# EFFECTIVE CATALYSTS OF THE SYNTHESIS OF QUINOLINE AND QUINOLINE DERIVATIVES

**A.T. Karimov, L.M. Meyliyeva, H.T. Tilovov, S.J. Kholikova, Kh.I. Kadyrov**

***Tashkent chemical-technological Institute, Republic of Uzbekistan***

**Abstract.** Highly effective and stable catalysts based on d-metal oxides and fluorides were developed, and their selectivity in the synthesis of compacted heterocycles was proven. A unique method for synthesizing quinoline and methylquinolines in the vapor phase was proposed. It was shown that when equimolecular amounts of aniline and acetaldehyde are passed over the catalyst surface at a temperature range of 380-440°C, quinoline derivatives are formed with high yields. The temperature, height of the catalyst layer, and rate of delivery of raw material to the reactor were determined for the yield of quinoline. Additionally, the mechanism of 4-methylquinoline formation, contrary to Scroop's rule, was established.

*Keywords:* condensed heterocyclic compounds, quinoline, alkylquinolines, catalysis, vapor phase, internal diffusion domain, acetaldehyde.

## Introduction.

The production of heterocyclic compounds is currently one of the most important tasks of the organic synthesis industry, and quinoline derivatives occupy a special place among them. Thousands of quinoline derivatives have been synthesized, and most have specific applications. Therefore, an important task is to obtain functional active substances with practical and useful properties by processing quinoline derivatives. In the world, the efficient production of heterofunctional compounds with predetermined properties through in-depth research is being pursued. Intensive scientific research is being carried out on obtaining condensed heterocycles with quinoline fragments that have molecules enriched with nitrogen, oxygen, halogen elements, and through hydrocarboxylation, hydroformylation, carbonylation, sulfurization, provision, and production of organic materials through etherification reactions.

The main goal of the research is to determine the optimal conditions for the synthesis of condensed heterocyclic compounds - quinoline derivatives.

It can be clearly seen that fused multi-ring nitrogen heteroatom heterocyclic compounds, including quinoline derivatives, exhibit antimalarial, antibacterial, antidiabetic, and anti-inflammatory activity. Polyquinolines obtained from quinoline derivatives can be used in the synthesis of nano- and mesostructured compounds.

76

Additionally, some quinoline derivatives, such as tetrahydro-quinoline, are rubber antioxidants and corrosion inhibitors [1-3]. There exist classical methods for the synthesis of quinoline nitrogen-heterocyclic compounds, as well as modern methods using metal complex catalysts [1].

Classic methods for forming the quinoline ring are based on the reaction of acids with glycerol, unsaturated aldehydes, ketones, and 1,3-dicarboxylic compounds according to Skraup, Debner-Miller [4], or Combe [5,6]. These methods are limited to polar functionalized quinolines due to high reaction temperatures and the use of strong acids or bases as catalysts. In recent years, a new page has been opened in the chemistry of quinolines by metal complex catalysis [7]. Catalytic methods for the synthesis of quinolines have several advantages over classical methods, including the tolerance of functional groups and the expansion of the range of substrates used in the construction of quinolines. Due to the use of transition metal complexes in a catalytic rather than stoichiometric amount, the process of separating the target products is facilitated by reducing the amount of waste [8-10]. Some problems related to synthesizing quinolines using metal complex catalysts are covered in monographs [11-16].

### Materials and methods

The catalysts are prepared by wet mixing the active components with a core, then shaping, drying, and curing. Benthanite and aluminum oxide (TU-6-03-7-14-78) from the Navoi region, which have been purified and separated from the amorphous part, are used as carriers.

**Table 1**

The main physical-mechanical and operational properties of prepared catalysts.

| | Composition, % mass. | Mechanical strength, MPa | Time of active operation until regeneration, hours | Productivity, g/kg·bed·h | product yield, % |
|---|---|---|---|---|---|
| . | ZnO -10,0 $Cr_2O_3$ - 5,0 $Al_2O_3$ - 85,0 | 5,2 | 78 | 81,0 | 56,0 |
| . | CdO - 10,0 $Cr_2O_3$ - 5,0 Bentonite -85,0 | 5,7 | 78 | 72,0 | 62,0 |
| . | $ZnF_2$ - 5,0 $CdF_2$ - 5,0 $Al_2O_3$ - 90,0 | 5,4 | 96 | 90,0 | 65,0 |

| | | | | |
|---|---|---|---|---|
| . | $ZnF_2$ - 5,0<br>$CdF_2$ - 5,0<br>$Cr_2O_3$ - 3,0<br>$Al_2O_3$ - 87,0 | 6,0 | 60 | 105,0 | 71,0 |
| . | $CdF_2$ - 10,0<br>$Cr_2O_3$ - 5,0<br>$Fe_2O_3$ - 5,0<br>Bentonite -80,0 | 6,2 | 100 | 120,0 | 68,0 |

93 g of aniline, 200 ml of methanol, and 60 ml of acetaldehyde are mixed in a 500 ml round-bottomed flask at a temperature of 0-5°C. The heterocyclization process is then carried out in a stainless steel continuous reactor with dimensions of d × h = 20 × 1000 mm, an external electric heater, and a catalyst loading of 100 cm³.

The experiments are carried out in the following order: a mixture of acetaldehyde, methanol, and aniline is transferred from a dropping funnel to the upper part of the reactor. The upper one-third of the reactor is filled with inert pieces of phosphorus. The vapor-gas mixture, acting on the surface of the catalyst, is collected in the collector capacity. Hydrogen-based gaseous products are released into the atmosphere. Methanol, water, and crotonaldehyde are separated from the catalyst by fractional distillation at 120°C. Then the grinding is continued in a vacuum of 8.0-10.0 mm Hg. Quinoline, 2-methylquinoline, and 4-methylquinoline are separated.

Catalyst composition analysis using gas-liquid chromatography was carried out on an LXM-8MD chromatograph of the first modification. The stationary layer was polysorb-1, and the column temperature was programmed to 200°C. The gas carrier used was hydrogen with a flow rate of 3 L/h. The internal standard used was N, N-dimethylaniline. The chromatogram of the obtained product is given in Figure 1.
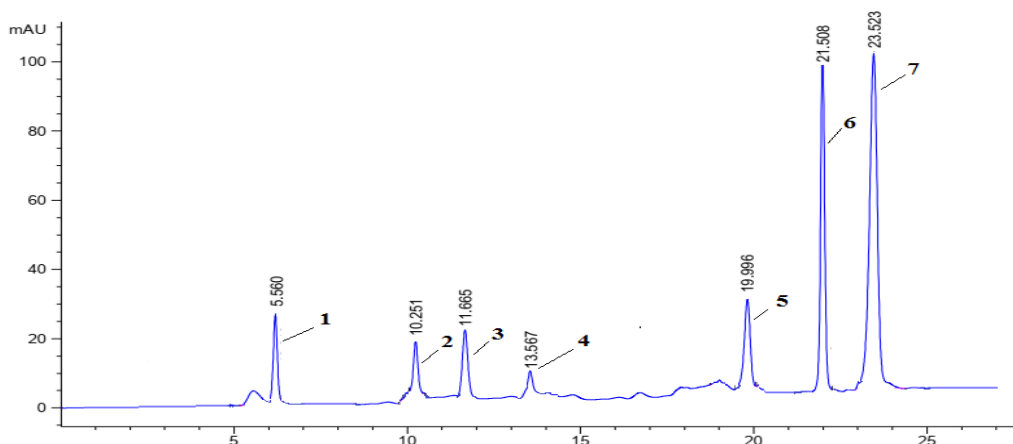


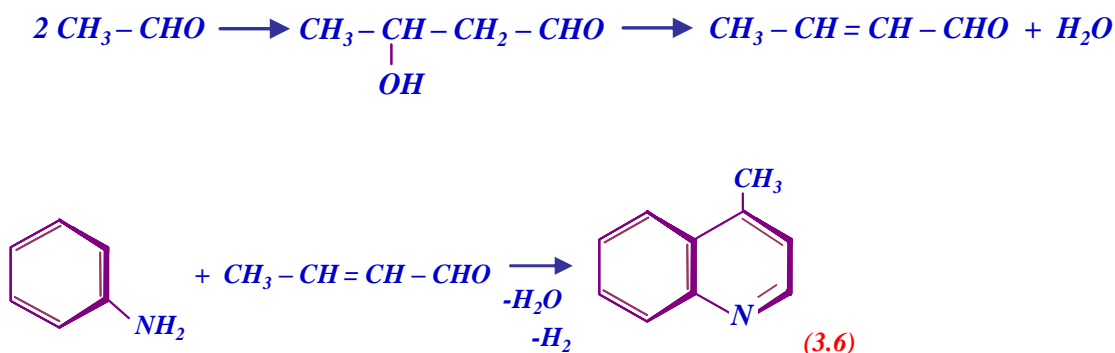**Fig 1. Chromatogram of the reaction product of heterocyclization of aniline and acetaldehyde**

Here: 1 - methanol; 2 - water; 3 - croton aldehyde; 4 - N,N - dimethylaniline; 5 - quinoline; 6 - 2-methylquinoline; 7 - 4-methylquinoline.

## Results and discussion

To expand the methods of synthesizing quinoline derivatives, the process of heterocyclization of aniline with acetaldehyde was studied. Using a 1:2 mole ratio of $C_6H_5NH_2:CH_3CHO$ and a temperature range of 320-460°C, the raw materials passed over the surface of the catalyst mainly formed 2-methylquinoline. The reaction takes place according to the following scheme:
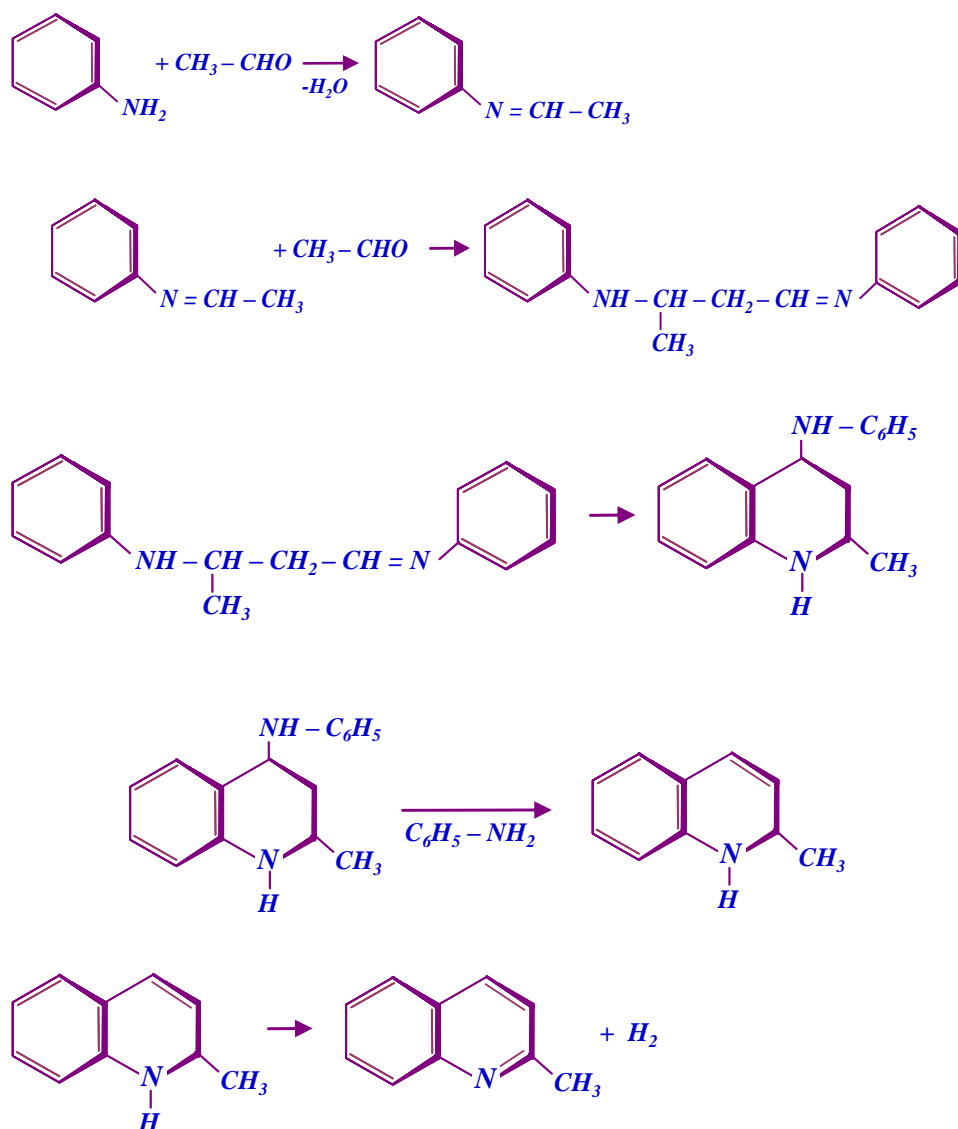
Along with 2-methylquinoline, under these reaction conditions, the formation of 4-methylquinoline has also been observed. The formation of 4-methylquinoline occurs through the condensation of acetaldehyde and cyclization with aniline, contrary to Skraupp's rule.

79

Eur. Chem. Bull. 2023, 12(Regular Issue 6), 76-86

$$2\ CH_3-CHO \longrightarrow CH_3-\underset{\underset{OH}{|}}{CH}-CH_2-CHO \longrightarrow CH_3-CH=CH-CHO\ +\ H_2O$$



Under the conditions defined as acceptable, 2-methylquinoline is formed with a yield of 32.0%, and 4-methylquinoline is formed with a yield of 39.0%. The temperature dependence of the heterocyclization process was studied in the range of 320-460°C (Table 2).

**Table 2**

Effect of temperature on the yield of 2- and 4-methylquinolines.
#5 catalysts; Woom. = 0.2 h−1; $S_6N_5NH_2$:$SN_3SNO$ = 1:4 mol

| Temperature, °C | Product yield relative to the reacted aniline, % | | Acetaldehyde conversion, % |
|---|---|---|---|
| | 2-Methylquinoline | 4-Methylquinoline | |
| 320 | 18,0 | 12,0 | 65,0 |
| 340 | 22,0 | 18,0 | 72,0 |
| 360 | 26,0 | 21,0 | 75,0 |
| 380 | 31,0 | 33,0 | 85,0 |
| 400 | 34,0 | 39,0 | 90,0 |
| 420 | 24,0 | 22,0 | 92,0 |
| 440 | 18,0 | 16,0 | 98,0 |
| 460 | 12,0 | 9,0 | 98,0 |

Table 2 shows that as the temperature increases from 320 to 400°C, the molar ratio of benzene $S_6H_5NH_2$:$SN_3SNO$ = 1:2, and the yield of 2- and 4-methylquinoline gradually increases. However, further temperature increases lead to a decrease in the reaction yield due to the formation of by-products as a result of secondary reactions. At the selected temperature of 400°C, the conversion of acetaldehyde reaches 90%. To determine the optimal synthesis conditions, another important indicator, the volumetric rate of transfer of the initial raw components to the reactor, was measured (Fig. 2).
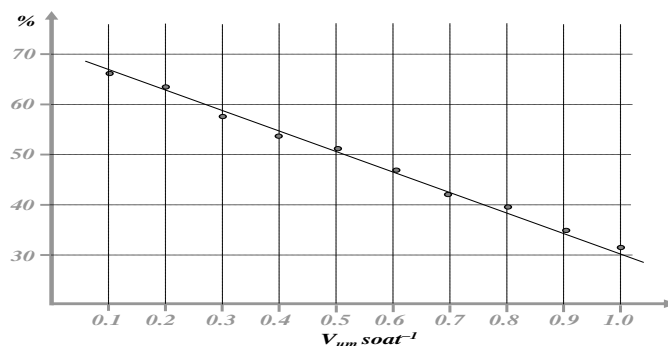
80

**Fig 2. Dependence of the production yield of methylquinolines on the rate of transfer of the initial raw materials to the reactor:**

#5 catalysts; temperature 400°C; The ratio of $S_6N_5NN_2$:$SN_3SNO$ is 1:2

Figure 2 shows that the yield of quinoline derivatives gradually decreases with the increase in the volumetric rate of feed of raw components to the reactor. This is another basis for the implementation of the process in internal diffusion fields. During the research, the chemical processes of catalytic reactions taking place inside the reactor - adsorption, effect on the surface of the catalyst, and desorption - were studied. The heterogeneous catalysts used (KXTB-5) have porous surfaces. Heterogeneous reactions of aniline and acetaldehyde in the vapor phase occur very quickly, and the sum of the speed of the catalysis process is the diffusion of reagents in the pores of the catalyst and the internal diffusion areas. The inner surface of the porous catalyst grains accounts for 99% of the total surface of the catalyst, and the mass transfer is determined by the catalytic reaction governed by the effective diffusion coefficient of aniline and acetaldehyde, and the effective rate constant adjusted to the unit of grain size (these constants are uniform over the size of the catalyst grain). Further studies were carried out to determine the optimal conditions, and the height of the catalyst layer for the conversion of raw materials and yield of methylquinolines was studied (Table 3).

**Table 3**

Dependence of catalyst layer height on heterocyclization process at 400 ° C temperature, $S_6N_5NN_2$:$SN_3SNO$ ratio 1:2.

Catalyst #5. Reactor d× l = 20× 1000 mm; Woom. = 0.2 h−1

| № | Layer height from the top of the reactor, mm | Conversion of aniline and acetaldehyde, % |
|---|---|---|
| 1 | 400 | 41,0 |
| 2 | 600 | 57,0 |
| 3 | 800 | 76,0 |
| 4 | 1000 | 86,0 |
| 5 | 1200 | 92,0 |
| 6 | At the exit from the reactor | 96,0-99,0 |

Table 3 shows that with an increase in the height of the catalyst layer, the conversion of aniline and acetaldehyde also increases and reaches maximum values at the limit of 1200 mm. However, at this height, optimal conditions for the realization of additional reactions are created, and the selectivity of the catalyst decreases.

Thus, the kinetics of quinoline production from aniline and acetaldehyde was studied, and chromium and iron catalysts with cadmium fluoride added as a promoter, forming the selectivity of quinoline derivative formation, were developed. The observed data indicate that internal diffusion does not affect the observed rate of acetaldehyde consumption. The influence of the catalyst composition, including the nature of the core-carrier, the reaction temperature, the ratio of initial reagents, and the volumetric rate of transfer on the yield of quinoline derivatives, was studied. The obtained computational data show that there are no internal diffusion barriers in the consumption reaction of acetaldehyde.

The composition and structure of the synthesized products were confirmed by IR-, PMR-spectroscopy, chromato-mass spectrometry, and thin-layer chromatogram methods (Figures 3, 4, 5).
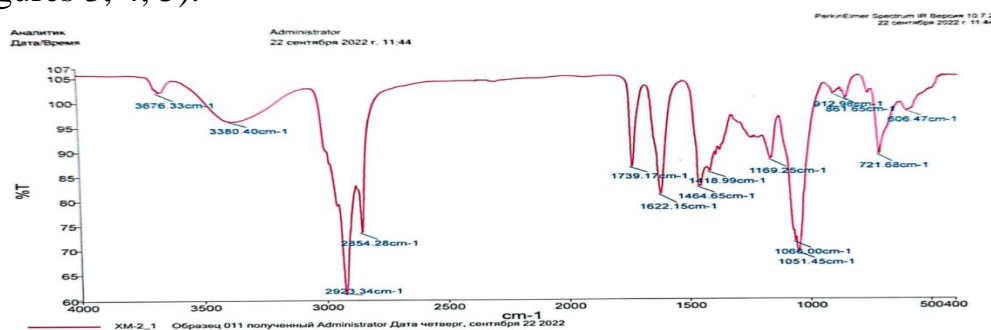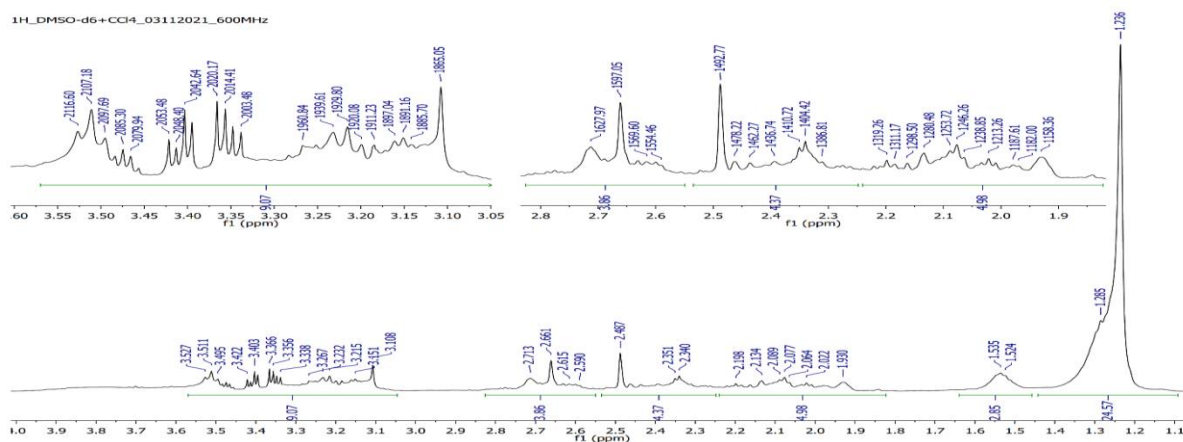


**Fig 3. IR-spectrum of reactions of heterocyclization of aniline with acetaldehyde.**

The IR spectrum of the products of the heterocyclization reactions of aniline with acetaldehyde (Fig. 4) showed absorption lines related to the composition of the original raw materials, including strong vibrations related to the S=O group of the

carbonyl bond at 1622.82 cm$^{-1}$ and bond valence vibrations of the S=S group related to the aromatic group at 1739.28 cm$^{-1}$. Additionally, the presence of C-N group valence vibrations in the 1066.38 and 1056.82 cm$^{-1}$ absorption lines and the S-N group valence vibrations in the 3393.64 cm$^{-1}$ region of the spectrum can be the basis for the presence of compacted heterorings. The structure of the composition resulting from the reaction of heterocyclization of aniline with acetaldehyde in the vapor phase was also studied using PMR-spectroscopy (Fig. 4).
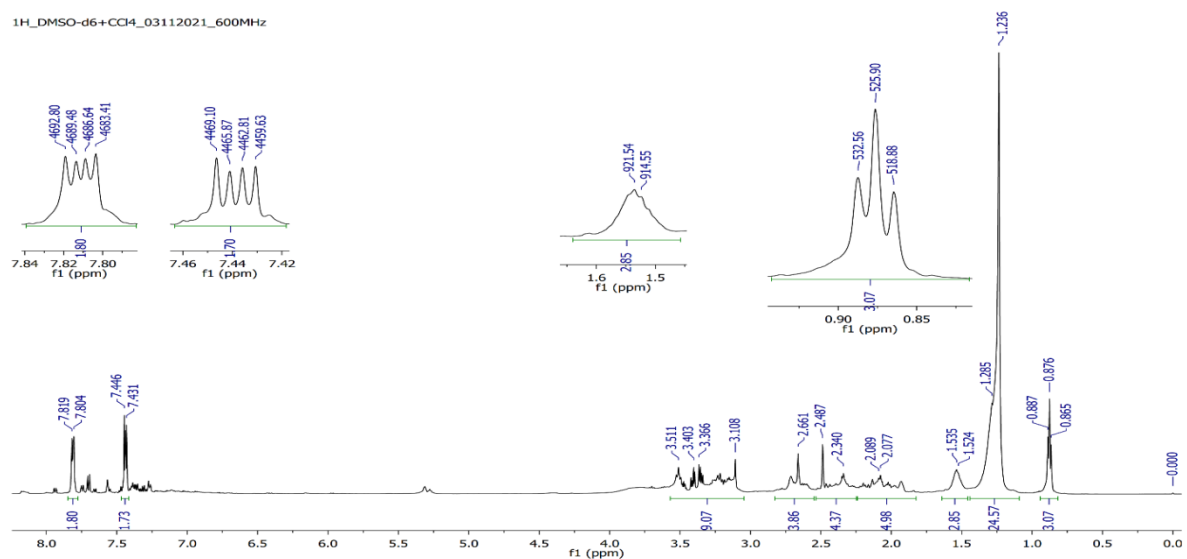


**Fig 4. PMR (1H)-spectrum of methylquinolines formed by the heterocyclization reaction of aniline and acetaldehyde.**

Figure 4 shows the analysis of the PMR (1H)-spectrum of 2-methylquinolines formed by the heterocyclization reaction of aniline and acetaldehyde. We took the ring of 2-methylquinoline containing a heteroatom as a basis, and the carbon atoms in the second and third states have the same strength relative to the nitrogen atom in the heteroatom ring. Therefore, the 2nd and 3rd carbon atoms exhibit different absorption bands than the 4th carbon atom. Doublet-doublet signals of protons located in the 2nd and 3rd state carbon atoms are observed at 6.332-6.321 ppm, while the doublet signals of protons on the 4th carbon atom are observed at 6.107 ppm. The doublet-doublet signals of the protons located on the 5th-8th carbon atoms of benzene are identified in the fields at 6.287-6.279 ppm. Singlet signals of protons of the S atom (SN=) were observed in the 6.087 ppm area, and doublet signals of protons of S atoms in the C=C bond were observed in the 6.05 ppm area. Figure **6** shows the chromato-mass spectrum of 2-methylquinoline.
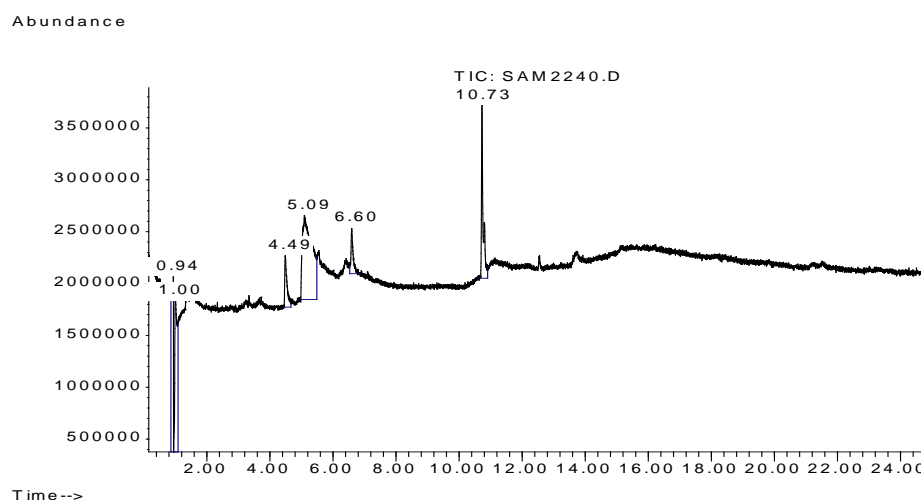
**Figure 6. Chromato-mass spectrum of 2-methylquinoline.**

**Conclusion.**

In conclusion, quinoline and alkylquinolines were successfully synthesized from heterocyclization reactions of aniline with acetaldehyde in the presence of various catalysts. The formation of quinoline bases involves complex, sequential, and interconnected processes, including nucleophilic addition of aldehydes to aromatic amines, dehydrogenation, dehydrocyclization, dehydrogenation, and other chemical reactions. Cadmium and zinc compounds were found to be catalysts of the reactions of nucleophilic addition of aldehydes to amines, and zinc, chromium, and iron catalysts containing compounds were recommended. The catalyst core (carrier) used was Navbahor bentonite from the Navoi region, purified from its amorphous part. Catalysts were prepared by wet mixing, shaping, drying, and curing.

During the research, a unique method for the synthesis of quinoline and methylquinolines in the vapor phase based on aniline and acetaldehyde was recommended. It was found that passing equimolar amounts of aniline and acetaldehyde over the surface of the catalyst at a temperature range of 380-440°C results in high yields of quinoline derivatives. The productivity of quinoline production was determined by temperature, height of the catalyst layer, and rate of transfer of raw materials to the reactor. Overall, the study provides valuable insights into the synthesis of quinoline derivatives and can be beneficial for further research in this area.

**References:**

1. F.A. Selimov, O.A. Ptashko, a.M. Джемилев. Synthesis of pyridine bases under the action of metal complex products. - Ufa: Gilha, 2002. - 304 p. https://www.researchgate.net/scientific-contributions/F-A-Selimov-77108439

2. A.R. Mahmutov, A.Yu. Kamatov, R.R. Nurtdinova, SM Usmanov. Photo-dietary condensation Anilina with hexon-1 // Bashkir chemical magazine. - 2016. - T. 23, No. 1. - P. 46-48. https://cyberleninka.ru/article/n/fotokataliticheskaya-kondensatsiya-anilina-s-geksenom-1

84

3. A.R. Mahmutov, A.Yu. Kamatov, R.R. Nurtdinova, SM Usmanov. Investigation of the architeks of the architeks with α-olefins // Natural and mathematical sciences in the modern world: Collection of articles on the materials of the XLI International Scientific and Practical Conference. - Novosibirsk: ed. ANS Sibak, 2016. - No. 4 (39). - S. 196-201.

4. R.J. Linderman, S.K. Kirollos. Regioselective Synthesis of Trifluoromethyl Substituted Quinolines from Trifluoroacetyl Acetylenes // Tetrahedron Lett. - 1990. -v. 31. - ISSUE 19. - P. 2689-2692.
https://www.researchgate.net/publication/264577646_ChemInform_Abstract_Regioselective_Synthesis_of_Trifluoromethyl-Substituted_Quinolines_from_Trifluoroacetylacetylenes

5. A.K. Agarwal, S.A. Jenekhe. New conjugated polyanthrazolines containing thiophene moieties in the main chain // Macromolecules. - 1991. - V. 24. - P. 6806-6808.
https://www.researchgate.net/scientific-contributions/Ashwini-K-Agrawal-74599955

6. Zhang X., Shetty A.S., Jenekhe S.A. Electroluminescence of multicomponent conjugated polymers. Roles of polymer/polymer interfaces in emission enhancement and voltage-tunable multicolor emission in semiconducting polymer/polymer heterojunctions // Macromolecules. - 2000. - V. 33. - P. 2069-2082.
https://www.researchgate.net/publication/231693731_Electroluminescence_of_Multicomponent_Conjugated_Polymers_2_Photophysics_and_Enhancement_of_Electroluminescence_from_Blends_of_Polyquinolines

7. Селимов Ф.А., Джемилев У.М., Пташко О.А. Металлокомплексный катализ в синтезе пиридиновых оснований. – М.: Химия, 2003. – С. 223-233.
https://cyberleninka.ru/article/n/poluchenie-hinolinovyh-osnovaniy-na-osnove-aromaticheskih-aminov-reaktsiey-s-karbonilnymi-soedineniyami-polucheniya-geterotsiklov-v

8. Agrawal A.K., Jenekhe S.A. Electrochemical properties and electronic structures of conjugated polyquinolines and polyanthrazolines. Chemistry of materials. 1996. Vol. No. 2. P. 579-589.
https://www.mindat.org/reference.php?id=2495257

9. Chen Y.L. et al. Synthesis and antibacterial evaluation of certain quinolone derivatives. Journal of Medicinal Chem-istry. 2001. Vol. 44. No. 14. P. 2374-2377.
https://pubmed.ncbi.nlm.nih.gov/11428933/

10. L.M. Meyliyeva, V.Z. Nurmukhamedova, Sh.A. Niyozova, B.U.Zokirov, Sh.Sh.Khasanov, O.N.Ashirov, J.M.Abdurakhmanov , Sh.A.Mutalov. Investigation of the conditions of alcoholization of secondary polyethylene terephthalate with triethanolamine Eur. Chem. Bull. 2023, 12(4), 888-895 doi: 10.31838/ecb/2023.12.4.0682023.25/04/2023

11. .Jones C.P., Anderson K.W., Buchwald S.L. Sequential Cu-catalyzed amidation-base-mediated camps cyclization: A two-step synthesis of 2-Aryl-4-quinolones from o-halophenones. The Journal of organic chemistry. 2007. Vol. 72. No. 21. P. 7968-7973. https://chemistry-buchwald.mit.edu/publications/sequential-cu-catalyzed-amidation-base-mediated-camps-cyclization%C2%A0-two-step-synthesis-2

12. Madapa S., Tusi Z., Batra S. Advances in the syntheses of quinoline and quinoline-annulated ring systems. Current Organic Chemistry. 2008. Vol. 12. №. 13. P. 1116-1183.
https://www.eurekaselect.com/article/12529

13. Roma G. et al. 1, 8-Naphthyridines IV. 9-Substituted N, N-dialkyl-5-(alkylamino or cycloalkylamino) [1, 2, 4] tria-zolo [4, 3-a] [1, 8] naphthyridine-6-carboxamides, new compounds with anti-aggressive and potent anti-inflammatory activities. European journal of medicinal chemistry. 2000. Vol. 35. No. 11. P. 1021-1035. https://europepmc.org/article/med/11137230

14. Tribute A. Professor Usein Memetovich Dzhemilev. ARKIVOC. 2011. Vol. 8. P. 1-19.
https://7universum.com/ru/tech/archive/item/8090

15. Yamashkin S. A., Oreshkina E. A. Traditional and modern approaches to the synthesis of quinoline systems by the Skraup and Doebner-Miller methods. Chemistry of Heterocyclic Compounds. 2006. Vol. 42. No. 6. P. 701-718. https://www.researchgate.net/publication/225344496_Traditional_and_Modern_Approaches_to_the_Synthesis_of_Quinoline_Systems_by_the_Skraup_and_Doebner-Miller_Methods

16. Yao C. et al. One-pot solvent-free synthesis of quinolines by C–H activation/C–C bond formation catalyzed by recy-clable iron (III) triflate. RSC Advances. 2012. Vol. 2. No. 9. P. 3759-3764. https://www.semanticscholar.org/paper/One-pot-solvent-free-synthesis-of-quinolines-by-C%E2%80%93H-Yao-Qin/13075d048269106419f3908202483aeaa8febf62

17. E.Egamberdiev, S. Turabdjanov, D. Mirzaeva, Kh. Khaydullaev, U. Sharipova, A. Shokhakimova, and O. Bakhtiyorov.: Effect of chitosan substance on the mechanical properties of paper obtained on the basis of flax cellulose. E3S Web of Conferences 371, 01045 (2023) https://doi.org/10.1051/e3sconf/202337101045

18. Ergashev Y.; Egamberdiev E.; Turabdzhanov S.; Akmalova G.; Isanova R.; Rashidov R.; Sobitov O.: Obtaining filter material from natural fiber composition and areas of its use. E3S Web of Conferences, 2023, 371, 01047, DOI 10.1051/e3sconf/202337101047

86

Eur. Chem. Bull. 2023, 12(Regular Issue 6), 76-86