Phytochemistry, 1978, Vol 17, pp 1068-1069. © Pergamon Press Ltd Printed in England

0031-9422/78/0601-1068 $02.00/0

ALKALOIDS OF *ZANTHOXYLUM OXYPHYLLUM*

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(*Revised received* 28 *October* 1977)

Key Word Index—*Zanthoxylum oxyphyllum*; Rutaceae; corydine; zanthoxyphylline (4,5,6-trimethoxy-*N*:*N* dimethyl aporphinium hydroxide); structural determination.

Zanthoxylum oxyphyllum Edgew. (N. O. Rutaceae) grows abundantly throughout the temperate and subtropical Himalaya from Garhwal to Sikkim and Bhutan mounts [1]. The plant is used for the treatment of various ailments in this sub-continent [2]. On reviewing the literature it has been found that the stem bark of *Z. oxyphyllum* has been analysed for its chemical constituents and an alkaloid, rhetsinine, has been isolated [3]. Since no work seems to have been done on the chemical analysis of the root of this plant, the opportunity to undertake the chemical examination of the roots was undertaken.

RESULTS AND DISCUSSION

The EtOH extract of the air-dried powdered root of *Z. oxyphyllum* yielded corydine (identified by mmp and IR with an authentic sample) and a new alkaloid provisionally named as zanthoxyphylline.

The presence of an aporphine skeleton in zanthoxyphylline, $C_{21}H_{27}NO_4$, was indicated by (i) formation of mellophanic acid mp 238°, on treatment with Ac_2O followed by HNO_3, (ii) UV spectrum: λ_{max}^{EtOH} at 230, 278 and 310 nm and (iii) MS: *m/e* 152 and 165 [4]. The alkaloid gave a positive response with citric acid and Ac_2O [5] and showed a PMR signal corresponding to 6 protons at δ 2.64 characteristic of a *N*-Me group [6] indicating the quaternary nature of the N atom. The IR band at 3300–3400 cm^{-1} suggests the presence of —OH group. The alkaloid on treatment with HI yielded an iodide which after passing through Amberlite IR 410 (OH form) regenerated zanthoxyphylline showing that the —OH group in the alkaloid is attached to the quaternary N atom. The presence of 3 OMe groups at C-4, C-5 and C-6 have been ascertained by PMR studies [4, 6].

Thus, zanthoxyphylline may be represented by the following tentative structure (4,5,6-trimethoxy-*N*:*N*-dimethylaporphinium hydroxide) (**1**).

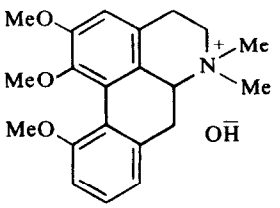
The formation of a few more abundant fragments $\mathbf{a}^+$, $\mathbf{b}^+$, $\mathbf{c}^+$ and $\mathbf{d}^+$ lends further support to the above structure for zanthoxyphylline [4]. The M^+ appeared at *m/e* 339 instead of 357 probably due to the facile loss of the OH group attached to the quaternary N atom in the form of a H_2O molecule.

Isothebaine on treatment with MeI and K_2CO_3 in Me_2CO, formed its methylated methiodide (**2**) which on passing through a column of Amberlite IR 410 (OH form) gave a product which was identical to zanthoxyphylline (mmp and superimposable IR).

EXPERIMENTAL

Extraction. Defatted powdered root bark (5 kg) of *Z. oxyphyllum* (supplied by United Chemical & Allied Products, Calcutta, identity checked by National Botanical Garden from Herbarium Sheet No P-560) was extracted exhaustively with EtOH. The EtOH extract was concd to a thick viscous mass, diluted with H_2O, acidified with HOAc and kept for 18 hr. A black mass settled out and the clear supernatant liquid was filtered. The aq. filtrate gave positive tests for alkaloids. It was concd to a thick viscous mass and extracted with $CHCl_3$. The $CHCl_3$ extract on removal of solvent yielded a crystalline alkaloid, corydine (2.3 g) mp 166–168°. The residual viscous mass was dissolved in MeOH and adsorbed onto a column of Al_2O_3 (10 × 4 cm diam.) which on elution with MeOH–$CHCl_3$ (1:1) yielded an alkaloid provisionally named zanthoxyphylline (4.2 g) mp 202° (decomp.), $[\alpha]^{22}$ + 51.66° (MeOH).

Zanthoxyphylline. The amorphous alkaloid gave a single spot on TLC (R_f = 0.78) with BuOH–HOAc–H_2O (4:1:5). λ_{max}^{EtOH} 230, 278 (inf.), 310 nm; ν_{max}^{KBr} 3400, 1635, 1598, 1512, 1450, 1379, 1311,



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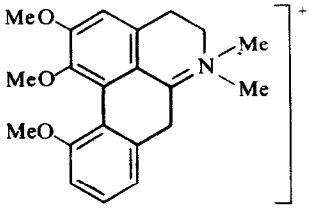
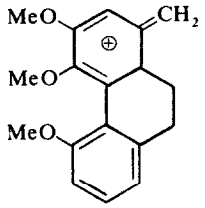
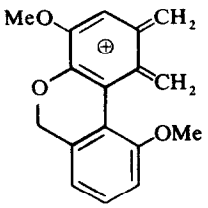


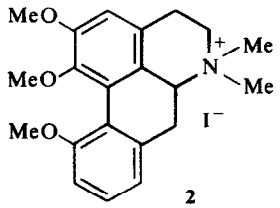
$\mathbf{a}^+$ (*m/e* 339)



$\mathbf{b}^+$ (*m/e* 283)



$\mathbf{c}^+$ (*m/e* 268)



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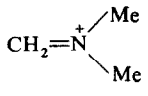

$\mathbf{d}^+$ (*m/e* 58)

1252, 1235, 1215, 1160, 1120, 1065, 1050, 840, 805, 772, 735, 725 cm^{-1}; PMR δ (in CF_3COOH) 6.86 (2H), 6.64 (1H), 650 (1H), 5.35 (1H), 3.59 (9H), 2.65 (6H), 3 (6H); MS *m/e* 339, 283, 268, 255, 212, 167, 165, 152, 58 (base peak); found C 70.51; H 7.62, N 3.85%; OMe 7.57%, $C_{21}H_{27}NO_4$ requires C 70.58, H 7.56, N 3.92%. OMe 8.68% (for 3 OMe groups).

Zanthoxyphylline hydroiodide. The alkaloid (100 mg) in 3 ml H_2O, on treatment with 1 ml HI gave a hydroiodide (90 mg), mp above 300°.

Partial synthesis of zanthoxyphylline. Isothebaine (80 mg), K_2CO_3 (500 mg) and MeI (5 ml) were refluxed in Me_2CO (20 ml) for 36 hr. Excess solvent was removed by distillation and the residue extracted with MeOH and passed through an Amberlite IR 410 column. The eluate yielded a crystalline compound (70 mg) which did not depress the mp of zanthoxyphylline when mixed.

Corydine. The alkaloid was recrystallized from $CHCl_3$, mp 166–168°, λ_{max}^{EtOH} 246, 285, 338 nm; ν_{max}^{Nujol} 3200, 1605, 1580, 1500, 1460, 1390, 1350, 1338, 1314, 1295, 1264, 1245, 1228, 1208, 1186, 1177, 1166, 1145, 1108, 1088, 1070, 1051, 1025, 995, 975, 961, 935, 900, 872, 855, 928, 820, 790, 770, 760, 730 cm^{-1}; PMR ($CDCl_3$), δ 6.88 (2H), 6.67 (1H), 3.82 (6H), 3.65 (3H), 2.45 (3H), 2.86 (6H); found C 70.56, H 6.86, N 4.2%; $C_{20}H_{23}NO_4$ requires C 70.38, H 6.74, N 4.05%.

Acknowledgements—The authors thank Drs D. S. Bhakuni, Central Drug Research Institute, Lucknow and T. R. Govindachari, Ciba-Geigy Research Centre, Bombay for their help in the spectral studies and Prof. A. R. Battersby, (Cambridge) who kindly provided a sample of isothebaine.

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Phytochemistry, 1978, Vol 17, pp. 1069–1070 © Pergamon Press Ltd. Printed in England 0031–9422/78/0601–1069$02.00/0

JASMINIDIN, EIN NEUES MONOTERPENALKALOID AUS *SYRINGA VULGARIS*

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(*Eingegangen* 21 *October* 1977)

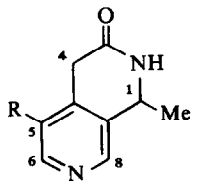
Key Word Index—*Syringa vulgaris*; Oleaceae; alkaloids; jasminidine; jasminine; tyrosol.

Bei Screening-Untersuchungen wurden in Blättern von *Syringa vulgaris* L. (Oleaceae) dragendorffpositive Substanzen nachgewiesen [1]. Wie im folgenden beschrieben, konnten die Monoterpenalkaloide Jasminidin und Jasminin isoliert werden, wenn die Blätter im Mai geerntet wurden. Dagegen erwiesen sich im September geerntete Blätter als alkaloidfrei.

Nach hochauflösender MS besitzt Jasminidin die Summenformel $C_9H_{10}N_2O$. Eine starke IR-Bande bei 1682 cm^{-1} zeigt an, daß ein N-Atom zu einer Amidgruppe gehört. Das gleichzeitige Vorkommen des schon strukturell aufgeklärten Jasminins (**2**) in dieser Pflanze (vgl. unten) legt nahe, für Jasminidin die Struktur des 1-Methyl-1,2,3,4-tetrahydro-2,7-naphthyridin-3-ons (**1**) anzunehmen, die mit den spektroskopischen Eigenschaften in Einklang steht. Das Absorptionsmaximum bei 259 nm entspricht einem 3,4-disubstituierten Pyridin [2]. Im PMR-Spektrum läßt sich die MeCH-Gruppierung durch ein Dublett bei δ 1.58 und ein Quartett bei 4.72 ppm erkennen. Die Protonen an C-4 ergeben ein Singulett, dessen Lage bei 3.58 ppm mit der Erwartung übereinstimmt [3]. Das 5-H-Dublett bei 7.07 ppm beweist ortho-Kopplung mit 6-H, die α-Protonen des Pyridinrings liefern ein Multiplett bei 8.45 ppm.

Das Hauptalkaloid besitzt nach hochauflösender MS die Summenformel $C_{11}H_{12}N_2O_3$ und nach IR eine Ester- sowie Amidgruppe. Es erwies sich nach Schmelzpunkt, Drehwert, UV, PMR und MS als Jasminin (**2**) [4]. Im PMR-Spektrum verschwindet nach Schütteln mit D_2O das Signal bei δ 7.70 ppm (NH) und das Multiplett bei 4.78 ppm (1-H) vereinfacht sich zu einem Quartett, was bei einer NHCHMe-Struktur zu erwarten ist. Abweichend vom beschriebenen Spektrum von **2** [4] befindet sich das Multiplett für die nichtäquivalenten Protonen an C-4 bei 4.05 ppm. Jasminin wurde bisher aus den Oleaceen *Jasminum gracile*, *J. lineare* und *Ligustrum novoguineense* isoliert [4]. Es ist kein Artefakt, das bei der Aufarbeitung mit NH_3 entsteht, sondern ein natürlich vorkommendes Alkaloid [4].

Jasminidin (**1**) und Jasminin (**2**) besitzen negative



1: R = H
2: R = CO_2Me

Cotton-Effekte bei etwa 256 (a −10.9°) bzw. 267 nm (a −2.0°). Aufgrund des chiroptischen Vergleichs mit Venoterpin und Actinidin [5] sollte ihnen die S-Konfiguration zukommen.