+)-(2S,6*R*)-*cis*-γ-irone (*1*)[1,9] suggested the synthesis of optically active C_{42}-carotenes in order to determine the absolute configuration of naturally occurring carotenoids of the same chromophore, containing the γ-end-group. We report now on the synthesis of (2*R*,6*S*,2′*R*,6′*S*)-2,2′-dimethyl-γ,γ-carotene (*5*) and (2*R*,2′*R*,6′*S*)-2,2′-dimethyl-β,γ-carotene (*6*).

RESULTS AND DISCUSSION

Naturally occurring (+)-(2*S*,6*R*)-*cis*-γ-irone (*1*) was the key building block for the synthesis of *5* and *6*. The numbering system for starting irone [9] and early intermediates differ from that of the carotenes; see Scheme 1.

Reaction of *1* with vinylmagnesium bromide gave (2*S*,6*R*)-vinyl-γ-ironol (*2*) in nearly quantitative yield. Treatment of *2* with triphenylphosphonium bromide gave the phosphonium salt *3* (possibly a mixture of *3a* and *3b*). Condensation of the phosphoran derived therefrom with the dial *4* gave two products (2*R*, 6*S*, 2′*R*, 6′*S*)-2,2′-dimethyl-γ,γ-carotene (*5*) and (2*R*,2′*R*, 6′*S*)-2,2′-dimethyl-β,γ-carotene (*6*). The latter product resulted from isomerization of the labile γ end-group to the thermodynamically more stable β end-group. A similar isomerization of a γ to a β end-group was previously noted during a Horner reaction with γ-ionone.[10,11] However, ^{1}H NMR analysis of the vinyl-γ-ironol (*2*) demonstrated that no isomerization occurred during the Grignard reaction from *1*. Isomerization may have been effected during formation of the phosphonium salt through intermediates *7* and *8* (Scheme 2), since compounds similar to *8* are

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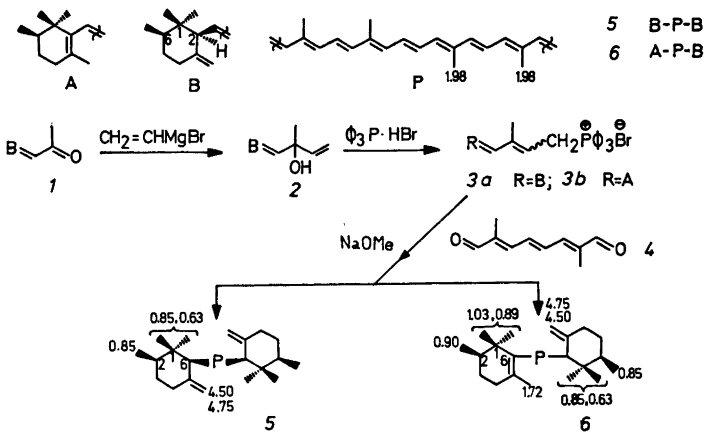
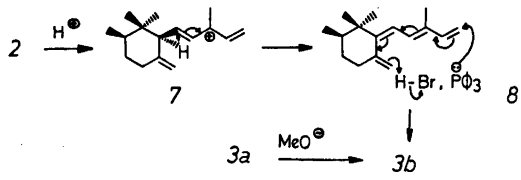


reported to provide phosphonium salts with triphenylphosphine hydrobromide.[12] Alternatively base catalyzed isomerization of *3a* may have occurred during generation of the phosphoran (Scheme 2). Either of these alternatives would lead to the *β*-type phosphonium salt *3b* and account for the presence of the dimethyl-*β,γ*-carotene *6* in the final reaction mixture.



The optically active C_{42}-carotenes *5* and *6* had electronic absorption spectra and IR spectra identical with their C_{40}-counterparts.[10,11] The mass spectra of *5* and *6* showed the predicted molecular ions and the typical loss of toluene (M − 92), xylene (M − 106) and also M − 158.[13] Other fragment ions originated from fragmentation patterns similar to those of the corresponding C_{40}-carotenes[10,11] with the exception that the *m/e* values were increased due to the methyl substitutents at C-2,2′. Qualitative CD spectra of *5* and *6* are given in Fig. 1.

The ^{1}H NMR and CD data reported here have been used for stereochemical correlation of naturally occurring C_{50}- and C_{40}-carotenoids containing the *γ* end-group.[8,14]

EXPERIMENTAL

Materials and methods. General methods, including instrumentation, chromatography and the GLC separation of irones from Iris oil have been described elsewhere.[1,2]

(+)-(2S,6R)-cis-γ-Irone (1). 1 isolated by preparative GLC was better than 98 % pure as measured by analytical GLC. *1* had the following properties: CD see Fig. 1; $[\alpha]_D^{20}$ (EPA) 589 nm = 4°, 578 nm = 5°, 546 nm = 6°, 436 nm = 21°,

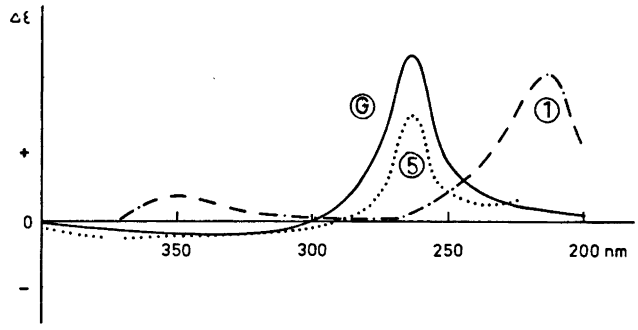


Fig. 1. Qualitative CD spectra in EPA solution of (2*S*,6*R*)-*cis*-*γ*-irone (*1*), (2*R*,6*S*,2′*R*,6′*S*)-2,2′-dimethyl-*γ,γ*-carotene (*5*), and (2*R*,2′*R*,6′*S*)-2,2′-dimethyl-*β,γ*-carotene (*6*).

365 nm = 112°; λ_{max} 222 nm (EPA), 227 nm (MeOH); IR(liq.) 3082 (m), 2965, 2937, 2860, 1650, 1630, 1455, 1370, 1258 (s), 1220, 1195, 1175 (m), 1145, 1110, 1049, 1025 (w), 1000 (s), 980, 960 (w), 895 (s) and 740 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.63, 0.88 (6 H, *gem.* dimethyl), 0.88 (d, 3 H, J 5 Hz, $>CH-CH_3$), 1.0–1.7 (5 H, complex, $>CH_2$, $>CH-CH_3$), 2.27 (3 H, $O=C-CH_3$), 2.56 (d, 1 H, J 10 Hz, $>CH-C=C$), 4.45, 4.80 (2 H, $>C=CH_2$), 6.03 (d, 1 H, J 16 Hz, $>CH-C=O$) and 6.95 (q, 1 H, J_1 16 Hz, J_2 10 Hz, $>CH=CH-C=O$; *m/e* 206 (M), 191 (M−15), 149 (M−57) and 121 (M−85).

(+)-(2S,6R)-cis-γ-Vinyl-ironol (2). *1* (570 mg) gave *10* (590 mg, 90 %) when reacted with vinylmagnesium bromide using earlier described methods.[3] *2* had $[\alpha]_D^{20}$ (EPA) 589 nm = 7°, 578 nm = 8°, 546 nm = 9°, 436 nm = 17°, 365 nm = 33°; IR (liq.) 3390 (s) 3082 (m), 2970, 2930, 2860, 1645 (s), 1455, 1410, 1390, 1370 (m), 1265, 1195, 1140, 1100 (w), 990, 920 (s), 895 (m), 740 (s) and 650 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.62, 0.88 (6 H, *gem.* dimethyl), 0.83 (d, 3 H, J *ca.* 5 Hz, $>CH-CH_3$), 1.0–1.7 (5 H, complex, $>CH_2$, $>CH-CH_3$), 1.38 (3 H, $CH_3-CH-OH$), 2.27 (d, 1 H, broad, $>CH-C=C<$), 3.65 (1 H, broad, OH), 4.73, 4.48 (2 H, $>C=CH_2$), 5.03 (q, 1 H, J_1 10 Hz, J_2 2 Hz, *cis* $-CH=CH_2$), 5.22 (q, 1 H, J_1 17.5 Hz, J_2 2 Hz, *trans* $-CH=CH_2$), 5.73 (1 H, $=CH-COH$), 5.70 (d, 1 H, J 9 Hz, $-CH=CH_2$), and 6.02 (q, 1 H, J_1 17.5 Hz, J_2 10.5 Hz, $-CH=CH-COH$); *m/e* 234 (M), 216 (M−18) and 263 (M−71).

(2S,6R)-cis-γ-Ironylidene-ethyltriphenylphosphonium bromide (3a). *3a* was prepared by reacting *2* with triphenylphosphonium bromide following earlier described procedure;[3] yield 70 % from *2* (570 mg).

(2R,6S,2'R,6'S)-2,2'-Dimethyl-γ,γ-carotene (5). The phosphoran generated from *3a* with sodium methoxide was reacted with 2,7-dimethylocta-2,4,6-trienedial (*4*, 15 mg) and the products isolated and purified by chromatography using procedures described earlier;[3] yield 17.5 mg, 31 % based on dial *4*. Both *5* and the isomerization product *6* were obtained. Crystallized from MeOH–$CHCl_3$ solution, *5* had m.p. 165–168 °C. The electronic absorption and IR spectra could not be distinguished from those of γ,γ-carotene;[10,11] CD spectrum is shown in Fig. 1; ^1H NMR signals are indicated on structure *5* in Scheme 1; *m/e* 564 (M), 485 (M−79), 472 (M−92), 458 (M−106), 427 (M−137), 406 (M−158), 460, (M−204), 347 (M−217), and 282. R_F = 0.33 on Schleicher & Schüll (S&S) 288 alumina paper developed with light petroleum.

(2R,2'R,6'S)-2,2'-Dimethyl-β,γ-carotene (6) was an isomerization product formed during the synthesis of *13;* yield *ca.* 5 mg. *6* had m.p. 156–158 °C after crystallization from MeOH–$CHCl_3$ solution. The electronic absorption and IR spectra could not be distinguished from those of β,γ-carotene.[10,11] The CD spectrum of *6* is reproduced in Fig. 1 and ^1H NMR signal assignments included in Scheme 1; *m/e* 564 (M), 485 (M−79), 472 (M−92), 458 (M−106), 427 (M−137), 413 (M−141), 406 (M−158), 460 (M−204), 347 (M−217) and 282. R_F = 0.40 on S&S 288 alumina paper developed with light petroleum.

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