posed on the CE at 290 nm. Consequently, the configuration of the C_1 center is determined only from the CE in the 200 nm region, an inversion of the sign of which on acidification is suffered by the threo form in α-hydrastine (V). In the erythro compounds d and l-β-hydrastines (VI, VII) the sign of the CE's in the 200 nm region does not change.

The assignment of the two new phthalide-isoquinoline alkaloids corledine and severtzine [4, 5] to the 1R,9R series has been confirmed by their CD spectra.

EXPERIMENTAL

The CD spectra were recorded on a JASCO J-20 spectropolarimeter. The concentration of the solutions was 1 mg/ml and the cell thicknesses 0.05 and 0.01 cm. Methanol was used as the solvent. On acidification, a drop of concentrated hydrochloric acid was added to 2 ml of a methanolic solution of the base. The changes in CD took place within an hour after the addition of the hydrochloric acid.

SUMMARY

1. It has been established that on protonation the threo isomers of phthalide-isoquinolines undergo an inversion of the signs of the CE's in the 290 and 200 nm regions, while in the case of the erythro compounds only the amplitudes of the corresponding CE's in the CD curves change.

2. An interconnection has been established between the preferred conformations of the threo and erythro forms and the relative intensities of the ^1L_b CE's in the CD curves of the phthalide-isoquinolines.

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ALKALOIDS OF *Delphinium biternatum*

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UDC 547.944/945

We have studied the epigeal part and roots of the plant *Delphinium biternatum* Huth collected in the budding-flowering stage on the slopes of the Fergana range at the Alchamaidan landmark. Iliensine has previously been isolated from the epigeal part of this plant [1, 2].

By chloroform extraction of the epigeal part of the plant we obtained 1.3% of the combined alkaloids from which, together with iliensine, we obtained five known alkaloids and three new ones. The constants and compositions of these bases are given below:

Alkaloid	Composition	mp, °C	$[\alpha]_D$, deg
Iliensine	$C_{24}H_{37}NO_7$	202—203	41
Acomonine	$C_{25}H_{41}NO_7$	208—210	25
Delphatine	$C_{26}H_{43}NO_7$	107	38,4
Anthranoyllycoctonine	$C_{32}H_{46}N_2O_8$	166	51
Browniine (I)	$C_{25}H_{41}NO_7$	110—112	33
Dehydrobrowniine (II)	$C_{25}H_{39}NO_7$	176—178	32
10-Benzoylbrowniine (VII)	$C_{32}H_{45}NO_8$	114—116	53
10-Benzoyliliensine (VIII)	$C_{31}H_{43}NO_8$	147—149	50
10-Dehydroiliensine (III)	$C_{24}H_{37}NO_7$	208—210	26

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The alkaloid (I), present in largest amount, crystallized from ether in the form of hexagonal prisms, and its perchlorate had mp 218°C (decomp., ethanol–ethyl acetate). The composition and spectral characteristics both of the base and of its salts coincided with those of browniine, which has been isolated from Delphinium rotundifolium (Afan.) Sosk. et Fachieva [3]. The latter was identified by a direct comparison of its acetate with an authentic sample of browniine acetate kindly provided by Prof. O. E. Edwards (Canada). It must be mentioned that Edwards et al. [4] have described borwniine as an amorphous base. For definitive identification with browniine, (I) was acetylated with acetic anhydride in pyridine, which gave a monoacetate with mp 128-130°C (hexane), identical with browniine acetate in all respects.

The base (II), mol. wt. 465, dissolved readily in chloroform and more sparingly in ether and methanol. The IR spectrum of (II) showed absorption bands at 3513 and 3455 cm^{-1} (hydroxy groups), 1755 cm^{-1} (carbonyl in a five-membered ring), and 1100 cm^{-1} (ether C–O bonds). According to its NMR spectrum, the alkaloid contained a N-ethyl group (three-proton triplet at 1.00 ppm) and four methoxy groups (six-proton singlet at 3.23 ppm and three-proton singlets at 3.26 and 3.32 ppm). The facts given permitted the conclusion that (II) was 10-dehydrobrowniine [5]. To confirm this, we reduced (II) with sodium tetrahydroborate and obtained browniine.

The new base (III), mol. wt. 451, dissolved readily in chloroform and acetone and less readily in ether and methanol. The IR spectrum of (III) showed absorption bands at 3455 and 3275 cm^{-1} (hydroxy groups), 1750 cm^{-1} (carbonyl in a five-membered ring), and 1100 cm^{-1} (ether C–O bonds). The NMR spectrum contained signals due to a N-ethyl group (three-proton triplet at 1.08 ppm) and to three methoxy groups (nine-proton singlet at 3.28 ppm). The mass spectrum, in which, apart from that of the molecular ion, peaks of the M – 15 (100%), M – 17, M – 31, and M – 33 ions were observed, was similar to those of acomonine [6, 7] and iliensine [2].

The acetylation of (III) with acetic anhydride in the presence of pyridine gave a monoacetate (IV) in the mass spectrum of which, as in the spectra of the acetates of acomonine (V) and of iliensine (VI), the maximum peak was that of the M – 59 ion [2, 6].

In the NMR spectrum of (IV), as in the spectra of (V) and (VI), at 4.75 ppm there is a one-proton quartet with $J_1 = 7$ Hz and $J_2 = 10$ Hz. The characteristics of the NMR and mass spectra show the presence of an α-hydroxy group at C_3 [2, 6].

The reduction of (III) with sodium tetrahydroborate gave iliensine. In view of the presence in (III) of only one secondary hydroxy group and a carbonyl in a five-membered ring, it may be concluded that (III) is 10-dehydroiliensine, not previously described in the literature.

The base (VII) dissolved readily in chloroform and acetone and less readily in ether and ethanol. Its IR spectrum showed absorption bands at 3460 cm^{-1} (hydroxy groups), 1715 cm^{-1} (ester grouping), 1610 and 1585 cm^{-1} (aromatic ring), and 1100 cm^{-1} (ether C–O bonds). The NMR spectrum of the alkaloid has the signals of a N-ethyl group (three-proton triplet at 1.01 ppm) of four methoxy groups (nine-proton singlet at 3.22 ppm and three-proton singlet at 3.32 ppm) and of five aromatic protons (7.42-8.10 ppm). The alkaline hydrolysis of (VII) gave an amino alcohol – browniine – and benzoic acid. The result of hydrolysis agreed completely with the features of the mass spectrum of (VII) which contains the peak of the molecular ion with m/e 571 and a strong peak of an ion with m/e 105 due to a benzoic acid residue. Consequently, (VII) was benzoylbrowniine, a and the position of the benzoyloxy group remained to be elucidated. In the weak field at 5.00 ppm, the NMR spectrum of (VII) contained a one-proton triplet with $J \approx 5$ Hz. On passing to browniine, it disappeared. In view of the presence of only one secondary hydroxy group in the browniine molecule the above-mentioned signal can be assigned unambiguously to the β-proton at C_{10} [8] geminal to the benzoyloxy group. Consequently, (VII) is 10-benzoylbrowniine, not previously described in the literature.

The base (VIII) readily dissolved in the usual organic solvents. The IR spectrum of (VIII) has absorption bands at 3460 cm^{-1} (hydroxy groups), 1715 cm^{-1} (ester grouping), 1585 and 1602 cm^{-1} (aromatic ring), and 1100 cm^{-1} (ether C–O bonds). The NMR spectrum showed the signals of a N-ethyl group (three-proton triplet, at 1.08 ppm), of three methoxy groups (nine-proton singlet at 3.27 ppm), and of five aromatic protons (7.43-8.06 ppm). In the mass spectrum of the base, the maximum peak was that of the M – 15 ion. The alkaline hydrolysis of (VIII) led to an amino alcohol – iliensine – and benzoic acid, which is in harmony with the mass spectrum of the base (M^+ 557 and peak of an ion with m/e 105). Thus, (VIII) was a benzoyliliensine and it remained to elucidate the position of the benzoyloxy group.

In the weak field at 5.01 ppm in the NMR spectrum of (VIII) there is the signal of a proton geminal to a benzoyloxy group, which permits the C_7 and C_8 positions to be excluded. The appearance of a signal in the form of a triplet with $J \approx 5$ Hz makes it possible to assign it to the β-proton at C_{10} [8]. Thus (VIII) is the previously unreported 10-benzoyliliensine.

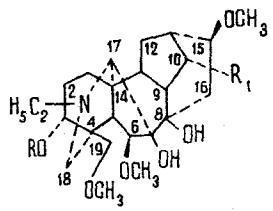
Chloroform extraction of 2.2 kg of the roots of the plant yielded 0.61% of combined alkaloids from which we isolated browniine, delphatine, and a new base which we have called delbiterine (IX), $C_{25}H_{41}NO_7$, with mp 137-138°C, mol.wt. 467. The IR spectrum of (IX) has absorption bands at 3495 cm^{-1} (hydroxy groups) and 1100 cm^{-1} (ether C–O bonds). According to its NMR spectrum, (IX) contains a N-ethyl group (three-proton triplet at 1.02 ppm) and four methoxy groups (three-proton singlets at 3.17 and 3.25 ppm and six-proton singlet at 3.38 ppm). The characteristics of its IR, NMR, and mass spectra enable (IX) to be assigned to the diterpene alkaloids with a lycoctonine skeleton and its formula to be developed in the following way:

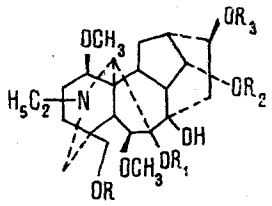
$$C_{19}H_{21}(>N-C_2H_5)(OH)_3(OCH_3)_4,$$

which is identical with the developed formulas of lycoctonine and browniine. A direct comparison of (IX) with lycoctonine and browniine showed their nonidentity. The mass spectrum of (IX), in which the peak of the M – 31 ion is the maximum peak, showed the presence of a methoxy group at C_1 [9] and its closeness to the mass spectra of lycoctonine and browniine.

The methylation of (IX) with methyl iodide in dioxane and the presence of sodium hydride led to compound (X), the perchlorate of which was identical in all respects with that of 7,19-di-O-methyllycoctonine [10]. The correlation performed confirmed the presence of a lycoctonine skeleton in (IX) and showed the positions of the substituents, including their configurations. It remained to elucidate the mutual positions of the substituents. The acetylation of (IX) with acetic anhydride in pyridine gave the monoacetate (XI), which shows the secondary nature of one of the hydroxy groups. The signal of the proton geminal to the acetoxy group appears in the NMR spectrum of (XI) at 4.73 ppm in the form of a one-proton quartet with $J_1 \approx 7$ Hz and $J_2 \approx 10$ Hz. In view of this, and also of the fact that there is a methoxy group at C_1, it may be concluded that the only position remaining for the secondary hydroxy group is C_{15}. According to Dreiding models and in view of the fact that ring D has a distorted chair conformation, the dihedral angle between the α proton at C_{15} and the β proton at C_{11} is 90-100°, that with the α proton at C_{16} is 20-30°, and that with the β proton at C_{16} is 140-150°. In the first case, $J_1 \approx 0$ Hz, in the second case $J_2 \approx 7$-8 Hz, and in the third case $J_3 \approx 10$ Hz.

Thus, delbiterine has the structure (IX).





III. R = H; R_1 = O.
IV. R = $COCH_3$; R_1 = O
Acomonine: R = H; R_1 = OCH_3
Iliensine : R = H; R_1 = OH
V. R = $COCH_3$; R_1 = OCH_3
VI. R = $COCH_3$; R_1 = OH
VIII. R = H; R_1 = $OCOC_6H_5$

I. R = R_3 = CH_3; R_1 = R_2 = H
VII. R = R_3 = CH_3; R_1 = H; R_2 = COC_6H_5
IX. R = R_2 = CH_3; R_1 = R_3 = H
X. R = R_1 = R_2 = R_3 = CH_3
XI. R = R_2 = CH_3; R_1 = H; R_3 = $COCH_3$
Lycoctonine: R = R_1 = H; R_2 = R_3 = CH_3

EXPERIMENTAL

The homogeneity of the substances was checked by chromatography in a thin layer of KSK silica gel in the benzene–methanol (4:1) and chloroform–methanol (20:1) systems and on alumina of "for chromatography" grade in the chloroform–methanol (50:1) system. The NMR spectra were taken in $CDCl_3$ on JNM-4H-100 /100 MHz instruments with HMDS as internal standard (the values are given on the δ scale) and the mass spectra on an MKh-13(instrument fitted with a system for direct introduction into the ion source. The specific rotations were determined on a JASCO J-20 specropolarimeter in chloroform.

Isolation of the Alkaloids from the Epigeal Part. The chloroform extraction of 2.62 kg of the air-dry epigeal part of D. biternatum gave 27 g of combined ether-soluble and 7 g of combined chloroform-soluble alkaloids. On treatment with acetone, the chloroform-soluble material yielded 2.2 g of iliensine. The combined ether-soluble alkaloids were dissolved in ethanol, and the solution was acidified with 10% alcoholic perchloric acid. The acid solution was diluted with water and washed with chloroform and then, with cooling, it wa made alkaline with sodium carbonate and was extracted with ether and with chloroform (to exhaustion). This gave chloroform washing fraction A (19.5 g), an alkaline ethereal fraction B (3.8 g), and an alkaline chloroform fraction C (3.4 g) of the total alkaloids. Fraction A, on treatment with acetone, yielded 5.9 g of a crystalline mixture of perchlorates. This was dissolved in water, and the solution was made alkaline with sodium carbonate with cooling and was extracted with ether and then with chloroform.

The ether-soluble fraction (4.7 g), on treatment with methanol, yielded 0.95 g of a crystalline mixture of two bases, which was chromatographed on a column of alumina (1:100). The alkaloids were eluted with ether – chloroform (10:1), 30-ml fractions being collected. Fractions 1-2, on treatment with methanol, yielded 0.4 g of dehydrobrowniine with mp 176-178°C, and fractions 6-18, again on treatment with ether, gave 0.28 g of browniine with mp 110-112°C. The mother liquor (containing 3.73 g of material), after the separation of 0.95 g of a mixture of bases, was chromatographed on a column of alumina. The alkaloids were eluted with ether, 250-ml fractions being collected. Fractions 3-18 of the ethereal eluate were combined and acetylated with acetic anhydride in pyridine. The product was separated into an alkaline hexane-soluble and an alkaline ether-soluble fraction. From the hexane fraction (1.15 g) 0.73 g of browniine acetate was separated with the aid of hexane [sic]. The mother solution (0.41 g), after the separation of the browniine acetate, was evaporated, the residue was dissolved in ethanol, and the solution was acidified with 10% alcoholic perchloric acid to give 0.18 g of delphatine perchlorate.

After the separation of 5.9 g of a crystalline mixture of perchlorates, the mother liquor was evaporated, the residue was dissolved in water, and the solution was made alkaline with sodium carbonate and was extracted with ether and with chloroform. The chloroform fraction, on treatment with acetone, yielded 0.55 g of iliensine. The ethereal fraction (11.48 g) was chromatographed on a column of alumina (1:70). The alkaloids were eluted with ether (15 fractions), with mixtures of ether and chloroform (10:1, fractions 16-23; 1:1, fractions 24-30), and with chloroform (fractions 31-34), and then with chloroform – methanol (10:1, fractions 35-37), 500-ml fractions being collected. On treatment with methanol, fraction 2 yielded 0.084 g of 10-benzoylbrowniine, and fraction 5, on treatment with ether, gave 0.041 g of 10-benzoyliliensine. On acidification with a 10% ethanolic solution of perchloric acid, fractions 10-13 deposited 0.44 g of delphatine perchlorate. By the action of methanol, fractions 27-28 yielded 0.25 g of acomonine, and fractions 32-33 gave 3.3 g of browniine perchlorate with mp 218 (ethanol – ethyl acetate). Fraction 38 gave 0.14 g of iliensine.

Fraction B was chromatographed on a column of alumina (1:100). The alkaloids were eluted with ether (fractions 1-14) and then with chloroform, 250-ml fractions being collected. Treatment of fraction 3 with acetone gave 0.14 g of anthrancyllycoctonine and treatment of fractions 4-5 with methanol yielded 0.19 g of 10-dehydroiliensine. From fraction 17 was obtained 0.1 g of iliensine perchlorate with mp 204°C (decomp.).

Fraction C was treated with acetone to give 1.5 g of iliensine, and the mother liquor (4.2 g) was chromatographed on a column of alumina (1:70), 250-ml fractions being collected. The alkaloids were eluted with ether (fractions 1-13) and then with chloroform (fractions 14-18). The action of acetone on fraction 2 gave 0.13 g of anthranoyllycoctonine, and the action of methanol on fraction 5 gave 0.035 g of 10-dehydroiliensine and that of acetone on fraction 14 gave 0.17 g of iliensine.

The 10-dehydrobrowniine, after one recrystallization from methanol, had mp 176-178°C.

Reduction of 0.1 g of the base with sodium tetrahydroborate [5] yielded 97 mg of browniine.

The 10-dehydroiliensine crystallized from methanol in the form of needles with mp 208-210°C.

Reduction of 10-Dehydroiliensine. In portions over one hour, 0.06 g of sodium tetrahydroborate was added to 0.05 g of the base in a mixture of 10 ml of methanol and 1 ml of water. The mixture was then boiled for 30 min. After the solvent had been evaporated off, the residue was treated with water, the mixture was made alkaline with sodium carbonate, and the reaction product was extracted with chloroform. The residue after the elimination of the chloroform was crystallized from acetone. This gave iliensine with mp 196-200°C.

Saponification of 10-Benzoylbrowniine. A mixture of 0.05 g of the base with 5 ml of 5% methanolic caustic soda was heated for 1 h. After the usual working up, 0.019 g of browniine perchlorate was obtained with mp 214°C (decomp., ethanol – ethyl acetate), together with benzoic acid having mp 120°C.

Saponification of 10-Benzoyliliensine. The base was heated in 5 ml of 5% methanolic alkali for 1 h, and iliensine was obtained with mp 194-198°C, together with benzoic acid.

Isolation of Alkaloids from the Roots. The chloroform extraction of 2.2kg of the roots of D. biternatum yielded 13.23 g of combined ether-soluble alkaloids and 0.27 g of combined chloroform-soluble alkaloids. The ether-soluble alkaloids were dissolved in the minimum amount of ethanol and the solution was acidified with 10% ethanolic perchloric acid. After 24 h, 11.6 g of a crystalline mixture of perchlorates with mp 215-217°C (decomp.) was isolated. Two recrystallization from methanol yielded 6.1 g of browniine perchlorate with mp 218°C (decomp.). The material from the mother liquor from the recrystallization of browniine perchlorate (5.46 g) was dissolved in water and the solution was made alkaline with sodium carbonate and was extracted with ether. The residue after the elimination of the solvent (4.7 g) was chromatographed on a column of alumina (1:100). The alkaloids were eluted with ether (fractions 1-10) and then with ether – methanol (10:1). Fraction

3 yielded 0.24 g of delphatine perchlorate with mp 219-220°C (decomp., ethanol). The combined fractions 5-11 were acidified with 10% ethanolic perchlorate and by means of a mixture of ethanol and ethyl acetate (1:10) 1.9 g of browniine perchlorate was isolated.

After the separation of 11.6 g of a crystalline mixture of perchlorates, the material from the mother liquor was dissolved in water, the solution was made alkaline with sodium carbonate, and it was extracted with chloroform. The residue after the elimination of the solvent (2.1 g) was chromatographed on a column of alumina (1:100). The alkaloids were eluted with ether (fractions 1-8), with ether–chloroform (10:1, fractions 9-18; and 1:1, fractions 19-23), and then with chloroform (fractions 24-28). Fractions 21-22 were combined, dissolved in ethanol, and acidified with 10% alcoholic perchloric acid, and 0.19 g of delphatine perchlorate was obtained. Fractions 24-25 yielded 0.75 g of browniine perchlorate. Fractions 26 and 27 were combined and treated with acetone to give 0.056% g of delbiterine.

Acetylation of Delbiterine. A mixture of 0.036 g of the base, 2 ml of acetic anhydride, and 0.5 ml of pyridine was left at room temperature for four days. After the usual working up, 0.04 g of a chromatographically homogeneous substance with M^+ 509 was obtained. NMR spectrum: 1.98 ppm ($OCOCH_3$).

Methylation of Delbiterine. A mixture of 0.043 g of the base, 5 ml of dioxane, 2 ml of methyl iodide, and 40 mg of sodium hydride was heated with stirring for 7 h. The sodium hydride was separated off, and the filtrate was evaporated to dryness. The residue was dissolved in 5% sulfuric acid, and the acid solution was washed with ether, made alkaline with sodium carbonate, and extracted with ether. The solvent was evaporated off, the residue was dissolved in methanol, and the solution was acidified with 10% methanolic perchloric acid. The action of a mixture of ether and methanol led to the isolation of 0.023 g of dimethyldelbiterine perchlorate with mp 109°C (foaming). Mass spectrum: M^+ 495, M – 15 (70%), M – 31 (100%), M – 33. NMR spectrum: 3.15 (3H), 3.24 (3H), 3.27 (3H), 3.32 (3H), 3.34 (3H), and 3.52 (3H).

SUMMARY

The combined alkaloids of the epigeal part and roots of Delphinium biternatum have been investigated. From the epigeal part, in addition to the iliensine detected previously, acomonine, browniine, dehydrobrowniine, delphatine, anthranoyllycoctonine, and three new bases for which the structures of 10-dehydroiliensine, 10-benzoyliliensine, and 10-benzoylbrowniine have been established, have been isolated.

From the roots have been isolated browniine, delphatine, and a new base, delbiterine. A lycoctonine skeleton has been established for delbiterine and the positions of the substituting groups have been determined.

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