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ANNONELLIPTINE, AN ALKALOID FROM *ANNONA ELLIPTICA*

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Key Word Index—*Annona elliptica*; Annonaceae; alkaloid; annonelliptine.

Abstract—Annonelliptine has been isolated from *Annona elliptica* and its structure has been identified as (*R*)-7-hydroxy-1-(4′-hydroxybenzyl)-5,6-dimethoxy-*N*-methyl-1,2,3,4-tetrahydroisoquinoline.

Application of UV, ^{1}H NMR and mass spectroscopy (see Experimental) indicated that annonelliptine isolated from *Annona elliptica* has the structure of a 1-(4′-hydroxybenzyl)-*N*-methyl-1,2,3,4-tetrahydroisoquinoline trisubstituted in ring A by one hydroxyl and two methoxyl groups. The main problem in the structural elucidation was the recognition of the substitution pattern in ring A. This was solved by NMR measurements. The signal for C-1 in the ^{13}C NMR spectrum (Table 1) was assigned by its doublet structure in the SFORD spectrum. The chemical shift of C-3 is in agreement with the corresponding signal of coclaurine [1] considering the shift differences by *N*-methylation. As the signal of the α-carbon should have approximately the same chemical shift in both alkaloids, the signal at δ 19.0 had to be assigned to C-4. The signals of C-1′ to C-6′ are in agreement in both alkaloids. The pH-induced shifts (cf. refs. [1, 2]) for the ensemble of the signals of C-4a to C-8a are in accordance with structure **1** and three other substitution patterns with hydrogen and hydroxyl in position 5/6, 6/7, or 7/6, respectively. The large chemical shift difference for C-4 in annonelliptine (Table 1) and coclaurine (29.0 ppm [1]) is only in agreement with an oxygen substituent at position 5 in annonelliptine (cf. ref. [3]), thus excluding the 5-hydro-6-hydroxy structure. In the NOE difference spectrum (200 MHz), a positive enhancement for the aromatic ring A proton was observed when H-1 was irradiated. This is only in agreement with structure **1**. Annonelliptine and (*R*)-coclaurine show negative Cotton effects at 282 or 286 nm ($a = -10.0°$ and $-17.1°$, respectively, cf. ref. [1]). 5,6,7-Trisubstituted and 6,7-disubstituted 1-benzyl-1,2,3,4-tetrahydroisoquinolines of the same absolute configuration at C-1 have the same sign of the Cotton effect for the α-band according to a theoretical approximation [4], thus annonelliptine possesses the (*R*)-configuration also. Negative effects in 6,7-disubstituted and 5,6,7-trisubstituted tetrahydroisoquinolines indicate (*M*)-helicity of the piperideine ring [4] and therefore a quasi-axial conformation of the benzyl group in (*R*)-coclaurine and (*R*)-annonelliptine.

EXPERIMENTAL

Plant material. A. elliptica R. E. Fries was collected in November in Valle de Viñales, Pinar del Río, Cuba, and identified by Tec. Ramona Oviedo, Havana. A voucher specimen has been deposited at the Herbarium of the Institute of Botany, Academy of Sciences of Cuba, Havana.

Annonelliptine (**1**). Dried (50°), ground leaves and stems of *A.*

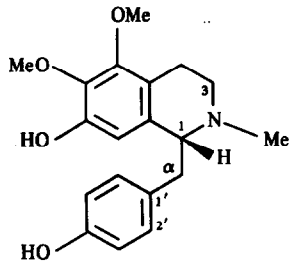

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Table 1. ^{13}C NMR chemical shifts of annonelliptine (**1**)

Carbon	δ in DMSO-d_6 (multiplicity)	δ in DMSO-d_6/NaOD (multiplicity)	Δδ
1	64.1 (*d*)		
3	45.9 (*t*)		
4	19.0 (*t*)		
4a	118.2 (*s*)	106.9 (*s*)	−11.3 *para**
5	150.1 (*s*)	149.9 (*s*)	−0.2 *meta*
6	138.6 (*s*)	141.5 (*s*)	+2.9 *ortho*
7	148.3 (*s*)	162.1 (*s*)	+13.8 *ipso*
8	110.4 (*d*)	114.5 (*d*)	+4.1 *ortho*
8a	133.5 (*s*)	133.5 (*s*)	±0.0 *meta*
α	39.9		
1′	130.2 (*s*)	121.6 (*s*)	−8.6 *para*
2′, 6′	130.1 (*d*)	129.4 (*d*)	−0.7 *meta*
3′, 5′	114.5 (*d*)	118.3 (*d*)	+3.8 *ortho*
4′	155.1 (*s*)	168.2 (*s*)	+13.1 *ipso*
NMe	42.2 (*q*)		
OMe	59.8 (*q*)		
OMe	60.0 (*q*)		

*Position relative to C-7 or C-4′ (*ipso*-carbons).

elliptica were extracted with EtOH at room temp. Evapn of the EtOH in *vacuo* gave a residue which was partitioned between 0.5 M HCl and C_6H_6–Et_2O (1:1). After addition of $KHCO_3$ to the aq. layer, the latter was extracted with $CHCl_3$–EtOH (2:1). Evapn of the solvents gave raw material, which was chromatographed over silica gel with $CHCl_3$–MeOH (19:1) and later over the same adsorbent with toluene–MeOH–15 N NH_3 (88:11:0.6). Crystallization from MeOH afforded **1**; yield 0.03%; needles, mp 198–200°, $[\alpha]_D^{22}$ −101.0° [$CHCl_3$–MeOH (1:1); *c* 0.38]. IR ν_{max}^{KBr} cm^{-1}: 1606, 1593, 1516. UV λ_{max}^{MeOH} nm (log ε): 282 (3.51), 225 (sh, 4.22). ORD (MeOH): $[\phi]_{290}$ −1450° (trough), $[\phi]_{275}$ −450° (peak), $[\phi]_{235}$ −6600° (trough). ^1H NMR (200 MHz, DMSO-d_6, TMS): δ 2.27 (*s*, 3H, NMe), 3.68 (*s*, 6H, OMe), 6.28 (*s*, 1H, 8-H), 6.60 (*d*, *J* = 8 Hz, 2H, H-3′, H-5′), 6.93 (*d*, *J* = 8 Hz, 2H, H-2′, H-6′), 8.90 (*s*, 1H, OH), 9.06 (*s*, 1H, OH). EIMS (6–16 eV) *m/z* (rel. int.): 222 [M − hydroxybenzyl]$^+$ (100), 107 [hydroxybenzyl]$^+$ (20). EAMS (2–4 eV) *m/z*: 328 [M − H]$^-$. (Found: C, 69.6; H, 7.5; N, 4.2. $C_{19}H_{23}NO_4$ requires: C, 69.3; H, 7.0; N, 4.2%.)

The NOE difference expts were carried out at 200 MHz using an automated sequence. The concn of **1** in DMSO-d_6 was < 5% (w/v) and the sample was examined without degassing.

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PYRROLIZIDINE ALKALOIDS FROM SEEDS OF *CROTALARIA SCASSELLATII*

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Key Word Index—*Crotalaria scassellatii*; Leguminosae; seeds; pyrrolizidine alkaloids; axillaridine; axillarine; desoxyaxillarine.

Abstract—Three pyrrolizidine alkaloids were isolated from the seeds of *Crotalaria scassellatii*. Axillaridine and axillarine were the two major alkaloids whereas the third minor alkaloid was a new compound. Its structure was determined as desoxyaxillarine.

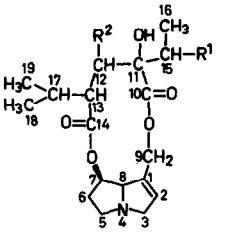
INTRODUCTION

Crotalaria species are known as a rich source of pyrrolizidine alkaloids. Therefore it was presumed that *C. scassellatii*, an East African species, also contained these compounds. After extraction and purification of the seeds of the plant, four alkaloids could be detected by TLC. We succeeded in the isolation of one minor and two major alkaloids. The two major alkaloids were identified as axillarine (**2**) and axillaridine (**1**), which were previously isolated from *C. axillaris* [1]. The minor alkaloid is new and the name desoxyaxillarine (**3**) is proposed.

RESULTS AND DISCUSSION

Methanol extraction of the seeds was followed by purification as previously described [2]. Two alkaloids were separated by low-pressure column chromatography (CC) from the resulting mixture. The mass spectra gave the formulae $C_{18}H_{27}NO_6$ (**1**) and $C_{18}H_{27}NO_7$ (**2**). The fragmentation patterns of both alkaloids and the agreement of the melting points with those given in an earlier paper [1] proved the structures to be axillaridine (**1**) and axillarine (**2**). This was also confirmed by the NMR data (Tables 1 and 2).

By investigation of the mother liquors of the CC fractions we succeeded in isolating a third, minor, alkaloid



R^1 = H; R^2 = OH : **1**
R^1 = R^2 = OH : **2**
R^1 = OH; R^2 = H : **3**