Journal of Natural Products
Vol. 58, No. 8, pp. 1278-1284, August 1995

POLYCERASOIDIN AND POLYCERASOIDOL, TWO NEW PRENYLATED BENZOPYRAN DERIVATIVES FROM *POLYALTHIA CERASOIDES*

M. CARMEN GONZALEZ, ANGEL SERRANO, M. CARMEN ZAFRA-POLO, DIEGO CORTES,*

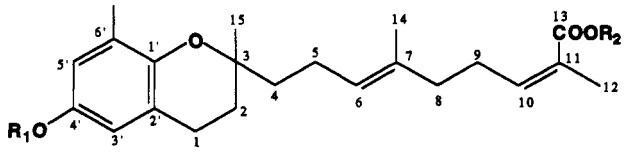
Departamento de Farmacología, Farmacognosia y Farmacodinamia, Facultad de Farmacia, Universidad de Valencia, 46100 Burjassot, Valencia, Spain

and K. SUNDAR RAO[1]

Department of Chemistry, University of Papua New Guinea, Papua New Guinea

ABSTRACT.—Two novel metabolites of mixed biogenesis, polycerasoidin [**1**] and polycerasoidol [**2**], have been isolated from the stem bark of *Polyalthia cerasoides*. Their structures were established on the basis of nmr spectroscopic techniques, including 2D correlated nmr spectroscopy (COSY 45, HMQC, and HMBC).

The genus *Polyalthia* includes more than 150 species of trees belonging to the family Annonaceae. It is considered one of the most unusual genera of this family and occurs in the tropical zones of Africa, Asia, and Oceania (1,2). Previous phytochemical studies on *Polyalthia* species have led to the isolation of different types of metabolites, namely, alkaloids (3–6), triterpenes (7), flavonoids (8), and diterpenes with a clerodane skeleton, some of which exhibit cytotoxic properties (9–11). *Polyalthia cerasoides* (Roxb.) Bedd., the subject of the present investigation, is a medium-sized tree occurring mainly in the deciduous forests of India and other Asiatic (12) and Oceanic areas. Only α-spinasterol and β-sitosterol have been reported previously from the leaves and stems of this plant (12). We describe herein the isolation and structure elucidation of two novel sesquiterpene benzopyran metabolites, polycerasoidin [**1**] and polycerasoidol [**2**], in which the first isoprene unit is arranged in a chromane nucleus. This type of metabolite, which must be considered a prenylated hydroquinone derivative, has been isolated from a broad range of phyla of marine organisms including brown algae (13–16), tunicates (17–19), octocorals (20,21), sponges (22–24), and mollusks (25), where the side-chain is a monoterpene, a drimane sesquiterpene, a linear diterpene, or more frequently a cyclic diterpene. Nevertheless, they are very rare in higher plants (26,27). The cytotoxicity against different tumor cell lines exhibited by some metabolites of this group (17,18,23,24) has raised inter-



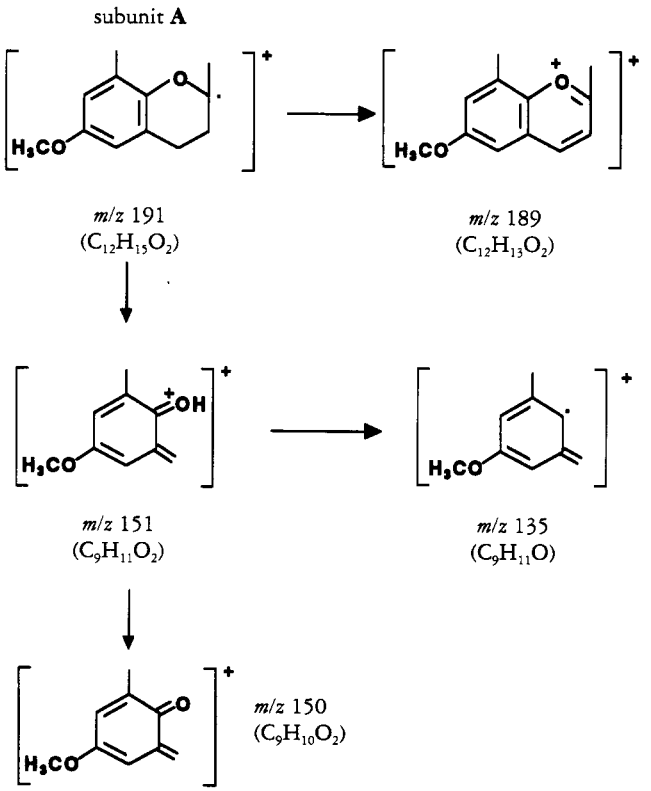
1 $R_1=CH_3$; $R_2=H$
2 $R_1=R_2=H$
3 $R_1=R_2=CH_3$
4 $R_1=COCH_3$; $R_2=H$

[1]Present address: Centre for Environmental Toxicology, University of Queensland, Cooper Plains, Queensland 4108, Australia.

est in these compounds. Also, their structural similarity with tocopherols has led several authors to assay these compounds as antioxidant and hypocholesterolemic agents, and such activity has been found for some of them (19,28,29).

Policerasoidin [**1**], the most abundant component of a CH_2Cl_2 extract of *P. cerasoides*, was obtained as an optically active yellowish oil, with $[\alpha]_D$ −16.2° (c=0.8, MeOH). Its hreims indicated a molecular ion at *m/z* 372.23000 [M^+], providing the formula $C_{23}H_{32}O_4$, requiring eight degrees of unsaturation. The ir spectrum revealed the presence of double bonds (1636 cm^{-1}), an α,β-conjugated carbonyl group (1686 cm^{-1}), and an aromatic ring (2926 and 1604 cm^{-1}); while uv absorptions at 294 nm and 236 nm were consistent with a chromane chromophore and a conjugated carbonyl group, respectively (14,15). The mass spectrum of **1** displayed diagnostically important fragment peaks at *m/z* 191 (62%), 189 (36%), 151 (base peak), and 135 (8%), strongly indicative of a partial benzopyran structure (subunit **A**) from which these peaks can originate according to Scheme 1.

Our structural hypothesis for **1** was supported by the 300 MHz ^{1}H-nmr spectrum (Table 1), which contained two singlets at δ 2.15 (3H) and δ 3.72 (3H) attributed to methyl and methoxy groups, respectively, linked to an aromatic nucleus. An AB system (δ 6.44 and δ 6.56, J=2.9 Hz) assignable to two meta-coupled protons; a methyl singlet at δ 1.26 attached to a carbon-bearing oxygen, and resonances at δ 2.73 (2H, t, J=7.5 Hz) and δ 1.60–1.70 (2H, m), including an ABX_2 system, completed the chromane moiety. This structure was also confirmed by the following features: (a) selective irradiation at δ 2.73 replaced the ABX_2 system with an AB system



SCHEME 1. Eims fragment ions of subunit **A** of **1**.

TABLE 1. ^{1}H- and COSY 45 Nmr Data of **1** (300 MHz, $CDCl_3$).

Proton	δ (*J* Hz)	Coupling in COSY 45 spectrum
1	2.73 t (7.5)	CH_2-2 (1.60–1.70)
2	1.60–1.70 m[a]	CH_2-1 (2.73)
4	1.60–1.80 m[a]	CH_2-5 (2.04–2.13)
5	2.04–2.13 m[a]	CH_2-4 (1.60–1.80)
6	5.16 dt (7.5, 1.2)	Me-14 (1.59)
8a	2.04 m[a]	CH-8b (2.13), CH_2-9 (2.61)
8b	2.13 m[a]	CH-8a (2.04), CH_2-9 (2.61)
9	2.61 ddd (15, 7.5, <1)	CH-8a (2.04), CH-8b (2.13)
10	6.07 dt (7.5, 1.2)	Me-12 (1.89)
12	1.89 d (1.2)	CH-10 (6.07)
13	10.31 s	—
14	1.59 br s	CH-6 (5.16)
15	1.26 s	—
3′	6.44 d (2.9)	CH-5′ (6.56)
5′	6.56 d (2.9)	CH-3′ (6.44), Me-6′ (2.15)
Me-6′	2.15 s	CH-5′ (6.56)
OMe-4′	3.72 s	—

[a]Overlapped with other signals.

(J_{AB}=13.2 Hz); (b) irradiation at δ 2.73 (CH_2-1) and δ 2.15 (Me-6′) produced an enhancement (nOe) of the doublets at δ 6.44 and δ 6.56, respectively, indicating that these protons are located at C-3′ and C-5′; and (c) a three-bond connectivity (HMBC) of the quaternary C-1′ (δ 146.25, in the ^{13}C-nmr spectrum) with the ^{1}H-nmr signals at δ 2.15, δ 2.73, δ 6.44, and δ 6.56, fixed the assignment of the methyl group at position 6′ (δ 16.24) and the position of the pyran nucleus. The carbon resonance at 152.14 ppm which correlated with H-3′ (δ 6.44) and a three-proton methoxy singlet (δ 3.72) could be ascribed to C-4′. Thus, subunit **A** was defined unambiguously (Figure 1 and Table 2).

The remaining portion of the structure ($C_{11}H_{17}O_2$) of **1** was elucidated using 1D and 2D nmr spectroscopic techniques. Both the ^{1}H- and ^{13}C-nmr spectra of **1** (Tables 1 and 2) supported the additional presence of a downfield singlet in the ^{1}H-nmr spectrum at δ 10.31 and the corresponding carbonyl resonance in the ^{13}C-nmr spectrum (δ 173.63), suggesting an α,β-conjugated carboxylic group (26), which was esterified (MeOH and H_2SO_4) to afford the methyl ester **3**. In addition, two olefinic protons at δ 5.16 and δ 6.07, allylically coupled with two vinyl methyls at δ 1.59 and δ 1.89, a signal at δ 2.61 (2H, ddd) and complex signals of three other methylene groups, were also observed (Table 1). These data are in agree-

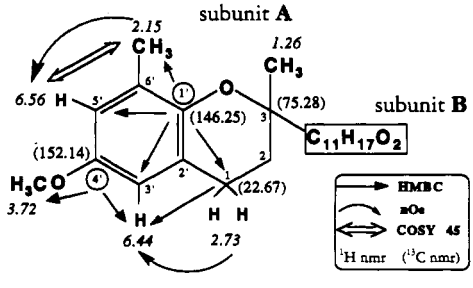


FIGURE 1. HMBC, nOe, and COSY 45 connectivities observed in subunit **A** of **1**.

TABLE 2. Heteronuclear Correlations (^{1}H-^{13}C-Nmr) of **1** (400 MHz, $CDCl_3$).

Carbon	δ	Multiplicity (^{13}C/DEPT)	HMQC	HMBC
1	22.67	CH_2	H-1	H-2, H-3′
2	31.44	CH_2	H-2	H-1, H-4, H-15
3	75.28	C	—	H-1, H-2, H-4, H-5, H-15
4	39.70	CH_2	H-4	H-2, H-5, H-15
5	22.19	CH_2	H-5	H-4, H-6
6	125.30	CH	H-6	H-4, H-5, H-14
7	134.20	C	—	H-5, H-8a, H-8b, H-9, H-14
8	39.04	CH_2	H-8	H-6, H-9, H-10, H-14
9	28.13	CH_2	H-9	H-8a, H-8b
10	146.25	CH	H-10	H-8a, H-8b, H-9, H-12
11	126.30	C	—	H-9, H-12
12	20.47	Me	H-12	H-10
13	173.63	C	—	H-12
14	15.73	Me	H-14	H-6, H-8a, H-8b
15	24.01	Me	H-15	H-2, H-4
1′	146.25	C	—	H-1, H-3′, H-5′, Me-6′
2′	120.86	C	—	H-1, H-2
3′	111.02	CH	H-3′	H-1, H-5′
4′	152.14	C	—	H-3′, OMe-4′
5′	114.79	CH	H-5′	H-3′, Me-6′
6′	127.17	C	—	Me-6′
Me-6′	16.24	Me	Me-6′	—
OMe-4′	55.58	Me	OMe-4′	—

ment with a linear olefinic chain (subunit **B**: Figures 1 and 2) linked to the subunit **A** at the C-3 position. An HMQC nmr experiment permitted the observation of protonated carbons in the ^{13}C-nmr spectrum. Assignment of the quaternary carbons was possible from the HMBC nmr spectrum, which also afforded additional evidence for the validity of structure **1** for polycerasoidin (Table 2). Thus, the correlation of the carboxyl group (C-13) to the three-proton signal at δ 1.89 (Me-12) and the correlation of this carbon at δ 20.47 (C-12) to the olefinic proton at δ 6.07 (CH-10), allowed the location of the carboxyl as the terminal group of the chain (for other HMBC correlations, see Figure 2 and Table 2). The ^{13}C-nmr chemical shift of Me-14 at δ 15.73 (less than 20 ppm) indicated an *E* geometry for $\Delta^{6,7}$, while the chemical shifts for Me-12 in both the ^{1}H- and ^{13}C-nmr spectra (δ 1.89 and δ 20.50, respectively) indicated the *Z* stereochemistry for $\Delta^{10,11}$ (30,31).

Polycerasoidol [**2**] was obtained as a clear oil and showed $[\alpha]_D$ +6.6° (*c*=0.45, MeOH); the eims revealed a fragment ion at *m/z* 358 [M^+], corresponding to a molecular formula of $C_{22}H_{30}O_4$, while the uv absorptions at 294 and 234 nm were indicative of the same carbon skeleton as **1**. The high degree of similarity

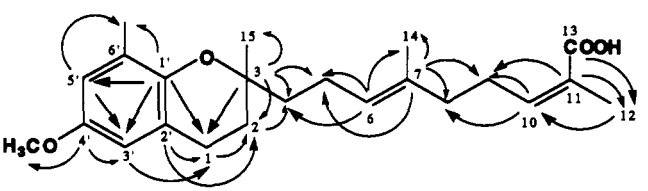


FIGURE 2. ^{1}H-^{13}C long-range correlations established from the HMBC nmr of **1**.

between the chemical shifts of the ^{1}H- and ^{13}C-nmr spectra of **1** and **2** indicated that their prenylated chains were identical. The most prominent difference between the ^{1}H-nmr spectra data of these compounds was the disappearance in **2** of the singlet signal of the methoxy group at δ 3.72. The substitution pattern of the aromatic ring in **2** was identical to that of the aromatic ring of polycerasoidin [**1**], due to the presence of an AB system at δ 6.47 and δ 6.37 (2H, J=2.7 Hz), and a singlet at δ 2.15 (3H). Therefore, a hydroxy group must be located at C-4′ in agreement with the strong ir absorption at 3358 cm^{-1}. Acetylation of **2** under the usual conditions afforded the monoacetate derivative **4**, which exhibited a new ir absorption at 1735 cm^{-1}, due to the ester carbonyl. The ^{1}H-nmr spectrum of **4** showed, in addition to the singlet signal at δ 2.26 (3H, s, OCOCH_3), a downfield shift (0.22 ppm) of the ortho protons as compared with similar chemical shifts in **2**, confirming the location at C-4′ for the hydroxy group (32) (Figure 3). Thus, polycerasoidol [**2**] appeared to be a demethylated analogue of polycerasoidin [**1**]. This was confirmed by the eims of **2**, m/z 358 [M$^+$], and the diagnostic peaks at m/z 177 ($C_{11}H_{13}O_2$) and m/z 137 ($C_8H_9O_2$), and the eims of **4**, m/z 400 [M$^+$].

The type of structure represented by polycerasoidin [**1**] and polycerasoidol [**2**] (prenylated benzopyran) is unique among the Annonaceae and within the genus *Polyalthia*. To our knowledge, compounds with a sesquiterpene unit linked to a chromane nucleus have been reported only in *Uvaria angolensis* (also Annonaceae) (33). In the compounds from *U. angolensis*, a cyclic sesquiterpene nucleus is coupled with an *o*-hydroxybenzyl unit and the cyclization occurs through the phenolic hydroxyl to give the benzopyran nucleus, while in **1** and **2** the first isoprene subunit is arranged in a chromane ring; thus, the biogenetic pattern of **1** and **2** is different from that of compounds isolated from *U. angolensis*.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Optical rotations were determined with a Perkin-Elmer 241 polarimeter. Ir spectra were run on a Perkin-Elmer 843 spectrometer. Uv spectra were obtained on a Perkin-Elmer Lambda 15 uv/vis spectrophotometer. Mass spectra were performed with direct injection at 70 eV on a Nermay-Sidar instrument or a VG Auto Spec Fisons spectrometer. ^{1}H- (250 and 300 MHz) and ^{13}C- (62.5 and 75 MHz) nmr spectra were recorded on Bruker AC-250 and Varian Unity-300 instruments, using the solvent as internal standard ($CDCl_3$ at δ 7.26 and δ 77.0). Multiplicities of ^{13}C-nmr resonances were determined by DEPT experiments. COSY 45, HMQC, and HMBC correlations were run using a Bruker AC-400 (400 MHz) instrument. Tlc was carried out on Si gel F_{254} precoated plates (Merck 5554). Compounds were detected by uv light (254 nm) or by spraying with phosphomolybdic acid or anisaldehyde-sulfuric acid. Prep. tlc was performed using Si gel (0.5-mm plates).

PLANT MATERIAL.—*Polyalthia cerasoides* was collected in the National Park of Varirata, located in the Central Province of Papua New Guinea in December 1992. A voucher specimen is deposited

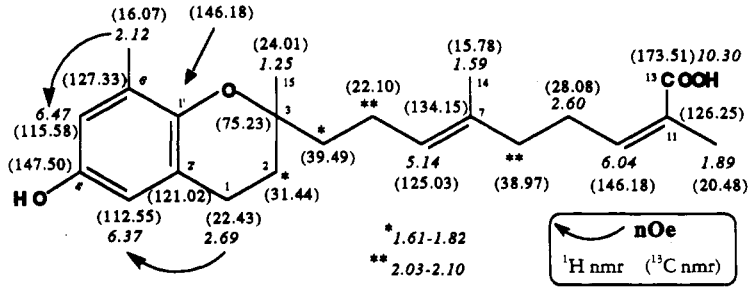


FIGURE 3. ^{1}H- (250 MHz) and ^{13}C-nmr (62.5 MHz, in parentheses) spectral data of **2** [$J_{1\text{-}2}$=7.2 Hz; $J_{6\text{-}5}$=6.6 Hz; $J_{6\text{-}14}$<1 Hz; $J_{9a\text{-}9b}$=15 Hz; $J_{9\text{-}10}$=7.2 Hz; $J_{10\text{-}12}$<1 Hz; $J_{3'\text{-}5'}$=2.7 Hz].

in the herbarium of the University of Papua New Guinea.

EXTRACTION AND ISOLATION.—Dried and powdered stem bark of *P. cerasoides* (550 g) was macerated with MeOH at room temperature. The concentrated MeOH extract (A) was partitioned between CH_2Cl_2 and 50% aqueous MeOH. The CH_2Cl_2-soluble extract (B, 4.70 g) was washed with 5% aqueous KOH to remove acidic substances, yielding a CH_2Cl_2 extract (C, 4.05 g) and an aqueous fraction. After neutralization, the aqueous fraction extracted with CH_2Cl_2 gave 0.51 g of a further CH_2Cl_2 extract (D). Extract D was applied to a Si gel 60H column (Merck 7736) and eluted with CH_2Cl_2-EtOAc (6:4); fractions 8–33 were combined and chromatographed on Si gel 60H and hexane-CH_2Cl_2-MeOH (3:6.5:0.5) as eluent, and pure **1** (160 mg) and **2** (5 mg) were obtained as oils. Flash cc on Si gel (Merck 9385) was applied to the extract C and developed with hexane containing gradually increasing amounts of CH_2Cl_2; fractions 7–8 eluted with hexane-CH_2Cl_2 (5:5) were purified by cc to afford more compound **1** (586 mg).

Polycerasoidin [**1**].—Oil, $[\alpha]_D$ −16.2° (*c*=0.8, MeOH); ir (film) ν max 2926, 2848, 1686, 1636, 1604, 1480, 1219, 1149, 1094 cm^{-1}; uv λ max (EtOH) (log ε) 294 (3.04), 236 (4.20) nm; hreims *m/z* [M^+] 372.23000 (75) (calcd for $C_{23}H_{32}O_4$, 372.23006), 218.13162 (5), 205.12298 (11), 203.10939 (5), 191.10608 (62), 189.08981 (36), 151.07641 (100), 150.06905 (42), 135.08024 (8), 123.08025 (9), 121.10097 (8), 105.06957 (7), 93.07072 (12), 91.05446 (23), 79.05595 (12), 55.05790 (19) (Scheme 1); ^{1}H- (300 MHz, $CDCl_3$) and ^{13}C- (75 MHz, $CDCl_3$) nmr data, see Tables 1 and 2 and Figures 1 and 2, respectively.

Polycerasoidol [**2**].—Oil; $[\alpha]_D$ +6.6° (*c*=0.45, MeOH); ir (film) ν max 3358, 2921, 2850, 1686, 1637, 1466, 1376, 1218, 1144, 1098 cm^{-1}; uv λ max (EtOH) (log ε) 294 (3.37), 234 (3.59) nm; eims *m/z* [M^+] 358 (100), 203 (14), 189 (27), 177 (51), 137 (69), 121 (43), 91 (36), 77 (22), 55 (53), 43 (32), 41 (28); ^{1}H- (250 MHz, $CDCl_3$) and ^{13}C- (62.5 MHz, $CDCl_3$) nmr data, see Figure 3.

METHYLATION OF **1** TO GIVE **3**.—Concentrated H_2SO_4 (0.5 ml) was added to a solution of **1** (5 mg) in MeOH (5 ml) and the mixture refluxed with stirring for 6 h. The solution was then neutralized with $NaHCO_3$ and extracted with CH_2Cl_2. Evaporation of the solvent gave a residue that was subjected to prep. tlc (hexane-CH_2Cl_2-MeOH, 8.5:1:0.5) to afford **3** (3.5 mg, 67%): oil; ir (film) ν max 2927, 2849, 1718, 1641, 1480, 1450, 1149, 1097 cm^{-1}; eims *m/z* [M^+] 386 (43), 259 (2), 218 (5), 205 (11), 203 (11), 191 (53), 189 (30), 175 (11), 151 (100), 150 (46), 135 (11), 121 (20), 105 (7), 93 (15), 91 (16), 77 (8), 47 (12); ^{1}H nmr (250 MHz, $CDCl_3$) δ 6.56 (1H, d, *J*=2.9 Hz, CH-5′), 6.44 (1H, d, *J*=2.9 Hz, CH-3′), 5.92 (1H, dt, *J*=7.5 and 1 Hz, CH-10), 5.14 (1H, dt, *J*=7.5 and 1 Hz, CH-6), 3.74 (3H, s, $COOCH_3$), 3.72 (3H, s, OCH_3), 2.72 (2H, t, *J*=7.2 Hz, CH_2-1), 2.55 (2H, ddd, *J*=15, 7.5, and 1 Hz, CH_2-9), 2.15 (3H, s, Me-6′), 2.07–2.14 (4H, m, CH_2-5 and CH_2-8), 1.89 (3H, d, *J*=1 Hz, Me-12), 1.60–1.80 (4H, m, CH_2-2 and CH_2-4), 1.59 (3H, br s, Me-14), 1.26 (3H, s, Me-15).

ACETYLATION OF **2** TO GIVE **4**.—Acetylation of **2** (3 mg) by Ac_2O/pyridine, overnight at room temperature and conventional work-up, gave the monoacetate **4** (quantitative yield): oil; ir (film) ν max 2959, 2923, 2851, 1735, 1687, 1641, 1465, 1375, 1259, 1097 cm^{-1}; eims *m/z* [M^+] 400 (14), 358 (33), 340 (6), 258 (5), 219 (12), 189 (14), 175 (27), 151 (9), 149 (11), 138 (16), 137 (48), 136 (19), 121 (25), 107 (12), 105 (7), 95 (13), 93 (17), 91 (11), 79 (22), 69 (19), 57 (22), 55 (37), 45 (18), 44 (31), 43 (100), 42 (93), 41 (52); ^{1}H nmr (250 MHz, $CDCl_3$) δ 6.69 (1H, d, *J*=2.7 Hz, H-5′), 6.59 (1H, d, *J*=2.7 Hz, H-3′), 2.26 (3H, s, $OCOCH_3$).

ACKNOWLEDGMENTS

This research was financially supported by the Generalitat Valenciana (grant GV1034/93) and CICYT (grant PB93-0682). We wish to thank Dr. B. Figadère, Faculty of Pharmacy, Châtenay-Malabry, France, for his encouragement. We are grateful to Mr. P. Wanganigi and Mr. Max Kuduk of the Biology Department of the University of Papua New Guinea, for the identification of the plant.

LITERATURE CITED

1. A. Le Thomas, in: "Flore du Gabon." Ed. by A. Aubréville, Museum National d'Histoire Naturelle, Paris, 1969, Vol. 16, p. 102.
2. R.E. Fries, in: "Die Natürlichen Pflanzen-Familien." Ed. by A. Engler and K. Prantl, Dunker and Humblot, Berlin, 1959, Vol. 17a II, p. 160.
3. Y.C. Wu, *Heterocycles*, **29**, 463 (1989).
4. M. Lavault, H. Guinaudeau, J. Bruneton, T. Sévenet, and H.A.A. Hadi, *Phytochemistry*, **29**, 3845 (1990).
5. Y.C. Wu, C.Y. Duh, S.K. Wang, K.S. Chen, and T.H. Yang, *J. Nat. Prod.*, **53**, 1327 (1990).
6. H. Guinaudeau, M. Leboeuf, and A. Cavé, *J. Nat. Prod.*, **57**, 1033 (1994).
7. H.Y. Li, N.J. Sun, Y. Kashiwada, L. Sun, J.V. Snider, L.M. Cosentino, and K.H. Lee, *J. Nat. Prod.*, **56**, 1130 (1993).
8. T.R. Seetharamam, *Fitoterapia*, **57**, 198 (1986).
9. G. Zhao, J.H. Jung, D.L. Smith, K.V. Wood, and J.L. McLaughlin, *Planta Med.*, **57**, 380 (1991).

10. M. Chakrabarty and A.C. Nath, *J. Nat. Prod.*, **55**, 256 (1992).
11. A. Kijjoa, M.M.M. Pinto, P.M.M. Pinho, and W. Herz, *Phytochemistry*, **34**, 457 (1993).
12. S. Dan, S.S. Dan, P. Mukhopadhyay, and M.K. Mukherjee, *Int. J. Crude Drug Res.*, **23**, 73 (1985).
13. V. Amico, G. Oriente, M. Piattelli, and G. Ruberto, *Gazz. Chim. Ital.*, **113**, 217 (1983).
14. C. Francisco, B. Banaigs, L. Codomier, and A. Cavé, *Tetrahedron Lett.*, **26**, 4919 (1985).
15. C. Francisco, B. Banaigs, M. Rakba, J. Teste, and A. Cavé, *J. Org. Chem.*, **51**, 2707 (1986).
16. R. Valls, L. Piovetti, B. Banaigs, and A. Praud, *Phytochemstry*, **32**, 961 (1993).
17. B.M. Howard, K. Clarkson, and R.L. Bernstein, *Tetrahedron Lett.*, 4449 (1979).
18. N.M. Targett and W.S. Keeran, *J. Nat. Prod.*, **47**, 556 (1984).
19. A. Sato, T. Shindo, N. Kasanuki, and K. Hasegawa, *J. Nat. Prod.*, **52**, 975 (1989).
20. F.J. McEnroe and W. Fenical, *Tetrahedron Lett.*, 1661 (1978).
21. B.N. Ravi and R.J. Wells, *Aust. J. Chem.*, **35**, 105 (1982).
22. P. Djura, D.B. Stierle, B. Sullivan, D.J. Faulkner, E. Arnold, and J. Clardy, *J. Org. Chem.*, **45**, 1435 (1980).
23. M. Ishibashi, Y. Ohizumi, J. Cheng, H. Nakamura, Y. Hirata, T. Sasaki, and J. Kobayashi, *J. Org. Chem.*, **53**, 2855 (1988).
24. J. Kobayashi, K. Naitoh, T. Sasaki, and H. Shigemori, *J. Org. Chem.*, **57**, 5773 (1992).
25. G. Cimino, S. De Rosa, S. De Stefano, R. Morrone, and G. Sodano, *Tetrahedron*, **41**, 1093 (1985).
26. F. Delle Monache, M. Marta, M.M. Mac-Quhae, and M. Nicoletti, *Gazz. Chim. Ital.*, **114**, 135 (1984).
27. G. Klink, A. Buchs, and F.O. Gülacar, *Phytochemistry*, **36**, 813 (1994).
28. B.C. Pearce, R.A. Parker, M.E. Deason, A.A. Qureshi, and J.J.K. Wright, *J. Med. Chem.*, **35**, 3595 (1992).
29. B.C. Pearce, R.A. Parker, M.E. Deason, D.D. Dischino, E. Gillespie, A.A. Qureshi, K. Volk, and J.J.K. Wright, *J. Med. Chem.*, **37**, 526 (1994).
30. E. Breitmaier and W. Voelter, "^{13}C-Nmr Spectroscopy," VCH, Weinheim, Germany, 1987.
31. A. Gaudemer, in: "Stereochemistry. Fundamentals and Methods." Ed. by H.B. Kagan, George Thieme, Stuttgart, 1977, Vol. 1.
32. M. Shamma and J.L. Moniot, *Tetrahedron Lett.*, 2291 (1974).
33. I. Muhammad and P.G. Waterman, *J. Nat. Prod.*, **51**, 719 (1988).

Received 24 January 1995