DOI: 10.6060/ivkkt.20246712.7065

СИНТЕЗ 1-ВИНИЛ-3(5)-МЕТИЛ-4-НИТРОПИРАЗОЛА И ИЗУЧЕНИЕ ЭФФЕКТА МЕТИЛЬНЫХ ЗАМЕСТИТЕЛЕЙ ПИРАЗОЛЬНОГО КОЛЬЦА ПРИ РАДИКАЛЬНОЙ ПОЛИМЕРИЗАЦИИ

Л.А. Бичахчян, А.Дж. Маркосян, А.Г. Шахатуни, К.С. Бадалян, О.С. Аттарян, А.Н. Хачатрян

Лилит Ашотовна Бичахчян (ORCID 0000-0002-8713-3724), Анна Дживановна Маркосян (ORCID 0000-0002-7293-3139)*, Карине Самсоновна Бадалян (ORCID 0000-0001-9872-9550), Оганес Саркисович Аттарян (ORCID 0000-0001-9790-2577), Асмик Нверовна Хачатрян (ORCID 0000-0002-2400-1679)

Лаборатория Проблем прикладной химии Института органической химии Научно технологического центра органической и фармацевтической химии, пр. Азатутян 26, г. Ереван, Республика Армения, 0014
E-mail: lilitbichakhchyan@mail.ru, a_markart@mail.ru*, karinebadalyan1947@gmail.com, hovelenatt@mail.ru, hasmikjasmin1@gmail.com

Алексан Геворкович Шахатуни (ORCID 0000-0002-2506-1091)

Лаборатория Ядерного магнитного резонанса Центра исследований строения молекулы Научно технологического центра органической и фармацевтической химии, пр. Азатутян 26, г. Ереван, Республика Армения, 0014
E-mail: shahkhatuni@gmail.com

Целью данной работы была разработка удобного препаративного метода прямого N-алкилирования 3(5)-метил-4-нитропиразола в условиях межфазного катализа (МФК). Необходимость разработки диктовалась еще тем, что продукты реакции одновременно являются промежуточными при синтезе важного класса соединений - винилпиразолов. При алкилировании 3(5)-метил-4-нитропиразола в стандартных условиях МФК (бензол-вода-КОН-ТЭБАХ (триэтилбехзиламмоний хлористый)) не привели к желаемому результату. По-видимому, бензол затрудняет перенос аниона нитропиразола из водной в органическую среду, в результате чего выход ожидаемого алкилированного соединения составляет лишь 50%. При алкилировании в отсутствие бензола, под воздействием гидроксида калия в воде легко протекает депротонирование и образуется соответствующая калиевая соль 3(5)-метил-4-нитропиразола, что блокирует дегидрохлорирование 1,2-дихлорэтана и приводит к селективному протеканию процесса алкилирования соответствующего нитропиразола. При эквимолярном соотношении нитропиразола и гидроксида калия выход смеси образующихся 1-(2-хлорэтил)-3- и 1-(2-хлорэтил)-5-метил-4-нитропиразолов достигает 80%. Исследовано также дегидрохлорирование полученных замещенных хлорэтилпиразолов в метанольном растворе, в условиях МФК и в водном растворе N-метилморфолин-N-оксида (NMO/H_2O), в присутствии гидроксида калия. Хотя гомогенный метод дегидрохлорирования технологически несовершенен, однако он позволяет с выходом 45% получить смесь изомеров 1-винил-3- и 1-винил-5-метил-4-нитропиразола. Дегидрохлорирование в условиях МФК является альтернативой гомогенному процессу, однако не способно обеспечить высокий выход ожидаемых соединений– 20%. Установлено, что дегидрохлорирование исследуемых 1-(2'-хлорэтил)-3(5)-метил-4-нитропиразолов значительно успешнее протекает в системе NMO/H_2O в присутствии КОН, приводя к суммарному выходу 1-винил-3- и 1-винил-5-метил-4-нитропиразолов до 60%. Изучены эффекты метильных заместителей пиразольного кольца при радикальной полимеризации. Идентифицированные мономеры в одинаковых условиях проявляют различную активность. Так, в процессе радикальной полимеризации изомер, в котором метильная группа находится в пятом положении пиразольного кольца, полимеризуется с большей скоростью, чем изомер, в котором метильная группа находится в третьем положении.

Ключевые слова: алкилирование, дегидрохлорирование, 3(5)-метил-4-нитропиразол, 1,2-дихлорэтан, радикальная полимеризация

SYNTHESIS OF 1-VINYL-3(5)-METHYL-4-NITROPYRAZOLE AND STUDY OF THE EFFECT OF METHYL SUBSTITUTES IN THE PYRAZOLE RING DURING RADICAL POLYMERIZATION

L.A. Bichakhchyan, A.J. Markosyan, A.G. Shakhatuni, K.S. Badalyan, O.S. Attaryan, A.N. Khachatryan

Lilit A. Bichakhchyan (ORCID 0000-0002-8713-3724), Anna J. Markosyan (ORCID 0000-0002-7293-3139)*, Karine S. Badalyan (ORCID 0000-0001-9872-9550), Hovhannes S. Attaryan (ORCID 0000-0001-9790-2577), Hasmik N. Khachatryan (ORCID 0000-0002-2400-1679)

Laboratory of Problems of Applied Chemistry, Institute of Organic Chemistry, Scientific and Technological Center for Organic and Pharmaceutical Chemistry, 26 Azatutyan ave., Yerevan, 0014, Republic of Armenia
E-mail: lilitbichakhchyan@mail.ru, a_markart@mail.ru*, karinebadalyan1947@gmail.com, hovelenatt@mail.ru, hasmikjasmin1@gmail.com

Aleksan G. Shakhatuni (ORCID 0000-0002-2506-1091)

Laboratory of Nuclear Magnetic Resonance of the Center for Research on the Structure of the Molecule of the Scientific and Technological Center for Organic and Pharmaceutical Chemistry, 26 Azatutyan ave., Yerevan, 0014, Republic of Armenia
E-mail: shahkhatuni@gmail.com

The aim of this work was to develop a convenient preparative method for the direct N-alkylation of 3(5)-methyl-4-nitropyrazole under conditions of phase-transfer catalysis (PTC). The need for development was also dictated by the fact that the reaction products are simultaneously intermediates in the synthesis of an important class of compounds - vinylpyrazoles. Alkylation of 3(5)-methyl-4-nitropyrazole under standard conditions of PTC (benzene-water-KOH-TEBACH (triethylbexylammonium chloride)) did not lead to the desired result. Apparently, benzene interrupts the transfer of the nitropyrazole anion from the aqueous organic medium, as a result of which the yield of the control alkyl compound is only 50%. During alkylation in the absence of benzene, under the influence of potassium hydroxide in water, deprotonation easily proceeds and the corresponding potassium salt of 3(5)-methyl-4-nitropyrazole is formed, which blocks the dehydrochlorination of 1,2-dichloroethane and leads to the selective course of the process of alkylation of the taken nitropyrazole. At an equimolar ratio of nitropyrazole and potassium hydroxide, the yield of a mixture of the resulting 1-(2-chloroethyl)-3- and 1-(2-chloroethyl)-5-methyl-4-nitropyrazoles reaches 80%. The dehydrochlorination of the obtained substituted chloroethylpyrazoles in a methanol solution, under conditions of PTC, and in an aqueous solution of N-methylmorpholine-N-oxide (NMO/H_2O), in the presence of potassium hydroxide was also studied. Although the homogeneous method of dehydrochlorination is technologically imperfect, however, it makes it possible to obtain a mixture of 1-vinyl-3- and 1-vinyl-5-methyl-4-nitropyrazole isomers with a yield of 45%. Dehydrochlorination under PTC conditions is an alternative to a homogeneous process; however, it is not able to provide a high yield of the expected compounds - 20%. It has been established that the dehydrochlorination of the studied 1-(2'-chloroethyl)-3(5)-methyl-4-nitropyrazoles proceeds significantly successfully in the presence of KOH in the NMO/H_2O system, leading to the total yield of 1-vinyl-3- and 1-vinyl -5-methyl-4-nitropyrazoles up to 60%. The effects of methyl substituents of the pyrazole ring during radical polymerization have been studied. The identified monomers exhibit different activities under the same conditions. Thus, in the process of radical polymerization, the isomer in which the methyl group is in the fifth position of the pyrazole ring polymerizes at a higher rate than the isomer in which the methyl group is in the third position.

Keywords: alkylation dehydrochlorination, 3(5)-methyl-4-nitropyrazole, 1,2-dichloroethane, radical polymerization

Для цитирования:
Бичахчян Л.А., Маркосян А.Дж., Шахатуни А.Г., Бадалян К.С., Аттарян О.С., Хачатрян А.Н. Синтез 1-винил-3(5)-метил-4-нитропиразола и изучение эффекта метильных заместителей пиразольного кольца при радикальной полимеризации. *Изв. вузов. Химия и хим. технология*. 2024. Т. 67. Вып. 12. С. 39–46. DOI: 10.6060/ivkkt.20246712.7065.

For citation:
Bichakhchyan L.A., Markosyan A.J., Shakhatuni A.G., Badalyan K.S., Attaryan O.S., Khachatryan A.N. Synthesis of 1-vinyl-3(5)-methyl-4-nitropyrazole and study of the effect of methyl substitutes in the pyrazole ring during radical polymerization. *ChemChemTech [Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.]*. 2024. V. 67. N 12. P. 39–46. DOI: 10.6060/ivkkt.20246712.7065.

INTRODUCTION

Nitrogen-containing heterocycles are an important class of chemical compounds. The special structure allows azole derivatives to bind easily to enzymes and receptors in organisms, thereby finding various applications in medicinal chemistry as drugs with better therapeutic results and fewer side effects [1].

Among other azoles, pyrazole and its substituted derivatives occupy leading positions in the synthesis of drugs [2, 3], pesticides [4, 5], polydentate ligands [6], and dyes [7, 8]. Therefore, continuous development of methods for obtaining pyrazoles with different functional groups is required.

Derivatives of azoles containing energetic groups (nitro-, nitramino-, polynitro-, azide) are used as components in explosive substances [9-11]. Vinylated products are interesting both as biological active cores and as universal building blocks for polymerization. They can be functionalized with either a heterocycle or a double bond (or both) [12-15]. The vinyl group can act both as a protecting group, which can be removed under relatively mild conditions [16], and as a subject of new heterocyclization [17].

For the synthesis of compounds containing various functional groups (vinyl, allyl, propargyl, butadienyl), azoles containing a mobile hydrogen atom are usually used [18].

Methods for preparing N-vinyl azole derivatives include vinylation with acetylene, which occurs without the formation of by-products. This reaction was originally implemented by Reppe [19], and is still used today with some optimizations [20]. The process takes place under pressure at a temperature of 150-200 °C. In recent years [21], as an alternative to high pressure acetylene, calcium carbide has shown very good results: a concept involving a solid acetylene reagent has been developed, where the reactivity of calcium carbide is generated in situ and acetylene is controlled by the addition of KF. Several other transformations leading to N-vinylazole derivatives can be mentioned, such as the vinyl exchange reaction between azoles and vinyl esters (vinyl acetate), catalyzed by the mercuric acetate-sulfuric acid system [22], such as the dehydrochlorination of N-chloroethyl-substituted compounds under PTC conditions and in the NMO system [23]. A method for the vinylation of azoles using heterogeneous catalysts has been developed. This method is based on the application of transition metal compounds (mercury(II) acetate) to organic polymers, which provides a simultaneous solution to the problem of wastewater treatment [24]. In search of developing new methods for the synthesis of various heterocyclic systems based on the reaction of 2,2-dichlorovinyl ketones with 2-(hydroxyethyl) hydrazine, approaches to the preparation of new chemoselective hydroxyalkyl-substituted and vinyl-substituted pyrazoles have been developed [25].

Polyvinylazoles exhibit specific properties inherent only to this class of heterocycles and can be used in various fields of science and technology.

It has been established that copolymers with grafted oligopropylamine fragments containing N-vinylazole units can interact with DNA oligonucleotide, stimulating their research as means of delivering nucleic acids into living cells [26]. Polymers based on N-vinylpyrazoles possess valuable proton-conducting, semiconducting and optical properties [27].

EXPERIMENTAL PROCEDURE

Alkylation of 3(5)-methyl-4-nitropyrazole was carried out under PTC conditions in the presence and absence of an organic solvent. Dehydrochlorination of the obtained products was conducted under PTC conditions and in the NMO/H_2O system. The composition and structure of the synthesized compounds were confirmed by NMR and IR spectroscopy methods and supported by elemental analysis data. Polymerization was carried out in a solution of DMF (dimethylformamide), in the presence of AIBN (azobisisobutyronitrile).

EXPERIMENTAL PART

1-(2'-Chloroethyl)-3(5)-methyl-4-nitro-1H-pyrazole (2a, b)

A mixture of 0.127 g (1 mmol) of 3(5)-methyl-4-nitro-1H-pyrazole, 0.056 g (1 mmol) of potassium hydroxide, 0.001 g of TEBAC in 0.50 ml of water was stirred for 1 h at a temperature of 70 °C. To the reaction mixture at this temperature 0.099 g (1 mmol) of dichloroethane was added, after which intense stirring was continued for another 8 hours.

After removing the solvent, the residue was distilled under reduced pressure. Yield 0.15 g (79%), boiling point 160-165/2 mmHg, n_D^{20} 1.5200. IR spectrum, ν, sm^{-1}: 1530 (ring). ^{1}H NMR spectrum (DMSO-d_6/CCl_4/1/3), δ, ppm: **2a)** 2.48 s (3H, 3-CH_3), 3.95 t

(2H, *J* 5.8 Hz, NCH_2); 4.43 t (2H, *J* 5.8 Hz, CH_2Cl), 8.70 s (1H, 5-H). **2b)** 2.69 s (3H, 5-CH_3); 3.92 t (2H, *J* 5.8 Hz, NCH_2), 4.47 t (2H, *J* 5.75 Hz, CH_2Cl), 8.07 s (1H, 3-H). ^{13}C NMR spectrum, (DMSO-d_6/CCl_4/1/3), δ, ppm: 10.2; 12.8; 41.6; 42.1; 50.3, 53.2; 129.5; 132.3; 132.5; 135.8; 139.8; 144.8. Found %: C 38.09, H 4.15, N 22.51. $C_6H_8ClN_3O_2$. Calculated, %: C 38.01, H 4.25, N 22.16.

3(5)-methyl-4-nitro-1-vinyl-1H-pyrazole (3a, b)

A mixture of 0.19 g (1 mmol) of 1-(2'-chloroethyl)-3(5)-methyl-4-nitro-1*H*-pyrazole **(2a, b)**, 0.056 g (1 mmol) of potassium hydroxide, 80 ml of methanol was stirred at temperature 60 °C for 1 h. After removing methanol, 20 ml of water to the residue was added and extracted with methylene chloride. After removing the solvent, the residue was distilled under reduced pressure. Yield 0.06 g (39%), boiling point 119-121/3 mmHg, n_D^{20} 1.5500. IR spectrum, ν, cm^{-1}: 1530 (ring). ^1H NMR spectrum (DMSO-d_6/CCl_4/1/3), δ, ppm: **3a)** 2.51 s (3H, 3-CH_3), 5.02 d.d. (1H, *J* 8.8 и 1.1 Hz, $=CH_2$), 5.82 d.d. (1H, *J* 15.5 и 1.1 Hz, $=CH_2$), 7.11 d.d. (1H, *J* 15.5 and 8.8 Hz, =CH), 8.95 s (1H, 5-H). ^{13}C NMR spectrum, (DMSO-d_6/CCl_4/1/3), δ, ppm: 96.0, 103.2, 129.5, 131.7, 136.4, 145.4. **3 b)** 2.73 s (3H, 5-CH_3), 5.15 ppm. (1H, *J* 8.7 и 0.4 Hz, $=CH_2$), 5.90 d.d. (1H, *J* 15.0 and 0.4 Hz, $=CH_2$), 7.26 d.d. (1H, *J* 15.0 и 0.87 Hz, =CH), 8.13 s (1H, 3-H). ^{13}C NMR, (DMSO-d_6/CCl_4/1/3), δ, ppm: 95.5, 105.4, 128.8, 136.4, 138.1, 152.4. Found %: C 47.18, H 4.81, N 27.67. $C_6H_7N_3O_2$. Calculated, %: C 47.06, H 4.61, N 27.44. %:

3(5)-methyl-4-nitro-1-vinyl-1H-pyrazole (3a, b) (TEBAC)

A mixture of 0.19 g (1 mmol) 1-(2'-chloroethyl)-3(5)-methyl-4-nitro-1*H*-pyrazole **(2a, b)**, 0.11 g (2 mmol) potassium hydroxide, 1 g TEBAC and 50 ml of a mixture of benzene: water (1:1 ratio) was intensively stirred for 3 h. The reaction product was extracted with benzene. After removing the solvent, the residue was distilled under reduced pressure. Yield 0.03 g (20%), boiling point 115-130/ 3 mmHg, n_D^{20} 1.5500.

3(5)-methyl-4-nitro-1-vinyl-1H-pyrazole (3a, b) (NMO)

A mixture of 0.19 g (0.001 mol) 1-(2'-chloroethyl)-3(5)-methyl-4-nitro-1*H*-pyrazole **(2a, b)**, 0.11 g (2 mmol) potassium hydroxide and 50 ml of 50% NMO aqueous solution was intensively stirred for 3 h at a temperature of 60 °C. The reaction mixture was extracted with methylene chloride. After removing the solvent, the residue was distilled under reduced pressure. Yield 0.09 g (59%), boiling point 123-127/2 mmHg, n_D^{20} 1.5500.

General procedure for the polymerization of 3-methyl-4-nitro- and 5-methyl-4-nitro-1-vinyl-1H-pyrazoles (3a and 3b)

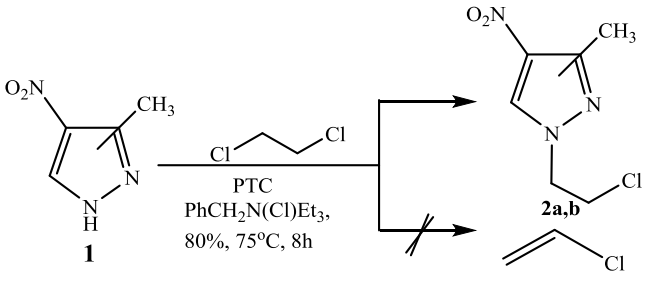
Before polymerization, the monomers were distilled twice in vacuum. Polymerizations were carried out in a solution of dimethylformamide (DMF), in the presence of azobisisobutyronitrile (AIBA) at a temperature of 70±1 °C, according to the procedure given in [28].

RESULT AND DISCUSSION

Direct alkylation of pyrazoles with 1,2-dichloroethane (DCE) under phase transfer catalysis (PTC) conditions showed that the direction of the reaction and the yields of alkylation products depend on the acidity of the pyrazoles. A decrease in the acidity of pyrazoles (correspondingly, the pKa of unsubstituted pyrazole is 20.4, 3(5)-methylpyrazole is 21.5, dimethylpyrazole is 22.5) leads to, along with alkylation, also the elimination of DCE.). Therefore, to prevent side processes during the alkylation of pyrazoles, it is necessary to increase the alkali consumption depending on the pKa of the alkylation object (2 times for pyrazole, 4 times for methylpyrazole, and 6 times for dimethipyrazole).

Transition to 3(5)-methyl-4-nitropyrazole (1), whose pKa is 10, under the influence of alkali (KOH), deprotonation easily occurs and the corresponding potassium salt of nitropyrazole is formed, which blocks the dehydrochlorination of 1,2-DCE and leads to selective the course of the alkylation process of pyrazole (**1**).

With an equimolar ratio of nitropyrazole and KOH, the yield of the mixture of the resulting 1-(2-chloroethyl)-3(5)-methyl-4-nitropyrazoles **(2a, b)** reaches 80% (Scheme 1):



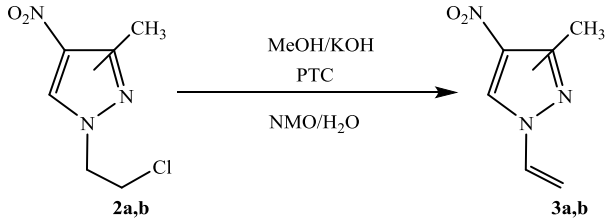
Scheme 1
Схема 1

Attempts to carry out alkylation under standard conditions of phase transfer catalysis (benzene-KOH-TEBAC) did not lead to the desired result. Apparently, benzene hinders the transfer of the nitropyrazole anion from an aqueous to an organic medium, as a result of which the yield of compound 2, in comparison with experiments without it, is only 50%.

According to the ^{1}H, ^{13}C NMR spectra, as well as those recorded using the NOESY method, the alkylation of nitro derivative 1 produces a mixture of isomeric pyrazoles – 1-(2'-chloroethyl)-3-methyl-4-nitro- and 1-(2'-chloroethyl)-5-methyl-4-nitropyrazoles (2 a, b) in a ratio of 1.5:1, respectively.

The isomeric forms of 3-Me and 5-Me were identified by the cross-peak of the proton of the pyrazole ring with the protons of the methylene group (a compound with a methyl group in the 5th position).

In order to obtain 1-vinyl-3(5)-methyl-4-nitropyrazoles **(3a, b)**, dehydrochlorination of compound **2a, b** was carried out in a methanol solution of KOH under PTC conditions, as well as a study of the dehydrochlorination process in an aqueous solution of N-Methylmorpholine-N-oxide (NMO) [23] (Scheme 2):



Scheme 2
Схема 2

Dehydrochlorination under PTC conditions is an alternative to the homogeneous process; however, it is not able to provide a high yield (20%) of compounds **3a, b**.

It was established that the dehydrochlorination of the studied 1-(2'-chloroethyl)-3(5)-methyl-4-nitropyrazoles **(2a, b)** proceeds significantly successfully in the presence of KOH, in the NMO/H_2O system, leading to a total yield of 1-vinyl- 3(5)-methyl-4-nitropyrazoles **(3a, b)** up to 60%.

The structure of the obtained 1-vinyl-3(5)-methyl-4-nitropyrazoles **(3a, b)** was confirmed by spectral methods (IR, ^{1}H, ^{13}C NMR).

Dehydrochlorination of compound **2a, b**, a mixture of isomeric 1-vinylpyrazoles **3a, b** is formed, the ratio of which, according to ^{1}H NMR data, is respectively 2.3:1. We were able to chromatographically separate and identify the corresponding 3-Me and 5-Me isomers of pyrazoles **3a** and **3b**.

In the ^{1}H NMR spectrum, the singlet signal of the protons of the methyl group of compound **3a** is observed at 2.51 ppm, while in compound **3b** the signal of the protons of the methyl group is observed in the region of 2.73 ppm, i.e., the shift towards the high field is 0.22 m.d.

A different picture is observed for the 3-H and 5-H protons of the pyrazole ring. Thus, in the ^{1}H NMR spectrum of compound **3a**, the 5-H proton is observed in the region of 8.95 ppm, while in the spectrum of compound **3b**, the 3-H proton appears in the region of 8.13 ppm.

Effects of methyl substituents on the pyrazole ring during the radical polymerization of 1-vinyl-3-methyl- and 1-vinyl-5-methyl-4-nitropyrazoles according to ^{1}H and ^{13}C NMR spectra

Vinylazoles are interesting objects for investigating the impact of structural factors on the activity of vinyl monomers in radical polymerization [29]. In the presented work, we examine the dependence of the polymerization activity of monomers **3a** and **3b** (Figure) on the position of the methyl group in the pyrazole ring. Monomers **3a** and **3b** exhibit different activities under the same conditions. Thus, during radical polymerization, isomer **3b**, in which the methyl group is located in the fifth position of the pyrazole ring, polymerizes at a higher rate than isomer **3a** (Table 1).

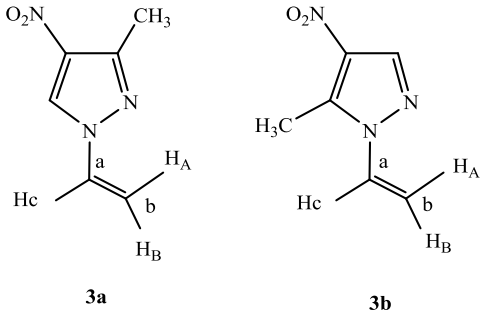


Fig. Structural formulas of 1-vinyl-3-methyl- and 1-vinyl-5-methyl-4-nitropyrazoles (**3a, 3b**)
Рис. Структурные формулы 1-винил-3-метил- и 1-винил-5-метил-4-нитропиразолов (**3a, 3b**)

Table 1

Polymerization parameters and inherent viscosities of polyvinyl nitropyrazoles obtained in DMF, [M]=1 mol/l, [I]= 0.001 mol/l, t=70 °C

***Таблица 1.* Параметры полимеризации и характеристические вязкости поливинилнитропиразолов, полученных в ДМФА, [M]=1 моль/л, [I]= 0,001 моль/л, t=70 °C**

Monomer	Duration of polymerization, min	Polymer yield, %	[η] in DMF, at 20 °C dl/g
3a	10	18.5	0.40
	20	29.7	
	30	53.2	
	40	75.5	
3b	10	45.5	0.52
	20	70.5	
	30	90.0	

The objective of the study was to identify a possible correlation between the spectral data (^{1}H, ^{13}C

NMR) characteristics of 1-vinyl-3-methyl-4-nitro- **(3a)** and 1-vinyl-5-methyl-4-nitropyrazoles **(3b)** with the polymerization ability of vinyl groups during radical polymerization.

As can be seen from Table 2, the chemical shift (CS) of the protons of the vinyl group weakly depends on the location of the methyl substituents, since they vary within a few hundredths of ppm, while the CS of the C_α and C_β carbon atoms of the vinyl group is reflected much more strongly by the interaction with the heterocycle.

Table 2

Parameters of ^{1}H and ^{13}C NMR spectra (ppm) of compounds 3a and 3b

***Таблица 2.* Параметры спектров ^{1}H, ^{13}C ЯМР (м.д.) соединений 3a и 3b**

Monomer	Chemical Shift ^{1}H, δ.ppm.			Chemical Shift ^{13}C, δ.ppm.		
	H_A	H_B	H_C	C_α	C_β	$\Delta\delta_{\alpha\beta}$
3a	5.82	5.02	7.11	129.52	103.23	26.29
3b	5.90	5.15	7.26	128.79	105.44	23.35

From Table 2, it can be seen that in monomer **3b**, which exhibits greater activity during polymerization, the C_β atom of the double bond is deshielded and its CS is shifted downfield compared to **3a** [30]. The chemical shift of the signal of the β-carbon atom ($\delta_{C\beta}$) of the vinyl group to a weaker field, reducing the difference between the chemical shifts C_α and C_β ($\Delta\delta_{\alpha\beta}$), increases the electrophilicity of the radical in monomer **3b**, which corresponds to its higher activity in radical polymerization compared to compound **3a**.

We studied the macromolecular parameters of polyvinyl-3(5)-methyl-4-nitropyrazole, since in practice we always obtain a mixture of these isomers – **3 a**, **b**. The obtained data indicate high molecular weights of the synthesized polymers ($\bar{M} = 1.3 \cdot 10^6$) a low degree of polydispersity $\frac{M_w}{M_n} \approx 1.5$, which supports the mechanism of square termination by macroradical recombination. The values of the constants K and α in the Mark-Houwink equation $[\eta] = K\bar{M}^\alpha$ have also been determined. It was found that $K = 0.85 \cdot 10^{-4}$ and $\alpha = 0.575$ (DMFA, 25 °C), indicating sufficient flexibility of the polymer macromolecules.

CONCLUSION

The presence of a nitro group in the 4th position in the 3(5)-methylpyrazole ring makes selective alkylation with dichloroethane possible under phase-transfer catalysis.

Due to the increased electrophilicity of the double bond, 5-methyl-4-nitro-1-vinylprazole is more active in radical polymerization than 3-methyl-4-nitro-1-vinylpyrazole.

ACKNOWLEDGEMENT

The work was supported by Grant 21T-1D020 of Higher Education and Science Committee of the RA MESCS. The authors declare the absence a conflict of interest warranting disclosure in this article.

The authors declare the absence a conflict of interest warranting disclosure in this article.

Работа поддержана грантом 21T-1D020 Комитета по высшему образованию и науке МОН РА. Авторы заявляют об отсутствии конфликта интересов.

Авторы заявляют об отсутствии конфликта интересов, требующего раскрытия в данной статье.

ЛИТЕРАТУРА

1. **Peng X-M., Cai G.-X., Zhou Ch.-H.** Recent developments in azole compounds as antibacterial and antifungal agents. *Curr. Top. Med. Chem.* 2013. V.13. N 16. P. 1963-2010. DOI: 10.2174/15680266113139990125.
2. **Li G. Cheng Y., Han Ch., Song Ch., Huang N., Du Y.** Pyrazole-containing pharmaceuticals: target, pharmacological activity, and their SAR studies. *RSC Med. Chem.* 2022. V. 13. P. 1300-1321. DOI: 10.1039/D2MD00206J.
3. **Lusardi M., Spallarossa A., Brullo Ch.** Amino-pyrazoles in medicinal chemistry: A review. *Int. J. Mol. Sci.* 2023. V. 24. P. 7834. DOI: 10.3390/ijms24097834.
4. **Fu C., Pei J., Ning Y., Liu M., Shan P., Liu J., Li Y., Hu F., Zhu Y., Yang H., Zou X.** Synthesis and insecticidal activities of novel pyrazole oxime ether derivatives with different substituted pyridyl rings. *Pest Manag. Sci.* 2013. V 70. P. 1207–1214. DOI: 10.1002/ps.3672.
5. **Cravedi J.P., Delous G., Zalko D., Viguie′ C., Debrauwer L.** Disposition of fipronil in rats. *Chemosphere*. 2013. V. 93. P. 2276-2283. DOI: 10.1016/j.chemosphere.2013.07.083.

REFERENCES

1. **Peng X-M., Cai G.-X., Zhou Ch.-H.** Recent developments in azole compounds as antibacterial and antifungal agents. *Curr. Top. Med. Chem.* 2013. V.13. N 16. P. 1963-2010. DOI: 10.2174/15680266113139990125.
2. **Li G. Cheng Y., Han Ch., Song Ch., Huang N., Du Y.** Pyrazole-containing pharmaceuticals: target, pharmacological activity, and their SAR studies. *RSC Med. Chem.* 2022. V. 13. P. 1300-1321. DOI: 10.1039/D2MD00206J.
3. **Lusardi M., Spallarossa A., Brullo Ch.** Amino-pyrazoles in medicinal chemistry: A review. *Int. J. Mol. Sci.* 2023. V. 24. P. 7834. DOI: 10.3390/ijms24097834.
4. **Fu C., Pei J., Ning Y., Liu M., Shan P., Liu J., Li Y., Hu F., Zhu Y., Yang H., Zou X.** Synthesis and insecticidal activities of novel pyrazole oxime ether derivatives with different substituted pyridyl rings. *Pest Manag. Sci.* 2013. V 70. P. 1207–1214. DOI: 10.1002/ps.3672.
5. **Cravedi J.P., Delous G., Zalko D., Viguie′ C., Debrauwer L.** Disposition of fipronil in rats. *Chemosphere*. 2013. V. 93. P. 2276-2283. DOI: 10.1016/j.chemosphere.2013.07.083.

6. **Kaddouri Y., Abrigach F., Ouahhoud S., Benabbes R., El Kodadi M., Alsalme A., Al-Zaqri N., Warad I., Touzani R.** Mono-alkylated ligands based on pyrazole and triazole derivatives tested against Fusarium oxysporum f. sp. albedinis: Synthesis, characterization, DFT, and phytase binding site identification using blind docking/virtual screening for potent fophy inhibitors. *Front. Chem*. 2020. V. 8. P. 559262. DOI: 10.3389/fchem.2020.559262.
7. **Tao T., Zhao X.-L., Wang Y.-Y., Qian H.-F., Huang W.** 5-Hydroxy-1-phenyl-1H-pyrazole-3-carboxylic acid based heterocyclic dyes. *Dyes Pigments.* 2019. V. 166. P. 226-232. DOI: 10.1016/j.dyepig.2019.03.046.
8. **Nitu S., Milea M.S., Boran S., Mosoarca G., Zamfir A.D., Popa S., Funar-Timofei S.** Experimental and computational study of novel pyrazole azo dyes as colored materials for light color paints. *Materials*. 2022. V. 15. 5507. DOI: 10.3390/ma15165507.
9. **Qu Y., Babailov S.P.** Azo-linked high-nitrogen energetic materials. *J. Mater. Chem. A.* 2018. V. 6. P. 1915-1940. DOI: 10.1039/c7ta09593g.
10. **Balachandar K.G., Thangamani A.** Novel high performance energetic materials of fluorine-containing 2,6-dinitro-4-(trifluoromethyl)phenol derivatives with substituted azoles. *J. Fluor. Chem.* 2021. V. 247. P. 109801. DOI: 10.1016/j.jfluchem.2021.109801.
11. **Srinivas V., Kommu N., Balaraju M., Sahoo A.K.** Synthesis and energetic properties of polynitro aryl-azole derivatives. *J. Phys.: Conf. Ser.* 2021. 1721. 012007. DOI: 10.1088/1742-6596/1721/1/012007.
12. **Gong T.-J., Xu M.-Y., Yu S.-H., Yu C.-G., Su W., Lu X., Xiao B., Fu Y.** Rhodium (III)-Catalyzed Directed C–H Coupling with Methyl Trifluoroacrylate: Diverse Synthesis of Fluoroalkenes and Heterocycles. *Org. Lett.* 2018. V. 20. P. 570. DOI: 10.1021/acs.orglett.7b03677.
13. **Sun J.-K., Kochovski Z., Zhang W.-Y., Kirmse H., Lu Y., Antonietti M., Yuan J.** General Synthetic Route toward Highly Dispersed Metal Clusters Enabled by Poly(ionic liquid)s. *J. Am. Chem. Soc.* 2017. V. 139. P. 8971. DOI: 10.1021/jacs.7b03357.
14. **Azpiroz R., Rubio-Perez L., Di Giuseppe A., Passarelli V., Lahoz F.J., Castarlenas R., Perez-Torrente J.J. Oro L.A.** Rhodium(I)-N-Heterocyclic Carbene Catalyst for Selective Coupling of N-Vinylpyrazoles with Alkynes via C–H Activation. *ACS Catal.* 2014. V. 4. N 12. P. 4244–4253. DOI: 10.1021/cs501366q.
15. **Hu B., DiMagno S.G.** Reactivities of vinyl azides and their recent applications in nitrogen heterocycle synthesis. *Org. Biomol. Chem.* 2015. V. 13. P. 3844-3855. DOI: 10.1039/C5OB00099H.
16. **Iddon B., Tonder J.E., Hosseini M., Begtrup M.** The N-vinyl group as a protection group of the preparation of 3(5)-substituted pyrazoles via bromine–lithium exchange. *Tetrahedron*. 2007. V. 63. P. 56-61. DOI: 10.1016/j.tet.2006.10.009.
17. **Grygorenko O.O., Nosik P.S.** Recent advances in (hetero)cyclizations of N-vinylazoles (microreview). *Chem. Heterocycl. Comp.* 2019. V. 55. N 3. P. 196-198. DOI: 10.1007/s10593-019-02440-6.
18. **Асратян А.Г., Алексанян А.Г., Данагулян Г.Г., Аттарян О.С.** Водный раствор N-метилморфолин-N-оксида как новая среда для алкилирования гетероциклических соединений. *Изв. вузов. Химия и хим. технология.* 2022. Т. 65. Вып. 1 С. 6-22. DOI: 10.6060/ivkkt.20226501.6485.
19. **Reppe W.** Vinylierung. *Justus Liebigs Ann. Chem.* 1956. V. 601. P. 132-134. DOI: 10.1002/jlac.19566010106.
20. **Semina E., Tuzina P., Bienewald F., Hashmi A.S.K., Schaub T.** Ruthenium-catalyzed synthesis of vinylamides

6. **Kaddouri Y., Abrigach F., Ouahhoud S., Benabbes R., El Kodadi M., Alsalme A., Al-Zaqri N., Warad I., Touzani R.** Mono-alkylated ligands based on pyrazole and triazole derivatives tested against Fusarium oxysporum f. sp. albedinis: Synthesis, characterization, DFT, and phytase binding site identification using blind docking/virtual screening for potent fophy inhibitors. *Front. Chem*. 2020. V. 8. P. 559262. DOI: 10.3389/fchem.2020.559262.
7. **Tao T., Zhao X.-L., Wang Y.-Y., Qian H.-F., Huang W.** 5-Hydroxy-1-phenyl-1H-pyrazole-3-carboxylic acid based heterocyclic dyes. *Dyes Pigments.* 2019. V. 166. P. 226-232. DOI: 10.1016/j.dyepig.2019.03.046.
8. **Nitu S., Milea M.S., Boran S., Mosoarca G., Zamfir A.D., Popa S., Funar-Timofei S.** Experimental and computational study of novel pyrazole azo dyes as colored materials for light color paints. *Materials*. 2022. V. 15. P. 5507. DOI: 10.3390/ma15165507.
9. **Qu Y., Babailov S.P.** Azo-linked high-nitrogen energetic materials. *J. Mater. Chem. A.* 2018. V. 6. P. 1915-1940. DOI: 10.1039/c7ta09593g.
10. **Balachandar K.G., Thangamani A.** Novel high performance energetic materials of fluorine-containing 2,6-dinitro-4-(trifluoromethyl)phenol derivatives with substituted azoles. *J. Fluor. Chem.* 2021. V. 247. P. 109801. DOI: 10.1016/j.jfluchem.2021.109801.
11. **Srinivas V., Kommu N., Balaraju M., Sahoo A.K.** Synthesis and energetic properties of polynitro aryl-azole derivatives. *J. Phys.: Conf. Ser.* 2021. 1721. P. 012007. DOI: 10.1088/1742-6596/1721/1/012007.
12. **Gong T.-J., Xu M.-Y., Yu S.-H., Yu C.-G., Su W., Lu X., Xiao B., Fu Y.** Rhodium (III)-Catalyzed Directed C–H Coupling with Methyl Trifluoroacrylate: Diverse Synthesis of Fluoroalkenes and Heterocycles. *Org. Lett.* 2018. V. 20. P. 570. DOI: 10.1021/acs.orglett.7b03677.
13. **Sun J.-K., Kochovski Z., Zhang W.-Y., Kirmse H., Lu Y., Antonietti M., Yuan J.** General Synthetic Route toward Highly Dispersed Metal Clusters Enabled by Poly(ionic liquid)s. *J. Am. Chem. Soc.* 2017. V. 139. P. 8971. DOI: 10.1021/jacs.7b03357.
14. **Azpiroz R., Rubio-Perez L., Di Giuseppe A., Passarelli V., Lahoz F.J., Castarlenas R., Perez-Torrente J.J. Oro L.A.** Rhodium(I)-N-Heterocyclic Carbene Catalyst for Selective Coupling of N-Vinylpyrazoles with Alkynes via C–H Activation. *ACS Catal.* 2014. V. 4. N 12. P. 4244–4253. DOI: 10.1021/cs501366q.
15. **Hu B., DiMagno S.G.** Reactivities of vinyl azides and their recent applications in nitrogen heterocycle synthesis. *Org. Biomol. Chem.* 2015. V. 13. P. 3844-3855. DOI: 10.1039/C5OB00099H.
16. **Iddon B., Tonder J.E., Hosseini M., Begtrup M.** The N-vinyl group as a protection group of the preparation of 3(5)-substituted pyrazoles via bromine–lithium exchange. *Tetrahedron*. 2007. V. 63. P. 56-61. DOI: 10.1016/j.tet.2006.10.009.
17. **Grygorenko O.O., Nosik P.S.** Recent advances in (hetero)cyclizations of N-vinylazoles (microreview). *Chem. Heterocycl. Comp.* 2019. V. 55. N 3. P. 196-198. DOI: 10.1007/s10593-019-02440-6.
18. **Asratyan A.G., Aleksanyan A.G., Attaryan H.S., Danagulyan G.G.** Aqueous solution of N-methylmorpholine-N-oxide as a new medium for the alkylation of heterocyclic compounds. *ChemChemTech [Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.]*. 2022. V. 65. N 1. P. 6-22 (in Russian). DOI: 10.6060/ivkkt.20226501.6485.
19. **Reppe W.** Vinylierung. *Justus Liebigs Ann. Chem.* 1956. V. 601. P. 132-134. DOI: 10.1002/jlac.19566010106.

at low acetylene pressure. *Chem. Commun*. 2020. V. 56. P. 5977−5980. DOI: 10.1039/D0CC01533D.
21. **Rodygin K.S., Bogachenkov A.S., Ananikov V.P.** Vinylation of a secondary amine core with calcium carbide for efficient post-modification and access to polymeric materials. *Molecules*. 2018. V. 23. P. 648. DOI: 10.3390/molecules23030648.
22. **Aleksanyan A.G., Hakobyan R.M., Aghekyan M.A., Kharatyan L.A., Attaryan H.S.** The vinilation of NH-pyrazole with vinil acetate in the present of mercure (II) acetate on the chitosan based polymer carrier. POLYCHAR-28, World Forum on Advanced Materials, Yerevan, 2022, 4-7 July. Abstract-Book. Yerevan. 2022. 50-50.
23. **Закарян Г.Б., Айоцян С.С., Аттарян О.С., Асратян Г.В.** Водный раствор N-метилморфолин-N-оксида как новая среда для алкилирования гетероциклических соединений. *ЖОХ*. 2016. Т. 86. С. 337-339.
24. **Алексанян А.Г., Агекян М.А., Акопян Р.М., Шахатуни А.Г., Шахатуни А.А., Аттарян О.С.** Ацетат ртути(II) на подложке из хитозана в качестве катализатора реакций трансвинилирования азолов. *Изв. вузов. Химия и хим. технология.* 2024. Т. 67. Вып. 3. С. 119-126. DOI: 10.6060/ivkkt.20246703.6942.
25. **Kobelevskaya V.A., Larina L.I., Popov A.V.** A regioselective synthesis of 5-chloro-1-vinyl- and 3-alkenyl-5-chloro-1H-pyrazoles. *Chem. Heterocycl. Comp*. 2022. V. 58. P. 588–597. DOI: 10.1007/s10593-022-03139-x.
26. **Strelova M.S., Danilovtseva E.N., Annenkov V.V.** Copolymers of methyl acrylate and vinylazoles: Synthesis, thermolabile properties, and grafting of polyamine chains. *Polym. Sci. Ser. B.* 2021. V. 63. P. 41–51. DOI: 10.1134/S1560090421010061.
27. **Son J., Hong Y., Han G., Nguyen T.S., Yavuz C.T., Han J.I.** Gold recovery using porphyrin-based polymer from electronic wastes: Gold desorption and adsorbent regeneration. *Sci. Total Environ.* 2020. 704. 135405. DOI: 10.1016/j.scitotenv.2019.135405.
28. **Макаров К.А., Воробьева Л.Н., Николаев А.Ф., Сюда Е.** Изучение процесса сополимеризации методом газожидкостной хроматографии. *Высокомол. Соед. Б.* 1968. Т. 10. С. 757-759.
29. **Kizhnyaev V.N., Golobokova T.V., Pokatilov F.A., Vereshchagin L.I., Estrin Y.I.** Synthesis of energetic triazole- and tetrazole-containing oligomers and polymers. *Chem. Heterocycl. Comp*. 2017. V. 53. N 6/7. P. 682-692. DOI: 10.1007/s10593-017-2109-6.
30. **Кижняев В.Н., Ратовский Г.В., Баженов Д.Н., Покатилов Ф.А.** Сравнительная оценка реакционной активности винилазолов в радикальной полимеризации. *Высокомол. соед. А*. 2005. Т. 47. Вып. 10. С. 1802-1811.

20. **Semina E., Tuzina P., Bienewald F., Hashmi A.S.K., Schaub T.** Ruthenium-catalyzed synthesis of vinylamides at low acetylene pressure. *Chem. Commun*. 2020. V. 56. P. 5977−5980. DOI: 10.1039/D0CC01533D.
21. **Rodygin K.S., Bogachenkov A.S., Ananikov V.P.** Vinylation of a secondary amine core with calcium carbide for efficient post-modification and access to polymeric materials. *Molecules*. 2018. V. 23. P. 648. DOI: 10.3390/molecules23030648.
22. **Aleksanyan A.G., Hakobyan R.M., Aghekyan M.A., Kharatyan L.A., Attaryan H.S.** The vinilation of NH-pyrazole with vinil acetate in the present of mercure (II) acetate on the chitosan based polymer carrier. POLYCHAR-28, World Forum on Advanced Materials, Yerevan, 2022, 4-7 July. Abstract-Book. Yerevan. 2022. 50-50.
23. **Zakaryan G.B., Hayotsyan S.S., Attaryan H.S., Hasratyan G.V.** Dehydrochlorination of 1-(2-chloroethyl)azoles in aqueous solution of N-methylmorpholine N-oxide. *Russ. J. Gen. Chem. [Journal obshch. Khim.]*. 2016. V. 86. P. 414-416. DOI: 10.1134/S1070363216020377. (in Russian).
24. **Aleksanyan A.G., Aghekyan M.A., Hakobyan R.M., Shahkhatuni A.G., Shahkhatuni A.A., Attaryan H.S.** Mercury(II) acetate on a chitosan substrate as a catalyst for azoles transvinylation reactions. *ChemChemTech [Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.]*. 2024. V. 67. N 3. P.119-126. DOI: 10.6060/ivkkt.20246703.6942.
25. **Kobelevskaya V.A., Larina L.I., Popov A.V.** A regioselective synthesis of 5-chloro-1-vinyl- and 3-alkenyl-5-chloro-1H-pyrazoles. *Chem. Heterocycl. Comp.* 2022. V. 58. P. 588–597. DOI: 10.1007/s10593-022-03139-x.
26. **Strelova M.S., Danilovtseva E.N., Annenkov V.V.** Copolymers of methyl acrylate and vinylazoles: Synthesis, thermolabile properties, and grafting of polyamine chains. *Polym. Sci. Ser. B.* 2021. V. 63. P. 41–51. DOI: 10.1134/S1560090421010061.
27. **Son J., Hong Y., Han G., Nguyen T.S., Yavuz C.T., Han J.I.** Gold recovery using porphyrin-based polymer from electronic wastes: Gold desorption and adsorbent regeneration. *Sci. Total Environ.* 2020. V. 704. P. 135405. DOI: 10.1016/j.scitotenv.2019.135405.
28. **Makarov K.A., Vorobyov L.N., Nikolaev A.N., Syuda E.** Study of the copolymerization process by gas-liquid chromatography. *Vysokomolek. Soed. B.* 1968. V. 10. P. 757-759 (in Russian).
29. **Kizhnyaev V.N., Golobokova T.V., Pokatilov F.A., Vereshchagin L.I., Estrin Y.I.** Synthesis of energetic triazole- and tetrazole-containing oligomers and polymers. *Chem. Heterocycl. Comp.* 2017. V. 53. N 6/7. P. 682-692. DOI: 10.1007/s10593-017-2109-6.
30. **Kizhnyaev V.N., Ratovsky G.V., Bazhenov D.N., Pokatilov F.A.** Comparative assessment of the reactivity of vinylazoles in radical polymerization. *Vysokomolek. Soed. A.* 2005. V. 47. N 10. P. 1802-1811 (in Russian).

Поступила в редакцию 13.02.2024
Принята к опубликованию 03.09.2024

Received 13.02.2024
Accepted 03.09.2024