Phytochemistry, Vol. 33, No. 2, pp. 383–387, 1993
Printed in Great Britain.

0031-9422/93 $6.00+0.00

PYRROLIZIDINE ALKALOIDS FROM *CRYPTANTHA* SPECIES

FRANK R. STERMITZ, MICHAEL A. PASS,* RONALD B. KELLEY† and J. RICHARD LIDDELL‡

Department of Chemistry, Colorado State University, Fort Collins, CO 80523, U.S.A.; *Department of Physiology and Pharmacology, The University of Queensland, St Lucia, Queensland 4072, Australia; †Department of Chemistry, Moorhead State University, Moorhead, MN 56563, U.S.A.; ‡Department of Chemistry, Rhodes University, Grahamstown 6140, South Africa

(*Received* 26 *October* 1992)

Key Word Index—*Cryptantha*; Boraginaceae; pyrrolizidine alkaloids; echiumine; *threo*-2″,3″-dihydroxyechiumine; *erythro*-3″-chloro-2″-hydroxyechiumine; 2″,3″-epoxyechiumine; 3′-acetylintermedine; ipanguline; isoipanguline; chemotaxonomy.

Abstract—In the first alkaloid investigation of the genus *Cryptantha* (Boraginaceae), pyrrolizidine alkaloids were identified from *C. cana*, *C. clevelandii*, *C. confertiflora*, *C. flava*, *C. fendleri*, *C. leiocarpa*, *C. thyrsiflora*, *C. virgata* and *C. virginensis*. Six perennial species from section (or subgenus) *Oreocarya* were similar in their alkaloid content, which was dominated by lycopsamine and intermedine and in some species with their acetyl derivatives. In two other species from this section, amabiline and tessellatine (heliospathine) were also major components. In contrast, in three annual species from section (or subgenus) *Krynitzkia*, the major pyrrolizidine alkaloids were angelylretronecine and echiumine derivatives. New pyrrolizidine alkaloids found were *threo*-2″,3″-dihydroxyechiumine, *erythro*-3″-chloro-2″-hydroxyechiumine and 2″,3″-epoxyechiumine.

INTRODUCTION

Cryptantha Lehm. ex G. Don (Boraginaceae) is a genus of about 150 species, two-thirds of which occur in the western U.S., with the remainder in the South American Andes [1]. They are plants of arid regions, many of which seem to prefer soils impregnated with mineral salts. The genus has been described as being of remarkable taxonomic and distributional interest [2]. Early botanists sometimes employed the generic concepts *Oreocarya* and *Krynitzkia* for the perennial/biennial and annual species, respectively, but more recent treatments have usually maintained these divisions as sections or subgenera under *Cryptantha*. One recent authority [3] recommended returning to a generic split, but the North American Flora currently under preparation will maintain all under *Cryptantha* (D. Wilken and W. Kelley, personal communication). The *Oreocarya* and *Krynitzkia* concepts are easily separable and distinct in the U.S., but South American species show intermediate characters and this fact seems to be the major one for placing all species within the unifying genus *Cryptantha* [2]. In a revision of the subgenus *Oreocarya* [4], groupings and phylogeny within that subgenus were also proposed. Genera of the Boraginaceae are often toxic due to their content of pyrrolizidine alkaloids and some are known to present severe poisoning problems to livestock of the western U.S. [5]. Several *Cryptantha* species were reported to be used in Ramah Navajo medicine [6]. The present work was undertaken to search for pyrrolizidine alkaloids in *Cryptantha* as a possible taxonomic aid and to determine if the genus represents a potential toxicity hazard.

RESULTS AND DISCUSSION

Cryptantha cana, *C. flava*, *C. thyrsiflora* and *C. virgata* (all of section *Oreocarya*) were very similar in both total pyrrolizidine alkaloid (PA) content (about 0.1–0.3% of the dry weight) and alkaloid pattern (80–90% intermedine and/or lycopsamine). The remaining PAs were mainly intermedine or lycopsamine 3′- and 7′-acetates (Table 1). The alkaloids were obtained only after zinc reduction and were therefore present in the plant as *N*-oxides. Complete NMR data for 3′-acetylintermedine have not previously been reported and are included in the Experimental. The alkaloid content of *C. thyrsiflora* was very similar to that of *Amsinckia menziesii* [7] a related genus of the Boraginaceae. Links to *Amsinckia* were also seen in the PA content of *C. confertiflora* and *C. virginensis*, also of section *Oreocarya*. These species contained major amounts of amabiline and tessellatine [8] (heliospathine [9]), alkaloids known from *Amsinckia* [8, 10]. On the basis of plant morphology, each of these *Cryptantha* species were placed in different phylogenetic groupings [4] so their very similar alkaloid content does not aid in evaluating these divisions.

In contrast, the alkaloid content of the three annual species from section *Krynitzkia* was considerably lower (*C. fendleri* 0.068%, *C. clevelandii* 0.029% and *C. leiocarpa* 0.014% of the dry weight) and the major PAs found (Table 2) were quite different from those of the section *Oreocarya* species. Most of the PAs in section *Krynitzkia* were angelylretronecines and their derivatives, compounds not found in section *Oreocarya*. Among the isolates were three previously undescribed alkaloids, **1**–**3**,

Table 1. Pyrrolizidine alkaloid content of *Cryptantha* species (section *Oreocarya*)

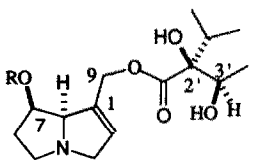
	Cryptantha spp.						
Alkaloid	*thyrsiflora*	*virgata*	*cana*	*flava*	*virginiensis*	*confertiflora A*	*confertiflora B*
Intermedine	38*	3	9	12	9	3	13
Lycopsamine	16	90	65	57	72	29	68
7-Acetylintermedine	10	T	T	1	—	—	—
7-Acetyllycopsamine	6	6	T†	6	—	—	—
3′-Acetylintermedine	27	T	18	12	—	—	—
3′-Acetyllycopsamine	2	—	7	7	—	—	—
Amabiline	—	—	—	—	3	50	1
Tessellatine‡	—	—	—	—	15	13	15
9-Acetyltessellatine	—	—	—	—	—	3	2

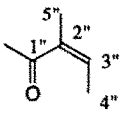
*Percentage of total alkaloids, determined from isolation and/or GC and GC-MS.
†Trace.
‡Also known as heliospathine.

Table 2. Pyrrolizidine alkaloid content of *Cryptantha* species (section *Krinitzkia**)

	Cryptantha spp.		
Alkaloid	*fendleri*	*leiocarpa*	*clevelandii*
7-Angelylretronecine	major	major	—
9-Angelylretronecine	major	trace	—
Echiumine	†	minor	minor
1	—	minor	major
2	—	minor	major
3	—	minor	major
Intermedine	—	minor	major
3′-Acetylintermedine	—	trace	major
Latifoline	minor	—	—
Neolatifoline	minor	—	—

*Relative amounts estimated from isolation and TLC spots and GC-MS (*C. clevelandii*).
†A trace of echiumine or its isomer symlandine was found.





Echiumine: R = angelyl =

1: R = *threo*-2",3"-dihydroxyangelyl

2: R = *erythro*-3"-chloro-2"-hydroxyangelyl

3: R = 2",3"-epoxyangelyl

described below. These are derivatives of echiumine, a rare PA from *Echium plantagineum* [11], but also described from *Amsinckia* species [12].

Thus, the two sections [2], subgenera [4] or genera [3] *Oreocarya* and *Krynitzkia* are chemically as well as morphologically distinct. It will be of interest to chemically examine the South American *Cryptantha* spp. which appear to be the key in determining the level of distinction among these taxa.

Structure elucidations. New PAs from *C. clevelandii* and *C. leiocarpa* were assigned structures **1–3** based on their mass and NMR spectra (Table 3). In general, the spectra could be compared with those for echiumine (7-angelylintermedine) and intermedine (Table 3). The ^1H and ^{13}C NMR spectra of the major PA of the four, **1**, included all the proper resonances for intermedine, including a C-5′ proton resonance at δ2.02 which distinguishes the trachelanthate from the viridiflorate (δ2.17) [7]. The MS showed *m/z* 415, which was consistent with a $C_{20}H_{33}NO_8$ formulation. If the 299 mass for intermedine was subtracted from the observed *m/z* 415, a mass of 116 remained, which corresponded to $C_5H_8O_3$. Since the δ5.44 broad singlet ^1H resonance was typical of a C-7-esterified PA, an acyl moiety must be present at the C-7 hydroxyl and this would correspond to $O{=}CC_4H_8O_2$.

Table 3. ^1H and ^{13}C NMR data ($CDCl_3$) for new pyrrolizidine alkaloids compared to echiumine and intermedine

	1		2		3		Echiumine	Intermedine	
Carbon no.	C	H	C	H	C	H	H	C	H
1	132.9	—	132.6	—	*	—	—	132.7	—
2	125.0	5.80	127.8	5.88	128.5	5.87	5.84	130.1	5.98
3u	63.3	3.37	62.4	3.36	62.7	3.40	3.40	62.5	3.43
3d		3.98		3.98		3.94	3.95		3.95
5u	54.0	2.60	53.7	2.60	53.6	2.64	2.66	53.8	2.73
5d		3.37		3.36		3.32	3.32		3.28
6	34.8	2.08	34.5	2.13	34.4	2.10	2.11	36.1	2.00
7	74.9	5.44	75.4	5.35	75.3	5.37	5.42	70.6	4.27
8	75.7	4.29	75.8	4.36	75.4	4.34	4.34	78.4	4.18
9u	63.0	4.74	62.3	4.74	62.5	4.68	4.67	62.3	4.79
9d		4.74		4.91		4.86	4.85		4.87
1′	174.9	—	173.6	—	175.1	—	—	175.2	—
2′	83.2	—	83.0	—	82.9	—	—	83.1	—
3′	69.8	4.13	69.4	4.07	69.4	4.06	4.03	69.1	4.12
4′	16.9	1.22	16.9	1.21	17.1	1.21	1.19	16.9	1.24
5′	33.2	2.02	33.0	2.05	33.0	2.04	2.04	33.0	2.04
6′	17.2	1.01	17.1	0.95	16.9	0.95	0.93	17.1	0.95
7′	17.2	0.94	17.3	0.94	17.3	0.93	0.94	17.1	0.94
1″	175.4	—	175.1	—	*	—	—	—	—
2″	78.7†	—	77.2	—	77.2	—	—	—	—
3″	71.5	3.80 *q*	62.8	4.19 *q*	60.0	3.04 *q*	6.09 *q*	—	—
4″	16.5	1.19 *d*	17.9	1.53 *d*	13.6	1.32 *d*	1.96 *m*	—	—
5″	22.1	1.24 *s*	23.0	1.36 *s*	19.3	1.49 *s*	1.81 *s*	—	—

*Obscured by noise.
†CD_3OD solvent.

The δ175.35 carbon resonance was assigned to the carbonyl carbon. In the normal $CDCl_3$ ^{13}C NMR spectrum only three of the required four peaks for the $C_4H_8O_2$ moiety were seen: δ16.46, 22.06 and 71.46. In CD_3OD, an additional resonance, which had been obscured by the $CDCl_3$ resonances, was seen at δ78.7 and such a peak was visible in the HMBC spectrum as well. In the ^1H NMR spectrum, a singlet methyl resonance was at δ1.24, while doublets ($J = 8$ Hz) were present at δ1.19 (3H) and 3.80 (1H). These data were all consistent with a 2,3-dihydroxyangelyl moiety at the C-7 hydroxyl. The resonances were virtually identical with the corresponding ones reported [13] for synthetic ethyl *threo*-2,3-dihydroxyangelate. Thus, **1** is *threo*-2″,3″-dihydroxyechiumine, with the absolute configuration unknown.

Dihydroxyangelyl side chains at the C-9 hydroxyl were recently reported [14] for the new PAs ipanguline and isoipanguline, but without assignment of relative stereochemistry. The ^1H NMR resonances reported for these side chains (δ3.77, 1.16 and 1.41 for ipanguline and δ3.91, 1.30 and 1.22 for isoipanguline) are virtually identical with those found for the synthetic *erythro* and *threo* models, respectively [13]. On the same basis, the *threo* stereochemistry can also be assigned to similar structural moieties in two unnamed PAs (**4** and **11** [15]) from *Senecio* species.

The NH_3CIMS of **2** showed double $[M]^+ + 1$ molecular ions at 434 and 436 (ratio 3:1) suggesting the presence of one chlorine atom and a calculated molecular formula of $C_{20}H_{32}ClNO_7$. All the expected NMR resonances were present for an intermedine moiety and the remainder could be analysed for an $O{=}CC_4H_7ClO$ acyl moiety at the C-7 hydroxyl. ^{13}C resonances for C-3″, C-4″ and C-5″ (δ77.2, 16.9 and 23.0) were comparable to the model dihydroxyangelyl derivatives [13], but the C-3″ resonance was at δ62.8 rather than at δ71–72. This could be accounted for by the presence of a Cl instead of an OH at C-3″. The macrocycle PA doronine contains a similarly arranged chlorohydrin functionality and the resonance for the carbon bearing the chlorine in that compound is δ63.0 [16]. The assignment was supported by the ^1H NMR spectrum where H-3″ was at δ4.19 (δ4.05 in doronine) and H-4″ at δ1.53 as opposed to the δ3.7–3.9 and δ1.15–1.22 resonances for the corresponding protons in the dihydroxyangelyl synthetics [13]. Thus, **2** is *erythro*-3″-chloro-2″-hydroxyechiumine, based on its close spectral correspondence with the macrocycle chlorohydrin doronine, whose stereochemistry is known from an X-ray study [17]. If **2** arises from the *trans*-epoxide **3** (see below), then it would indeed have the *erythro* configuration. Since H_2SO_4 and not HCl was used in the isolation procedures, **2** is presumed to be a natural constituent.

Compound **3** had a M_r of 397 (mass spectrum) or 18 mass units less than **1**. All ^1H and ^{13}C NMR resonances were again present for an intermedine moiety and the remainder could be accounted for by the epoxyangelyl side chain at C-7. The macrocycles ligularizine, petasitenine, neopetasitenine and an episenecicannabine are all *trans*-substituted epoxides with the methine proton appearing at δ3.02–3.04 and the methyl at δ1.27–1.48. The macrocycles jacobine, senecicannabine, florosenine and

otosenine are all *cis*-substituted epoxides having the methine proton at δ2.91–2.96 and the methyl at δ1.17–1.23. The corresponding resonances in **3** are at δ3.03 and 1.27 and we thus assigned it as a *trans*-substituted epoxide. Echiumine [11] was a trace component of two plant species and was isolated slightly contaminated by other PAs. Its mass spectrum (molecular ion *m/z* 381) and previously unpublished ^{1}H NMR spectrum (Table 3), again in comparison with that for intermedine, were consistent with its structure as 7-angelylintermedine, the expected precursor of **1–3**.

EXPERIMENTAL

NMR spectra were determined in $CDCl_3$ with TMS as int. standard at 300 MHz (^{1}H) and 75 MHz (^{13}C) at Colorado State, except for 2D ^{1}H NMR spectra which were run at 400 MHz at Rhodes University. TLC data are for silica gel plates developed with $CHCl_3$–MeOH–25% NH_4OH, 85:14:1. GLC was performed on a 30 m DB-1 0.32 mm i.d. column (0.1 μ film), He carrier gas at 2 ml min^{-1}. The oven was programmed at 165° for 14 min, then ramped to 275° at 20° min^{-1} with a final hold time of 10 min. GC-MS data were obtained as described previously [18].

Plant collections. Cryptantha cana (A. Nels.) Payson: Weld Co., CO, sandstone buttes at Forest Road 681 west of Pawnee Buttes on 26 May 1991 (voucher FRS 428, CSU herbarium, identified by W. A. Weber, University of Colorado Museum, Boulder); *C. clevelandii* Greene: Monterey Co., CA, County Road G-18 west of U.S. 101, on 28 March 1980 (James N. Roitman voucher JR 80-05) and on 17 June 1991 (R. B. Kelley voucher RBK 308); identified by R.B.K., in comparison with material in the Jepson Herbarium, University of California from the same location; *C. confertiflora* (Greene) Payson Collection A: Mono Co., CA, Hot Creek thermal area on 9 August 1989 (voucher RBK 266) and Collection B: Inyo Co., CA, State Road 168 east of Westgard Pass in the White Mtns on 9 June 1986; *C. flava* (A. Nels.) Payson: San Juan Co., NM off SH 544 between Aztec and Bloomfield on 31 May 1991 (voucher FRS 431, CSU, identified by W. A. Weber); *C. fendleri* (Gray) Greene: Chaffee Co., CO, west of U.S. 285 just north of Nathrop on 3 August 1990 (voucher FRS 415, CSU, identified by W. A. Weber); *C. leiocarpa* (F.&M.) Greene: Sonoma Co., CA, in sand dunes west of dormitories on Bodega Marine Reserve on 13 April 1992 (voucher FRS 440, CSU, identified by P. Conners, botanist, University of California, Bodega Marine Reserve); *C. thyrsiflora* (Greene) Payson: Chaffee Co., CO, west of Rd 321, 3 miles south of Buena Vista on 24 June 1990 (voucher FRS 406, CSU, identified by W. A. Weber); *C. virgata* (Porter) Greene; Larimer Co., CO, at Kelly Flats, SH 14 30 miles west of Fort Collins (voucher FRS 406, CSU, identified by W. A. Weber); *C. virginensis* (M. E. Jones) Payson: Esmeralda County, NV, off U.S. 95 near Goldfield Summit on 9 June 1986 (R.B.K.).

Isolations. Dried and milled plant material of *C. cana*, *C. flava*, *C. clevelandii*, *C. leiocarpa*, *C. thyrsiflora* and *C. virgata* was soaked in MeOH at room temp. for 24 hr (×3). The combined extracts were concd to dryness *in vacuo* and the residue was partitioned between 0.1 M H_2SO_4 and $CHCl_3$. The aq. layer was washed with $CHCl_3$ (×3) and stirred with Zn dust for at least 3 hr. The Zn was removed by filtration, the filtrate made basic to pH 9–10 with aq. NH_3 and the alkaloids extracted into $CHCl_3$ (×5). Results were as follows (plant, dry wt extracted, wt of alkaloid fr., per cent yield): *C. cana* (287 g, 440 mg, 0.15%), *C. clevelandii* (305 g, 89 mg, 0.03%), *C. flava* (374 g, 680 mg, 0.18%), *C. leiocarpa* (438 g, 62 mg, 0.014%), *C. thyrsiflora* (90 g, 112 mg, 0.12%). For *C. cana*, separate plant parts were analysed: roots (0.29%), stems (0.10%) and leaves (0.60%). Separation and purification of individual alkaloids was achieved by prep. TLC on silica gel. Identification of known alkaloids was by ^{1}H NMR and/or GLC or GC-MS in comparison with authentic standards.

Plant material of *C. confertiflora*, *C. clevelandii* and *C. virginensis* was similarly treated using the detailed methods described previously [10] and analysed by GC-MS, also as described in detail [18]. Alkaloid yields were: *C. confertiflora* Collection A (0.36%) and Collection B (0.39%), *C. clevelandii* (0.004%) and *C. virginensis* (0.35%). In these GC-MS studies, the following trace amounts (less than 1% of the total) of alkaloids were found in addition to those described above or in Table 1: *C. confertiflora* Collection A (3′-acetylmyoscorpine, myoscorpine, 3′-acetylamabiline), *C. confertiflora* Collection B (supinine, myoscorpine, amabiline, 3′-acetyllycopsamine) and *C. virginensis* (supinine). Amabiline, echiumine, 3′,7-diacetylintermedine and myoscorpine were also found in small amounts in the crude base fraction of *C. clevelandii* analysed by GC-MS.

Threo-2″,3″-*dihydroxyechiumine* (**1**). Brown gum, R_f 0.32, R_t 19.76 min; EIMS: 415 (0.4), 371 (2), 254 (56), 236 (3), 210 (26), 166 (5), 138 (30), 136 (37), 120 (100), 93 (70), 80 (29); NH_3CIMS 416 (72), 370 (46), 326 (33), 300 (13), 272 (100), 254 (28), 238 (6), 210 (22), 162 (27), 138 (24). NMR data (Table 3) assignments verified by COSY and HMBC. Copies of the NMR spectra are available from F.R.S.

Erythro-3″-*chloro*-2″-*hydroxyechiumine* (**2**). Brown gum, R_f 0.39, R_t 20.03 min; NH_3CIMS 436 (39), 434 (100), 414 (18), 180 (44), 118 (23); EIMS 435 (0.5), 274 (37), 273 (32), 272 (92), 254 (10), 236 (13), 208 (9), 138 (10), 136 (28), 121 (26), 120 (100), 94 (32), 93 (45), 80 (19), 71 (19). NMR data (Table 2) assignments were verified by HETCOR and HMBC spectra. Copies of the NMR spectra are available from F.R.S.

2″,3″-*Epoxyechiumine* (**3**). Brown gum, R_f 0.47, R_t 19.05 min; NH_3CIMS 398 (100), 336 (36), 308 (9), 254 (56), 238 (71), 236 (51); EIMS 397 $[M]^+$, 254 (9), 237 (33), 236 (100), 164 (17), 157 (4), 138 (4), 136 (19), 121 (24), 120 (85), 94 (27), 93 (44), 80 (12), 71 (4), 43 (30). NMR data (Table 3) assignments made in comparison with data for **1** and **2**. Copies of the NMR spectra are available from F.R.S.

Echiumine. Brown gum, R_f 0.45, R_t 18.60 min; NH_3CIMS 381 (12), 336 (18), 238 (20), 222 (23), 118 (100); EIMS 381 (1), 337 (1), 281 (2), 255 (1), 238 (9), 221 (37), 220 (100), 141 (14), 138 (7), 136 (45), 121 (30), 120 (73), 94 (20),

93 (49), 83 (24), 80 (17), 55 (35). ^{1}H NMR data (not previously published, Table 3). Assignments were verified by comparison with data for intermedine and for 7-angelyl PAs from the literature.

3′-*Acetylintermedine*. EIMS: 341 (3), 298 (2), 255 (3), 198 (2), 181 (4), 139 (20), 138 (100), 136 (14), 120 (10), 99 (7), 94 (45), 93 (79), 80 (13), 43 (34); NMR data, not previously published: carbon or hydrogen number (^{13}C resonance, ^{1}H resonance): C-1 (132.5), C-2 (130.8, 5.91), C-3 (62.9, 3.42, 3.95), C-5 (53.9, 2.73, 3.28), C-6 (36.1, 2.00), C-7 (71.0, 4.31), C-8 (78.5, 4.18), C-9 (62.9, 4.72, 4.85), C-1′ (174.5), C-2′ (81.7), C-3′ (72.1, 5.21), C-4′ (14.1, 1.25), C-5′ (32.6, 2.06), C-6′ (17.2, 0.96), C-7′ (16.6, 0.92), C=O (169.9), MeCO (21.0, 2.04).

Acknowledgements—This work was supported by the Colorado State University Agriculture Experiment Station as part of Western Regional Research Project W-122. J.R.L. was partially supported by Rhodes University while on leave at Colorado State. We thank the Department of Chemistry at Rhodes University for obtaining part of the NMR and MS data, J. A. Edgar and J. N. Roitman for standard samples and J. N. Roitman for the collection of *Cryptantha clevelandii*. The Facility for Advanced Instrumentation, University of California, Davis provided support and use of GCMS instrumentation.

REFERENCES

1. Cronquist, A. (1984) in *Intermountain Flora* (Cronquist, A., Holmgren, A. H., Holmgren, N. H., Reveal, J. L. and Holmgren, P. K., eds), Vol. 4, pp. 223–268. The New York Botanical Garden, New York.
2. Payson, E. B. (1927) *Ann. Missouri Bot. Gard.* **14**, 211–359.
3. Weber, W. A. (1987) in *Colorado Flora: Western Slope*, pp. 164–166. Colorado Associated University Press, Boulder, CO.
4. Higgins, L. C. (1971) *Brigham Young Univ. Sci. Bull.* **13** (4), pp. 1–62.
5. Knight, A. P., Kimberling, C. V., Stermitz, F. R. and Roby, M. R. (1984) *J. Am. Vet. Med. Assoc.* **185**, 647.
6. Vestal, P. A. (1952) in *Papers of the Peabody Museum*, Vol. 40, p. 40. Harvard University.
7. Roitman, J. N. (1983) *Aust. J. Chem.* **36**, 769.
8. Kelley, R. B. and Seiber, J. N. (1992) *Phytochemistry* **31**, 2513.
9. Röder, E., Breitmaier, E., Birecka, H., Frohlich, M. W. and Badzies-Crombach, A. (1991) *Phytochemistry* **30**, 1703.
10. Kelley, R. B. and Seiber, J. N. (1992) *Phytochemistry* **31**, 2369.
11. Culvenor, C. C. J. (1956) *Aust. J. Chem.* **9**, 512.
12. Culvenor, C. C. J. and Smith, L. W. (1966) *Aust. J. Chem.* **19**, 1955.
13. Greiner, A. and Ortholand, J.-Y. (1992) *Tetrahedron Letters* **33**, 1897.
14. Jenett, K., Kaloga, M. and Eich, E. (1991) *Planta Med.* **57**, A102, Suppl. 2.
15. Bohlmann, F., Zdero, C., Jakupovic, J., Grenz, M., Castro, V., King, R. M., Robinson, H. and Vincent, L. P. D. (1986) *Phytochemistry* **25**, 1151.
16. Röder, E., Wiedenfeld, H. and Knoezinger-Fischer, P. (1984) *Planta Med.* **50**, 203.
17. Wong, R. Y. and Roitman, J. N. (1984) *Acta Cryst.* **C40**, 163.
18. Kelley, R. B., Seiber, J. N., Jones, A. D., Segall, H. J. and Brower, L. P. (1987) *Experientia* **43**, 943.