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SYNTESIS OF A NEW DERIVATIVE OF COLCHAMINE AND AMINOCOLCHAMIN WITH PROPARGYL ESTER OF ACRYLIC

Abstract: *A method is proposed for the synthesis of a new derivative of aminocolchamine with methylethylenethylcarbinol and the synthesized compound is identified on 4- (aminocolchamino N / 1,1-methylethylbutin-2) carbinol by thin-layer and paper chromatography. The structures of the synthesized colchamine derivative are confirmed by the data of IR and PMR spectra. Based on the obtained data of IR spectra, it was found that the synthesized substance differs from the starting compounds from the ester and carbonyl groups.*

Key words: *aminocolchamine, propargyl, methylethylethynylcarbinol, 4- (aminocolchamino N / 1,1-methylethylbutin-2) carbinol.*

Language: *English*

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Introduction

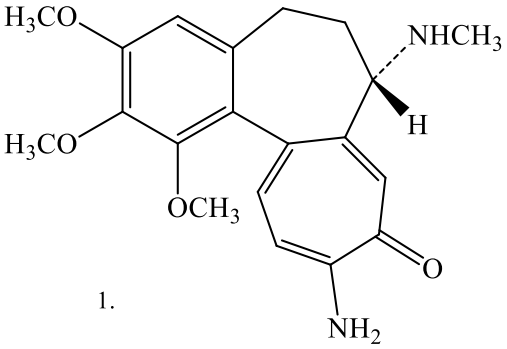
Colchamine is one of the alkaloids isolated from the corms of the Colchicum marius (Colchicum SpeciosumStev.), Fam. Liliaceae (Liliaceae). The second alkaloid contained in these corms is colchamine (Colchicinum). Both alkaloids have similar pharmacological properties, while colchamine is less toxic (7-8 times). Both drugs have anti-mitotic (anti-cell division) activity, have a karyoclastic (anti-cell division) effect, and inhibit leuko- and lymphopoiesis (the formation of white blood cells and lymphocytes).

Among the numerous chemical compounds with antitumor activity, much attention is paid to tropolonlilium alkaloids. In order to find less toxic compounds in this series, a large number of derivatives of colchicine and colchamine were synthesized.

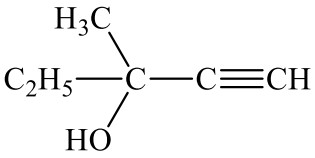
It is known that the introduction of acetylene bond groups into the drug molecule significantly reduces their toxicity. Due to the fact that such work in the field of colchicine alkaloids has not previously been carried out, we synthesized derivatives of

aminocolchamine (1) with methylethylethynylcarbinol (2) [1].

Starting compounds for the synthesis of acetylene derivatives of aminocolchamine.



1.



2.

The condensation reaction of aminocolchamine with acetylene compounds was carried out according to Mannich [2], in equimolecular ratios of the reagents:

The main starting compound, colchamine (1), was synthesized from the Colchicum luteum baker in the Surkhandarinsky region for the syntheses.

As a result, we synthesized; 4-(aminocolchamino N / 1,1-methylethylbutin-2) carbinol (3) [3].

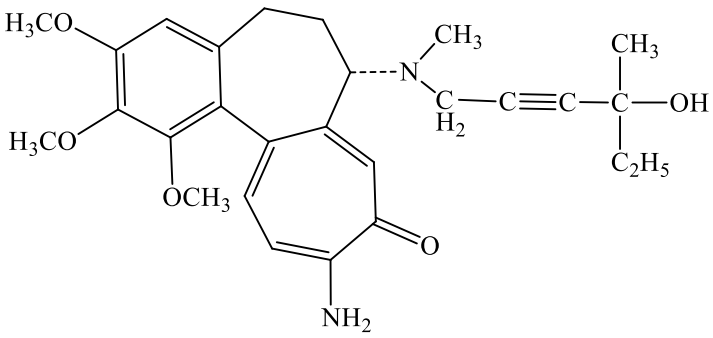
The compounds obtained are light yellow powders with R_f values close to each other. At the same time, they differ greatly in chromatographic mobility from the original aminocolchamine, having a high R_f value.

A characteristic feature of all acetylene derivatives is the presence of a two-proton doublet from the bridging N-CH_2 group in their NMR spectra, which appears in the region of 3.32-3.38 ppm. The bridge OCH_3 group present in compounds 4-5 forms a narrow two-proton doublet in the region of 4.53-4.70 ppm.

The structures of the synthesized compounds are confirmed by the data of IR and PMR spectra. The IR spectra of compounds with an ester moiety (3-4) show absorption bands of the carbonyl group (1735-1730 cm^1).

The colchamin fragments of the synthesized compounds in the 1H-NMR spectra do not differ significantly: the signals of the N-methyl group appear at 2.20-2.22 ppm, the methoxy groups at 3.56-3.60 (at C-1) and 3.82 -3.85 ppm (at C-2, C-3 C-10), proton H-4 - at 6.44-6.51 ppm, H-8 - 7.90-7.96 ppm, H- 11 - 6.68-6.75 ppm. and H-12 - 7.17-7.22 ppm.

Synthesized Acetylene Derivatives



The experimental part. Acetylene alcohols and amino alcohols and their various derivatives exhibit biological and pharmacological activity [4,5].

The individuality and authenticity of the substances was controlled by PC and TLC methods.

a) Derivatives of aminocolchamine with methylethylethynylcarbinol. A portion of 1.0 g of aminocolchamine was dissolved in 17 ml of dried and freshly distilled dioxane, and 0.12 g of paraform, 0.01 g of hydroquinone and 0.03 g of copper monochloride were added to the solution. After adding another equimolecular amount of methylethylethynylcarbinol to the solution, the contents of the flask were mixed well. Reaction conditions table 1.

Table 1. Reaction conditions of methylethylethynylcarbinol with colchamine

№	Reagent	Estimate damount of reagent	Reagent taken	Product yield (%)
1.	Aminocolchamine	0,74	1,0	91

The reaction mixture was heated in a glycerin bath under reflux at 70-90°C for 4-6 hours. The end of the reaction was determined by thin layer chromatography of the reaction mixture.

After the practical completion of the reaction, insoluble in dioxane substances were separated by filtration and the solvent (dioxane) was distilled off on a rotary unit. The residue was dissolved in 20-30 ml of chloroform, the resulting very dark chloroform solution was extracted three times with 20 ml of 5% acetic acid.

The acetic acid extract contains unreacted aminocolchamine, which was isolated by alkalizing the acidic solution with ammonia and extracting it with chloroform.

The chloroform solution of the reaction product, after separation of the starting aminocolchamine, was dried over anhydrous sodium sulfate, the sulfate was filtered off and the filtrate was passed through a small layer (5-7 g) of aluminum oxide. In this case, the dark extract is greatly clarified. The solvent was distilled off and the reaction product was dried in a vacuum desiccator.

The final reaction products are obtained as non-crystalline light yellow powders.

4- (aminocolchamino N / 1,1-methylethylbutin-2) carbinol (3).

IR spectrum: 1120, 1170, 1720, 2570, 2950, 3410, 3540 cm^{-1}.

NMR spectrum: 1.26; 1.45; 1.49 (CH_3CH_2), 1.98 (CH_3), 2.16 (N-CH_3), 3.58; 3.85 x2, 3.88 (3H x 4, ss, 4OCH_3), 5.16 (OH), 6.48 (H-$_4$), 6.94 (H-11), 7.24 (H-12 and H-8) ppm.

Findings.

1. Synthesized new derivatives of aminocolchamine with methylethylenethylcarbinol.

2. The synthesized compounds are confirmed by PMR and IR spectral data.

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