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Abstract

Full Text

Chemistry

R. P. Evstigneeva, Yu. Brayer, and N. A. Preobrazhenskii

Synthesis of the Alkaloid Emetamine

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Emetamine is one of the representatives of the group of alkaloids isolated from ipecacuanha roots. In the plant it is present in an insignificant amount and is very difficult to isolate in pure form. It was established that emetamine differs from the principal alkaloid of ipecacuanha—emetine—by a lower hydrogen content (by 4 atoms). It was suggested that emetamine contains an isoquinoline ring in its composition, whereas emetine is a derivative of tetrahydroisoquinoline ((^{1})). The principal transformations of the alkaloid confirmed this possibility. However, the formula proposed at that time was based on an incorrect structure of emetine. After the structure of emetine (I) had been established, formula II was adopted for emetamine.

I II

In recent times the correctness of structure II has been confirmed by the conversion of emetamine bisbenzyl chloride (III), upon oxidation with permanganate, into N-benzylisoquinolone (IV) ((^{2})).

III $\longrightarrow$ IV

On the basis of analogous transformations of *o*-methylpsychotrine bisbenzyl chloride (V), which led to the preparation (in good yield) of benzyl-

corydaldine (VI), it may be considered that the double bond of the isoquinoline derivative IV could not have formed during oxidation.

[structural formulas V and VI]

In the present communication the synthesis of racemic emetamine is described, as a result of which the structure of this alkaloid may be regarded as definitively established.

The synthesis was carried out according to the scheme developed by us earlier for the preparation of emetine ((^{3})).

[synthetic scheme VII + VIII → IX → II]

Fig. 1. Ultraviolet absorption spectra in water: 1—synthetic rubremetamine bromide, 2—rubremetamine bromide from the natural alkaloid (5)

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Methyl ester of 4 ,5 -dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydrobenz-((1,2:1 ,2))-quinolizin-7-acetic acid (VII) is obtained by the method described by us, using a skeletal nickel catalyst for the reduction of the quaternary chloride ((⁀3)). The melting point of the hydrochloride (crystalline hydrate) is 195–195.5° (decomposes at 189°). -(3,4-Dimethoxyphenyl)- -methoxyethylamine (VIII) is obtained from vanillin ((⁀4)). B.p. 112–115°/1 mm.

On heating ester VII with amine VIII at 180–200° in a stream of nitrogen, amide IX is obtained, which is isolated from anhydrous ethyl alcohol in the form of colorless crystals. M.p. 172.5–173.5°.

Found, %:		*C* 68.66; 68.45;		*H* 7.97; 7.83;		*N* 5.49; 5.48	
$C_{30}H_{42}O_6N_2$. Calculated, %:		*C* 68.44;		*H* 8.02;		*N* 5.31	

Cyclization of the amide with phosphorus oxychloride in toluene gives emetamine. The base is isolated as a white amorphous substance, which is converted into the oxalate.

M.p. 141.5–142.5° (from ethyl alcohol). Before analysis the preparation was dried at 117° and 1 mm for one hour.

Found, %:		*C* 60.23; 60.64;		*H* 6.16; 6.12;		*N* 3.89; 3.84	
$C_{29}H_{36}O_4N_2 \cdot 2C_2H_2O_4$	Calculated, %:	*C* 60.34;		*H* 6.14;		*N* 4.27	

The emetamine base, isolated from the oxalate, has m.p. 124–125° (deforms at 70°):

$C_{29}H_{36}O_4N_2$.	Found %:	C 73.46;	H 7.58;	N 5.55
	Calculated %:	C 73.10;	H 7.62;	N 5.88

On oxidation of the racemic emetamine base with bromine, rubremetamine bromide was obtained in the form of orange-red crystals. M.p. 170–185°.

Fig. 1. Ultraviolet absorption spectra in water:
1—synthetic rubremetamine bromide,
2—rubremetamine bromide from the natural alkaloid (5)

The ultraviolet absorption spectrum of synthetic rubremetamine bromide is identical (Fig. 1) to the spectrum of rubremetamine bromide obtained from the natural alkaloid (5).

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Note: Figure translations are in progress. See original paper for figures.