STRUCTURE OF ISOREGECOLINE

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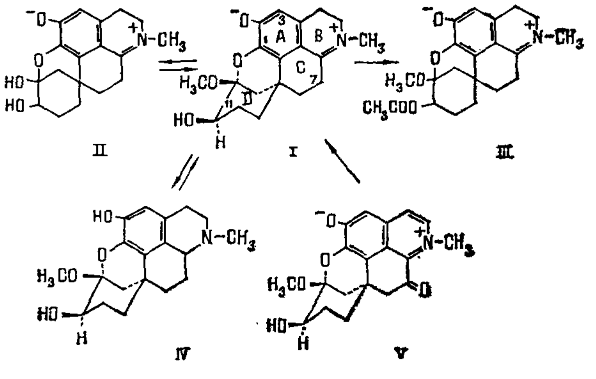
The structure of the alkaloid isoregecoline (I) with the composition $C_{19}H_{23}O_4N^+$, mp. 284-286°C, isolated previously from Colchicum kesselringii Regel growing in the flood plains of the R. Chirchik has been established. It has been shown by IR, PMR and mass spectroscopy and chemical transformations that (I) is an epimer of regecoline isolated from a plant of the same species.

We have previously [1] reported the isolation from the epigeal parts of Colchicum kesselringii Regel (Kesselring's autumn crocus) collected in the flood plain of the R. Chirchik of – together with isoregelinone [1, 2] – an alkaloid with mp 284-286°C which has been called isoregecoline.

Isoregecoline has the composition $C_{19}H_{23}O_4N^+$ and exhibits in its IR spectrum the absorption bands of active hydrogen (3380, 3250 cm^{-1}) of methylene groups (2930, 1450, 1440 cm^{-1}), of a N=C bond (1630 cm^{-1}), and of a benzene ring (1595 cm^{-1}). The PMR spectrum of the base (Fig. 1) shows the signals of the proton of a benzene ring (6.65 ppm), of two methyl groups (3.50 and 3.34 ppm), and of three protons, obviously, of methylene and methine groups (3 H, 4.23-3.78 ppm). The appearance of the signal of a proton geminally arranged in relation to a hydroxy group in position 11 in this region is characteristic for homoproaporphine alkaloids with a spirocyclohexanol ring [3, 4], and the downfield shift of the signals of the protons of the methylene group in position 7 when a 6=6a double bond is present in isoquinoline bases has been reported previously for the aporphine alkaloid 6,6a-dehydronorglaucine [5].

In the mass spectrum of isoregecoline there are the peaks of the main ions with m/z 329 (M^+, 100%), 327 $(M-2)^+$, 314 $(M-15)^+$ (100%), 310, 298, 296, 270, 228.

In its spectral characteristics, this base proved to be close to regecoline [6]. Starting from this and the physical constants of the base, it was assumed that it was an epimer of regecoline differing from the latter by the configuration of the hydroxy group in position 11. In view of the fact that in regecoline this hydroxy group has the axial orientation, isoregecoline is represented by structure (I) (scheme) with the equatorial orientation of this group.



Structure and transformations of isoregecoline

To confirm the structure proposed for the base, we studied some of its chemical transformations. Acid hydrolysis gave the 1-demethylated derivative (II) which was reconverted into (I) on methanolysis. The acetylation of (I) with acetic anhydride and anhydrous sodium acetate led to the monoacetyl derivative (III). The reduction of (I) by heating it with zinc in acetic acid led to a comopund identical with luteine (IV) [7]. In addition, the passage

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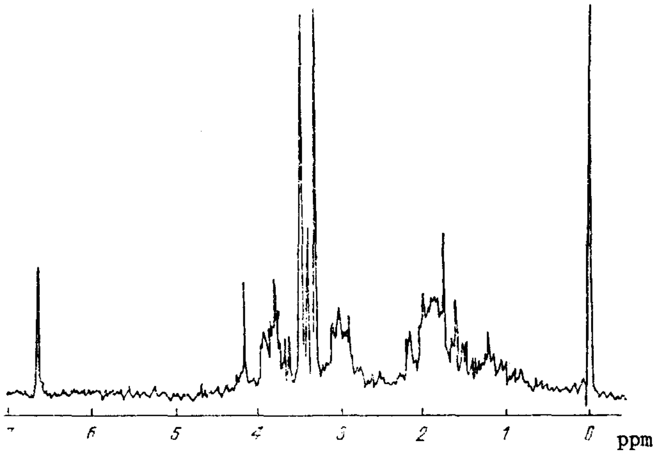

Fig. 1. PMR spectrum of isoregecoline (in CD_3OD).

to (I) from isoregelinone (V) was effected [2] by reduction with zinc in acetic acid under milder conditions.

The transformations of isoregecoline given above confirm structure (I) for it. The structure of its spirocyclohexene ring D follows from the facts presented for isoregelinone [1].

EXPERIMENTAL

The individuality of the substances was studied by thin-layer chromatography on glass plates coated with type LS 5/40 μm silica gel fixed with 13% of gypsum in the chloroform–methanol–acetone–benzene–25% ammonia (10:8:6.5:3:5) system.

IR spectra were recorded on a UR-10 double-beam spectrometer, PMR spectra on a XL-100 instrument, and mass spectra on a Varian MAT-311 spectrometer.

12-Demethylisoregecoline (II). A solution of 0.1 g of (I) in 8 ml of 7% hydrochloric acid was heated on the water bath for 2 h. The solution was evaporated and the residual substance was treated twice with a 9:1 mixture of acetone and methanol, the mother liquor being decanted off. Compound (II) was isolated with R_f 0.21. The initial (I) had R_f 0.58.

PMR spectrum (in CD_3OD, ppm): 6.70 (1 H, s, H_3); 3.50 (3 H, s, $^+N{-}CH_3$); 4.23-3.78 (3 H).

Isoregecoline from (II). A solution of 0.06 g of (II) in 10 ml of methanol containing 7% of hydrogen chloride was heated with a reflux condenser and a calcium chloride tube for 1 h. The solvent was evaporated off in vacuum and the residual substance was decanted twice with 3 ml of acetone each time. A compound identical in its R_f and IR spectrum with isoregecoline (I) was isolated.

Acetylisoregecoline (III). One drop of concentrated sulfuric acid was added to a solution of 0.07 g of (I) in 3 ml of acetic anhydride. After 3 h, the excess of reagent was evaporated off in vacuum with the addition of methanol. Compound was isolated with R_f 0.78.

PMR spectrum ($CDCl_3$, ppm): 6.66 (1 H, s, H_3); 4.96 (1 H, m, H_{11}); 3.42 (3 H, s, $^+N{-}CH_3$); 3.31 (3 H, s, OCH_3); 2.04 (3 H, s, $COCH_3$).

Mass spectrum (*m/z*): 371 (M^+; 100%), 369 $(M-2)^+$ (50%), 312 (100), 310, 308, 296, 294, 282, 280, 270.

Reduction of (I) to Luteine (IV). A solution of 0.07 g of (I) in 12 ml of 30% acetic acid was treated with 0.2 g of zinc dust and the mixture was heated on the water bath for 8 h. The precipitate was separated off and washed with water, the filtrate was neutralized with ammonia, and the reaction product was extracted with chloroform. A compound was isolated with mp 226-228°C (from acetone), identical in its R_f value (0.67) and IR spectrum with luteine (IV) [7].

Isoregecoline from Isoregelinone (V). A solution of 0.06 g of (V) in 10 ml of 10% acetic acid was treated with 0.5 g of zinc dust at room temperature for 4 h. The solid matter was separated off, the filtrate was evaporated in vacuum, and the residual substance was washed successively with ether and acetone. Compound (I) was isolated (from acetone), R_f 0.58.

SUMMARY

The structure of the new alkaloid isoregecoline isolated from *Colchicum kesselringii* Regel has been established on the basis of the results of a study of IR-, PMR-, and mass-spectral characteristics and chemical transformations.

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