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SYNTHESIS OF PYRIDINE BASED COMPOUNDS CONTAINING DIFFERENT FUNCTIONAL GROUPS.

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Abstract : In general, the results of the research carried out in this article provide a comprehensive description of synthesized nitrogen-containing organic substances. They also allow, to a certain extent, to evaluate the purity and individuality of each of these products separately, as well as to compare them with other compounds of similar classes. It has been shown that in the case of 3-substituted pyridine-N-oxides, the reaction under study is regioselective and can be used for the targeted synthesis of pyridinyl ureas containing a substituent in position 5 of the pyridine ring.

Keywords: pyridine, 3-substituted pyridine-N-oxides, 4-nitropyridine 1-oxide., IR spectroscopy.

INTRODUCTION

Pyridines are one of the most common heterocycles, the derivatives of which are widely used in pharmaceuticals, agrochemistry, and also in the production of new materials [1]. Pyridine and piperidine rings are very common structural elements and are found in numerous natural biologically active substances. Thus, pyridine- and piperidine-containing alkaloids represent a wide class of natural compounds with a unique structure and a wide range of biological properties [2–4]. Many of these alkaloids have activities associated with the treatment of cancer, neurological disorders, and other diseases, and continue to be valuable research objects that stimulate the discovery of new drugs [5-9].

Numerous pyridine derivatives act as medicines , herbicides and fungicides [22, 23]. Some of the world's leading drugs, such as esomeprazole, pioglitazone, and eszopiclone, represent only a small part of the huge variety of drugs that contain pyridine derivatives in their structure [24]. A significant number of newly approved drugs in recent years are natural compounds of pyridine or its synthetic derivatives [25].

As follows from the literature review, pyridine nitro derivatives have a variety of chemical properties and great practical value. Modification of their structure by introducing new functional groups makes it possible to obtain new compounds that can act as potential drugs, pesticides, dyes, etc.

RESEARCH METHODS

IR spectra of the starting reagents and synthesized substances were obtained on a SHIMADZU IR-100 spectrometer. Thermoanalytical studies of the synthesized samples were carried out on a Netzsch Simporary Analyzer STA 409 PG instrument (Germany) equipped with a K-type thermocouple and aluminum crucibles (Low RG Silver). Mass spectrometers were obtained using a 6420 TripleQuad LC/MS mass spectrum (Agilent Technologies, USA) using the APCI-ionization method (atmospheric pressure chemical ionization).

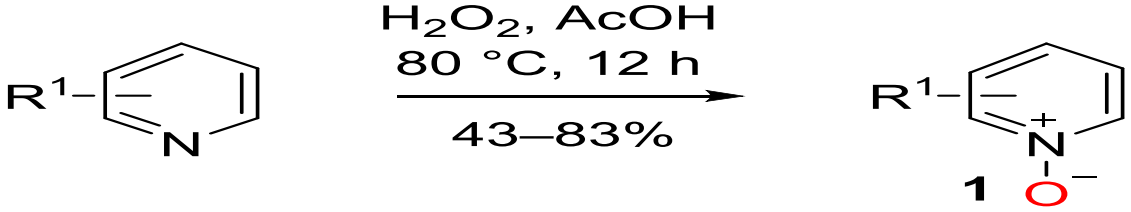
RESULTS.

Synthesis of pyridine-N-oxides

To assess the limits of applicability of the method under study, a wide range of substituted pyridine-N-oxides was synthesized. Most of them were obtained from the corresponding pyridines by their oxidation in a mixture of acetic acid and hydrogen peroxide. An aqueous solution of H_2O_2 (75 ml, 30%) was added to a solution of substituted pyridine (30 g) in glacial acetic acid (160 ml), and the reaction mixture was stirred at 80°C for 12 hours. After that, the solution was cooled to room temperature, and most of the acetic acid was evaporated on a rotary evaporator. The residue was processed according to one of two methods. The rest of the reaction mixture was basified with saturated aqueous Na_2CO_3 (100 ml) and solid K_2CO_3 to pH = 8, and the resulting solution was extracted with EtOAc (4 × 75 ml). The combined organic fractions were washed with saturated aqueous NaCl (100 ml), dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator. The product was distilled in vacuo or recrystallized from a suitable solvent.

All the obtained substances were first thoroughly cleaned from possible impurities. Their purity was evaluated by various chromatographic methods. In addition, their elemental composition was determined. Based on the obtained results, the individuality of the studied products was determined in general. Some directions of their use were determined by certain methods.

The reaction mixture was diluted with acetone (100 ml), the precipitate was filtered off, washed with an acetone/hexane (1/1) mixture, and dried in a vacuum at 40°C for 3 h.



N-oxide pyridine in the IK-spectrum (Fig. 1) the peaks at 1270 cm-1 are spectra related to the tertiary amino group; In the region of 1468 cm-1 and 850 cm-1, absorption frequencies belonging to the N →O group are observed.

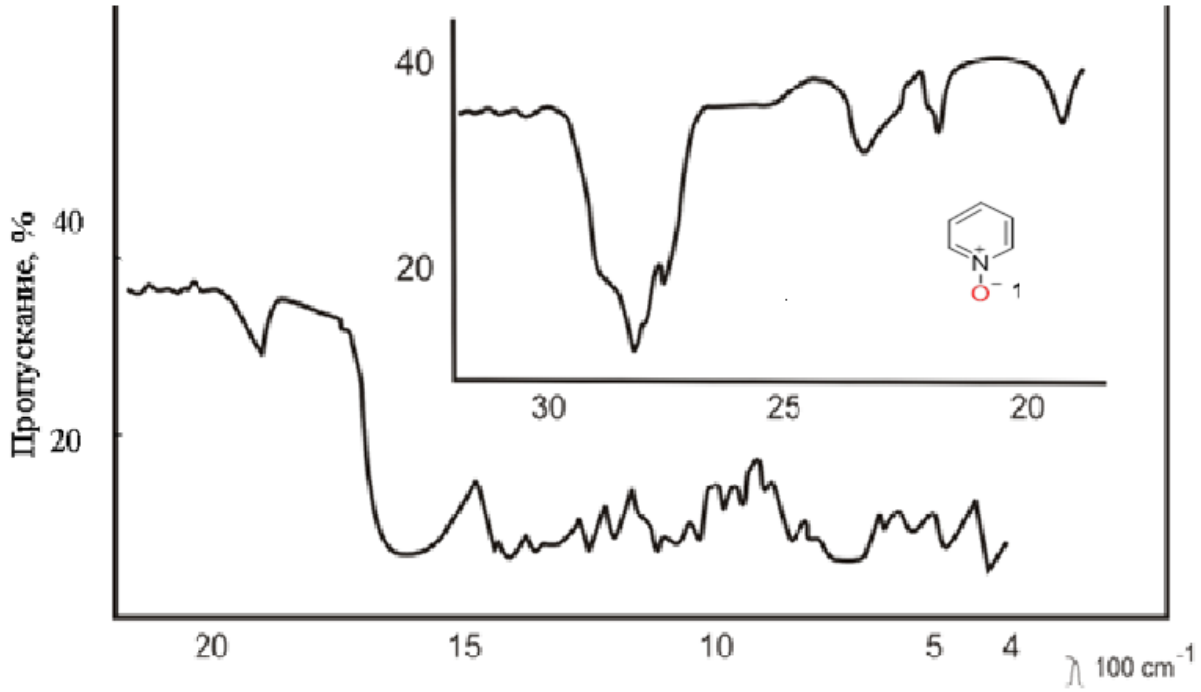


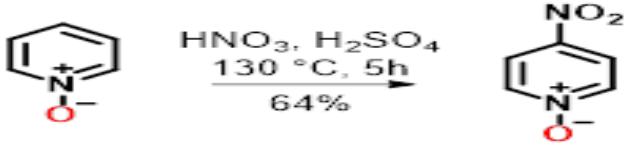
Figure 1. IR spectrum of pyridine N-oxide.

Заключение

Synthesis of 4-nitropyridine 1-oxide.

Fuming HNO3 (12 ml) was slowly added to a solution of pyridine 1-oxide (10.2 g, 107 mmol) in concentrated H2SO4 (23 ml), and the resulting solution was stirred at 130°C for 5 hours. The reaction mixture was poured onto ice, neutralized with saturated Na2CO3 solution, and extracted with CH2Cl2 (3 × 30 ml). The combined organic fractions were dried over anhydrous Na2SO4 and concentrated on a rotary evaporator. The product was recrystallized from acetone. Yield 9.60 g (64%), yellow crystals, mp. = 160.5–161.5 °C, lit. 117 m.p. = 163 °C.

4-Nitropyridine-N-oxide was obtained by nitration of unsubstituted pyridine-N-oxide in a mixture of concentrated sulfuric and fuming nitric acid.



CONCLUSIONS

1. It has been established that substituents in positions 2 and 4 in pyridine-N-oxides do not have a visible effect on the reaction rate. In the case of 3-substituted pyridine-N-oxides, the methoxy group significantly slows down the reaction rate.

2. It has been shown that in the case of 3-substituted pyridine-N-oxides, the reaction under study is regioselective and can be used for the targeted synthesis of pyridinyl ureas containing a substituent in position 5 of the pyridine ring.

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