Pergamon

PII: S0031-9422(98)00016-8

Phytochemistry, Vol. 48, No. 3, pp. 581–582, 1998

Printed in Great Britain
0031 9422/98 $19.00 + 0.00

VOLATILE ALKALOIDS FROM *ARECA CATECHU*

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(*Received* 27 *October* 1997)

Key Word Index—*Areca catechu*; Palmae; betel nut; nicotinic esters; tetrahydropyridine-3-carboxylic esters; piperidine-3-carboxylic esters.

Abstract—High resolution GC-mass spectral analysis of the volatile bases present in fruits of *Areca catechu* confirmed the presence of arecoline and guvacoline, but also indicated the presence of six other related, but hitherto undetected, alkaloids. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Areca catechu is the only one of 54 *Areca* species known to contain alkaloids [1, 2]. In early work [3–7], arecoline and guvacoline (methyl 1-methyl-1,2,3,6-tetrahydropyridine-3-carboxylate and methyl 1,2,3,6-tetrahydropyridine-3-carboxylate, respectively) and the corresponding carboxylic acids were isolated but since that time no other alkaloids have been isolated, nor has any significant instrumental or other analytical work [cf 8] been conducted on the *Areca* species of palms. In this paper, we describe our study by GC-mass spectrometry of the volatile basic components of betel nuts.

RESULTS AND DISCUSSION

Extraction of crushed macerated nuts with either dichloromethane or ethanol-free chloroform under mild conditions yielded a mixture of basic compounds (constituting 0.1–0.15% of the total nut) from which, by GC-mass spectral analysis, we have identified eight compounds **1**–**8** (Table 1), which amounted to ~98% of the extracted material.

The aromatic nicotinates (**1** and **2**) and arecoline (**3**) were identified by comparison of their R_ts and fragmentation data with those of authentic samples. Mass spectral data for the nicotinates (**1** and **2**) arecoline (**3**) guvacoline (**4**) and nicotine (**8**), were identical with the data reported in the literature [8–12]. The identification of the ethyl ester analogue of arecoline (**5**), was based upon the M_r and mass spectral fragmentation pattern which, after loss of the ethyl group, was virtually identical to that of arecoline. The mass spectra of the piperidine derivatives (**6** and **7**), were consistent with their structures being closely similar to each other and with that for methyl piperidine-3-carboxylate and its 1-propyl derivative [13]; the base peaks at m/z 142 correspond with the loss of the *O*-alkyl groups.

The result of our analysis clearly establishes that betel nuts contain a family of closely related alkaloids with varying degrees of hydrogenation and the unexpected identification of nicotine (**8**), albeit in only trace quantities, supports a single biogenetic pathway to the synthesis of 3-substituted pyridine alkaloids [cf 14, 15] in *A. catechu* palms.

The carboxylic acids, which had been noted earlier, were not detected, as they were retained in the aqueous extracts during isolation of the volatile bases. The identification of the ethyl esters is significant. They were not artefacts of the isolation of the bases and, to the best of our knowledge, they are the first recorded pyridine-based ethyl esters isolated from natural sources.

We found no evidence for the presence of "arecolidine" (3,4-dimethoxy-1-methyl-1,2-dihydropyridine) for which isolated reports [e.g. 16] without sustainable structural evidence have been made. It is possible that this compound has been confused with **6**, which has a similar molecular formula or with an isomer of **3**.

EXPERIMENTAL

Extraction

Green, immature, fruits of *Areca catechu* L. were husked and seeds (500 g) chopped, crushed and extracted using a Soxhlet extractor with CH_2Cl_2 (4 l), made slightly basic with conc. NH_4OH. The cooled organic soln was extracted with H_2SO_4 (2 M, 25 ml). The aq. extracts were neutralised with aq. NaOH (6 M) and then extracted with CH_2Cl_2 (3 × 10 ml). Dried

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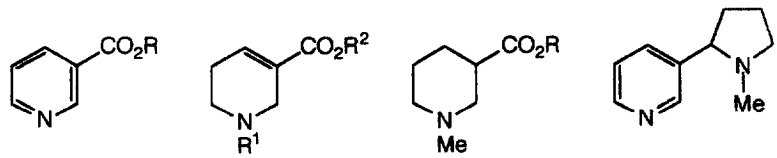

1 R = Me
2 R = Et
3 R^1 = Me, R^2 = Me
4 R^1 = H, R^2 = Me
5 R^1 = Me, R^2 = Et
6 R = Me
7 R = Et
8

Table 1. GC-mass spectral analysis of betel nut volatile base

Retention time (min)	%	M_r	Major MS peaks (m/z)	Identity
8.10	1.80	137	137, 106,[a] 78, 51	Methyl nicotinate (**1**)[b]
8.18	0.20	157	157, 156, 142,[a] 126, 98	Methyl *N*-methylpiperidine-3-carboxylate (**6**)
9.40	0.21	171	171, 156, 142,[a] 126, 98	Ethyl *N*-methylpiperidine-3-carboxylate (**7**)
9.36	0.49	151	151, 123, 106,[a] 78, 51	Ethyl nicotinate (**2**)[b]
10.11	69.83	155	155, 140,[a] 124, 96, 81	Arecoline (**3**)[c]
10.21	0.70	141	141, 126, 110, 82,[a] 81	Guvacoline (**4**)[d]
10.75	24.44	169	169, 140,[a] 124, 96, 92, 81	Ethyl *N*-methyl-1,2,5,6-tetrahydro-pyridine-3-carboxylate (**5**)
11.43	ca 0.02	162	162, 161, 133, 119, 84[a]	Nicotine (**8**)

[a] Base peak.
[b] Identical with authentic samples synthesized from nicotinic acid.
[c] Methyl *N*-methyl-1,2,5,6-tetrahydropyridine-3-carboxylate. Identical with authentic commercially available (Aldrich) sample.
[d] Methyl 1,2,5,6-tetrahydropyridine-3-carboxylate.

($MgSO_4$) (0.5 μl) samples of the CH_2Cl soln were subjected to GC-MS analysis. Virtually identical results were obtained when chopped betel nuts were extracted at room temp. with $CHCl_3$ (4 × 250 ml), which had been washed well sequentially with H_2SO_4 and H_2O, and made slightly basic with conc. NH_4OH.

Analysis

GC separation prior to MS analysis was effected on a capillary column (50 m × 0.32 mm) with a 5% diphenyl polysiloxane: 95% dimethyl polysiloxane stationary phase at a flow rate of He of 1 cm^3 min^{-1} over a temp. gradient of 5° min^{-1} from 50 to 200°.

EIMS of the separated alkaloids were obtained using a quadrupoler mass spectrometer operating at 70 eV.

Acknowledgement—We thank Miss Nurdiyanah Goh binte Abdullah of the Department of Chemistry, University of Brunei Darussalam, for her help in the extraction of alkaloids from betel nuts.

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