International Journal of Engineering Sciences &Research Technology

(A Peer Reviewed Online Journal)
Impact Factor: 5.164

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THOMSON REUTERS

[Alikulov, *et al.*, 8(10): October, 2019]
IC™ Value: 3.00

ISSN: 2277-9655
Impact Factor: 5.164
CODEN: IJESS7

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INTERNATIONAL JOURNAL OF ENGINEERING SCIENCES & RESEARCH TECHNOLOGY

SYNTHESIS OF A NEW DERIVATIVE OF COLCHINE WITH PROPYLETHYNYLCARBINOL

Alikulov R.V.[*1], GeldievYu.A.[2], SuyunovZh.R.[3], RuzievaB.Yu.[4] & Atamuratova D.M.[5]
[*1,2,3,4&5]Termez State University

DOI: 10.5281/zenodo.3522963

ABSTRACT

A new method for the synthesis of a colchamine derivative with propylethynylcarbinol is proposed. The resulting substance was identified by thin layer and paper chromatography of 4- (colchamino N / 1-propylbutin-2) carbinol. The structures of the synthesized compound are confirmed by the data of IR and PMR spectra. The resulting compounds are light yellow powders with close R_f values. At the same time, they are very different in chromatographic mobility from the original colchamine, having high R_f values.

KEYWORDS: Colchamine, propylethynylcarbinol, 4- (colchamino N / 1-propylbutin-2) carbinol.

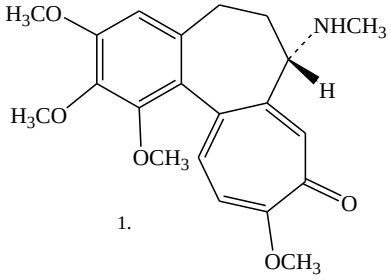
1. INTRODUCTION

Colchamine was isolated in 1952 by V.V., Kiselev, G.P. Menshikov, and A.A. Beer from Colchisumliparochiadis by extracting the juice of fresh colchicum bulbs with chloroform, which extracts a mixture of the bases. To separate impurities, the chloroform extract is treated with diluted sulfuric acid and washed with an alkali solution at a pH of 6–5.5,colchamine is released (0.02–0.03% of the weight of the feed). Colchamine - a white or yellowish crystalline powder, so pl. 181-182°, [α] D 125°, soluble in about 1%, chloroform, somewhat more difficult in alcohol and acetone insoluble in ether. Aqueous solutions of an alkaline reaction. In dilute mineral acids, colchamine is readily soluble to form yellow solutions. When boiling with dilute hydrochloric acid, the hydrolysis of the methoxy group occurs [1].

The structure and chemical transformations of the base were studied mainly by Kiselev [2] and Shantava by an employee [3]. Colchamine is 7-8 times less toxic than colchicine.

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 colchamine (1) with propylethynylcarbinol (2) [4].

The starting compounds for the synthesis of acetylene derivatives of colchamine (1):



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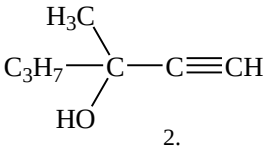

2.

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The condensation reaction of colchamine with acetylene compounds was carried out by Mannicho [5], 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.

2. MATERIALS AND METHODS

a) Derivatives of colchamine with propylethynylcarbinol. A portion of 1.0 g of colchamine 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 pro-ethynylcarbinol to the solution, the contents of the flask were mixed well.

Table 1.Reaction conditions of propylethynylcarbinol with colchamine

№	Reagent	Estimatedamountof reagent	The amount of reagent taken	Productyield (%)
1.	Kolhamin	0,78	1,0	93

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 colchamine, 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 colchamine, 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.

3. RESULTS AND DISCUSSION

As a result, we synthesized; 4- (colchamino N / 1-propylbutin-2) carbinol (3) [6].

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 colchamine, having a high R_f value.

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.

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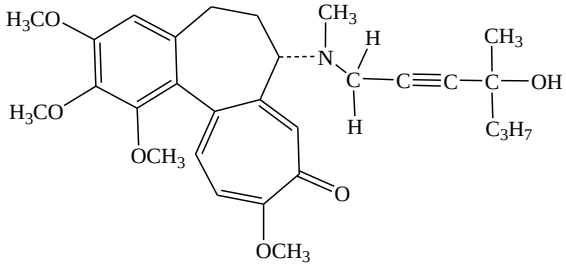
Synthesize dacetylene derivative



4- (colchamino N / 1-propylbutin-2) carbinol (3).

IR spectrum: 1100, 1170, 1720, 2570, 2950, 3400, 3540 cm -1.
PMR spectrum: 1.28; 1.51; 1.53 (CH3CH2), 1.90 (CH3), 2.86 (N-CH3), 3.58; 3.85 x 2, 3.88 (3H x 4, ss, 4OCH3), 5.64 (OH), 6.48 (H-4), 6.95 (H-11), 7.28 (H- 12 and H-8) ppm.

4. CONCLUSION

- Synthesized derivatives of kolhamine with propylethynylcarbinol.
- The structures of the synthesized compounds were confirmed by IR and PMR spectra.

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