É. Kh. Batirov, S. A. Khamidkhodzhaev, V. M. Malikov, and S. Yu. Yunusov

The plant <u>Lolium cuneatum</u> Nevski (family Gramineae) is a poisonous weed found among plantings of wheat, barley, and flax in the grain regions of central Asia. Continuing an investigation of the alkaloids of <u>L. cuneatum</u> [1], by the chloroform extraction of seeds collected in 1972 in the Hissar region of the Tadzhik SSR we have isolated 0.23% of a mixture of bases (A).

We introduced the same seeds into the territory of the Kibrai sovkhoz [communal farm], Tashkent oblast. From the seeds of the introduced plant we obtained 0.24% of combined alkaloids (B). The mixture of bases was separated by the preparation of various salts and by chromatography in a column of alumina. From the total alkaloids A we isolated the known alkaloids loline, norloline, lolinine [1, 2], and bases (I) and (II).

The mass spectrum of the base $C_{9}H_{16}N_{2}O$ (I) had strong peaks of ions with m/e 168 (M⁺), 153 (M - 15)⁺, 82 (100%), and others, which are characteristic for alkaloids of the loline group [2]. The molecular weight of (I) differed from that of loline by 14 m/e. In the NMR spectrum of (I) (CCl₄), we observed the signals of the protons of an $-N(CH_3)_2$ group at 2.21 ppm (6H, singlet). This permits the assumption that (I) is probably N-methylloline. A comparison of the properties of (I) and N-methylloline obtained from loline by a known method [1] confirmed this hypothesis.

The spectral characteristics of base (II) coincide with those of N-acetylnorloline [3]. To establish the authenticity of the N-acetylnorloline we hydrolyzed (II), after which we isolated norloline. Consequently, (II) has the spectrum of N-acetylnorloline.

By separating the combined alkaloids B, we isolated loline, lolinine, N-acetylnorloline, and a base (III).

By its mass, IR, and NMR spectra and some chemical reactions, (III) was identified as N-formylloline [3]. From the water-soluble fraction of combined bases (B) we isolated a quaternary base in the form of an iodide with the composition $C_{10}H_{17}N_2O_2I$ with mp 179-180°C. Its IR spectrum showed an absorption band at 1680 cm⁻¹ (amide carbonyl). The NMR spectrum of the base (D₂O) was similar to that of N-formylloline but differed by the presence of an additional signal of an N-CH₃ group at 3.69 ppm (3H, singlet).

Thus, the alkaloid is N-formylloline methiodide. The facts given are also in harmony with its mass spectrum which shows the peaks of ions with $m/e 182 (M-CH_3I)^+$, 153 $(182 - CHO)^+$, 142 $(CH_3I)^+$, and others characteristic for the loline alkaloids [2].

A mixture with N-formylloline methiodide gave no depression of the melting point. Consequently, the alkaloid that we have isolated is a quaternary derivative of N-formylloline and its structure is expressed by formula (IV).



It must be noted that the qualitative and quantitative compositions of the combined alkaloids A and B differ and are in agreement with laws found previously [4].

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The alkaloid present in greatest amount in the bases A is loline (45%) and in the alkaloids B it is lolinine (41.7%).

N-Methylloline and norloline were obtained from alkaloids A, while they were not detected in alkaloids B. N-Formylloline and its quaternary derivative were isolated from the combined alkaloids B.

EXPERIMENTAL

The mass spectra were taken on an MKh-1303 mass spectrometer fitted with a system for the direct introduction of the sample into the ion source, the IR spectra on a UR-10 instrument, and the NMR spectra on a JNM-4H 100/100 MHz spectrometer (δ scale).

The homogeneity of the substances was checked by chromatography in a thin layer of KSK silica gel in the chloroform-methanol system (4:1).

The crushed seeds (110 kg) were moistened with 10% ammonia and extracted with chloroform. The alkaloids were extracted from the chloroform solution with 10% sulfuric acid. The acid solution was washed with ether and made alkaline with gaseous ammonia, and the alkaloids were extracted with chloroform. This gave 256 g (0.23\%) of combined alkaloids.

When the combined alkaloids were treated with ether $(3 \times 0.5 \text{ liter})$, 1.47 g of an ether-soluble fraction was obtained. The residue was dissolved in 300 ml of ethanol and the solution was acidified with an ethanolic solution of hydrogen chloride, giving a precipitate of 118 g of loline dihydrochloride.

The mother solution was evaporated to small volume and an ethanolic solution of sodium perchlorate was added. This gave 81.0 g of loline diperchlorate. The ethanol was evaporated off from the mother solution, the residue was made alkaline with 25% ammonia, and the alkaloids were extracted with chloroform. Yield 122.0 g. The mother solution of the combined alkaloids (40.0 g) was chromatographed on a column of alumina (1:20). Elution was performed with chloroform—benzene (3:1 and 9:1), chloroform, and chloroform—methanol (99:1 and 98:2). The eluate was collected in 30-ml portions. The chloroform—benzene (3:1) fraction yielded 10.23 g of lolinine, R_f 0.56. Elution with chloroform—benzene (9:1) gave 2.87 g of a mixture of alkaloids with R_f 0.45 and 0.42. The rechromatography of this mixture on a column of alumina (1:50) yielded 0.7 g of N-methylloline and 1.7 g of N-acetylnorloline. When elution was continued with chloroform, loline (7.2 g) and norloline (0.37 g) were isolated.

N-Methylloline. Oil, $[\alpha]_D^{20}$ +13.7° (c 2.44; acetone). Dihydrochloride, mp 246-247°C (decomp.).

<u>N-Acetylnorloline</u>. Oil, $[\alpha]_{D}^{20}$ + 49.8° (c 2.23; chloroform); hydrochloride with mp 232-235°C (decomp.); M⁺ 182. IR spectrum (hydrochloride); 3200-3250 cm⁻¹ (NH), 1670 cm⁻¹ (=N-C-). NMR spectrum (CDCl₃):

1.95 ppm (3H, singlet) (Ac-) and 7.04 ppm (NH).

<u>Hydrolysis of N-Acetylnorloline</u>. A solution of 0.08 g of the base in 5 ml of 1 Nhydrochloric acid was heated at 80°C for 2h. This gave 0.05 g of an oil with R_f 0.17. Carbonate with mp 141-142°C, M^+ 140.

A mixture with norloline carbonate gave no depression of the melting point.

By the method described above, 9.1 kg of the seeds of the introduced plant yielded 21.62 g (0.24%) of combined alkaloids.

Quaternary Derivative of N-Formylloline. After repeated extraction with chloroform, the aqueous alkaline solution continued to show the reaction for alkaloids, and therefore it was evaporated at room temperature to a volume of 10 ml. The crystals of the organic substances that deposited were separated off, and potassium iodide was added to the solution. This gave another precipitate. After recrystallization from acetonemethanol (2:1), mp 179-180°C. Yield 0.25 g.

When the combined chloroform-soluble alkaloids were separated, loline (4.43 g), lolinine (8.47 g), N-acetylnorloline (0.42 g), and N-formylloline (0.17 g) were isolated.

<u>N-Formylloline</u>. Silky crystals with mp 93-94°C, $[\alpha]_D^{20}$ +47.9° (c 0.73; chloroform), M⁺ 182. IR spectrum: 1670 cm⁻¹ (N-C-). NMR spectrum (CDCl₃): 2.90 and 3.10 ppm (singlets) (N-CH₃), 8.00 and 8.27 O O O O O O O <u>N-Formylloline</u>. This was hydrolyzed in the same way as N-acetylnorloline. From 0.03gof the base was obtained 0.022 g of an oil with R_f 0.32. Its dihydrochloride had mp 244-246°C (decomp). A mixture with loline dihydrochloride showed no depression of the melting point.

<u>N-Formylloline Methiodide</u>. A solution of 0.03 g of N-formylloline in 5 ml of acetone was treated with 0.025 g of methyl iodide. Yield 0.05 g, mp 180°C. A mixture of (IV) gave no depression of the melting point.

SUMMARY

In addition to three known alkaloids, the seeds of <u>L</u> <u>cuneatum</u> have yielded N-formylloline, N-acetylnorloline, and the new alkaloids N-methylloline and N-formylloline methiodide.

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LOLIDINE - A NEW CHLORINE-CONTAINING ALKALOID

FROM THE SEEDS OF Lolium cuneatum

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By chromatographing the ether-soluble fraction of the combined alkaloids on a column of silica gel we have isolated a new unusual chlorine-containing base – lolidine – with the composition $C_{18}H_{27}N_4O_4Cl$ (M⁺ 398), mp 225-226°C, $[\alpha]_D^{20}$ +146° (c 2.0; chloroform). Lolidine was also isolated without using chlorine-containing solvents in all stages of isolation and purification.

The IR spectrum of the base has absorption bands at 3170-3180 cm⁻¹ (NH), 1635 cm⁻¹ (NCOCH₃), and 1665 cm⁻¹ (C=N-C-O-). Lolidine is not acetylated by acetic anhydride and acetyl chloride, which is prob- \parallel O

ably due to the presence of $an = NHCOCH_3$ group.

The NMR spectrum of the alkaloid (CDCl₃, δ scale, JNM 100/100 MHz) shows the signals of an = N-COCH₃ group (1.96 ppm, 3H, singlet) and an = N-CH₃ group (2.63 ppm, 3H, singlet).

The mass spectrum of lolidine (Fig. 1) confirms the suggested composition and is characteristic for alkaloids of the loline group [1]. The mass spectrum shows a series of peaks of chlorine-containing ions which are distinguished by the presence of the characteristic isotopic peaks.

The molecular ion appears in the form of a doublet with m/e 398 and 400, the ratio of the intensities of the 398/400 peaks being 3:1, which shows the presence of one covalently bound chlorine atom [2]. The peaks of ions with m/e 363 and 362 correspond to the elimination of chlorine and of hydrogen chloride from the molecular ion. The high molecular weight and also the presence of strong peaks of ions with m/e 153 and 181 in the mass spectrum permit the assumption that lolidine is a bimolecular compound consisting of fragments of loline and N-acetylnorloline [1, 3]. The number of protons calculated from the integral curve of the NMR spectrum is in agreement with this hypothesis and corresponds to the alkaloids just mentioned.

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