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Bacterial Carotenoids. 51.* Chirality and Chiroptical Properties of (2*S*)-2-Isopentenyl-3,4-dehydrorhodopin (C.p. 482) and Related C_{45}-Carotenoids

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Dehydration of C.p. 482 (2-*iso*pentenyl-3,4-dehydrorhodopin; 2-(3-methyl-2-butenyl)-3,4-didehydro-1,2-dihydro-ψ,ψ-caroten-1-ol) with $POCl_3$ provided a *tert* chloride, a conjugated and a non-conjugated anhydro product in varying yields depending on reaction conditions.

Chiroptical properties of C.p. 482 and its trimethylsilyl ether were considered.

The 2*S*-chirality of C.p. 482 was demonstrated by chiroptical comparison of its non-conjugated anhydro derivative with the same (2*S*)-carotenoid, here prepared by total synthesis.

The dehydration to the non-conjugated anhydro derivative only slightly modified the CD curve but reduced $\Delta\varepsilon$ values significantly.

For further chiroptical studies (2′*S*)-2′-(3-methyl-2-butenyl)-1′,16′,3′,4′-tetradehydro-1′,2′-dihydro-β,ψ-carotene was synthesized. The 2′-*iso*pentenyl substituent had a similar influence on the Cotton effects of the monochiral monocyclic C_{45}-, the monochiral aliphatic C_{45}- and the homodichiral aliphatic C_{50}-carotenes considered.

The bacterial C_{45} carotenoid C.p. 482 from *Corynebacterium poinsettiae* has been assigned the aliphatic conjugated dodecaene structure *1*, Scheme 1, from spectroscopic and chemical evidence.[1,2] The chirality of the C_{50} conjugated tridecaene bisanhydrobacterioruberin (*2*), produced by the same bacterium, and containing two identical end groups A, Scheme 1, has been established as 2*S*,2′*S*.[3] While biogenetic considerations would favour the same chirality for C.p. 482 at C-2, the chirality has not yet been proven.

RESULTS AND DISCUSSION

The Cotton effect of C.p. 482 (*1*) was essentially unaltered upon silylation to the trimethylsilyl ether *3*, Fig. 1. The CD curves of *1* and *3* in the 250–350 nm region are similar to that [3,4] of (2*S*,2′*S*)-bisanhydrobacterioruberin (*2*) after allowing for a 10 nm hypsochromic displacement to compensate for chromophoric differences. This correlation suggested 2*S* chirality for C.p. 482. However, an unequivocal correlation must be based on chiroptical comparison of structurally identical compounds.

Dehydration of C.p. 482 (*1*) with $POCl_3$ in pyridine [5,6] provided the tertiary chloride *4*, the conjugated tridecaene *5* and the anhydro product *6* with terminal methylene, in varying yields, depending on reaction conditions, see Scheme 1.

Besides *1* and *4–6*, water soluble pigments, presumably phosphate esters, were always formed. The dehydrated products represented no more than 20 % yield, consistent with the low yields obtained in related dehydrations, particularly of 2′-substituted *tert.* caroten-1-ols.[3,7]

Chlorinated products have not previously been characterized upon dehydration of carotenols

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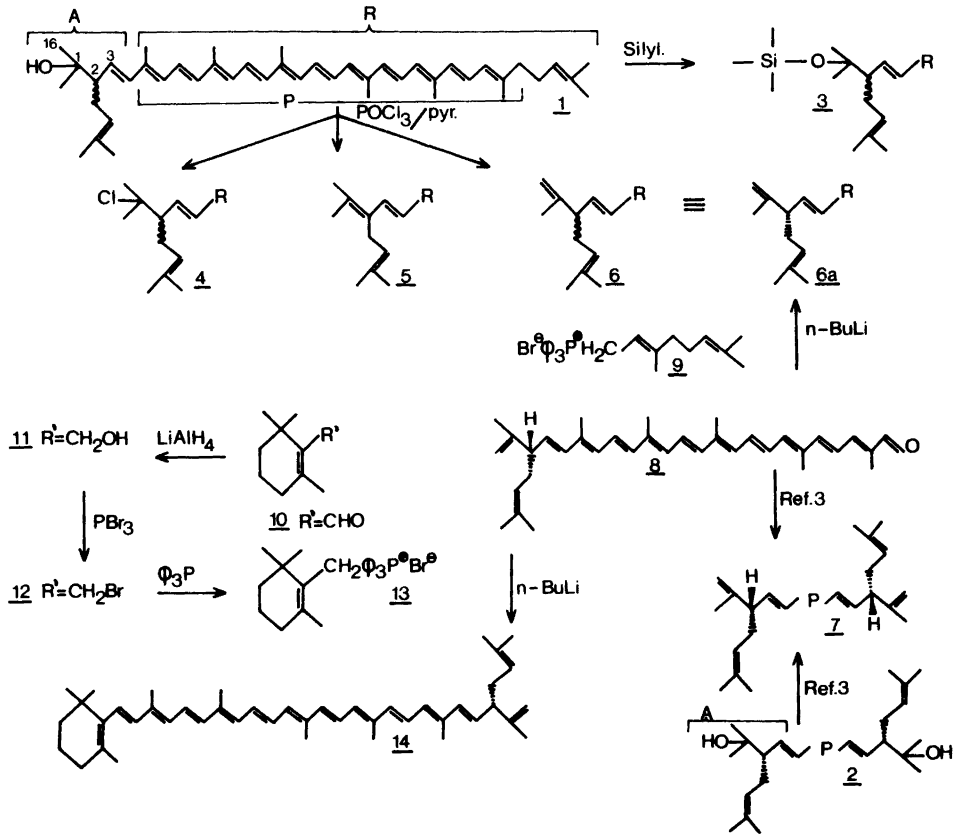

Scheme 1.

with $POCl_3$. Formation of the chloride *4* may be rationalized by an S_N1 mechanism via a *tert.* carbocation. The formation of the conjugated anhydro product *5*, obtained at the expense of *4* at 160 °C, may be rationalized by a competing E1 reaction from the same carbocation. The unconjugated anhydro product *6* must involve elimination of a proton from CH_3-16 or CH_3-18, sterically less hindered than H-2, by a concerted E2 type elimination or less likely an E1 reaction. Tetraanhydrobacterioruberin (*7*) with two end groups identical to that of *6* has previously been obtained by analogous dehydration of bacterioruberin and bisanhydrobacterioruberin (*2*).[3,7]

The chiral aldehydic synthon *8*, available from the previous synthesis of tetraanhydrobacterioruberin (*7*),[3] was condensed in a Wittig reaction with geranyltriphenylphosphonium bromide (*9*) to give the monochiral (2*S*)-C_{45}-carotene *6a* with the same CD properties as the semisynthetic anhydro product *6* from C.p. 482 (*1*), Fig. 2. This direct CD correlation unambiguously defines 2*S*-configuration for C.p. 482 (*1a*) as predicted from biogenetic considerations.

The shape of the CD curve of (2'*S*)-C.p. 482 (*1a*) was only slightly changed upon dehydration to the anhydro product *6a*, Figs. 1 and 2, consistent with previous results for bisanhydrobacterioruberin (*2*) and tetraanhydrobacterioruberin (*7*).[3] In further agreement with the CD results for *2* and *7*,[3] the $\Delta\varepsilon$ values for synthetic and semisynthetic anhydro C.p. 482 (*6a*) are significantly reduced upon dehydration of the *tert.* carotenol C.p. 482 (*1a*).

Synthon *8* was also used for the condensation with β-cyclogeranyltriphenyl phosphonium bromide (*13*),[8,9] prepared by a general sequence from β-cyclocitral (*10*) via β-cyclogeraniol (*11*)

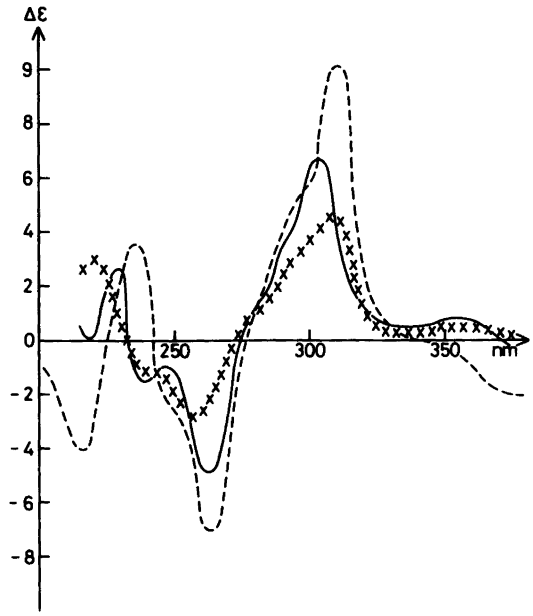

Fig. 1. CD spectra in EPA solution. ———, C.p. 482 (*1*); ×, C.p. 482 TMS ether (*3*); – – –, Bisanhydrobacterioruberin (*2*),[3] displaced hypsochromically 10 nm.

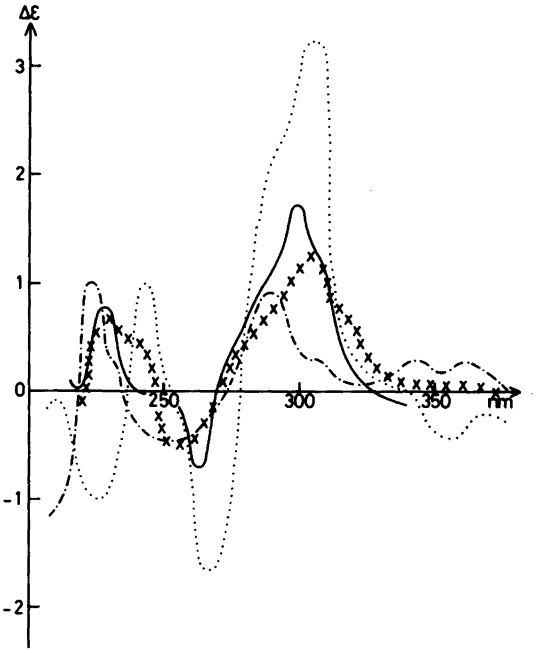

Fig. 2. CD spectra in EPA solution. ———, Synthetic anhydro-C.p. 482 (*6a*); ×, Semisynthetic anhydro C.p. 482 (*6*); –·–, Synthetic *14*; ···, Tetraanhydrobacterioruberin (*7*),[3] displaced hypsochromically 10 nm.

and its bromide *12*. The CD spectrum of the monocyclic C_{45}-carotene *14*, Fig. 2, resembled that of semisynthetic *6a* as well as that[3] of the dichiral (2*S*,2′*S*)-tetraanhydrobacterioruberin (*7*), 10 nm bathochromically displaced (for chromophoric correction). Thus, the 2′-*iso*pentenyl substituent has a similar effect on the CD spectra of the monochiral, monocyclic C_{45}-*14*, the monochiral aliphatic C_{45}-*6a* and the homodichiral aliphatic C_{50}-*7* carotenes considered.

The synthetic model C_{45}-carotene *14* has been useful for a chiroptical correlation with the monocyclic heterodichiral C_{50}-carotenoid C.p. 473[2,10] as treated elsewhere.[11]

EXPERIMENTAL

Biological material. Extracts of *Corynebacterium poinsettiae* from an earlier study[2] were the source of C.p. 482.

Materials and methods. These were as described elsewhere[12] when not specified. Visible spectra were recorded in acetone; ^{1}H NMR spectra in $CDCl_3$ at 100 MHz; CD spectra in EPA (ether–isopentane–ethanol, 5:5:2). General precautions for work with carotenoids were taken.

C.p. 482 (1, *2-(3-Methyl-2-butenyl)-3,4-didehydro-1,2-dihydro-ψ,ψ-caroten-1-ol*). *1* was isolated from extracts by TLC on Kieselgel 60 F_{254} plates developed with Me_2CO–hexane (20+80); R_F=0.47. Vis. λ_{max} nm 455, 482, 513; % III/II=67.[13] ^{1}H NMR δ 1.98 s (four in-chain methyls); 1.92 s (C-5 methyl); 1.82 s (C-5′ methyl); 1.68 s, 1.60 s (four isopropylidene methyls); 1.22 s, 1.18 s (two methyls attached to *tert.* hydroxyl); 5.10 (broad, C-2′ *H*); 5.06 (broad, olefinic H on isopentenyl substituent); 5.49 dd (H-3, $J_{3,2}$=8 Hz, $J_{3,4}$=14 Hz). MS *m/z* 620 (M^+, 100 %), M–18 (8 %), M–58 (10 %), M–92 (14 %), M–106 (57 %). CD Fig. 1.

C.p. 482 TMS ether (2). *2* was obtained in virtually quantitative yield from *1* by the standard silylation procedure.[14] R_f=0.91 on Kieselgel developed with Me_2CO-hexane (10+90). Vis λ_{max} nm 455, 482, 514; % III/II=71. MS *m/z* 692 (M^+, 100 %), M–90 (10 %), M–92 (10 %), M–106 (64 %). CD. Fig. 1.

Dehydration of C.p. 482 (1). General procedure: To *1* (0.1–0.2 mg) in dry pyridine (2 ml,

distilled over KOH and stored over molecular sieves) was added $POCl_3$ (distilled before use, 0.25 ml of a 20 % solution in pyridine). The mixture was heated in a sealed tube purged with nitrogen. The procedure was tested for 1,2,1′,2′-tetrahydro-ψ,ψ-carotene-1,1′-diol.

At 25 °C the dehydration of *1* was very slow and provided only traces of the desired product *6*. After 1–1.5 h at 60 °C the pigment recovery followed by the usual extractive isolation was 10 %. Products *4*, *5*, *6* and some starting *1* were isolated. Under conditions where the reaction temperature was raised to 160 °C over a period of 15 min and then quenched, only *5* and *6* were formed; pigment recovery *ca.* 20 %.

C.p. 482 chloride (4, 1-chloro-2-(3-methyl-2-butenyl)-3,4-didehydro-1,2-dihydro-ψ,ψ-carotene). *4* was isolated from the above dehydration. R_f=0.56 on Kieselgel plates developed with Me_2CO-hexane. Vis λ_{max} nm 455, 482, 515; % III/II=60. MS *m/z* (M^+, ^{37}Cl, 6 %), 638 (M^+, ^{35}Cl, 13 %), M−36 (100 %), M−142 (91 %).

Conjugated anhydro C.p. 482 (5, 2-(3-methyl-2-butenyl)-3,4-dehydro-ψ.ψ-carotene). *5* was isolated from the dehydration of *1*. R_f=0.46 Kieselgel plates (Me_2CO−hexane; 2+98). Vis λ_{max} nm 460, 490, 525.

Unconjugated anhydro C.p. 482 (6, 2-(3-methyl-2-butenyl)-1,16,3,4-tetradehydro-1,2-dihydro-ψ,ψ-carotene. The least polar dehydration product of *1* had R_f=0.60 on Kieselgel plates (Me_2CO-hexane; 2+98). Vis λ_{max} nm 455, 482, 504; % III/II=50. ^1H NMR δ 1,92 s (four in-chain methyls); 1.91 s (C-5 methyl); 1.83 s (C-5′ methyl); 1.69 s (three methyls; two from isopropylidene and one from C-1); 1.62 s (two methyls from isopropylidene); 4.78 s (terminal methylene at C-1); 5.1 (broad, two olefinic signals; one from C-2′ and the second from *iso*pentenyl substituent), 5.6 dd (H-3′, $J_{3,4}$=14 Hz, $J_{3,2}$=6 Hz). MS *m/z* 602 (M^+, 51 %), M−106 (100 %), M−175 (25 %).

Geranyltriphenylphosphonium bromide (9). Linalool (2.2 g, 0.014 m) and triphenylphosphonium bromide (3.4 g, 0.01 M) were refluxed in $CHCl_3$ (25 ml) for 4 h. Evaporation of solvent followed by trituration with Et_2O, then recrystallization from CH_2Cl_2−EtOAc gave *9*, 3.6 g (75 %). ^1H NMR δ 1.35 s, 1.31 s (C-3 methyl; *cis, trans*); 1.58 s, 1.50 s (non-equivalent *gem.* methyls); 1.67 m (CH_2-4); 1.96 m (CH_2-5), 4.70 dd (CH_2-1, $J_{H,P}$=14 Hz, $J_{H,H}$=7 Hz); 4.88 m (H-2), 5.10 m (H-6).

Synthetic anhydro C.p. 482 (6a, (2S)-2-(3-methyl-2-butenyl)-1,16,3,4-tetradehydro-1,2-dihydro-ψ,ψ-carotene). n-Butyl lithium was added dropwise to a slurry of *9* (0.25 g) in Et_2O (15 ml) until the deep red colour of the phosphorane was formed. The phosphorane was added in aliquots to the aldehyde *8* (1 mg in 10 ml Et_2O−CH_2Cl_2) and the reaction monitored by TLC. After 1 h, water was added, the crude product extracted into ether, dried over Na_2SO_4 and concentrated. Chromatography on Kieselgel (Me_2CO−hexane; 2+98) gave *6a* in 30 % yield. Vis λ_{max} nm 458, 483, 505; % III/II=28. ^1H NMR same as for *6*. MS *m/z* 602 (M^+, 52 %), M−69 (10 %), M−92 (10 %), M−106 (100 %), M−175 (25 %). CD Fig. 2.

β-Cyclogeranyltriphenylphosphonium bromide (13). β-Cyclocitral (*10*, 2 g) in Et_2O (25 ml) was reduced at 0 °C with $LiAlH_4$. The reaction was monitored by TLC and upon completion β-cyclogeraniol (*11*) was isolated by extraction with Et_2O. ^1H NMR (carotenoid numbering is used for all cyclogeraniol derivatives) of the semisolid showed δ 1.04 (C-1 *gem.* methyls); 1.75 (C-5 methyl) and 4.14 (s, CH_2OH). Conversion to the bromide *12* was effected at −30 °C with dropwise addition of 10 % excess PBr_3 (1.3 g in 10 ml pentane−Et_2O; 1+1) to *11* (2.0 g in 25 ml pentane−Et_2O; 1+1) over 1 h. The reaction was stirred an additional 2 h at −30 °C, then at room temp. overnight. Aqueous $NaHCO_3$ was added and after Et_2O extraction and concentration the bromide *12* showed ^1H NMR signals at δ 1.10 (two *gem.* methyls); 1.75 (C-5 methyl); 4.08 s ($-CH_2Br$).

β-Cyclogeranyl bromide (*12*, 2 g) and triphenylphosphine (2.41 g) in EtOAc (25 ml) were refluxed for 1 h. After cooling, the crude phosphonium salt *13* was filtered off and recrystallized from CH_2Cl_2−EtOAc; 0.86 g (22 %). ^1H NMR δ 0.78 (two *gem.* methyls); 1.05 d (C-5 methyl; *J*=4 Hz); 4.37 d ($J_{H,P}$=14 Hz).

Synthetic cyclic C_{45}-carotene (14, (2′S)-2′-(3-methyl-2-butenyl)-1′,16′,3′,4′-tetradehydro-β,ψ-carotene). *13* and *8* were converted to *14* in a manner analogous to the synthesis of *6a*. The purified product *14* had vis. λ_{max} nm 448, 473, 504; % III/II=40. ^1H NMR δ 1.98 s (four in-chain methyls); 1.70 s, 1.62 s (isopropylidene methyls); 1.69 s (C-1′ methyl); 1.72 s (C-5 methyl); 4.77 s (C-1′ methylene). MS *m/z* 602 (M^+, 65 %), M-69 (8 %), M−106 (100 %), M−106−69 (31 %). CD Fig. 2.

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