Phytochemistry, Vol. 27, No. 9, pp. 2979–2981, 1988.
Printed in Great Britain.

0031-9422/88 $3.00 + 0.00
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ARALIOPDIMERINES A, B, AND C, DIMERIC QUINOLONE ALKALOIDS FROM THE BARK OF *ARALIOPSIS TABOUENSIS*

BONAVENTURE T. NGADJUI, JOHNSON F. AYAFOR, BEIBAM L. SONDENGAM, MICHEL KOCH,* FRANCOIS TILLEQUIN,* and JOSEPH D. CONNOLLY†

Department of Organic Chemistry, University of Yaounde, BP 812, Yaounde, Cameroon; * Department of Pharmacognosy, University Rene Descartes, Paris V 75270, France; † Department of Chemistry, University of Glasgow, Glasgow, G12 8QQ, Scotland

(*Received* 22 *December* 1987)

Key Word Index—*Araliopsis tabouensis*; Rutaceae; bark; dimeric 2-quinolone alkaloids; araliopdimerines A, B, and C.

Abstract–Araliopdimerines A, B, and C, three new dimeric 2-quinolone alkaloids have been isolated from the bark of *Araliopsis tabouensis* and their structures assigned on the basis of ^{1}H and ^{13}C NMR evidence and chemical correlation.

INTRODUCTION

It has been reported [1–3] that *Araliopsis tabouensis* Aubrev et Pellegr (Rutaceae) contains several quinolone alkaloids and large amounts of flindissol. Recently, in addition to vepridimerines A(**1**), B(**2**), C(**3**), and D(**4**) [4], we isolated a new quinolone alkaloid araliopsinine (**5**) [5] from the bark of this plant. In this study [5] we also obtained an unresolved mixture of dimeric 2-quinolone alkaloids apparently different from the vepridimerines. We now report that re-investigation of this mixture has led to the isolation of three new dimeric quinolone alkaloids araliopdimerines A(7), B(9), and C(11).

RESULTS AND DISCUSSION

Repeated column chromatography and preparative TLC of the unresolved mixture obtained in our previous study [5] yielded, in addition to vepridimerine A (**1**) [4], skimmianine [2, 3] and araliopsinine (**5**) [5], the new dimers (**7**), (**9**), and (**11**).

The ^{1}H and ^{13}C NMR chemical shifts of araliopdimerine A(**7**) and B(**9**) are listed in Tables 1 and 2. Both compounds contain two 7,8-dimethoxy-2-quinolone moieties, presumably derived from veprisine (**12**). The presence of four *C*-methyl groups suggested a close relationship of (**7**) and (**9**) to paraensidimerine B(**6**) [6] and D(**8**) [7, 8] respectively. Comparison of their spectro-

Table 1. ^{1}H NMR chemical shifts and coupling constants of araliopdimerine A (**7**) and B (**9**)

H	7	9
3, 12	6.86 (*d*, 9.0), 6.78 (*d*, 9.0)	6.79 (*d*, 9.0), 6.84 (*d*, 9.0)
4, 13	7.73 (*d*, 9.0), 7.75 (*d*, 9.0)	7.71 (*d*, 9.0), 7.72 (*d* 9.0)
6a	2.14 (*br d*, 3.6)	2.38 (*br d*, 3.4)
7	3.84 (obs *d*, 9.4)	3.25 (*br dd*, 6.2, 2.0)
14a	5.47 (*d*, 3.6)	5.41 (*d*, 3.4)
17	5.27 (*br d*, 9.4)	1.90 (*dd*, 16.0, 2.0)
		1.75 (*dd*, 16.0, 6.2)
19 (Me)	1.93 (*d*, 0.9)	1.26 (*s*)
20 (Me)	1.68 (*br s*)	1.29 (*s*)
OH	–	4.97
N-Me	3.75, 3.79	3.74, 3.76
OMe	3.90, 3.91	3.88, 3.92
	3.95, 3.98	3.94, 3.95
C-Me	1.72, 1.20	1.72, 1.15

Coupling constants (Hz) are given in parentheses.

Table 2. ^{13}NMR chemical shifts of araliopdimerine A (**7**) and B (**9**)

C	7	9
1.10	136.4, 136.7	136.6, 136.5
2, 11	155.9, 155.7	155.8, 155.7
3, 12	107.0, 106.9	107.3, 107.0
4, 13	119.7, 119.9	119.6, 119.8
4a, 13a	111.7 (2)	111.5, 111.4
4b, 13b	156.0, 156.9	156.0, 156.9
6	80.3	80.9
6a	29.7	25.8
7	45.1	44.6
7a, 14b	105.9, 101.7	107.3, 101.5
8, 15	164.1 (2)	164.0, 164.5
2NMe	33.4, 33.6	33.5 (2)
9a, 16a	133.4, 135.3	133.3, 135.1
14a	64.2	64.1
17	127.7	52.2
18	132.2	69.9
19, 20	18.2, 25.9	29.0, 31.1
2CMe	21.0, 29.2	21.0, 29.3
4OMe	56.2 (2)	56.1 (2)
	61.6, 61.7	61.6 (2)

Multiplicities were assigned from DEPT spectra.

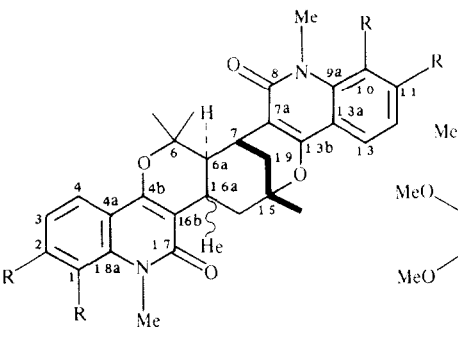
scopic properties confirmed this relationship and established araliopdimerine A as (**7**) and B as (**9**). Chemical correlation of A(**7**) and B(**9**) was achieved by Markovnikov hydration [9] of (**7**) with mercuric acetate to give (**9**).

It was clear from the spectroscopic properties of araliopdimerine C(**11**) that it is also a dimer of veprisine (**12**). The presence of four methoxyls, three *C*-methyl group, two 2-quinoline carbonyl groups and a trisubstituted double bond [δ_H 7.50 (*br s*, H-16); δ_C 127.4 (*d*, C-16), 130.3 (*s*, C-16a)] led to the conclusion that araliopdimerine C is the tetramethoxy-derivative of paraensidimerine G(**10**) [6]. Oxidation of vepridimerine A(**1**) and B(**2**) with DDQ afforded araliopdimerine C(**11**) accompanied by traces of a second product, presumably the isomer (**13**) [6].

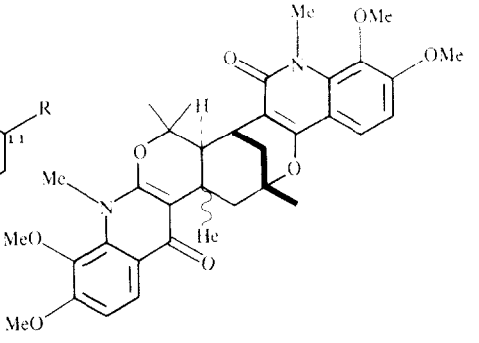
The isolation of araliopdimerines A, B, and C increases the members of the small group of dimeric quinolone alkaloids which includes pteledimerine and pteledimeridine [10, 11], paraensidimerines A–G [6, 7, 8], vepridimerines A–E [4, 12] and geijedimerine [13]. All these dimers have been isolated from the Rutaceae and all are optically inactive.

EXPERIMENTAL

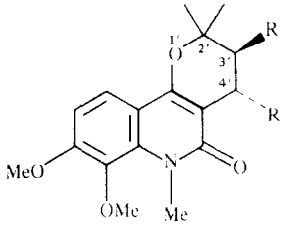
Mps: uncorr. UV spectra were obtained, in EtOH and IR spectra as (KBr discs. NMR spectra were run in $CDCl_3$ solution at 25° 200.13 M Hz for ^1H (shifts relative to $CDCl_3$ at δ_H 7.25) and at 50.32 M Hz for ^{13}C (shifts relative to $CDCl_3$ at δ_C 77.0). EIMS were obtained at 70 eV. Optical rotations were measured on an AA-100 digital polarimeter.



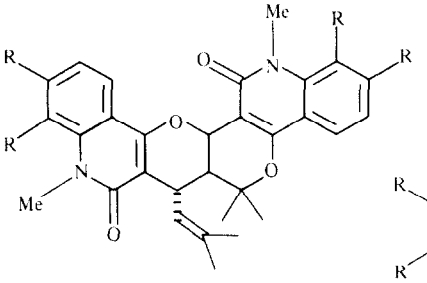
1 α He, R = OMe
2 β He, R = OMe
10 $\Delta^{16,16a}$, R = H
11 $\Delta^{16,16a}$, R = OMe
13 $\Delta^{6a,16a}$, R = OMe



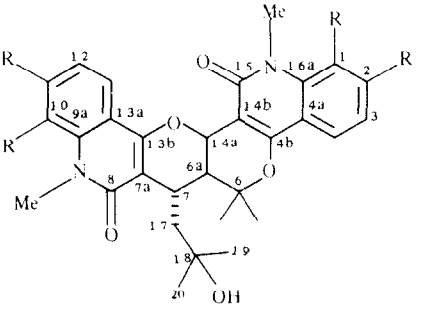
3 α He
4 β He



5 R = OH
12 R = H, $\Delta^{3',4'}$



6 R = H
7 R = OMe



8 R = H
9 R = OMe

Isolation. The mixture (4 g) of dimers, obtained from bark (5 kg) of *A. tabouensis* in the previous study [5], was chromatographed on silica gel (Merck Kieselgel 60, 100 g) eluting successively with hexane, hexane–ethyl acetate and ethyl acetate. Fractions were combined on the basis of TLC. Preparative TLC and crystallisation afforded three new alkaloids, in addition to some known compounds [5]. The new compounds are presented in order of increasing polarity.

Araliopdimerine A (**7**): Colourless crystals (hexane–$CHCl_3$) (280 mg) m.p. 259–260°, $[\alpha]_D^{25} \pm 0$ ($CHCl_3$; *c* 1.0); ν_{max} 1630, 1580, 1560, 1495, 1450, 1400, 1380, 1300, 1255, 1170, 1120, 1055, and 1000 cm^{-1}; λ_{max} (ε) 300sh (11 800), 317 (15, 100), 300 (18, 400), 258sh (36 400), 250sh (43 000), 239 (69 800), and 235sh (66 800) nm: *m/z* (rel. int.) 602 (M^+) (20), 533 (12), 368 (13), 302 (15), 301 (48), 287 (20), 286 (100), 256 (24), and 77 (13). [Found: C, 68.00; H, 6.10; N, 4.75; M^+ 602.2550. $C_{34}H_{38}N_2O_8$ requires C, 67.80; H, 6.30; N, 4.60%; M^+ 602.2628].

Araliopdimerine C (**11**). Colourless needles (hexane–$CHCl_3$) (90 mg) mp 254–255°, $[\alpha]_D^{25} \pm 0$ ($CHCl_3$; *c* 1.1) ν_{max} 1620, 1580, 1480, 1450, 1380, 1320, 1250, 1170, 1120, 1060, 1000, 870 and 800 cm^{-1}; λ_{max} (ε) 348sh (10,000), 330 (11,500), 320 (13,000), 303sh (11,000), 272sh (30 000), and 237 (43 000) nm: δ_H 7.69 and 7.68 (both *d*, $J = 9.0$ Hz, H-4 and H-13), 7.50 (*br s*, H-16), 6.80 (2H, *d*, $J = 9.0$ Hz, H-3 and H-12), 3.90, 3.89, 3.85 and 3.82 (4 × OMe), 3.68 and 3.67 (2 × NMe), 3.53 (*br t*, H-7), 2.58 (*br s*, H-6a), 1.95, 1.70, and 1.29 (3 × CMe), 1.92 (*dd*, $J = 14$, 2.2 Hz, H-19), and 1.74 (*br dd*, $J = 14$, 2.5 Hz, H-19); δ_C 163.9, 162.8 (C-8, C-17), 155.5, 155.8 (C-2, C-11), 155.3, 154.7 (C-4b, C-13b), 136.1, 136.5 (C-1, C-10), 134.0, 133.8 (C-9a, C-18a), 130.3 (C-16a), 127.4 (C-16), 119.2, 119.9 (C-4, C-13), 111.8, 112.3, (C-4a, C-13a), 108.3, 102.9 (C-7a, C-16b), 106.9, 106.8 (C-3, C-12), 82.0 (C-6), 73.2 (C-15), 61.5 (2), 56.2, 56.1 (4 × OMe), 47.9 (C-6a), 33.3 (2) (2 × NMe), 31.3 (C-19), 26.1 (C-7), 27.8, 27.7, and 22.6 (3 × CMe); *m/z* (rel. int.) 600 (M^+) (20), 585 (15), 527 (15), 366 (25), 365 (40), 351 (27), 350 (100), 320 (25), 300 (10), 286 (13), and 178 (12). [Found: C, 68.25; H, 6.15; N, 4.40; M^+ 600.2702. $C_{34}H_{36}N_2O_8$ requires C, 68.05; H, 6.05; N, 4.70%; M^+ 600.2659].

Araliopdimerine B (**9**). Yellow granules (Et_2O) (120 mg) mp 246–247°, $[\alpha]_D^{25} \pm 0$ ($CHCl_3$; *c* 1.4) ; ν_{max} 3350, 2930, 1630, 1570, 1495, 1450, 1400, 1380, 1320, 1300, 1280, 1255, 1120, 1000, 975 and 920 cm^{-1}; λ_{max} (ε) 326sh (11,600), 315 (13,000), 298 (15,500), 288sh (14,00), 256sh (31,000), 248 sh (38,200) and 237 (62,000) nm; *m/z* (rel. int.) 620 (M^+) (10), 302 (35), 301 (35), 287 (16), 286 (100), 256 (24), 128 (10) , 107 (20), and 77 (20). [Found: C, 65.60; H, 6.60; N, 4.30; M^+ 620.2719. $C_{34}H_{40}N_2O_9$ requires C, 65.80; H, 6.45; N, 4.50%; M^+ 620.2788].

Hydration of araliopdimerine A (**7**). Dimer (**7**) (100 mg) was added slowly to a stirred solution of $Hg(OAc)_2$ (0.55 g) in H_2O (5 ml) and THF (5 ml) at 25°C. After the addition was complete the reaction mixture was stirred for 3 h. Following the addition of NaOH solution (3 M, 10 ml) and aqueous $NaBH_4$ solution (0.5 M; 10 ml) the aqueous phase was decanted and extracted with $CHCl_3$ in the usual way. The crystallization of the crude product from Et_2O afforded araliopdimerine **B**(**9**) (80 mg) m.p. 247–248°, identical in all respects with authentic (**9**).

Oxidation of vepridimerines A(**1**) *and B*(**2**). An equimolar mixture (210 mg) of **1** and **2** was refluxed for 4 hr in dry C_6H_6 (40 ml) containing DDQ (700 mg). The reaction mixture was diluted with $CHCl_3$ and washed with aq. $NaHCO_3$ and H_2O. The crude product (180 mg), which showed one major spot on TLC, was purified by prep. TLC and crystallization from $CHCl_3$–hexane to yield araliopdimerine C (**11**) (130 mg) as colourless needles mp 254–255°, identical in all respects with authentic (**11**). A minor product (10 mg) is probably the isomer(**13**).

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