Phytochemistry, Vol. 28, No. 9, pp. 2415–2418, 1989.
Printed in Great Britain.

0031-9422/89 $3.00 + 0.00

SESQUITERPENE LACTONES AND OTHER CONSTITUENTS FROM *CALEA PRUNIFOLIA* AND *C. PECKII*

V. CASTRO, G. TAMAYO-CASTILLO and J. JAKUPOVIC

Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, F.R.G.

(*Received* 16 *September* 1988)

Key Word Index—*Calea prunifolia*, *C. peckii*; Compositae, sesquiterpene lactones; eudesmanolides; guaianolides; heliangolides; bisabolene derivatives; aromatic compounds.

Abstract—A re-investigation of *Calea prunifolia* afforded, in addition to compounds reported previously, a new eudesmanolide, a costol acetate hydroperoxide and four aromatic compounds. *Calea peckii* gave a large variety of aromatic compounds, three new bisabolene derivatives, a further guaianolide and, in addition to a known one, a further heliangolide. The structures were elucidated by high field NMR techniques.

INTRODUCTION

From the large genus *Calea* (tribe Heliantheae, subtribe Neurolaeninae) many species have been studied chemically especially by N. H. Fischer and his group [1 and refs cited therein). Most species contain heliangolides and/or furoheliangolides with an 8β-acyloxy group. However, there are several species which contain other sesquiterpene lactones or other constituents. Previous studies of *C. prunifolia* H. B. K. gave no lactones [2]. We have now reinvestigated material collected at different stages of growth and a further species, *C. peckii* Rob. Both species are from Costa Rica. The results are discussed in this paper.

RESULTS AND DISCUSSION

The aerial parts of *C. prunifolia* collected in May 1986 gave in addition to compounds reported previously [2] the benzofuranes **2** [2] and **6** [3], the prenyl phenol **17**, the lactone **4** [4], the sesquiterpene lactones **19** [5], **20** [6] and **21** [7] as well as the unusual dibenzofurane **16**. From the extract of a second collection made in August 1986 the aerial parts gave in addition to lactone **5**, the aldehyde **8** and the costol derivative **23**.

The structure of **2** has been studied again to establish the position of the methoxy groups. As one methoxy group showed a NOE effect with the low field singlet at δ6.68 while another showed an effect with the singlet at δ6.77 a 4,5,6-trimethoxy derivative was present.

The ^{1}H NMR spectrum of **17** (Experimental) indicated that a substituted hydroquinone methyl ether was present. The nature of the substituents was easily deduced from the typical signals of a senecioyl group and the relative position followed from the presence of a hydrogen bonded hydroxy group.

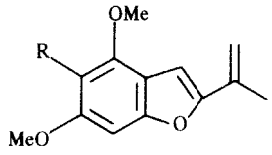
The molecular formula ($C_{22}H_{20}O_4$) and the ^{1}H and the ^{13}C NMR spectrum of **16** indicated a polycyclic aromatic compound with two methoxy, two methyl and one hydroxy group (Experimental). The relative positions of the substituents and the arrangement of the rings were determined by spin decoupling and the observed NOE's. Clear effects were obtained between H-1, H-15 and one methoxy group, between H-4 and the other methoxy group, between 11-OH, H-7 and H-12, between H-17 and H-6 as well as between H-16, H-12 and H-14. It is likely that compound **16**, which we have named caleprunifolin, is formed by a Diels–Alder reaction of 4-desmethoxy **2** with an 8,9-dehydrothymol derivative followed by oxidative elimination of C-10 from the thymol moiety.

The structure of **5** followed from the spectral data which were close to those of **4** [4]. A NOE between H-5, OMe (δ3.25) and H-13 established the positions of the methoxy groups. Obviously this lactone was formed by oxidation of **2**. Similarly, the ^{1}H NMR spectrum of **8** (Experimental) indicated that a trimethoxy derivative of salicylaldehyde was present. A NOE between the methoxy group (δ4.04), H-7 and OMe (δ3.79) as well as between the third methoxy group and H-6 established the relative position of the substituents.

The ^{1}H NMR spectral data of **23** (Experimental) were in part similar to those of costol acetate. However, spin decoupling indicated that H-5 was missing. A broadened singlet at δ7.47 required a hydroperoxide group which had to be placed at C-5. Comparison of the chemical shifts with those of costol acetate showed that a 5α-hydroperoxide was most likely.

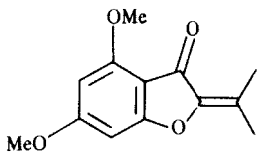
The aerial parts of *C. peckii* afforded in addition to widespread compounds (Experimental) the benzofuranes **3**, **6** [8] and **7** [8], the chromene derivatives **9**–**15** [9–13], the bisabolene derivatives **24**–**26** and **27** [14], the guaianolides **28**, **29** [15] and **30** [15] and the heliangolides **31** and **32** [15]. The structure of **3** followed from its ^{1}H NMR spectrum (Experimental) which was similar to that of **4**. As expected, the presence of a keto group at C-3 caused some shift differences.

The structures of **24** and **25** followed from their ^{1}H NMR spectra (Table 1) which were in part similar to those of 1α- and 1β-hydroxybisabolene [16]. As followed from the couplings of H-1 the ketones only differed in the configuration at C-1. Inspection of models indicated, as pointed out previously [16], that the isomer **24** should be that with the broadened doublet for H-1. The absolute

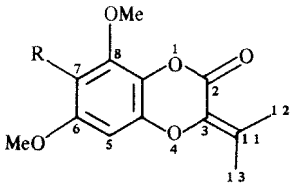


1 **2**

R H OMe

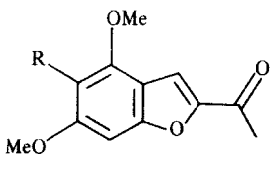


3



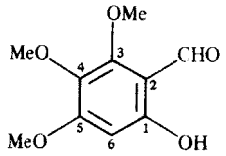
4 **5**

R H OMe

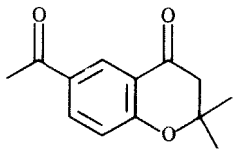


6 **7**

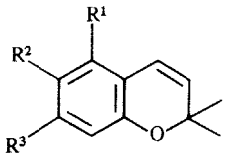
R H OMe



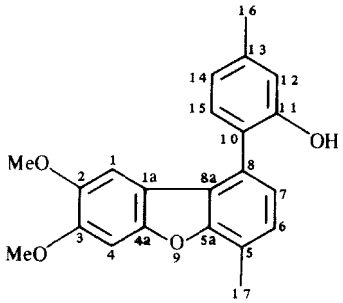
8



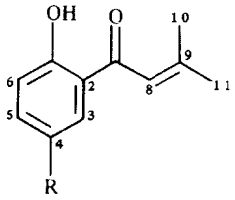
15



	9	**10**	**11**	**12**	**13**	**14**
R^1	OMe	H	H	OMe	H	H
R^2	H	CHMe(OMe)	COMe	OMe	OMe	$COCH_2OH$
R^3	OMe	OMe	OH	OMe	OMe	H

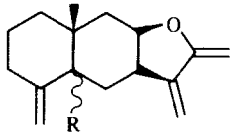


16



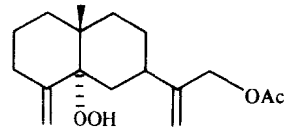
17 **18**

R OMe CH(OH)Me

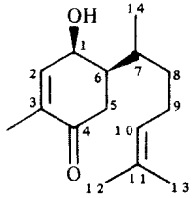


19 **20** **21** **22**

R αOH αOOH βOH βOOH

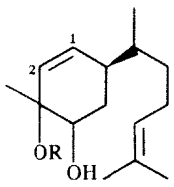


23



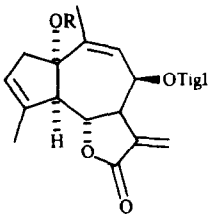
24 **25**

1αOH

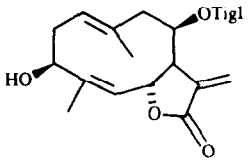


26 **27**

R Me H



	28	29	30
R	OH	H	H
			$\Delta^{10(14)}$



31

32 1β-10α epoxide

Table 1. ^{1}H NMR spectral data of compounds **24**–**26** ($CDCl_3$, 400 MHz, δ-values)

H	24	25	26
1	4.36 *br d*	4.43 *br dd*	5.75 *dd*
2	6.67 *dq*	6.76 *dq*	5.59 *dd*
4	—	—	3.89 *br d*
5	2.40 *dd*	2.52 *dd*	1.88 *ddd*
5′	2.12 *dd*	2.44 *dd*	1.65 *br dd*
6	2.2–2.0 *m*	1.80 *dddd*	2.26 *br m*
7	1.6 *m*	1.67 *m*	1.6 *m*
8	1.28 *dt*	1.59 *m* 1.20 *m*	1.41 *m* 1.25 *m*
9	2.2–2.0 *m*	2.05 *m* 1.95 *m*	2.1–1.9 *m*
10	5.08 *tqq*	5.11 *tqq*	5.90 *br t*
12	1.68 *br s*	1.69 *br s*	1.68 *br s*
13	1.59 *br s*	1.61 *br s*	1.60 *br s*
14	0.88 *d*	0.96 *d*	0.87 *d*
15	1.78 *dd*	1.81 *br s*	1.24 *s*
OMe	—	—	3.23 *s*

J[Hz]: compound **24**: 1,2 = 1,15 = 2,15 = 10,12 = 10,13 ~ 1.5; 1,6 = 9.5; 5,5′ = 15; 5,6 = 3; 5′,6 = 14; 7,14 = 9,10 = 7; compound **25**: 1,2 = 5; 1,6 = 3; compound **26**: 1,2 = 10; 1,6 = 3.5; 2,6 = 2; 4,5 = 4.5; 5,5′ = 13.5; 5,6 = 6.5; 9,10 = 11.5.

configuration is not known, the proposed one is that of bisabolone from Compositae [17]. The structure of **26** clearly followed from the comparison of the ^{1}H NMR data with those of **27** [14].

The structure of **28** was readily deduced from a comparison of the ^{1}H NMR data (Table 2) with those of **29** [15]. The presence of a hydroperoxide group followed from the singlet at δ7.69 and a NOE between the latter and H-5 supported the configuration. Similarly the ^{1}H NMR data (Table 2) of **31** were close to those of **32** [15]. Spin decoupling allowed the assignment of all signals. The couplings and the chemical shifts indicated that a heliangolide with 3β and 8β oxygen functions was present. The relative position of the ester group followed from the chemical shift of H-8.

Table 2. ^{1}H NMR spectral data of compounds **28** and **31** (400 MHz, $CDCl_3$, δ-values)

H	28	31
1	—	5.19 *m*
2	2.66 *br d*	2.69 *ddd*
2′	2.54 *br d*	2.22 *dddq*
3	5.46 *br s*	4.51 *br dd*
5	3.33 *br d*	5.25 *dq*
6	4.51 *dd*	6.34 *dd*
7	3.48 *dddd*	2.92 *dddd*
8	5.87 *br dd*	5.25 *ddd*
9 9′	5.82 *dq*	2.77 *br dd* 2.39 *br dd*
13	6.31 *d*	6.33 *d*
13′	5.54 *d*	5.70 *d*
14	1.92 *br s*	1.78 *dd*
15	1.98 *br s*	1.74 *d*
OCOR	6.72 *qq*	6.82 *qq*
	1.76 *br d*	1.76 *dq*
	1.75 *br s*	1.79 *dq*

J[Hz]: compound **28**: 2,2′ = 17; 5,6 = 11; 6,7 = 9; 7,8 = 7,13 = 3; 8,9 = 6; 3′,4′ = 7; compound **31**: 1,2 = 9; 1,2′ = 7; 1,14 = 2′, 14 = 1; 2,2′ = 14; 2,3 = 2′,3 = 3; 5,6 = 10; 5,15 = 6,7 = 7,8 ~ 1.5; 7,13 = 2.5; 7,13′ = 2; 8,9 = 3.5; 8,9′ = 3; 9,9′ = 14.5.

EXPERIMENTAL

Extraction and separation was carried out as reported previously [18]. Only the conditions of the final separation are presented below. The extract of *C. prunifolia* (100 g, collected in May 1986 in San Isidro del General, Costa Rica, voucher 125939, deposited in the Univ. of Costa Rica) gave in addition to compounds reported previously [2] 2 mg **17** (TLC: Et_2O–petrol, 1:2, R_f 0.52), 2 mg **2** (TLC: same solvent, R_f 0.48), 2 mg **4**, 40 mg **19**, 1 mg **6**, 4 mg **16** (TLC: Et_2O–petrol, 1:2, R_f 0.40), 10 mg **20**, 4.5 mg **21** and 115 mg **22**. A further collection made in August 1987 (2 kg) gave in addition 1 mg **5** (HPLC, RP 8, MeOH–H_2O, 1:1), 1 mg **23** (HPLC, RP 8, MeOH–H_2O, 17:3) and 115 mg **8** (HPLC, RP 8, MeOH–H_2O, 4:1).

The extract of *C. peckii* (1.6 kg aerial parts, collected in March 1988 in Limon, Costa Rica, voucher C.R. 126609, deposited in the Univ. of Costa Rica) gave 160 mg zingiberene, 90 mg α-curcumene, 10 mg **4**, 70 mg **10**, 1 mg tocopherol, 20 mg lupeyl-acetate, 10 mg **11**, 4 mg **12**, 700 mg **13**, 300 mg **9**, 1 mg **6**, 40 mg **15**, 2 mg **14**, 2 mg **18**, 2 mg **24** (HPLC, RP 8, MeOH–H_2O, 4:1, R_t 7.0 min), 2 mg **25** (same cond., R_t 8.5 min), 5 mg 9-hydroxy-dehydrothymol, 1.2 mg **28** (same cond., R_t 7.0 min), 2 mg **26** (same cond., R_t 10.0 min), 1 mg **29**, 1 mg **30**, 5 mg **31** (HPLC, RP 8, MeOH–H_2O, 4:1, R_t 4.0 min), 1 mg **7**, 2 mg **3** (HPLC, R_f 8, MeOH–H_2O, 4:1, R_t 8.0 min), 1 mg **27** and 1 mg **32**. Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material.

4,6-Dimethoxy-2-isopropylidene-3-oxo-2,3-dihydrobenzofurane (**3**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1620 (PhCOC=C); MS *m/z* (rel. int.): 234.089 [M]$^+$ (100) (calc. for $C_{13}H_{14}O_4$: 234.089), 219 [M − Me]$^+$ (14), 216 (36), 215 (32), 205 (10), 201 (11); ^{1}H NMR ($CDCl_3$): δ 6.02 (*d*, H-5), 6.22 (*d*, H-7), 2.32 (*s*, H-9), 2.03 (*s*, H-10), 3.91 and 3.87 (*s*, OMe); *J* [Hz]: 5,7 = 2.

7-Methoxycaleteucrin (**5**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750 (lactone); MS *m/z* (rel. int.): 280.095 $[M]^+$ (100) (calc. for $C_{14}H_{16}O_6$: 280.095), 265 $[M-Me]^+$ (94), 237 $[265-CO]^+$ (10); ^1H NMR (C_6D_6): δ6.17 (*s*, H-5), 2.12 (*s*, H-13), 1.70 (*s*, H-14), 3.80, 3.75, 3.25 (*s*, OMe); NOE: H-5 with H-14 and OMe (δ3.25).

3,4,5-Trimethoxysalicylaldehyde (**8**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500–2700, 1635, 1600 (*O*-hydroxyaldehyde); MS *m/z* (rel. int.): 212.068 $[M]^+$ (100) (calc. for $C_{10}H_{12}O_5$: 212.068), 197 $[M-Me]^+$ (88), 169 $[197-CO]^+$ (40), 137 $[169-MeOH]^+$ (34); ^1H NMR ($CDCl_3$): δ6.14 (*s*, H-6), 10.05 (*s*, H-7), 12.10 (*s*, OH), 4.04, 3.90, 3.79 (*s*, OMe); NOE: OMe (δ3.90) with H-6; OMe (δ4.04) with OMe (δ3.79) and H-7.

Caleprunifolin (**16**). Colourless gum; MS *m/z* (rel. int.): 348.136 $[M]^+$ (100) (calc. for $C_{22}H_{20}O_4$: 348.136), 333 $[M-Me]^+$ (7), 301 $[333-MeOH]^+$ (14), 273 $[301-CO]^+$ (3); ^1H NMR ($CDCl_3$): δ6.74 (*s*, H-1), 7.14 (*s*, H-4), 7.25 (*d*, H-6), 7.16 (*d*, H-7), 6.93 (*br s*, H-12), 6.89 (*br d*, H-14), 7.26 (*br d*, H-15), 2.43 (*s*, H-16), 2.63 (*s*, H-17), 3.69, 3.96 (*s*, OMe), 5.04 (*s*, OH); *J* [Hz]: 6,7 = 14,15 = 7.5; NOE: H-1 with H-15 and OMe (δ3.69), H-4 with OMe (δ3.96); OH with H-1, H-7 and H-12; H-16 with H-12 and H-14; H-17 with H-6; ^{13}C NMR ($CDCl_3$, C-1–C-8): δ103.9, 145.7, 149.8, 95.2, 122.7, 130.4, 124.2, 140.0; C-1a, 4a, 5a, 8a: δ115.2 151.2, 155.3, 122.8; C-10–C-17: 121.5, 152.8, 116.0, 127.1, 121.4, 127.0, 21.4, 15.2; OMe: 56.2, 56.1 (some signals may be interchangeable).

2-Senecioyl-hydroxyquinone-4-O-methyl ether (**17**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500–2700, 1650, 1590 (*O*-hydroxyketone); MS *m/z* (rel. int.): 206.094 $[M]^+$ (15) (calc. for $C_{12}H_{14}O_3$: 206.094), 191 $[M-Me]^+$ (100), 151 $[M-C_4H_7]^+$ (23), 123 $[151-CO]^+$ (10); ^1H NMR ($CDCl_3$): δ7.72 (*br s*, H-3), 7.08 (*dd*, H-5), 6.93 (*d*, H-6), 6.73 (*br s*, H-8), 2.21 (*d*, H-10), 2.06 (*d*, H-11), 3.81 (*s*, OMe), 12.35 (*s*, OH); *J* [Hz]: 3,5 = 2; 5,6 = 8; 8,10 = 8,11 = 1.

5α-Hydroperoxy-costol acetate (**23**). Colourless oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (OH), 1720 (OAc); MS *m/z* (rel. int.): 278.188 $[M-O]^+$ (9) (calc. for $C_{17}H_{26}O_3$), 261 $[M-HO_2]^+$ (8), 201 $[261-HOAc]^+$ (36), 95 (100); ^1H NMR ($CDCl_3$): δ1.83 (*ddd*, H-1α), 1.03 (*br d*, H-1β), 1.65 (*m*, H-2), 2.50 (*m*, H-3α, H-7), 2.20 (*m*, H-3β, H-6α), 1.45 (*dd*, H-6β), 1.55 (*m*, H-8), 1.75 (*m*, H-9α), 1.22 (*dt*, H-9β), 4, 85 and 4.47 (*br d*, H-12), 5.11 and 5.05 (*br s*, H-13), 0.94 (*s*, H-14), 5.05 and 4.73 (*br s*, H-15); *J* [Hz]: 1α,1β = 1α,2β = 13; 1α,2α = 7; 6α,6β = 6β, 7 ~ 13; 8α,9β = 8β,9β = 3.5; 9α,9β = 12,12′ = 13.

1β-Hydroxy-Bisabola-2,10-dien-4-one (**24**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1680 (C=CC=O); MS *m/z* (rel. int.): 236.178 $[M]^+$ (18) (calc. for $C_{15}H_{24}O_2$: 236.178), 218 $[M-H_2O]^+$ (10), 189 (70), 136 (38), 125 (56), 109 (58), 69 (100); $[\alpha]_D^{24°}$ + 33 ($CHCl_3$; *c* 0.2).

1α-Hydroxy-Bisabola-2,10-dien-4-one (**25**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1685 (C=CC=O); MS *m/z* (rel. int.): 236.178 $[M]^+$ (12) (calc. for $C_{15}H_{24}O_2$: 236.178), 218 $[M-H_2O]^+$ (16), 203 $[218-Me]^+$ (6), 136 (52), 109 (100), 69 (62); $[\alpha]_D^{24°}$ −27 ($CHCl_3$; *c* 0.37).

4-Hydroxy-3-methoxybisabola-1,10-diene (**26**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); MS *m/z* (rel. int.): 252.209 $[M]^+$ (4.5) (calc. for $C_{16}H_{28}O_2$: 252.209), 220 $[M-MeOH]^+$ (9), 205 $[220-Me]^+$ (8), 125 (96), 71 (100), 69 (95).

1α-Hydroperoxy-8β-tigloyloxyguaia-3,9,11(13)-trien-12,6α-olide (**28**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3530 (OOH), 1775 (γ-lactone), 1710 (C=CCO$_2$R); MS *m/z* (rel. int.): 343.155 $[M-OH]^+$ (8) (calc. for $C_{20}H_{23}O_5$: 343.155), 337 $[M-OOH]^+$ (0.3), 227 $[327-RCO_2H]^+$ (6), 83 $[RCO]^+$ (100), 55 $[83-CO]^+$ (62).

3β-Hydroxy-8β-tigloyloxyheliangolide (**31**). Colourless gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH), 1770 (γ-lactone), 1710 (C=CCO$_2$R); MS *m/z* (rel. int.): 246.126 $[M-RCO_2H]^+$ (6) (calc. for $C_{15}H_{18}O_3$: 246.126), 228 $[246-H_2O]^+$ (8), 83 $[RCO]^+$ (100), 55 $[83-CO]^+$ (76); $[\alpha]_D^{24°}$ −79 ($CHCl_3$; *c* 0.43).

Acknowledgements—We wish to thank the Deutscher Akademischer Austauschdienst for financial support and Mr Bot. Luis Poveda for the identification of plant material.

REFERENCES

1. Ober, A. G., Fronczek, F. R. and Fischer, N. H. (1987) *Phytochemistry* **26**, 604.
2. Castro, V., Jakupovic, J. and Bohlmann, F. (1984) *J. Nat. Prod.* **47**, 802.
3. Ober, A. G., Fronczek, F. R. and Fischer, N. H. (1985) *J. Nat. Prod.* **48**, 242.
4. Bohlmann, F. and Jakupovic, J. (1974) *Phytochemistry* **18**, 119.
5. Benesova, V., Herout, V. and Sorm, F. (1961) *Coll. Czech. Chem. Comm.* **26**, 1350.
6. Appendino, G., Garriboldi, P. and Nono, G. M. (1982) *Phytochemistry* **21**, 2767.
7. del Castillo, J. D., Ferrero, M. T. M., Luis, F. R., Obis, J. C. R. and Bueno, P. V. (1984) *Rev. Latinoam. Quim.* **15**, 96.
8. Burke, J. M., Stevenson, R. (1986) *J. Nat. Prod.* **49**, 522.
9. Alertsen, R. (1961) *Acta Polytech. Scand.* Ser 13, No 10, 1.
10. Bohlmann, F. and Grenz, M. (1977) *Chem. Ber.* **110**, 295.
11. Bjeldanes, L. F. and Geissman, T. (1971) *Phytochemistry* **10**, 1079.
12. Bohlmann, F., Gupta, R., Jakupovic, J., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 2899.
13. Bohlmann, F. and Le Van, N. (1978) *Phytochemistry* **17**, 1173.
14. Zdero, C., Bohlmann, F. and Scott, R. (1987) *Phytochemistry* **26**, 1999.
15. Ober, A. G., Urbatsch, L. and Fischer, N. H. (1985) *Phytochemistry* **24**, 795.
16. Bohlmann, F., Tsankova, E. and Jakupovic, J. (1984) *Phytochemistry* **23**, 1103.
17. Müller, F. (1981) Dissertation, University of Dortmund.
18. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1979.