SUMMARY

6,6'-Methylenebisdeoxyvacisinone and its homologs have been synthesized by the reaction of methylenebisanthranilic acid with lactams (γ-butyrolactam, δ-valerolactam, ε-caprolactam, and α-chloro- and α,α-dichloro-ε-caprolactams). The condensation of anthranilic acid and its derivatives (4-nitro-, 5-bromo-, 5-iodo-, and 5-nitroanthranilic acids) with α,β-dichloro-ε-caprolactam has given seven-membered analogs of deoxyvasicinone containing two chlorine atoms in the polymethylene ring.

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ALKALOIDS OF Papaver Bracteatum

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Papaver bracteatum Lindl. (great scarlet poppy) is a representative of the section Oxytona Bernh., and is a perennial endemic plant of the northern Caucasus [1]. The alkaloids isothebaine, oripavine, bracteine, and bractamine have been isolated previously from this plant collected in Transcaucasia [2]. Cultivated forms of P. bracteatum have been studied abroad and more than 15 alkaloids have been isolated [3-7].

We have investigated the epigeal part of P. bracteatum collected in the region of Mt. Beshtau (Pyatigorsk) in the end of flowering to beginning of fruit-bearing period. Methanolic extraction yielded 0.6% of combined alkaloids, which were separated into phenolic and nonphenolic fractions. Treatment of the nonphenolic fraction with methanol yielded thebaine [8]. Repeated treatment of the mother solution with ethanol gave thebaine and mecambridine [9].

After the separation of these alkaloids, the mother liquor was chromatographed on a column. Elution with benzene and benzene–methanol yielded isothebaine, oripavine, orientalidine [10], salutaridine [11], alpinigenine [4, 12, 13], floripavidine [11, 14], a base with mp 119-120°C, and two amorphous bases (I) and (II). The alkaloids thebaine, oripavine, salutaridine, and floripavidine were identified by direct comparison with authentic samples, and isothebaine, mecambridine, orientalidine, and alpinigenine by comparison of their properties and spectral characteristics with those given in the literature. The crystalline base with mp 119-120°C was identical in its spectral characteristics with alpinine, which has been found in the amorphous form in P. alpinum [12, 13] and has been obtained by the methylation of alpigenine [4]. From the ether-soluble fraction of the combined phenolic alkaloids we isolated isothebaine, oripavine, thebaine and bracteoline, which was identified by comparison with an authentic sample isolated from Corydalis gortschakovii [15].

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EXPERIMENTAL

For chromatography we used type KSK silica gel. The UV spectra were taken on a Hitachi spectrometer (in ethanol), the IR spectra on a UR-20 spectrophotometer (molded tablets with KBr), the mass spectra on a MKh 1303 mass spectrometer, and the NMR spectra on a JNM-4H 100/100 MHz instrument with hexamethyldisiloxane as internal standard (δ scale).

Isolation and Separation of the Combined Alkaloids. The air-dry comminuted epigeal part of *P. bracteatum* (6 kg) was charged into a percolator and covered with methanol. After a day, the solvent was poured off and the raw material was covered with a fresh portion of methanol. This was repeated eight times. Then the solvent was distilled off in vacuum to a volume of one liter. The last traces of solvent were evaporated off at room temperature. The methanolic extract so obtained was treated with 3% acetic acid. The acetic acid solution was washed with ether and was brought with Na_2CO_3 to pH 7-8, and the alkaloids were extracted with ether (fraction A, 12.4 g) and with chloroform (fraction B, 14.5 g). After this, the alkaline solution was saturated with NH_4Cl and the alkaloids of phenolic nature were extracted with ether (fraction C, 5.2 g) and with chloroform (fraction D, 4.1 g).

Fraction A was treated with ethanol, and 5.1 g of thebaine was isolated. By fractional crystallization from ethanol the mother liquor yielded an additional 1.5 g of thebaine and 0.8 g of mecambridine. After treatment with ethanol, fraction B yielded 4.3 g of oripavine. Fractional crystallization from ethanol of the residue from the mother liquor yielded 0.8 g of oripavine, 2.1 g of thebaine, 0.52 g of mecambridine, and 0.62 g of isothebaine. After the isolation of these alkaloids, fractions A and B were combined (11.2 g) and chromatographed on a column of silica gel (350 g), using mixtures of benzene and methanol (99:1, 98:2, 97:3, 95:5, and 9:1).

The benzene–methanol (99:1) eluate yielded alpinine (0.25 g) and alpigenine (0.59 g); the (98:2) mixture yielded orientalidine (0.65 g), mecambridine (3.9 g), and isothebaine (0.51 g); the (97:3) eluate yielded salutaridine (0.05 g) and floripavine (0.08 g); the (95:5) mixture yielded 5.3 g of thebaine and 0.5 g of oripavine; and the (9:1) fraction yielded 8 mg of base (I) and 10 mg of base (II). On treatment with ethanol, fraction C yielded 2.5 g of oripavine, and then the mother liquor gave 0.81 g of isothebaine. The mother liquors of fractions C and D were combined and were chromatographed on a column of silica gel. Elution with mixtures of benzene and methanol (99:1, 98:2, 97:3, 96:4, 95:5, and 9:1) yielded 1.9 g of oripavine, 1.7 g of isothebaine, 0.2 g of thebaine, and 0.08 g of bracteoline.

Thebaine, mp 192-193°C (ethanol), $[\alpha]_D -217°$ (c 0.8; chloroform).

Oripavine, mp 201-202°C (ethanol), $[\alpha]_D -230°$ (c 1.2; chloroform).

Isothebaine, mp 202-203°C (ethanol), $[\alpha]_D + 272°$ (c 0.6; chloroform).

Salutaridine, mp 200-201°C (ethanol), $[\alpha]_D + 90°$ (c 1.2; chloroform).

Floripavidine, mp 241-242°C (ethanol), $[\alpha]_D -156°$ (c 1.6; methanol).

Orientalidine, mp 193-194°C (ethanol), $[\alpha]_D -236°$ (c 0.8; chloroform).

Mecambridine, mp 176-177°C (ethanol), $[\alpha]_D -260°$ (c 0.6; chloroform).

Alpinine, mp 119-120°C methanol), $[\alpha]_D +280°$ (c 0.6; chloroform).

$\lambda_{max}^{ethanol}$ 233, 286 nm (log ε 4.23, 3.80). Mass spectrum: 415 $(M)^+$, 400, 384, 222, 208, 206, 193. NMR spectrum: 2.26 (s, $N-CH_3$), 3.50 (s, OCH_3), 3.85 (s, 4 OCH_3), 6.62, 7.29 (s, para aromatic protons), 6.86, 7.19 (d, J = 8 Hz, ortho aromatic protons), 5.78 (s, 1H), 3.96, 5.51 (d, 2H, J = 9 Hz), 3.10-3.90 ppm (m, 4H).

Alpigenine, mp 192-193°C (ethanol), $[\alpha]_D +290°$ (c 1.0; chloroform).

Bracteoline, mp 218-220°C (ethanol), $[\alpha]_D +32°$ (c 1.2; chloroform).

SUMMARY

From the epigeal part of *Papaver bracteatum* Lindl. (family Papaveraceae) growing in the region of Mt. Beshtau (Pyatigorsk) 12 bases have been isolated: isothebaine and oripavine, isolated previously, and thebaine, mecambridine, orientalidine, alpinine, alpigenine, salutaridine, floripavidine, bracteoline, and bases (I) and (II), isolated for the first time.

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THE BIOSYNTHESIS OF THE ALKALOIDS OF Goebelia pachycarpa

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We have previously [1-4] shown a possible route for the interconversion of the matrine alkaloids in Goebelia pachycarpa C. A. Mey. In the present paper we give concrete information on this question obtained as the result of a detailed study of the alkaloids isolated after feeding the plant with various labelled precursors. In order to determine the optimum time of feeding we studied the dynamics of the accumulation of alkaloids in the plant. The qualitative composition of the combined alkaloids was studied by thin-layer chromatography on alumina and by paper chromatography in various systems.

The combined alkaloids, obtained by a known method, [1] were separated by ascending thin-layer chromatography on plates coated with alumina by a method described previously [3]. The amounts of the individual alkaloids were determined by titration with silicotungstic acid in parallel with standard solutions of the corresponding alkaloids (Table 1).

Analysis of Table 1 shows that the main alkaloids in the initial growth period are present in the epigeal and hypogeal parts of the plant in approximately equal amounts; in the period of vigorous flowering and fruit-bearing, the maximum synthesis and accumulation take place in the epigeal parts of the plants.

Beginning with the fruit-bearing period, the alkaloid content gradually falls, and therefore to feed the plant with assumed precursors of the matrine alkaloids we selected the period of flowering and budding (Table 2).

The results of a study of the percentage inclusion of labelled precursors in the matrine alkaloids (see Table 2) show that in the periods considered an intensive biosynthesis of the alkaloids takes place.

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