Phytochemistry, Vol 25, No 5, pp 1175–1178, 1986.
Printed in Great Britain

0031-9422/86 $3.00 + 0.00

DIMERIC GUAIANOLIDES AND OTHER CONSTITUENTS FROM *GOCHNATIA* SPECIES

FERDINAND BOHLMANN, CHRISTA ZDERO, GUILLERMO SCHMEDA-HIRSCHMANN, JASMIN JAKUPOVIC, XORGE A. DOMINGUEZ*, ROBERT M. KING† and HAROLD ROBINSON†

Institute for Organic Chemistry, Technical University of Berlin, D-1000 Berlin 12, West Germany; *Departamento de Quimica, I.T.E.S.M., Monterrey, Mexico; †Smithsonian Institution, Department of Botany, Washington, DC 20560, U.S.A.

(*Revised received* 1 *August* 1985)

Key Word Index—*Gochnatia polymorpha*; *G. hypoleuca*; Compositae; sesquiterpene lactones; dimeric guaianolides; germacranolides; bisabolene derivatives.

Abstract—The roots of *Gochnatia polymorpha* afforded two new bisabolene derivatives and four dimeric guaianolides, two of them being isolated previously from *G. paniculata*. The aerial parts gave two further dimeric guaianolides. The aerial parts of *G. hypoleuca* afforded three new germacran-8,12-olides, a germacranolide acid and four additional dimeric guaianolides, which may be characteristic for this genus, while the presence of oxygenated germacranolides seems to be typical for the whole subtribe.

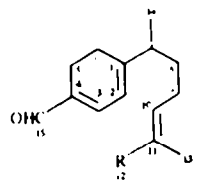
INTRODUCTION

The large genus *Gochnatia* (Compositae, tribe Mutisieae, subtribe Gochnatiinae) is concentrated in the Tropical Andes and Brazil, but also distributed in Mexico and Southern U.S.A. Two species are present in South Eastern Asia [1]. So far six species have been investigated chemically [2–6]. In addition to triterpenes [2, 3] and bisabolene derivatives [5, 6] several sesquiterpene lactones were isolated [3–6] including germacranolides, guaianolides and unusual dimeric guaianolides. We now have studied a further species, *G. polymorpha* (Less.) Cabrera and reinvestigated *G. hypoleuca* (DC.) A. Gray. The results are discussed in this paper.

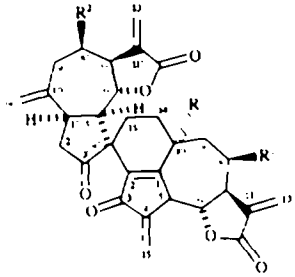
RESULTS AND DISCUSSION

The roots of *G. polymorpha* afforded the bisabolene derivatives nuciferal [7], 15-oxo-nuciferal [5], **1**, **2**, 13-oxo-bisabol-1-one [8], costunolide, dehydrocostus lactone [9] as well as the dimeric guaianolides **3**, **5** [5], **7** [5] and **8**, while the aerial parts gave costunolide, 15-oxonuciferal, **2** and **3**–**8**. The structures of **1** and **2** followed from the ^{1}H NMR spectra (Table 1). If compared with the spectra of nuciferal and 15-oxonuciferal the signals of the aromatic protons were replaced by pairs of broadened doublets for both compounds and the signals of the side chain differed in the expected way.

The structure of **3** followed from the molecular formula ($C_{30}H_{30}O_6$), the ^{1}H NMR (Table 2) and the ^{13}C NMR spectrum (Table 3). The ^{1}H NMR spectral data were close to those of the dimeric guaianolide gochnatiolide A (**5**) [5]. Therefore **3** was proposed to be the 10-desoxy derivative of **5** as the molecular formula showed that **3** had one oxygen less. Careful spin decoupling allowed the assignment of all ^{1}H NMR signals of **3**. As the broadened three-fold doublet at δ2.71 could be assigned to H-10 the proposed difference between **3** and **5** was established. The couplings of H-10 indicated a 10α-proton. Inspection of models showed that a boat-like conformation of the seven-membered ring would be in agreement with the large coupling observed for $J_{9\beta,10\alpha}$ and with the ^{13}C NMR signals of C-7 and C-10, which were at higher fields when compared with the shifts of **9** (see below). This shielding effect can be deduced from a model. By NOE difference spectroscopy, the stereochemistry could be established. Clear NOEs were observed between H-5 and H-7 and H-10, between H-10 and H-5, H-7, H-14$_1$ and H-



1 R = Me
2 R = CHO



	3	4	5	6	7*	8†	9	10	11	12
R	αH	αH	αOH	αOH	αH	αH	βH	βH	βH	βH
R¹	H	OH	H	OH	H	H	H	H	OH	OH
R²	H	H	H	H	H	H	H	OH	H	OH

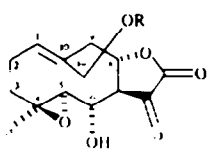
* 2α OH 1,10-dehydro
† 11,13H 11,13'H

14_2, between H-8β and H-6, between H-7 and H-8' and H-15', H-8'β and H-15'α, between H-7' and H-5', H-8_1', H-9_1' and H-1' as well as between H-9'α and H-1 and H-7'. A model shows that these results required the proposed configuration at C-4' and at C-10.

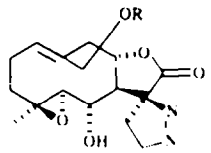
In the ^{1}H NMR spectrum of **4** a broadened low field double doublet at δ4.21 was that of H-8 as could be shown by spin decoupling. The β-orientation followed from the couplings of H-8. The ^{13}C NMR of **4** (Table 3) also supported this assumption as a new low field doublet at δ70.5 was accompanied by downfield shifts of the signals of C-7 and C-9 while the chemical shifts of the other carbons were nearly identical with those of **3**.

In the ^{1}H NMR spectrum of **6** (Table 2) again the downfield shift of the H-8 signal indicated a 8-hydroxyl group. The absence of a H-10 signal and the additional low field singlet in the ^{13}C NMR spectrum (Table 3) at δ71.8 together with a downfield shift of the C-14 signal showed that a 10-hydroxyl group was present. As the remaining ^{1}H NMR signals, except that of H-7 which was deshielded by the 10α-hydroxyl group, as well as the ^{13}C NMR signals were nearly the same as those of **3**, the stereochemistries obviously were identical in both lactones.

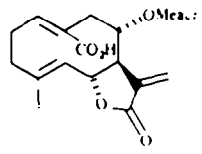
The ^{1}H NMR spectrum of **8** (Table 2) clearly differed from those of **3–6**. Though the molecular formula together with a γ-lactone band in the IR again indicated the presence of a dimeric sesquiterpene lactone ($C_{30}H_{34}O_6$), the ^{1}H NMR spectrum showed no signals of a methylene lactone. However, from a methyl doublet at δ1.16 (6H) the presence of a bis-11,13-dihydro derivative was proposed. Spin decoupling indeed led to sequences requiring H-11 protons which showed a 7 Hz coupling with H-7. Accordingly, 11β-methyl groups were present. All data therefore agreed with the structure of a bis-11α,13-dihydro derivative of **5**.



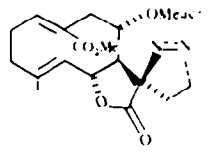
13 R = Meac
15 R = Tig
17 R = iBu



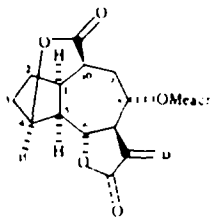
14 R = Meac
16 R = Tigl



18



19



20

The aerial parts of *Gochnatia hypoleuca* (DC.) A. Gray were studied previously but only triterpenes were isolated [2]. We now have reinvestigated this species. The aerial parts gave in addition to triterpenes dehydrocostus lactone, the dimeric guaianolides **9–12** and the germacranolides **13**, **15**, **17** and **18**.

The molecular formula of **9** indicated that this compound was most likely an isomer of **3**. If the ^{1}H and ^{13}C NMR spectra (Tables 2 and 3) were compared, it was obvious that again a dimeric guaianolide was present, which only differed from **3** by the stereochemistry. Careful spin decoupling with **9**, especially in deuterobenzene, allowed the assignment of all proton signals leading to sequences which were identical with those of **3**. A clear difference was seen for the H-10 signal which showed in the spectrum of **9** (Table 2) two large couplings while the chemical shift indicated that H-10 was more deshielded in **3**. Comparison of the ^{13}C NMR spectral data of **9** with those of **3** (Table 3) further showed especially differences in the chemical shifts of C-7, C-10 and C-15'. These agreed with the proposed changed configuration at C-10 as models showed that now no pressing effect between C-7 and C-10 and no γ-effect between C-9 and C-15' should be present. Also the changed couplings of H-10 supported the configuration and indicated that H-9α, H-10β and H-14α were in a *trans,trans*-diaxial conformation. NOE difference spectroscopy further established the configuration. Clear NOEs were observed between H-7 and H-5 and H-9α, between H-10 and H-6, H-8β, H-9β, H-14β and H-15β, between H-5' and H-7' and H-2'α, between H-6' and H-8'β, H-14α and H-15'α, between H-8β and H-6 and H-10, between H-9α and H-7 and between H-9β and H-10.

If the spectral data of **10** were compared with those of **9** it was obvious that a β-hydroxyl group was at C-8'. Accordingly the ^{13}C NMR signals of **10** only differed from those of **9** in the chemical shifts of C-6' C-10'. The broadened singlet at δ4.46 in the ^{1}H NMR spectrum of **10** was coupled with a pair of double doublets at δ2.69 and 2.47 as well as with H-7'. The latter signal could be distinguished from that of H-7 by spin decoupling, especially as a clear assignment of H-5 was possible. This signal was shifted downfield due to its double allylic position and the coupling $J_{1,5}$ was missing, while the H-5' signal was a clear double doublet. All other signals also could be assigned in this way. A few overlapped signals could be separated by addition of deuteriobenzene.

The spectral data of **11**, again together with systematic spin decoupling and NOE difference spectroscopy, led to the proposed structure. Comparison of the ^{13}C NMR signals (Table 3) with those of **9** and **10** showed that in **11** a 8β-hydroxy group was present. Accordingly, the signals of C-7–C-9 were shifted downfield, while that of C-10 was shifted upfield due to the γ-effect of the 8β-hydroxyl group. All the other signals of **11** were nearly identical with those of **9**. Furthermore clear NOEs were present between H-5 and H-7, H-6 and H-10, between H-8α and H-13_2, between H-14_2' and H-2β', between H-6' and H-15'α and H-8'β as well as between H-8'β and H-7'.

Compound **12** was isolated in minute amounts. However, the molecular formula ($C_{30}H_{30}O_8$) and the ^{1}H NMR spectrum (Table 2) allowed the assignment of the structure. The ^{1}H NMR signals of one part of the dimer corresponded to those of **10** while those of the second part agree with those of **11**. As the couplings in **12** were the same as in **10** and **11** the stereochemistry also was clear.

Obviously all dimers (**3**–**12**) are formed by cycloaddition of zaluzanin C with 1,2-dehydrozaluzanin C or with the corresponding lactones with a 8β-hydroxy group. These Diels Alder-like additions would lead first to dimers with a 1,10-double bond, which only is present in **7**, where, however, a hydroxyl group was introduced by allylic oxidation. In all the other dimers the double bond had shifted to the 1,2-position leading to the two series with a 10α-H (**3**, **4**, **7** and **8**) and with a 10β-H (**9**–**12**).

The structures of **13**, **15** and **17** followed from the ^{1}H NMR spectra and from those of the corresponding pyrazolines **14** and **16** obtained by addition of diazomethane (Table 4). The signals in the spectra of **13**, **15** and **17** were extremely broad. Accordingly, only the nature of the ester groups could be deduced from these data. The similarity with the spectrum of a corresponding acetate, which was isolated from a *Schistostephium* species [10] was an indication that the new lactones may differ only in the nature of the ester groups. The pyrazolines **14** and **16** gave clear ^{1}H NMR spectra (Table 4) which allowed the assignment of all signals by spin decoupling. The chemical shifts and couplings nicely agreed with those of the pyrazoline of corresponding acetate [10]. Due to the addition of diazomethane from the β-face the signals of H-6 and H-8 were shifted downfield by the azo group and that of H-7 was not influenced. The remaining configurations already were assigned in the case of the acetate [10] and as the couplings in **14** and **16** were identical the whole stereochemistry of the new lactones were settled.

The last lactone **18** gave a very poorly resolved ^{1}H NMR spectrum (Table 4). However, again addition of diazomethane led to a pyrazoline (**19**). Its clear ^{1}H NMR spectrum (Table 4) allowed the assignment of all signals by spin decoupling and the presence of an acid group in **18** followed from the methyl ester group in the reaction product. The downfield shifts of H-6 and H-8 again indicated an attack of diazomethane from the β-face. The couplings observed led to the proposed stereochemistry thus indicating that **18** corresponds to an angelate which was isolated from *Gochnatia vernonioides* [6]. In the latter case heating of the angelate gave an interesting dilactone. For a final proof **18** was heated in benzene at 200°. Again only one product was obtained, the dilactone **20**. All ^{1}H NMR spectral data were similar to those of the corresponding angelate [6] except those of the ester part. As the stereochemistry of the angelate was established by careful NOE difference spectroscopy, the configuration of **20** also was settled.

Though the number of species investigated chemically are limited, the general picture indicates that sesquiterpene lactones are widespread in the subtribe Gochnatiinae. For *Gochnatia* itself, which is the largest genus of this group, dimeric guaianolides and germacranolides with oxidation at C-14 seem to be characteristic. A surprising feature is the fact that in this genus the 8,12-germacranolides predominate, but of forms with C-14 oxygenated to an aldehyde or acid group, only 6,12-lactones have been isolated so far. Oxygenated germacranolides are also typical from *Dicoma* species [11–13] and some other genera placed in the Gochnatiinae [14–17]. From the two genera *Pleiotaxis* and *Pertya* guaianolides related to dehydrocostuslactone are reported [18, 19]. The subtribe Gochnatiinae is suggested to be the oldest with *Gochnatia* as the basic genus [20]. The chemistry differs characteristically from that of the other three subtribes, where so far no common sesquiterpene lactones were reported. This may be an indication that the ability to produce sesquiterpene lactones, which surely is a general feature for the Compositae, can be lost during evolution.

EXPERIMENTAL

The air dried plant material was worked-up in the usual fashion [21]. *Gochnatia polymorpha* was collected in Paraguay

Table 5.* Infra-red and mass spectral data for compounds **1**–**4**, **6**, and **8**–**19**

	IR (CCl_4)	MS
1	2720, 1690, 1680	218.167 [M]$^+$ (46) ($C_{15}H_{22}O$), 119 (100)
2	2710, 1690	232.146 [M]$^+$ (12) ($C_{15}H_{20}O_2$), 107 (100)
3	1770, 1740, 1690†	486.204 [M]$^+$ (43) ($C_{20}H_{38}O_6$), 55 (100)
4	3610, 1770, 1740, 1690†	502.199 [M]$^+$ (22) ($C_{30}H_{30}O_7$), 55 (100)
6	3480, 1760, 1740, 1690†	518.194 [M]$^+$ (2) ($C_{30}H_{30}O_8$), 55 (100)
8	1770, 1740, 1690†	490.236 [M]$^+$ (22) ($C_{30}H_{34}O_6$), 55 (100)
9	1760, 1720, 1685†	486.204 [M]$^+$ (100) ($C_{30}H_{30}O_6$)
10	3600, 1770, 1740, 1695†	502.199 [M]$^+$ (54) ($C_{30}H_{30}O_7$), 55 (100)
11	3580, 1770, 1735, 1690†	502.199 [M]$^+$ (58) ($C_{30}H_{30}O_7$), 55 (100)
12	3600, 1770, 1690	518.194 [M]$^+$ (100) ($C_{30}H_{30}O_8$)
13	3560, 1780, 1725	348.157 [M]$^+$ (0.5) ($C_{19}H_{24}O_6$), 69 [C_3H_5CO]$^+$ (100)
14	3560, 1775, 1720†	362 [M − N_2]$^+$ (0.5), 69 [C_3H_5CO]$^+$ (100)
15	3560, 1775, 1720	362.173 [M]$^+$ (0.5) ($C_{20}H_{26}O_5$), 83 [C_4H_7CO]$^+$ (100)
16	3560, 1775, 1715†	376 [M − N_2]$^+$ (2), 83 [C_4H_7CO]$^+$ (100)
17	3560, 1775, 1735	350.173 [M]$^+$ (0.5), 71 [C_3H_7CO]$^+$ (100)
18	3600 2700, 1710, 1775, 1720	346.142 [M]$^+$ (0.3) ($C_{19}H_{22}O_6$), 69 [C_3H_5CO]$^+$ (100)
19	1770, 1720†	402 [M]$^+$ (1) ($C_{21}H_{26}N_2O_6$), 69 [C_3H_5CO]$^+$ (100)

*NMR data (Tables 1–4) are deposited in the National Data Bank and copies may be obtained from the Editorial Office of the Journal at Reading.

†In $CHCl_3$.

(voucher deposited in the U.S. National Herbarium). CC fractions (SiO_2) of the extract of the roots (1 kg) were as follows: 1 (petrol), 2 (Et_2O–petrol, 1:10), 3 (C_6H_6–CH_2Cl_2, 1:1), 4 (Et_2O–C_6H_6–CH_2Cl_2, 1:5:5), 5 (Et_2O–C_6H_6–CH_2Cl_2, 1:1:1) and 6 (Et_2O–MeOH, 5:1). Fraction 1 gave nothing of interest. TLC (SiO_2, PF 254) of fraction 2 (Et_2O–petrol, 1:10) gave 3 mg nuciferal (R_f 0.57) and TLC of fraction 3 (Et_2O–petrol, 1:4, two developments) afforded a mixture (R_f 0.6). Repeated TLC (Et_2O–C_6H_6–CH_2Cl_2, 1:6:6) gave 2 mg nuciferal, 2 mg **1** (R_f 0.47) and a mixture (R_f 0.2). Repeated TLC of this mixture (Et_2O–C_6H_6–CH_2Cl_2, 1:2:2) gave 7 mg costunolide (R_f 0.6) and 8 mg dehydrocostuslactone (R_f 0.65). Fraction 4 on standing at −20° gave an amorphous ppt, which was separated by TLC (Et_2O–C_6H_6–CH_2Cl_2–MeOH, 20:20:20:3, two developments) and gave 20 mg **3** (R_f 0.62) and 3 mg **8** (R_f 0.55). TLC of the soluble part of fraction 4 (Et_2O–C_6H_6–CH_2Cl_2, 1:6:6) gave 2 mg 15-oxonuciferal (R_f 0.62), 2 mg **2** (R_f 0.45) and 3 mg **5** (R_f 0.35). TLC of fraction 5 (Et_2O–C_6H_6–CH_2Cl_2, 1:1:1) gave 10 mg **3** and TLC of fraction 6 (Et_2O–MeOH, 10:1) gave a mixture, which by HPLC (RP 8, MeOH–H_2O, 11:9, flow rate 3 ml/min, 200 bar) gave 2 mg **5** (R_t 5.8 min) and 1 mg **7** (R_t 5.0 min). The extract of the aerial parts (500 g) gave CC fractions as follows: 1 (C_6H_6–CH_2Cl_2, 1:1), 2 (Et_2O–C_6H_6–CH_2Cl_2, 1:5:5), 3 (Et_2O–C_6H_6–CH_2Cl_2, 1:1:1) and 4 (Et_2O–MeOH, 5:1). TLC of fraction 1 (C_6H_6–CH_2Cl_2, 1:1) gave 10 mg costunolide and 10 mg dehydrocostuslactone. TLC of fraction 2 (Et_2O–C_6H_6–CH_2Cl_2, 1:5:5) afforded 10 mg 15-oxonuciferal and 7 mg **2**, while TLC of fraction 3 (Et_2O–C_6H_6–CH_2Cl_2, 1:1:1) gave 5 mg **3**. TLC of fraction 4 (Et_2O–C_6H_6–CH_2Cl_2,–MeOH, 20:20:20:3, two developments) gave 2 mg **3** and two mixtures. The less polar fraction was separated by HPLC (same conditions as above) affording 4 mg **5** (R_t 5.8 min), 2 mg **7** (R_t 5.0 min) and the more polar one (R_f 0.15) was separated by TLC ($CHCl_3$–MeOH, 49:1, two developments) which gave 10 mg **6** (R_f 0.30) and 10 mg **4** (R_f 0.20).

The aerial parts of *Gochnatia hypoleuca* (collected near Monterrey, Mexico, voucher deposited in the U.S. National Herbarium) was worked-up as usual [21]. CC fractions were as follows: 1 (Et_2O–petrol, 1:20 and 1:10) 2 (Et_2O–petrol, 1:3 and 1:1) and 3 (Et_2O and Et_2O–MeOH, 10:1).

TLC of fraction 1 (Et_2O–petrol, 1:10) gave 50 mg lupeyl acetate. TLC of fraction 2 (Et_2O–petrol, 1:3) gave 50 mg lupeol, 10 mg taraxasterol and crude dehydrocostuslactone which was isolated as its pyrazoline derivative (2 mg) after TLC (Et_2O–petrol, 1:1, R_f 0.22). Fraction 3 was further separated by medium pressure CC (60 g SiO_2). Fractions collected were (25 ml): 1–12 (Et_2O–petrol, 1:1) nothing of interest, 13 and 14 (Et_2O) (I), 15–18 (Et_2O) (II), 19–21 (Et_2O–MeOH, 100:1) nothing of interest, 22–29 (Et_2O–MeOH, 20:1) (III) and 30–36 (Et_2O–MeOH, 10:1) (IV). TLC of I (Et_2O–petrol, 3:1) gave 30 mg **18** (R_f 0.58). TLC of II (Et_2O–petrol, 3:1) gave a mixture of **13**, **15** and **17** ($R_f \sim 0.5$). Repeated TLC (Et_2O–C_6H_6–$CHCl_3$, 1:2:2) gave 200 mg **13** (R_f 0.4) and a mixture which was separated by repeated HPLC (RP 8, MeOH–H_2O, 3:2, flow rate 3 ml/min, 200 bar) affording 5 mg **15** (R_t 2.9 min), 5 mg **17** (R_t 2.1 min) and 100 mg **13** still containing **17**. TLC of III ($CHCl_3$–MeOH, 200:1) gave 20 mg **9** (R_f 0.52). TLC of IV ($CHCl_3$–MeOH, 100:1) gave two bands (IVa R_f 0.58 and IVb R_f 0.50). HPLC of IVa (RP 8, MeOH–H_2O, 11:9) gave 5 mg **10** (R_t 2.5 min) and 4 mg **11** (R_t 4.3 min) and HPLC of IVb (same conditions) 1 mg **12** (R_t 1.6 min).

The homogeneity of all compounds was tested by TLC in different solvents and by high field ^1H NMR. Known compounds were identified by comparing the 400 MHz ^1H NMR spectra with those of authentic material.

Acknowledgements—We thank the Deutsche Forschungsgemeinschaft for financial support. G. S.-H. thanks the UNESCO for a grant.

REFERENCES

1. Cabrera, A. L. (1971) *Rev. Mus. La Plata (N.S.)* **12**, 1.
2. Dominguez, X. A., Franco, K. and Cano, G. (1978) *Rev. Latinoam. Quim.* **9**, 214.
3. Bohlmann, F., Jakupovic, J., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20**, 109.
4. Bohlmann, F. and Zdero, C. (1979) *Phytochemistry* **18**, 95.
5. Bohlmann, F., Ahmed, M., Jakupovic, J., King, R. M. and Robinson, H. (1983) *Phytochemistry* **22**, 191.
6. Bohlmann, F., Schmeda-Hirschmann, G., Jakupovic, J., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1989.
7. Sakai, T., Nishimura, K. and Hirore, T. (1965) *Bull. Chem. Soc. Japan* 381.
8. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 2389.
9. Mathur, S. B., Hiremath, S. V., Kulkarni, G. H., Kelkar, G. R. and Bhattacharyya, S. C. (1965) *Tetrahedron* **21**, 3575.
10. Bohlmann, F., Jakupovic, J., Ahmed, M. and Schuster, A. (1983) *Phytochemistry* **22**, 1623.
11. Bohlmann, F. and Le Van, N. (1978) *Phytochemistry* **17**, 570.
12. Bohlmann, F., Singh, P. and Jakupovic, J. (1982) *Phytochemistry* **21**, 2122.
13. Bohlmann, F., Singh, P. and Jakupovic, J. (1982) *Phytochemistry* **21**, 2029.
14. Bohlmann, F. and Zdero, C. (1979) *Phytochemistry* **18**, 95.
15. Bohlmann, F., Zdero, C., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20**, 1631.
16. Bohlmann, F., Ludwig, G. W., Jakupovic, J., King, R. M. and Robinson, H. (1984) *Liebigs Ann.* 228.
17. Jin, H. (1982) *Yakugaku Zasshi* **102**, 911.
18. Naguno, S., Izawa, K., Higashiyama, K. and Nagai, M. (1980) *Yakugaku Zasshi* **100**, 427.
19. Bohlmann, F. and Zdero, C. (1982) *Phytochemistry* **21**, 1434.
20. Cabrera, A. L. (1977) *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L., eds) p. 1039. Academic Press, London.
21. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1984) *Phytochemistry* **23**, 1979.