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Method for the Synthesis and Bioavailability of Phenol-4-Methoxyphenoxyacetate by Nucleophilic Exchange Reaction

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Abstract

Phenol was first carried out in the presence of catalytic iron salts and the composition of the resulting product was determined. The reaction mechanism suggested. Research has been conducted to synthesize the individual substance and a method for the synthesis of phenylchloroacetate in benzene solution has been developed. Reactions with 4-methoxyphenol under different conditions were carried out in order to synthesize a new organic substance. As a result of the research, a new organic substance phenyl-4-methoxyphenoxyacetate was synthesized and its structure was proved by physicochemical methods. This substance has been proven to have biological activity.

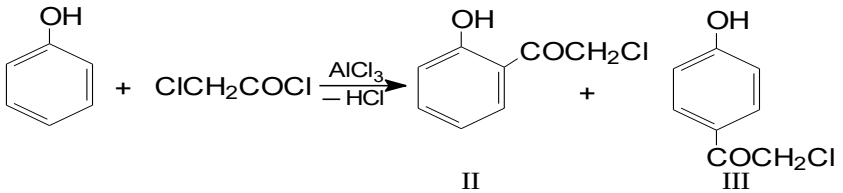
Keywords: phenol, acylation, catalyst, temperature, chloroacetyl chloride, gas-liquid chromatography, complex, electronegative, synthesis, biological, vacuum, bactericidal, fungicide, extraction

Introduction

German scientists carried out the reaction of chloroacetylation of phenol in the presence of $AlCl_3$, in a solution of CS_2 at 0^0 , and found that the O-acidification reaction took place to form phenylchloroacetate:

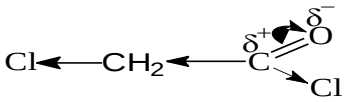
I

British scientists [1-2] also carried out the same reaction at higher temperatures (10-20 ^{0}C) and in excess phenol, where the S-acidification reaction took place and 2- and 4-hydroxyphenacylchlorides were formed:



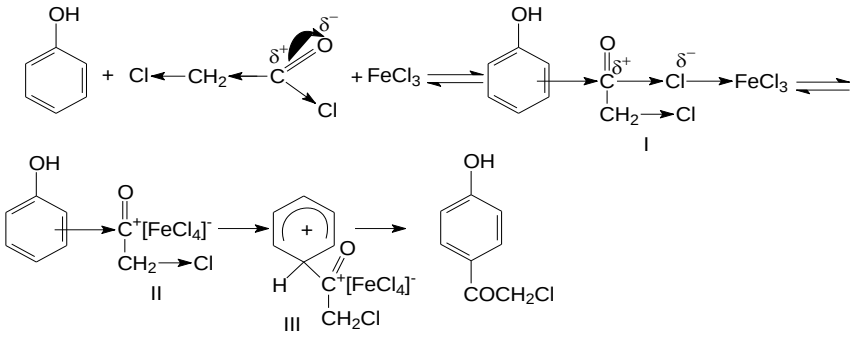
II III

In the study of the chloroacetylation reaction, we used chlorohydride of chloric acid as an aqueous agent. This is because, on the one hand, most of the compounds held by the chloroacetyl group have high biological activity, while on the other hand, it is a strong acytic agent. This is because the carbon atom in the carbonyl group has an additional positive charge due to the induction effect of the halogen in chloroacetyl chloride.

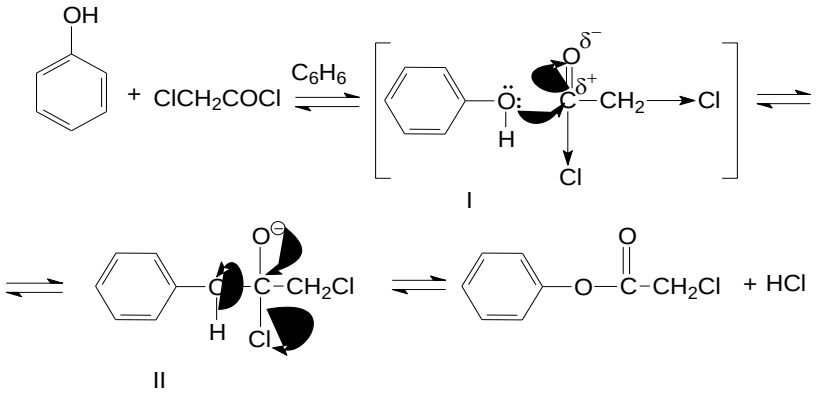


and facilitates the course of the electrophilic exchange reaction.

In order to study in more detail the course of the chloroacetylation of phenol, it was carried out only in solvents without solvents and catalysts in the presence of catalytic amounts of $FeCl_3$, $FeCl_3 \bullet 6H_2O$,$Fe_2(SO_4)_3$, TAA. When the reaction product was examined by gas-liquid chromatography, it was found that 15% phenylchloroacetate and 85% 4-hydroxyphenacyl chloride were formed [3-4]. Given the charge distribution in the s-complex formed during electrophilic exchange in the aromatic ring, the -OH group in the phenol nucleus is more exposed to this complex when directed to the p-state, and therefore p-hydroxyphenacyl chloride is formed. The reaction mechanism is as follows:

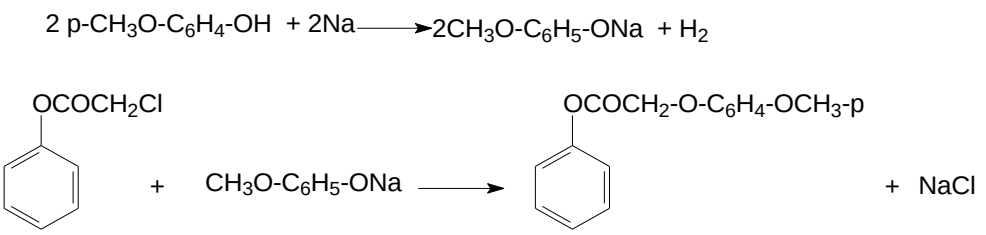


Phenol chloroacetylation reaction abs. when carried out in benzene solution only the O-acylation reaction takes place and phenylchloroacetate is formed with 94% yield. The scheme of formation of phenylchloroacetate can be described as follows [115]:



During the reaction of phenol and chloroacetyl chloride, the electron density in the chloroacetyl chloride molecule shifts toward electromagnetic oxygen, and the oxygen has a partially negative charge. As a result of the action of electromagnetic chlorine and oxygen atoms, the carbon atom has a partially positive charge and interacts with the double electrons of the hydroxyl group in the phenol molecule to form complex I. During the reaction, a valence bond is formed between oxygen and carbon, forming Complex II, from which the reaction product with hydrogen chloride is separated.

Nucleophilic exchange reactions with 4-methoxyphenol were carried out to synthesize new substances based on phenylchloroacetate and to study their biological properties, and a new organic substance phenyl-4-methoxyphenoxyacetate was synthesized.



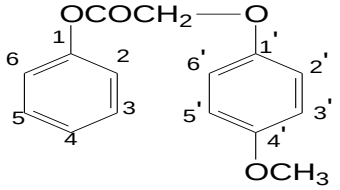
Solvent: dimethylformamide, benzene; Conditions for obtaining

Methodology

GSX, IR-, PMR-spectra The products of the chloroacetylation reaction of phenol in the presence of catalytic catalysts were also analyzed in LXM-8-MD equipment under the following conditions: column length 2 m, stationary phase 20% apiezon L cellite, column and detector temperature 1500S, hydrogen velocity 25 ml /min.

The IR spectrum of the ether synthesized on the basis of phenylchloroacetate tolylchloroacetates was obtained in the form of a cake with potassium bromide on Philips PYE Unicam SP 3-080 [5]. PMR spectrum 1) INM-4-H-100 MGTs; 2) Tesla 567 100 MHz; 3) Option XL-100 was written using TMS and GMDS internal standards on MGTs (solvent CCl_4, CD_3Cl) equipment.

Table 1. IR-PMR spectra of synthesized phenyl-4-methoxyphenoxyacetate.

Structural formula of phenyl-4-methoxyphenoxyacetate	
IQ spectrum (ν, sm^{-1})	$\nu_{c=o}$=1777, $\nu_{c=c}$=1600, 1588, ν_{c-o-c}=1071, 1159, 1254 $\nu_{=CH}$=3007, 3061, $v^{as}CH_2CH_3$=2993, 2971 δ_{CH} = 856, 845 (1,4 rep.) (mono rep.) $\delta^{s}CH_3$=1348, $\delta^{as}CH_3$=1463, $v^{s}CH_2CH_3$=2837
PMR spectrum (δ м.у)	δOCH_3=3,72 m.sh. (d), $\delta COCH_3$=4,86 m.sh. (s), δ_{Ar-CH}=6,73-7,41 m.sh. (m)

Biological activity of phenyl-4-methoxyphenoxyacetate.

One of the technical crops in the Republic of Uzbekistan is cotton. In recent years, due to climate change, root rot and Gonorrhea have become widespread in cotton varieties. This leads to a decrease in productivity.

The synthesized substance is a microorganism that causes homozygous disease — Xantamanas malvacearum E bacterium and a microorganism that causes black root disease — Th. Basicola has been tested against black root rot.

Table 2. Biological activity of phenyl-4

№	The name of the substance	The zone of growth inhibition of microorganisms as a

		percentage.	
		X. malvacearum E (bactericidal)	Th. Basicola (fungitcide)
1.	phenyl-4-methoxyphenoxyacetate	49	62
2.	Comparative “Fentiuram”	41,2	45

The test results showed that the bactericidal and fungicidal properties of the synthesized phenyl-4-methoxyphenoxyacetate were more active than the comparator.

Experimental Part

Experiment № 1. Chloroacetylation of phenol.

9.4 g (0.1 mol) phenol, 11.3 g (0.1 g mol) chloroacetyl chloride, 0.04 g (2.5 (10-4 g mol) $FeCl_3$ mixture at 118-1200C for 3 hours heated. Phenol, which did not react after the cessation of hydrogen chloride gas. Then 13.6 g (80%) of the main product was driven at 138-140^{0}C / 30 mm wire. Gas-liquid chromatography showed that the reaction product consisted of phenylchloroacetate and 85% 4-hydroxyphenacyl chloride. When the chloroacetylation reaction of phenol is carried out in the presence of temiracetylacetonate (TAA), a single substance, 4-hydroxyphenacyl chloride, is formed. The reaction yield is 83%. T. liquid (148^0. 148 ^{0}C) according to the literature [6].

Experiment № 2. Obtaining phenylchloroacetate

a) In a round flask with a return cooler, 9.4 g (0.1 g-mol) of phenol was dissolved in 30 ml of pyridine and 11.3 g (0.1 g-mol) of chloroacetyl chloride was added. The reaction mixture was boiled and turned dark red during boiling. To it was added 10 ml of dilute sulfuric acid solution and cooled with ice water. The reaction product was separated as an oily substance. To separate the pyridine from the mixture, a solution of diethyl ether and dilute acid was added. The ether portion was separated and dried with $CaCl_2$. After the solvent was pumped, phenylchloroacetate was pumped under vacuum. The reaction yield was 10.2 g (60%). T.boil. 120-122^{0}C / 20 mm. sim. ust.

b) 9.4 g (0.1 g-mol) phenol, 50 ml abs, in a round tube with a tube fitted to the return refrigerant for the release of hydrogen chloride. dissolved in benzene, 11.3 g (0.1 g-mol) of chloroacetyl chloride was added and boiled for 10 h. After the hydrogen chloride output was stopped, the mixture was washed in alkaline water, extracted in benzene, and dried in $CaCl_2$. Benzene is under normal conditions, and the substance in vacuum is 120-122^0 / 20 mm. sim. ust. drove in.

c) 14.1 g (0.15 g-mol) of phenol, 5.65 g (0.05 g-mol) of chloroacetyl chloride, 8.01 g (0.05 g-mol) of AlCl3 at 00S by the above method 5.95 g (70%) of phenylchloroacetate was synthesized. T.qayn. 120-122 ^{0}C / 20 mm. sim. ust.

Gas-liquid chromatogram of the substances obtained by the three methods was analyzed on LXM-8MD equipment under the following conditions: column length 2 m, stationary phase 20% apiezon L cellite, column and detector temperature 150 ^{0}C, hydrogen velocity 25 ml / min. GSX showed that the product obtained by the three methods contained 1 substance, and its physical constants correspond to the data on phenylchloroacetate in the literature.

Experiment № 3. Synthesis of phenyl-4-methoxyphenoxyacetate

a) 4.71 g (0.038 g-mol) of 4-methoxyphenol was added to a two-mouth flask fitted with a return cooler and stirrer and dissolved in 50 ml of absolute benzene. A small amount of 0.9 g (0.038 g-atom) of purified sodium metal was placed on top of it. After the reaction slowed, the mixture was heated in a water bath for 6 h. A hungry blue precipitate formed. Then 6.48 g (0.038 g-mol) of phenylchloroacetate was added dropwise and the reaction mixture was boiled for 8 h.

The completion of the reaction was determined using a Belshtein sample. The reaction mixture was washed in alkaline water, extracted three times in benzene, and dried with $CaCl_2$. After benzene was pumped in a water pump, the product was pumped in a vacuum. Phenyl-4-methoxyphenoxyacetate yielded 5.97 g (61%). T.boil. 215-220^{0}C (16 mm.sim. Ust. T. liquid. 76-78 ^{0}C (alcohol).

b) 25 ml of DMFA 4.71 g (0.038 g-mol) 4-methoxyphenol was added to the flask and 0.9 g (0.038 g-atom) of the purified sodium metal was gradually added to it. During the reaction, the solution turned a reddish color. The reaction lasted 15 minutes. The reaction mixture was cooled, 6.48 g (0.038 g-mol) of phenylchloroacetate was added slowly, and the reaction mixture was boiled for 6 h. At the end of the reaction, the product was filtered and separated T.boil. 215-220^{0}C (16 mm. Mm.sim. Ust. T. liquid. 76-78^{0}C (alcohol).

Calculated%: C 69.76; H 5.48. $C_{15}H_{14}O_4$

Found%: C 69.80; H 5.50. $C_{15}H_{14}O_4$.

REFERENCES

Cullinane N.M., Edwards F.R. Comparison of the Fries and Friedel-Crafts reactions ??J.Appl. Chem. -1959. -Vol. 9. -P.133-136.

Dorofenko. G.N. and other Preparative chemistry of pyrillic salts. Rostov on Dono. Ed. Rostov University. Issue 1.-1972.-250 p

Tojimuhamedov.H.S., Shohidoyatov H.M. Reactivity of organic compounds. Part II. Mechanisms of organic reactions. Tashkent. "ABU Ali Ibn Sino". -2001. -210 b.

Mamatkulov N.N., Abdushukurov A.K. Chloroacetylation of o-cresol in the presence of small amounts of catalysts // Chemistry of Natural Sciences. connect. -Tashkent. -1999. Special issue. -FROM. 74-75.

V.A. Mironov, S.A. Yankovsky. Spectroscopy in organic chemistry Moscow: Chemistry, 1985. -232 p.

Cullinane N.M., Edwards F.R. Comparison of the Fries and Friedel-Crafts reactions ??J.Appl. Chem. -1959. -Vol. 9. -P.133-136.

Н.К.Мадусмонова, З.А.Сманова, И.И.Жураева Свойство нового аналитического реагента 2-гидрокси-3-нитрозонафтольдегида//ЖАХ том 75 №1, 2020, с. 92-96.

Kist JA, Zhao H, Mitchell-Koch KR, Baker GA. The study and application of biomolecules in deep eutectic solvents. Journal of Materials Chemistry B. 2020.

Feng J, Hse CY, Wang K, Yang Z, Jiang J, Xu J. Directional liquefaction of biomass for phenolic compounds and in situ hydrodeoxygenation upgrading of phenolics using bifunctional catalysts. Energy. 2017 Sep 15;135:1-3.

Long J, Zhang Q, Wang T, Zhang X, Xu Y, Ma L. An efficient and economical process for lignin depolymerization in biomass-derived solvent tetrahydrofuran. Bioresource technology. 2014 Feb 1;154:10-7.