ALKALOIDS OF Sophora alopecuroides

NEOSOPHORAMINE – A NEW ISOMER OF SOPHORAMINE

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UDC 547–94

We have studied the epigeal part of Sophora alopecuroides collected by M. G. Pimenov in Central Asia (near the town of Samarkand on May 20, 1971, in the flowering stage). The combined alkaloids (2.0%) were obtained by the usual dichloroethane method. From the fraction soluble in petroleum ether, by separation according to basicity in combination with chromatography on alumina, we isolated the alkaloids sophoridine, sophoramine, sophocarpine, aloperine, a base A with the composition $C_{15}H_{20}N_2O$, mp 124-125°C, $[\alpha]_D^{20}$ −29.4° (c 1.53), and a liquid base B with the composition $C_{19}H_{23}NO_3$. The sophoridine, sophoramine, sophocarpine, and aloperine were identified by direct comparison with standard samples.

The presence in the molecule of the alkaloid A of a 6-monosubstituted α-pyridone ring was confirmed by its NMR characteristics (HA-100D, CCl_4, 20°C, 0 – HMDS; 7.03 ppm, q, $J_1 = 9.5$ Hz, $J_2 = 6.8$ Hz; 6.06 ppm, q, $J_1 = 9.5$ Hz, $J_2 = 1.8$ Hz; 5.75 ppm, q, $J_1 = 6.8$ Hz, $J_2 = 1.8$ Hz) and its IR spectrum, which is given in Fig. 1 ($\nu = 1650$ cm^{-1} – C=O of an α-pyridone ring). In the mass spectrum of this base, peaks of ions with m/e 146 and 160 are observed which are also evidence of the presence of this fragment [1].

The composition $C_{15}H_{20}N_2O$, with mol. wt. 244, may correspond to alkaloids of the sparteine or the matrine series, and also to alkyl derivatives of cytisine. However, the latter can easily be excluded on the basis of the NMR spectrum. The characteristics of the mass spectra enabled a choice to be made between the first two groups. The known sparteine alkaloid anagyrine [1], with the same elementary composition, has in its mass spectrum as the strongest peaks those of ions with m/e 98 (100%), M^+ 244 (56%), 146 (16%), 160 (10%), 190 (6%), and others. In the mass spectrum of base A, however, the peak of the ion with m/e 98 is absent, and the strongest peaks are those of ions with m/e 136 (100%), 244 (M^+) (90%), M−1 (66%), and others characteristic for the mass spectrum of sophoramine [2]. The results of a comparison of the mass spectra of base A and sophoramine taken under identical conditions confirm this fact (Fig. 2).

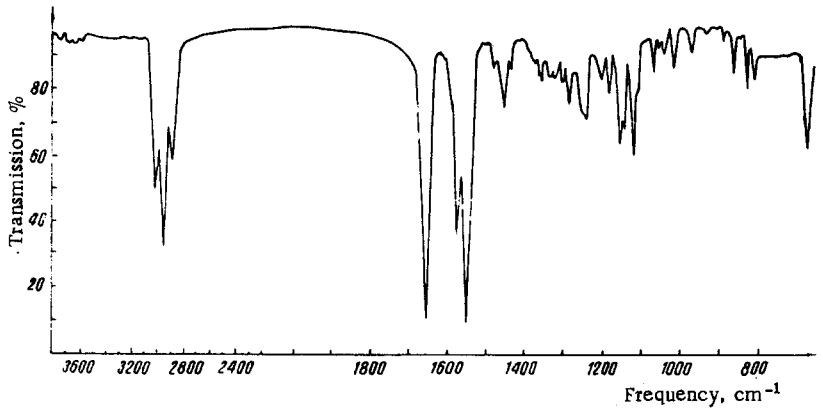


Fig. 1. IR spectrum of neosophoramine.

All-Union Scientific-Research Institute of Medicinal Plants. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 472-476, July-August, 1974. Original article submitted March 15, 1973.

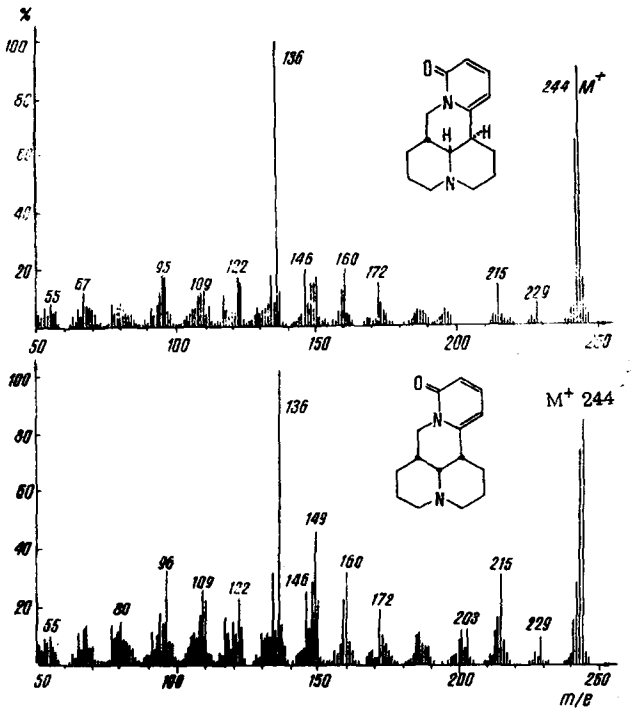


Fig. 2. Mass spectra of neosophoramine and sophoramine.

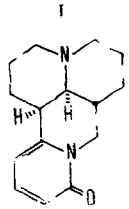
In the NMR spectrum of the base, the protons at C_{17} give two quartets with $\delta_1 = 4.27$, $J_{gem} = 15.2$ Hz, J_{vic}, e, $a = 5.4$ Hz, and $\delta_2 = 2.71$, $J_{gem} = 15.2$ Hz, J_{vic}, a, $a = 11.5$ Hz; it follows from the existence of a trans-diaxial coupling constant $J_{17a,5}$ of 11.5 Hz that the proton at C_5 is axial. In this case, only three variants of the linkage of rings A, B, and C are possible: A/C cis, B/C cis, and A/B trans (sophoramine), A/C trans, B/C trans, and A/B trans (isosophoramine) and, finally, A/C trans, B/C and A/B cis. The IR spectrum of the alkaloid A lacks Bohlmann frequencies, which shows a cis-quinolizidine structure. Thus, only the third variant satisfies this condition. Base A is a new A/C-trans, A/B-cis, B/C-cis isomer of sophoramine, and in view of this we have called it neosophoramine (I).

The catalytic hydrogenation of this base over platinum oxide in ethanolic solution formed a tetrahydro derivative $C_{15}H_{24}N_2O$ the IR spectrum of which contained absorption bands at 1620 cm^{-1} (amide carbonyl), while Bohlmann absorption bands in the 2700-2800-cm^{-1} region were absent. Its mass spectrum is characteristic for compounds of the matrine series: M^+ 248 (30%) M−1 (35%), 205 (11%), 191 (8%), 177 (14%), 150 (38%), 136 (32%), 122 (22%), 96 (100%), 55 (86%) and others.

In contrast to the base, on hydrogenation in hydrochloric acid solution its hydrochloride gave a mixture of two products: the tetrahydro derivative mentioned above and an oxygen-free ditertiary base $C_{15}H_{26}N_2$. The IR spectrum of the latter exhibited absorption bands at 2750-2800 cm^{-1} (Bohlmann bands) and lacked the absorption band of an amide carbonyl group. Its mass spectrum was characteristic of a matrine alkaloid and had the same main ionic peaks as in matrine [3] but with somewhat different intensities: M^+ 234 (65%); 233 (13%), 219 (5%), 205 (11%), 191 (18%), 177 (24%), 150 (66%), 151 (69%) 137 (60%), 136 (42%), 122 (24%), 110 (15%), 98 (70%), 97 (47%), 96 (100%), 84 (30%), 55 (45%).

The presence of the Bohlmann frequencies in the IR spectrum of the oxygen-free compound at 2750-2800 cm^{-1} apparently indicates the trans linkage of rings C/D. The hydrogenation products obtained, according to their physicochemical properties and IR spectra, differ sharply from isosophoridine and isosophoridane, which have the A/B-cis structure.

I



EXPERIMENTAL

The IR spectra were taken on a UR-10 instrument, the mass spectra on a Varian CH-8 instrument at 20-30°C with an energy of the ionizing electrons of 70 eV, and the NMR spectra on a Varian HA-100D instrument (in CCl_4, 0 – HMDS). The melting points were determined on a Kofler block. The analyses of all the compounds corresponded to the calculated figures.

Isolation of the Alkaloids. The comminuted herb Sophora alopecuroides (35 kg) was wetted with 10% ammonia, and the alkaloids were exhaustively extracted with dichloroethane. The dichloroethane extracts were treated with 10% sulfuric acid. The sulfuric acid solution was made alkaline with ammonia, and the alkaloids were re-extracted with chloroform, the evaporation of which yielded 700 g (2%) of combined alkaloids.

Separation of the Alkaloids. The combined alkaloids (700 g) were exhaustively extracted with petroleum ether at the boil under reflux, and then the petroleum ether was evaporated. This gave 300 g of combined bases soluble in petroleum ether. On standing, this material partially crystallized, 18 g of sophoridine separating out. The remainder of the mixed bases was dissolved in 20% sulfuric acid (pH 3), and the solution was made alkaline with sodium bicarbonate and extracted with benzene, seven fractions being obtained: I – 1.75 g, II – 81.46 g, III – 89.74 g, IV – 76.56 g, V – 4.8 g, VI – 5.32 g and VII – 6.37 g.

Fraction I contained mainly sophoramine. Fraction II, by separation on a column of alumina, yielded 11 g (0.031%) of sophoramine, mp 163-164°C (a mixture with an authentic sample of the alkaloid gave no depression of the melting point, and their IR spectra were identical) and 17.17 g (0.051%) of sophocarpine with mp 53-55°C (a mixture with an authentic sample gave no depression of the melting point, and their IR spectra were identical).

Fraction III was separated on a column of alumina (activity grade IV) in a ratio of 1:50.

A benzene eluate yielded 3 g (0.06%) of sophoridine (a mixture with an authentic sample of the alkaloid gave no depression of the melting point, and their IR spectra were identical). From a benzene–5% chloroform eluate was isolated 0.6 g of neosophoramine with mp 124-125°C (from ether), $[\alpha]_D^{20}$ –29.4° (c 1.53; ethanol); hydrochloride with mp 285°C (decomp.).

The separation of fraction (IV) on a column (alumina, activity grade IV, in a ratio of 1:50) gave a) from a benzene eluate, aloperine (6.86 g of the hydrochloride), mp 265°C (a mixture with an authentic sample of the hydrochloride gave no depression of the melting point, and their IR spectra were identical); and b) from a benzene–5% chloroform eluate, 0.3 g (0.0025%) of neosophoramine.

The combined fractions V and VI yielded 4 g of aloperine hydrochloride.

The hydrochlorides of the mother liquors from fractions IV-VI were combined, converted into the bases, and separated on a column of alumina (activity grade IV) in a ratio of 1:50. A benzene eluate yielded 0.2 g (0.00057%) of a liquid base, $C_{19}H_{23}O_3N$, with M^+ 313. A benzene–5% chloroform eluate gave 2 g (0.036%) of aloperine hydrochloride.

Hydrogenation of Neosophoramine. A solution of 0.1 g of neosophoramine in 2 ml of ethanol was treated with 0.05 g of platinum oxide and hydrogenated at atmospheric pressure for 6 h. Then the catalyst was filtered off, the ethanol was evaporated off, and the hydrogenation product was recrystallized from acetone. This gave a compound with the composition $C_{15}H_{24}N_2O$, mp 152-154°C, $[\alpha]_D^{20}$ –21° (c 1.9; ethanol), M^+ 248.

Hydrogenation of Neosophoramine Hydrochloride. A solution of 0.13 g of neosophoramine hydrochloride in 2 ml of 5% hydrochloric acid was treated with 0.05 g of platinum oxide and hydrogenated for 6 h. The catalyst was separated off, the filtrate was made alkaline with 25% ammonia, and the base was extracted with ether. Evaporation of the ether yielded a crystalline mixture of two substances which were separated preparatively on a plate coated with alumina (activity grade IV). This gave 0.06 g of a substance with the composition $C_{15}H_{26}N_2$, mp 104-106°C (from ether), $[\alpha]_D^{20}$ +12.5° (c 3.2; ethanol), M^+ 234, and 0.04 g of a substance with the composition $C_{15}H_{24}N_2O$, mp 152-154°C, M^+ 248, identical with the compound obtained in the preceding experiment.

SUMMARY

The following alkaloids have been isolated from the epigeal part of Sophora alopecuroides in the flowering phase: sophoridine (0.06%), sophoramine (0.036%), sophocarpine (0.051%), aloperine (0.03%), a

liquid base $C_{19}H_{23}NO_3$ (0.00057%), and a new base $C_{15}H_{20}N_2O$ (0.0025%) which we have called neosophoramine and for which the structure of the A/B and B/C-cis, A/C-trans isomer of sophoramine is proposed.

LITERATURE CITED

1. N. Neuner-Jehle, H. Nesvadba, and G. Spiteller, Monatsh. Chem., 95, No. 3, 687 (1964).
2. N. S. Vul'fson, V. G. Zaikin, Z. S. Ziyavidinova, Yu. K. Kushmuradov, Kh. A. Aslanov, and A. S. Sadykov, in: Seventh International Symposium on the Chemistry of Natural Compounds [in Russian], Riga (1970).
3. S. Iskandarov and S. Yu. Yunusov, Khim. Prirodn. Soedin., 106 (1968).