Allyl and Propargyl Ethers of Dihaloalkanols: Synthesis and Study of Them as Antimicrobial Additives

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Based on the catalytic addition of dimethylacetylenecarbinol to allyl halides with the participation of *N*-bromosuccinimide and molecular iodine, methods for the synthesis of simple 2-methyl-3-butyn-2-ol ethers of dihaloalkanols (chlorine, bromine and iodine derivatives) have been proposed. The resulting compounds were studied as antimicrobial additives for lubricating oils and fuels. The antimicrobial effectiveness of the studied compounds was determined by the zonal diffusion method using microorganisms: *Pseudomonas aeruginosa, Mycobacterium phlei, Aspergillus niger, Penicillium chrysogenum, Cladosporium resinae*. It was revealed that 2-methyl-3-butyn-2-ol ethers of dihaloalkanols with two iodine atoms significantly inhibit the growth of microorganisms at low concentrations. It has been established that iodoethers are 2-4.5 times more effective than ethanol. Unsaturated ethers do not decompose and cannot be corrosive; their use for these purposes does not cause side effects.

Introduction

One of the methods for improving the quality of motor oils and fuels is the use of effective additives. They slow down the corrosion process [1] and reduce wear of engine parts [2]. An effective method for protecting petroleum products from microbiological damage is the chemical method. introduction of antimicrobial additives – biocides – into their composition [3-5]. Heteroatomic organic compounds are widely used as antioxidant, anticorrosion and antimicrobial additives for oils and fuels [6].

The purpose of the work is to use 2-methyl-3-butyn-2-ol ethers of dihaloalkanols and study their biocidal properties as antimicrobial additives for oils (T-22 synthetic oil) and fuels (Gasoline-95). It should be noted that propargyl ethers, including iodoethers [7,8], do not decompose and cannot be corrosive agents. Therefore, their use for these purposes does not cause side effects [9,10].

Most modern additives must be multifunctional. In these cases, halogenated ethers are more effective.

Study of the antimicrobial activity of compounds (**1-5**). The synthesized compounds (**1-5**) were studied as antimicrobial additives in synthetic oil – succinic acid diether, in T-22 base oil and fuel – gasoline-95. Analysis was carried out using the zonal diffusion method. For the development of bacteria, meat-peptone agar (MPA) was chosen as a nutrient medium; for fungi, wort agar was chosen. The exposure time for bacteria was 2 days, for fungi – 3-4 days. Samples were taken in three concentrations, %: 0.25, 0.5 and 1.0. The results of the study were compared with the data of the control drug – sodium pentachlorophenolate.

Experimental part

IR spectra were recorded on a Specord 75 IR (Germany). ^{1}H and ^{13}C NMR spectra of compounds ($CDCl_3$ is a solvent) were recorded on a Bruker SF-300 instrument with operating frequencies of 300.13 MHz for hydrogen and 75 for carbon ^{13}C MHz, internal standard - hexamethyldisiloxane (HMDS). The elemental composition of the samples was determined on a Karlo Erba 1106 elemental analyzer.

The starting compounds were: allyl chloride [cat. No. 401310500, 99%, Biochem], allyl iodide (99%, Chemical Line LLC), sodium hydroxide (reagent grade, EKOS-1 JSC), potassium hydroxide (reagent grade, EKOS-1 JSC "). The solvents used were ethyl alcohol (reagent grade, JSC "VEKTON"), diethyl ether (cat. no. 176830010, 99+%, Acros Organics) and isopropyl alcohol (reagent grade, cat. no.: 211138, LLC TD "Khimmed") purified by distillation.

3-[(1,3-Dibromopropan-2-yl)oxy]-3-methylbut-1-yne (1). To an equimolar mixture of 3.8 g of allyl bromide and 1.8 g (0.032 mol) dimethylacetylenecarbinol, cooled to -5ºC, 2.6 g of N-bromosuccinimide was gradually added, preventing the temperature of the reaction mixture from increasing above 0ºC. After 3 hours, the resulting succinimide was separated by filtration, the residue was made alkaline with a solution of 15 g of NaOH in 100 ml of water, extracted with diethyl ether and dried with $CaCl_2$. After removing the ether under reduced pressure, 66.9 g (69% yield) of compound (I) was isolated. bp 138–140ºC ºC (1 mm Hg). IR spectrum, (ν, cm^{-1}): 685, 1104, 1254, 1371, 1382, 2110, 3310. ^{1}H NMR spectrum (δ, ppm): 1.02 s (6H, $2CH_3$), 2.49 s (1H, ≡CH), 3.34 dd (2H, CH_2Br, *J* 15.4, 9.8 Hz). 3.41 dd (2H, CH_2Br, *J* 15.4, 9.8 Hz), 3.45 m (1H, OCH). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 29.11 (CH_3), 31.83 (CH_3), 35.75 (CH_2Br), 43.17 (CH_2Br), 62.49 (OCH), 65.31 (OCH_2), 71.33 (≡CH), 82.75 (C≡). Found, %: C 33.63; H 4.36; Br 56.28. $C_8H_{12}Br_2O$. Calculated, %: C 33.83; H 4.26; Br 56.27. Similarly, from allyl chloride, dimethylacetylenecarbinol and N-bromosuccinimide, it was obtained in 68.7% yield.

4-[(1-Bromo-3-chloropropan-2-yl)oxy]-4-methylbut-1-yne (2). Yield 68%, bp 146–148ºC (1 mm Hg). IR spectrum (ν, cm^{-1}): 660, 1253, 1366, 1383, 2108, 3311. ^1H NMR spectrum (δ, ppm): 1.02 s (6H, $2CH_3$), 2.49 s (1H, ≡CH), 3.41 dd (1H, CH_2Br, J 15.4, 9.8 Hz), 3.46 dd (1H, CH_2Br, *J* 15.4, 9.8 Hz), 3.47-3.53 m (1H, CHO), 3.61 dd (1H, CH_2CI, *J* 15.4, 9.9 Hz), 3.69 dd (1H, CH_2CI, *J* 15.4, 9.9 Hz). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 30.45 (CH_3), 31.63 (CH_3), 42.25 (CH_2Br), 54.57 (CH_2Cl), 64.86 (OCH_2), 71.13 (≡CH), 82.35 (≡C). Found, %: C 28.83; H 3.62; Br 24.14; I 38.31. $C_8H_{12}BrIO$. Calculated, %: C 29.03; H 3.65; Br 24.14; I 38.34.

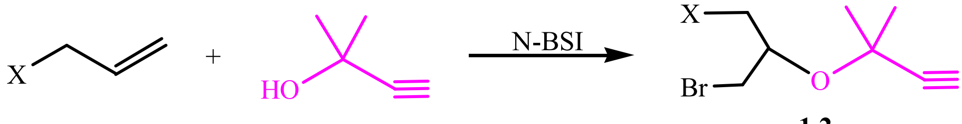
4-[(1,3-Diiodopropan-2-yl)oxy]-4-methylbut-1-yne (3). 2.6 g of HgO was added to a mixture of 1.4 g of dimethylacetylenecarbinol and 4.5 g of allyl iodide, cold to –5-0°C and intensively stirred, and then 31.5 g of finely ground crystalline iodine was added in portions of 1 g. stiring was continued at room temperature for another 3-4 hours, then the mixture was filtered, the filter was washed with $Na_2S_2O_3$ solution and extracted with ether. The extract was dried with $CaCl_2$, the ether was removed under low light, *and the residue was recrystallized from ethanol.* Yield 67%. bp 52-54 ºC (1 mm Hg). IR spectrum (ν, cm^{-1}): 660, 1254, 1366, 1383, 2100, 3310. ^1H NMR spectrum (δ, ppm): 1.02 s (6H, $2CH_3$), 2.51 s (1H, ≡CH), 3.20 dd (2H, CH_2I, *J* 15.4, 9.6 Hz), 3.29 dd (2H, CH_2I, *J* 15.4, 9.6 Hz), 3.42 m (1H, CHO). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 2.7 (CH_2I), 29.36 (CH_3), 30.64 (CH_3), 65.92 (OCH_2), 68.13 (OCH), 70.17 (≡CH), 80.37 (C≡). Found, %: C 25.12; H 3.23; I 67.34. $C_8H_{12}I_2O$. Calculated, %: C 25.42; H 3.20; I 67.15

3-[3-Chloro-2-(chloromethyl)propoxy-3-methylbut-1-yne (4). 0.8 g of allyl chloride was added to a mixed mixture of 1.0 g of propargyloxy(dimethyl)methylene chloride and 1 g of powdered $ZnCl_2$ to obtain. After the end of the exothermic regime, the mixture was *stirred* at a temperature of 60°C for 1.5 hours, and then the reaction mass was distilled in vacuum. Yield 1.3 g (69%). bp 82–84 ^{0}C ºC (1 mm Hg). IR spectrum (ν, cm^{-1}): 660, 1252, 1383, 2100, 3310. ^1H NMR spectrum (δ, ppm): 1.02 s (6H, $2CH_3$), 2.50 s (1H, ≡CH), 3.34 d. d (1H, CH_2O, *J* 15.1, 2.8 Hz), 3.45 m (1H, OCH), 3.21 dd (2H, CH_2CI, *J* 15.4, 9.9 Hz), 3.52 dd (2H, CH_2CI, *J* 15.4, 9.9 Hz), ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 31.36 (CH_3), 32.64 (CH_3), 44.54 (CH_2), 58.28 (CH_2Cl), 66.86 (OCH_2), 71.19 (≡CH), 82.36 (≡C). Found, %: C 51.54; H 6.78; Cl 33.77. $C_9H_{14}C1_2O$. Calculated, %: C 51.69; H 6.75; Cl 33.91.

Similarly, **3-[2-(Bromomethyl)-3-chloropropoxy]-4-methylbut-1-yne (5)** was obtained from allyl bromide, propargyl-oxy(dimethyl)methylene chloride and $ZnCl_2$. Yield 60%. bp 96–98 ºC (1 mm Hg). IR spectrum (ν, cm^{-1}): 663, 1255, 1382, 2100, 3310. ^1H NMR spectrum (δ, ppm): 1.01 s (6H, $2CH_3$), 2.48 s (1H, ≡CH), 3.34 d. d (1H, CH_2O, J 15.1, 2.8 Hz), 3.40 dd (1H, CH_2Br, *J* 15.4, 9.8 Hz), 3.45 m (1H, OCH), 3.46 dd (1H, CH_2Br, *J* 15.4, 9.8 Hz), 3.47 dd (1H, CH_2Br, *J* 15.4, 9.8 Hz), 3.49 dd (1H, CH_2Br, *J* 15.4, 9.8 Hz), 3.56 dd (1H, CH_2O, *J* 15.1, 9.8 Hz). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 30.69 (CH_3), 31.43 (CH_3), 42.25 (CH_2Br), 44.54 (CH_2), 58.25 (CH_2Cl), 66.83 (OCH_2), 71.14 (≡CH), 82.38 (≡C). Found, %: C 37.66; H 4.45; Br 27.62; Cl 24.41. $C_9H_{14}BrClO$. Calculated, %: C 37.40; H 4.88; Br 27.65; Cl 24.53.

Results and discussion

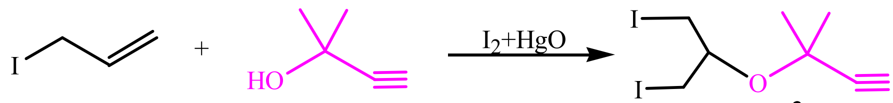
One of the rational ways to obtain β-haloethers is the alkoxyhalogenation of the double bond in the environment of C_3-unsaturated alcohols in the presence of N-bromosuccinimide (N-BSI) [11,12]. Alkoxyhalogenation of allyl halides (bromine, chlorine) with dimethylacetylenecarbinol leads to dihalogene ethers (**1,2**) (**Scheme 1**).



X= Br (**1**), CI (**2**)   **1,2**

Scheme 1.

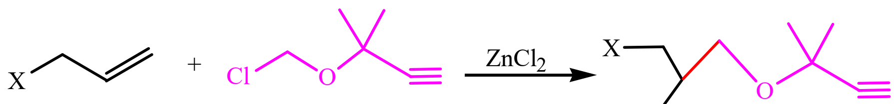
Or alkoxyhalogenation of allyl iodide with dimethylacetylenecarbinol leads to diiodoethers (3) with the participation of iodine and HgO [13] (**Scheme 2**).



3

Scheme 2.

The synthesis of 3-[3-chloro-2-(chloromethyl)propoxy-3-methylbut-1-yne 4, 3-[2-(bromomethyl)-3-chloropropoxy]-4-methylbut-1-yne 5 was carried out with a yield of 68% reaction of propargyloxydimethylmethine chloride with allyl halides in the presence of $ZnCl_2$ [14] (**Scheme 3**).



X= CI(**4**), Br (**5**)   **4,5**

Scheme 3.

Table 1. Characteristics of the antimicrobial properties of unsaturated ethers of dihaloalkanols

Compound	Concentration, %	Microbial growth inhibition zone, cm				
		Synthetic oil (succinic acid diether)	T-22 oil		Fuel (Gasoline-95)	
		Bacteria (Pseudomonas aeruginosa, Mycobacterium phlei)	Bacteria (Pseudomonas aeruginosa, Mycobacterium phlei)	Mushrooms (Aspergillus niger, Penicillium chrysogenum)	Bacteria (Pseudomonas aeruginosa, Mycobacterium phlei)	Mushrooms (Cladosporium resinae)
1	1,0	1,4-1,5	1,5-1,5	+++	—	—
	0,5	1,0-1,1	1,0-1,1	+++	1,6-1,7	+++
	0,25	+++	+++	+++	1,2-1,2	+++
2	1,0	2,5-2,5	2,0-2,0	1,0-1,0	no inhibition	no inhibition
	0,5	2,4-2,5	2,0-2,0	1,0-1,0	1,3-1,4	+++
	0,25	1,4-1,4	1,2-1,3	+++	1,1-1,1	+++
3	1,0	3,0-3,2	2,5-3,0	1,4-1,6	no inhibition	no inhibition
	0,5	2,4-2,5	2,0-2,0	1,0-1,0	1,3-1,4	+++
	0,25	1,4-1,4	1,2-1,	+++	1,1-1,1	+++
4	1,0	3,0-3,0	2,2-2,5	1,4-1,2	no inhibition	no inhibition
	0,5	1,8-2,0	2,0-1,8	1,0-1,0	1,5-1,6	+++
	0,25	1,0-1,0	1,1-1,0	+++	1,4-1,4	+++
5	1,0	2,8-3,0	2,2-2,5	1,4-1,2	no inhibition	no inhibition
	0,5	1,8-2,0	2,0-1,8	1,0-1,0	1,8-2,0	1,0-1,2
	0,25	1,0-1,0	1,1-1,0	+++	1,4-1,4	+++
Standard (sodium pentachloro phenolate)	1,0	1,3-1,4	1,3-1,4	1,3-1,4	no inhibition	no inhibition
Control	0,25	1,4-1,4	1,2-1,3	+++	1,1-1,1	+++

Note: (+++)—development of microorganisms, (–) - No inhibition

The reaction proceeds predominantly strictly regioselectively, as evidenced by the data of the ^{1}H NMR spectra. Thus, the protons of the methylene groups CH_2Br and CH_2Cl of compound **(5)** are diasterotopic in the form of two doublet signals at 3.40 dd (1H, CH_2Br, *J* 15.4, 9.8 Hz), 3.46 dd (1H, CH_2Br, *J* 15.4, 9.8 Hz), 3.47 dd (1H, CH_2Br, *J* 15.4, 9.8 Hz), 3.49 dd (1H, CH_2Br, *J* 15.4, 9.8 Hz). The signals of the methylene groups of compounds 4,5 are presented similarly in the ^{1}H NMR spectrum: 3.34 dd (1H, CH_2O, *J*=15.1, 2.8 Hz), 3.54 dd (1H, CH_2O, *J*=15.1, 9.8 Hz) m.d. In the IR spectrum, the two geminal methyl groups in compounds **1-5** have a clear absorption in the region of bending vibrations of the C-H bond, giving a doublet with absorption bands of equal intensity in the ranges 1384-1382 and 1371-1366 cm^{-1}. As a result of the tests, it was established that the synthesized compounds **1-5** have high antimicrobial activity, while at a concentration of 1.0%, compounds with two iodine atoms in the composition showed high bactericidal properties (2.5-3.0 cm), almost twice as large as those of the reference compound - sodium pentachlorophenolate. Compounds **1** and **2** showed the same result as the standard (1.3-1.6 cm). All the studied halogen ethers (see **Table 1**) have biocidal properties, but their inhibition of the growth of microorganisms in lubricating oil and fuel occurs differently, although they are 2÷4.5 times more effective than sodium pentachlorophenolate.

A comparison of the biocidal properties of acyclic halogen ethers **1-5** showed that iodoether 3 is significantly more effective than chloro- and bromoanalogues **1,2,4,5**. It should be noted that propargyl ether iodoether **3** is effective in both lubricating oil and fuel environments.

The structure of the resulting compounds (**1-5**) was confirmed by ^{1}H, ^{13}C NMR and IR spectroscopy data, as well as elemental analysis data.

Conclusions

Simple 2-methyl-3-butyn-2-ol ethers of dihaloalkanols (chlorine, bromine and iodo derivatives) were synthesized by the catalytic addition of dimethylacetylenecarbinol to allyl halides. It has been established that 2-methyl-3-butyn-2-ol ethers of dihaloalkanols with two iodine atoms significantly suppress the growth of microorganisms at low concentrations.

References

[1] Baret N, Dulcere J, Rodriguez J, Pons J, Faure R. The Cohalogenation of 1-N-Vinylpyrimidinediones: A New Approach to Nucleoside Analogs. European Journal of Organic Chemistry 2000;2000(8):1507-1516.

[2] Luz G, Sousa B, Guedes A, Barreto C, Brasil L. Biocides Used as Additives to Biodiesels and Their Risks to the Environment and Public Health: A Review. Molecules 2018;23(10):2698.

[3] Kahrilas G, Blotevogel J, Stewart P, Borch T. Biocides in Hydraulic Fracturing Fluids: A Critical Review of Their Usage, Mobility, Degradation, and Toxicity. Environmental Science & Technology 2014;49(1):16-32.

[4] Pastor A, Gámiz B, Cruz-Yusta M, Sánchez L, Pavlovic I. Carbendazim-clay complexes for its potential

use as antimicrobial additives in mortars. Building and Environment 2020;183:107214.

[5] Lemire J, Harrison J, Turner R. Antimicrobial activity of metals: mechanisms, molecular targets and applications. Nature Reviews Microbiology 2013;11(6):371-384.

[6] Benincá T, Schmidt L, Thomé Cardoso L, Rossini Augusti P, da Silva Malheiros P. Carvacrol as a food additive: Toxicological aspects and the role of nanotechnology in enhancing its antimicrobial and antioxidant properties. Food Research International 2024;197:115256.

[7] Yeasmin R, Zhang H, Zhu J, Cadieux P. Fabrication and analysis of antimicrobial additives for powder coated surface. Progress in Organic Coatings 2019;127:308-318.

[8] Dutta P, Wang B. Zeolite-supported silver as antimicrobial agents. Coordination Chemistry Reviews 2019;383:1-29.

[9] Cui J, Shao Y, Zhang H, Zhang H, Zhu J. Development of a novel silver ions-nanosilver complementary composite as antimicrobial additive for powder coating. Chemical Engineering Journal 2021;420:127633.

[10] Arunachalam S, Padma Priya N, Boopathi K, Jayabalakrishnan C, Chinnusamy V. Biocidal and catalytic efficiency of ruthenium(III) complexes with tridentate Schiff base ligands. Applied Organometallic Chemistry 2010;24(7):491-498.

[11] Priya N, Arunachalam S, Manimaran A, Muthupriya D, Jayabalakrishnan C. Mononuclear Ru(III) Schiff base complexes: Synthesis, spectral, redox, catalytic and biological activity studies. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2009;72(3):670-676.

[12] Talybov G, Ezizbeyli A, Mammadbayli E, Gurbanov G. Alkoxyhalogenation of Dichlorostyrenes in Unsaturated C3-Alcohols. Russian Journal of Organic Chemistry 2020;56(1):34-37.

[13] Talybov G. Heterocyclization of Allyloxyiodination Products of Halogen-Substituted Styrenes. Russian Journal of Organic Chemistry 2021;57(6):1009-1011.

[14] Talybov G, Ezizbeyli A, Mammadbayli E, Shirinova N, Guliyeva N. Regioselective Alkoxyiodination of Allyl Ethers in Unsaturated C3-Alcohols. Russian Journal of Organic Chemistry 2020;56(3):552-554.