ЕҢБЕК ҚЫЗЫЛ ТУ ОРДЕНДІ
«Ә. Б. БЕКТҰРОВ АТЫНДАҒЫ
ХИМИЯ ҒЫЛЫМДАРЫ ИНСТИТУТЫ»
АКЦИОНЕРЛІК ҚОҒАМЫ

ҚАЗАҚСТАННЫҢ ХИМИЯ ЖУРНАЛЫ

ХИМИЧЕСКИЙ ЖУРНАЛ КАЗАХСТАНА

CHEMICAL JOURNAL of KAZAKHSTAN

АКЦИОНЕРНОЕ ОБЩЕСТВО
ОРДЕНА ТРУДОВОГО КРАСНОГО ЗНАМЕНИ
«ИНСТИТУТ ХИМИЧЕСКИХ НАУК
им. А. Б. БЕКТУРОВА»

3 (63)

ИЮЛЬ – СЕНТЯБРЬ 2018 г.

ИЗДАЕТСЯ С ОКТЯБРЯ 2003 ГОДА

ВЫХОДИТ 4 РАЗА В ГОД

АЛМАТЫ
2018

UDC 547.655.1.260.2.824+543.429.23

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SYNTHESIS DIACETYLENIC GLYCOLS BASED ON 1,5-DI(PROP-2-INILOXY)NAPHTHALINE

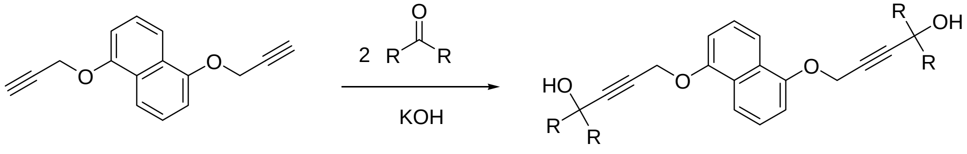
Abstract. Conditions of synthesis of new potentially biologically active diacetylenic glycols were developed. The reaction of nucleophilic addition 1,5-di (prop-2-ynyloxy)naphthalene at the carbonyl group of the cyclic ketones (cyclohexanone and N-substituted piperidones) was studied. Structure of new compounds were established based on the analysis by ^{1}H and ^{13}C NMR spectral data.

Keywords: 1,5-di(prop-2-ynyloxy)naphthalene, ethynylation, diacetylenic glycols, cyclohexanone, N-substituted piperidones.

Introduction. At the beginning of the 20-th century A. E. Favorsky showed that in the presence of strong bases the carbonyl compounds react with acetylene and its monosubstituted derivatives formed the corresponding acetylenic alcohols. The ethynylation reaction successfully used such strong bases such as hydroxides of K, Na, Rb, Mg, alkaline amides and alkaline earth metal alkoxides, and quaternary ammonium ion exchange resins [1]. The condensation of ketones with acetylenes are widely used for the synthesis of structurally simplest acetylenic alcoholic of complex analogues of natural physiologically active compounds which are used in the development of anticancer drugs, hemorheologic agents [2], plant growth regulators [3] and fungicides [4, 5].

Results and Discussion. The reaction of nucleophilic addition 1,5-di(prop-2-ynyloxy)naphthalene at the carbonyl group of cyclic ketones of cyclohexanone, 1-methylpiperidin-4-one, 1-propylpiperidin-4-one and 1-benzyl-4-piperidone were studied in order to synthesize of new potentially biologically active compounds in the series of diproparpylic ethers of naphthols. The reaction was carried out in the presence of a 4-fold excess of technical KOH at room temperature in diethyl ether. As a result of ethinylation of cyclohexanone and N-substituted piperidoneswith 1,5-di (prop-2-ynyloxy) naphthalene, were obtained the corresponding tertiary diacetylenic glycols.

After appropriate treatment of the reaction mixture the following diacetylenic glycols were obtained in individual state:1,1'-(3,3'-(naphthalene-1,5-diylbis(oxy))bis(prop-1-yne-3,1-diyl))dicyclohexanol1, 4,4'-(3,3'-(naphthalene-1,5-diylbis(oxy))bis(prop-1-yne-3,1-diyl))bis(1-methylpiperidin-4-ol)2, 4,4'-(3,3'-(naphthalene-1,5-diylbis(oxy))bis(prop-1-yne-3,1-diyl))bis(1-propylpiperidin-4-



1-4

1 R-R=$(CH_2)_5$; 2 R-R=$(CH_2)_2NCH_3(CH_2)_2$;

3 R-R=$(CH_2)_2N$ $C_3H_5(CH_2)_2$; 4 R-R=$(CH_2)_2N(CH_2)_2$;

CH_2Ph

Figure 1 – Scheme of the nucleophilic addition reaction of 1,5-di(prop-2-ynyloxy)naphthalene

ol)3 and 4,4'-3,3'-(naphthalene-1,5-diylbis(oxy))-bis(prop-1-yn-3,1-diyl))bis(1-benzylpiperidin-4-ol) 4 in yield 50, 82, 75, 87%, respectively.

The structure of synthesized compounds 1-4 was confirmed by IR spectra and NMR ^1H, ^{13}C, COZY (^1H–^1H) and HMQC (^1H–^{13}C) spectroscopy. The data of ^1H and ^{13}C NMR spectra are given in the tables 1 and 2.

In IR spectra, diacetylenic glycols 1–4 are characterized by the presence of broadened absorption bands in the 3400–3500 cm^{-1} region, characteristic for valence vibrations of hydroxyl groups, weak intensity peaks in the region of 2100 cm^{-1} indicate the presence of a triple acetylenic bond.

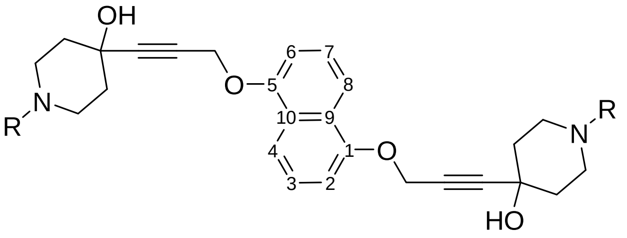


Table 1 –^1H NMR(δ, ppm) spectral data for compounds 1 – 4

Comp.	A type spectrum	PMR,δ, ppm						
		O–CH_2	N–R (CH_3, $CH_2CH_2CH_3$, CH_2Ph)	CH_2(cycle)	OH	Protons of naphthalene cycle		
						$C^{2,6}H$	$C^{3,7}H$	$C^{4,8}H$
1	e^1	4,97	–	1,38-2,22	3,56	7,07 д	7,4 т	7,74 д
	c^2	4,91	–	1,34-2,15	3,58	6,94	7,20	7,80
2	e^1	5,0	2,03	1,59-2,32	2,46	7,06 д	7,4 т	7,72 д
	c^2	4,91	2,31	1,99-2,10	2,92	6,94	7,20	7,80
3	e^1	4,94	0,71;1,25;2,01	1,52-2,41	3,40	7,01д	7,33т	7,65д
	c^2	4,91	0,86;1,47;2,59	1,90-2,28	2,92	6,94	7,20	7,80
4	e^1	4,97	3,50; 7,22-7,30	2,28-2,58	3,58	7,05 д	7,41 т	7,79 д
	c^2	4,91	3,47; 7,13-7,18	2,02-2,12	3,47	6,93	7,63	7,82
Notes. e – is the experimental spectrum; c-spectrum calculated according to the «MestReNova» program.								

Table 2 – ^{13}C NMR(δ, ppm) spectral data for compounds 1 – 4

Comp.	A typespectrum	$O–\underline{C}H_2$	$\underline{C}\equiv C$	$C\equiv\underline{C}$	$>C<$	CH_2(cycle)	N–R (CH_3, $CH_2CH_2CH_3$, CH_2Ph)
1	e^1	56,53	78,47	93,01	67,20	24,84; 26,97; 41,86	–
	c^2	58,40	80,41	89,94	68,52	23,40; 25,40; 39,58	–
2	e^1	56,73	78,47	92,32	65,09	40,50; 40,71	46,16
	c^2	58,40	80,41	90,13	66,99	35,48; 50,17	45,83
3	e^1	56,78	79,12	92,20	65,64	39,51; 50,11	12,31; 20,14; 60,08;
	c^2	58,40	80,41	90,13	66,85	37,63; 50,17;	12,05; 20,25; 60,80
4	e^1	56,49	78,83	79,60	61,34	41,21; 52,79	61,34;127,55; 128,74; 129,20
	c^2	58,40	80,41	90,13	66,99	37,45; 48,71	58,97; 129,44; 128,89; 131,48

Comp.	Carbon atoms of the naphthalene ring				
	A typespectrum	C^1C^5	C^2C^6	C^3C^7	C^4C^8	C^9C^{10}
1	e^1	153,15	107,29	125,97	114,83	126,58
	c^2	147,70	109,35	125,38	114,52	124,85
2	e^1	153,23	107,57	125,91	114,75	126,67
	c^2	147,70	109,35	125,38	114,52	124,85
3	e^1	153,18	107,46	125,82	114,72	126,65
	c^2	147,70	109,35	125,38	114,52	124,85
4	e^1	153,18	107,14	125,92	114,90	126,60
	c^2	147,70	109,35	125,00	114,52	124,85

Notes. e – is the experimental spectrum; c-spectrum calculated according to the «MestReNova» program.

In the ^1H NMR spectra of diacetylenic glycols 1-4 appear broadened singlets for the protons of the hydroxyl groups in the region 2.46–3.58 ppm, which indicates the occurrence of nucleophilic addition of 1,5-di (prop-2-ynyloxy)naphthalene at the carbonyl group of the cyclic ketones.

In the ^1H NMR spectra of the glycol 4 (figure 2), in the strong field region of the spectrum, the chemical shifts for protons in the region 2.29 and 2.58 ppm were assigned to the cyclic protons forthe symmetrical methylene groups of two piperidine rings. The chemical shift in the region 4.96 ppm belongs to the protons of OCH_2 methylene groups. The protons of methylene substituents at the nitrogen atom are resonated as a broadened singlet in the region of 3.50 ppm. The signals for the protons of the naphthalene nucleus and of the benzene nucleus appear in the weak-field regions 7.05–7.79 ppm and 7.22–7.30 ppm, respectively.

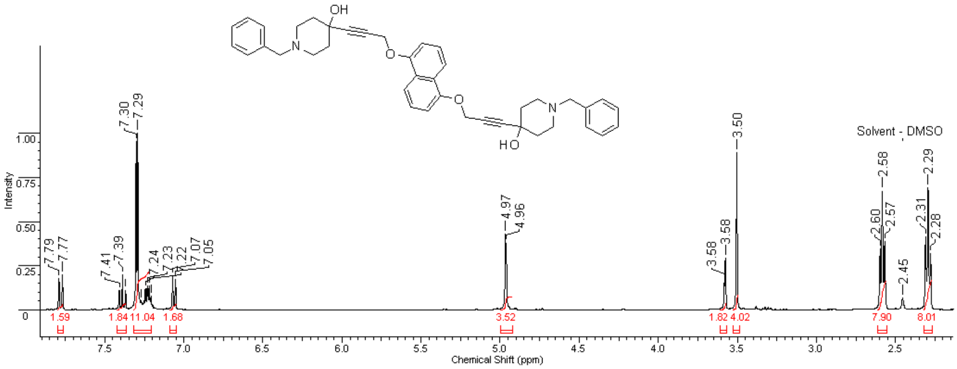


Figure 2 – ^1H NMR spectra
of 4,4'-3,3'-(naphthalene-1,5-diylbis(oxy))bis(prop-1-yn-3,1-diyl))bis(1-benzylpiperidin-4-ol)

In the ^{13}C spectra of diacetylenic glycols 1–4 (table 2) resonance signals appear in the corresponding region 61.34 –68.52 ppm characteristic for quaternary carbon atoms of saturated nitrogen cycles.

In the ^{13}C NMR spectra of glycol 4 (4,4'-(3,3'-(naphthalene-1,5-diylbis-(oxy))bis(prop-1-yn-3,1-diyl))bis(1-benzylpiperidin- 4-ol)) shown in figure 3, the most characteristic carbon atoms of the –C≡C– acetylenic bond resonate in the region 78.83 and 79.60 ppm.Chemical shifts for carbon atoms of the symmetric CH_2 groups of the piperidine rings are observedin the strong field region 41.21 and 52.79 ppm.Quaternary carbon atoms of the saturated nitrogen cycles resonate in the region δ 61.34 ppm.

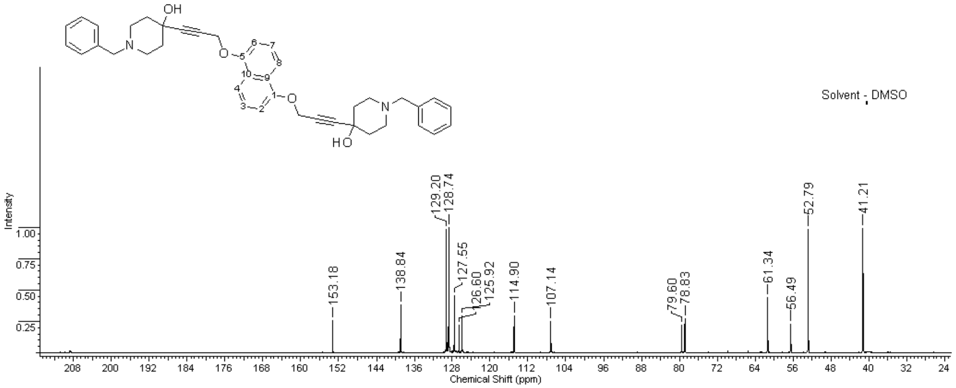


Figure 3 – ^{13}CNMR spectra
of 4,4'-3,3'-(naphthalene-1,5-diylbis(oxy))bis(prop-1-yn-3,1-diyl))bis(1-benzylpiperidin-4-ol)

It should be noted that the chemical shifts for the methylene group of the benzyl substituent appear in the more weaker region (61.34 ppm) compared to the carbon atoms of the oxymethylene group (56.49 ppm), which is due to the influence of the nitrogen atom of the piperidine ring. In the weak field region 107.14 – 153.18 ppm and 127.55 –129.20 ppm the signals for the carbon atoms of the naphthalene and benzyl rings are observed.

The correct interpretation of the resonance signals is confirmed by the coincidence of the values of the chemical shifts observed in the experimentally obtained spectra with the corresponding values in the spectra calculated by the «MestReNova» program.

The results of the interpretation of the two dimensional spectrum in the HMQC (^{1}H –^{13}C) format make it possible to determine the correlation between chemical shifts of protons and carbon nuclei, spin –spin interaction between nuclei, which confirms the nature of heteronuclear interaction.

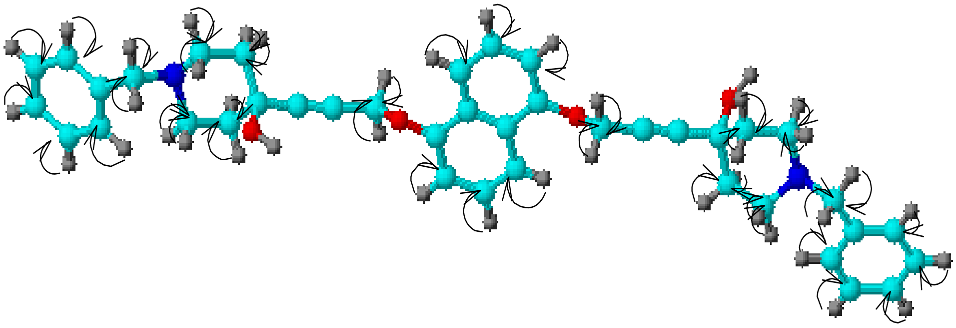


Figure 4 – Scheme of correlations of HMQC (^{1}H –^{13}C) 4,4'-3,3'-(naphthalene-1,5-diylbis(oxy))bis(prop-1-yn-3,1-diyl))bis(1-benzylpiperid-4-ol)

Conclusion. Summarizing the obtained data on the synthesis of new diacetylene glycols, it can be noted that 1,5-di (prop-2-ynyloxy) naphthalene readily reacts in Favorsky'sethynylation reaction and allows one to move relatively easily to an important class of tertiary acetylenic alcohols, which due to the presence in their structures acetylenic and tertiary alcohol groups can serve as initial synthons in the further synthesis of natural substancesanalogues.

Thus, as a result of studying the reactivity of 1,5-di(prop-2-ynyloxy)naphthalene in the Favorsky reaction with various cyclic ketones, formation of diacetylenic glycols in 50-87% yields was established. The structure of synthesized glycols was established based on the analysis of the ^{1}H and ^{13}C NMR spectral data.

EXPERIMENTAL PART

The course of the reactions and the purity of the products were monitored by thin-layer chromatography on "Silufol UV–254" plates, the eluent was a mixture of benzene and ethanol (1:3) with the appearance of substances spots with iodine vapor. The IR spectra were recorded on a Nicolet 5700 spectrometer in KBr tablets. The ^{1}H and ^{13}C NMR spectra of the samples were recorded in DMSO-D$_6$ using a JNM-ECA 400 (Jeol) spectrometer with operating frequencies 400 (^{1}H), 100 MHz (^{13}C).

1,1'-(3,3'-(naphthalene-1,5-diylbis(oxy))bis(prop-1-yne-3,1-diyl))dicyclohexanol 1. A **s**olution of0.5 g (0.0021 mol) of 1,5-di (prop-2-ynyloxy)naphthalene in 10 ml of etherwas added to a mixture of 0.47 g (0.0084 mol) of powdered technical KOH in 15 ml of ether. After 30 minutes 0.41 g (0.0042 mol) of cyclohexanone in 10 ml of ether was slowly added dropwise with stirring. After the end of the reaction, the mixture was decomposed with water(15 ml) under ice-cooling. The ether was separated, the aqueous layer was extracted with ether(5x20 ml), the ether extract was dried with potash. After distilling off the ether,diacetylene glycol 1 was obtainedin 0.45 g (50%) yield.

4,4'-(3,3'-(naphthalene-1,5-diylbis(oxy))bis(prop-1-yne-3,1-diyl))bis(1-methyl-piperidin-4-ol) 2 was synthesized analogouslyfrom 0.5 g (0.0021 mole) of 1,5-di(prop-2-ynyloxy)naphthalene with 0.48 g (0.0042 mol) of 1-methyl-piperidin-4-one in the presence of 0.47 g (0.0084 mol) of powdered technical KOH in ether at room temperature. The yield was 0.8 g (82%).

4,4'-(3,3'-(naphthalene-1,5-diylbis(oxy))bis(prop-1-yne-3,1-diyl))bis(1-propylpiperidin-4-ol)3 was synthesized analogouslyfrom 1.0 g (0.0042 mole) of 1,5-di (prop-2-ynyloxy)naphthalene with 1.19 g (0.0084 mol) of 1-methylpiperidin-4-one in the presence of 0.94 g (0.016 mol) of powdered technical KOH in ether at room temperature. The yield was 1.66 g (75%).

4,4'-3,3'-(naphthalene-1,5-diylbis(oxy))-bis(prop-1-yn-3,1-diyl))bis(1-benzylpiperidin-4-ol)4 was synthesized analogouslyfrom 0.5 g (0.0021 mole) of 1,5-di (prop-2-ynyloxy)naphthalene with 0.8 g (0.0042 mol) of 1-methylpiperidin-4-one in the presence of 0.47 g (0.0084 mol) of powdered technical KOH in ether at room temperature. The yield was 1.14 g (87%).

REFERENCES

[1] Kotlyarevsky I.L. Reactions of acetylenic compounds / I.L. Kotlyarevsky, M.E. Schwarzberg, L.B. Fisher. Novosibirsk: Nauka, 1967. 384 p.

[2] Kurmankulov N.B., Basenova A.T. New naphthoxypropynyl alcohols and naphthopyrans, their haemorheological activity // All-Russian Conf. on the chemistry of heterocycles. Suzdal, 2000. P. 253.

[3] Yerzhanov K.B., Vizer S.A., Sycheva Ye.S. Creation of innovative plant growth regulators of broad spectrumaction. Almaty, 2017. 158 p.

[4] Yerzhanov K.B., Akhmetova A.A., Almaniazov E.A., Sadykov T.S., Kurmankulov N.B. New fungicides against solid cereals // Materials of International scientific-practical conference "Processing of medicinal raw materials and production of phytopreparations for medicine and agriculture". Almaty, 1996. P. 102.

[5] Yerzhanov K.B., Kurmankulov N.B., Akhmetova A.A., Patsaev A.K. New fungicides against dry rot of potato tubers // Proceedings of the scientific and practical conference on topical issues of agricultural chemistry. Tashkent, 2002. P. 79.

Резюме

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СИНТЕЗ ДИАЦЕТИЛЕНОВЫХ ГЛИКОЛЕЙНА ОСНОВЕ 1,5-ДИ(ПРОП-2-ИНИЛОКСИ)НАФТАЛИНА

Разработаны условия синтеза новых потенциально биологически активных диацетиленовых гликолей. Изучена реакция нуклеофильного присоединения 1,5-ди-(проп-2-инилокси)нафталина по карбонильной группе циклических кетонов (циклогексанона и N-замещенных пиперидонов). Строение новых соединений установлено на основании анализа данных спектроскопии ЯМР ^{1}Н и ^{13}С.

Ключевые слова: 1,5-ди(проп-2-инилокси)нафталин, этинилирование, диацетиленовые гликоли, циклогексанон, N-замещенные пиперидоны.

Резюме

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1,5-ДИ(ПРОП-2-ИНИЛОКСИ)НАФТАЛИН НЕГІЗІНДЕ ДИАЦЕТИЛЕНДІ ГЛИКОЛЕЙН СИНТЕЗІ

Жаңа тұрғыдағы биологиялық активті диацетиленді гликолдер синтезінің жүзге асыру жағдайлары қарастырылды. Тұйың сақиналы кетондардың (циклогексанон және N-орынбасқан пиперидондар) карбонил тобы бойынша 1,5-ди(проп-2-инилокси)нафталиннің нуклеофильді қосылу реакциясы зерттелінді. Жаңа қосылыстардың құрылымы ЯМР ^{1}Н және ^{13}С спектроскопиялық талдау негізінде ан-ықталынды.

Түйін сөздер: 1,5-ди(проп-2-инилокси)нафталин, этинилдеу, диацетиленді гликолдер, циклогексанон, N-орынбасқан пиперидондар.