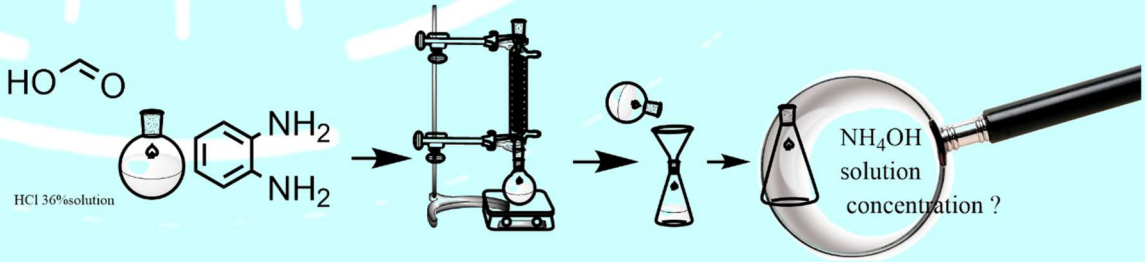
# SYNTHESIS OF BENZIMIDAZOLE BASED ON THE PHILIP METHOD AND THE DEPENDENCE OF THE CONCENTRATION OF AMMONIA SOLUTION ON THE REACTION YIELD

**Tolibjon Egamberdiyev**
*Karakalpakstan Research Institute of Natural Sciences Academy of Sciences*
*PhD student.*
*E-mail: tolibjonchemical@gmail.com*
*Tel:(93) 487 14 46*
**Iqboljon Yuldashev**
*Faculty of Chemistry, PhD, National University of Uzbekistan*
**Toshov Hamza**
*Faculty of Chemistry, PhD, National University of Uzbekistan*
**Gulsara Berdimbetova**
*Karakalpakstan Research Institute of Natural Sciences, Academy of Sciences,*
*Senior researcher*
*E-mail:Gulsara2@rambler.ru*
*Tel:(90) 727 69 53*
**Alisher Khaitbaev**
*Professor of the National University of Uzbekistan*
*E-mail:polyphenol-10@yandex.ru*
*Tel:(93) 549 99 66*




**Abstract.** The article is devoted to the synthesis of benzimidazole from ophenylenediamine using optimal reaction conditions. The main steps of the process are considered, including the role of the catalyst, the concentration of the precipitate, the reaction time, and other factors affecting the yield and purity of the final product. The concentration of the ammonia solution was studied in different cases and the reaction yield was estimated accordingly. The advantages of the method, such as simplicity and economy, as well as possible disadvantages associated with the use of concentrated acids and precipitants, are described. The optimal reaction parameters are given, ensuring high efficiency of the synthesis of benzimidazole.

**Key words**: o-phenylenediamine , synthesis, benzimidazole, ammonium hydroxide, hydrochloric acid



ISSN 3030-3907

**Annotatsiya.** Maqola optimal reaksiya sharoitlaridan foydalangan holda o-fenilendiamindan benzimidazol sinteziga bag‘ishlangan. Jarayonning asosiy bosqichlari, jumladan, katalizatorning roli, cho‘kma konsentratsiyasi, reaksiya vaqti va yakuniy mahsulotning hosildorligi va sofligiga ta’sir qiluvchi boshqa omillar ko‘rib chiqiladi. Ammiak eritmasining konsentratsiyasi turli holatlarda o‘rganildi va reaksiya unimdorligi shunga mos ravishda baholandi. Usulning soddaligi va tejamkorligi kabi afzalliklari, shuningdek, konsentrlangan kislotalar va cho‘ktiruvchilardan foydalanish bilan bog‘liq mumkin bo‘lgan kamchiliklari tasvirlangan. Benzimidazol sintezining yuqori samaradorligini ta’minlaydigan optimal reaksiya parametrlari keltirilgan.

**Kalit so‘zlar**: o-fenilendiamin, sintez, benzimidazol, ammoniy gidroksid, xlorid kislota

**Аннотация.** Статья посвящена синтезу бензимидазола из о-фенилендиамина с использованием оптимальных условий реакции. Рассмотрены основные стадии процесса, включая роль катализатора, концентрацию осадка, время реакции и другие факторы, влияющие на выход и чистоту конечного продукта. Изучена концентрация раствора аммиака в различных случаях и оценен выход реакции. Описаны преимущества метода, такие как простота и экономичность, а также возможные недостатки, связанные с использованием концентрированных кислот и осадителей. Приведены оптимальные параметры реакции, обеспечивающие высокую эффективность синтеза бензимидазола.

**Ключевые слова**: о-фенилендиамин, синтез, бензимидазол, гидроксид аммония, соляная кислота

## Introduction

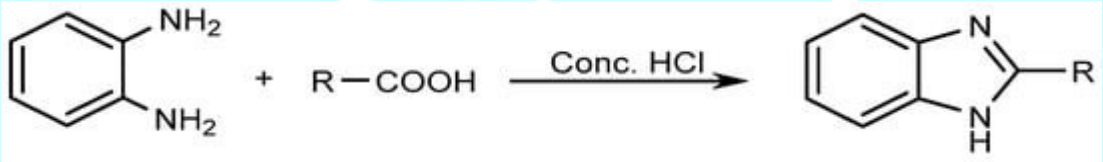
The methods for the synthesis of benzimidazoles have become a focus of synthetic organic chemists, as they are useful building blocks for the development of important therapeutic compounds in medicine Benzimidazole derivatives, which were first discovered in 1944, are a diverse group of nitrogen-containing heterocyclic compounds. The benzimidazole nucleus consists of a benzene ring fused to an imidazole ring. The chemistry of benzimidazole has been an interesting field of study for a considerable time. It is one of the most promising moieties that is present in many clinically useful drugs and possesses various biological activities [1] They have been recognized for their potential as biologically active compounds and have been extensively studied. The benzimidazole nucleus and its derivatives have proven to be valuable therapeutic agents, particularly in the treatment of conditions such as ulcers and parasitic infections. The natural and synthetic source of different benzimidazole derivatives play a vital role in medicinal chemistry. The structure similarity of 2-aminobenzimidazole with purine shed the light on the



ISSN 3030-3907

development of such nucleus for different biological activities.[2] Additionally, these derivatives have demonstrated various pharmacological activities, including antimicrobial, anticancer, anti-inflammatory, and analgesic effects.

The most typical synthetic approach for producing several benzimidazole derivatives is known as Phillip's method, which entails the condensation of o-phenylenediamine (IV) with carboxylic acids (V) itself or its derivatives, and which involves heating the reagents in the presence of concentrated HCl (Scheme 1).[3]




Structure with properties of Benzimidazole
Empirical Formula :C7H6N2
SMILES. C1=CC=C2C(=C1)NC=N2.
InChI Key HYZJCKYKOHLVJF-UHFFFAOYSA-N,
CAS Number:51-17-2
Molecular weight: 118.g/mole

**Materials and methods**

Formic acid - 0.67 ml (0.015 mol)
O – phenylenediamine - 1.08 g (0.01 mol)
Charchol(activated carbon) - 0.15 g
$NH_3$ solution - 10 ml (10%)
Synthesis for Benzimidazole by o-Phenylenediamines:

First, a 50 ml round-bottomed flask was taken, 1.08 g (0.01 mol) of O – phenylenediamine was added to it, then 0.67 ml (0.015 mol) of formic acid was added, and 10 ml of HCl (8 ml of 36% HCl solution mixed with 2 ml of pure distilled water) was poured onto it. Then, the reaction mixture was heated on an electric stove with a reflux condenser at a temperature of 200 ˚C. At this time, a light pink solid salt was formed in the initial reaction mixture, which gradually dissolved over time, changing the mixture to a light yellow color. After heating the reaction mixture for 1 hour, 0.15 g of activated carbon was ground in a mortar and added to the reaction mixture and boiled for 15 minutes. Then, the reaction mixture was filtered, and 10 ml of (10% -20%-25%) $NH_3$ solution was added to the clear solution passed through the filter. When the pH of the solution was 8-9, a white precipitate formed. Then, the precipitate was filtered using a Buncher funnel in a vacuum pump. The separated light yellow substance was taken, placed in a Petri dish and dried thoroughly in a thermostat at 50-60 ˚C.

**Results and discussion**

Thin layer chromatography method


ISSN 3030-3907

The purity of the synthesized benzimidazole was checked by (silufol plate 15x15). A mixture of hexane:ethanol in a ratio of 1:4 was used as the eluent. An iodine chamber was used to detect invisible spots. TLC gave a single spot with an Rf value of 0.83.

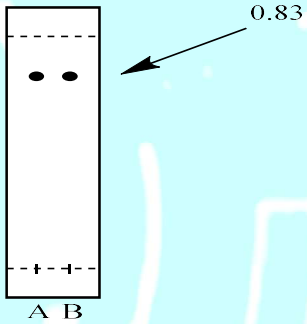



**Figure 1. TLC plate**

IR analysis method

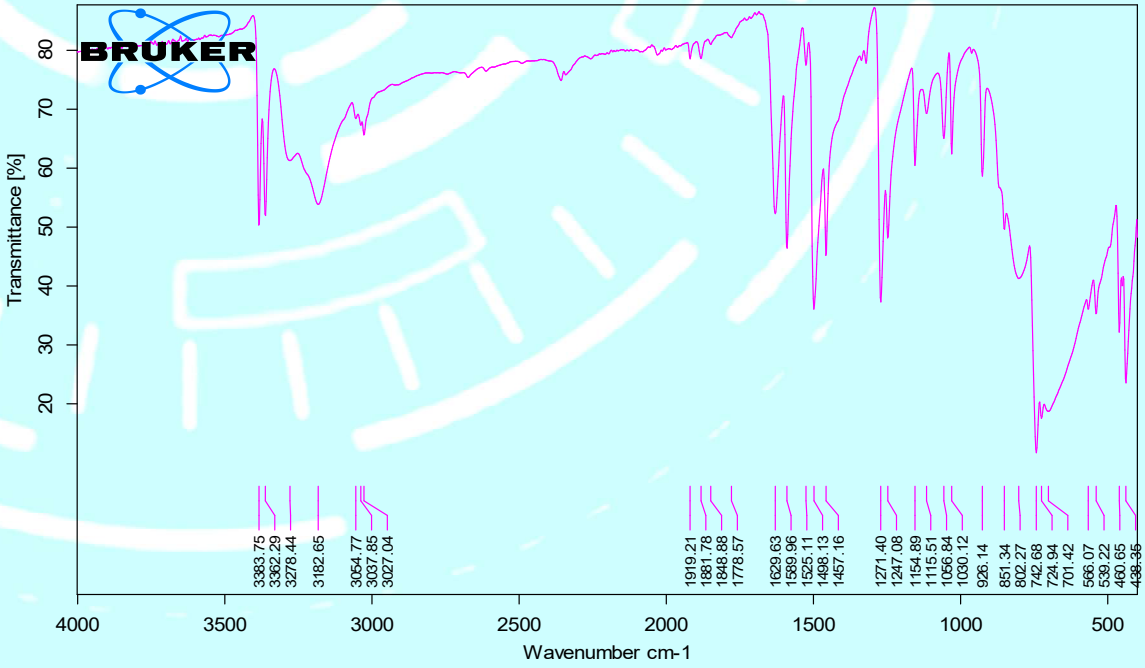



**Figure 2. IR spectrum of o-phenylenediamine**

In the IR spectrum of the obtained o-phenylenediamine, absorption spectra due to the stretching vibrations of the -N-H bond in the primary amino group were observed in the region of 3362-3383 $cm^{-1}$. The absorption spectra of the $sp^2$ hybridized -C-H bond in the aromatic ring appeared in the region of 3054 cm-1. The deformation vibration of the $sp^2$ hybridized -Ar-H bond in the region of 1629.68 cm-1 and the 1,2-substitution of the aromatic ring in the region of 742.68 $cm^{-1}$ can also be observed.


ISSN 3030-3907

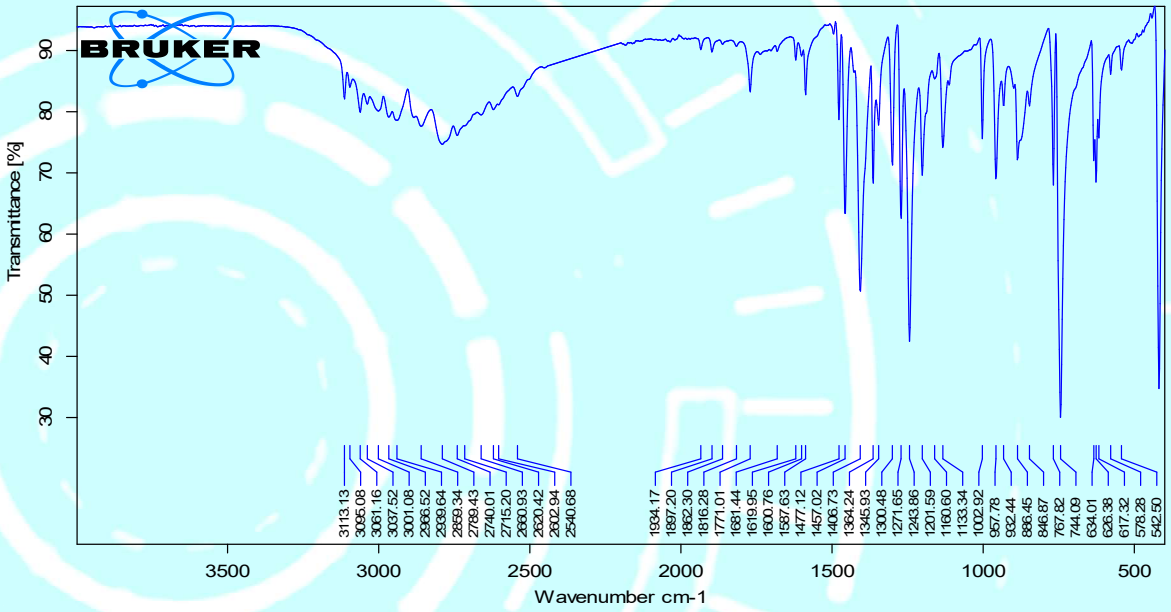



**Figure 3. IR spectrum of benzimidazole**

The disappearance of the absorption spectrum characteristic of the primary amine in the original o-phenylenediamine and the formation of a broadened signal characteristic of the stretching vibrations of the -N-H bond in the secondary amino group of the synthesized benzimidazole in the region of 3113 $cm^{-1}$ were observed. Also, the absorption spectra of the $sp^2$ hybridized -Ar-H bond in the aromatic ring appeared in the region of 3037-3061 $cm^{-1}$.

**Conclusion**

Three different concentrations of ammonia solution were used in the synthesis process: 10%, 20%, and 25%. The highest and optimal value was observed in the 25% ammonia solution.

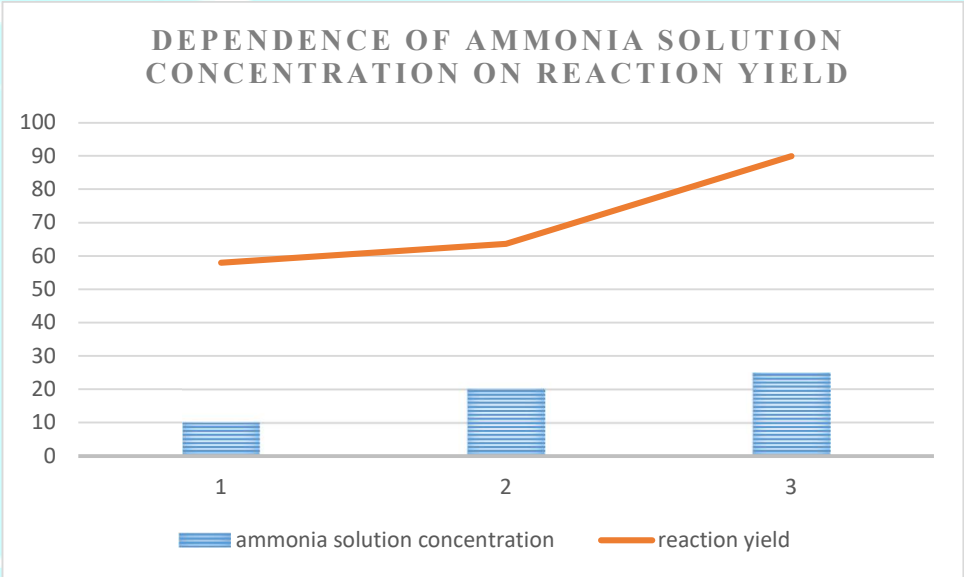



**Figure 4.Dependence of ammonia solution concentration on reaction yield**


ISSN 3030-3907

## REFERENCES

1. Digwal C.S.,Yadav U.,Sakla A.P., Sri Ramya P.V., Aaghaz S., Kamal A., . VOSO4 catalyzed highly efficient synthesis of benzimidazoles, benzothiazoles, and quinoxalines. Tetrahedron Lett.. 2016;57(36):4012-4016.
2. Chen M., Su S., Zhou Q., Tang X., Liu T., Peng F., He M., Luo H., Xue W., Antibacterial and antiviral activities and action mechanism of flavonoid derivatives with a benzimidazole moiety. J. Saudi Chem. Soc.. 2021;25(2):101194.
3. Vijayalakshmi, PB; Haridasan, AP Nelamuchchalaning farmakognostik va dastlabki fitokimyoviy bahosi (Gymnostachyum Febrifugum Benth.). Int. J. Res. Ayush Pharm. Sci. 2017, 1, 1–6.


ISSN 3030-3907