Chemistry

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Abstract

Full Text

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THE STRUCTURE OF UNGERINE

From *Ungernia Severtzovii* we have isolated a number of alkaloids, including a new alkaloid, ungerine (1,2); further study of the latter leads to the composition $C_{18}H_{19}O_5N$ and to the expanded formula

$$C_{14}H_{11}(=N—CH_3)(CH_2O_2)(OCH_3)(—COO—)(=).$$

The IR spectrum of ungerine contains a band at 1725 cm^{-1}, indicating the presence of a δ-lactone group. In addition, on boiling ungerine with an alcoholic alkali solution, an oxyamino acid (II) is formed. In the IR spectrum of II there is an absorption band at 3340 cm^{-1}, characteristic of a hydroxyl group. On heating with dilute sulfuric acid the oxyamino acid is converted into the original ungerine.

Reduction of ungerine with both $LiAlH_4$ and $NaBH_4$ gave tetrahydroungerine (III) of composition $C_{18}H_{23}O_5N$. The presence of two active hydrogen atoms was established in tetrahydroungerine. In the IR spectrum of III a band appears at 3370 cm^{-1}, characteristic of hydroxyl groups, and the absorption band of the carbonyl group disappears. On catalytic hydrogenation of tetrahydroungerine III, *d*- and *l*-hexahydroungerines of composition $C_{18}H_{25}O_5N$ are formed, with the expanded formula

$$C_{16}H_{15}(=N—CH_3)(CH_2O_2)(CH_3O)(OH)_2.$$

All these reactions confirm the presence of a δ-lactone grouping in the ungerine molecule.

Comparison of the UV absorption spectrum of ungerine with the spectra of hippeastrine and homolycorine showed that it belongs to alkaloids of the homolycorine type ($\lambda_{\max}$227, 228, 306 mμ in alcohol).

When silver hydroxide acts on the methiodide of dihydroungerine, amorphous des-N-methyldihydroungerine is obtained, which gives a well-crystallizing nitrate, picrate, and methiodide. In the molecule of des-N-methyldihydroungerine $C_{18}H_{23}O_5N$, the methylenedioxy, methoxy, and δ-lactone groups are retained:

$$C_{14}H_{12}\left(—N\begin{matrix}CH_3\\CH_3\end{matrix}\right)(CH_2O_2)(OCH_3)(—COO—)(=).$$

Further degradation of the methiodide of des-N-methyldihydroungerine in the presence of silver oxide does not occur. On heating the methiodide with alcoholic alkali, trimethylamine is liberated, and a nitrogen-free substance of composition $C_{16}H_{12}O_4$ is formed, with the expanded formula $C_{12}H_6(CH_2O_2)(—CH=CH_2)(COOH)$.

The nitrogen-free substance dissolves well in alkalis; in an acidic medium a precipitate separates. In the second stage of Hofmann degradation a methoxy group is split off.

Oxidation of the nitrogen-free product with potassium permanganate (4 g-at. of oxygen) in alkaline medium gave an acid identical with 4,5-methylenedioxydiphenyl-2,3-dicarboxylic acid, obtained by oxidation of the nitrogen-free product of dihydrohippeastrine.

The products obtained from the transformation of ungerine, dehydroungerine, indicate that ungerine belongs to the alkaloids of the homolycorine type and has structural formula (I), in which the positions of the methoxyl group and of the double bond were established by carrying out the conversion of ungerine into the known (3) alkaloid hippeastrine (IV).

Ungerine was also isolated from the bulbs of *U. Severtzovii* and *Leucojum aestivum* by N. F. Proskurnina, and the conversion of dihydroungerine into dihydrohippeastrine (4) was carried out, confirming the correctness of the structure of ungerine.

Some physicochemical properties of the alkaloid nivaline, isolated from *Galanthus nivalis* (5), coincide with the properties of ungerine. It is possible that it will prove identical with ungerine, which can be decided by direct comparison of the two alkaloids.

[Reaction scheme showing the conversion among structures labeled (III), (II), (I), and (IV).]

Experimental Part

Tetrahydroungerine is formed when ethereal solutions of ungerine and lithium aluminum hydride are mixed; m.p. 155–156°, $[\alpha]_D^{20} - 40^\circ$ (C 1118°, ethanol).

$C_{18}H_{23}O_5N$.	Found, %:	C 64.80; H 7.72; N 4.16; OCH_3 8.22; NCH_3 6.99; H′ 0.58
	Calculated, %:	C 64.84; H 6.95; N 4.20; OCH_3 9.3; NCH_3 8.71; 2H′ 0.60

Hexahydroungerine was obtained by reduction of tetrahydroungerine in the presence of a platinum catalyst. By recrystallization from ether and methanol it was separated into optical antipodes with m.p. 167-168°, $[\alpha]_D^{20} - 49^\circ$ (C 1.49°, chloroform) and with m.p. 186-187°, $[\alpha]_D^{30} + 40.3^\circ$ (C 0.338°, methanol). A mixed sample of the two antipodes gives no depression of the melting point.

$C_{18}H_{25}O_5N$.	Found, %:	C 64.48; H 7.45; N 4.01; NCH_3 5.90
	Calculated, %:	C 64.45; H 7.51; N 4.17; NCH_3 7.6

Oxyamino acid is formed on boiling ungerine with a 10% KOH solution; m.p. 182-183° (with foaming), $[\alpha]_D^{27} - 42^\circ$ (C 0.614°, water).

$C_{18}H_{21}O_6N$.	Found, %:	N 3.62; OCH_3 8.6; H' 0.60
	Calculated, %:	N 4.03; OCH_3 8.93; $2H'$ 0.58

On heating in a 2% solution of sulfuric acid, the oxyamino acid is converted back into ungerine.

Dihydroungerine methiodide is formed when an acetone solution of dihydroungerine is mixed with methyl iodide, as an amorphous powder.

Des-N-methyldihydroungerine. On treatment of dihydroungerine methiodide with silver oxide in methanol, a des-base is formed as a yellow powder. The nitrate has m.p. 182-183° (with foaming).

$C_{19}H_{23}O_5N \cdot HNO_3$.	Found, %:	N 6.58; OCH_3 7.3
	Calculated, %:	N 6.85; OCH_3 7.59

Picrate melts at 239-240° (with decomposition).

$C_{25}H_{26}N_4O_{12}$.	Found, %:	N 10.12
	Calculated, %:	N 9.73

Iodomethylate has m.p. 297-298° (from water), $[\alpha]_D^{27} - 52.65^\circ$ (C 0.321°, water).

$C_{19}H_{23}O_5N \cdot CH_3J$.	Found, %:	J 25.5
	Calculated, %:	J 26.04

A **nitrogen-free substance** is formed with elimination of trimethylamine on boiling the iodomethylate of des-N-methyldihydroungerine with a concentrated solution of KOH. It crystallizes from methanol and ether, m.p. 180-181°.

$C_{16}H_{12}O_4N$.	Found, %:	C 71.5; H 5.02
	Calculated, %:	C 71.63; H 4.49

4,5-Methylenedioxy-diphenyl-2,3′-dicarboxylic acid was obtained by oxidation of 0.45 g of the nitrogen-free product of dihydroungerine in alkaline medium with 0.9 g of potassium permanganate for 30 min. It has m.p. 220-230°. A mixed sample of this acid gives no depression of the melting point with 4,5-methylenedioxy-diphenyl-2,3′-dicarboxylic acid obtained by oxidation of the nitrogen-free product of dihydrohippeastrine.

IR spectrum of 4,5-methylenedioxy-diphenyl-2,3-dicarboxylic acid: 2700, 2530, 1700, 1620, 1030, 980 cm^{-1}; UV–$\lambda_{\max}$ 224, 260, 292 mμ, $\lg\varepsilon$ 4.42, 3.83, 3.72.

The **conversion of ungerine into hippeastrine** was carried out by boiling 0.4 g of ungerine with 20 ml of 17% hydrochloric acid for 6 h. Descending paper chromatography established the presence of two alkaloids: one of them, with R_f 0.58, was the starting ungerine, and the other, with R_f 0.44, was hippeastrine. System: *n*-butanol—water—acetic acid (100 : 100 : 5). Developer: UV rays and iodine vapors.

Separation of the two alkaloids was carried out on a column packed with aluminum oxide. It was washed first with benzene and then with ethyl acetate. From the ethyl acetate fraction a crystalline alkaloid (0.04 g) with m.p. 205-206° was isolated; a mixed sample of this alkaloid with hippeastrine gives no depression (hippeastrine 214-215°).

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