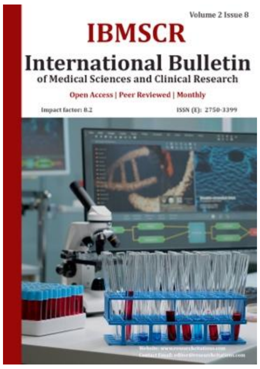

SYNTHESIS OF ACETYLENE SERIES TRIOLS AND THEIR INVESTIGATION

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Abstract

This study is devoted to the synthesis of monoesters of acetylene triols as biologically active compounds and the investigation of their properties. The aim of the research was to obtain new compounds with practical and pharmacological significance. The monoesters were synthesized by condensation of 1-alkoxy-4-pentyn-2-ols with acetone under Favorskii reaction conditions. The reaction was carried out in liquid ammonia medium at low temperatures (from −35 to −40 °C) in the presence of potassium hydroxide. As a result, six new monoester derivatives of acetylene triols were obtained. It was established that the structure of the alkyl radical significantly affects the yield of the final products. Higher yields were observed for methyl and ethyl derivatives, whereas the yield decreased with increasing alkyl chain length. The almost complete absence of by-products indicates the high selectivity of the reaction. The structure and purity of the synthesized compounds were confirmed by thin-layer chromatography (TLC), IR spectroscopy, and elemental analysis. Characteristic absorption bands corresponding to OH, C≡C, and C–O–C groups were identified in the IR spectra.

Introduction

The results of studies aimed at obtaining biologically active compounds belonging to the acetylene series are presented. Methods for the synthesis of simple monoesters of acetylene triols have been developed, including the condensation of 1-alkoxy-pentyn-2-ols with acetone in a liquid ammonia medium at temperatures of −30 to −35 °C in the presence of powdered caustic potash under Favorskii reaction conditions.

Using this method, six new representatives of simple monoesters of acetylene series triols were synthesized. It was established that the highest yields of the final products were observed for ether radicals containing methyl and ethyl groups. As the length of the alkyl radical increases, the yield of the final products decreases.

To confirm the composition and structure of the synthesized compounds, decomposition reactions into the starting products — 1-alkoxy-pentyn-2-ols and acetone — by heating in the presence of K_2CO_3 (reverse Favorskii reaction), as well as IR spectral data and elemental analysis methods, were used.

Pharmacological studies conducted to date have shown that monoesters of acetylene triols exhibit hypotensive (blood pressure lowering), spasmolytic, and other biologically active properties. Some of these compounds have demonstrated the ability to reduce blood pressure.

Reagents and Equipment Used

The purity of all substances was checked by thin-layer chromatography (TLC) using the following solvent systems:

A. Diethyl ether + heptane (2:1)
B. Ethanol + benzene (1:9)
C. Chloroform
D. Benzene + chloroform (5:1)

The chromatograms were treated with iodine vapor. IR spectra of the synthesized compounds were recorded on a UR-10 instrument using thin films with a thickness of 10–15 µm. NMR spectra were measured relative to HMDS on a Tesla-B-487 instrument at an operating frequency of 80.80 MHz in CCl_4 solvent.

During stirring, 0.8 mol of freshly distilled 1-alkoxy-2,3-epoxypropane dissolved in 100 ml of ether was added over 2 hours. The mixture was then stirred for an additional 6 hours under a slow stream of acetylene. Afterwards, the reaction mixture was left to evaporate the ammonia.

To the alcoholic suspension of alkoxyacetylene alcohol, 200 ml of ether was added, followed by decomposition with a saturated ammonium chloride solution (250 ml) at 0 °C. After stirring for 45 minutes, the ether layer was separated, while the aqueous layer was extracted with ether (2 × 100 ml).

The ether solution was dried over magnesium sulfate. After removal of the solvent, the reaction product was fractionated under vacuum. Identification of the target products was monitored by TLC in system B.

Synthesis of 1-Ethoxy-4-pentyn-2-ol

A three-neck flask equipped with a dropping funnel, a gas outlet tube, and a mechanical stirrer was charged with 1.5 L of liquid ammonia. Purified acetylene was passed through the gas outlet tube for 2 hours under vigorous stirring conditions.

The mixture was stirred for 2 hours under a weak acetylene flow, after which 7 g of finely powdered metallic lithium was added over 1 hour, followed by additional stirring for 30 minutes.

Then, 81.6 g (0.8 mol) of freshly distilled 1-ethoxy-2,3-epoxypropane dissolved in 100 ml of ether was added over 2 hours with continuous stirring. The mixture was further stirred for 6 hours under a weak acetylene stream. The reaction mixture was then left until the ammonia had completely evaporated.

To the suspension of acetylene and ethoxy alcohol, 200 ml of ether was added, followed by neutralization at 0 °C with 250 ml of saturated ammonium chloride solution. After stirring for 45 minutes, the ether layer was separated, while the aqueous layer was extracted twice with ether (2 × 200 ml).

The ether extracts were dried over magnesium sulfate. After evaporation of the solvent, the product was fractionated under reduced pressure, and the fraction boiling at 72 °C / 10 mmHg was collected.

received product: 86 g (84%)

Physicochemical Constants

- n^{20D} = 1.4420
- d^{20D} = 0.9601

- MRD found = 35.20
- MRD calculated = 35.63

Example I. Synthesis of 6-Ethyl-1-ethoxy-heptyn-4-diol-2,6

A mixture of 12.8 g (0.1 mol) of 1-ethoxy-pentyn-4-ol-2 and 5.8 g (0.1 mol) of acetone in 50 ml of dry ether was prepared. The reaction mixture was maintained under reaction conditions for 1.5 hours and then left for an additional 9 hours. The reaction mass was kept until the ammonia had completely evaporated.

The resulting complex was decomposed with water and extracted with ether. The ether extracts were dried over magnesium sulfate. After evaporation of the solvent, the product was fractionated under reduced pressure, yielding 13.58 g (73%) of 6-methyl-1-ethoxy-4-heptyn-diol. The identity of the product was confirmed by TLC in system B.

Physicochemical Properties

Boiling point: 126–128 °C / 2 mmHg

Found composition, %: C – 64.81; 64.93; H – 10.05; 9.99

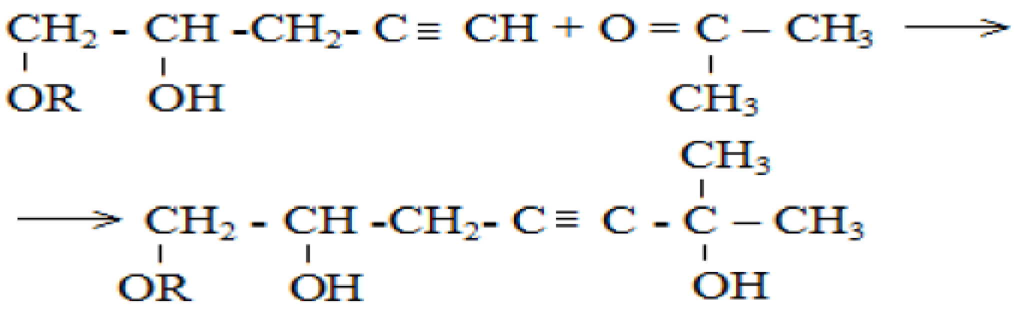
Calculated composition, %: C – 64.5; H – 9.7

Results Obtained and Their Analysis

Despite the large number of studies devoted to the synthesis and investigation of acetylene triols and their mono-, di-, and triesters, interest in discovering new representatives of this class of compounds remains significant.

In the course of this work, special attention was paid to the possibility of obtaining monoesters of primary, secondary, and tertiary triols, since such compounds are rarely described in the literature and are of considerable theoretical and practical interest.

By condensation of 1-alkoxy-4-pentyn-2-ols with acetone, we obtained monoesters of primary, secondary, and tertiary triols.



$$\underset{OR}{CH_2} - \underset{OH}{CH} - CH_2 - C \equiv CH + O = \underset{CH_3}{C} - CH_3 \longrightarrow$$

$$\longrightarrow \underset{OR}{CH_2} - \underset{OH}{CH} - CH_2 - C \equiv C - \overset{CH_3}{\underset{OH}{C}} - CH_3$$

Chemical Process and Results

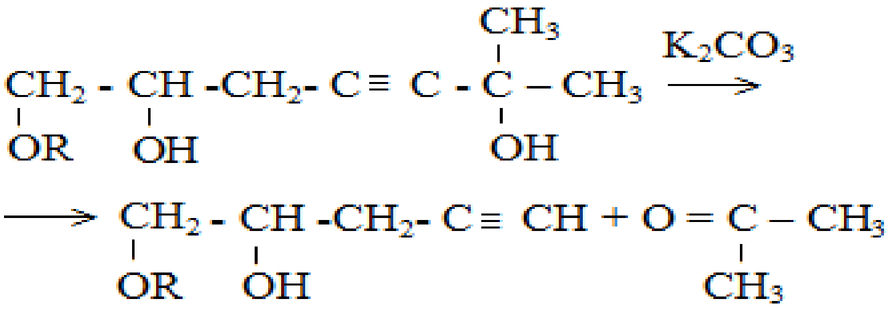
Here: R = C_2H_5, nC_3H_7, C_4H_9, C_6H_{13}, C_7H_{15}, $C_6H_5CH_2$.

The reaction was carried out in liquid ammonia in the presence of powdered KOH at a temperature of –35 to –40 °C. It was observed that an increase in the size of the alkyl radical led to a decrease in the yield of the final product. The absence of by-products indicates that the initial 1-alkoxy-4-pentyn-2-ols are sufficiently stable in alkaline medium. The highest product yield was obtained at a molar ratio of acetylene glycol : KOH : acetone equal to 1:4:2. By this method, six types of acetylene triol monoesters were synthesized.

A characteristic feature of acetylene alcohols, glycols, and triols obtained by condensation of acetylene compounds with ketones is that they decompose into the original products when heated in the presence of alkaline substances [6]. This method serves as one of the approaches for confirming the correctness of the product structure.

Therefore, we decided to investigate 6-methyl-1-alkoxy-4-heptyn-2,6-diols under reverse Favorskii reaction conditions using potassium instead of calcium.

For this purpose, the obtained compounds (I–VI) were heated under reduced pressure in the presence of a small amount of potassium carbonate.



$$\underset{OR}{CH_2} - \underset{OH}{CH} - CH_2 - C \equiv C - \overset{CH_3}{\underset{OH}{C}} - CH_3 \xrightarrow{K_2CO_3}$$

$$\longrightarrow \underset{OR}{CH_2} - \underset{OH}{CH} - CH_2 - C \equiv CH + O = \underset{CH_3}{C} - CH_3$$

.

Here: R = C_2H_5, nC_3H_7, C_4H_9, C_6H_{13}, C_7H_{15}, $C_6H_5CH_2$.

The structure of the decomposition products was determined by IR spectroscopy and compared with the IR spectra of the initial compounds.

In addition, the structure of the obtained compounds was confirmed by elemental analysis and IR spectral measurements.

The IR spectra of acetylene triol monoesters showed characteristic absorption bands in the following frequency ranges:

3350–3400 cm^{-1} – stretching vibrations of OH groups
2220 cm^{-1} – stretching vibrations of the C≡C bond
1110 cm^{-1} – vibrations of the C–O–C bond

Conclusion

In order to study the reactivity of 1-alkoxy-4-pentyn-2-ols, new monoesters of primary, secondary, and tertiary acetylene triols were synthesized. These compounds were obtained by the addition of acetone to alkoxypentynols under Favorskii reaction conditions.

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