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AZOTLI ORGANIK BIRIKMA PIRIDINNING N-OKSIDINI OLISHNI OPTIMALLASHTIRILGAN SHAROITLARI VA REAKSION MEXANIZMI

Аннотация

Ushbu maqolada piridin hosilalarining qishloq xo'jaligi, tibbiyot va sanoatdagi qo'llanilishi hamda ularni olishning zamonaviy sintetik usullari yoritilgan. Piridin π -elektron tanqis geterosiklik birikma sifatida elektrofil reaksiyalarga nisbatan past reaktivlikka ega ekanligi va uning oksidlanish jarayonlari sharoitga bog'liqligi tahlil qilingan. Tadqiqotda piridinni vodorod peroksid va chumoli kislotaga ishtirokida oksidlash reaksiyasi o'rganilib, piridin N-oksid hosil bo'lish mexanizmi bosqichma-bosqich izohlangan. Reaksiya sharoitlarining (harorat, vaqt va reagentlar nisbati) mahsulot unumiga ta'siri aniqlanib, optimal sharoit sifatida 80°C harorat va 12 soat davomiylikda 84–86% gacha unumga erishilganligi ko'rsatilgan. Olingan mahsulotning tuzilishi IQ-spektr tahlili orqali tasdiqlangan. Natijalar piridin N-oksidlarini samarali olish uchun qulay va optimallashtirilgan usul mavjudligini ko'rsatadi. **Kalit so'zlar:** Piridin, vodorod peroksid, chumoli kislotaga, piridin oksid, peroksiformil kislotaga, reaksiya mexanizmi.

ОПТИМИЗИРОВАННЫЕ УСЛОВИЯ ПОЛУЧЕНИЯ N-ОКСИДА АЗОТСОДЕРЖАЩЕГО ОРГАНИЧЕСКОГО СОЕДИНЕНИЯ ПИРИДИНА И РЕАКЦИОННЫЙ МЕХАНИЗМ

Аннотация

В данной статье рассматриваются применение производных пиридина в сельском хозяйстве, медицине и промышленности, а также современные синтетические методы их получения. Проведен анализ низкой реакционной способности пиридина как π -электронодефицитного гетероциклического соединения по отношению к электрофильным реакциям и зависимости его окислительных процессов от условий реакции. В исследовании изучена реакция окисления пиридина в присутствии перекиси водорода и муравьиной кислоты, а также поэтапно описан механизм образования N-оксида пиридина. Установлено влияние условий реакции (температура, время и соотношение реагентов) на выход продукта, при этом оптимальными условиями являются температура 80°C и продолжительность реакции 12 часов, обеспечивающие выход до 84–86%. Структура полученного продукта подтверждена методом ИК-спектроскопии. Результаты показывают, что существует эффективный и оптимизированный метод получения N-оксидов пиридина.

Ключевые слова: Пиридин, перекись водорода, муравьиная кислота, пиридин-N-оксид, пероксиформилиновая кислота, механизм реакции.

OPTIMIZED CONDITIONS FOR THE SYNTHESIS OF PYRIDINE N-OXIDE AS A NITROGEN-CONTAINING ORGANIC COMPOUND AND ITS REACTION MECHANISM

Annotation

This article discusses the applications of pyridine derivatives in agriculture, medicine, and industry, as well as modern synthetic methods for their preparation. The low reactivity of pyridine as a π -electron-deficient heterocyclic compound toward electrophilic reactions and the dependence of its oxidation processes on reaction conditions were analyzed. The study investigates the oxidation of pyridine in the presence of hydrogen peroxide and formic acid, and the step-by-step mechanism of pyridine N-oxide formation is described. The influence of reaction conditions (temperature, time, and reagent ratio) on product yield was determined, with optimal conditions identified as 80°C and 12 hours, achieving a yield of 84–86%. The structure of the obtained product was confirmed by IR spectroscopic analysis. The results demonstrate an efficient and optimized method for the synthesis of pyridine N-oxides.

Key words: Pyridine, hydrogen peroxide, formic acid, pyridine N-oxide, peroxyformic acid, reaction mechanism.

Introduction. Derivatives of nitrogen-containing organic compounds are widely used in various fields of agriculture and industry. They are important as insecticidal and fungicidal agents, as well as herbicides with selective and stable effects. In addition, these compounds play a significant role in the synthesis of monomers and polymers, in the production of oil additives, as corrosion inhibitors for metals, and as extractants in the process of recovering precious metals. They are also used as stabilizers and in suspension systems.

Nitropryrin and 2-chloro-6-(trichloromethyl)pyridine act as stabilizers that help maintain the stability of nitrogen fertilizers in soil. Based on these compounds, a number of biologically active preparations have also been developed. Among them, drugs such as ftivazid, saluzid, and metazid, which are used in the treatment of tuberculosis, occupy an important place. [1–3].

The wide practical application of pyridine derivatives has significantly increased interest in methods for synthesizing compounds of this class. As a result, since the second half of the last century, numerous research studies in this field have been published in foreign scientific literature. These studies extensively describe the use of carbonyl compounds, including aldehydes and ketones, as well as ammonia, as the main raw materials for obtaining pyridine structures.

Among heterocyclic compounds, pyridine is considered a π -electron-deficient (π -poor) system. For this reason, it does not readily undergo reactions with electrophilic reagents. In particular, in acidic media, pyridine becomes protonated and is converted into the pyridinium ion, which has an even greater deficiency of π -electrons. As a result, its reactivity in electrophilic substitution reactions is significantly lower compared to aromatic hydrocarbons. Pyridine can react only with very strong electrophiles and under strictly controlled, optimal conditions.

This property can be explained by its tendency to form complex compounds with various functional groups. In this regard, the oxidation processes of pyridine are of particular importance and are typically carried out in a system involving pyridine, hydrogen peroxide, and acetic acid.

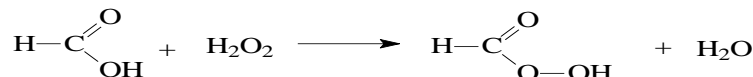
The oxidation of pyridine was carried out in a system consisting of pyridine, hydrogen peroxide, and formic acid. Initially, when the experiment was conducted at a temperature close to room temperature (20°C) for 4 hours, the reaction yield was found to be 40%.

In the next stage, it was observed that an increase in temperature had a significant effect on the course of the reaction. As the temperature was raised, an increase in product yield was recorded. Based on the experimental results, the optimal conditions were determined to be a temperature of 80°C and a reaction time of 12 hours. Under these conditions, the reaction yield was found to reach up to 86%.



Mechanism of pyridine oxidation in the presence of formic acid and hydrogen peroxide. The oxidation of pyridine to pyridine N-oxide in the presence of hydrogen peroxide and formic acid proceeds through performic acid formed during the reaction. The process consists of two main stages.

In the first stage, hydrogen peroxide and formic acid interact with each other to form a highly reactive oxidizing agent in equilibrium - performic acid (HCOOOH):



The formed performic acid has electrophilic properties and acts as an oxidizing agent in the next stage.

In the second stage, the lone electron pair of the nitrogen atom in the pyridine molecule performs a nucleophilic attack on the terminal oxygen atom of performic acid. As a result of this attack, the O–O peroxide bond is cleaved, and simultaneously an N–O bond is formed. Consequently, pyridine N-oxide and formic acid are regenerated.



This mechanism corresponds to the classical electrophilic oxidation process of heterocyclic amines via peroxyacids. In this case, formic acid plays not only the role of a reaction medium component but also a crucial role as a reagent that generates the active oxidizing species - performic acid.

Due to the high reactivity of performic acid, the process generally proceeds rapidly; however, this also increases the likelihood of side reactions. Therefore, strict control of reaction conditions (temperature, reagent ratios) is required.

The influence of various factors on the reaction progress, including temperature, reaction time, and molar ratios of the starting materials, was investigated. The interaction of these parameters was found to have a direct effect on product yield, as clearly demonstrated by the experimental results.

Table 1

Variation of reaction yield under different temperatures and reaction times

Reagents	Reaction time (hours)	Temperature (°C)	Reaction yield (%)
1. Pyridine	4	20	40
2. Formic acid	6	30	45
3. Hydrogen peroxide	8	50	65
	10	70	80
	12	80	86

The yields of products synthesized under different molar ratios and reaction conditions were determined as percentages, and the obtained results were presented in the form of a table and a graph. This enabled the identification of optimal conditions and the evaluation of reaction efficiency (Table 1 and Figure 1).

Methods and materials

Method for the synthesis of pyridine N-oxide. To a mixture consisting of 160 mL of formic acid and 30 mL of a pyridine solution, 75 mL of a 30% hydrogen peroxide (H₂O₂) solution was added. The resulting reaction mixture was then stirred continuously using a magnetic stirrer at 80°C for 12 hours. After completion of the reaction, the mixture was cooled to room temperature, and the excess formic acid was removed by evaporation using a rotary evaporator (rotavap).

The remaining residue was further processed using two methods.

a) The remaining portion of the reaction mixture was neutralized to pH 8 using 100 mL of a saturated aqueous sodium carbonate (Na_2CO_3) solution and solid potassium carbonate (K_2CO_3). The resulting solution was then extracted with ethyl acetate (75 mL, 4% solution). After separation of the organic layer, it was washed with saturated sodium chloride (NaCl) solution (100 mL) and dried over anhydrous sodium sulfate (Na_2SO_4). The dried solution was concentrated using a rotary evaporator, after which the obtained product was vacuum-distilled and recrystallized using an appropriate solvent.

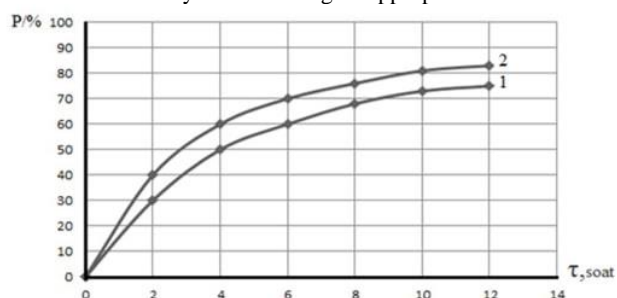


Figure 1. Difference in product yield obtained from pyridine and formic acid at different molar ratios under the same temperature and reaction time conditions: 0.5 : 1.5 mol, 0.3 : 2 mol

b) After completion of the reaction, the resulting mixture was diluted with 100 mL of acetone. The precipitate formed was then isolated by filtration. The obtained solid was subsequently washed with a mixture of acetone and hexane (1:1 ratio). Finally, the product was dried under vacuum at 40°C for 3 hours.

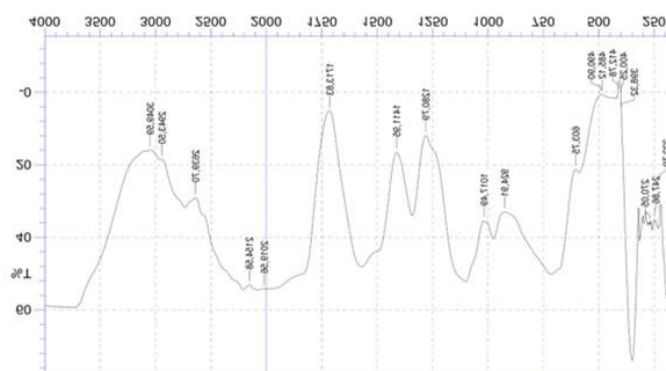


Figure 2. IR spectrum of pyridine N-oxide

According to the obtained results, when the initial molar ratio of reactants was 0.3:2 mol, the product was formed with an 86% yield at a reaction time of 12 hours. The optimal conditions for the formation of pyridine N-oxide were determined to be a temperature of 80°C and a reaction time of 12 hours.

In order to determine the structure of the synthesized pyridine N-oxide, IR spectral analysis was performed, and the results are presented in Figure 2.

According to the obtained IR spectral data, pyridine N-oxide exhibited the following absorption bands (cm^{-1}): (C–C) 1404; $\nu(\text{C–N})$ 1273; $\nu(\text{C–H})$ 3049; $\nu(\text{C=C})$ 1713; and the asymmetric stretching vibration of the NO group at 1014 cm^{-1} .

Conclusion. During the synthesis of the nitrogen-containing organic compound pyridine N-oxide, the properties of the initial reagents and the course of the reaction mechanism were studied in relation to temperature, time, and product yield. In this study, the oxidation of pyridine was carried out in a system containing pyridine, hydrogen peroxide, and formic acid. Initial experiments conducted at conditions close to room temperature (20°C) for 4 hours showed a reaction yield of 40%.

In subsequent stages, it was observed that an increase in temperature had a significant effect on reaction efficiency. Based on the obtained results, the optimal conditions were determined to be a temperature of 80°C and a reaction time of 12 hours, under which the product yield reached 86%. In addition, the influence of the molar ratios of the starting materials and various reaction conditions on the reaction yield was systematically investigated. The obtained results were presented in the form of tables and graphs showing percentage product yields.

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