INNOVATIVE TECHNOLOGICA
METHODICAL RESEARCH JOURNAL
ISSN: 2776-0987 Volume 2, Issue 6, June, 2021

# PREPARATION OF PYRAZOLES BASED ON PROPARHYL ETHERS OF SUBSTITUTED PHENOLS

Yunusova D.
Doctor of Chemical Sciences,
Professor of the Department of Physics and Chemistry.

Madikhanov N
Doctor of Chemical Sciences,
Professor of the Department of Physics and Chemistry.

Abdugafurov I. A.
Doctor of Chemical Sciences,
Associate Professor of the Department of General Chemistry and Oil Gas.

Usmanova S. G.
senior Lecturer of the Department of Physics and Chemistry.
Andijan Agricultural and Agrotechnological Institute, Tashkent National University

## Annotation

Pypzole derivatives were obtained by the reaction of 1,3-dipolar cycloaddition of the propargyl ether of substituted phenols with diazomethane. The structure is proved by IR, PMR, UV spectroscopy and mass spectrometry.

**Keywords:** Propargyl ethers of phenols, diazomethane, physical methods of analysis.

Acetylene is a highly reactive compound that readily converts to other more complex organic compounds, especially heterocyclic compounds.

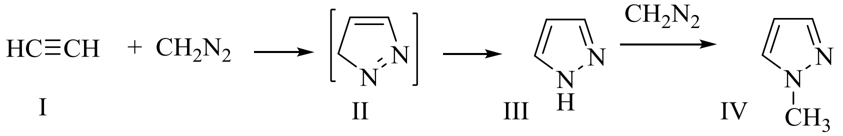
In modern synthetic organic chemistry, one of the tasks is useful and effective methods for the synthesis of new biologically active compounds that meet the needs of the national economy, especially meditation, agriculture, tezniks and others.

The rapidly developing chemistry of acetylene compounds attracts the attention of many researchers both in our country and abroad. This is combined with those rich possibilities of various chemical transformations, which are represented by acetylene groups, which are highly reactive. The presence of a triple carbon-carbon bond and a mobile hydrogen atom promotes the reactions of 1,3-dipolar cycloaddition of diazomethane with propargyl ethers of phenols and naphthols.

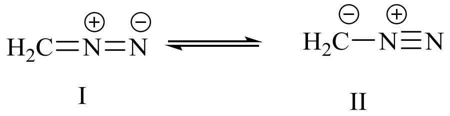
Acetylene compounds are widely used in reactions with pyrazole and its derivatives, which are also based on processes such as 1,3-dipolar cycloaddition, intramolecular cyclization, etc.

The high reactivity of the pyrazole ring makes it possible to use pyrazole derivatives as starting and intermediate products in the synthesis of various organic compounds, many of which have found practical application.

H. Pekhman [1] passing directly acetylene into an ethereal solution of diazomethane obtained pyrazoleIII.Thepyrazole yield was 50%. Under pressure, it is formed quantitatively, with an excess of diazomethane - its methyl derivative IV



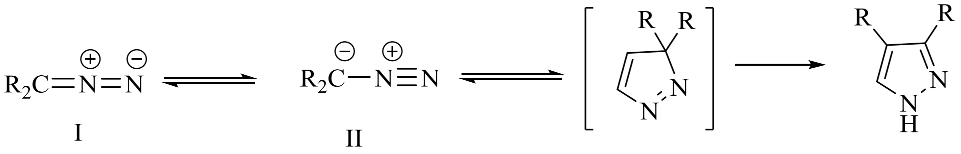
This reaction is 1,3-cycloaddition, diazomethane is here a 1,3-dipolar compound. Having the following spacer structures:



$$\underset{\text{I}}{H_2C=\overset{\oplus}{N}=\overset{\ominus}{N}} \rightleftharpoons \underset{\text{II}}{H_2\overset{\ominus}{C}-\overset{\oplus}{N}\equiv N}$$

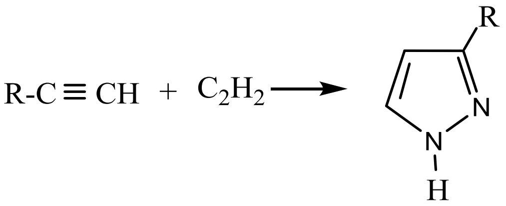
It enters into a cycloaddition reaction with dipolarophiles of the acetylene series.

Basically the most reactive structure III capable of containing a nitrogen atom lacking an electron octet



The principle of 1,3-bipolar cycloaddition proposed by Husgen [2-4] is based on the formation of two new β-bonds, in the result of electron transfer within a cyclic transition state and the neutralization of formal charges in the initial compounds. The principle of 1,3-dipolar cycloaddition correlates well with the experimental data on stereospecificity and also with the absence of the solvent effect on the rate and stereochemistry of the reaction [5].

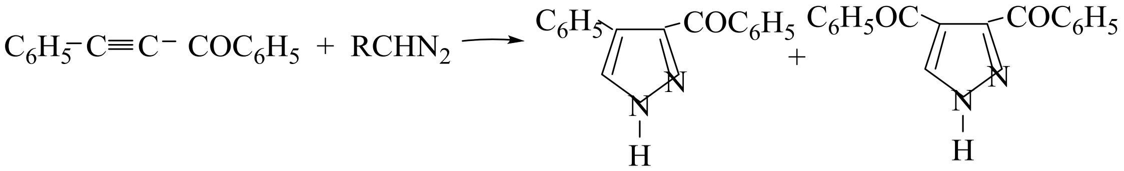
The main problem of the 1,3-cycloaddition reaction of diazo compounds to asymmetrically substituted unsaturated compounds is the mutual orientation of polar groups in space. In many cases, regloselectivity obeys the Auwers rule: a carbon atom carrying a diazo group forms a σ bond with the most electrophilic alkyne atom, which leads to pyrazole with an electron-reactor substituent at position 3 (5) of the ring [6,7] 3 (5) - Substituted pyrazoles are formed when interactions of acetylenes having electron-withdrawing groups at a triple bond [8] (aryl, carbonyl, carboxyl, etc.)



где, R = n-NO$_2$ C$_6$H$_4$–; - COCH$_3$ ; - COC$_6$H$_5$ ; CONH$_2$ ; - CN ; - CHO

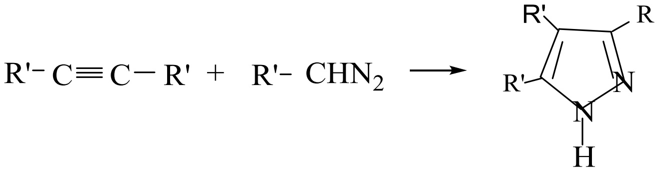
The ratio of isomers changes with an increase in the volume of substituents [9]

The ratio of isomers is influenced by the volumes of the avengers and diazomethane [10-11]

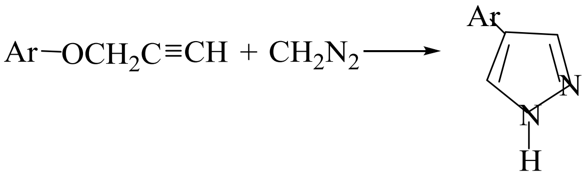


| | | |
|---|---|---|
| R= H | 100% | — |
| R= CH$_3$ | 60% | 40% |
| R = C$_6$H$_5$ | 62% | 38% |

In [12], a regularity was followed: the reaction of diazomethane with alkynes always proceeds with the formation of 1H-pyrazoles.



The authors of [13] synthesized pyrazole derivatives based on propargyl ethers of phenols and naphthols with diazomethane.



где : Ar = C$_6$H$_5$ - ; o - ; м - ; n – ClC$_6$H$_4$ ; 2,4 –Cl$_2$C$_6$H$_3$ - ;

2,4,6 – $Cl_3C_6H_2$ - ; 2,3,4,5,6 – $Cl_5$ $C_6$- ;

The resulting pyrazole derivatives are either viscous or crystalline substances of white or light yellow color.

The progress of the reaction, separation and purification of the reaction products was monitored by thin-layer chromatography on $Al_2O_3$ of the II degree of activity.

When studying the reaction products by thin-layer chromatography, it was found that the cyclization reaction proceeds with the formation of only one target product.

It was found that it is expedient to carry out the cyclization reaction at room temperature, since this temperature favors the approach of the active reagent to the conjugated acetylene bond. Lowering the temperature leads to a decrease in the electrophilicity of the propargyl ether of substituted phenols, due to the decrease in its reactivity, which leads to a decrease in the yield of the final product.

It was found that the yield of the whole product of the 1,3-dipolar cycloaddition reaction depends significantly on temperature. For example: propargyl ether of n-chlorophenol with diazomethane enters into a cyclization reaction with a yield of 81% at a temperature of + 18-20 ° C. When the temperature rises to + 25 ° C, the yield decreases to 70.5%, which is apparently explained by the evaporation of the ether solution of diazomethane and a decrease in its concentration in the reaction medium. Reducing the temperature by + 10 ° C, the yield of the final product is 45%.

To determine the effect of solvents, diethyl ether, diethyl ether + dioxane, diethyl ether + DMF were taken. This choice of a mixture of solvents is due to the fact that diazotmethane itself is a gas. It was found that the nature of the solvent does not significantly affect the yield of the target products, which is in full agreement with the literature data [2-5].

At the same time, it was found that the most suitable solvent is diethyl ether, which favors the approach of the attacking reagent to the triple bond and thereby somewhat increases the yield of the final product.

It was also studied the effect on the reactivity of pyrazole in the reaction under consideration is exerted by electro-acceptor substituents in the n-position. This is due to the high inductive effect of the halogen in the n-position. The influence in the o- and m-positions is less pronounced. As a result, the yield of products in the n-position is higher than in the o- and m-positions.

The decrease in the yield of the target product depending on the products and the number of substitutes in the phenyl ring can be represented as follows: three > di mono. This is due to the fact that with an increase in the number of halogens in the benzene ring, its electron acceptor ability increases, the conjugation effect becomes stronger, which contributes to the shift of the electron density towards the benzene ring and at the same time facilitates the cleavage of the bond in the acetylene group when attacked by a nucleophilic reagent.

Thus, the reciprocal orientation of the dipolarophiles and the dipolar promotes the 1,3-dipolar cycloaddition reaction with the formation of pyrazoles with a substitute in the C% position, which is consistent with Husgen's generalizations.

The composition of the synthesized compounds is subject to elemental analysis, and the structure of IR, PMR, UV spectroscopy and mass spectroscopy.

In the IR spectra of all the obtained compounds there are absorption bands in the range 1224-1760 cm$^{-1}$, characteristic of the C – O – C group, in the region of 1430-1480 cm$^{-1}$ for - $CH_2$–. The absorption region 1540-1584 cm$^{-1}$ corresponds to the pyrazole ring and a blurred band in the region of 3200-3408 cm$^{-1}$ for the NH group of the heterocycle.

For example, in the IR spectrum of4- (p-chlorophenoxymethyl) -pyrazole, the absorption bands in the region of 1248 cm$^{-1}$ of the C – O – C group, in the region of 1450 cm$^{-1}$ –$CH_2$–, in the region of 1540-1550 cm$^{-1}$ of pyrazole rings and for the NH group in the region of 3246 cm $^{-1}$.

Comparison of the IR spectra of the obtained pyrazole derivatives with the known ones [13-18] confirms the expected structure. The observed small shifts of stretching vibrations in the spectra are apparently explained by the influence of substituents in the phenyl ring.

The assignment of PMR spectra was carried out by comparing them with the spectra of compounds [17-20].

The PMR spectrum of 4- (p-chlorophenoxymethyl) -pyrazole at 4.97 and 12.73 ppm shows singlet signals with an integrated intensity ratio of 1: 2, which we assigned to the protons of the methylene group and the NH group of the pyrazole ring.In the area of 6.677.04 ppm. Two doublets from 4 protons of the sub-substituted aromatic ring with an integral intensity ratio of 2: 2 and a spin-spin coupling constant of 8 Hz are clearly manifested. Two doublets with an integral intensity ratio of 1:1 and a spin-spin coupling constant of 2 Hz, located at 6.17 and 7.35 ppm, are due to the protons of the pyrazole ring.

Absorption of light energy in the ultraviolet region is characteristic of heteroaromatic systems. The UV spectra of pyrazole derivatives exhibit absorption bands corresponding to $\pi \rightarrow \pi$□ transitions. In the UV spectrum of 4- (p-chlorophenoxymethyl) -pyrazole, the pyrazole ring absorbs the 228 nm region, which is characteristic of the conjugated system of the phenyl radical, this is consistent with the data [21-22]. The observed some bachromic shift in the remaining spectra depends on the nature of the substitute.

To determine the regnospecificity and regnoselectivity of the reaction of 1,3-dipolar cycloaddition of diazomethane to the propargyl ester of n-chlorophenol, fragmentation of molecular ions was carried out under the action of electron impact. Mass spectra of 4- (p-phenoxymethyl) -pyrazole contain molecular ion peaks. The main fragmentation ions are formed by breaking the weakest bond $–O – CH_2–$.

The work considers the mass spectra of 4- (p-phenoxymethyl) -pyrazole. The decay of these compounds under the action of electron impact is very selective and the mass spectra consist mainly of three intense peaks due to the formation of fragment ions. The formation of stable fragment ions is explained by the formation of ions of n-substituted phenols and methylene pyrazole ions with m / z 81, and the intensity of the peak of the latter is maximum in the spectrum. In the strength of the propagation of chlorine isotopes in a ratio of 1:3. So for the compound under consideration, the value of m/z and relative intensities (% of max) of the main fragments correspond to: 208/210 ($M^+$, 15/5), 128/130 (9/3) .81 (100) where $m^+$- is the molecular and he.

Thus, the spectroscopic study of the pyrazole ring makes it possible to judge the position of the molecule, the mutual orientation of atoms and the effect of substitutes in the benzene ring and the intensity of the absorption band.

## Experimental part

### Preparation of 4- (p-chlorophenoxymethyl) -pyrazole

In a flat-bottomed flask with a ground stopper was placed 1.59 g (0.01 mol) of propargyl ether of n-chlorophenol, poured 50 ml of an ethereal solution of diazomethane, the flask with the reaction mixture was placed in a place protected from light at room temperature. As the color of diazomethane became discolored, portions were added over a period of three days. After a lapse of time, the solvent was evaporated, the product after three times recrystallization from benzene and hexane taken in a ratio of 1: 2 has so.pl. 101-102$^o$C. TLC was performed using a petroleum ether – benzene system (1: 2). Rf 0.36. Yield 1.7 (81.3%). $C_{10}H_9N_2ClO$. Found: C 57.51; 57.52; H 4.25; 4.27; N 13.48; 13.34%. Calculated: C 57.55; H 4.32; N 13.42%.

Thus, pyrazole derivatives were obtained by the reaction of 1,3-dipolar cycloaddition of the propargyl ether of substituted phenols with diazomethane.

Analysis of the obtained mass spectroscopic data and IR, PMR, UV spectroscopic data of the compounds indicates the formation of a zanoproduct of the reaction.

## REFERENCES

1.Pechmann H.V. Pyrozolausacetilen und Diazomelkan. Ber. 1898. Br/ 31. S. 2950-2951.

2.Huisgen R.1,3-Dipolar Cycloaddittonen.-And.Chem. 1969.v.75.P.604-637.

3.Hussigen R. KinetikandMechanisme 1,3-Dipolar Cycloaddittonen. -And.Chem.1963. v.75.p.743-754.

4.HusigenR.On the Mechanisim of 1,3-Dipolar Cycloaddittos. -Org.Chem.1969. v.33.p.2291.

5. HusigenR.FerschriftzurZchnjahresfer des Fonde der chemieche-nindustrie.-Dusseldorf. 1960.p.73.

6.Ledwith A.1,3-Dipolar CycloadditionReastione of Diascalkanes. Substituent Effecte.cn the kinnettes of ReactioneBetween Diazomethane and some unsaturatedBeters. Chem. Soc. 1967. №1. p.84-85.

7. Ried W. Omran I. 3- Acyl-PyrazoleausDiazoketonen und monosubetituieztenAlkinen. Lieb.Ann., 1963,v.666.p.144-147.

8.Day A.,WittinngM.Allens and 1,3- Dienies from the photolysis of Pyrozolenines. ChemCommen.1965.

9. TzugeO.Shinkai I. Koga M. Renction of 2-Diazoacenaphthenone With ozefine and Acetylenes J. Org. Chem., 1971.v.36. № 6. P. 745-749.

10.Huttel R. Riedel. J. Matin A. Eranke K. Unsetzung von Acetylen-derivatenmitdisubsutituiertenDiazometanverbindungen.Chem. Ber., 1960, v. 93.p.1425

11.Huttel R., Franke K., Martin H., Riedel J. ZurKenntine der Umlagerung 3,3-disubstituierterv Pyrazolenine.- nChem. Ber. -1960. V.93. p.1433.

12.Makhsumov A.G., Yunusova D.F., Madikhanov N., Abdugafurov I.A. Chemistry of acetylene II. Synthesis of pyrazolederivatives.Scientific Bulletin of Andijan State University.Andijan.2011.No. 2. P. 031-36.

13.VinokurovV.G., TrotskayaV.S., SolokhinaN.D., GrandbergI.I. IRspectraof 4-acetylpyrazoles, theirsaltsandmetalderivatives.Journal of Organ Chemistry, 1963, vol. 33, pp. 506-510.
14.Bellamy L. Infrared spectra of complex molecules. Moscow, 1963.-243s.
15. Shuster Ya.A., Kozlova V.A. Seraya V.I. Spectrophotometric study of some N-substituted 3 (5) -methylpyrazole and their complexes with CuCl.Chemistryofheterocycle. connection.1974. No. 12.1585-1728.c.
16.Makhsumov A.G., Yunusova D.F., Ibragimov.Kh.G., Nasrdinov S.D. Synthesis spectroscopic study of pyrazole derivatives. Dokl. AcademyofSciencesofUz.SSR. 1970. # 1.s.48-50.
17.Makhsumov A.G., Yunusova D.F., Madikhanov N., Nasrdinov S.D. Synthesis and antimicrobial activity of pyrazole derivatives. Fiziol.active substances."NaukovaDumka" Kiev. 1979.No.11.p.101-103.
18.Makhsumov A.G., Zakirov U.B., Yunusova D.F., Madikhanov N.
S.D. Anti-inflammatory activity of halogenated 4-aryloxymethylpyrazoles. Fiziol.active substances."NaukovaDumka" Kiev. 1984, No. 16, pp. 68-69.
19.Zhunke A. Nuclear magnetic resonance in oranic chemistry. M.: MIR. 1974.175
20.Dyer John R. Applications of adsorption spectroscopy of organic compounds. M. Chemistry. 1970, 163, p.
21.Mayson S.F. In kN, Physical methods in the chemistry of heterocyclic compounds ML: Chemistry. 1966, p. 370.
22.Grandberg I.I. Tabak S.B., Kost A.A. UV and fluorescence spectra of some 1-phenyl pyrazoles. Ortho-effect of substituents at position 5.Chemistry of Heterocycle Compounds.1965.No. 6. P. 901-908.