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N-FORMYLCYTISINE: A NEW ALKALOID FROM *THERMOPSIS CHINENSIS*

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Abstract—A new base have been isolated from *Thermopsis chinensis* along with *N*-methylcytisine, cytisine, anagyrine and lupanine. The new alkaloid have been shown to be *N*-formylcytisine.

INTRODUCTION

THE PLANTS of the genus *Thermopsis* (Leguminosae) are known as a rich source of lupine alkaloids.[1-3] Cytisine has been isolated from *Thermopsis chinensis* (= *T. fabaceae*)[4] by Rjabinin *et al.*[5] and Jarzebinska.[6] Further chemical examination of the alkaloids obtained from the ethanolic extract of the roots of *Thermopsis chinensis*, collected in April in Okinoerabu-jima, Amami islands, Japan, has resulted in the isolation of five more basic constituents, the characterization of which is described in the present communication.

RESULTS

N-Methylcytisine (0·042%), cytisine (0·005%), anagyrine (0·025%) and lupanine (trace) were identified by comparison with authentic samples by method previously described[7] (MS, m.m.ps, co-TLC, and superimposable IR spectra). The fifth alkaloid, a new compound, was isolated in 0·0007% yield. Its UV spectrum (see Experimental) was typical of a modified cytisine chromophore.[8] The IR spectrum showed the presence of a carbonyl group (broad band at 1650–1660 cm^{-1}) but there were no bands due to hydroxy or amine absorption.

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The molecular ion peak of the base on the MS appeared at *m/e* 218 which was 28 m.u. more than that of cytisine, and the main fragment pattern below *m/e* 190 was superimposable to that of cytisine. Moreover, two fragmentation processes of $M^+ \rightarrow m/e$ 146 and $M^+ \rightarrow m/e$ 190 $\rightarrow m/e$ 147 $\rightarrow m/e$ 146 were proved by the presence of appropriate metastable ions,[9,10] and the latter process was completely analogous to the behaviour of cytisine.[11,12] Furthermore, the base was hydrolyzed by refluxing in 20% HCl to cytisine, and also was easily reduced with diborane[13] to *N*-methylcytisine. From these results, the base was identified as *N*-formylcytisine. This structural assignment was confirmed by comparing the natural compound with synthetic material (m.m.p., MS, IR, and co-TLC). *N*-Formylcytisine also has been tentatively found (unpublished results) in the ethanolic extracts of the aerial parts of *Euchresta japonica* (Leguminosae).

EXPERIMENTAL

The m.ps were determined on the Kofler block and uncorrected. The UV spectra were measured in 95% EtOH (aldehyde-free), the IR spectra in KBr pellets.

Isolation of the alkaloids. Air-dried and finely ground roots of *T. chinensis* (6 kg) were soaked in 70% EtOH and extracted 5× with the same solvent as previously described.[7] The crude alkaloid mixture was chromatographed over alumina: the C_6H_6–Et_2O (1:0 and 1:1) eluates were mixed together and the major components in this fraction (lupanine, anagyrine, and *N*-methylcytisine) were isolated by repeated chromatography on alumina by method previously described.[7] The combined CH_2Cl_2–MeOH (1:0, 50:1 and 1:1) eluates containing *N*-methylcytisine, *N*-formylcytisine, cytisine and an unknown alkaloid were chromatographed on a silica gel column in CH_2Cl_2–MeOH–conc. NH_4OH (95:4:0·3). Rechromatography of these fractions on a column of silica gel followed by preparative TLC on silica gel with CH_2Cl_2–MeOH–conc. NH_4OH (90:9:1) separated *N*-methylcytisine, *N*-formylcytisine and cytisine. *N*-Formylcytisine crystallized from CH_2Cl_2–Et_2O as stout needles (yield 0·0007%), m.p. 170–172°, $[\alpha]_D^{20}$ −233° (*c* 0·43, EtOH), UV: λ_{max}^{EtOH} 232, 309 nm (log ε: 3·82, 3·85). IR: ν_{max}^{KBr} 1650–1660 cm^{-1} (*b*, C–O). MS: *m/e* 218 (M^+, 81%), significant peaks at *m/e* 190(14), 160(17), 147(63), 146(100) (Found: C, 65·98; H, 6·27; N, 12·72. $C_{12}H_{14}N_2O_2$ requires: C, 66·03; H, 6·47; N, 12·84%).

Hydrolysis of N-*formylcytisine.* *N*-Formylcytisine was hydrolyzed in boiling 5 N HCl for 4 hr under reflux, to give cytisine (m.m.p., co-TLC, MS and superimposable IR spectra).

Reduction of N-*formylcytisine.* BF_3-etherate (0·5 ml) in diglyme (1 ml) was added dropwise with stirring to a solution of *N*-formylcytisine (30 mg) and $NaBH_4$ (100 mg) in diglyme (2 ml). The reaction mixture was stirred for 0·5 hr at room temp., and then most of the diglyme was removed by evaporation under vac. at 60°. MeOH (7 ml) was added and the mixture boiled under reflux for 1 hr to decompose the boron complexes. The MeOH was then distilled off and the residue taken up in CH_2Cl_2 and H_2O. The H_2O layer was separated, made alkaline by NaOH, then extracted with CH_2Cl_2 to give *N*-methylcytisine in 75% yield. *N*-Methylcytisine was recrystallized from Et_2O, m.p. 137°, and identified with an authentic specimen[7] by m.m.p., co-TLC, MS and IR.

Synthesis of N-*formylcytisine.* Cytisine (20 mg), isolated from *T. chinensis* or *Sophora tomentosa*[14], was refluxed with 98% HCO_2H (5 ml) for 10 hr to give *N*-formylcytisine in 95% yield.

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