THE ALKALOIDS OF Dipthychocarpus strictus

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Several sulfur-containing bases belonging to various groups of alkaloids have been described in the literature [1-11]. It is known that plants of the family Cruciferae produce sulfur-containing organic compounds. We have investigated the alkaloids of Dipthychocarpus strictus (Fisch) Trautv. (family Cruciferae) collected in the Chimkent region of the Kazakh SSR in the environs of Dastur-Tau and Kirk-Kuduk. In the early period the plant contains considerably more alkaloids than in the later period [12], and the maximum accumulation has been found in the period up to budding, with 0.2% in the epigeal part and 0.72% in the roots, and in the period of full fruit-bearing with from 0.05% (Kirk-Kuduk) to 0.3% (Dastur-Tau) of combined alkaloids in the seeds.

By separating the mixture of bases of the epigeal part according to their solubilities in various organic solvents, and also by chromatography on columns of alumina and silica gel, we isolated a hydrocarbon $C_{31}H_{64}$, acetamide, and the alkaloids diphthocarpamine, diphthocarpidine, diphthocarpaine, diphthocarpamidine, and base No. 5. A study of the seeds (Dastur-Tau) showed that they contained 0.3% of total alkaloids. Two alkaloids were isolated from the mixture of bases – diphthocarpine and diphthocarpinine.

Diphthocarpaine, diphthocarpamine, and diphthocarpidine are very close in their physicochemical properties. They do not undergo hydrogenation by Adams' method or acetylation and do not give methiodides and salts, because they are weak bases; however, they are fairly stable to the action of acids and alkalis. In their UV spectra, each of these bases has a maximum at 210 nm. In the IR spectrum, absorption bands of active hydrogen, of an amide carbonyl group, and of the stretching and deformation vibrations of methyl, methylene, and methine groups are shown.

The hydrogenation of diphthocarpaine on Raney nickel gave an optically inactive crystalline compound with mp 107-109°C, which shows the destruction of the optical center of diphthocarpaine on hydrogenation. The hydrogenation products did not contain sulfur. An almost similar pattern was observed in the reduction of diphthocarpaine with zinc dust in 20% hydrochloric acid. The reduction product, with mp 117-118°C, had no optical center, but it did still contain sulfur.

Base No. 4 (I), with the composition $C_7H_{16}N_2O$, showed a narrow band at 3350 cm^{-1} in the IR spectrum which we assigned to the absorption of an NH group, and absorption in the region of the stretching and deformation vibrations of methyl and methine groups and of an amide carbonyl group – at 1630 and 1580 cm^{-1}.

The NMR spectrum contained a 12-proton doublet at 1.1 ppm, which corresponds to the signals of the methyl protons of two isopropyl groups. In the 3.64 ppm-region was found a multiplet with an intensity of four proton units. This probably includes the signals of two NH groups and also of the methine protons of two isopropyl groups attached to nitrogen. In the NMR spectrum of the deutero derivative, the intensity of the signal at 3.64 ppm had decreased to two proton units through the deuteration of the protons of the NH groups.

The molecular weight of the alkaloid, determined mass spectrometrically, showed that the base contains two nitrogen atoms, and the intensity of the absorption band of the $N-C=O$ group showed that they are both amide nitrogen atoms. The mass spectrum of the base contained peaks of ions with m/e 144 (M^+), 129 $(M-15)^+$, 58, and 44 (100%). The presence of only these ion peaks in the mass spectrum showed the symmetrical nature of the amide, since if it had been unsymmetrical the formation of various fragments would have been possible as the result of double α cleavage and C–N cleavage accompanied by the migration of hydrogen. However, the absence of the corresponding ions permits the symmetry of the molecule of the base to be deduced [13].

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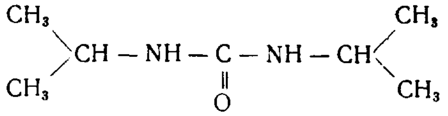
TABLE 1

Alkaloid	Composition	mp, °C	$[\alpha]_D$, deg	Rf value (system 1*)
Diphthocarpamine	$C_{11}H_{24}N_2O_2S$	100–101	–58,21 (methanol)	0,40
Diphthocarpidine	$C_{18}H_{32}O_3N_2S_2$	135–136	–70,54 (methanol)	0,27
Diphthocarpaine	$C_8H_{18}N_2OS$	124–125	– 80.33 (ethanol)	0,17
Diphthocarpamidine base No. 4	$C_7H_{16}N_2O$	190–192		0,55
Base No. 5	—	bp 193–195 (4 mm)	–49,23 (chloroform)	0,85
Diphthocarpine sulfate	—	300		0,32
Diphthocarpinine	—	91–92		0,50

*TLC. Chloroform–methanol (9 : 1) system.

All that has been said above and the composition, physicochemical constants, and spectral characteristics of the base, and also a comparison with literature information [14], permits the assumption that compound (I) is N,N'-diisopropylurea, and we are the first to have isolated it from a plant:



The base gave no depression of the melting point with a sample of N,N'diisopropylurea which we obtained from urea and isopropylamine.

EXPERIMENTAL

Isolation of the Combined Alkaloids of the Epigeal Part. The previously comminuted plant (10 kg) was moistened with 5% NH_4OH and the alkaloids were exhaustively extracted with chloroform. The concentrated chloroform extract (~ 8 liters) was treated with a 10% solution of H_2SO_4 (~ 1.2 liter), and the extract was saturated with NH_3 until it had an alkaline reaction, and the alkaloids were reextracted with chloroform. When the chloroform extract was concentrated, 7.5 g of total bases was obtained.

The concentrated chloroform extract was evaporated to dryness and the viscous residue was dissolved in ether (~ 2 liters). By the above-mentioned treatment, this solution yielded 20 g of combined alkaloids.

The alkaloid-containing alkaline solution, after evaporation to dryness, was treated with chloroform, into which acetamide (~ 3.8 g) passed, and with chloroform–methanol (19 : 1). The latter gave a mixture of alkaloids in the form of a viscous oil (~ 10 g).

Separation of the Mixture of Bases of the Epigeal Part. The total alkaloids of the chloroform residue (20 g) were treated with ether. Concentration of the ethereal solution yielded a mixture of crystals, from which, on separation according to solubility in acetone–methanol (9 : 1), 0.02 g of a neutral substance with mp 57-58°C and 0.26 g of a base with mp 135-136°C were isolated. The residue from the combined alkaloids was exhaustively extracted with ether, the ether-insoluble fraction amounting to 9 g. The ethereal solution of alkaloids was treated with 10% HCl solution. The acid solution was shaken with ether, and from the ether on concentration was obtained 0.7 g of base No. 4 with mp 190-192°C. The acid solution, after being made alkaline with 25% NH_4OH, yielded 5.4 g of total bases. The latter were combined with the 9 g of ether-insoluble fraction and chromatographed on a column of alumina with elution successively by ether, chloroform, chloroform–methanol (19 : 1 and 9 : 1), and methanol. The ethereal eluates yielded base No. 4 with mp 190-192°C. The mother liquor consisted of a liquid oil with bp 193-195°C (4 mm) (4.2 g). The chloroform eluates yielded 0.35 g of a base with mp 100-101°C and 0.29 g of a base with mp 135-136°C. From the chloroform–methanol (19 : 1) fraction, 0.3 g of a base with mp 124-125°C was isolated.

The main fraction of combined alkaloids (7.5 g) was chromatographed on a column of Al_2O_3. This yielded 0.2 g of acetamide and 0.17 g of a base with mp 135-136°.

The combined alkaline residue (10 g) was chromatographed on a column of silica gel, which gave 0.6 g of a base with mp 124-125°C.

Hydrogenation of Diphthocarpaine on Raney Nickel. A mixture of the base (0.1 g) and Raney nickel (1 g) in 10 ml of ethanol was shaken under a current of hydrogen for 2 h. The catalyst was filtered off with suction, the ethanolic filtration was concentrated to 1 ml, and 5 ml of ether was added. This led to the precipitation of scale-like crystals with mp 107-108°C (0.08 g), $[\alpha]_D \pm 0$.

Reduction of Diphthocarpaine with Zinc Dust in Hydrochloric Acid. In portions, 4 g of zinc dust was added to a solution of 0.1 g of the substance in 10 ml of 20% hydrochloric acid. After a day, the appropriate working up of the reaction mixture yielded 0.086 g of reduction product with mp 116-117°C (from acetone), $[\alpha]_D \pm 0$.

Separation of the Combined Alkaloids of the Seeds. From 1200 g of comminuted and previously ether-defatted seeds, by the above-described method, 1.9 g of ether-soluble and 1.7 g of chloroform-soluble alkaloids were obtained. The treatment of the ethereal fraction of the combined alkaloids with acetone yielded 0.24 g of a crystalline substance which was purified by reprecipitation of a methanolic solution with acetone; mp > 300°C, decomp. The addition of an aqueous solution of barium chloride to an aqueous solution of the crystals gave a precipitate of barium sulfate. The crystals (the sulfate of a base) were decomposed with caustic alkali and extracted with ether. This gave the liquid base diphthocarpine.

On treatment with acetone, the chloroform-soluble fraction of the total alkali yielded 0.15 g of crystals of diphthocarpinine with mp 91-92°C.

Synthesis of N,N'-Diisopropylurea. A mixture of isopropylamine hydrochloride (1.9 g) and urea (1.2 g) was dissolved in distilled water (5 ml), and the solution was heated on the water bath for 6 h. Then the aqueous solution was shaken with ether. When the ethereal extract was concentrated, crystals with mp 190-192°C were obtained.

SUMMARY

1. A study of the dynamics of the accumulation of the alkaloids of *D. strictus* according to the vegetation period showed the maximum accumulation of alkaloids in the period before budding with 0.2% in the epigeal part and 0.72% in the roots, and in the period of full fruit-bearing with 0.05-0.3% of combined alkaloids in the seeds.

2. The separation of a mixture of bases of the epigeal part and of the seeds yielded seven alkaloids, six of which contained sulfur: diphthocarpamine, diphthocarpidine, diphthocarpaine, diphthocarpamidine, dipthocarpine, diphthocarpinine, and base No. 5.

3. A study of the chemical properties and spectral characteristics of diphthocarpamidine has shown that it is N,N'-diisopropylurea, and we are the first to have isolated it from a plant.

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