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BAICALINE — A NEW APORPHINE ALKALOID FROM *Thalictrum baicalense*

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A new aporphine base — baicaline — has been isolated from the epigeal part of *Thalictrum baicalense*. Its structure has been established as 1,9,10-trimethoxy-2,3-methylenedioxynoraporphine. Magnoflorine and berberine have been isolated from the roots of the plant.

Continuing a study of Far Eastern species of *Thalictrum*, we have investigated the peculiar East Asian species *Th. baicalense* Turcz. [Baikal meadow-rue], which, according to "Flora SSSR" ["Flora of the USSR"] belongs to the section *Physocarpum* DC [1], but which is well distinguished from other meadow-rues by its swollen ovate-spherical woody fruit. On the basis of features of the structure of the generative organs, M. Emura [2] isolated this species into a monotypical section *Baicalensia* (Tamura) Eruma. The Baikal meadow-rue is distributed in the southern part of Eastern Siberia in the Soviet Far East in the basin of the R. Amur, and on the Karelian peninsular, where it grows among valley woods and on their outskirts in thickets.

For the investigation we took the roots and epigeal part of *Th. baicalense* Turcz., collected on June 20, 1976 in the environs of the village of Kuldur, Khabarov district. The methanolic extraction of the roots yielded 0.7% of combined bases, from which magnoflorine and berberine were extracted. The epigeal part was extracted with chloroform. From the mixture of alkaloids (0.50% on the weight of the raw material), a crystalline optically active base (I) was isolated. UV spectrum of (I), $\lambda_{max}^{ethanol}$, nm: 220, 246, 287, 303, 315.

The PMR spectrum of (I) contained the signals of the protons of three methoxy groups (nine-proton singlet at 3.91 ppm), of a methylenedioxy group (broadened two-proton singlet at 6.03 ppm), and of two aromatic protons at 6.82 and 7.94 ppm (singlets, one proton each). The mass spectrum contained the peaks of ions with m/z 355 (M^+) 354. 340, and 326 $(M - 29)^+$. The combination of UV, NMR, and mass-spectroscopic characteristics showed that (I) was a new pentasubstituted noraphorphine base. We have called it baicaline. The noraporphine nature of (I) was confirmed by the preparation of N-methyl- and N-acetylbaicalines (II and III).

In the study of the structure of baicaline, the largest amount of information was provided by NMR spectra. One-proton singlets at 6.82; 7.94; 6.70, 7.80; 6.63, 7.75 ppm in the spectra of (I), (II), and (III) are due to the H-8 and H-11 protons, respectively [3]. Consequently, baicaline is a 1,2,3,9,10-pentasubstituted aporphine base in which the methylenedioxy group may be present at C-1,2; C-2,3; or C-9,10. A methylenedioxy group at C-1,2 appears in the form of two one-proton doublets at about 6.0 and 5.75 ppm ($J \simeq 1.5$ Hz), and one in the 9,10 position is revealed in the form of a two-proton singlet at ≅6.0 ppm [4]. In the case of 2,3-substitution (ocokryptine (IV) and O-methylocokryptine (V)) close one-proton doublets are observed at 5.98, 5.92 and 5.91, 5.88 ppm [5]. In the structure of (II) and (III), the protons of the CH_2O_2 group appear in the form of two broadened singlets at 5.91, 5.89 and 5.83, 5.86, respectively. On the basis of what has been said above, the 2,3 position is suggested for the methylenedioxy group in baicaline. Furthermore, 3,9,10-trimethoxy-1,2-methylenedioxynoraporphine (northalicmine (VI) [6]) is not identical (melting point, IR and NMR spectra) with baicaline, nor is N-acetyl-1,3,4-trimethoxy-9,10-methylene-

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TABLE 1

Substance	NCH$_3$	OCH$_3$						CH$_2$O$_2$	Ar–H		NCOCH$_3$
		1	2	3	9	10	11		H-8	H-11	
I		3,91			3,91	3,91		6.03 (s)	6,82	7,94	
II	2,49	3,84			3,84	3,84		5,91; 5,89*	6,70	7,80	
III		3,81			3,81	3,81		5,83; 5,86*	6,63	7,75	2,12
IV	2,50	3,91				3,91		5,98; 5,92 (dd)	6.77		
V	2,49	3,86				3,97	3,63	5,91; 5,88 (dd)	6,82 (д)		
VI				3,82	3,82	3,85		5.92; 5.75 (dd, J=1,5 Hz)	6,60	7,45	
VII		3,68	3,83	3,90				5,87 (s)	6,63	7,77	2,20

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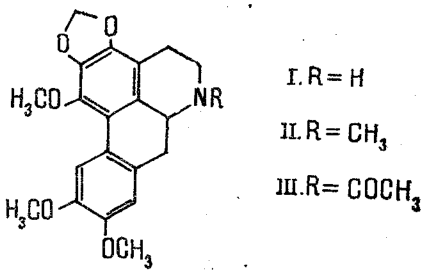
*Broadened one-proton singlets; s — singlet; d — doublet.

dioxynoraporphine (VII) [7] identical with N-acetylbaicaline. Consequently, baicaline has the structure of 1,9,10-trimethoxy-2,3-methylenedioxynoraporphine (I).



The strong positive Cotton effect at 240 nm shows that (I) has the S configuration [7].

EXPERIMENTAL

UV spectra were taken in ethanol on a EPS-3T spectrophotometer (Hitachi), IR spectra on a UR-20 instrument (tablets with KBr), NMR spectra on a JNM-C-60/60 MHz spectrophotometer (0 — HMDS, δ scale, in CDCl$_3$), and mass spectra on a MKh-1303 mass spectrometer.

Extraction of the Roots. The comminuted air-dry roots (90 g) were extracted with methanol. The methanolic extract was evaporated to dryness and the residue was dissolved in a mixture of 5% CH$_3$COOH and 20% H$_2$SO$_4$. The acid extract was washed with ether and was then made alkaline with concentrated ammonia solution and the bases were extracted with chloroform. The chloroform extract was dried with sodium sulfate and distilled. This gave 0.78 g of total material.

Magnoflorine. A saturated solution of potassium iodide was added to the alkaline mother solution after the extraction of the tertiary bases. The resin that deposited was separated off and treated with methanol, to give 0.63 g of technical magnoflorine.

Berberine. The combined tertiary bases were chromatographed on a column of silica gel. The column was washed with chloroform and with mixtures of chloroform with 1, 3, 5, and 10% of methanol. The fraction obtained with chloroform containing 10% of methanol yielded 0.01 g of berberine.

Extraction of the Epigeal Part. The comminuted air-dry raw material (130 g) was moistened with a 5% solution of sodium carbonate and extracted with chloroform. The bases were extracted from the chloroform solution with 10% sulfuric acid and the sulfate that then deposited (0.24 g) was filtered off. The filtrate was washed with ether and made alkaline with concentrated ammonia solution, and the bases were extracted with chloroform. This gave 0.58 g of total material.

Baicaline (I). The sulfate (0.24 g) was suspended in 10% caustic soda solution. The mixture was extracted with ether. The ethereal extract was washed with water, dried with sodium sulfate, and evaporated. Baicaline crystallized from the concentrated extract, with mp 169-170°C; $[\alpha]_D$ +48° (methanol).

N-Methylbaicaline (II). A mixture of 0.048 g of baicaline, 1 ml of 37% formaldehyde solution, and 1 ml of formic acid was heated in the boiling water bath under reflux for 6 h.

Then the reaction mixture was cooled with ice, a 30% solution of potash was added to it dropwise (pH ≈ 9-10), and the base was extracted with chloroform. The solvent was evaporated off, and the residue (0.044 g) was chromatographed on a column of alumina (4.5 g). The base was eluted with benzene. The yield of (II) was 0.035 g, and it had the form of a slightly yellowish oil with m/z 369 (M^+, 100%), 368, 354, 338, 326, 311, 295.

N-Acetylbaicaline (III). A mixture of 0.069 g of baicaline, 3 ml of freshly distilled acetic anhydride, and 0.2 ml of pyridine was left at room temperature (30°C) for three days. Then the reaction mixture was poured into a beaker containing ice, a 34% solution of caustic soda was added slowly dropwise (pH ≈ 10), and extraction was carried out with chloroform. The chloroform extract was washed with water, dried with sodium sulfate, and evaporated. The residue (0.062 g) was chromatographed on a column of silica gel (6 g). The column was washed with chloroform and 50-ml fractions were collected. Fractions 2 and 3 yielded 0.058 g of (III) with $[\alpha]_D$ +262° (c 1.3; ethanol); λ_{max} 218, 243, 292, 307, 317 nm (log ε 4.56, 4.30, 4.10, 4.15, 4.15); IR, ν_{max}: 1650 cm^{-1} ($HCOCH_3$); m/z 397 (M^+).

N-Acetylnorthalicmine was obtained as described above. The substance melted at 97-100°C resolidified at 115°C, and melted again at 167-168°C. $[\alpha]_D$ +233° (c 1.03; chloroform); λ_{max}: 222, 240 infl., 287, 305, 317 (log ε 4.51, 4.38, 4.18, 3.18, 4.20, 4.19); IR, ν_{max}: 1638-1650 cm^{-1} ($NCOCH_3$); n/z 397 (M^+); NMR spectrum, ppm: 2.11 (s, $NCOCH_3$); 3.89, 3.82, 3.89 (3 × OCH_3); 5.96 and 5.81 (broadened one-proton singlet, CH_2O_2); 6.63 (s, H-8), and 7.52 (s, H-11).

CONCLUSION

Thalictrum baicalense, which has not previously been studied chemically, has yielded magnoflorine, berberine, and the new base baicaline. On the basis of spectral characteristic and chemical transformations, the structure of 1,9,10-trimethoxy-2,3-methylenedioxynoraporphine has been established for baicaline.

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