Pergamon

PII: S0031-9422(96)00714-5

Phytochemistry, Vol. 44, No. 8, pp. 1535–1536, 1997

0031-9422/97 $17.00+0.00

CADINANOLIDES AND OTHER CONSTITUENTS FROM *VERNONIA FRUTICULOSA* AND *VERNONANTHURA DISCOLOR**

JOSÉ N. BAZON, JOÃO L. CALLEGARI LOPES,† WALTER VICHNEWSKI, DIONES A. DIAS, KENJI NAGAMITI, WILSON R. CUNHA‡ and WERNER HERZ§

Departamento de Física e Química, Faculdade de Ciências Farmaceuticas de Ribeirão Preto-USP, 14040-903 Ribeirão Preto, São Paulo, Brazil; ‡Departamento de Química, Universidade de Franca-UNIFRAN, 14404-600, Franca, São Paulo, Brazil; §Department of Chemistry, The Florida State University, Tallahassee, FL 32306-3006, U.S.A.

(*Received* 21 *August* 1996)

Key Word Index—*Vernonia fruticulosa*; *Vernonanthura discolor*; Vernonieae; Asteraceae; sesquiterpene lactones; cadinanolides.

Abstract—Aerial parts of *Vernonia fruticulosa* furnished a large amount of glaucolide B, two known and one new cadinanolide as well as three known flavonoids. The silica gel catalysed rearrangement of glaucolide B to one of the cadinanolides supports the proposal that cadinanolides isolated from Vernoniinae may be artefacts derived from glaucolide type precursors. Aerial parts of *Vernonanthura discolor* afforded friedelanol, friedelin and β-sitosterol. Copyright © 1997 Elsevier Science Ltd

INTRODUCTION

The literature contains numerous reports on the phytochemistry of *Vernonia* species *sensu lato*. Sesquiterpene lactones of all types are common, but undoubtedly glaucolides and similar lactones are characteristic of *Vernonia* and related species [1]. In a few instances, glaucolides are accompanied by cadinanolides [2–5] and it has been suggested [3, 6] that these, like the more common hirsutinolides, are artefacts resulting from the isolation procedure.

RESULTS AND DISCUSSION

In the present instance a hexane–ethyl acetate extract of a collection of *V. fruticulosa* Mart. from São Paulo State, Brazil, afforded unusually large amounts of glaucolide B (**1**) [7], while an ethanol extract furnished three cadinanolides (**2a–c**) and the flavonoids isorhamnetin, acacetin and tamarixetin. Cadinanolides **2a** and **2b** were earlier reported from *V. jalcana* [2] while **2c** is new. The structure was established on the basis of its ^{1}H and ^{13}C NMR spectra (see Experimental). The ^{1}H NMR spectrum was similar to that of **2a**; however, the three singlets of the acetate groups in the ^{1}H NMR spectrum of **2a** were replaced by signals of three hydroxyl groups which disappeared on addition of D_2O. The ^{13}C NMR spectrum of **2c** supported the proposed structure.

Reaction of **1** with silica gel in the manner described in ref. [3] gave a 40% yield of **2a**, which lends further support to the notion that cadinanolides of type **2** isolated from *Vernonia* species *sensu lato* are artefacts since in all instances silica gel was used as a stationary phase in the process of isolation and purification. However, an earlier report [8] briefly mentions the isolation of **1** and the 1-acetoxyhirsutinolide **3** from a Brazilian collection of *V. fruticulosa*. Hirsutinolides of type **3** with acetoxy and sometimes other acyl functions on C-1 have been encountered occasionally [5, 8, 9] and it is difficult to see how in the absence of acetic or other carboxylic acids acylation might have occurred during the isolation and purification process.

The hexane–ethyl acetate extract of the aerial parts of *Vernonanthura discolor* (Less.) H. Robinson, an arboreal species (syn. *Vernonia discolor* Less.), furnished friedelin, friedelanol and β-sitosterol. Sesquiterpene lactones were not detected in the more polar fractions.

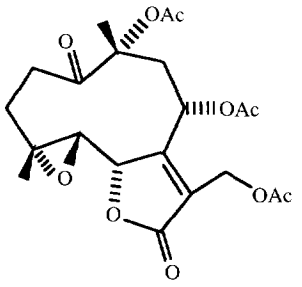
EXPERIMENTAL

General. Known compounds were identified by comparison with authentic samples (GC, TLC, ^{1}H NMR).

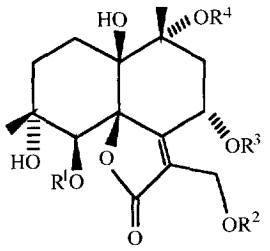
Plant material. Vernonanthura discolor (Less.) H. Robinson was collected near Miracatu, SP, Brazil, and *V. fruticulosa* Mart. near Termópolis, Minas

*Dedicated to the memory of our friend and botanist colleague Prof. Hermógenes de Freitas Leitão Filho who died 23 February 1996.

†Author to whom correspondence should be addressed.



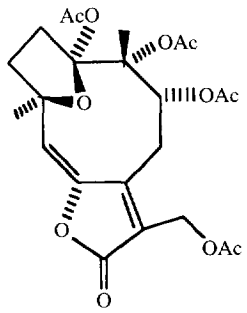
1



2a R^1, R^3, R^4, = Ac, R^2 = Me

b R^1, R^3, R^4, = Ac, R^2 = H

c R^1, R^3, R^4, = H, R^2 = Me



3

Gerais, Brazil, in July 1992. Species were identified by the late Prof. Hermógenes de Freitas Leitão Filho, Instituto de Biologia, Unicamp, SP. Vouchers are deposited in the Herbarium of the same Institute.

Extraction and isolation. Dried and pulverized aerial parts of *V. fruticulosa* (5.4 kg) were extracted with hexane–EtOAc (4:1) and EtOH. The hexane–EtOAc extract (203 g) was dissolved in MeOH–H_2O (9:1), extracted with $CHCl_3$ and concd *in vacuo*. Both extracts were chromatographed (VLC) over silica gel D, all frs being analysed by TLC. Frs containing material with the same R_f were combined and further purified by repeated CC (silica gel) and prep. TLC. The dried $CHCl_3$ layer (44 g) afforded 30 g **1**. The EtOH extract (100 g) furnished isorhamnetin (240 mg), acacetin (15 mg), tamaraxetin (10 mg) and cadinanolides **2a** (210 mg), **2b** (20 mg) and **2c** (10 mg).

Dried and pulverized aerial parts of *V. discolor* (10 kg) were extracted with hexane–EtOAc (4:1) to give 148 g crude extract. A 30-g sample of the extract on chromatography afforded 300 mg friedelin, 600 mg friedelanol and 400 mg β-sitosterol.

(1S*, 4R*, 5S*, 6S*, 8S*, 10R*)-1,4,5,8,10-*Pentahydroxy*-13-O-*methylcadin*-7(11)-*en*-6,12-*olide* (**2c**). Gum; CI MS (NH_3) *m/z* (rel. int.): 362 $[M+NH_4]^+$ 100, 344 (43.5), 326 (52.7), 160 (74.1); IR ν_{max} cm^{-1}: 3450 (-OH), 1785 (conjug. lactone); ^1H NMR (300 MHz, $CDCl_3$): δ 5.82 (*s*, H-5), 5.50 (*dd*, J = 9, 2.5 Hz, H-8), 4.50 (centre of AB system of H-13a and H-13b), 3.35 (*s*, 3p, -OMe), 2.50 (*m*, H-2a), 2.40 (*m*, H-3a), 2.18 (*dd*, J = 16, 9 Hz, H-9a), 1.95 (*m*, H-3b), 1.65 (*s*, 3p, H-14), 1.58 (*m*, H-2b), 1.20 (*s*, 3p, H-15), H-9b signal obscured; ^{13}C NMR (75 MHz, $CDCl_3$): C-1–C-15, δ 102.0*s*, 28.3*t*, 38.5*t*, 73.3*s*, 76.8*d*, 76.9*s*, 153.6*s*, 63.0*d*, 37.2*t*, 82.2*s*, 128.2*s*, 167.0*s*, 62.2*t*, 28.1*q*, 25.1*q*, -OMe 57.9*q*.

Acid catalysed rearrangement of 1.0 g **1** by the method of ref. [3] furnished 0.40 g **2a**.

Acknowledgements—Work in Ribeirão Preto was supported by CAPES, CNPq and FAPESP. We wish to thank Professor Gil Valdo J. Silva (FFCLRP-USP) for some of the NMR spectra.

REFERENCES

1. Herz, W., in *Proceedings of the International Compositae Conference, Kew*, 1994, Vol. 1, *Systematics*, eds D. J. N. Hind, H. Beentje, and G. V. Pope. Royal Botanical Garden, Kew, U.K., 1996, pp. 229–251.
2. Jakupovic, J., Schmeda-Hirschmann, G., Schuster, A., Zdero, C., Bohlmann, F., King, R. M., Robinson, H. and Pickardt, J., *Phytochemistry*, 1986, **25**, 145.
3. Martinez, V. M., Sanchez, F. A., Lopez, B. G. and Joseph-Nathan, P., *Zeitschrift Naturforschung*, 1986, **41C**, 1119.
4. Bardón, A., Kamiya, N. I., Ponce de Leon, C. A., Catalán, C. A. N., Díaz, J. G. and Herz, W., *Phytochemistry*, 1992, **31**, 609.
5. Bardón, A., Montanaro, S., Catalán, C. A. N., Díaz, J. G. and Herz, W., *Phytochemistry*, 1993, **34**, 253.
6. Martinez-Vázquez, M., Sepúlveda, S., Belmont, A., Rubio, M. and Joseph-Nathan, P., *Journal of Natural Products*, 1992, **55**, 884.
7. Padolina, W. G., Yoshioka, H., Nakatani, N., Mabry, T. J., Monti, S. A., Davis, R. E., Cox, P. J., Sim, G. A., Watson, W. H. and Wu, I. B., *Tetrahedron*, 1974, **30**, 1161.
8. Bohlmann, F. and Zdero, C., *Revista Latinoamer. Quimia*, 1988, **19**, 63.
9. Bohlmann, F., Mahanta, P. K. and Dutta, L. N., *Phytochemistry*, 1979, **18**, 289.