Acknowledgements—We thank the IMIB-CNR, Napoli, for the FAB mass spectra; the Centro Interdipartimentale di Metodologie Chimico-Fisiche, Università di Napoli, for NMR Spectra; and the Ministero della Pubblica Istruzione, Roma, for financial support of this work.

# REFERENCES

- Kaneda, N., Nakanishi, H., Kuraishi, T. and Katori, T. (1983) Yakugaku Zaasshi 103, 1133.
- 2. Zhu, Y., Yan, K. and Tu, G. (1987) Phytochemistry 26, 2873.

Phytochemistry, Vol. 29, No. 5, pp. 1699 1701, 1990. Printed in Great Britain.

- Nakanishi, H. and Kaneda, N. (1987) Yakugaku Zaasshi 107, 780.
- Adinolfi, M. Barone, G., Corsaro, M. M., Mangoni, L., Lanzetta, R. and Parrilli, M. (1988) *Tetrahedron*, 4981.
- Adinolfi, M. Barone, G. Corsaro, M. M., Mangoni, L., Lanzetta, R. and Parrilli, M. (1988) Can. J. Chem., 64, 2787.
- Budzikiewicz, H., Djerassi, C. and Williams, D. H. (1964). in Structure Elucidation of Natural Products by Mass Spectrometry, Vol. 2, p. 110, Holden-Day, San Francisco.
- 7. Mahato, S. B., Sahu, N. P., Ganguly, A. N., Kasai, R. and Tanaka, O. (1980) Phytochemistry 19, 2017.
- Seo, S., Tomita, Y., Tori, K. and Yoshimura, Y. (1978) J. Am. Chem. Soc. 100, 3331.

0031-9422/90 \$3.00+0.00 © 1990 Pergamon Press plc

# A DEGRADED LIMONOID FROM FAGAROPSIS GLABRA

JOËL BOUSTIE, CLAUDE MOULIS, JACQUELINE GLEYE, ISABELLE FOURASTE, PHILIPPE SERVIN\* and MARYSE BON\*

Laboratoire de Pharmacognosie, Faculté de Pharmacie, Université Toulouse III, 31 Allées Jules-Guesde F-31400, Toulouse, France; \*Laboratoire des IMRCP, Université Toulouse III, 118 route de Narbonne F-31062, Toulouse Cédex; France

(Received in revised form 13 October 1989)

Key Word Index—Fagaropsis glabra; Rutaceae; trunk bark; limonoids; fraxinellonoe; fraxinellone; isofraxinellone.

Abstract—The structure and absolute configuration of fraxinellonone isolated from *Fagaropsis glabra* was established as  $3\alpha$ -(3'-furanyl)- $3a\alpha$ ,7-dimethyl-4,5-dihydro-1,6-isobenzofurandione, by NMR and CD comparison with fraxinellone. Complete carbon assignments for fraxinellone and isofraxinellone were achieved by  ${}^{13}C{}^{-1}H$  COSY experiments.

# **INTRODUCTION**

Limonoids are polyoxygenated triterpenoid derivatives and have been widely investigated in the Rutaceae family for their chemotaxonomic and commercial interest [1]. Fraxinellone (2) [1–5], isofraxinellone [4, 5] and calodendrolide [4, 6] belong to a small group of degraded limonoids from the Rutaceae. In this paper, we report the complete elucidation of the structure of fraxinellonone (1), a new natural relative of fraxinellone, isolated from the trunk bark of *Fagaropsis glabra* Capuron, a Madagascan Rutaceae.

# **RESULTS AND DISCUSSION**

Enhanced absorption at 1669 cm<sup>-1</sup> in the IR spectrum of 1 and a bathochromic shift in the UV spectrum relative to 2 suggested the presence of a second conjugated carbonyl function. The mass spectral fragmentation and <sup>1</sup>H NMR spectrum were consistent with a C-7/C-7a double bond and a carbonyl group at C-6, and the molecular ion at m/z 246 corresponds to the molecular formula C<sub>14</sub>H<sub>14</sub>O<sub>4</sub>. Structure 1 for fraxinellonone is in full accord with the carbon and proton assignments listed in Table 1. A <sup>13</sup>C<sup>-1</sup>H COSY experiment on fraxinellone (2) permitted the unambiguous assignment of the protonated carbons as follows:  $\delta 32.1$  (C-6), 31.6 (C-4), 20.3 (C-9), 18.6 (C-8), 18.3 (C-5). The values for C-4 and C-6 have been interchanged [5]. Similarly, the remaining carbons for isofraxinellone [5] were assigned as follows:  $\delta 22.0$  (C-8), 21.8 (C-5), 21.1 (C-9).

Initially, the relative stereochemistry of 1 presented a problem. The Me-9 protons of 1 and epifraxinellone resonate at  $\delta 1.07$  [7], suggesting a *trans*-relationship. However, the CD curve,  $[\theta]_{233} - 13\,100\,[\theta]_{272} + 25\,500$  (MeOH; c 0.015), indicated that the chirality of 1 was the same as that of other known natural limonoids at the corresponding centres [6, 8]. Therefore, the Me-9 and



	<sup>1</sup> H*			<sup>13</sup> C	
Position	$\delta$ (ppm) mult.	J (Hz)	Config.	$\delta$ (ppm) GATED DEC. mult. J (Hz)	
1				168.68 s	
3	5.24 br s			82.85 d (150.0)	
3a				43.95 s	
4	$4_{\rm A} = 2.22 \dagger ddd$	${}^{2}J_{4A-4B} = 12.9, \; {}^{3}J_{4A-5A} = 14.2$ ${}^{3}J_{4A-5B} = 5.1 \; Hz$	ax'	31.99 br t (129.0)	
	$4_{\rm B} = 2.02 \ ddd$	${}^{2}J_{4B-4A} = 12.9, {}^{3}J_{4B-5A} = 5.5$ ${}^{3}J_{4B-5B} = 2.2 \text{ Hz}$	eq'		
5	$5_{\rm A} = 2.70 \ ddd$	${}^{2}J_{5A-5B} = 18.3, {}^{3}J_{5A-4A} = 14.2$ ${}^{3}J_{5A-4B} = 5.5 \text{ Hz}$	ax'	32.96 t (130.5)	
	$5_{\rm B} = 2.53  ddd$	${}^{2}J_{5B-5A} = 18.3, {}^{3}J_{5B-4A} = 5.1$ ${}^{3}J_{5B-4B} = 2.2 \text{ Hz}$	eq'		
6		50 40		198.08 s	
7				139.51 br s	
7a				145.20 s	
8	2.09 s			10.11 q (130.2)	
9	1.07 s			$18.95 \ br \ q \ (130.0)$	
2′	7.60† ddd	${}^{4}J_{2'-5'} = 1.7,  {}^{4}J_{2'-4'} = 1.0$ ${}^{4}J_{2'-3} = 0.9 \text{ Hz}$		140.15 ddd (204.0, 10.5, 6.2)	
3′				119.28 br s	
4′	6.48 ddd	${}^{3}J_{4'-5'} = 1.9,  {}^{4}J_{4'-2'} = 1.0$ ${}^{4}J_{4'-3} = 0.3 \text{ Hz}$		108.30 dddd (174.0, 13.8, 5.4, 3.0)	
5'	7.57† dd	${}^{3}J_{5'-4'} = 1.9,  {}^{4}J_{5'-2'} = 1.7 \text{ Hz}$		144.04 ddd (203.7, 10.0, 7.4)	

Table 1. <sup>1</sup>H (300 MHz, CD<sub>3</sub>OD) and <sup>13</sup>C (75.45 MHz, CDCl<sub>3</sub>) NMR data of compound 1

\*All assignments were confirmed by the <sup>1</sup>H-<sup>1</sup>H COSY experiment. † Partially overlapped signal.

furanyl substituents are both  $\alpha$  and the downfield chemical shift of Me-9 can be explained by the O=C-6 anisotropy effect. This is confirmed by the upfield chemical shift of the Me-9 protons,  $\delta 0.95$ , of the secondary alcohol (3) prepared from 1 by sodium borohydride reduction.

The most likely conformation of 1 (Fig. 1) is supported by  ${}^{1}H^{-1}H$  NOESY results which also confirm the proton assignments in Table 1. The pseudo-axial signals appear further downfield than the corresponding pseudo-equatorial ones, because they are deshielded by the O=C-6 carbonyl group.

Fraxinellonone (1) is a genuine natural product because it can be detected in the initial extracts and its relative concentration does not change with time. Its origin can clearly be related to limonoids, like those found in *Fagaropsis angolensis* [9] and which are still under investigation in *F. glabra*.

### **EXPERIMENTAL**

General. Mps: uncorr. Analytical TLC was on silica gel GF<sub>254</sub> and furanyl compounds visualized with spraying Ehrlich reagent, followed by immersing in HCl vapour. NMR: <sup>1</sup>H, 300.13 MHz; <sup>13</sup>C, 75.43 MHz, TMS as ref. in CD<sub>3</sub>OD (<sup>1</sup>H NMR, homonuclear 2D spectra) and CDCl<sub>3</sub> (<sup>1</sup>H, <sup>13</sup>C NMR and <sup>13</sup>C-<sup>1</sup>H COSY). EIMS: direct inlet, 70 eV.

Plant material. Fagaropsis glabra Capuron trunk bark was collected in the Sambava country (NE coast of Malagasy) and authenticated at source by the ORSTOM centre of Tananarive.

Extraction and isolation. Dried, powdered trunk bark (900 g) of Fagaropsis glabra was defatted by petrol and then extracted with  $CH_2Cl_2$  (12 l). The extract was chromatographed over Amberlite XAD-2. An aliquot of the extract eluted with MeOH-H<sub>2</sub>O (17:3) was chromatographed over silica gel. Iso-fraxinellone (80 mg), fraxinellone (2) (60 mg) and fraxinellonone



Fig. 1. Molecular structure and significant NOEs in compound 1.

(1) (25 mg) eluted with  $CH_2Cl_2$ -MeOH (49:1) were purified by CCC (Chromatotron) on silica plates eluted with hexane-EtOAc (19:1 to 17:3). The physical and spectral data of fraxinellone (2) and isofraxinellone were comparable to published results [2, 5].

Fraxinellonone (1). Needles (MeOH), mp 143–145°;  $[\alpha]_D^{25}$ -82° (CHCl<sub>3</sub>; c 0.94); UV  $\lambda_{max}^{MeOH}$  nm (log c) 208 (3.88), 248 (3.94); IR  $\nu_{max}^{MBc}$  cm<sup>-1</sup>: 1751 (γ-lactone), 1669 (C=C-C=O), 3138, 1502, 877, 813 (furan). EIMS, m/z (rel. int.): 246 [M]<sup>+</sup> (3), 150 [M -C<sub>5</sub>H<sub>4</sub>O<sub>2</sub>]<sup>+</sup> (100), 122 [150-CO]<sup>+</sup> (62), 107 [122-Me]<sup>+</sup> (3), 79 [94-Me]<sup>+</sup> (28); <sup>1</sup>H and <sup>13</sup>C NMR: Table 1.

Reduction of 1. A MeOH soln of 1 (7 mg) was treated with excess of NaBH<sub>4</sub>. After work-up in the usual way, the product was purified on Chromatotron (silica plate, hexane–EtOAc (1:1)) and afforded an amorphous solid, 3 (5 mg). UV  $\lambda_{max}^{MeOH}$  nm: 213, 230sh; IR v<sub>max</sub><sup>KBr</sup> cm<sup>-1</sup>: 3430 (OH), 1753 (y-lactone), 1500, 1028, 876, 806 (furan); <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$ 0.95 (3H, s, H-9), 1.6 (1H, D<sub>2</sub>O exchange, 6-OH), 1.75 (3H, m, H-4, H-5), 2.2 (3H, s, H-8), 2.2 (1H, m, H-5), 4.25 (1H, br t, H-6), 4.9 (1H, br s, H-3), 6.3 (1H, m, H-4'), 7.44 (1H, m, H-5'), 7.46 (1H, m, H-2').

#### REFERENCES

- Dreyer, D. L. (1983) in Chemistry and Chemical Taxonomy of the Rutales (Waterman P. G. and Grundon M. F., eds), p. 215. Academic Press, London.
- Pailer, M., Schaden, G., Spiteller, G. and Fenzl, W. (1965) Monatsh. Chem. 96, 1324.
- Coggon, P., McPhail, A. T., Storer, R. and Young, D. W. (1969) J. Chem. Soc. Chem. Comm. 828.
- 4. Koch, V. and Kubeczka, K. H. (1984) Fresenius Z. Anal. Chem. 243.
- 5. Blaise, A. J. and Winternitz, F. (1985) Phytochemistry 24, 2379.
- 6. Cassady, J. M. and Liu, C. S. (1972) J. Chem. Soc. Chem. comm. 86.
- 7. Tokoroyama, T., Fukuyama, Y., Kubota, T. and Yokotani, K. (1981) J. Chem. Soc. Perkin Trans I 1557.
- 8. Dreyer, D. L. (1968) Tetrahedron 24, 3273.
- Waterman, P. G. and Khalid, S. A. (1981) Biochem. Syst. Ecol. 9, 45.

Phytochemistry, Vol. 29, No. 5, pp. 1701-1704, 1990. Printed in Great Britain. 0031-9422/90 \$3.00+0.00 © 1990 Pergamon Press plc

# (+)-ISOALTHOLACTONE: A FURANOPYRONE ISOLATED FROM GONIOTHALAMUS SPECIES

# Steven M. Colegate, Laily B. Din,\* Abdul Latiff,† Kamarudin Mat Salleh,‡ Mohd W. Samsudin,\* Brian W. Skelton, Kin-ichi Tadano,|| Allen H. White§ and Zuriati Zakaria\*

School of Veterinary Studies, Murdoch University, Murdoch, Western Australia, 6153; \*Department of Chemistry, Universiti Kebangsaan Malaysia, 43600 UKM Bangi, Malaysia; †Department of Botany, Universiti Kebangsaan Malaysia, 43600 UKM Bangi, Malaysia; ‡Department of Biology, Universiti Kebangsaan Malaysia, Sabah Campus, Locked Bag 62, 88996 Kota Kinabalu, Malaysia; \$Department of Physical and Inorganic Chemistry, University of Western Australia, Nedlands, Western Australia, 6009; #Department of Applied Chemistry, Faculty of Science and Technology, Keio University, Hiyoshi, Kohoku-Ku, Yokohama 223, Ianan

(Received in revised form 24 October 1989)

Key Word Index—Goniothalamus malayanus, G. montanus, G. tapis; Annonaceae; structural studies; furano-pyrone; (+)-isoaltholactone.

Abstract—(+)-Isoaltholactone, (2S,3S,3aR,7aS)-3-hydroxy-2-phenyl-(2H,3aH)-furano[3,2-b]pyran-5-one was isolated from stembark of Goniothalamus malayanus, stembark and leaves of G. montanus and roots of G. tapis.

## INTRODUCTION

Shrubs and trees of the genus *Goniothalamus* occur in south-eastern Asia and throughout Malaysia. The most common medicinal usage of plants of this genus seems to be connected with the procurement of abortion and for undefined post-natal treatments [1].

## **RESULTS AND DISCUSSION**

(+)-Isoaltholactone (1) was obtained as optically active needles following chromatographic purification of extracts of the plants Goniothalamus malayanus, G. montanus and G. tapis. A molecular formula of  $C_{13}H_{12}O_4$ was implied by the high resolution EIMS. The major