(+)-4#-Hydroxyhernandulcin, A New Sweet Sesquiterpene from the Leaves and Flowers of Lippia dulcis

Norito Kaneda, Ik-Soo Lee, Mahabir P. Gupta, D. Doel Soejarto, and A. Douglas Kinghorn

J. Nat. Prod., **1992**, 55 (8), 1136-1141• DOI: 10.1021/np50086a016 • Publication Date (Web): 01 July 2004

Journal of Natural Products
Vol. 55, No. 8, pp. 1136-1141, August 1992

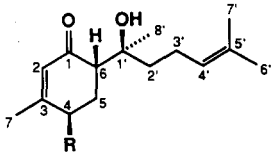
(+)-4β-HYDROXYHERNANDULCIN, A NEW SWEET SESQUITERPENE FROM THE LEAVES AND FLOWERS OF *LIPPIA DULCIS*[1]

NORITO KANEDA, IK-SOO LEE, MAHABIR P. GUPTA,[2]
D. DOEL SOEJARTO, and A. DOUGLAS KINGHORN*

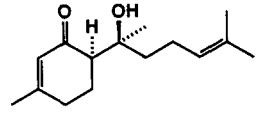
Program for Collaborative Research in the Pharmaceutical Sciences, Department of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, University of Illinois at Chicago, Chicago, Illinois 60612

ABSTRACT.—From the leaves and flowers of *Lippia dulcis* collected in Panama, a new sweet sesquiterpene identified as (+)-4β-hydroxyhernandulcin [**2**] was isolated, accompanied by (+)-hernandulcin [**1**], (−)-epihernandulcin [**3**] (a novel natural product), and 6-methyl-5-hepten-2-one [**4**]. Acteoside (verbascoside) [**5**], a known bitter phenylpropanoid glycoside, was isolated from the flowers of *L. dulcis*. The structure of (+)-4β-hydroxyhernandulcin was established by interpretation of its spectral data.

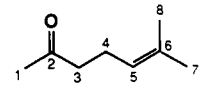
(+)-Hernandulcin [**1**] was first isolated as a sweet bisabolane sesquiterpene constituent of *Lippia dulcis* Trev. (Verbenaceae) leaves and flowers collected in Mexico (2). It was rated by a taste panel as being 1000 times as sweet as sucrose on a molar basis (2). The racemic form of this compound was synthesized by directed aldol-condensation starting from the two commercially available ketones, 6-methyl-5-hepten-2-one and 3-methyl-2-cyclohexen-1-one. (±)-Hernandulcin was neither acutely toxic for mice at single doses of up to 2 g/kg body wt, nor positive in a forward mutation assay, when evaluated both in the presence and absence of a metabolic activating system (2,3). Attempts to synthesize derivatives of hernandulcin [**1**] with improved hedonic parameters resulted in the discovery of no further sweet-tasting analogues. However, as a result of



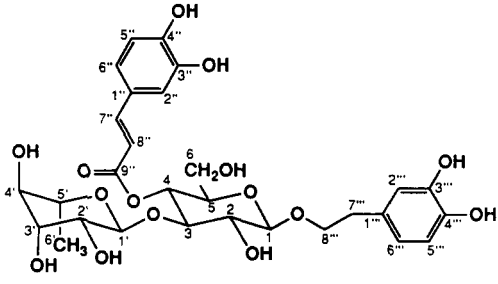
1 R=H
2 R=OH



3



4



5

[1]Paper No. 26 in the series, "Potential Sweetening Agents of Plant Origin." For part 25, see Fullas *et al.* (1).

[2]Address: FLORPAN, Unidad de Investigaciones Farmacognosticas, Universidad de Panamá, Panama, Republic of Panama.

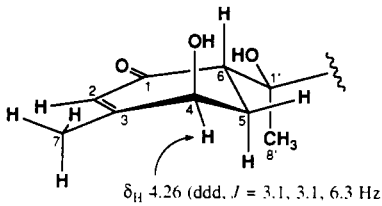
such investigations, it was concluded that the C-1 keto group, the C-1′ tertiary hydroxyl group, and the double bond between C-4′ and C-5′ must be present in order for compound **1** to exhibit sweetness (4).

Both (+)- and (±)-hernandulcin [**1**] have been synthesized by other groups (5–10). Thus, Mori and Kato (5,6) have synthesized (+)-hernandulcin [**1**] from *(R)*-(+)-limonene, and thereby established that the absolute configuration of naturally occurring hernandulcin [**1**] is 6*S*,1′*S*. Furthermore, they showed by synthesizing the other three stereoisomers (6*S*,1′*R*; 6*R*,1′*R*; and 6*R*,1′*S*) of this compound from appropriate isomers of limonene that only the 6*S*,1′*S* enantiomer is sweet (6). Racemic hernandulcin [**1**] has been synthesized variously from a cyclohexadiene derivative using boron and silicon enolates (7), by an intramolecular nitrile oxide cycloaddition route from (2*Z*,6*E*)-farnesal (8,9), and from an *E*-dienyl carbonate by titanium chloride catalysis (10). The naturally occurring form of this sweet sesquiterpene, (+)-hernandulcin [**1**], has been produced from both hairy root cultures (11) and shoot cultures (12) of *L. dulcis*.

In the present communication, we report the isolation and characterization of a second sweet bisabolane sesquiterpene, the novel (+)-4β-hydroxyhernandulcin [**2**], along with several analogues, including (+)-hernandulcin [**1**] in high yield, from *L. dulcis* leaves and flowers collected in Panama. A sample of *L. dulcis* [which is listed in the *Flora of Panama* under the name *Phyla scaberrima* (A.L. Juss.) Moldenke] (13), was obtained from a medicinal plants' market in Valle de Antón, Coclé, where it was on sale for the treatment of respiratory ailments.

RESULTS AND DISCUSSION

The molecular formula of compound **2** was determined as $C_{15}H_{24}O_3$ (*m/z* 252.1715) from its hrms data, indicating that it was a structural analogue of (+)-hernandulcin [**1**]. On comparison of its $[\alpha]_D$, ^{13}C-nmr (δ 67.5), and eims spectra ($[M]^+$ 252) with those of **1** ($[M]^+$ 236), **2** was considered to be a hydroxylated derivative. Initial spectral assignments of compound **2** were made after ^{1}H-, ^{13}C-nmr, ^{1}H-^{1}H COSY, and ^{1}H-^{13}C HETCOR nmr experiments were performed. The position of the additional hydroxyl group in **2** was deduced as being attached to C-4, on the basis of resonance enhancements at chemical shift values corresponding to C-2, C-3, C-6, and C-7, which were observed upon irradiation ($^3J_{CH} = 6$ Hz) of H-4 (δ 4.26) in a selective INEPT nmr experiment (14). The assignment of the hydroxyl group at C-4 position was confirmed by proton homonuclear decoupling nmr experiments. Thus, irradiation of H-5ax at δ 1.91 transformed H-4 (δ 4.26, ddd, $J = 3.1, 3.1, 6.3$ Hz) to a narrower multiplet peak similar to a broad singlet, and caused H-6 (δ 2.90, dd, $J = 12.9, 4.6$ Hz) to collapse to a doublet with a smaller J value (4.6 Hz). When H-5eq (δ 2.11) was irradiated, both the H-4 and H-6 peaks were simplified to a narrower multiplet and a doublet with a larger J value (12.9 Hz), respectively. An analysis of the individual spin system constituted by H-4, H-5, and H-6 led to the conclusion that the stereochemistry of hydroxyl group at the C-4 position is β (axial), a summary of which is shown in Figure 1. Thus, based on the observed coupling constants between H-4 and H-5 and between H-5 and H-6, together with a consideration of the absolute stereochemistry of **1**, in which H-6 is in the β configuration (5,6), it may be suggested that the actual splitting pattern (pseudo-quintet) of H-4α is caused by the spin-spin interactions between H-4α(eq) and H-5β(eq) ($J = 3.1$ Hz), H-4α(eq) and H-5α(ax) ($J = 3.1$ Hz), and H-4α(eq) and 4β-O*H*(ax) ($J = 6.3$ Hz). Likewise, the spin system of H-6β(ax) was influenced by H-5β(eq) ($J = 4.6$ Hz), and by H-5α(ax) ($J = 12.9$ Hz), to give a well resolved doublet of doublets signal. Further supportive evidence for the stereochemistry of 4β-hydroxyhernandulcin [**2**] was obtained by comparing the observed ^{1}H-^{1}H



2

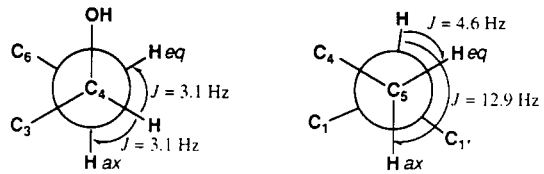


FIGURE 1. A partial perspective view and Newman projection models of compound **2**.

coupling constants ($^1J_{HH}$) between H-4 and H-5 and between H-5 and H-6, with those predicted by molecular mechanics calculations, in which J values were given as 2.6 Hz for $J_{H4\alpha\text{-}H5\alpha(ax)}$, 3.6 Hz for $J_{H4\alpha\text{-}H5\beta(eq)}$, 3.5 Hz for $J_{H6\beta\text{-}H5\beta(eq)}$, and 12.3 Hz for $J_{H6\beta\text{-}H5\alpha(ax)}$. Therefore, the chemical structure of this new sesquiterpene was elucidated as (+)-4β-hydroxyhernandulcin [**2**]. The sweetness potency of this compound relative to sucrose was not determined because of the small amount isolated. 4β-Hydroxyhernandulcin [**2**] is significant in being only the second naturally occurring or synthetic hernandulcin analogue reported to have a sweet taste.

(+)-Hernandulcin [**1**] was obtained in a much higher overall yield in this Panamanian sample of *L. dulcis* (0.154% w/w) than in the sample collected in Mexico (0.004% w/w) (15). It is interesting to note that there was no evidence of camphor in the Panamanian specimen; camphor, however, was the major volatile oil constituent of *L. dulcis* collected in Mexico (15). More precise ^{1}H-nmr coupling constant assignments were made in the present investigation for **1** than those published previously (2). Compound **3** exhibited levo-rotation at 589 nm, but it resembled (+)-hernandulcin in its other spectral data (uv, ir, ^{1}H and ^{13}C nmr) and exhibited the same base (*m/z* 237) and fragment peaks (*m/z* 219, 109) in the eims spectrum, suggesting the possibility of its being a diastereomeric counterpart because of its ease of separation by tlc. It was established as (−)-epihernandulcin [**3**] (a new natural product) by comparison of spectral data with the (±)-, (+)-, and (−)-forms of this compound, which have been obtained previously by chemical synthesis (2,3,6). (−)-Epihernandulcin [**3**], the absolute configuration of which was assigned as 6*R*,1′*S*, has been determined as being devoid of sweetness in a previous study (6). Compound **4** was identified as a known compound, 6-methyl-5-hepten-2-one, from its ^{1}H- and ^{13}C-nmr data. Although hernandulcin [**1**] is known to degrade to **4** by thermal dissociation at 140° (3), there was no evidence of its formation when an aqueous solution of **1** was stored at room temperature for two weeks at neutral pH. Accordingly, it may be inferred that **4** is a natural product.

The methanol extract of *L. dulcis* flowers was examined to see if any glycosides of hernandulcin [**1**] were present. Although no such compounds were detected, the major constituent of the MeOH-soluble extract was the known phenylpropanoid glycoside, acteoside (verbascoside) [**5**], which was identified by comparison with published physical and spectroscopic data (16–19). This compound was initially characterized by Birkofer

et al. (20) and was obtained as a bitter-tasting principle of *Conandron ramoidioides* (Gesneriaceae) (21). This substance has been recently isolated from *Lantana camara*, another plant in the family Verbenaceae (22), and exhibits significant cytotoxicity for P-388 cells (23) and antimicrobial, immunosuppressive, and protein kinase C inhibitory effects (22).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Optical rotations were measured with a Perkin-Elmer Model 241 polarimeter. Uv spectra were obtained on a Beckman DU-7 spectrometer. Ir spectra were taken with a Midac Collegian FT-IR spectrophotometer. ^{1}H-nmr and ^{13}C-nmr spectra were measured with TMS as internal standard, employing a Varian XL-300 instrument operating at 300 MHz and 75.6 MHz, respectively. ^{1}H-^{1}H COSY and ^{1}H-^{13}C HETCOR nmr experiments were also performed on a Varian XL-300, using standard Varian pulse sequences. Selective INEPT nmr experiments were conducted on a Nicolet NT-360 spectrometer operating at 90.8 MHz. Eims, cims, and hreims were obtained using a Finnigan MAT 90 instrument. Conformational analysis in order to compute nmr coupling constants was performed by optimization of structures using molecular mechanics energy calculations, with the use of MacroModel software (24), run on a Digital Equipment Corporation VAX 11/785 computer interfaced to a Tektronix 4107 graphics display terminal.

PLANT MATERIAL.—The leaves and flowers of *L. dulcis* were purchased in May 1991, from a marketplace in Valle de Antón, Coclé, Panama. The identity of the sample was confirmed by a taxonomist (D.D.S.). A voucher specimen (Florpan 743) representing this collection has been deposited at the Herbarium of the Field Museum of Natural History, Chicago.

EXTRACTION AND ISOLATION.—The air-dried and powdered aerial parts (leaves and flowers) (1.1 kg) of *L. dulcis* were exhaustively extracted with petroleum ether (6 × 2 liters). The petroleum ether layer was combined with that obtained from a similar extraction of *L. dulcis* flowers (70 g), after confirming the similarity of their tlc profiles. This combined petroleum ether layer was concentrated to dryness, and the residue (25 g) was chromatographed over a Si gel column (500 g) by elution, in turn, with toluene/hexane, toluene, toluene/Me_2CO, and toluene/Me_2CO/MeOH, with (+)-hernandulcin **[1]** to guide the fractionation. Additional Si gel cc with toluene-EtOAc (15:1) as eluent was carried out on the second fraction (5.6 g) from the original column, obtained from elution with toluene, to afford 6-methyl-5-hepten-2-one **[4]** (0.5 g, 0.043% w/w) and (+)-hernandulcin **[1]** (1.8 g, 0.154% w/w). From the third fraction (1.8 g) of the original cc, eluted with toluene/Me_2CO, (−)-epihernandulcin **[3]** (0.47 g, 0.040% w/w) was purified by further cc over Si gel with cyclohexane-EtOAc (5:1). Likewise, from the fourth fraction (3.7 g) of the original cc eluted with toluene/Me_2CO/MeOH, **2** (9.5 mg, 0.0008% w/w) was obtained by subsequent cc using $CHCl_3$-Me_2CO (15:1) and toluene-EtOAc (2:1) as solvents. This compound exhibited a similar orange-brown color in visible light to **1** when visualized with 10% H_2SO_4 (heated at 110°, 10 min).

The air-dried flowers (70 g) of *L. dulcis* were exhaustively extracted with MeOH (3 × 1 liter) at room temperature, and MeOH was removed under vacuum. This extract was taken up in MeOH (50 ml), and the resultant suspension in H_2O (50 ml) was washed consecutively with petroleum ether (3 × 100 ml) and Et_2O (3 × 100 ml). The aqueous MeOH layer was then treated with *n*-BuOH (2 × 100 ml). The *n*-BuOH layer was concentrated to dryness, and the residue (3.5 g) was subjected to chromatography over a Si gel (200 g) column with $CHCl_3$-MeOH (8:1) as eluent, to afford acteoside (verbascoside) **[5]** (1.6 g, 2.3% w/w).

(+)-*Hernandulcin* **[1]**.—Colorless oil: $[\alpha]^{20}D$ +105.1° (c = 3.3, $CHCl_3$); ^{1}H nmr ($CDCl_3$) δ 1.17 (3H, s, H-8′), 1.47 (2H, dd, J = 8.3, 8.3 Hz, H-2′), 1.62 (3H, s, H-7′), 1.70 (1H, m, H-5ax), 1.68 (3H, s, H-6′), 1.98 (3H, s, H-7), 2.03 (1H, m, H-5eq), 2.05 (1H, m, H-3′), 2.13 (1H, m, H-3′), 2.30 (1H, m, H-4), 2.35 (1H, m, H-4), 2.42 (1H, dd, J = 14.0, 4.6 Hz, H-6), 5.12 (1H, tt, J = 7.2, 1.3 Hz, H-4′), 5.30 (1H, s, 1′-O*H*), 5.88 (1H, s, H-2); eims *m/z* (rel. int.) $[M+1]^+$ 237 (100), 219 (64), 109 (78). For uv, ir and ^{13}C-nmr spectral data of **[1]**, see Compadre and co-workers (2,3).

(+)-*4β-Hydroxyhernandulcin* **[2]**.—Colorless oil: $[\alpha]^{23}D$ +103.0° (c = 0.77, $CHCl_3$); uv λ max (EtOH) (log ε) 232 (4.29) nm; ir ν max (film) 3405 (br), 2970, 2920, 2860, 1650, 1440, 1380, 1220 cm^{-1}; ^{1}H nmr ($CDCl_3$) δ 1.16 (3H, s, H-8′), 1.48 (2H, dd, J = 8.4, 8.4 Hz, H-2′), 1.63 (3H, s, H-7′), 1.68 (3H, s, H-6′), 1.91 (1H, ddd, J = 13.4, 13.4, 3.7 Hz, H-5ax), 2.07 (3H, s, H-7), 2.11 (1H, m, H-5eq), 2.14 (1H, m, H-3′), 2.18 (1H, m, H-3′), 2.33 (1H, d, J = 5.6 Hz, 4-O*H*), 2.90 (1H, dd, J = 12.9, 4.6 Hz, H-6), 4.26 (1H, ddd, J = 3.1, 3.1, 6.3 Hz, H-4), 4.98 (1H, s, 1′-O*H*), 5.11 (1H, tt, J = 6.6, 1.3 Hz, H-4′), 5.84 (1H, s, H-2); ^{13}C nmr ($CDCl_3$) δ 18.0 (q, C-7′), 21.9 (t, C-3′), 22.0 (q, C-7), 24.2 (q, C-8′), 26.1 (q, C-6′), 33.6 (t, C-5), 40.5 (t, C-2′), 46.9 (d, C-6), 67.5 (d, C-4), 74.3 (s, C-1′), 124.7 (d, C-4′), 128.5 (d, C-2), 132.0 (s, C-5′), 159.8 (s, C-3), 203.9 (s, C-1); eims *m/z*

(rel. int.) $[M]^+$ 252 (6), 234 (16), 169 (15), 151 (22), 125 (58), 109 (100), 82 (25), 69 (54), 55 (31); hreims *m/z* $[M]^+$ 252.1715 (calcd for $C_{15}H_{24}O_3$ 252.1725).

(−)-*Epihernandulcin* [**3**].—Colorless oil; $[\alpha]^{20}D$ −180.6° (*c* = 1.03, $CHCl_3$) [lit. (6) $[\alpha]^{22}D$ −133° (*c* = 0.108, EtOH)]; uv λ max (EtOH) (log ε) 237 (4.13) nm; ir ν max (film) 3440, 2970, 2915, 2860, 1650, 1430, 1380, 1215 cm^{-1}; ^1H nmr ($CDCl_3$) δ 1.19 (3H, s, H-8′), 1.40 (1H, ddd, *J* = 12.7, 12.7, 5.0 Hz, H-2′), 1.54 (1H, dd, *J* = 12.1, 4.9 Hz, H-2′), 1.60 (3H, s, H-7′), 1.66 (3H, s, H-6), 1.75 (1H, dddd, *J* = 12.8, 12.8, 12.8, 5.6 Hz, H-5ax), 1.89–2.11 (2H, m, H-5eq and H-3′, 1.97 (3H, s, H-7), 2.18 (1H, m, H-3′), 2.24–2.40 (2H, m, H-4), 2.35 (1H, dd, *J* = 13.7, 4.8 Hz, H-6), 5.08 (1H, s, 1′-O*H*), 5.09 (1H, m, H-4′), 5.84 (1H, s, H-2); ^{13}C nmr ($CDCl_3$) δ 17.6 (q, C-7′), 22.1 (t, C-3′), 24.1 (q, C-7), 25.0 (t, C-5), 25.4 (q, C-8′), 25.7 (q, C-6′), 31.5 (t, C-4), 37.1 (t, C-2′), 55.3 (d, C-6), 74.3 (s, C-1′), 124.8 (d, C-4′), 127.4 (d, C-2), 131.1 (s, C-5′), 163.6 (s, C-3), 203.4 (s, C-1); eims *m/z* (rel. int.) $[M + 1]^+$ 237 (100), 219 (88), 109 (70).

6-Methyl-5-hepten-2-one [**4**].—Colorless oil: ir ν max (film) 2970, 2920, 2860, 1720, 1440, 1360, 1160 cm^{-1}; ^1H nmr ($CDCl_3$) δ 1.62 (3H, s, H-8), 1.67 (3H, s, H-7), 2.13 (3H, s, H-1), 2.25 (2H, dd, *J* = 14.5, 7.5 Hz, H-4), 2.46 (2H, t, *J* = 7.4 Hz, H-3), 5.07 (1H, tt, *J* = 7.1, 1.4 Hz, H-5); ^{13}C nmr ($CDCl_3$) δ 17.3 (q, C-8), 22.3 (t, C-4), 25.3 (q, C-7), 29.5 (q, C-1), 43.4 (t, C-3), 122.5 (d, C-5), 132.3 (s, C-6), 208.2 (s, C-2); cims *m/z* (rel. int.) $[M + 1]^+$ 127 (93), 125 (51), 119 (61), 117 (57), 109 (100).

Acteoside (=verbascoside) [**5**].—Amorphous powder: $[\alpha]^{20}D$ −82.8° (*c* = 0.39, MeOH) [lit. (17) $[\alpha]^{15}D$ −70.2° (*c* = 4.0, MeOH); lit. (16) $[\alpha]^{20}D$ −66.5° (*c* = 1.0, MeOH)]; fabms *m/z* $[M + 1]^+$ 625. For uv and ir spectral data of **5**, see Kitagawa *et al.* (16) and Lahloub *et al.* (18); for ^1H-, and ^{13}C-nmr spectral data, see Jia *et al.* (17), Lahloub *et al.* (18), and Andary *et al.* (19).

ACKNOWLEDGMENTS

This investigation was funded by grant R01-DE-08937 from the National Institute of Dental Research, NIH, Bethesda, Maryland. Professor Mireya Correa, of the University of Panama, is thanked for providing valuable input on the taxonomic aspects of the material used in this investigation. Thanks are also due to the Regional Program for Scientific and Technological Development of the Organization of American States and the Commission of European Communities for supporting FLORPAN in Panama. We acknowledge the Nuclear Magnetic Resonance Laboratory of the Research Resources Center, University of Illinois at Chicago, for expert assistance and for provision of spectroscopic equipment used in this study. We thank Dr. M.E. Johnson for useful suggestions concerning the use of MacroModel software, and Mr. R.B. Dvorak, of the Department of Medicinal Chemistry and Pharmacognosy, University of Illinois at Chicago, for recording the mass spectral data.

LITERATURE CITED

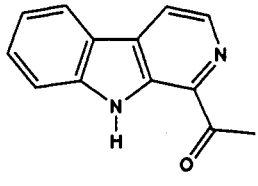
1. F. Fullas, R.A. Hussain, E. Bordas, J.M. Pezzuto, D.D. Soejarto, and A.D. Kinghorn, *Tetrahedron*, **47**, 8515 (1991).
2. C.M. Compadre, J.M. Pezzuto, A.D. Kinghorn, and S.K. Kamath, *Science*, **227**, 417 (1985).
3. C.M. Compadre, R.A. Hussain, R.L. Lopez de Compadre, J.M. Pezzuto, and A.D. Kinghorn, *J. Agric. Food Chem.*, **35**, 273 (1987).
4. C.M. Compadre, R.A. Hussain, R.L. Lopez de Compadre, J.M. Pezzuto, and A.D. Kinghorn, *Experientia*, **44**, 447 (1988).
5. K. Mori and M. Kato, *Tetrahedron Lett.*, **27**, 981 (1986).
6. K. Mori and M. Kato, *Tetrahedron*, **42**, 5895 (1986).
7. Y.N. Bubnov and M.E. Gurskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1448 (1986); *Chem. Abstr.*, **107**, 40102u (1987).
8. G.-C. Zheng and H. Kakisawa, *Bull. Chem. Soc. Jpn.*, **62**, 602 (1989).
9. G.-C. Zheng and H. Kakisawa, *Chin. Sci. Bull.*, **35**, 1406 (1990).
10. P.F. De Cusati and R.A. Olofson, *Tetrahedron Lett.*, **31**, 1409 (1990).
11. M. Sauerwein, T. Yamazaki, and K. Shimomura, *Plant Cell Rep.*, **9**, 579 (1991).
12. M. Sauerwein, H.E. Flores, T. Yamazaki, and K. Shimomura, *Plant Cell Rep.*, **9**, 663 (1991).
13. H.N. Moldenke, *Ann. Missouri Bot. Gard.*, **60**, 60 (1973).
14. A. Bax, *J. Magn. Reson.*, **57**, 314 (1984).
15. C.M. Compadre, E.F. Robbins, and A.D. Kinghorn, *J. Ethnopharmacol.*, **15**, 89 (1986).
16. S. Kitagawa, H. Tsukamoto, S. Hisada, and S. Nishibe, *Chem. Pharm. Bull.*, **32**, 1209 (1984).
17. Z. Jia, Z. Liu, and C. Wang, *Phytochemistry*, **30**, 3745 (1991).
18. M.F. Lahloub, A.M. Zaghloul, S.A. El-Khayaat, M.S. Afifi, and O. Sticher, *Planta Med.*, **57**, 481 (1991).
19. C. Andary, R. Wylde, C. Laffite, G. Privat, and F. Winternitz, *Phytochemistry*, **21**, 112 (1982).

20. L. Birkofer, C. Kaiser, and U. Thomas, *Z. Naturforsch., Teil B*, **23**, 1051 (1968).
21. G. Nonaka and I. Nishioka, *Phytochemistry*, **16**, 1265 (1977).
22. J.M. Herbert, J.P. Maffrand, K. Taoubi, J.M. Augereau, I. Fouraste, and J. Gleye, *J. Nat. Prod.*, **54**, 1595 (1991).
23. G.R. Pettit, A. Numata, T. Takemura, R.H. Ode, A.S. Narula, J.M. Schmidt, G.M. Cragg, and C.P. Pase, *J. Nat. Prod.*, **53**, 456 (1990).
24. F. Mohamadi, N.G.J. Richards, W.C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson, and W.C. Still, *J. Comput. Chem.*, **11**, 440 (1990).

Received 24 February 1992

ERRATUM

For the paper by Dillman and Cardellina entitled "Aromatic Secondary Metabolites from the Sponge *Tedania ignis*," *J. Nat. Prod.*, **54**, 1056 (1991), structure **3** should be a β-carboline, not a carbazole. The corrected structure drawing is as follows:



3