

N-Formylloline. This was hydrolyzed in the same way as N-acetylnorloline. From 0.03 g of 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.

N-Formylloline Methiodide. 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 *L. cuneatum* have yielded N-formylloline, N-acetylnorloline, and the new alkaloids N-methyloline 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 $C_{13}H_{27}N_4O_4Cl$ (M^+ 398), mp 225–226°C, $[\alpha]_D^{20} +146^\circ$ (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} ($NCOCH_3$), and 1665 cm^{-1} ($C=N-C-O-$). Lolidine is not acetylated by acetic anhydride and acetyl chloride, which is prob-



ably due to the presence of an $=NCOCH_3$ group.

The NMR spectrum of the alkaloid ($CDCl_3$, δ scale, JNM 100/100 MHz) shows the signals of an $=N-COCH_3$ group (1.96 ppm, 3H, singlet) and an $=N-CH_3$ 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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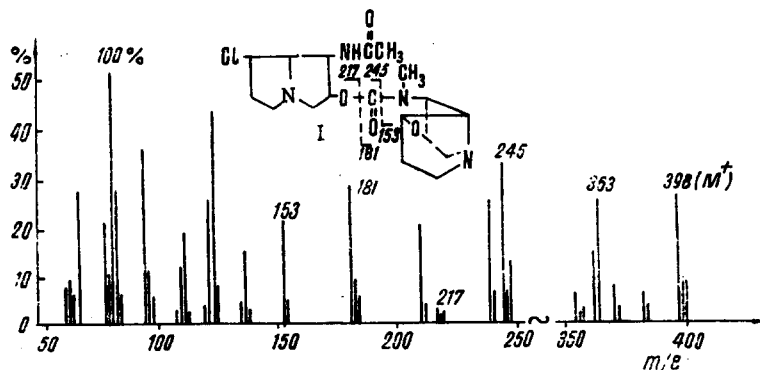


Fig. 1. Mass spectrum of lolidine.

The peak of the ion with m/e 245 ($M - 153$)⁺ corresponds to the detachment of a loline radical from the molecular ion [1]. The absorption band at 1665 cm^{-1} in the IR spectrum and the paramagnetic shift of the signal of the $=N-CH_3$ group by 0.26 ppm in comparison with that of loline shows that the loline (R) is attached to the other part of the molecule through a CO group ($-CO-R$). Consequently, the chlorine atom is in the N-acetylnorloline part of the molecule.

On the basis of a comparative study of the mass and NMR spectra of chlorohydroxyloline and lolidine it may be concluded that in the N-acetylnorloline moiety of the alkaloid the oxygen "bridge" has opened and the chlorine occupies the C_6 position [4].

The IR and mass spectra show the absence of a hydroxy group from lolidine. This means that the hydroxy group formed at C_2 after the opening of the oxygen bridge is substituted through a carbonyl group by the loline radical.

The facts given above permitted the suggestion for lolidine of a structure which agrees well with the mass spectrum. In the mass spectrum of D-lolidine, the peaks of ions with m/e 245 and 217 are displaced by unity in the direction of high mass numbers, which confirms the position of the $-NHCOCH_3$ group in the chlorine-containing part of the molecule. For a definitive confirmation of the structure of lolidine we hydrolyzed it in an acid medium. In the hydrolysis products we detected loline and norloline chromatographically. Norloline is obtained in the hydrolysis of lolidine from the chlorine-containing moiety by cyclization on alkalization with the formation of an oxygen bridge, as has been found previously [4].

Thus, lolidine has the structure (I). The native nature of lolidine was confirmed by its isolation from the combined alkaloids obtained by extracting the raw material with methanol.

EXPERIMENTAL

The homogeneity of the substances was checked by chromatography in a thin layer of type KSK silica gel in the chloroform-methanol (20:5 + 2 drops of 25% ammonia solution) system.

Isolation of Lolidine. The ether-soluble fraction of the combined alkaloids A (1.47 g) was chromatographed on a column of silica gel (1:50). Elution was performed with benzene-ether (1:4), ether, ether-chloroform (9:1), ether-chloroform (4:1), and chloroform. From the ether-chloroform (4:1) fraction we isolated 0.21 g of a mixture of bases with R_f 0.86 and 0.65. The latter was treated with methanol; a base with the composition $C_{18}H_{27}N_4O_4Cl$, R_f 0.86, crystallized out. Yield 64 mg, mp $225-226^\circ\text{C}$ (methanol), $[\alpha]_D^{20} +146^\circ$ (c 2.0; chloroform).

The base with R_f 0.65 was identified as loline.

Hydrolysis of Lolidine. A solution of 8 mg of lolidine in 3 ml of 3% hydrochloric acid was heated at 80°C for 2 h. Then the reaction mixture was neutralized with 20% aqueous caustic soda; after 30 min the alkaloids were extracted with chloroform. Yield 5 mg.

The hydrolysis product showed two spots with R_f 0.17 and 0.40, which were stained by the Dragendorff reagent and the R_f values of which coincided with those of norloline and loline.

Methanolic Extraction of the Seeds. The comminuted seeds (10 kg) were extracted with methanol. Five extractions were performed. The extract was filtered and the solvent was distilled off under vacuum. The concentrated extract was acidified with 10% sulfuric acid and washed with ether until the ethereal layer was

colorless. Then it was made alkaline with a 25% solution of ammonia, and the alkaloids were extracted with ether and chloroform. This gave 0.20 g of ether-soluble and 7.30 g of chloroform-soluble alkaloids.

The ether-soluble alkaloids were chromatographed on a column of alumina (1:30). The alkaloids were eluted with hexane-benzene (1:4), benzene, benzene-methanol (99:1), and benzene-ethanol (49:1). Elution with the benzene-methanol (99:1) mixture yielded 7 mg of lolidine.

SUMMARY

A new chlorine-containing alkaloid, lolidine, has been isolated from the seeds of L. cuneatum Nevski. On the basis of its spectral characteristics and the production of loline and norloline on hydrolysis, structure (I) has been established for it.

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