INVESTIGATION OF ACONITE ALKALOIDS

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The alkaloids of the *Aconitum* plants (family Ranunculaceae) have been described in a large number of papers [1-9], but many representatives of this large genus growing in the territory of the U. S. S. R. have not been investigated up to the present time.

We have examined the Manchurian (*kirinense*), Korean (*coreanum*), Altai (*altaicum*), and sylvan (*nemorosum*) species of *Aconitum*.

A. kirinense. The material was collected at the end of July in the (Russian) far east. From the epigeal part of the plants investigated we isolated a mixture of alkaloids in which four alkaloids were detected by paper chromatography*, the mixture making up 0. 2% by weight of the air-dry plant. On separating the mixture of alkaloids with respect to the different basicities of the components, it was possible to obtain a base in the form of the nitrate (mp 134. 5°, composition $C_{26}H_{41}O_8N \cdot HNO_3$). The substance contained four OH groups, three OCH_3 groups, and one NCH_3 group. The IR spectrum had absorption bands at 3480, 3384, 3240, 3100, and 1737 cm^{-1}. Alkaline saponification of the alkaloid gave an aminoalcohol (mp 85°, composition $C_{23}H_{37}O_7N$) and acetic acid. By substituting the functional groups in the developed formula of the aminoalcohol $C_{19}H_{21}(NCH_3)(OCH_3)_3(OH)_4$ by hydrogen, we obtain the nucleus $C_{19}H_{29}N$.

The aconite alkaloids studied up to the present time with a nucleus of this composition belong to the lycoctonine group and it may therefore be assumed that the lycoctonine skeleton is also present as the basis of the aminoalcohol obtained. Oxidation of the aminoalcohol with iodic acid showed the presence of an α-glycol grouping which also agrees with our assumption.

A. altaicum. The roots of a plant collected in mid-July in the Altai were investigated. The content of a mixture of alkaloids was 0. 2%, and paper chromatography gave two substances. From the mixture a base with R_f 0. 62 and composition $C_{33}H_{45}O_{11}N$ was isolated, mp 200-202°.

Alkaline saponification of the alkaloid gave an aminoalcohol (mp 125-126°, composition $C_{24}H_{39}O_9N$) and acetic and benzoic acids. The constants of the base and the products of its saponification are close to those of mesaconitine [10] and mesaconine. A comparison of the IR spectra showed their identity.

A. coreanum. A plant collected in mid-June in the (Russian) far east contained 0. 14% of a mixture of alkaloids. Paper chromatography showed the presence of four substances. A substance was isolated from the mixture in the form of a hydrobromide with R_f 0. 85, mp 210°, composition $C_{35}H_{41}O_{10}N \cdot HBr$, $[\alpha]_D^{27}$ – 18. 7° (c 4. 27; alcohol).

IR spectrum: 3608, 3420, 3200, 3100, 1741, and 1608 cm^{-1}.

A. nemorosum. The roots of a plant collected at the end of June in province Poltava contained 0. 2% of a mixture of alkaloids. Paper chromatography of the mixture showed the presence of five substances; separation of the mixture gave a base with R_f 0. 41, mp 244-246°, composition $C_{20}H_{25}O_3N$, the IR spectrum of which had absorption bands at 3372, 3080, and 1713 cm^{-1}, and also a base in the form of a hydrochloride with R_f 0. 50, mp 270-272°, and composition $C_{23}H_{29}O_6N \cdot HCl$.

The bases isolated from *A. kirinense*, *A. coreanum*, and *A. nemorosum* have not previously been described in the literature.

EXPERIMENTAL

Isolation of alkaloids from *Aconitum kirinense*. Ten kilograms of the dry comminuted herb was moistened with 5 liters of 5% Na_2CO_3 solution and the alkaloids were exhaustively extracted with toluene (1: 7). The bases were extracted from the toluene solution with 5% H_2SO_4 and, after the sulfate solutions had been made alkaline with crystalline soda (NA_2CO_3), the alkaloids were extracted with ether and then with chloroform.

The evaporation of the ethereal extract gave 20 g of a mixture of bases, and that of the chloroform extract gave 1. 5 g.

Paper chromatography of the ethereal and chloroform fractions of the total alkaloids showed the presence of four substances with R_f values 0. 62, 0. 52, 0. 40, and 0. 29.

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* For chromatography, in all experiments we used Leningrad type B paper. System: butyl alcohol – 5% acetic acid (1: 1); detecting agent: Dragendorf's reagent.

Separation of the total alkaloids. A solution of 20 g of the total material in 54 ml of 1 N H_2SO_4 was fractionally basified by the addition of 5.4-ml portions of 1 N caustic soda solution. After each addition of alkali, the alkaloids were extracted with ether. Ten fractions of non-crystalline bases were obtained.

Fractions 3-7 were combined and dissolved in alcohol, and then nitric acid was added to give an acid reaction (to Congo Red). A precipitate of an alkaloid nitrate (0.5 g) deposited, and, after recrystallization from alcohol, this melted at 134.5°.

Found %: C 56.15; 56.54; H 7.72; 7.77; N 5.09; 4.92; H (labile) 0.70; 0.72; OCH_3 17.02; 16.59; NCH_3 2.97; 2.88. $C_{26}H_{41}O_8N \cdot HNO_3$. Calculated %: C 55.90; H 7.57; N 6.01; H (labile) 0.70; OCH_3 16.6; NCH_3 5.19.

IR spectrum: 3480, 3384, 3240, 3100, 1737 cm^{-1}.

Saponification of the base. A solution of 2 g of the nitrate in 40 ml of alcohol and 8 ml of 40% aqueous caustic soda was boiled for half an hour under reflux, and then 20 ml of water was added and the mixture was heated for a further 30 min. The alcohol was distilled off in vacuum. On cooling, the aqueous solution deposited a crystalline aminoalcohol (1.5 g) which melted at 85° after recrystallization from a mixture of acetone and hexane (3:1); mp 85°.

Found %: C 63.84; 63.42; H 8.70; 8.36; N 3.51; 3.58. $C_{23}H_{37}O_7N$. Calculated %: C 62.84; H 8.46; N 3.18.

The alkaline mother liquor, after acidification and distillation with steam, yielded acetic acid, which was identified by the preparation of acetanilide; mp 113-114°.

Isolation of the alkaloids from A. altaicum. By the method described for A. kirinense, 3 kg of the dry roots yielded 6.05 g of total bases, including 3.5 g of a crystalline mixture of substances (fraction *a*) obtained by evaporating the ethereal extract to small volume, 1.05 g of a substance (fraction b) from the mother liquor after the separation of fraction *a*, and 1.5 g of a substance (fraction c) from the chloroform extract.

Treatment of fraction *a*. A solution of 3.5 g of fraction *a* in 5% H_2SO_4 was treated with a saturated solution of potassium bromide. After recrystallization from water, the hydrobromide which precipitated (1.2 g) consisted of a mixture of two substances with R_f values of 0.57 and 0.65, which it was impossible to separate. After the separation of the hydrobromide, the mother liquor was made alkaline and was extracted with ether. On evaporation of the ethereal solution, 0.85 g of crystals with R_f 0.62 and mp 200-202° (from alcohol), deposited.

Found %: C 63.33; 63.34; H 7.43; 7.35; N 2.38; 2.43; H (labile) 0.51; 0.50; OCH_3 20.74; 21.81; N CH_3 2.6; 2.4. $C_{33}H_{45}O_{11}N$. Calculated %: C 63.2; H 7.18; N 2.21; H (labile) 0.47; OCH_3 19.64; N CH_3 4.59.

IR spectrum: 3508, 1606, and 1715 cm^{-1}.

Saponification of the base. A mixture of 0.5 g of substance, 10 ml of alcohol, and 2 ml of 40% NaOH was boiled under reflux for 1 hr. The alcohol was evaporated off, and the residue was treated with 5 ml of water and was extracted with ether. Evaporation of the ether to small bulk led to the precipitation of an aminoalcohol (0.38 g) with mp 125-126° (from a mixture of acetone and hexane, 2:1).

Found %: C 60.13; H 8.58; N 2.85; 2.75. $C_{24}H_{39}O_9N$. Calculated %: C 59.37; H 8.09; N 2.86.

Acetic and benzoic acids were isolated from the mother liquor.

Isolation of alkaloids from A. coreanum. By the method described for A. kirinense, 6 kg of the dry herb gave 7 g of total bases, including 5 g from the evaporation of the ethereal extract and 2 g from the chloroform extract. Paper chromatography showed the presence in the ethereal and chloroformic fractions of the total material of substances with R_f values of 0.35, 0.46, 0.56, 0.63, and 0.70.

Separation of the total alkaloids. A saturated solution of potassium bromide was added to a solution of 7 g of the total bases in 1% H_2SO_4. The hydrobromide was recrystallized from 70% aqueous alcohol, mp 210°, $[\alpha]^{27}_{D}$ – 18.7° (c 4.27; alcohol).

Found %: C 59.19; 59.13; H 6.08; 6.18; N 1.98; 1.98; Br 10.33; 10.02. $C_{35}H_{41}O_{10}N$. HBr. Calculated %: C 58.64; H 5.90; N 1.95; Br 11.15.

IR spectrum: 3608, 3420, 3200, 3100, 2780, 1741, and 1608 cm^{-1}.

Isolation of alkaloids from A. nemorosum. Two kilograms of dry comminuted roots were wetted with aqueous ammonia and extracted with dichloroethane. The bases were extracted from the dichloroethane solution with 5% sulfuric acid. After the sulfate solutions had been made alkaline with crystalline sodium carbonate, the alkaloids were extracted with ether. Evaporation of the ether gave 6.3 g of total bases. Paper chromatography showed the presence of five substances with R_f values of 0.35, 0.46, 0.56, 0.63, and 0.70.

Separation of the total alkaloids. A saturated solution of sodium perchlorate was added to a solution of 6.3 g of the bases in hydrochloric acid. The resinous residue of perchlorate which deposited was washed with water and was then crystallized from alcohol. This gave 1.35 g of a mixture of crystalline perchlorates consisting of four substances with R_f values of 0.68, 0.62, 0.56, and 0.46 (fraction *a*).

1.35 g of the perchlorate was suspended in 5% ammonia solution and the alkaloids were extracted with chloroform. The resulting mixture of bases (1.1 g) was dissolved in 3 ml of alcohol, and 35% aqueous hydrochloric acid and absolute ether were added to turbidity. This gave 0.5 g of hydrochloride which, after 3-fold recrystallization from alcohol, melted at 270-272°. R_f 0.50.

Found %: C 61.84; 61.68; H 7.02; 7.06; N 3.14; Cl 7.78; 7.78. $C_{23}H_{29}O_6N \cdot HCl$. Calculated %: C 61.10; H 6.69; N 3.09; Cl 7.84.

After the separation of fraction *a*, the alcoholic mother liquor was evaporated to dryness and the perchlorates were converted into the bases; these were suspended in 5% ammonia solution and the alkaloids were extracted with ether. Trituration of the mixture with acetone gave a crystalline base with a yield of 0.08 g, R_f 0.41, mp 244-246° (from acetone).

Found %: C 73.55; 73.29; H 7.83; 7.91; N 4.49; 4.42. $C_{20}H_{25}O_3N$. Calculated %: C 73.38; H 7.69; N 4.29.

SUMMARY

The composition of the alkaloids in plants of the genus Aconitum – A. kirinense, A. altaicum, A. coreanum, and A. nemorosum – has been studied. Four new alkaloids of composition $C_{26}H_{41}O_8N \cdot HNO_3$, $C_{35}H_{41}O_{10}N \cdot HBr$, $C_{20}H_{25}O_3N$, and $C_{23}H_{29}O_6N$ have been isolated.

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