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

ARTHUR G. ANDREWES,** GUNNER BORCH and SYNNØVE LIAAEN-JENSEN

*Organic Chemistry Laboratories, Norwegian Institute of Technology, University of Trondheim, N-7034 Trondheim-NTH, Norway and **Chemistry Department A, Technical University of Denmark, DK-2800, Lyngby, Denmark

Dehydration of C.p. 482 (2-isopentenyl-3,4-dehydrorhodopin; 2-(3-methyl-2-butenyl)-3,4-didehydro-1,2-dihydro-\(\psi,\psi\)-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 2S-chirality of C.p. 482 was demonstrated by chiroptical comparison of its non-conjugated anhydro derivative with the same (2S)-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 (2'5')-2',2'-[(3-methyl-2-butenyl)-1',16',3',4'-tetrahydroxy-1',2'-dihydro-\(\psi\)-carotene was synthesized. The 2'-isopentenyl substituent had a similar influence on the Cotton effects of the monocyclic mononuclear \(C_{45}\), the monochiral aliphatic \(C_{45}\)- and the homodichiral aliphatic \(C_{50}\)-carotenones 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 2S,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 \(^4\) of (2S,2'S)-bisanhydrobacterioruberin (2) after allowing for a 10 nm hypsochromic displacement to compensate for chromophoric differences. This correlation suggested 2S 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.\(^7\)

Chlorinated products have not previously been characterized upon dehydration of carotenols.
with POCl₃. Formation of the chloride 4 may be rationalized by an S₉1 mechanism via a tert. carboxation. 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 carboxation. The unconjugated anhydro product 6 must involve elimination of a proton from CH₃-16 or CH₃-18, sterically less hindered than H-2, by a concerted E2 type elimination or less likely an E1 reaction. Tetraanhydrobacteriokerberin (7) with two end groups identical to that of 6 has previously been obtained by analogous dehydration of bacteriokerberin and bisanhydrobacteriokerberin (2).³,⁷

The chiral aldehyde synthon 8, available from the previous synthesis of tetraanhydrobacterioberin (7),³ was condensed in a Wittig reaction with geranyltriphenylphosphonium bromide (9) to give the monochiral (2S)-C₄₅-carotene 6a with the same CD properties as the semisynthetic anhydro product 6 from C.p. 482 (I), Fig. 2. This direct CD correlation unambiguously defines 2S-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 bisanhydrobacteriokerberin (2) and tetraanhydrobacteriokerberin (7).³ In further agreement with the CD results for 2 and 7,³ the Δe 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 prepared by a general sequence from β-cycloctital (10) via β-cyclogeraniol (11).
Fig. 1. CD spectra in EPA solution. ———, C.p. 482 (1); ×, C.p. 482 TMS ether (3); ---, Bisanhydrobacterioruberin (2), 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 of the dichiral (2S,2'S)-tetraanhydrobacterioruberin (7), 10 nm bathochromically displaced (for chromophoric correction). Thus, the 2'-isopentenyl substituent has a similar effect on the CD spectra of the monocyclic, monocyclic C_{45}-14, the monocyclic aliphatic C_{45}-6a and the homodichiral aliphatic C_{59}-7 carotenes considered.

The synthetic model C_{45}-carotene 14 has been useful for a chiroptical correlation with the monocyclic heterodichiral C_{59}-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; ^1H NMR spectra in CDCl$_3$ at 100 MHz; CD spectra in EPA (ether-isopentane-ethanol, 5:5:2).


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

General precautions for work with carotenoids were taken.

C.p. 482 (1, 2-(3-Methyl-2-butenyl)-3,4-didehydrosso-1,2-dihydro-\(\gamma\)-\(\gamma\)-caroten-1-ol). 1 was isolated from extracts by TLC on Kieselgel 60 F$_{254}$ plates developed with Me$_2$CO–hexane (20+80); $R_f$=0.47. Vis. $\lambda_{\text{max}}$ nm 455, 482, 513; % III/II=67.13. $^1$H NMR $\delta$ 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 isopropylidine 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$_2$CO–hexane (10+90). Vis $\lambda_{\text{max}}$ 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 POCl₃ (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-β,γ-carotene-1,1'-diol.

At 25 °C the dehydration of I 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 I 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-β,γ-carotene). 4 was isolated from the above dehydrochlorination. R₅=0.56 on Kieselgel plates developed with Me₆CO-hexane. Vis λₘₚax nm 455, 482, 515; % III/II=60. MS m/z (M⁺, 37Cl, 13 %), 638 (M⁺, 0.7 %), M–36 (100 %), M–142 (91 %).

Conjugated anhydro C.p. 482 (5, 2-(3-methyl-2-butenyl)-3,4-dehydro-β,γ-carotene). 5 was isolated from the dehydrochlorination of 4. R₅=0.46 Kieselgel plates (Me₂CO-hexane; 2+98). Vis λₘₚax nm 460, 490, 515.

Unconjugated anhydro C.p. 482 (6, 2-(3-methyl-2-butenyl)-1,6,3,4-tetrahydro-1,2-dihydro-β,γ-carotene). The least polar dehydrochlorination product of 4 had R₅=0.60 on Kieselgel plates (Me₂CO-hexane; 2+98). Vis λₘₚax 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); 1.78 s (terminal methylene at C-1); 5.1 (broad, two olefinic signals; one from C-2' and the second from isopentenyl substituent). 5.6 dd (H-3', J₄,₅=14 Hz, J₃,₂=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 tripheylphosphonium bromide (3.4 g, 0.01 M) were refluxed in CHCl₃ (25 ml) for 4 h. Evaporation of solvent followed by trituration with Et₂O, then recrystallization from CH₂Cl₂-Et₂O gave 9. 3.6 g (75 %). 1H NMR δ 1.35 s, 1.31 s (C-3 methyl; cis, trans); 1.58 s, 1.5 s (non-equivalent gem. methyls). 1.67 m (CH₂=CH₂); 1.96 m (CH₂=CH₂), 4.70 dd (CH₂=CH₂, JHH=14 Hz, J₃,₂=7 Hz); 4.88 m (H-2), 5.10 m (H-6).

Synthetic anhydro C.p. 482 (6a, 2S)-2-(3-methyl-2-butenyl)-1,6,3,4-tetrahydro-1,2-dihydro-β,γ-carotene). n-Butyl lithium was added dropwise to a slurry of 9 (0.25 g) in Et₂O (15 ml) until the deep red colour of the phosphoran was formed. The phosphoran was added in aliquots to the aldehyde 8 (1 mg in 10 ml Et₂O-CH₂Cl₂) and the reaction monitored by TLC. After 1 h, water was added, the crude product extracted into ether, dried over Na₂SO₄ and concentrated. Chromatography on Kieselgel (Me₂CO–hexane; 2+98) gave 6a in 30 % yield. Vis λₘₚax 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-Cyclogeranyltriphenyolphosphonium bromide (13). β-Cycloctiron (10, 2 g) in Et₂O (25 ml) was reduced at 0 °C with LiAlH₄. The reaction was monitored by TLC and upon completion β-cyclogeranone (11) was isolated by extraction with Et₂O. 1H NMR (carotenoid numbering is used for all cyclogeranone derivatives) of the semisolid showed δ 1.04 (C-1 gem. methyls); 1.75 (C-5 methyl) and 4.14 (s, CH₃OH). Conversion to the bromide 12 was effected at –30 °C with dropwise addition of 10 % excess PbBr₃ (1.3 g in 10 ml pentane-Et₂O; 1:1) to 11 (2.0 g in 25 ml pentane-Et₂O; 1:1) over 1 h. The reaction was stirred an additional 2 h at –30°C, then at room temp. overnight. Aqueous NaHCO₃ was added and after Et₂O 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 (–CH₂Br).

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 CH₂Cl₂–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 (JHH=14 Hz).

Synthetic cyclic C₄₀-carotene (14, (2'S)-2-(3-methyl-2-butenyl)-1,16',3',4'-tetrahydro-β,γ-carotene). 13 and 8 were converted to 14 in a manner analogous to the synthesis of 6a. The purified product 14 had vis. λₘₚax 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.

Acknowledgements. We thank Dr. H. Mayer, Hoffmann-La Roche, Basel, for a sample of β-cycloctiron and for the detailed procedure for the phosphonium salt formation from β-cyclogeranyl bromide. AGA was supported by a grant from Hoffmann-La Roche and held a Fulbright fellowship.

REFERENCES


Received March 12, 1984.