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C_{50}-Carotenoids. 18.* Syntheses and Chirality of Aliphatic C_{50}-Carotenoids

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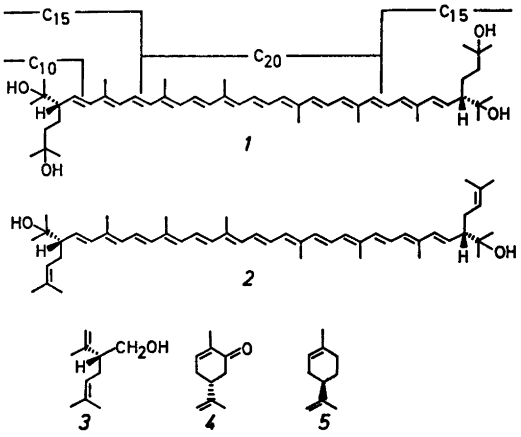
Details regarding the total syntheses of (2*R*,2′*R*)-tetradesoxybacterioruberin (*13*) and (2*S*,2′*S*)-tetraanhydrobacterioruberin (*18*) from (−)-lavandulol (*3*) are given.

A low yield synthesis of optically inactive bacterioruberin (*1a*) is reported.

The formation of octanor by-products in the final Wittig condensation to C_{50}-carotenoids with crocetindial (*12*), ascribed to the elimination of toluene, is rationalized on a mechanistic basis.

Chiroptical correlation of tetraanhydrobacterioruberin (*18*), obtained by dehydration of natural bacterioruberin (*1*) and of natural bisanhydrobacterioruberin (*2*), with synthetic *18*, proved the 2*S*,2′*S*-configuration for *1* and *2*. Synthetic (2*R*,2′*R*)-tetradeoxybacterioruberin (*13*) was not a valid CD-model.



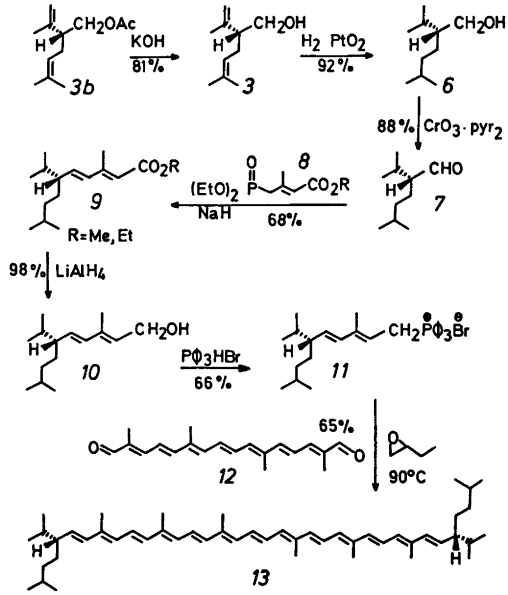
Scheme 1.

Total syntheses of aliphatic C_{50}-carotenoids and chiroptical correlations revealing the absolute configuration of bacterioruberin (*1*) and of bisanhydrobacterioruberin (*2*), Scheme 1, have been reported in a priority note.[1] Further details [2] are now published.

RESULTS AND DISCUSSION

Total syntheses

These are based on racemic [3] or (−)-(*R*)-lavandulol (*3*),[4,5] an irregular monoterpene, as the key synthon, using a $(C_{10}+C_5)+C_{20}+$



Scheme 2.

* No. 17. See Ref. 1.

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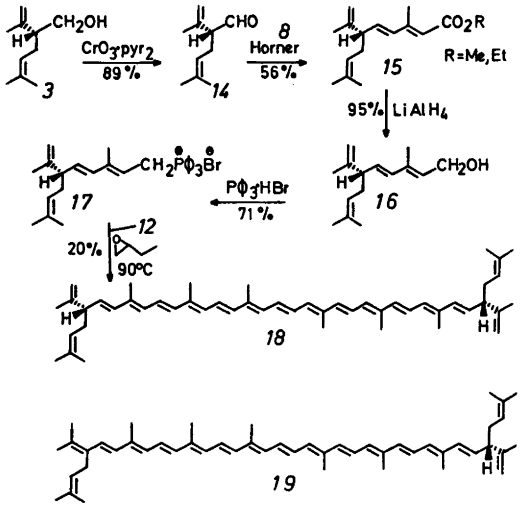
($C_{10}+C_5$) approach. Unsuccessful attempts using a $C_{10}+C_{30}+C_{10}$ approach involving (−)-carvone (*4*) or (+)-limonene (*5*) as chiral synthons are described elsewhere.[2]

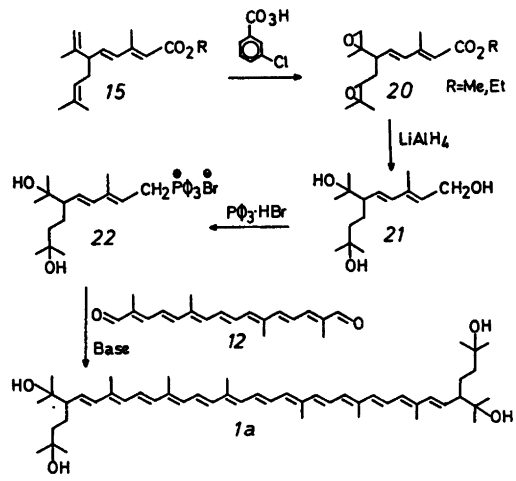
(2R,2'R)-Tetradeoxybacterioruberin (*13*). The route outlined in Scheme 2 with minor modifications was first tested with racemic lavandulol.[2] Since it had been experienced that the lavandulyl moiety could suffer double bond migration with racemization and cyclization [2] this route *via* tetrahydrolavandulol (*6*) was aimed at optically active tetradeoxybacterioruberin (*13*). Oxidation of *6* at essentially neutral conditions [6] provided optically active tetrahydrolavandulal (*7*). The olefination to the C_{15}-ester *9* with the phosphonate *8* proved sufficiently efficient to outrun racemization of 7 through enolization. The C_{15}-ester *9* was converted *via* the corresponding allylic alcohol *10* to the phosphonium salt *11* and subsequently condensed with crocetindial (*12*) in a Wittig reaction, using 1,2-butylene oxide as proton acceptor, to the target compound (*13*).



Scheme 3.

(2S,2'S)-Tetraanhydrobacterioruberin (*18*) was obtained by an analogous route, Scheme 3. The route was first tested with (±)-lavandulol, providing optically inactive tetraanhydrobacterioruberin.[2] After the final Wittig reaction to the chiral product *18* a tetradecaene by-product *19* was also isolated. Judged by ^{1}H NMR and GC analysis of lavandulal (*14*) no isomerization of the terminal double bond of *3* into conjugation had occurred during the oxidation, but UV-data for the ester *15* suggested that such partial isomerization had occurred during the subsequent Horner reaction. The unsaturated intermediates *15* and *16* (as well as *9* and *10* Scheme 1) were obtained as *cis-trans* mixtures. Separation of *cis-trans* isomers was not effected at the C_{15}-level, but postponed until the C_{50}-stage. Pure all-*trans* *18* was obtained after chromatography (Al_2O_3) and crystallization.

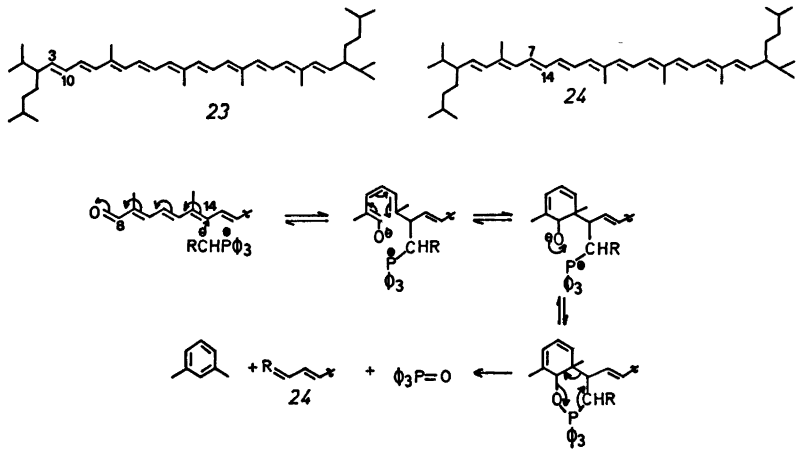
Optically inactive bacterioruberin (1a). Several approaches were attempted.[2] Bacterioruberin (*1a*) was obtained in low yield by the route outlined in Scheme 4. Regioselective epoxida-



Scheme 4.

tion of the C_{15}-ester *15* with *m*-chloroperbenzoic acid gave the diepoxide *20* as a mixture of stereoisomers. Critical steps were the subsequent reduction and phosphonium salt formation. Thus bacterioruberin (*1a*) was obtained in the final step together with considerable amounts of less polar products whose visible and mass spectra were compatible with anhydro- and epoxy derivatives of *1a*. Acidic conditions should be avoided in further attempts to synthesize bacterioruberin, *e.g.* by employing a sulfone reaction [7] for the $C_{15}+C_{20}+C_{15}$ step.

Norcarotenoid by-products. In the final Wittig reactions to (2*S*,2'*S*)-tetradeoxybacterioruberin



Scheme 5.

(*13*, Scheme 2) and (2*R*,2′*R*)-tetraanhydrobacterioruberin (*18*, Scheme 3), as well as to the corresponding optically inactive C_{50}-carotenoids,[2] a yellow by-product representing *ca.* 5 % of the product mixture, was obtained in each case. The electronic spectra, revealing an aliphatic decaene chromophore, and the mass spectra were consistent with octanor derivatives with carbon skeletons as for *23* and *24*, Scheme 5, whose formation could be rationalized in terms of a formal loss of xylene from the corresponding C_{50}-carotenoids. Pyrolysis of carotenoids is known to yield toluene, xylene and dimethylnaphthalene.[8,9] Corresponding reactions also occur in the mass spectrometer as a combination of electron impact and thermally induced rearrangements.[10] Thermal degradation of the C_{50}-carotenoid during the Wittig reaction leading to its formation was disfavoured by separate experiments with optically inactive tetradeoxybacterioruberin (*13a*). An alternative process involving xylene expulsion during the Wittig reaction, Scheme 5, allows for the formation of products of skeletal type *24* only and rationalizes the lack of heptanorcarotenoids formally derived by the expulsion of toluene from the preformed C_{50}-carotenoid expected in a thermal degradation. Side-reactions of this type during Wittig condensations appear not to have been reported.

Comparative study of natural and synthetic carotenoids. Isolation and derivatization

Natural bisanhydrobacterioruberin *ex Corynebacterium poinsettiae* [11] was available. Bacterioruberin was isolated from *Halobacterium salinarium*.[11] Synthetic optically inactive bacterioruberin had electronic, ^{1}H NMR and mass spectral properties consistent with those of natural bacterioruberin and could not be separated from the latter.

Natural bisanhydrobacterioruberin and bacterioruberin were both dehydrated with phosphorus oxychloride in pyridine [12] to give optically active tetraanhydrobacterioruberin.

Chiroptical correlations. Tetraanhydrobacterioruberin prepared above was identical in all respects including CD properties (Fig. 1) with synthetic (2*S*,2′*S*)-tetraanhydrobacterioruberin (*18*). The chirality of natural bisanhydrobacterioruberin (*2*) and of bacterioruberin (*1*) was consequently proved to be the same as for *18*.

The previously reported CD spectra of natural bacterioruberin (*1*) and bisanhydrobacterioruberin (*2*)[13] correspond to that of their tetraanhydro derivative *18*. However, the synthetic model (2*R*,2′*R*)-tetradeoxybacterioruberin (*13*) with the same chirality as *18* exhibited the opposite Cotton effect (Fig. 2), thus demonstrating that *13* was not a valid model for CD correlation with *18*, *2* and *1*. In this respect it is interesting to note that

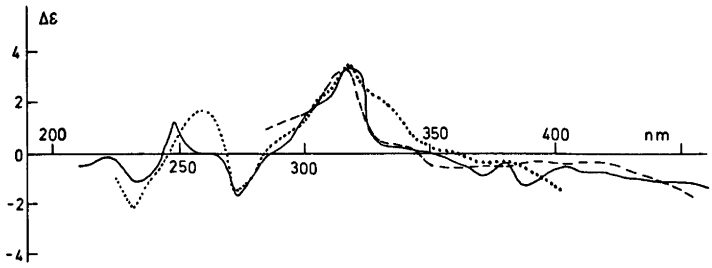


Fig. 1. CD spectra in EPA solution of (2*S*,2′*S*)-tetraanhydrobacterioruberin (*18*): —— synthetic, - - - *ex* natural bisanhydrobacterioruberin (*2*) and · · · *ex* natural bacterioruberin (*1*).

while (−)-(*R*)-lavandulol (*3*) had $[\alpha]_D^{16} = -10.20$, its tetrahydro derivative *6* had $[\alpha]_D^{16} = +12.84$.[4]

CONCLUSION

(2*R*,2′*R*)-Tetradeoxybacterioruberin (*13*) and (2*S*,2′*S*)-tetraanhydrobacterioruberin (*18*) are the first optically active C_{50}-carotenoids prepared synthetically. The preparation of optically inactive bacterioruberin (*1b*)[2] represented the first total synthesis of a naturally occurring C_{50}-carotenoid. Optically inactive decaprenoxanthin with wrong relative stereochemistry has now been synthesized.[14]

The results demonstrate that aliphatic C_{50}-carotenoids (*1* and *2*) have the same chirality at C-2,2′ as the bicyclic carotenoids with ε-,[15,16] β-[17] and λ-[18,19] end groups, thus indicating a common biosynthetic pathway for the presumed isopentenylation of C_{50}-carotenoids.

EXPERIMENTAL

Materials and methods. Lavender oil was provided by Givaudan, Dübendorf, Switzerland. Analytical grade solvents and chemicals were generally used. Technical grade acetone and hexane were distilled before use while technical grade ether was passed through alumina activity grade 1 [20] to remove peroxides. Spectroscopic grade solvents were used for crystallizations and spectroscopy. Merck silica gel was used for column and thin layer chromatography.

Melting points were determined on an Electrothermal melting point apparatus and are uncorrected. Gas liquid chromatography was carried out on a Perkin Elmer F11 instrument with flame ionization detector. Electronic spectra were recorded on a Coleman Hitachi 124 spectrometer, CD spectra on a Rousell-Jouan dicrographe in EPA (ether − isopentane − ethanol 5:5:2) solution, ^{1}H NMR spectra on a Jeol JNM-FX (100 MHz) pulsed Fourier transform instrument, and mass spectra on an AEI 902 instrument with a direct inlet system. Optical rotations were measured on a Zeiss model 31759 polarimeter.

General precautions for work with carotenoids [21] were taken. Further experimental details are available.[2]

Synthesis of (2*R*,2′*R*)-tetradeoxybacterioruberin (*13*)

(−)-(*R*)-*Lavandulyl acetate* (3b) was isolated from lavender oil by a modification [2] of previous procedures.[4,22] The lavender oil (500 g) was saponified in 5 % KOH and the crude product acetylated. Fractionation on a Widmer column, monitored by GC (carbowax column, 105 °C) and ^{1}H NMR, gave the *3b*-enriched fraction (49 g) at 84 − 105 °C/8.5 Torr. Further chromatography on a silica gel column, followed by fractionation through a Widmer column gave *3b* (2.8 g; *ca* 90 % pure; main impurity bornyl acetate) judged by IR, ^{1}H NMR and MS;[2] $[\alpha]_D^{24.5} = -7.82°$.

(−)-(*R*)-*Lavandulol* (*3*). *3b* (4.0 g) upon saponification in 5 % KOH, followed by extractive isolation and distillation gave *3* (2.7 g), b.p. 85 − 90 °C/0.4 Torr; ν_{max} (liq.) 3350 (s), 3075 (w), 2970, 2925 (s), 1644, 1446, 1377 (m), 1111 (w), 1039 (m), 891 (s) and 838 (w) cm^{-1}; δ ($CDCl_3$) 0.86 (imp.), 1.62 s and 1.71 m (3 + 6H; 3 × CH_3), 1.9 − 2.5 (4H; OH, CH and CH_2), 3.52 d (2H, J = 6 Hz; CH_2O), 4.75 − 4.95 (2H; = CH_2) and 5.08 (1H; = CH); *m/e* (70 °C) 154 (M, 5.0 %), 136 (M − 18, 3.7 %), 123 (M − 31, 14 %), 111 (M − 43, 22 %) and 69 (100 %); $[\alpha]_D^{24.5} = -5.96°$; purity 91 % as estimated from reported specific rotations: $[\alpha]_D^{16} = -10.20$ for *3* [4] and $[\alpha]_D^{20} = +37.7$ for *d*-borneol.[23]

(+)-(R)-*Tetrahydrolavandulol* (*6*). *3* (2.7 g) in acetic acid was hydrogenated in the presence of platinum oxide; yield *6* (2.5 g, 92 %); ν_{max} (liq.) 3340, 2955, 2930, 2870 (s),

1468, 1386, 1368 and 1054 cm^{-1}; δ ($CDCl_3$) 0.90 d (12H, $J=6$ Hz; CH_3), 1.2–2.1 (7H; CH, CH_2), 3.09 s (1H; OH) and 3.55 d (2H, $J=5$ Hz; CH_2O); *m/e* (70 °C) 140 (M–18, 29 %) and 57 (100 %), $[\alpha]_D^{26}=+17.90°$; reported $[\alpha]_D^{20}=+12.84°$.[4]

(–)-(R)-Tetrahydrolavandulal (7). *6* (1.0 g) in dry methylene chloride was oxidized with chromium trioxide–pyridine.[6] Chromium trioxide (3.8 g) was added to a stirred solution of dry pyridine (6.2 ml) in dry ethanol-free dichloromethane (95 ml) in a flask provided with a drying tube. After 15 min stirring, *6* (1.0 g) was added in one portion. Stirring was continued for 15 min, the solution decanted and the residue washed with ether (125 ml). The combined organic extracts were stirred for 5 min and precipitated inorganic material removed by filtration through celite. The organic extract was washed extensively with water, dried and the solvent evaporated; yield crude *7* (0.87 g; 88 %); ν_{max} (KBr) 2960, 2870 (s), 2700 (w), 1726 (s), 1471 (m), 1386 and 1369 (w); δ ($CDCl_3$) 0.82–1.00 ($4\times CH_3$), 1.1–2.2 (CH and CH_2) and 9.46 d ($J=2.7$ Hz, CHO); $[\alpha]_D^{25}=-9.46°$.

Methyl and ethyl (6R)-3,9-dimethyl-6-(1-methylethyl)-2,4-decadienoate (9). Diethyl 3-carbomethoxy-2-methylprop-2-enylphosphonate (*8*, 3.0 g) was added dropwise to a stirred suspension of sodium hydride (0.62) in dry ether (5 ml). After 1 h *6* (0.75 g) in dry ether (10 ml) was added dropwise and allowed to react for 1 h. TLC (silica gel PF_{254}) gave *9* (0.85 g, 68 %) as a 7:3 mixture of methyl and ethyl esters, ν_{max} (ethanol) 267 nm ($\varepsilon=21\,200$); ν_{max} (liq.) 2955, 2930, 2870, 1718 (s), 1634, 1612, 1467, 1368, 1240 (m), 1157 (s), 1053, 984, 971 and 922 (w) cm^{-1}; δ ($CDCl_3$) 0.85 d ($J=5$ Hz; $4\times CH_3$), 1.26 t ($J=7$ Hz, OCH_2CH_3), 2.00 and 2.92 s (in-chain CH_3, *cis+trans*?), 3.69 s (OCH_3), 4.16 q ($J=7$ Hz; OCH_2CH_3) and 5.4–7.7 (olefinic H, complex); *m/e* (70 °C) 266 (M, ethyl ester, 2.1 %), 252 (M, methyl ester, 19 %), 123 (100 %); $[\alpha]_D^{26.5}=-20.00°$.

(6R)-3,9-Dimethyl-6-(1-methylethyl)-2,4-decadienol (10). *9* (0.79 g) was reduced with $LiAlH_4$ in dry ether; yield crude *10* (0.76 g, 98 %); λ_{max} (methanol) 238 nm ($\varepsilon=24\,300$); ν_{max} (KBr) 3330, 2955, 2930, 2870 (s), 1468, 1386, 1368 (m), 1086 (w), 1002 and 968 (m) cm^{-1}; δ ($CDCl_3$) 0.78–0.90 ($4\times CH_3$), 1.1–1.8 (CH, CH_2), 1.76 s and 1.84 s (allylic CH_3, *cis+trans*?), 2.66 s (OH), 4.23 d ($J=7$ Hz; CH_2OH) and 5.2–6.5 (olefinic H); *m/e* (70 °C) 224 (M, 51 %), 206 (M–18, 12 %), 181 (M–42, 31 %) and 69 (100 %); $[\alpha]_D^{24.5}=-13.56°$.

(6R)-3,9-Dimethyl-6-(1-methylethyl)-2,4-decadienyltriphenylphosphonium bromide (11). *10* (0.62 g) was reacted with triphenylphosphonium bromide (0.90 g) in methylene chloride by standard procedure; yield crude *11* (1.03 g, 66 %); δ ($CDCl_3$) 4.82 s and 0.94 s ($4\times CH_3$) 1.1–2.35 (CH, CH_2 and allylic CH_3), 4.72 dd ($J_{H-P}=16$ Hz, $J_{1-2}=7$ Hz; CH_2P), 5.1–6.2 (olefinic H) and 7.6–8.1 (aromatic H).

(2R,2'R)-Tetradeoxybacterioruberin (13) was prepared from crocetindial (*12*, 20 mg) and *11* (230 mg) by treatment with 1,2-butylene oxide (3 ml) in chloroform (3 ml) at 90 °C for 3 h in a sealed tube; yield *13* (29.7 mg, 65 %). Crystallization from acetone-hexane gave all-*trans* *13* (8.4 mg); m.p. 118–124 °C after recrystallization m.p. 124–133 °C; λ_{max} (hexane) 245, 275, 307, 319, (370), 387, 464, 493 ($E_{1\%,\,1cm}=2890$) and 527 nm; ν_{max} (KBr) 3030 (w), 2955,

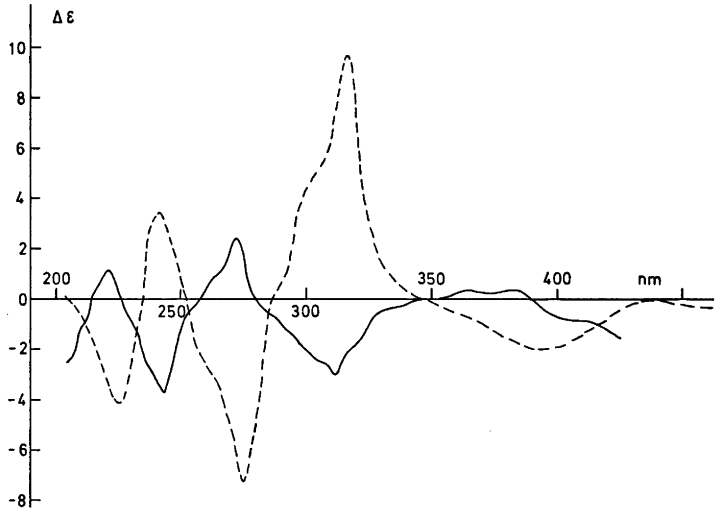


Fig. 2. CD spectra in EPA solution of – – – natural (2*S*,2'*S*)-bisanhydrobacterioruberin (*2*) and —— synthetic (2*R*,2'*R*)-tetradeoxybacterioruberin (*13*).

2925, 2865 (s), 1544, 1469, 1384, 1368 (m), 1038, 1003 (w), 964 (s), 835 and 824 (w) cm^{-1}; δ ($CDCl_3$) 0.87 d (18H, $J=5$ Hz; *gem.* dimethyl), 1.93 s (6H; $CH_3-18,18'$), 1.98 s (12H; $CH_3-19,20,19',20'$), 1.1–2.3 (14H; CH_2, CH) and 5.2–7.0 (20H; olefinic); *m/e* (220 °C) 676 (M, 100 %), 661 (M–15, 0.6 %), 633 (M–43, 0.9 %), 584 (M–92, 5.4 %), 570 (M–106 96 %) and 518 (M–158, 7.5 %); $\Delta\varepsilon$ (EPA) Fig. 2.

Stability tests: 13 (5.8 mg) in 1,2-butylene oxide (1 ml) and chloroform (1 ml) were heated to 90 °C in a sealed tube for 3 h; recovery of *18* 5.2 mg (90 %) after TLC. Only a trace of an impure decaene could be detected.

Recovered *13* (5.2 mg), geranyltriphenylphosphonium bromide (100 mg) and 1.2-butylene oxide (1 ml) in chloroform (1 ml) were kept at 90 °C for 6 h; recovery of *18* was 1.7 mg (33 %) after TLC. No decaene products were formed.

(2R,2'R)-8,9,10,11,12,13,19,20-Octanortetradeoxybacterioruberin (20) (or the corresponding 3,4,6,7,8,18,19-octanor compound *19*), obtained as a by-product during the synthesis of *13*, was less polar than *13*, had λ_{max} (hexane 278, 329, 343, 424, *449* and 480 nm; *m/e* (190 °C) 570 (M, 100 %), 427 (M–43, 1.5 %), 478 (M–92, 3.3 %) and 464 (M–106, 2.5 %); $\Delta\varepsilon$ (EPA) 217 (0), 241 (+2.5), 278 (–2.0), 327 (+1.1), 333 (+0.9), 343 (+1.2), 400 (–2.0) and 490 (–1.0) nm.

Synthesis of (2*S*,2'*S*)-tetraanhydrobacterioruberin (*19*)

(–)-(R)-Lavandulal (14) was prepared from (–)-(*R*)-lavandulol (*3*) by the same procedure as *7* above; yield *14* (0.88 g, 89 %); ν_{max} (liq.) 3080 (w), 2975, 2915 (m), 2720 (w), 1726 (s), 1777, 1746, 1442, 1379 and 900 (m) cm^{-1}; δ ($CDCl_3$) 1.62–1.69 ($3\times CH_3$), 1.9–3.1 (CH, CH_2), 4.7–5.2 ($=CH_2$, $=CH$) and 9.49 d ($J=2$Hz; CHO); *m/e* (70 °C) 152 (M, 9.3 %), 123 (M–29, 14 %) and 69 (100 %), $\Delta\varepsilon$ (EPA) 205 (–0.2), 217 (+0.1), 304 (–1.5), 345 (0) nm;[1] $[\alpha]_D^{19} = -114.20°$, reported $[\alpha]_D = -132.10°$.[22]

Methyl and ethyl (6S)-3,9-dimethyl-6-(1-methylethyl)-2,4,8-decatrienoate (15) was prepared from *14* (0.85 g) as described for *9* above; yield *15* (0.79 g, 56 %); λ_{max} (methanol) 268 ($\varepsilon=18\,200$) and 319 ($\varepsilon=71\,000$) nm; ν_{max} (liq.) 2970, 2920 (m), 1714 (s), 1634, 1604, 1436, 1369, 1242 (m), 1156 (s) and 893 (m) cm^{-1}; δ ($CDCl_3$) 1.27 t ($J=7$ Hz; OCH_2CH_3), 1.61 s and 1.70 s ($3\times CH_3$), 1.98 and 2.27 (2-CH_3, 2-*cis* and 2-*trans*), 3.58 s (OCH_3), 4.15 q ($J=7$ Hz; OCH_2CH_3), 4.7–4.9 ($=CH_2$), 5.08 m ($(CH_3)_2C=CH$) and 5.45–7.8 (olefinic H); $[\alpha]_D^{18} = +5.74°$.

(6S)-3,9-Dimethyl-6-(1-methylethenyl)-2,4,8-decatrienol (16). 15 (0.77 g) was reduced with $LiAlH_4$ in ether. Column chromatography gave *trans-16* (0.27 g, 40 %); λ_{max} (methanol) 240 ($\varepsilon=16\,500$) and 282 ($\varepsilon=1770$) nm; λ_{max} (liq.) 3310, 2970, 2925 (s), 2820, 1645, 1440, 1379, 1016, 963 and 890 (m) cm^{-1}; δ ($CDCl_3$) 1.62 s, 1.68 s and 1.83 s ($4\times CH_3$), 2.0–3.0 (CH, CH_2), 4.24 ($J=7$ Hz, CH_2OH), 4.75–4.85 ($=CH_2$), 5.07 m ($(CH_3)_2C=CH$) and 5.45–6.7 (olefinic H); *m/e* (70 °C) 220 (M, 22 %), 202 (M–18, 0.9 %), 151 (M–69, 26 %) and 69 (100 %); $\Delta\varepsilon$ (EPA) 205 (+2.8), 220 (–1.0), 230 (–1.2) and 250 (0) nm. A *cis* isomer of *16* was also characterized.[2]

(6S)-3,9-Dimethyl-6-isopropenyl-2,4,8-decatrienyltriphenylphosphonium bromide (17). 16 (0.23 g) was reacted with triphenylphosphonium bromide (0.35 g) in methylene chloride affording crude *17* (0.43 g, 71 %); δ ($CDCl_3$) 1.5–1.85 ($4\times CH_3$), 2.0–3.0 (CH, CH_2), 4.5–6.5 (olefinic H) and 7.5–8.1 (aromatic H).

(2S,2'S)-Tetraanhydrobacterioruberin (18). Sodium ethoxide (0.94 N, 0.05 ml) was added to a solution of *17* (230 mg) in dry ethanol (1.5 ml) and stirred for 1 min. Crocetindial (*12*, 20 mg) in methylene chloride (5 ml) was added and stirring continued for 2.5 h. More phosphorane, generated externally from *17* (130 mg) in dry ethanol (1.0 ml) and sodium ethoxide (0.094 N, 0.025 ml) was added and stirring continued for 1 h. The reaction mixture was diluted with ether and water, and the pigments extracted with ether. TLC on SiO_2 (1 % acetone in hexane) followed by chromatography on Al_2O_3 activity grade III (1 % ether in hexane) provided *18* (60 mg). Crystallization from acetone-hexane gave all-*trans 18* (1.0 mg); m.p. 108–112 °C; λ_{max} (hexane) 306, 318, (370), 387, 464, 493 ($E_{1\%,1cm}=2500$) and 527 nm; ν_{max} (KBr) 3030 (w), 2970 (m), 2915 (s), 2855, 1644 (m), 1543 (w), 1438, 1376 (m), 1002 (w), 962 (s) and 820 (w) cm^{-1}; δ ($CDCl_3$) 1.26 (imp.), 1.61 and 1.69 (*gem.* dimethyl and $CH_3-16,16'$, 1.80 ($CH_3-18,18'$), 1.98 ($CH_3-19,20,19',20'$), *ca* 4.75 ($=CH_2$), 5.05 ($(CH_3)_2C=CH$) and 5.4–7.0 olefinic H); *m/e* (220 °C) 668 (M, 11 %), 599 (M–69, 1.4 %), 576 (M–92, 0.6 %), 562 (M–106, 48 %), 510 (M–158, 0.5 %), 493 (M–175, 5.5 %) and 69 (100 %); $\Delta\varepsilon$ (EPA) Fig. 1.

(2'S)-Δ-1-Tetraanhydrobacterioruberin (19), more polar than *18*, was isolated as a by-product, yield crude *19 ca* 5 mg; ν_{max} (ether) (383), 400, 473, *501* and 536 nm; *m/e* (220 °C) 668 (M, 15 %), 599 (M–69, 1.1 %), 576 (M–92, 0.8 %), 562 (M–106, 47 %), 510 (M–158, 0.7 %), 493 (M–175, 1.4 %), 91 (100 %) and 69 (88 %).

Synthesis of bacterioruberin (*1b*)

(±)-Methyl and ethyl-6-(1-methyl-epoxyethyl)-8,9-epoxy-3,9-dimethyldeca-2,4-dienoate (16). 15 (0.5 g) was reacted with *m*-chloroperbenzoic acid (1.12 g) in $CHCl_3$ (22 ml) at 0 °C for 3 h. Crude *16* (0.55 g, 98 %) had λ_{max} (methanol)

266 nm (ε = 12 500); ν_{max} (liq.) 3430, 2975, 1712 (s), 1637, 1613, 1440, 1381, 1240, 1160 (m) and 756 (s) cm^{-1}; δ ($CDCl_3$) 1.1–1.4 (CH_3), 2.03 and 2.28 (in-chain CH_3), 3.85 s (OCH_3); *m/e* (100 °C) 294 (M, ethyl ester 3.2 %), 280 (M, methyl ester, 17 %) and 83 (100 %).

(±)-3,9-Dimethyl-6-(1-hydroxy-1-methyleth-yl)-2,4-decadien-1,9-diol (20). 16 (0.30 g) was reduced with $LiAlH_4$ (0.18 g) in dry ether for 20 h; yield crude *16* (0.25 g, 93 %).

(±)-9-Hydroxy-6-(1-hydroxy-1-methylethyl)-3,9-dimethyl-2,4-decadienyltriphenylphosphonium bromide (21). Crude *16* (0.40 g) was reacted with triphenylphosphonium bromide (0.54 g) in methylene chloride; yield crude *21* (0.64 g, 70 %).

Bacterioruberin (1b). 21 (0.6 g), crocetindial (*12*, 28 mg) and 1,2-butylene oxide (2.5 ml) in chloroform (2.5 ml) were kept at 90 °C in a sealed tube under N_2 for 2 h. The complex reaction mixture afforded upon TLC from the most polar fraction *1b* (*ca* 0.2 mg); λ_{max} (hexane) 273, 305, 318, (370), 386, 465, *493* and 526 nm; δ ($CDCl_3$) 1.18, 1.23, 1.26 (imp. and *gem.* dimethyl), 1.94 and 2.00 (in-chain methyl); *m/e* (230 °C) 740 (M, 15 %), 722 (M−18, 3.8 %), 704 (M−36, 1.0 %), 682 (M−58, 3.8 %), 664 (M−76, 2.5 %), 648 (M−92, 2.5 %), 634 (M−106, 11 %) and 59 (100 %); inseparable from natural *1* (TLC, SiO_2, 35 % acetone in hexane).

Isolation and derivatization

Bacterioruberin (1). Frozen, centrifuged cells of *Halobacterium salinarium* (850 g) provided by the previous isolation procedure[13] 17.7 mg *1*. *H. volcanii*[25,26] (490 g) gave 107 mg *1*. *1* could not be separated from synthetic *trans 1b*.

Semisynthetic tetraanhydrobacterioruberin (18). (a) *From bacterioruberin (1). 1* (59.6 mg) in dry pyridine (10 ml) was treated with phosphorus oxychloride (0.2 ml) at 50 °C for 3 h. TLC gave *18* (3.4 mg after rechromatography); λ_{max} (hexane) (371), 388, 468, *495* and 529 nm; δ ($CDCl_3$) 0.81, 0.89 and 1.25 (imp.), 1.60 and 1.69 (*gem.* dimethyl, CH_3–16,16′), 1.91 (CH_3–18,18′), 1.98 (CH_3–19,20,19′,20′), 4.65–4.80 (=CH_2), 5.05 ($(CH_3)_2C{=}CH$) and 5.4–7.0 (olefinic H); *m/e* (220 °C) 668 (M, 37 %), 599 (M−69, 3.6 %), 576 (M−92, 2.4 %), 562 (M−106, 82 %), 510 (M−158, 2.2 %), 493 (M−175, 8.2 %), 91 (100 %) and 69 (82 %), $\Delta\varepsilon$ (EPA) Fig. 1.

(b) *From bisanhydrobacterioruberin (2).* 2[12] (16.1 mg) was dehydrated by the same procedure as *1* above; *18* (0.47 mg) had λ_{max} (ether) 246, 276, 308, 320, 372, 388, (468), 493 and 526 nm; ν_{max} (KBr) 3030 (w), 2960 (m), 2925 (s), 2455 (m), 1644 (w), 1452, 1377 (m), 1002 (w), 962 (s), 888 (m) and 820 (w) cm^{-1}; *m/e* (220 °C) 668 (M, 16 %), 599 (M−69, 1.9 %), 576 (M−92, 0.5 %), 562 (M−106, 50 %), 510 (M−158, 0.4 %), 493 (M−175, 6.1 %) and 69 (100 %), $\Delta\varepsilon$ (EPA) Fig. 1.

Semisynthetic *18* and synthetic *18* could not be separated.

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