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SYNTHESIS AND DETERMINATION OF THE ABSOLUTE CONFIGURATION OF MONOETHERS OF α-GLYCOLS OF ALLYL AND PROPARGYL ALCOHOLS BY NMR ^{1}H SPECTROSCOPY

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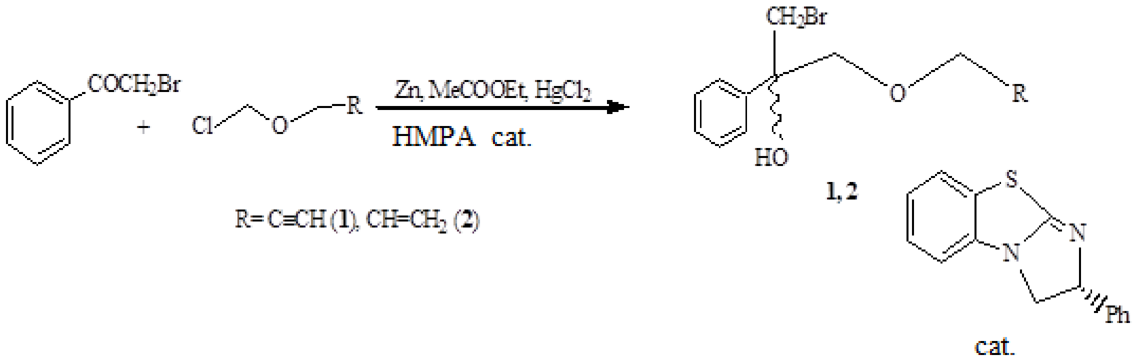
The interaction of chloromethylpropargyl (allyl) ether with phenacylbromide with the participation of the chiral catalyst - (+) - benzotetramisole leads to aromatic allyl and propargyl alcohol monoethers. By the chiral derivative agent (CDA) chloride anhydride-α-trifluoro-methyl-phenyl-acetic acid (MTPA-Cl) the absolute configuration of compounds was determined. Due to comparing the $\Delta\delta^{R/S}$ data in the NMR ^{1}H spectra during such interaction it was found that they converted to diastereomers.

Keywords: chloromethylpropargyl (allyl) ether, (+)-benzotetramisole, Mosher method, chiral derivative agent, diasteromer.

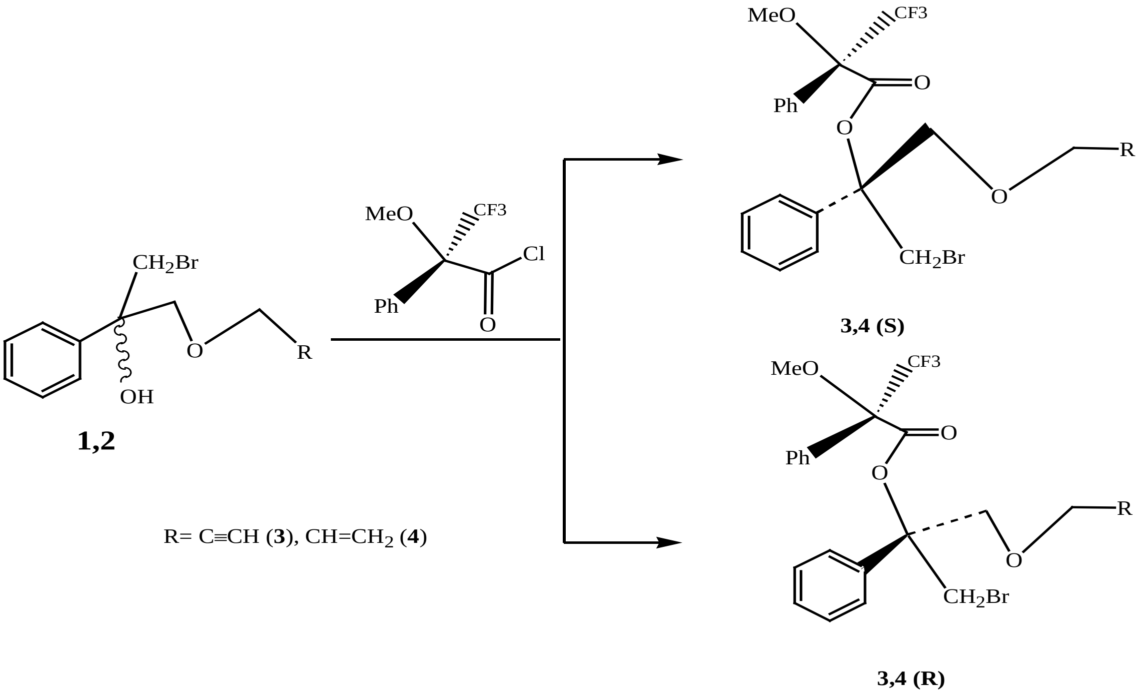
INTRODUCTION. The determination of the absolute configuration has gained great development in recent decades and is an important tool for modern organic chemistry, where it is necessary to know the three-dimensional structure of chiral structures (natural products, asymmetric synthesis, analysis of pharmaceutical preparations, etc.) [1,2]. It is known that the interaction of chloromethylpropargyl ether with carbonyl compounds with the participation of metallic zinc leads to unsaturated oxyethers [3]. The interaction of chloromethylpropargyl(allyl) ether with phenacyl bromide, with the participation of the chiral catalyst - (+)-benzotetramisole, can lead to the production of monoethers of α-glycols of allyl and propargyl alcohol of the aromatic series (1,2) (Scheme 1).

Then compounds (1,2) are reacted with a chiral derivatizing reagent (CDR) - α-methoxytrifluoromethylphenylacetic acid chloride (MTPA-Cl, Mosher's reagent), which converts them into the corresponding diastereoisomers (3,4) (Scheme 2).

Mosher's reagent is mainly used to determine the configuration of secondary alcohols [4–9], however, in rare cases, it is also



Scheme 1



Scheme 2

used to determine tertiary alcohols. The proton signals of the propargyl (allyl) oxymethyl group are shifted to the weak field, and the proton signals of phenyl groups are shifted to a strong field. The chemical shift of halogenomethylene protons at 3.69 d (1H, *J*=10.5), 3.77 d (1H, *J*=10.5 Hz) remains almost unchanged. No significant effect of multiple bonds on the $\Delta\delta^{R/S}$ data is observed. The anisotropic effect of the phenyl group in the acid chloride of α-methoxytrifluoromethylphenylacetic acid (MTPA-Cl) on the halogenaryl group leads to screening of the latter, and this, in turn, leads to a shift to a strong field and positive values of $\Delta\delta^{R/S}$, while proton signals of the less bulky group are shifted to a weaker field with a negative value of $\Delta\delta^{R/S}$ (Fig. 1).

EXPERIMENT AND DISCUSSION OF THE RESULTS. The NMR spectra of sub-

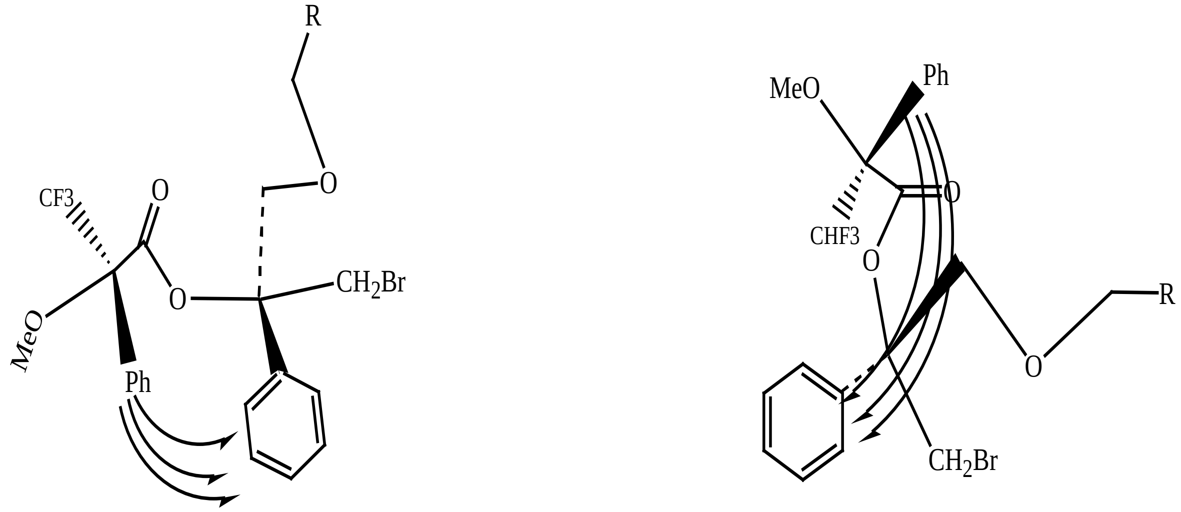


Fig. 1.The anisotropic effect of the phenyl group in the acid chloride of α-methoxytrifluoromethylphenylacetic acid

stances in a solution of $CDCl_3$ were recorded on a Bruker SF-300 instrument with an operating frequency of 300.13 MHz, the internal standard is HMDS.

General procedure for the synthesis of unsaturated oxyether (1,2): A mixture of 15 mg-atom of finely divided zinc chips, a catalytic amount of $HgCl_2$, 6 mmol of chloromethylpropargyl ether, 2 mmol of phenacyl bromide, 0.15 g of (+)-benzotetramisole, 10 ml of anhydrous benzene, 5 ml of anhydrous ethyl acetate, and 1 ml of HMPTA was boiled for 4 hours in an inert nitrogen atmosphere, then cooled. The solution was decanted, then 15 ml of 5% HCl was added, stirred for 1 h at room temperature, the organic layer was separated. From the aqueous layer, the reaction products were extracted with ethyl acetate (2×25 ml). After the extract was dried with anhydrous sodium sulfate, the solvent was distilled off. Then the reaction mixture was concentrated in vacuum, the residue was chromatographed on a column with SiO_2 (petroleum ether-ethyl acetate, 2:1).

General procedure for the synthesis of esters of MTPA (3,4) (R,S): To a mixture of 17 mmol of unsaturated alcohol (1) in dry pyridine (31 mmol) and dry CH_2Cl_2 (20 ml) was added dropwise MTPA-Cl (16 mmol) at 0 °C under nitrogen and the mixture was stirred at room temperature for 5 hours. After evaporation of the solvents, the excess pyridine was azeotropically removed together with dry toluene (20 ml×2) to obtain a raw product. The two diastereomeric esters were separated by silica gel column chromatography (CH_2Cl_2) to get (S)-MTPA esters and (R)-MTPA esters (3,4 (R, S)).

(2R)-1-Chloro-2-phenyl-3-[(prop-2-yn-1-yl)oxy]propan-2-yl (5S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanate (S)-3). Oily yellow substance. $[\alpha]_D$=-24.2 (s 1.2, $CDCl_3$). ^1H NMR spectra, δ, ppm: 2.51 t (1H, ≡CH, ^4J=2.4 Hz), 3.05 d (1H, CH, *J* 15.9 Hz), 3.17 d (1H, CH, *J* 15.9 Hz), 3.43 s (3H,

CH_3O), 3.69 d (1H, CH, *J* 10.5 Hz), 3.77 d (1H, CH, *J* 10.5 Hz), 3.83 d.d (1H, ≡$CC\underline{H}_2O$, ^2J 16.2 Hz, ^4J=2.4 Hz), 4.05 d.d (1H, ≡$CC\underline{H}_2O$, ^2J 16.2 , ^4J 2.4 Hz), 7.28-7.51 m (5H, Ph), 7.38-7.42 m (5H, Ph).

(2R)-1-Chloro-2-phenyl-3-[(prop-2-en-1-yl)oxy]propan-2-yl (5R)-3,3,3-trifluoro-2-methoxy-2-phenylpropanate (S)-4). Oily yellow substance. $[\alpha]_D$ =-17.2 (s 0.7, $CDCl_3$). ^1H NMR spectra, δ, ppm: 3.05 d (1H, CH, *J* 15.9 Hz), 3.17 d (1H, CH, *J* 15.9 Hz), 3.43 s (3H, CH_3O), 3.69 d (1H, CH, *J* 10.5 Hz), 3.77 d (1H, *J* 10.5 Hz), 4.00 d.d (2H, CH_2O, ^3J 5.67 and ^4J 1.47 Hz), 5.17 d.d.t (1H, $\underline{H}_2C$=, J^{cis} =10.37, ^2J=^4J 1.57 Hz), 5.26 d.d.d (1H, $\underline{H}_2C$=, J^{trans} =17.31 and ^2J=^4J 1.66 Hz), 5.89 d.d.t (1H, CH=, J^{cis}=10.37, ^2J=^4J 1.57 and J^{trans}17.31 Hz), 7.28-7.51 m (5H, Ph), 7.38-7.42 m (5H, Ph).

(2R)-1-Chloro-2-phenyl-3-[(prop-2-en-1-yl)oxy]propan-2-yl (5S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanate (R)-4). Oily yellow substance. $[\alpha]_D$=+34.9 (s 1.1, $CDCl_3$). ^1H NMR spectra δ, ppm: 3.12 d (1H, CH, *J* 15.9 Hz), 3.21 d (1H, *J* 15.9 Hz), 3.49 s (3H, CH_3O), 3.69 d (1H, CH, *J* 10.5 Hz), 3.77 d (1H, CH, *J* 10.5 Hz), 4.07 d.d (2H, CH_2O, ^3J=5.67 and ^4J=1.47 Hz), 5.21 d.d.t (1H, $\underline{H}_2C$=, J^{cis} =10.37, ^2J=^4J 1.57 Hz), 5.32 d.d.d (1H, $\underline{H}_2C$=, J^{trans} =17.31 and ^2J=^4J 1.66 Hz), 5.92 d.d.t (1H, CH=, J^{cis}=10.37, ^2J=^4J 1.57 and J^{trans}17.31 Hz), 7.22-7.45 m (5H, Ph), 7.42-7.48 m (5H, Ph).

CONCLUSIONS. Thus, the synthesis of previously unknown unsaturated aromatic oxyethers was carried out by reaction of chloromethylpropargyl(allyl) ether with phenacyl bromide, with the participation of the chiral catalyst - (+)-benzotetramisole, and their configurations were also established.

СИНТЕЗ И ОПРЕДЕЛЕНИЕ АБСОЛЮТНОЙ КОНФИГУРАЦИИ МОНОЭФИРОВ α-ГЛИКОЛЕЙ АЛЛИЛОВОГО И ПРОПАРГИЛОВОГО СПИРТОВ МЕТОДОМ ПМР СПЕКТРОСКОПИИ

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Взаимодействие хлорметилпропаргил(аллил)ового эфира с фенацилбромидом при участии хирального катализатора – (+)-бензотетрамизола приводит к моноэфирам α-гликолей аллилового и пропаргилового спиртов ароматического ряда. Определена их абсолютная конфигурация путем взаимодействия последних с хиральном дериватирющим агентом (ХДА) – хлорангидридом трифторметилфенилуксусной кислотой (MTPA-Cl), превращая α- их соответствующие диастеромеры и сравнивая данные $\Delta\delta^{R/S}$ в спектрах ЯМР.

Ключевые слова: Хлорметилпропаргил(аллил)овый эфир, (+)-бензотетрамизол, метод Мошера, хиральный дериватирющий агент, диастеромер.

СИНТЕЗ І ВИЗНАЧЕННЯ АБСОЛЮТНОЇ КОНФІГУРАЦІЇ МОНОЕСТЕРІВ α –ГЛІКОЛЕЙ АЛЛІЛОВОГО ТА ПРОПАРГІЛОВОГО СПИРТІВ МЕТОДОМ ПМР СПЕКТРОСКОПІЇ

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Взаємодія хлорметілпропаргіл (аллил) ефіру з фенацілбромідом за участю хірального каталізатора - (+) - бензотетрамізола призводить до моноефіру ароматичного аллила і пропаргілового спирту. За допомогою хірального деріватуючого агенту (ХДА) хлорітангідріду –α -тріфторметілфенілуксусной кислоти (MTPA-Cl) була визначена абсолютна конфігурація сполук. В результаті порівняння даних ΔδR / S в спектрах ЯМР ^{1}H під час такої взаємодії було виявлено, що вони перетворюються в діастереомери.

Ключові слова: хлорметилпропаргіловий (алліловий) етер, (+) - бензо тетрамізол, метод Мошера, хіральний похідний агент, діастереомер.

REFERENCES

1. Peter I. Dalko. Comprehensive Enantioselective Organocatalysis. *Wiley-VCH Verlag GmbH & Co. KGaA, Boschstr. Germany*. 2013. P.1438.
2. Cimmino A., Masi M., Evidente M., Superchi S., Evidente A. Application of Mosher's method for absolute configuration assignment to bioactive plants and fungi metabolites. *Journal of pharmaceutical and biomedical analysis*. 2017. **144**: 59-89. doi: 10.1016/j.jpba.2017.02.037.
3. Talybov G. New synthesis of 1, 2-diol monopropargyl ethers. *Russian Journal of Organic Chemistry*. 2017. **53**(1):123. doi: 10.1134/S1070428017010225
4. García R., Seco J. M., Vázquez S. A., Quinoá E., Riguera R. Absolute configuration of secondary alcohols by 1H NMR: in situ complexation of α-methoxyphenylacetic acid esters with barium (II). *The Journal of organic chemistry*. 2002. **67**(13):4579-4589. doi: 10.1021/jo0256989
5. Thomas J. Wenzel. Strategies for using NMR spectroscopy to determine absolute configuration. *Tetrahedron: Asymmetry.* 2017.**28**(10):1212. doi: 10.1016/j.tetasy.2017.09.009/
6. Jose Manuel Seco, Li-Hong Tseng, Markus Godejohann, Emilio Quinoa and Ricardo Riguera. Simultaneous enantioresolution and assignment of absolute configuration of secondary alcohols by directly coupled HPLC–NMR of 9-AMA esters. *Tetrahedron: Asymmetry*. 2002. **13**(19): 2149. doi: org/10.1016/S09574166(02)00510-4.
7. Latypov Sh. K., Seco J. M ., Quinoa E., Riguera R. Are Both the (R)- and the (S)-MPA Esters Really Needed for the Assignment of the Absolute Configuration of Secondary Alcohols by NMR? The Use of a Single Derivative. *J. Am. Chem. Soc.* 1998. **120**(5): 877. doi: org/10.1021/ja9700055.
8. Latypov S. K., Seco J. M., Quinoa E., Riguera R. Determination of the absolute

stereochemistry of chiral amines by 1H NMR of arylmethoxyacetic acid amides: the conformational model. *The Journal of Organic Chemistry*. 1995. **60**(6):1538-1545.
doi: org10.1021/jo0011a010.

9. Haruko Takahashi, Naoko Kato, Makoto Iwashima, Kazuo Iguchi. Determination of Absolute Configurations of Tertiary Alcohols by NMR Spectroscopy. *Chem. Let*. 1999.**28**(11):1181.
doi: 10.1246/cl.1999.1181.

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