Impact Factor:					
	ISRA (India) = 6.317	SIS (USA) = 0.912	ICV (Poland) = 6.630
	ISI (Dubai, UAE) = 1.582	РИНЦ (Russia) = 3.939	PIF (India) = 1.940
	GIF (Australia) = 0.564	ESJI (KZ) = 9.035	IBI (India) = 4.260
	JIF = 1.500	SJIF (Morocco) = 7.184	OAJI (USA) = 0.350

SOI: 1.1/TAS DOI: 10.15863/TAS

International Scientific Journal

Theoretical & Applied Science

p-ISSN: 2308-4944 (print) **e-ISSN:** 2409-0085 (online)

Year: 2021 **Issue:** 12 **Volume:** 104

Published: 21.12.2021 **http://T-Science.org**

QR – Issue QR – Article

R. V. Alikulov
Termez State University
researcher
rv_aliqulov@rambler.ru

Safarov A. M.
Termez State University
researcher

Bozorov Y. Sh.
Termez State University
researcher

Khamraeva M. F.
Termez State University
researcher

SYNTHESIS OF A NEW AMINOCOLCHAMINE DERIVATIVE WITH METHACRYLIC ACID PROPARGYL ESTER

Abstract: *New esters of methacrylic acid 4- (aminocolhamino-N-butin-2-yl) esters of methacrylic acids have been synthesized. The structures of the synthesized compound were confirmed by the data of IR and PMR spectra.*

Key words: *Colchamin, aminocolchamin, propargyl, methacrylic acid.*

Language: *English*

Citation: Alikulov, R. V., Safarov, A. M., Bozorov, Y. Sh., & Khamraeva, M. F. (2021). Synthesis of a new aminocolchamine derivative with methacrylic acid propargyl ester. *ISJ Theoretical & Applied Science, 12 (104),* 782-785.

Soi: http://s-o-i.org/1.1/TAS-12-104-82 ***Doi***: https://dx.doi.org/10.15863/TAS.2021.12.104.82

Scopus ASCC: *1600.*

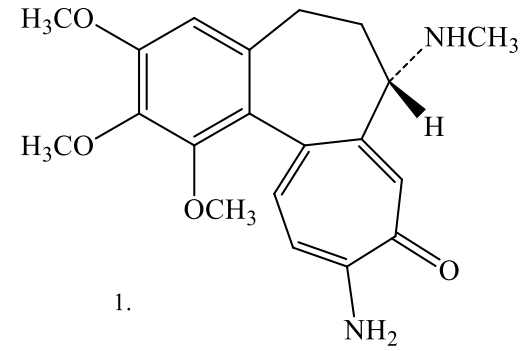
Introduction

Recently, propargyl ethers have attracted attention due to a wide range of useful properties (propargyl ethers exhibit biological activity, inhibiting corrosion and promoting the flotation of rare metals, increasing the energy intensity of complex rocket fuels). However, up to now in the literature there are practically no generalizing reviews on the methods of synthesis, physical, chemical and applied properties of this class of heteroatomic acetylenes [1].

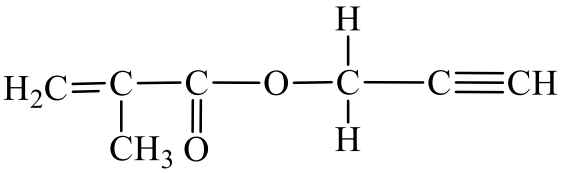
Among the numerous chemical compounds with antitumor activity, much attention is paid to the tropolone alkaloids of liliaceae. In order to find less toxic compounds in this series, a large number of colchicine and colchamine derivatives have been synthesized.

It is known that the introduction of groups containing an acetylene bond into a drug molecule significantly reduces their toxicity. In view of the fact that such work in the field of colchicine alkaloids has not been carried out previously, we synthesized derivatives of aminocolchamine with propargyl ester of methacrylic acid (3) [2].

Starting compounds for the synthesis of acetylene derivatives of aminocolchamine:



1.



The condensation reaction of amincolhamine with acetylenic compounds was carried out according to Mannich [3], in equimolecular ratios of the reagents:

The main starting compound - aminokolchamin (1) for the carried out synthesis obtained the isolated colchamine from Colchicum luteum baker growing in the Surkhandara region.

As a result, we have synthesized; aminocolchamin-4- (aminocolhamino-N-butin-2-yl) esters of methacrylic (5) (Table 1) [4].

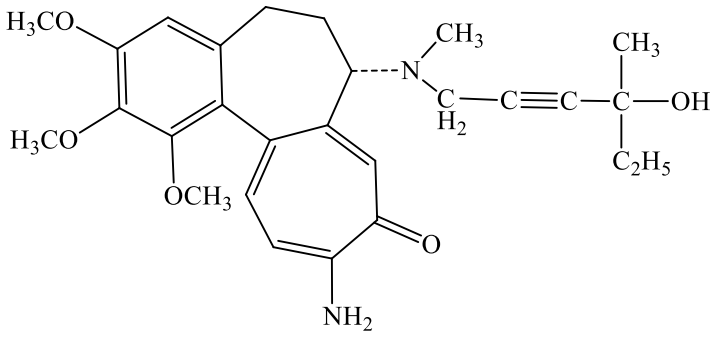
Upon hydrolysis of ester 4, 4- (colhamino-n-butin-2-yl) alcohol 6 is formed.

The resulting compounds are light yellow powders with close Rf values. At the same time, in terms of chromatographic mobility, they strongly differ from the starting aminocolchamines, having high Rf values.

The structures of the synthesized compound were confirmed by the data of IR and PMR spectra. The IR spectra of compounds with the ester group (3-4) show absorption bands of the carbonyl group (1735-1730 см^{1}).

Aminocolchaminic fragments of the synthesized compounds in the PMR spectra do not differ significantly: the signals of the N-methyl group appear at 2.20-2.22 ppm, methoxyl groups - 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.

Table 1. Synthesis of acetylene derivatives



A characteristic feature of all acetylene derivatives is the presence in their PMR spectra of a two-proton doublet from the bridging N-CH2 group, which manifests itself in the region of 3.32-3.38 ppm. The bridging OCH3 group present in compounds 4-5 forms a narrow two-proton doublet in the range of 4.53-4.70 ppm.

Signals of C-alkyl groups appear in the strongest field of the spectrum (1.4-2.0 ppm) and are easily deciphered. The olefinic protons of methacrylic esters resonate at 5.98 ppm. (cis-) and 3.48 ppm. (trans-

protons). The most complex spectra of colchamine and aminocolhamine with propargyl ether propargyl ether of methacrylic acid, in which the signals of the protons of two benzene rings overlap.

Experimental part. IR spectra - on a UR-10 two-beam spectrometer in KBr, PMR spectra - on a Varian XL-100 instrument in $CDCl_3$

a) Derivatives, aminocolhamina with esters of organic acids. A weighed 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 that, adding an equimolecular amount of methacrylic acid propargyl ester to the solution, the contents of the flask were mixed well.

Table 2. Reaction conditions methacrylic acid propargyl ester with colchamine amine.

№	Reagent	Estimated amount of reagent	Taken amount of reagent	Product yield (%)
1.	Aminokolchamin	0,35	0,51	78

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

After the reaction was practically completed, the dioxane-insoluble 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 each.

The acetic acid extract contains unreacted colchamine, which was isolated by alkalinization of the acidic solution with ammonia and extraction 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 alumina. In this case, the dark extract is strongly lightened. The solvent was distilled off and the reaction product was dried in a vacuum desiccator.

The end products of the reaction were obtained in the form of non-crystalline light yellow powders.

Due to the alkyl (and not acyl) nature of the substituents introduced into the amino group, the resulting derivatives retain some basicity (especially with the pyridine ring), which makes it difficult to separate the colchamin impurity from the reaction products. Therefore, for this purpose, they resorted to the method of chromatography on alumina (eluents of a mixture of ether-acetone, acetone and acetone-methanol).

4- (aminocolhamino-N-butyn-2-yl) esters of methacrylic acid (5).

IR – spectrum. 1100, 1170, 1720, 2570, 2950, 3400, 3540 $см^{-1}$.

PMR spectrum. 1,26; 1,45; 1,49 (CH_3CH_2), 1,98 (CH_3). 2,16 (N-CH_3), 3,58; 3,85 x 2, 3,88 (3H x 4, cc, 4 OCH_3) , 5,16 (OH), 6,48 (H-4), 6,94 (H-11), 7,24 (H-I2 и H-8) м.д.

1. Synthesized a derivative of aminocolchamine with propargyl ester of methacrylic acid.
2. The structures of the synthesized compounds were confirmed by IR and PMR spectra.

References:

1. Karaev, S.F., & Garayeva, Sh.V. (1980). Propargyl ethers. *Uspekhi khimii*, 49, 1774.
2. Alikulov, R.V. (1993). *Alkaloids Colchicum kesselringii Rgl. and Merendera robusta Bge. Structures of new homoproporphine and homoaporphine alkaloids.* Diss. for a degree student Ph.D., (pp.53-57). Tashkent.
3. Vatsuro, K.V., & Mishchenko, G.L. (1976). *Nominal reactions in organic chemistry*. Moscow.
4. Yusupov, M.K., & Alikulov, R.V., & Makhsumov, A.G. (1992). New antineoplastic compounds based on colhamine and propargyl ethers. *The third regional meeting of the*

republics of Central Asia and Kazakhstan on chemical reagents. Abstracts of the report. and messages, Tashkent, Vol.2, p.72.

5. Kurbanov, A.I., Sirlibaev, T.S., Turgunov, E., Kultaev, K.K., Kablov, R.K., & Tarikov, S. (1986). The biological activity of some acetylene amino alcohols and halogen-containing products based on them. *Agrochemistry*, No. 4, p. 86.
6. Alikulov, R.V., Kenjaev, D.R., Normurodov, B.A., & Maulyanov, S. (2015). Alkaloidy Colchicum luteum Baker. *Own MU News 2015*, №3 / 1, p.219.
7. Alikulov, R.V., Turaev, X.X., Kasimov, Sh., & Normurodov, B.A. (2014). *Alkaloids colchicum c. kesselringii RGL*. IV Republican scientific-practical conference "Actual problems of analytical chemistry", Termez May 1-3, 2014.
8. Alikulov, R.V., Kenjaev, D.R., Umbarov, I.A., Normurodov, B.A., Alimnazarov, B.X., & Geldiev, Yu.A. (2014). *Vydelenie alkaloids from klubnelukovits bezvremennika jyoltogo*. IV Republican scientific-practical conference "Actual problems of analytical chemistry", Termez May 1-3, 2014.
9. Alikulov, R.V., Alimnazarov, B.Kh., Geldiev, Yu.A., & Ruzieva, B.Yu. (2018). The structure of the new homoproporphine alkaloid 12-demethylluteine. *Universum: Chemistry and biology electron. scientific. zhurn.*, No. 3 (45).
10. Alikulov, R.V., Alimnazarov, B.Kh., Nuraliev, G.T., & Geldiev, Yu.A. (2019). The structure of the new homoproporphine alkaloid regecolquine. *Universum: Chemistry and biology electron. scientific. zhurn*., No. 2 (56).