Pergamon

PII: S0031-9422(96)00510-9

Phytochemistry, Vol. 44, No. 3, pp. 549–551, 1997

0031-9422/97 $17.00 + 0.00

TETRALONES FROM *ANCISTROCLADUS COCHINCHINENSIS*

NGUYEN HOANG ANH, HELMUT RIPPERGER,* ANDREA PORZEL,* TRAN VAN SUNG and GÜNTER ADAM*†

Institute of Chemistry, National Centre of Scientific Reasearch of Vietnam, Nghia Do, Tu Liem, Hanoi; *Institute of Plant Biochemistry, Weinberg 3, D-06120 Halle (Saale), Germany

(*Received in revised form* 10 *June* 1996)

Key Word Index—*Ancistrocladus cochinchinensis*; Ancistrocladaceae; leaves; tetralones; NMR.

Abstract—From leaves of *Ancistrocladus cochinchinensis*, along with plumbagin, (+)-isoshinanolone, 3,3′-biplumbagin, 8,8′-biplumbagin, lupeol and betulin, three new tetralones have been isolated. Their structures were established as (2*R**, 4*S**)-4,5-dihydroxy-2-methyltetralone, (2*R**,4*R**)-4,5-dihydroxy-2-methyltetralone and (3*R**, 4*S**)-3,4,8-trihydroxy-3-methyltetralone, respectively, by NMR spectroscopic data. Copyright © 1997 Elsevier Science Ltd

INTRODUCTION

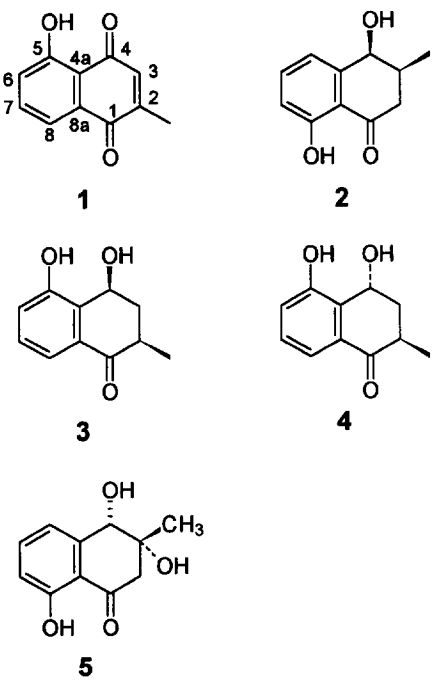
Ancistrocladus cochinchinensis is a large hooking climber growing as an endemic species in the south of Vietnam. [1], the constituents of which have not yet been investigated. In folk medicine, it is used as diuretic, antifebrile and antiphlogistic agent. In continuation of our studies on bioactive constituents of Vietnamese plants [2], we have obtained from leaves of *A. cochinchinensis*, in addition to the known compounds plumbagin (**1**) [3], (+)-isoshinanolone (**2**) ([4], absolute configuration tentatively assigned [5]), 3,3′-biplumbagin [6], 8,8′-biplumbagin [5], lupeol and betulin, three new tetralones. Their structures were elucidated mainly on the basis of NMR data as (2*R**, 4*S**)-4,5-dihydroxy-2-methyltetralone (**3**), (2*R**, 4*R**)-4,5-dihydroxy-2-methyltetralone (**4**) and (3*R**, 4*S**)-3,4,8-trihydroxy-3-methyltetralone (**5**), respectively, as outlined below.

RESULTS AND DISCUSSION

The elemental compositions of compounds **3**–**5** were shown to be $C_{11}H_{12}O_3$, $C_{11}H_{12}O_3$ and $C_{11}H_{12}O_4$, respectively, by high-resolution mass spectrometry.

The constitution of compound **3** followed from the ^{1}H, ^{1}H COSY and HMBC spectra; Tables 1 and 2 contain the ^{1}H and ^{13}C NMR data. HMBC measurements indicated all H–C correlations via $^2J(^1H–^{13}C)$ and $^3J(^1H–^{13}C)$ expected for structure **3**, with the exception of H-2/C-8a, H-7/C-6, H-7/C-8 and H-8/C-8a. The ^{1}H–^{1}H coupling constants (Table 1) are in agreement with the relative configuration assuming a half-chair conformation with an equatorial 2-methyl group. NOEs between H-2 and 2-methyl, H-3a, H-4, as well as between H-3e and H-2, 2-methyl, H-4, corroborated these conclusions.

The ^{1}H–^{1}H COSY and HMBC spectra of compound **4** were in accordance with the given structure. HMBC correlations via ^2J and ^3J were detected, with the exception of H-2/C-8a, H-6/C-7, H-7/C-8, H-8/C-1, H-8/C-7 and H-8/C-8a. The ^{1}H, ^{1}H coupling constants (Table 1) suggested the relative configuration with a half-chair conformation and an equatorial 2-methyl group. NOEs between H-4 and H-3a, as well as H-3e, supported this structure but a NOE between the



*Author to whom correspondence should be addressed.

Table 1. ^{1}H NMR data of compounds **3**–**5** (500 MHz, $CDCl_3$, ^{1}H–^{1}H coupling constants (Hz) in parentheses, TMS)

	3		**4**		**5**	
H	δ	J (H/H)	δ	J (H/H)	δ	J (H/H)
Me	1.26	6.7 (Me/2)	1.24	7.0 (Me/2)	1.30	
2a	2.58	13.5 (2*a*/3*a*)	3.00	9.0 (2*a*/3*a*)	2.80	17.1 (2*a*/2*e*)
2e	–	4.0 (2*a*/3*e*)	–	5.7 (2*a*/3*e*)	3.01	
3a	1.95	12.5 (3*a*/3*e*)	2.23	13.7(3*a*/3*e*)	–	
3e	2.51		2.32		–	
4	5.36	10.5 (3*a*/4)	5.33	4.9 (3*a*/4)	4.76	
5	–	5.1 (3*e*/4)	–	5.0 (3*e*/4)	7.10	7.6 (5/6)
6	7.08	8.0 (6/7)	7.09	8.2 (6/7)	7.52	8.2 (6/7)
7	7.28	7.7 (7/8)	7.28	8.0 (7/8)	6.93	0.9 (5/7)
8	7.53	1.2 (6/8)	7.55	1.2 (6/8)	–	
4-OH	3.26	6.4 (4-OH/4)	–		–	
5-OH	8.72		7.66		–	
8-OH	–		–		12.2	

2-methyl and H-4 indicated a further conformation with an axial methyl group. Line broadening at -55° agreed with a conformational equilibrium.

Structure **5** was in agreement with the ^{1}H–^{1}H COSY and HMBC spectra. ^{1}H–^{13}C couplings via two or three bonds were detected, with the exception of H-2a/C-8a, H-5/C-4a, H-5/C-6, H-6/C-5, H-6/C-7, H-7/C-6 and H-7/C-8. The ^{1}H NMR low-field shift of the 8-hydroxyl group (Table 1) is caused by a hydrogen bridge to the carbonyl. A NOE between H-2a and H-4 suggested a *cis* and axial relationship of these two protons and, thus, a half-chair conformation. HMBC indicated correlation of C-8a to H-2e (torsional angle *ca* 180°) but not to H-2a (torsional angle *ca* 90°), in agreement with the assumed conformations of the 2-protons. A NOE between 3-methyl and the axial H-4 localized the methyl group in the equatorial position (*cis* to the axial H-2 and H-4, formula **5**) also expected from thermodynamic reasons. Further NOEs between H-2e and 3-methyl, as well as between H-4 and H-5, are in agreement with structure **5**, however, a NOE between H-2a and 3-methyl was not detected.

Table 2. ^{13}C NMR data of compounds **3**–**5** (76 MHz, $CDCl_3$, TMS)

C	**3**	**4**	**5**
Me	14.9	15.2	22.1
1	199.1	200.1	202.2
2	40.7	38.1	49.8
3	41.1	38.3	74.0
4	69.1	64.0	75.4
4a	128.6	128.3	143.4
5	156.2	155.2	117.7*
6	122.0	121.5	137.2
7	129.5	129.7	117.6*
8	119.2	119.5	162.6
8a	132.4	131.9	114.8

*May be exchanged.

The tetralones described herein can be regarded as nitrogen-free biosynthetic metabolites of naphthylisoquinoline alkaloids, typical constituents of the Ancistrocladaceae [7]. Studies of such alkaloids from *A. cochinchinensis* are under way. It should be also mentioned that 3,3′-biplumbagin and 8,8′-biplumbagin were found for the first time in the Ancistrocladaceae.

EXPERIMENTAL

Plant material and extraction. Leaves of *A. cochinchinensis* Gagn. were collected at Binh Dinh in December 1993. The species was identified by Dr Nguyen Van Tap, Hanoi. A voucher specimen is deposited in the Herbarium of the Institute of Materia Medica, Hanoi. Leaves were dried at 40°, ground and extracted (580 g) with 95% MeOH at room temp. This soln was extracted with *n*-hexane, the MeOH evapd *in vacuo* and the aq. soln extracted with EtOAc. From the *n*-hexane extract, plumbagin (**1**) [3] (yield 0.04%), (+)-isoshinanolone (**2**) [4] (yield 0.028%), 3,3′-biplumgabin [6] (yield 0.003%), 8,8′-biplumgabin [5] (yield 0.005%), lupeol (yield 0.026%) and betulin (yield 0.005%) were isolated by chromatographic methods. They were identified by comparison with published spectroscopic data (IR, UV, ^{1}H, ^{13}C NMR) or in the case of both triterpenes, by direct comparison with authentic samples (TLC, mp, $[\alpha]_D$, MS).

(2*R**, 4*S**)-4,5-*Dihydroxy*-2-*methyltetralone* (**3**). Flash CC of the residue of the EtOAc extract over silica gel with *n*-hexane–EtOAc (7:3) followed by prep. TLC on silica gel using *n*-hexane–EtOAc (3:2) gave compound **3**. Oil, yield 0.007%. R_f 0.60 (silica gel, $CHCl_3$–MeOH (9:1)]. $[\alpha]_D^{23}$ + 36.9° ($CHCl_3$; *c* 0.71). CD ($CHCl_3$): $\Delta\varepsilon_{338} = +0.61$, $\Delta\varepsilon_{304} = -1.50$. EI-MS (70 eV) *m/z* (rel. int.): 192.0777 $[M]^+$ ($C_{11}H_{12}O_3$, calcd 192.0786) (28), 174.0671 $[M - H_2O]^+$ ($C_{11}H_{10}O_2$, calcd 174.0681) (100), 159.0456 $[M - H_2O - Me]^+$ ($C_{10}H_7O_2$, calcd 159.0446) (18).

(2*R**, 4*R**)-4,5-*Dihydroxy*-2-*methyltetralone* (**4**).

Flash CC of the residue of the EtOAc extract over silica gel with $CHCl_3$ followed by prep. TLC on silica gel using $CHCl_3$–MeOH (9:1) gave compound **4**. Oil, yield 0.003% R_f 0.43 (conditions see above). $[\alpha]_D^{23}$ + 14.7° ($CHCl_3$; *c* 0.34). CD ($CHCl_3$): $\Delta\varepsilon_{314} = +0.03$ EI-MS (70 eV) *m/z* (rel. int.): 192.0783 $[M]^+$ ($C_{11}H_{12}O_3$, calcd 192.0786) (88), 174.0686 $[M - H_2O]^+$ ($C_{11}H_{10}O_2$, calcd 174.0681) (100), 159.0445 $[M - H_2O - Me]^+$ ($C_{10}H_7O_2$, calcd 159.0446) (22).

(3*R**, 4*S**)-3,4,8-*Trihydroxy*-3-*methyltetralone* (**5**). Flash CC over silica gel with $CHCl_3$–MeOH (49:1) followed by prep. TLC on silica gel using EtOAc–*n*-hexane (7:3) gave compound **5**. Amorphous, yield 0.004% R_f 0.28 (conditions see above). $[\alpha]_D^{23}$ + 10.1° ($CHCl_3$; *c* 0.33). CD ($CHCl_3$): $\Delta\varepsilon_{324} = -0.37$. EI-MS (70 eV) *m/z* (rel. int.): 208.0722 $[M]^+$ ($C_{11}H_{12}O_4$, calcd 208.0736) (63), 190.0622 $[M - H_2O]^+$ ($C_{11}H_{10}O_3$, calcd 190.0630) (88), 121 (100).

Acknowledgements—We thank the Volkswagenstiftung and the Bundesministerium für Bildung, Wissenschaft, Forschung und Technologie, Bonn, for financial support, Dr J. Schmidt for MS measurements, and Dr Nguyen Van Tap, Hanoi, for identification of plant material.

REFERENCES

1. Pham-Hoang Ho (1991) *Cayco Vietnam, An Illustrated Flora of Vietnam*, Vol. 1, p. 555. Mekong Printing, Santa Ana.
2. Nguyen Hoang Anh, Ripperger, H., Porzel, A., Tran Van Sung and Adam, G. (1996) *Phytochemistry*, **42**, 1167.
3. Bhattacharyya, J. and De Barcalho, V. R. (1986) *Phytochemistry* **25**, 764.
4. Hanson, S. W., Crawford, M. and Thanasingh, D. P. J. (1981) *Phytochemistry* **20**, 1162.
5. Tezuka, M., Takahashi, C., Kuroyanagi, M., Satake, M., Yoshihira, K. and Natori, S. (1973) *Phytochemistry* **12**, 175.
6. Sidhu, G. S. and Sankaram, A. V. B. (1971) *Tetrahedron Letters*, 2385.
7. Bringmann, G. and Pokorny, F. (1995) *Alkaloids* **46**, 127.