Phytochemistry, Vol 23, No 11, pp 2706–2707, 1984
Printed in Great Britain

0031–9422/84 $3 00 + 0 00

(−)-(*R*,*R*)-7′-*O*-METHYLCUSPIDALINE FROM THE LEAVES OF *ARISTOLOCHIA ELEGANS*

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(*Received* 6 *February* 1984)

Key Word Index—*Aristolochia elegans*, Aristolochiaceae, 11,12′-linked bisbenzyltetrahydroisoquinoline alkaloids, (−)-(*R*,*R*)-7′-*O*-methylcuspidaline

Abstract—The chloroform extract of the defatted leaves of *Aristolochia elegans* has yielded a bis-1-benzyltetrahydroisoquinoline alkaloid with one diphenyl ether link between rings C and C′ On the basis of spectroscopic analysis this has been identified as the previously unreported (−)-(*R*,*R*)-7′-*O*-methylcuspidaline

INTRODUCTION

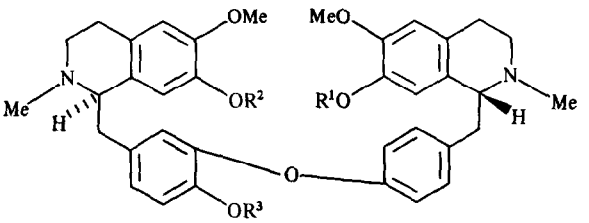
Aristolochia elegans is a Brazilian species that is grown in Egypt as an ornamental plant It has been reported that this species contains an alkaloid causing contraction of the uterus [1] and that an extract has mitotic activity [2] Previous work by one of us (N S) has revealed the presence of sitosterol, (−)-cubebin, ent-kaurane-16,17-diol, allantoin, magnoflorine and aristolochic acid in the roots [3, 4] In addition two basic compounds have been reported from the aerial parts [5] but not identified We now report the results of an examination of the leaves of this species and the isolation of a hitherto unrecorded 11,12′-linked 1-benzyltetrahydroisoquinoline dimer which has been assigned structure **1** Alkaloids of this type appear to be rare in *Aristolochia* species, the only previous record being for (−)-curine from *A indica* [6] This study failed to show the presence of any nitro compounds in the leaves of *A elegans*

RESULTS AND DISCUSSION

After preliminary defatting with petrol (bp 60–80°) the leaves of *A elegans* were extracted with chloroform The chloroform extract was concentrated and then extracted with 1 N HCl Basification of the acid extract and re-extraction into chloroform gave a mixture of bases from which the major component was separated by circular prep TLC, in a yield of 0 0005%

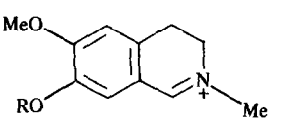
The alkaloid, which was obtained only in an amorphous form, exhibited a bathochromic shift in the UV spectrum indicating that it was phenolic The ^{1}H NMR spectrum, which showed sharp singlets at δ2 46 and 2 54 (2 × NMe) and at δ3 59, 3 80, 3 81 and 3 84 (4 × OMe), together with the mass spectrum, which gave a weak $[M]^+$ *m/z* 624 that analysed for $C_{34}H_{44}N_2O_6$, suggested that the alkaloid was a bisbenzyltetrahydroisoquinoline

The facile fragmentation of the alkaloid in the EIMS to give major ions at *m/z* 206 (**2**) and 192 (**3**) is typical of dimeric bisbenzylisoquinolines with a single ether link between the C and C′ rings [7] and the presence of both ions indicates that the OH substituents must be placed in one of the isoquinoline moieties and not in ring C, thereby eliminating the known alkaloid dauricine (**4**) Minor ions at *m/z* 417 ($C_{26}H_{27}NO_4$) and 326 ($C_{19}H_{20}NO_4$) containing four oxygen atoms and therefore derived from ABC-C′ and ABC rings, respectively, must in view of the number of carbons present, contain only 2 methoxyl groups and the hydroxyl must be assigned to either C-6 or



	R¹	R²	R³
1	Me	H	Me
4	Me	Me	H
5*	H	Me	Me
6	H	H	Me

*(*S*,*S*)−configuration



	R
2	Me
3	H

C-7 in ring-A This eliminates the only other known tetramethoxy-*N*,*N*-dimethyl bis alkaloid, thalibrine (**5**) [6]

The assignment of the hydroxyl substituent to C-7 comes from an analysis of the resonance positions of the methoxyl substituents in the ^{1}H NMR spectrum An examination of published spectral data for alkaloids of this class [6], and for 6,7,4′-substituted *N*-methylcoclaurines [8], shows clearly that shielded OMe resonances (*ca* δ3 60) arise from substituents at C-7 while resonances for C-6, and C-12 (C-4′ of monomers) methoxyl groups occur at *ca* δ3 80 Thus, in dauricine (**4**) there are two signals at δ3 60 and others at δ3 80 and 3 83 [9], while in thalibrine (**5**) there is only one at δ3 60 with the other three above δ3 75 [6] In cuspidaline (**6**) all three methoxyl resonances are found at δ3 83 [6] (cf δ3 80, 3 81 and 3 84 for deshielded methoxyl resonances in the isolated alkaloid) On this basis the fourth methoxyl resonance at 3 59 in the isolated alkaloid must be assigned to C-7′ and the isolated alkaloid must be 7′-*O*-methylcuspidaline (**1**) These arguments are supported by the occurrence of H-8 and H-8′ signals at δ6 05 and 6 36, the former being a typical resonance where there is an adjacent hydroxyl substituent, the latter where there is an adjacent alkoxy substituent [8]

The final problem, concerning the stereochemistry of the new alkaloid at C-1 and C-1′, is resolved by the strongly negative OR which requires that it has the usual *R*,*R* stereochemistry [6]

EXPERIMENTAL

UV MeOH ^{1}H NMR $CDCl_3$ at 250 MHz with TMS as int standard EIMS 70 eV, probe 200°

Plant material Aerial parts of *A elegans* Mast were collected from the El Nozha Garden, Alexandria The identity of this species was confirmed by the late Dr V Tackholm and a voucher has been deposited in the Faculty of Pharmacy, University of Alexandria

Extraction and isolation of alkaloid Dried, powdered, leaves (1 kg) were extracted in a Soxhlet, first with petrol (bp 40–60°) and then with $CHCl_3$ The $CHCl_3$ extract was concd and partitioned with 1 N HCl (5 × 25 ml) The combined acid fractions were basified with NH_4OH and re-extracted into $CHCl_3$ (5 × 25 ml) The combined $CHCl_3$ extract so obtained was concd to dryness and the residue subjected to prep circular TLC on silica gel (toluene–Me_2CO–EtOH–NH_4OH, 40 40 3 1) to give **1** (5 mg) which was then pptd from $CHCl_3$ by the addition of petrol

(−)-(R,R)-7′-O-*Methylcuspidaline* (**1**) Pptd as an amorphous powder $[\alpha]_D$ −105° (*c* 0 001, $CHCl_3$) Found $[M]^+$ 624 3188, $C_{38}H_{44}N_2O_6$ requires 624 3199 UV λ_{max} nm 285 (log ε3 98), (+ NaOH) 285, 305 ^{1}H NMR δ2 46 (3H, *s*, 2-NMe), 2 54 (3H, *s*, 2′-NMe), 3 59 (3H, *s*, 7′-OMe), 3 80, 3 81, 3 84 (3 × 3H, 3 × *s*, 3 × OMe), 6 05 (1H, *s*, H-8), 6 36 (1H, *s*, H-8′), 6 47, 6 56 (2 × 1H, 2 × *s*, H-5 and H-5′), 6 62 (1H, *d*, *J* = 1 7 Hz, H-10), 6 78, 7 00 (4H, ABq, *J* = 8 Hz, C′-ring protons), 6 86 (1H, *dd*, *J* = 8 2 and 1 7 Hz, H-14), 6 91 (1H, *d*, *J* = 8 2 Hz, H-13) EIMS *m/z* (rel int) 624 (1), 417 1914 $[C_{26}H_{27}NO_4]^+$ (2), 326 1679 $[C_{19}H_{20}NO_4]^+$ (2), 211 0755 $[C_{14}H_{11}O_2]^+$ (2), 206 (99), 192 (100), 191 (26), 177 (34)

Acknowledgements—One of us (N S) extends her thanks to the British Council for the award of a travel scholarship under the auspices of which this work was carried out Ilias Mohammad, Phytochemistry Research Laboratories, University of Strathclyde, is thanked for technical assistance and valuable discussion

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