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ALKALOIDS OF THE RUTOIDEAE: TRIBE DIOSMEAE*

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Key Word Index—*Agathosma*; *Coleonema*; *Diosma*; *Empleurum*; *Phyllosma*; Rutaceae; Diosmeae; alkaloids; halfordamine, skimmianine; chemotaxonomy.

Abstract—The aerial parts of 42 taxa of the genera *Agathosma*, *Coleonema*, *Diosma*, *Empleurum* and *Phyllosma* (tribe Diosmeae) were screened for alkaloids. Positive results were obtained for five *Agathosma* species and the compounds were identified as halfordamine and skimmianine.

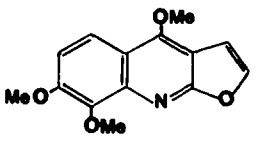
INTRODUCTION

As part of our continuing phytochemical investigation of the Diosmeae, one of the five tribes of the Rutoideae, we have tested 42 species from five genera for alkaloids. Furoquinoline alkaloids with a variety of oxygenation patterns occur widely in the protorutaceous genera, *Zanthoxylum* (Rutoideae) and *Toddalia* (Toddalioideae), and in more advanced genera of Rutoideae, Toddalioideae and Flindersioideae [2]. The only previous reported occurrence of an alkaloid from this tribe was that of skimmianine (**1**), in *Agathosma virgata* (Lam.) Bartl. et Wendl. [3].

RESULTS AND DISCUSSION

HCl extracts of plant material from the genera *Agathosma*, *Coleonema*, *Diosma*, *Empleurum* and *Phyllosma* were tested with the Dragendorff reagent and with iodoplatinic acid and positive results were obtained for five species from the genus *Agathosma*. One of the taxa, *Agathosma capensis*, is the most widely distributed and most polymorphic of the *Agathosma* species [4], and for this reason four collections (two from coastal areas and two from mountainous areas) were investigated. The trimethoxyfuro[2,3b]quinoline alkaloid, skimmianine (**1**) and the trimethoxy-2(1*H*)-quinolinone alkaloid, halfordamine (**2**), were isolated from *A. bisulca*, all four collections of *A. capensis* and from a species as yet undescribed. *A. peglerae* and *A. thymifolia* gave (**1**) as the sole product. The yield of (**1**) varied from 200 μg/g dry wt (0.02% in *A. capensis*, Bean 170) to 1000 μg/g dry wt (0.1% in *A. peglerae*), and that of (**2**) from 10 μg/g dry wt (0.001% in *A. capensis*, Bean 1436) to 90 μg/g dry wt (0.009% in *A. bisulca*).

The genus *Agathosma* is among the most advanced of the genera of the Diosmeae. Moreover, the 33 species of the genus, which have been investigated to date, have been provisionally grouped into an advanced group and a less advanced or more primitive group. All five taxa, reported on in this paper, together with *A. virgata* are regarded as members of the advanced group. Normal rutaceous alkaloids thus do occur in the Diosmeae, but they are rare and the evidence to date seems to indicate that they are confined to the genus *Agathosma*.



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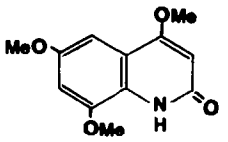

2

EXPERIMENTAL

Mps are uncorr. UV and IR spectra were recorded in EtOH and as KBr discs, respectively. ^{1}H NMR spectra were measured in $CDCl_3$ solns (90 MHz, int. standard TMS). MS were determined at 70 eV.

Plant material. Collection details for the species which gave a positive alkaloid test are given in Table 1.

Extraction and isolation of alkaloids. Ground air-dried aerial parts were extracted with EtOH. The solvent was removed under red. pres. and the residue dissolved in H_2O and acidified with dil. HCl. The ppd fats were filtered and the filtrate extracted with Et_2O (30 ml × 3). The aq. soln was basified with conc. NH_3, extracted with $CHCl_3$ (50 ml × 3), and the $CHCl_3$ dried and removed to give the crude extract which was chromatographed over alumina using $CHCl_3$ as eluant. Mixtures were separated by prep. TLC (silica gel: solvent C_6H_6–EtOAc–Et_2NH, 7:2:1).

Skimmianine (**1**). Colourless prisms, mp 178–179° (Me_2CO–petrol, lit. 177° [5]). Found [M^+] 259.0839; $C_{14}H_{13}NO_4$ requires 259.0845.

Halfordamine (**2**). Colourless prisms, mp 242–243° (benzene, lit. 240–241° [6]. UV λ_{max}^{EtOH} nm (log ε): 250 (4.41), 290 sh (3.35), 301 sh (3.59), 312 (3.72), 328 sh (3.53), 342 (3.39). IR ν_{max}^{KBr} cm^{-1}: 3160 (NH), 1640 (amide CO) 1618, 1578, 1485, 810. ^{1}H NMR: δ3.83, 3.91 and 3.95 (each 3H, *s*, OMe), 5.93 (1H, *s*, 3-H), 6.61 (1H, *d*, *J* = 3 Hz, 7-H), 6.83 (1H, *d*, *J* = 3 Hz, 5-H), 8.73 (1H, *s*, NH). EIMS (probe) *m/z* (rel. int.): 235 [M]$^+$ (100), 234 [M − H]$^+$ (57),

*Part 2 in the series "Chemosystematic Studies in the Genera of the Diosmeae". For part 1 see ref. [1]

Table 1. Plant material

Species	Locality	Date collected	Collector and No.	Herbarium deposition
Agathosma bisulca (Thunb.) Bartl. and Wendl.	Velddrift district, West Coast.	February 1979	Bean 181	Bolus
A. capensis (L.) Düm.	Gysmanshoek pass, Langeberg mountains.	December 1978	Bean 170	Bolus
A. capensis (L.) Düm.	Sebrafontein, Outeniqua mountains.	July 1980	Bean 373	Bolus
A. capensis (L.) Düm.	De Hoop Nature Reserve.	April 1981	Bean 575	Bolus
A. capensis (L.) Düm.	Moeras river valley, Mossel Bay district.	April 1984	Bean 1436	Bolus
A. peglerae Düm.	Albany District, Eastern Cape.	February 1979	Cock *s.n.*	Albany
A. thymifolia Schldl.	Hopefield District, West Coast.	February 1978	Bean 180	Bolus
A. spec. nov.	Moeras river valley, Mossel Bay district.	April 1984	Bean 1428	Bolus

220 $[M-Me]^+$ (20), 206 $[M-CHO]^+$ (30), 205 $[M-CH_2O]^+$ (23), 192 $[220-CO]^+$ (20), 190 $[205-Me]^+$ (11), 177 $[192-Me]^+$ (7), 162 $[190-CO]^+$ (6), 149 $[177-CO]^+$ (7).

Agathosma bisulca: 244.2 mg (0.07%) skimmianine **1** and 35.7 mg (0.009%) halfordamine **2** from 361.5 g aerial parts. *A. capensis* (Bean 170): 223.2 mg of **1** (0.02%) and 30.2 mg of **2** (0.003%) from 972 g. *A. capensis* (Bean 373): 260.3 mg of **1** (0.04%) and 40.2 mg of **2** (0.006%) from 650 g. *A. capensis* (Bean 575): 305.4 mg of **1** (0.04%) and 38.7 mg of **2** (0.005%) from 705 g. *A. capensis* (Bean 1436): 48.3 mg of **1** (0.007%) and 8.4 mg of **2** (0.001%) from 707 g. *A. peglerae*: 1.11 g of **1** (0.1%) from 1.04 kg. *A. thymifolia*: 383.7 mg of **1** (0.06%) from 661 g. *A. spec. nov.*: 217.6 mg of **1** (0.02%) and 49.7 mg of **2** (0.005%) from 993 g.

The following taxa gave negative tests: *Agathosma abrupta* Pillans, *A. affinis* Sond., *A. barosmaefolia* E. and Z., *A. cedrimontana* Düm., *A. ciliaris* Druce, *A. collina* E. and Z., *A. dielsiana* Schltr., *A. eriantha* Stend., *A. geniculata* Pillans, *A. glandulosa* Sond., *A. hispida* Bartl. and Wendl., *A. lanceolata* Engl., *A. latipetala* Sond., *A. marifolia* E. and Z., *A. martiana* Sond., *A. mucronulata* Sond., *A. mundtii* Cham. and Schldl., *A. ovata* Pillans, *A. puberula* Fourcade, *A. pungens* Pillans, *A. recurvifolia* Sond., *A. roodebergensis* Compton, *A. rosmarinifolia* Bartl., *A. salina* E. and Z., *A. scaberula* Düm., *A. serpyllacea* Licht., *A. spinosa* Sond., *A. unicarpellata* Pillans, *Coleonema album* Bartl. and Wendl., *Diosma acmaeophylla* E. and Z., *D. avilana* Williams, *D. prama* Williams, *D. ranosissima* B. and W., *D. recurva* Clan., *Empleurum unicapsulare* (Linn. f.) Skeels and *Phyllosma capensis* Bolus.

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