*Phytochemistry*, Vol. 21, No. 8, pp. 2087–2090, 1982.
Printed in Great Britain.

0031-9422/82/082087-04$03.00/0


# CHIRALITY OF PLECTANIAXANTHIN*

HARALD RØNNEBERG, GUNNER BORCH,† RICHARD BUCHECKER,‡ NOEL ARPIN§ and SYNNØVE LIAAEN-JENSEN

Organic Chemistry Laboratories, Norwegian Institute of Technology, University of Trondheim, N-7034 Trondheim-NTH, Norway; †Chemistry Department A, The Technical University of Denmark, DK-2800 Lyngby, Denmark; §Laboratoire de Mycologie associé au C.N.R.S., Service de Phytochimie, Faculté des Sciences, Lyon, France

(*Received* 16 *December* 1981)

**Key Word Index**—*Plectania coccinea*; Ascomycetes; chirality; characteristic carotenoid; plectaniaxanthin; (2′*R*)-3′, 4′-didehydro-1′, 2′-dihydro-β, ψ-carotene-1′, 2′-diol.

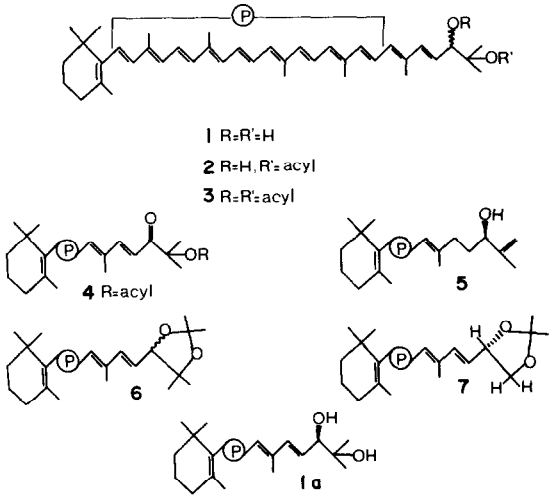
**Abstract**—The chirality of plectaniaxanthin, a carotenoid *vic.* glycol from *Plectania coccinea*, could not be determined by the modified Horeau method. Chiroptical correlation of plectaniaxanthin acetonide and (2′*S*)-16′, 17′-dinorplectaniaxanthin acetonide was taken as proof of 2′*R* chirality for natural plectaniaxanthin and its mono- and diesters. The synthesis of the chiral model carotenoid was effected from D-mannitol via 2, 3-*O*-isopropylidene-D-glyceraldehyde as key synthon.

## INTRODUCTION

*Plectania coccinea* (Scop ex Fr.) Fuck. synthesizes as characteristic carotenoids plectaniaxanthin (**1**), the monoacyl ester **2**, the diacyl ester **3**, and 2′-didehydro-1′-ester **4** [1] (Scheme 1).

Several monocyclic carotenoids have end-groups of undetermined chirality related to the aliphatic end-group of plectaniaxanthin (**1**) [2].

We now report the re-isolation of **1** and the determination of its absolute configuration by a synthetic approach involving chiroptical correlations.




Scheme 1.

*Part 12 in the series "Fungal Carotenoids".

‡Present address: Organisch-chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland.

## RESULTS AND DISCUSSION

Establishment of the chirality of *sec.* carotenols such as the 2′-ol aleuriaxanthin (**5**) [3, 4] has been successfully carried out by the modified Horeau method [5]. The application of this method to *vic.* diols has also been reported [6]. However, plectaniaxanthin (**1**) unexpectedly showed no preferential esterification with *R* or *S*-α-phenylbutyric acid. This result indicated at least partial racemization of plectaniaxanthin (**1**) at C-2′.

Attempts to demonstrate a partly racemic nature of plectaniaxanthin (**1**) using a chiral $^1$H NMR shift reagent [Eu(tfc)$_3$] [7] or by HPLC separation of diastereomeric camphanates [8] prepared from **1**, failed.

Whereas the CD spectrum at room temperature of plectaniaxanthin diester (**3**) exhibited a characteristic Cotton effect of medium intensity, natural plectaniaxanthin (**1**) and plectaniaxanthin derived from the diester **3** either by alkaline hydrolysis or by $LiAlH_4$ reduction, showed very weak and indistinct CD. However, at −100° the Cotton effect of plectaniaxanthin (**1**) of different origin changed in sign and magnitude and became similar to that of the diester **3** (Fig. 1). This result is compatible with a labile conformation for plectaniaxanthin (**1**) which becomes more rigid at lower temperature and in the natural diester (**3**).

CD correlation with any known carotenoid of established chirality was not feasible and a synthetic approach was considered. Since the chiral centre of plectaniaxanthin (**1**) carries an allylic hydroxy group conservation of the configuration during a synthesis was a problem. Efforts were therefore made to synthesize a suitable, chiral derivative.

Natural plectaniaxanthin (**1**) was derivatized with acetone in the presence of $CuSO_4$ [9] to give optically active plectaniaxanthin acetonide (**6**) (Scheme 1). This

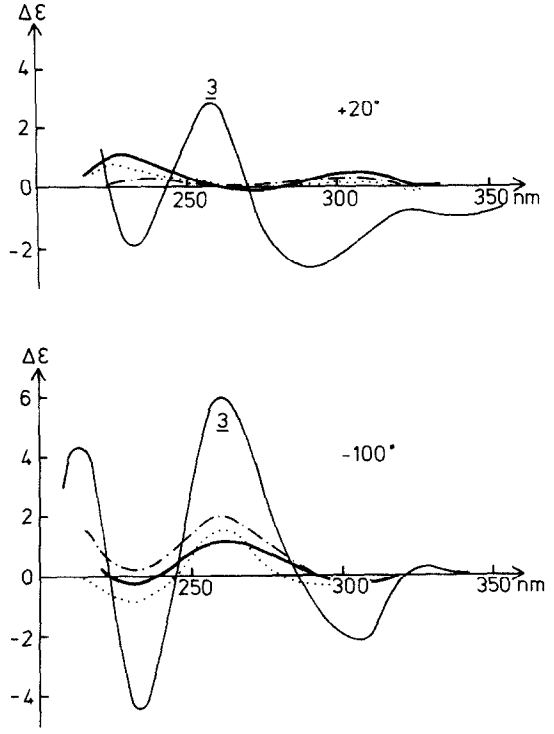
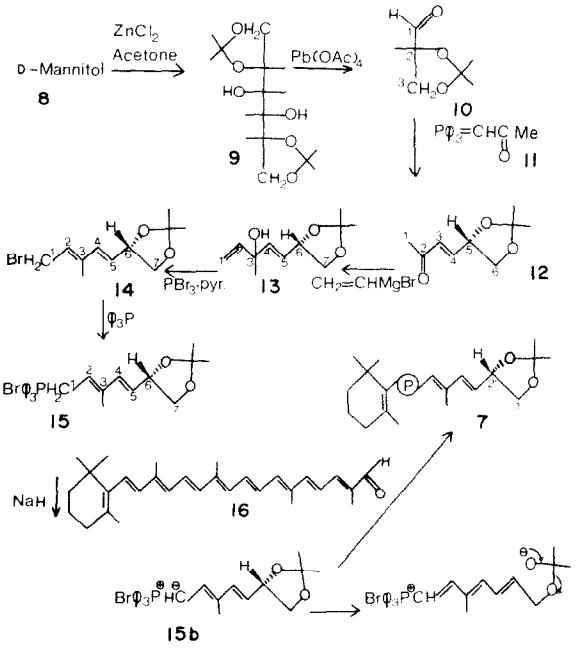



Fig. 1. CD spectra at room temperature and at −100° in EPA (diethyl ether–isopentane–ethanol, 5:5:2). —, Plectaniaxanthin (**1a**, natural); · · ·, plectaniaxanthin [**1a**, ex $LiAlH_4$-reduced diester (**3**)]; —·—, plectaniaxanthin [**1a**, ex saponified diester (**3**)]; —, plectaniaxanthin diester (**3**).




Scheme 2.

condensation is considered to occur with retention of configuration [10, 11]. The acetonide (**7**) of (2′*S*)-16′, 17′-dinorplectaniaxanthin was considered an appropriate model for chiroptical correlation. The two acetonides **6** and **7** differ only in the replacement of two methyl groups in **6** with two hydrogen atoms in **7**. Methyl vs hydrogen are of comparable electronegativity and neither carry lone-pair electrons. Inspection of models revealed no steric conflicts which could lead to different conformations.

The synthesis of the chiral 16′, 17′-dinor derivative was effected as outlined in Scheme 2. D-Mannitol (**8**) was converted to 1, 2; 5, 6-di-*O*-isopropylidene-D-mannitol (**9**) by condensation with acetone [12]. Oxidation of the *vic.* glycol **9** with Pb $(OAc)_4$ provided 2, 3-*O*-isopropylidene-D-glyceraldehyde (**10**) by a known procedure [13]. This aldehyde (**10**) was reacted with the phosphorane **11** in a Wittig reaction to yield the optically active ketone **12**, which was transformed in a Grignard reaction with vinyl magnesium bromide to the *tert.* alcohol **13**. Substitution with $PBr_3$ in pyridine afforded with allylic rearrangement the primary bromide **14**, which was further converted to the phosphonium salt **15**. Finally, a Wittig reaction with *β*-apo-8′-carotenal (**16**), using NaH as preferential base, provided the target compound **7** in 16% yield. Elimination from the ylid **15b** (Scheme 2) is considered responsible for the low yield. The formation of an achiral C-2′ methyl ether as the major product when NaOMe was used as base in an alternative attempted route to the acetonide **7** has been discussed elsewhere by Rønneberg [14].

The product **7** was chromatographically homogeneous and from its electronic spectrum considered to be all-*trans*. In any case, partial *cis*-configuration at Δ7′ (unlikely since sterically hindered), Δ5′ or Δ3′ compatible with the synthetic route employed, is not likely to invert the non-conservative Cotton effect of a monocyclic carotenoid [15, 16].

The CD spectra of the synthetic (2′*S*)-16′,17′-dinorplectaniaxanthin acetonide (**7**) and of plectaniaxanthin acetonide (**6**) are given in Fig. 2. Provided the model **7** is valid for chiroptical correlation with plectaniaxanthin acetonide (**6**), the result proves the opposite configuration at C-2′ and hence 2′*R*-configuration for plectaniaxanthin (**1a**, Scheme 1).

The agreement in the magnitude of the Cotton effects of the acetonides **6** and **7** (Fig. 2) and also of plectaniaxanthin (**1**) as natural diol and as a saponification product from its mono and diesters does not favour the possibility of natural plectaniaxanthin (**1**) being partly racemized.

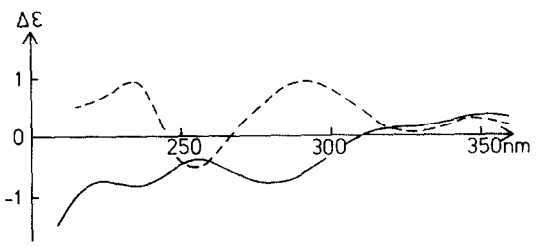



Fig. 2. CD spectra at room temperature in EPA solution. – – – –, Plectaniaxanthin acetonide (**6**); ———, (2′*S*)-16′, 17′-dinorplectaniaxanthin acetonide (**7**).

A chiroptical correlation between plectaniaxanthin derivatives (**1–3**) and carotenoids with related 2′-substituted end-groups will be published separately.

## EXPERIMENTAL

*Biological material. P. coccinea* (Scop ex Fr.) Fuck. [= *Sarcoscypha coccinea* (Fr. Lamb)] collected in 1975 near Lyon, France, was used. The carotenoids were re-isolated by the previous procedure [1]. After TLC (Si gel) the total yield was 114 mg, consisting of β, β-carotene (22% of total), plectaniaxanthin diester (**3**, 55%), 2′-dehydroplectaniaxanthin ester (**4**, 16%), plectaniaxanthin monoester (**2**, 1%) and plectaniaxanthin (**1a**, 6%) given in order of increasing adsorption.

*Plectaniaxanthin* (**1a**), vis. $\lambda_{max}^{Et_2O}$ nm: 450, 474 and 503; CD (EPA) Fig. 1; $^1$H NMR [1]. Treatment of the diester (**3**, 6.3 mg) with $LiAlH_4$ in dry $Et_2O$ or alkaline hydrolysis of the diester (**3**, 6.3 mg) in 5% KOH MeOH–$Et_2O$ gave optically active **1a** (CD, Fig. 1).

Racemic plectaniaxanthin (**1a** + enant.) was prepared by $LiAlH_4$ reduction of 2′-didehydroplectaniaxanthin ester (**4**, 18 mg).

*Horeau experiments.* These were carried out as previously described [14]. (+)-Natural **1a** (6.2 mg) gave by comparison with the standard reaction for cyclohexanol the corrected ratio for R,S-amide: R,R-amide 1:0.98, (2). Plectaniaxanthin (**1a**, 3.3 mg, obtained by saponification of the diester 3) gave the same ratio 1:0.98, (3). Racemic plectaniaxanthin (**1a** + enant., 2.5 mg, obtained by $LiAlH_4$-reduction of **4** above) gave the corrected ratio 1:0.39 and (4): (−)-R-Menthol gave the corrected ratio 1:0.79.

*2′-Camphanates of plectaniaxanthin.* The camphanates were prepared with (−)-camphanoyl chloride by the general procedure [8, 17]. Neither the camphanate prepared from optically active plectaniaxanthin (**1a**) or racemic plectaniaxanthin (**1a** + enant.) gave diastereomeric esters which could be resolved by HPLC.

*$^1$H NMR with chiral shift reagent.* Racemic plectaniaxanthin (**1a** + enant., 16 mg) in $CDCl_3$ with successive additions to 5, 8, 14.3 and 29.8 mg $Eu(tfc)_3$ gave no resolution of the C-1′ Me signals. Shifts of the H-2′ or H-3′, 4′ signals (both *br*) could not be observed. Modification of the solvent system gave no positive results.

*Plectaniaxanthin acetonide* (**6**). Natural plectaniaxanthin (**1a**, 2.6 mg) in $Me_2CO$ (7 ml) and $CuSO_4$ (75 mg) were reacted for 20 min at room temp.; pigment recovery 50% after TLC (Si gel). The acetonide **6** (0.94 mg, 36%) was less strongly adsorbed than **1a**; vis. $\lambda_{max}^{hexane}$ nm: 446, 471 and 501, % III/II [18] = 35; CD (EPA) Fig. 2; $^1$H NMR ($CDCl_3$): δ 1.03 (*s*, Me − 1), 1.13 (*s*) and 1.21 (*s*, Me − 1′), 1.39 (*s*) and 1.48 (*s* $Me_2C$, acetonide), 1.72 (*s*, Me-5), 1.94 (*s*, Me-5′), 1.98 (*s*, Me-9, 13, 9′, 13′), 2.03 (H-4), 4.2 (*d*, H-2′, $J$ = 8 Hz), 5.8–6.9 (*m*, olefinic H); MS *m/z* (rel. int.): 608 $[M]^+$ (25), 593 $[M-15]^+$ (3), 577 $[M-31]^+$ (9), 565 $[M-43]^+$ (6), 563 $[M-45]^+$ (6), 551 $[M-57]^+$ (14), 550 $[M-58]^+$ (10), 549 $[M-59]^+$ (11), 537 $[M-69]^+$ (10), 523 $[M-85]^+$ (13), 509 $[M-99]^+$ (7), 502 $[M-106]^+$ (12), 44 (100), for discussion of fragmentation pattern see refs. [10, 14].

*Synthesis of* (2′S)-16′, 17′ *dinorplectaniaxanthin acetonide* (**6**) 1.2; 5.6-Di-*O*-isopropylidene-D-mannitol (**9**) was prepared from D-mannitol (**8**, 85 g) according to Baer [12]. Yield 37 g (30%), mp (corr.) 116.5–117.5° (lit [12] 117–119°).

2, 3-*O*-Isopropylidene-D-glyceraldehyde (**10**) was prepared by the procedure of ref. [13] from 1.2; 5.6-di-*O*-isopropylidene-D-mannitol (**9**, 5.2 g) by $Pb(OAc)_4$ oxidation in $C_6H_6$. Yield 3.7 g (73%); $^1$H NMR ($CDCl_3$): δ 1.42 (*s*) and 1.48 (*s*, 6H, $(Me_2C)$, 4.0–4.5 (*m*, 3H, H-2, 3), 9.5 (*d*, 1H, H-1, $J_{1,2}$ = 1.5 Hz); IR $\nu_{max}^{liq.}$ cm$^{-1}$: 3000–2800 (CH), 1735 (C=O), 1480 and 1460 ($CH_2$, Me), 1370 (Me), 1250 (C–O), 1180 (C–O); $[\alpha]_D^{25}$ ($C_6H_6$) 44.3 ± 2.2°, reported $[\alpha]_D^{21}$ = 64.9° [13].

*Triphenylphospineacetylmethylene* (**11**) was prepared according to ref. [19] from acetyltriphenylphosphonium chloride (4.8 g). Yield 4.3 g (100%); mp 203–208°, UV and IR as previously reported [18].

*(5S)-5, 6-Dihydroxy-5, 6-O-isopropylidene-3-hexen-2-one* (**12**). To 2, 3-*O*-Isopropylidene-D-glyceraldehyde (**10**, 2.5 g) dissolved in $C_6H_6$–$Et_2O$ (1:1, 140 ml) was added triphenylphosphineacetylmethylene (**11**, 6.5 g). The reaction mixture was worked up after 22 hr at room temp. by evap. to dryness, transfer to $Et_2O$, removal of $P\phi_3$=O by filtration and high vac. distillation. **12** (3.0 g, 93%) had $^1$H NMR ($CDCl_3$): δ 1.4 (*s*) and 1.45 (*s*, 6H, $Me_2$ C), 2.25 (*s*, 3H, H-1), 3.4–4.9 (*m*, 3H, H-5, 6), 6.0–7.0 (*m*, 2H, H-3, 4); IR $\nu_{max}^{liq.}$ cm$^{-1}$: 3000–2800 (CH), 1680 (C=O), 1630, 1375, (Me), 1250 (C–O), 1160 (C–O); MS *m/z*: 170 $[M]^+$ (1), 155 $[M-15]^+$ (58), 140 $[M-30]^+$ (16), 113 $[M-57]^+$ (53), 43 (100); $[\alpha]_D^{25}$ ($C_6H_6$) 49.5 ± 8°.

(6S)-6, 7-O-*Isopropylidene-3-methyl*-1, 4-*heptadiene*-3, 6, 7-*triol* (**13**). To Mg (2 g) was added vinyl bromide (8.8 g) in dry THF (20 ml). After formation of the Grignard reagent (5*S*)-5, 6-dihydroxy-5, 6-*O*-isopropylidene-3-hexen-2-one (**12**, 2.8 g) in dry THF (20 ml) was added dropwise with stirring at 0°. The reaction was stopped after 1 hr by addition of $NH_4Cl$ and extraction with $Et_2O$. CC ($SiO_2$, $CHCl_3$ in hexane) gave **13** (2 g, 59%); $^1$H NMR ($CDCl_3$): δ 1.37 (*s*, Me−3); 1.37 (*s*) and 1.41 (*s*, Me) (2:1–2:2 (OH, OH, confirmed by $D_2O$ exchange), 3.3–4.7 (*m*, 3H, H − 6.7), 4.8–6.3 (*m*, 4H, H − 1, 2, 4, 5); IR $\nu_{max}^{liq.}$ cm$^{-1}$: 3420 (OH), 3000–2800 (CH), 1640, 1450, ($CH_2$, Me), 1370 (Me), 1230 (C–O), 1155 (C–O) cm$^{-1}$; MS *m/z*: 183 $[M-15]^+$ (7), 180 $[M-18]^+$ (1), 168 $[M-30]^+$ (1), 155 $[M-43]^+$ (1), 140 $[M-58]^+$ (7), 43 (100); $[\alpha]_D^{20}$ 21.2°.

(6S)-1-*Bromo*-3-*methyl*-6, 7-O-*isopropylidene*-2, 4-*heptadiene*-6, 7-*diol* (**14**). To a chilled (−18°) soln of (6*S*)-6, 7-*O*-isopropylidene-3-methyl-1.4-heptadiene-3, 6, 7-triol (**13**, 0.47 g) in pyridine (0.07 ml) and dry hexane (3 ml) was added $PBr_3$ (0.26 g). The temp. in the reaction mixture was raised to −10° over 2 hr. Cold, saturated aq. $NaHCO_3$ was added and the product extracted with $Et_2O$ and dried by azeotropic distillation with $C_6H_6$; yield of **14** (0.47 g, 75%); $^1$H NMR ($CDCl_3$): δ 1.39 (*s*) and 1.43 (*s*, 6H, $Me_2C$), 1.84 (*s*, 3H, Me − 3, $J$ = 2 Hz), 3.3–4.7 (*m*, 5H, H-1, 6, 7), 5.5–6.5 (*m*, H-2, 4, 5); IR $\nu_{max}^{liq.}$ cm$^{-1}$: 3000–2800 (CH), 1630 (C=C), 1380 and 1370 (Me), 1250 (C–O), 1160 (C–O), 680 (C–Br); MS *m/z*: 262/260 $[M]^+$ (2), 247/245 $[M-15]^+$ (5), 181 $[M-Br]^+$ (57), 150 $[M-111/109]^+$ (5), 43 (100); $[\alpha]_D^{20}$ ($C_6H_6$) − 7.75°.

(6S)-6, 7-*Dihydroxy*-O-*isopropylidene*-3-*methyl*-2, 4-*heptadienyl triphenylphosphonium bromide* (**15**). The bromide **14** (0.47 g) was reacted with triphenylphosphine (590 mg) in ether for 84 hr at room temp. The semicrystalline product was precipitated several times from $CHCl_3$ with $Et_2O$, yield of **15** 552 mg (59%). A strong red ylid colour was developed upon addition of NaH to an aliquot in $CH_2Cl_2$.

(2′S)-16′, 17′-*Dinorplectaniaxanthin acetonide* (**7**). The phosphonium salt **15** (30 mg) and β-apo-8′-carotenal (**16**, 9 mg) dissolved in $CH_2Cl_2$ (3 ml) were added to NaH (6 mg) in $CH_2Cl_2$ (2 ml) and the mixture stirred for 23 hr at room temp. Saturated aq. $NH_4Cl$ was added and the pigments extracted with $Et_2O$. Prep. TLC ($SiO_2$) gave **7** (2 mg, 16%). The total pigment recovery was 90%. **12** had vis. $\lambda_{max}^{Me_2CO}$ nm:

447, 472 and 502, % III/II = 32; CD (EPA) Fig. 2; $^1$H NMR ($CDCl_3$): $\delta$ 1.04 (*s*, Me − 1), 1.43 (*s*) and 1.47 (*s*, $Me_2C$), 1.73 (*s*, Me − 5), 1.94 (*s*, Me − 5′), 1.99 (*s*, Me − 9, 13, 9′, 13′), 2.04 (H-4), 5.8–6.9 (*m*, olefinic H); MS *m/z*: 580 $[M]^+$ (15), 565 $[M-15]^+$ (2), 551 $[M-29]^+$ (5), 550 $[M-30]^+$ (3), 549 $[M-31]^+$ (4), 548 $[M-32]^+$ (37), 537 $[M-43]^+$ (4), 523 $[M-57]^+$ (6), 509 $[M-71]^+$ (4), 495 $[M-85]^+$ (5), 488 $[M-92]^+$ (1), 474 $[M-106]^+$ (30), 43 (100).

*Acknowledgements*—H.R. was supported by a grant from The Technical University of Norway and R. B. by a postdoctoral fellowship from the Schweizerischen Nationalfonds zur Förderung der wissenschaftlichen Forschung.

## REFERENCES

1. Arpin, N. and Liaaen-Jensen, S. (1967) *Phytochemistry* **6**, 995.
2. Straub, O. (1976) *Key to Carotenoids*. Birkhäuser, Basel.
3. Arpin, N., Kjøsen, H., Francis, G. W. and Liaaen-Jensen, S. (1973) *Phytochemistry* **12**, 2751.
4. Buchecker, R., Arpin, N. and Liaaen-Jensen, S. (1976) *Phytochemistry* **15**, 1013.
5. Brooks, C. J. W. and Gilbert, J. D. (1973) *Chem. Commun.* 194.
6. Hamond, P. P. G., Massy-Westropp, R. A. and Pipithakul, T. (1974) *Aust. J. Chem.* **27**, 2199.
7. Fraser, R. R., Petit, M. A. and Saunders, J. K. (1971) *J. Chem. Soc. Chem. Commun.* 1450.
8. Vecchi, M. and Müller, R. K. (1979) *J. High Res. Chrom. Chrom. Commun.* 195, 2.
9. McCloskey, J. A. and McClellend, M. J. (1965) *J. Am. Chem. Soc.* **87**, 5090.
10. Hurd, C. D. (1966) *J. Chem. Educ.* **43**, 527.
11. March, J. (1977) *Advanced Organic Chemistry*, 2nd edition, p. 810. McGraw-Hill, New York.
12. Baer, J. (1945) *J. Am. Chem. Soc.* **67**, 338.
13. Fischer, J. O. L. and Baer, E. (1936) *Helv. Chim. Acta* **19**, 519.
14. Rønneberg, H. (1980) Ph.D. thesis, University of Trondheim.
15. Noack, K. and Thomson, A. J. (1979) *Helv. Chim. Acta* **62**, 1902.
16. Sturzenegger, V., Buchecker, R. and Wagniére, G. (1980) *Helv. Chim. Acta* **63**, 1074.
17. Renstrøm, B., Borch, G. and Liaaen-Jensen, S. (1981) *Comp. Biochem. Physiol*, **69B**, 621.
18. Ke, B., Imsgard, F., Kjøsen, H. and Liaaen-Jensen, S. (1970) *Biochim. Biophys. Acta* **210**, 139.
19. Raminez, F. and Dershowitz, S. (1957) *J. Org. Chem.* **22**, 41.