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STRUCTURE OF PETILINE

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From the epigeal part of Petilium raddeana Rgl. we have isolated imperialine [1-9], edpetiline, [10] and a new alkaloid, petiline with mp 205-206° C, $[\alpha]_D$ − 51.07°, and composition $C_{27}H_{43}O_2N$. This base contains four C-methyl groups, and forms a crystalline hydrochloride, hydrobromide, and oxime.

The IR spectrum of petiline has absorption bands of hydroxy, carbonyl, and NH groups and of a double bond, and the UV spectrum has absorption bands with λmax 240, 290 mμ (log ε 2.66, 1.9) (Fig. 1), which are characteristic for α, β-unsaturated ketones [11, 12].

The acetylation of petiline gave a neutral O, N-diacetyl derivative. The IR spectrum of this compound has absorption bands of ketone, amide, and ester carbonyl groups and of a double bond. Consequently, petiline is a secondary base in which one atom of carbon is present in the form of a hydroxy group and the other in the form of a carbonyl group. The hydrogenation of petiline formed tetrahydropetiline. The IR spectrum of the latter had no absorption bands for a double bond or a carbonyl group. On oxidation with chromic acid, tetrahydropetiline gave dihydropetilinone, the IR spectrum of which has the absorption band of a carbonyl group and lacks absorption bands for a double bond or a hydroxy group.

The formation of a diketone shows the secondary nature of the hydroxy group of petiline.

The UV spectrum of dihydropetilinone has an absorption band with λmax 280 mμ (log ε 1.09) (see Fig. 1) which is characteristic for steroid alkaloids[10].

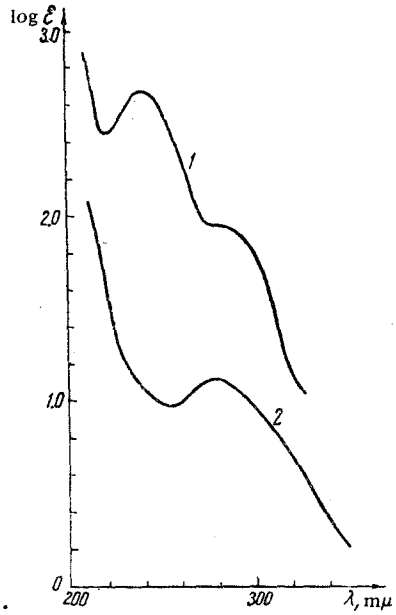
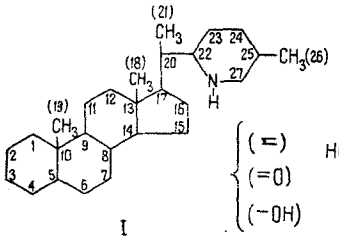
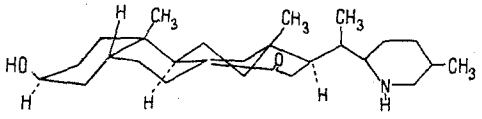


Fig. 1. UV spectra (in ethanol) of petiline (1) and dihydropetilinone (2).

The NMR spectra of petiline, N, O-diacetylpetiline, and tetrahydropetiline show that these substances have two secondary and two tertiary methyl groups. The data presented give grounds for assigning petiline to the solasodine or solanidine group of alkaloids [13]. The absence from petiline of an inert oxygen atom in the form of an ether, as in solasodine, the presence in the mass spectrum of petiline of the peak of maximum intensity for an ion with m/e 125, and the similarity of the IR spectra of tetrahydrosolasodine and tetrahydropetiline in the 1400-800 cm^{-1} region permit the suggestion of structure (I) for petiline.



I



II

This structure is confirmed by the NMR spectra of petiline, N, O-diacetylpetiline, and tetrahydropetiline, and by the mass spectrum of petiline.

The NMR spectrum of petiline has signals from chemically equivalent protons: singlets at 9.37 τ (3H, C-18 CH_3), 9.32 τ (3H, C-19 CH_3) and doublets at 9.17 τ (3H, C-21 CH_3) and 8.99 τ (3H, C-26 CH_3). The NMR spectrum of O, N-diacetylpetiline has singlets at 9.43 τ (3H, C-18 CH_3), 9.31 τ (3H, C-19 CH_3), 8.05 τ (3H, $OCOCH_3$), and 7.94 τ (3H > > N—COH_3), doublets at 9.11 τ (3H, C-21 CH_3) and 8.86 τ (3H, C-26 CH_3), and multiplets at 5.4 τ (α-H, H at C_3 and C_{22}) and 4.9 τ (2H at C_{27}) (Fig. 2). In the NMR spectrum of tetrahydropetiline there are singlets at 9.38 τ (3H, C-18 CH_3) and 9.03 τ (3H, C-19 CH_3) and doublets at 9.27 τ (3H, C-21, CH_3) and 9.10 τ (3H, C-26 CH_3) [14-21].

Under mass spectrometry conditions, the action of electronic impacts decomposes petiline in the same way as the steroid alkaloids [22] with the formation of fragments having m/e 97, 98, 111, 125, 151, 165, $(M - 57)^+$, $(M - 43)^+$, $(M - 29)^+$, $(M - 18)^+$, $(M - 15)^+$ and 413 (M^+) (Fig. 3).

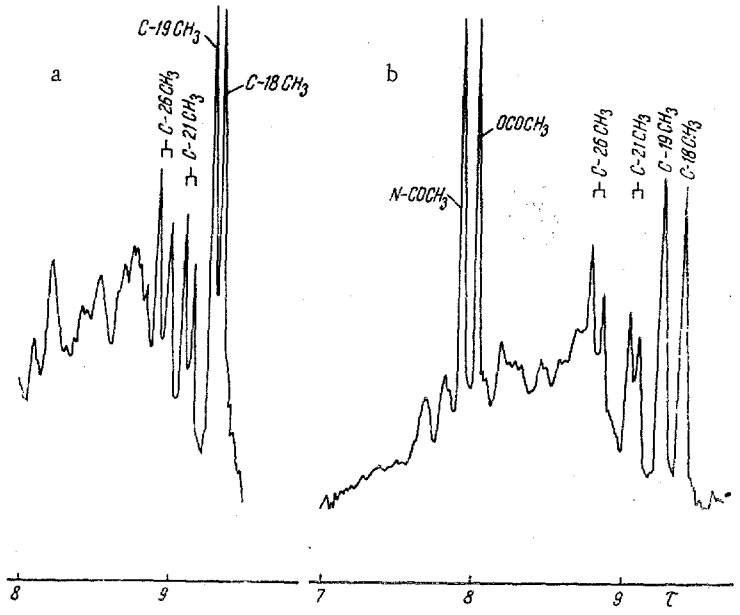


Fig. 2. NMR spectra of petiline (a) and diacetylpetiline (b).

The NMR spectra given show that petiline has a 3β-OH group. This is confirmed by the formation with digitonin of a digitonide insoluble in ethanol.

The double bond in petiline can be only between C_8 and C_9, C_8 and C_{14}, C_{17} and C_{20}, or C_{20} and C_{22}. The other positions are excluded because of the absence from the NMR spectrum of the signal of an olefinic proton. According to the UV spectrum, the carbonyl group must be conjugated with the double bond. Consequently, this group may be present in position 7, 11, 15, 16, or 23. If the double bond is between C_8 and C_9, the carbonyl group may occupy position 7

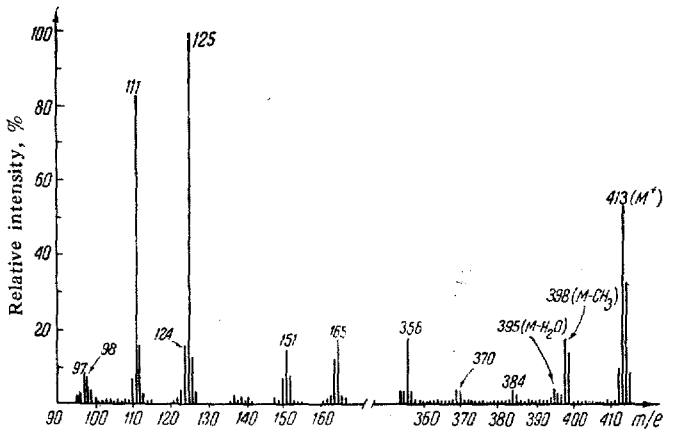


Fig. 3. Mass spectrum of petiline.

or 11. In both cases, the signal from the protons of the C-19 methyl group must appear at 8.85-8.9 τ, i.e., strongly displaced toward the weak-field region. In petiline, this signal is found in a comparatively strong field at 9.32 τ. Consequently, the double bond conjugated with the carbonyl group cannot be in the positions mentioned. The formation from petiline under the conditions of mass spectrometry of fragments with m/e 111 and 125 excludes the location of the double bond between C_{17} and C_{20} or C_{20} and C_{22}, and position 16 or 23 for the carbonyl group. Moreover, the double bond cannot be located in these positions because the NMR spectrum of petiline and its conversion products lack a signal from the protons of a methyl group attached to an unsaturated carbon atom. Consequently, the double bond in petiline is located between C_8 and C_{14} and the carbonyl group is in position 7 or 15. If the carbonyl group were at position 7, the

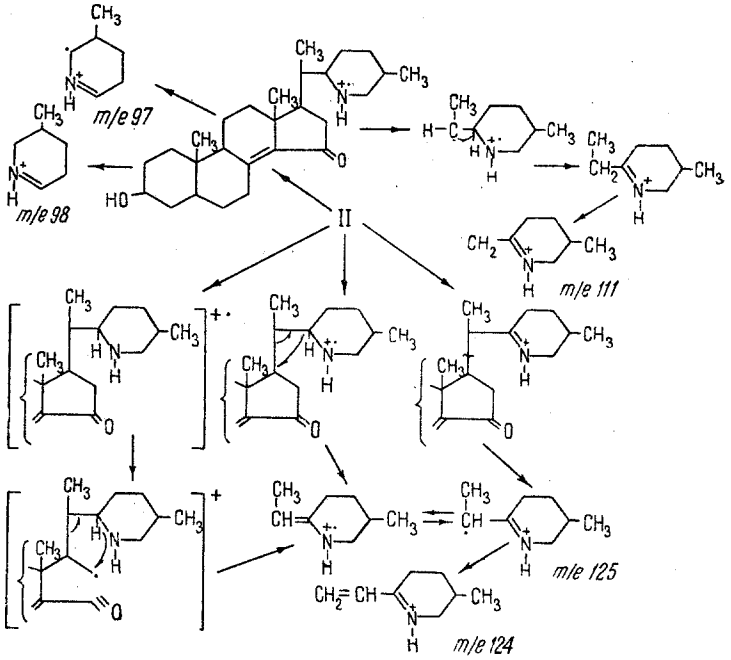
signal from the protons of the C-18 methyl group should be observed in a weak field, i.e., at approximately 8.9–9.1 τ. In petiline, the signal from the C-18 methyl group is strongly shielded and is located at 9.37 τ. Thus, the carbonyl group in petiline is located in position 15.

In the NMR spectrum of tetrahydropetiline, the signal from the protons of the C-19 methyl group is found at 9.03 τ. Such a chemical shift of the protons of a C-19 methyl group in steroids is found only with a cis-linkage of rings A and B, the C-19 methyl group and the hydrogen at C_5 being in the β positions.

Moreover, in tetrahydropetiline the resonance signal from the C-18 methyl group is found at 9.38 τ, which shows the α position of the hydrogen atom at C_{14} and the β position of the C-18 methyl group.

On the basis of the data given, we propose for petiline the most probable structure and partial configuration II. In the mass spectrometry of petiline (II), the fragment with m/e 98 is formed by α-bond cleavage. This cleavage with migration of a hydrogen atom from C_{27} to C_{20} leads to the appearance of an ion with m/e 97. Because of β-cleavage and the migration of hydrogen from C_{22} to C_{20} with subsequent loss of the C-21 methyl group, an ion with m/e 111 is formed.

Cleavage of the bond between C_{15} and C_{16}, migration of hydrogen from C_{22} to C_{16}, and further cleavage of the bond between C_{17} and C_{20} form the ion with m/e 125. The fragment with m/e 125 may also arise from the ion with m/e



412 (M – 1) on β-cleavage and from the molecular ion on cleavage of the bond between C_{17} and C_{20} and migration of a hydrogen atom from C_{22} to C_{17}. The ion with m/e 124 is obtained after the elimination of hydrogen from the fragment with m/e 125.

Experimental

By the usual chloroform extraction, from 70 kg of the epigeal part of P. raddeana collected in the flowering and fruit-bearing stage on the Chindirskii Road in the Kizyl-Arvat region, (Ashkhabad Oblast of TurkmSSR), we obtained 512.2 g of ether-soluble and 190.4 g of chloroform-soluble alkaloids (1% of the weight of the dry plant).

From the total chloroform alkaloids, by treatment with methanol, we isolated 67.2 g (9.6%) of edpetiline (from methanol).

When the ethereal solution was concentrated, 296.5 g of imperialine deposited (from methanol). The mother liquor from the imperialine was evaporated in vacuum and the dry residue (215.7 g) was dissolved in methanol and the solution was then mixed with an ethanolic solution of hydrochloric acid. Petiline hydrochloride was formed, with mp 281–284° C. Yield 42.1 g, mp 288–289° C (from acetone–methanol).

The hydrochloride was decomposed with ammonia, and the base was extracted with chloroform. Evaporation of the solvent yielded 25.8 g of petiline with mp 205–206° C (from acetone). The methanolic mother liquor from the petiline hydrochloride was evaporated in vacuum, the residue was dissolved in water, a 5% solution of hydrochloric acid

was added, and the solution was exhaustively extracted with chloroform. The acid solution was made alkaline with 12.5% ammonia solution and the alkaloids were extracted with ether (26.8 g) and chloroform (3.2 g). By treatment with acetone, the 26.8 g of mixed bases yielded 21.7 g of imperialine. The acid chloroform extract was made alkaline with 12.5% ammonia. The alkaline solution was separated off and the chloroform extract was treated with 5% sulfuric acid. The washed acid solution was made alkaline with ammonia and extracted with ether and chloroform. Concentration of the ethereal extract yielded 9.6 g of petiline.

Petiline is readily soluble in methanol, ethanol, and chloroform, moderately soluble in ether and acetone, sparingly soluble in petroleum ether, and insoluble in water. IR spectrum: ν_{max} 3310 (>NH); 3400 (OH), 2840-2940; 1470 (C—CH_3), 1718 (C=O); 1675 (C=C) cm^{-1}, $[\alpha]_D$ −51.07° (c 1.2; C_2H_5OH), R_f 0.75 [ethyl acetate—petroleum ether—ethanol (5:5:1.5)].

Found, %: C 78.2, 78.4; H 10.40, 10.5; N 3.35, 3.36. Calculated for $C_{27}H_{43}NO_2$, %: C 78.40; H 10.47; N 3.38; mol. wt. 413 (mass spectroscopy).

Hydrochloride—mp 288-289° C [acetone—methanol (3:1)].

Found, %: Cl 7.8, 7.94. Calculated for $C_{27}H_{43}NO_2 \cdot HCl$, %: Cl 7.89.

Hydrobromide, mp 314-316° C [acetone—methanol (3:1)].

N,O-Diacetylpetiline. A mixture of 0.29 g of petiline, 4 ml of dry pyridine, and 3 ml of acetic anhydride was left at 30° C for 72 hr. The melting point of the diacetylpetilidine formed was 188-189° C (from acetone); IR spectrum: ν_{max} 1745, 1260 ($OCOCH_3$), 1718 (C=O); 1680 (C=C), 1660 cm^{-1} (N—$COCH_3$).

Found, %: C 74.65; H 9.48. Calculated for $C_{31}H_{43}NO_2$, %: C 74.8, H 9.5.

Petiline oxime, obtained by the usual method, had mp 218-220° C [from methanol—water (2:1)].

N-Methylpetiline. A mixture of 0.2 g of petiline, 0.1 ml of formalin, and 0.05 ml of 98% formic acid was heated in the water bath for 4 hr. The melting point of the N-methylpetiline was 219-221° C (from acetone).

Tetrahydropetiline. In 30 ml of ethanol, 1.1 g of petiline and a platinum catalyst (from 0.3 g of PtO_2) was shaken in an atmosphere of hydrogen. The tetrahydropetiline formed had mp 209-210° C (from methanol), $[\alpha]_D$ −11.5° [c 1.3; methanol—chloroform (1:1)].

Dihydropetilinone. A mixture of 0.3 g of tetrahydropetiline, 0.15 g of chromic anhydride, and 12 ml of acetic acid was heated at 50° C for 30 min. The melting point of the dihydropetilinone obtained was 229-231° C (from acetone); IR spectrum: ν_{max} 1722 cm^{-1} (C=O). The melting point of dihydropetilinone dioxime obtained by the usual method was 161-163° C [from methanol—water (3:1)].

Deoxohexahydropetilinone, obtained by the Huang-Minlon reduction of dihydropetilinone had mp 171-172° C (from acetone), $[\alpha]_D$ −29.2° (c 0.48; chloroform).

N-Acetyldeoxohexahydropetilinone. A mixture of 0.05 g of deoxohexahydropetilinone, 0.7 ml of pyridine, and 0.5 ml of acetic anhydride was left at 30° C for 72 hr. The melting point of the N-acetyldeoxohexahydropetilinone was 155-156° C (from acetone).

The IR spectra were recorded on a UR-10 double-beam spectrophotometer (molded tablets with KBr); the UV spectra on an SF-4 spectrophotometer (ethanolic solutions); the mass spectra on a MKh-1303 mass spectrometer with a glass inlet system at 40 eV and 50 mA; and the NMR spectra (in deuterochloroform) on a JNM-4H-100 instrument with hexamethyldisiloxane as internal standard.

Conclusions

1. Imperialine, edpetilidine, and the new alkaloid petiline $C_{27}H_{43}O_2N$ have been isolated from the epigeal part of P. raddeana.

2. On the basis of a study of the chemical properties and the IR, UV, NMR, and mass spectra a most probable structure and a partial configuration have been proposed for petiline.

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