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NEROLIDOL-5,8-OXIDES FROM THE ESSENTIAL OIL OF *SANTOLINA OBLONGIFOLIA*

J. DE PASCUAL-T., S. VICENTE, M. S. GONZÁLEZ and I. S. BELLIDO

Department of Organic Chemistry, Salamanca University, Salamanca, Spain

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Key Word Index—*Santolina oblongifolia*; Compositae; nerolidol derivatives; α-oplopenone.

Abstract—From the essential oil of *Santolina oblongifolia*, three new dihydrofurane sesquiterpenoids, related to nerolidol, and a bicyclic sesquiterpene, named α-oplopenone, have been isolated. Their structures and stereochemistry have been assigned by spectroscopic methods.

INTRODUCTION

Santolina oblongifolia, Boiss. (tribe Anthemideae, Compositae), is a perennial plant whose distribution area is the SW of the Iberian Peninsula. It is widely spread in the Sierras of Gredos, Bejar and Gata, and it is commonly known as 'Gredos camomile'*.

There have been only a few investigations on the components of plants belonging to the *Santolina* genus. The essental oil from the roots of *S. chamaecyparisuss* has been examined [1, 2] and acetylenic compounds have been reported from the roots of *S. rosmarinifolia* [3], *S. pinnata* [4] and *S. chamaecyparisuss* [5, 6]. We have recently reported the isolation of several sesquiterpenes and aromatic acetylenes from the essential oil of *S. rosmarinifolia* [7].

In the present paper, we report the components of the essential oil from the aerial parts of *S. oblongifolia* collected at the beginning of June in the Sierra of Béjar (Salamanca, W. Spain).

*The material was identified by Professor B. Casaseca Mena, from the Botany Department of Salamanca University, where a specimen is held (herbarium No. 20.412).

RESULTS AND DISCUSSION

The steam-distilled fraction from the hexane extract of the air-dried and finely ground aerial parts of *S. oblongifolia*, was first dry-chromatographed and the different fractions were then analysed by GC. Pure components were isolated by CC and the known ones, were identified by comparison of their R_f and IR, NMR and mass spectra with those of authentic samples. The structural assignments of the unknown components, were made on the basis of spectroscopic observations.

The oil contained 24.5% of monoterpenoids, 13.6% of sesquiterpenoid hydrocarbons and 61.0% of oxygenated sesquiterpenes. The results of this systematic study of the essential oil are summarized in Table 1.

Compound **11**, which was named α-oplopenone, because of its relationship with oplopenone (**10**), is a viscous oil with $[M]^+$ at m/z 220 ($C_{15}H_{24}O$) and it showed IR absorptions due to a carbonyl group (1705 cm^{-1}) and one

Table 1. Constituents of the essential oil of *S. oblongifolia*.

No.	Compound	%	Ref.	No.	Compound	%	Ref.
1	α-Pinene*	1.8	—	**14**	α-*trans*-Bejarol	13.1	—
2	Δ^1-*p*-Menthene*	1.6	—	**15**	*cis*-Bejarol	10.0	—
3	Limonene*	1.1	—	**16**	Fokienol	2.5	[16]
4	β-Cariophillene	3.1	[8]	**17**	Isofokienol	2.3	—
5	β-Farnesene	1.6	[9]	**18**	γ-Eudesmol	2.0	[17, 18]
6	δ-Cadinene	3.6	[10, 11]	**19**	α-Eudesmol	1.6	[17, 18]
7	β-Maalliene	4.9	[12]	**20**	β-Eudesmol	2.7	[17, 18]
8	*Artemisia* ketone	18.0	[7]	**21**	Espatulenol	3.5	[19, 20]
9	Cariophillene oxide	2.3	[13]	**22**	Elemol	5.4	[16]
10	Oplopenone	2.7	[14]	**23**	Nerolidol	2.3	[21]
11	α-Oplopenone	3.6	—	**24**	Hydroxifokienol	1.8	—
12	Epoxizerumbone	4.0	[15]	**25**	Herniarin	1.2	[22]
13	β-*trans*-Bejarol	3.1	—				

*Identified by comparison with authentic samples.

trisubstituted double bond (3010, 1640, 820 cm^{-1}). The ^1H NMR spectrum (see Experimental) and the mass spectral fragmentation pattern were very similar to those exhibited by **10**, and agree with the proposed structure. This was confirmed by treatment of oplopanone [23] with sulphuric acid–acetic acid, which afforded a 4:1 mixture of **10** and **11**.

Compounds **13–15**, were all isolated as viscous oils with a pleasant smell resembling that of the fresh plant. They were chromatographically and spectroscopically very much alike, and showed a molecular ion $[M]^+$ at *m/z* 236 ($C_{15}H_{24}O$) and the same fragmentation pattern. Their IR spectra showed absorptions due to hydroxyl groups and double bonds, which were confirmed by the ^1H NMR spectra (see Experimental). The IR and NMR spectra were both very similar to those exhibited by nerolidol (**23**) [21]. The only significant differences with the ^1H NMR spectrum of **23**, were one additional signal due to two *O*-geminal protons and the absence of the signal due to a CH_2 group in the α-position with respect to a double bond.

These spectral data, suggested that **13–15** were isomers and they were all related to nerolidol (**23**) with one *O*-bridge between C-5 and C-8.

The fragmentation patterns agreed with the proposed structure (Scheme 1).

The stereochemistry of these compounds was easily deduced from the ^1H NMR spectra, because in **13** and **14**, the chemical shifts due to the C-5 and C-8 protons were seen at δ4.35 and 4.45, respectively ($J_{5,8}$ = 3 Hz). This is evidence for a *trans*-configuration in 2,5-disubstituted 2,5-dihydrofuranes [24]. Compound **15** showed the signals due to the same protons, at δ4.05 and 4.15, respectively, which is also proof for the *cis*-stereochemistry [24].

In the ^1H NMR spectrum of **13**, the signal due to the H-6, appeared as a broad singlet at δ5.20, which agrees with an H-5–H-6 dihedral angle of *ca* 80°. Thus, the H-5 must be in a pseudoaxial position [25].

In **14**, the signal due to the H-6 proton was seen as a doublet (J = 5 Hz) centred at δ5.15, indicative of an H-5–H-6 dihedral angle of *ca* 40°, with the H-5 in a pseudo-equatorial position [25].

The stereochemistry at C-3 is unknown, but we suggest it is the same as found in (+)-nerolidol [26] because of their possible biogenetic relationships.

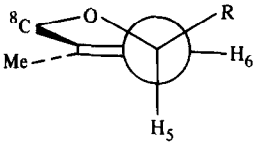
As the ^1H NMR spectrum of **15** showed the same signals as **13** for the olefinic protons we have assigned to it the stereochemistry depicted in structure **15**.

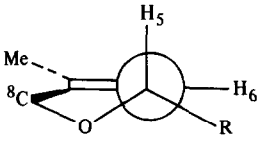
The proposed structures for **13–15**, are: *trans*-3,7,11-trimethyl-3-hydroxy-5,8-epoxidodeca-1,6,11-triene or '*α-trans*-bejarol' and *trans*-3,7,11-trimethyl-3-hydroxy-5,8-epoxidodeca-1,6,11-triene or '*β-trans*-bejarol' for **13** or **14** and *cis*-3,7,11-trimethyl-3-hydroxy-5,8-epoxidodeca-1,6,11-triene or '*cis*-bejarol' for **15**.

Compounds **16** and **17**, are also isomers, with $[M]^+$ at *m/z* 220 ($C_{15}H_{24}O$). Their UV spectra showed absorptions at 225 and 231 nm, respectively, which is evidence for a conjugated dienic system. This was confirmed by the presence of IR absorption bands at 1640 and 1610 cm^{-1}.

Compound **16** was identical with fokienol isolated from the hexane extract of *Solanum melongena* [16].

The ^1H NMR spectrum of **17** (see Experimental) was very similar to that of **16**. The only significant difference was a signal which in **16** appeared as a doublet centred at





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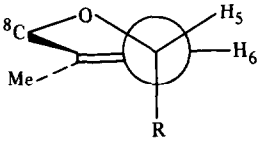

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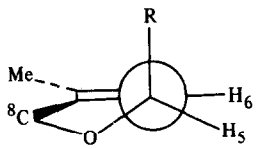

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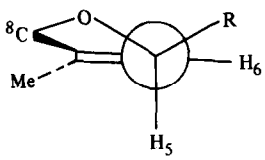

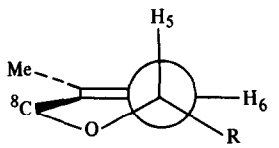

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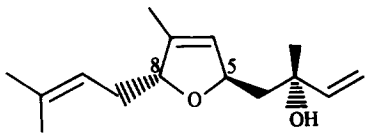
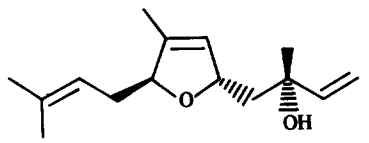
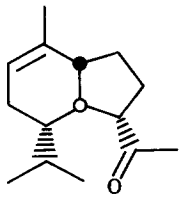


13–14

or



13–14



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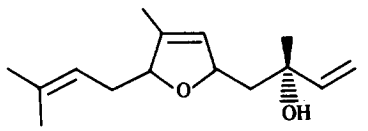
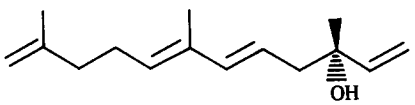


15 *cis*



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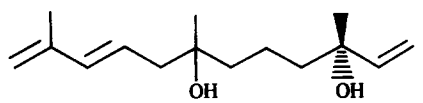


24

δ2.70 (J = 7 Hz), assigned to the methylene group at C-8, between two double bonds, while **17** showed a signal at 2.35, due to a C=CH=CH$_2$–C–OH group, which is in good agreement with the proposed structure.

Compound **24** (UV λ_{max}^{EtOH} at 226 nm), was a diol with $[M]^+$ at m/z 238 ($C_{15}H_{26}O_2$) and a fragmentation pattern very much like that of **16**. The ^{1}H NMR spectra of **16** and **24** were also very similar, except for the absence of the signals due to the trisubstituted double bond at C-6, and one additional signal due to a Me–OH, which suggests that **24** is a hydroxy derivative of fokienol.

EXPERIMENTAL

UV spectra were recorded in EtOH; ^{1}H NMR were recorded using TMS as int. standard. Analytical TLC was performed on Si gel G (E. Merck No. 7731), prep. TLC, on Si gel $PF_{234-336}$ (E. Merck No. 7748) and CC on Si gel 60 (E. Merck No. 7734); GC was performed on Carbowax-20M columns (temp. 100–200°).

Extraction and isolation. The air-dried and finely ground aerial parts of the plant (7.0 kg), collected in the Sierra of Béjar (Salamanca), were extracted with hot hexane. The concd hexane extract was steam-distilled to yield 28.0 g of essential oil (0.40% of the dry plant total weight). This oil was directly chromatographed on a Si gel dry column (hexane–Et_2O, 7:3) to give six fractions. Fr. 1, 8.04 g (28.7%) **1–8**. Fr. 2, 4.37 g (15.6%) **7–11**. Fr. 3, 6.77 g (24.2%) **13–15**. Fr. 4, 3.02 g (10.8%) **12, 15–17**. Fr. 5, 4.26 g (15.2%) **18–22**. Fr. 6, 1.48 g (5.3%) **23–25**. Each fraction, was rechromatographed on Si gel–$AgNO_3$ (20%), to give pure samples of the different components.

α-Oplopenone (**11**). Viscous oil, $[\alpha]_D$ = −14.5° ($CHCl_3$; c 0.80); IR ν_{max} cm^{-1}: 1705 (C=O), 3010, 1640, 820 (C=CH); ^{1}H NMR (CCl_4): δ0.70 and 0.88 (6H, 2d, J = 7 Hz), 1.70 (3H, s), 2.10 (3H, s), 5.25 (1H, *br s*); MS m/z (rel. int.): 220 $[M]^+$ (6), 205 $[M-Me]^+$ (14), 177 $[M-MeCO]^+$ (100), 161 (36), 150 (78), 134 (52), 119 (17), 109 (65), 107 (46), 93 (13).

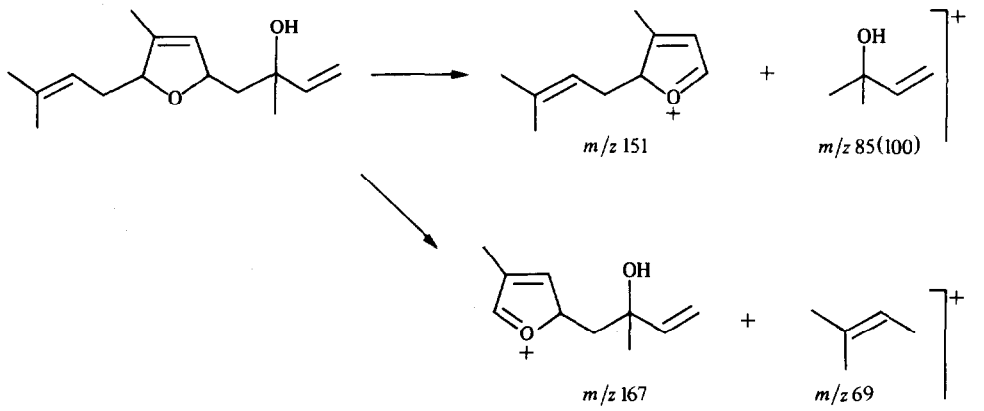
Synthesis of α-oplopenone. A mixture of 100 mg oplopanone and H_2SO_4–HOAc (1:3), was heated for 1 hr and then extracted with Et_2O. The product was chromatographed on Si gel, giving 15 mg **11**, identical in all respects with the natural compound, and 60 mg **10**, mp 57°, $[\alpha]_D$ = −9.6°; IR ν_{max} cm^{-1}: 3080, 1705, 1650, 1160, 890; ^{1}H NMR (CCl_4): δ0.63 and 0.88 (6H, 2d, J = 7 Hz), 2.08 (3H, s), 4.51 (2H, m); $[M]^+$ at m/z 220 ($C_{15}H_{24}O$).

β-trans-Bejarol (**13**). $[\alpha]_D$ = −9.5° ($CHCl_3$; c 1.1) and $n_D^{25°}$ = 1.4820. IR ν_{max} cm^{-1}: 3500, 1640, 1280, 1190, 1105, 1070, 990, 930, 890, 830; ^{1}H NMR (CCl_4): δ1.24 (3H, s, Me-3), 1.35 (1H, m, H-4), 1.71 (6H, s, Me-7 and Me-11), 1.85 (1H, m, H-9), 4.30 (1H, td, J = 7, 3 Hz, H-5), 4.42 (1H, td, J = 7, 3 Hz, H-8), 4.85 (1H, dd, J = 10, 2 Hz, H-1 *cis*), 4.97 (1H, dd, J = 17, 2 Hz, H-1 *trans*), 5.00 (1H, *br s*, H-10), 5.20 (1H, *br s*, H-6), 5.76 (1H, dd, J = 17, 10 Hz, H-2); MS m/z (rel. int.): 236 $[M]^+$ (15), 167 (20), 151 (45), 123 (19), 122 (12), 109 (66), 107 (23), 95 (17), 91 (19), 85 (100).

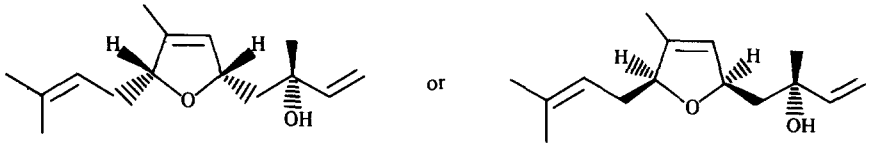
α-trans-*Bejarol* (**14**). $[\alpha]_D$ = −15.7° ($CHCl_3$; c 0.90) and $n_D^{25°}$ = 1.4816. IR ν_{max} cm^{-1}: 3500, 1650, 1280, 1200, 1110, 990, 930, 890, 830; ^{1}H NMR (CCl_4): δ1.13 (3H, s, Me-3), 1.67 (3H, s, Me-11), 1.72 (3H, s, Me-7), 1.35 (1H, m, H-4), 1.85 (1H, m, H-9), 4.30 (1H, tdd, J = 7, 5, 3 Hz, H-5), 4.42 (1H, td, J = 7, 3 Hz, H-8), 4.98 (1H, dd, J = 10, 2 Hz, H-1 *cis*), 5.12 (1H, *br s*, H-10), 5.15 (d, J = 5 Hz, H-6), 5.20 (1H, dd, J = 17, 2 Hz, H-1 *trans*), 5.76 (1H, dd, J = 17, 2 Hz, H-2); MS m/z (rel. int.): 236 $[M]^+$ (20), 167 (35), 151 (65), 123 (15), 109 (48), 107 (21), 95 (16), 85 (100).

cis-*Bejarol* (**15**). $[\alpha]_D$ = −41.4° ($CHCl_3$; c 0.76) and $n_D^{25°}$ = 1.4942. IR ν_{max} cm^{-1}: 3500, 1650, 1205, 1150, 990, 920, 890, 830, 690; ^{1}H NMR (CCl_4): δ1.13 (3H, s, Me-3), 1.66 (3H, s, Me-11), 1.73 (3H, s, Me-7), 1.44 (1H, m, H-4), 1.88 (1H, m, H-9), 4.00 (1H, t, J = 8 Hz, H-5), 4.15 (1H, t, J = 7 Hz, H-8), 4.94 (1H, dd, J = 10, 2 Hz, H-1 *cis*), 5.12 (2H, *br s*, H-6 and H-10), 5.20 (1H, dd, J = 17, 2 Hz, H-1 *trans*), 5.76 (1H, dd, J = 17, 10 Hz, H-2); MS m/z (rel. int.): 236 $[M]^+$ (11), 167 (42), 151 (31), 123 (29), 122 (10), 109 (66), 107 (13), 95 (27), 91 (12), 85 (100).

Fokienol (**16**). $[\alpha]_D$ = −14° ($CHCl_3$; c 0.90). UV λ_{max}^{EtOH} nm: 225 (ε = 19.600); IR ν_{max} cm^{-1}: 3450, 1640, 1610, 1235, 1160, 1110, 970, 930, 890, 830; ^{1}H NMR (CCl_4): δ1.22 (3H, s, Me-3), 1.57 (3H, s, Me-7), 1.80 (3H, s, Me-11), 1.30 (1H, t, J = 7 Hz, H-4), 2.10 (1H, m, H-5), 2.67 (1H, d, J = 7 Hz, H-8), 4.78 (1H, s, H-12), 4.92 (1H, dd, J = 10, 2 Hz, H-1 *cis*), 5.00 (1H, t, J = 7 Hz, H-6),



Scheme 1.



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5.10 (1H, *dd*, J = 17, 2 Hz, H-1 *trans*), 5.60 (1H, *dt*, J = 18, 7 Hz, H-9), 5.82 (1H, *dd*, J = 17, 10 Hz, H-2), 6.10 (1H, *d*, J = 18 Hz, H-10); MS m/z (rel. int.): 220 $[M]^+$ (5), 205 $[M-Me]^+$ (10), 202 $[M-H_2O]^+$ (11), 187 (6), 159 (15), 151 (6), 149 (23), 133 (22), 131 (29), 119 (52), 109 (44), 107 (53), 105 (57), 93 (79), 91 (100), 85 (74).

Isofokienol (**17**). $[\alpha]_D = -8.5°$ ($CHCl_3$; c 0.65). UV λ_{max}^{EtOH} nm: 231 (ε = 16.140); IR ν_{max} cm^{-1}: 3500, 3070, 1640, 1610, 1170, 1110, 990, 970, 890, 830; ^1H NMR (CCl_4): δ1.28 (3H, *s*, Me-3), 1.60 (3H, *s*, Me-11), 1.68 (3H, *s*, Me-7), 2.20 (2H, *m*, H-9 and H-10), 2.35 (1H, *d*, J = 7 Hz, H-4), 4.90 (1H, *s*, H-12), 5.02 (1H, *dd*, J = 10, 2 Hz, H-1 *cis*), 5.10 (1H, *br s*, H-8), 5.20 (1H, *dd*, J = 17, 2 Hz, H-1 *trans*). 5.72 (1H, *dt*, J = 18, 7 Hz, H-5), 5.95 (1H, *dd*, J = 17, 10 Hz, H-2), 6.15 (1H, *d*, J = 18 Hz, H-6); MS m/z (rel. int.): 220 $[M]^+$ (12), 205 (10), 202 (11), 189 (20), 151 (13), 136 (16), 123 (16), 121 (22), 109 (58), 107 (51), 105 (17), 95 (30), 93 (100), 91 (32), 85 (29).

Hydroxyfokienol (**24**). UV λ_{max}^{EtOH} nm: 226 (ε = 23.200); IR ν_{max} cm^{-1}: 3400, 3080, 1640, 1610, 1130, 1040, 980, 930, 890, 795; ^1H NMR (CCl_4: δ1.20 (6H, *s*, Me-3 and Me-7), 1.80 (3H, *s*, Me-11), 1.60 (3H, *m*, H-4–H-6), 2.30 (1H, *d*, J = 7 Hz, H-8), 4.80 (1H, *br s*, H-12), 4.90 (1H, *dd*, J = 10, 2 Hz, H-1 *cis*), 5.11 (1H, *dd*, J = 17, 2 Hz, H-1 *trans*), 5.60 (1H, *dt*, J = 18, 7 Hz, H-9), 5.85 (1H, *dd*, J = 17, 10 Hz, H-2), 6.10 (1H, *d*, J = 18 Hz, H-10); MS m/z (rel. int.): 238 $[M]^+$ (14), 230 $[M-H_2O]^+$ (21), 205 $[220-Me]^+$ (10), 202 $[220-H_2O]^+$ (14), 187 (15), 152 (23), 149 (32), 131 (55), 119 (66), 109 (37), 107 (43), 93 (100), 91 (87), 85 (28).

REFERENCES

1. Zalkow, L. H., Brannon, D. R. and Uecke, J. W. (1964) *J. Org. Chem.* **29**, 2786.
2. Thomas, A. F. and Williams, B. (1964) *Tetrahedron Letters* 3775.
3. Bohlmann, F. and Zdero, C. (1973) *Ber.* **106**, 845.
4. Bohlmann, F., Bornowski, H. and Schonwsky, H. (1962) *Ber.* **95**, 1733.
5. Bohlmann, F. and Ardt, C. (1966) *Ber.* **99**, 135.
6. Bohlmann, F. and Zdero, C. (1968) *Ber.* **101**, 2062.
7. De Pascual-T., J., Bellido, I. S., González, M. S., Vicente, S. and De Dios, M. A. (1981) *Riv. Ital. Essenze, Profumi, Piarte Off. Aromi Saponj Cosmet.* **62**, 355.
8. Corey, E. J., Mitra, R. B. and Lledo, H. (1964) *J. Am. Chem. Soc.* **86**, 485.
9. Naves, Y. R. (1966), *Helv. Chim. Acta* **49**, 1029.
10. Wenninger, J. A., Yates, R. L. and Dolinsky, M. J. (1967) *J. Assoc. Off. Analyt. Chem.* **50**, 1313.
11. Andersen, N. H., Ohta, Y., Li, C. B., Kramer, C. M., Allison, K. and Huneck, S. (1977) *Phytochemistry* **16**, 1727.
12. Buchi, G., Greuter, F. and Tokoroyana, T. (1962) *Tetrahedron Letters* 827.
13. Ramaswami, D. K. and Bhattachariyya, S. C. (1962) *Tetrahedron* **18**, 575.
14. De Pascual-T., J., San Feliciano, A., Miguel del Corral, J. M. and Barrero, A. F. (1978) *An. Quim.* **74**, 680.
15. Kalsi, P. S., Kumar, K. S. and Wadia, M. S. (1971) *Chem. Ind.* 31.
16. Stoessl, A., Stothers, J. B. and Ward, E. W. B. (1975) *Can. J. Chem.* **53**, 3351.
17. McQuillin, F. J. and Parrack, J. D. (1956) *J. Chem. Soc.* 2973.
18. Frandadt, M., Grieder, A. and Ohloff, G. (1972) *Helv. Chim. Acta* **55**, 235.
19. Bowyer, R. C. and Jefferies, P. R. (1963) *Chem. Ind.* 1245.
20. Abe, H., Kawashima, T., Maruta, I., Kodama, H. and Ito, S. (1971) *Phytochemistry* **10**, 3330.
21. Vlad, P. and Soucek, M. (1962) *Collect. Czech. Chem. Commun.* **27**, 1726.
22. Herz, W., Bhat, S. V. and Santhanam, P. S. (1970) *Phytochemistry* **9**, 891.
23. Rowe, J. W., Ronald, R. C. and Nagassmpagi, A. (1972) *Phytochemistry* **11**, 365.
24. Barbier, C., Gagnaire, D. and Vottero, P. (1968) *Bull. Soc. Chim. Fr.* 2330.
25. Erickson, L. E. (1963) *J. Am. Chem. Soc.* **87**, 1867.
26. Kimland, B. and Norin, T. (1967) *Acta Chem. Scand.* **21**, 825.