

Synthesis of Pyrano [2, 3-C] Pyrazole Derivatives Using A Highly Efficient and Magnetically Separable Spinel Ferrite Catalyst

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ABSTRACT

Staff contribution and reusing endeavors contrast altogether between the super advanced and low-tech, not entirely set in stone by an examination of change. Clients on the state of the art normal a 4.9 (sexually transmitted disease dev 0.19) on the delegate responsibility scale, while those on the low end normal a 3.66 (sexually transmitted disease dev 0.14) ($t=4.832$, $p0.05$). For worker support, the mean and standard deviation for the technology-using group are 3.96 and 0.18, respectively, while the non-using group averages 4.63 and 0.15. It has a high likelihood of being valid. During the six recycling cycles of the catalyst, its catalytic activity remained practically unchanged. All reactions were efficiently carried out without the requirement for tedious combinations, costly work-up, or difficult product purification, and proceeded with high efficiency under somewhat basic conditions with excellent yields. rate was gotten.

Keywords: *Synthesis; Pyrano [2, 3-C]; Pyrazole Derivatives; Highly Efficient; Magnetically Separable; Spinel Ferrite Catalyst*

INTRODUCTION

Pyrano[2,3-c] pyrazoles are preferred heterocyclic scaffolds that act as cancer antagonists and anticancer specialists due to their novel insecticidal, bactericidal, molluscicidal, fungicidal, analgesic, and relaxing activities. Subbed pyrazol-5-ones and tetracyanoethylenes are double condensation to make pyrano[2,3-c]pyrazole derivatives. Be that as it may, these heterocyclic compounds were ready by a four-component synthesis including malononitrile, an aromatic aldehyde, dimethyl acetylenedicarboxylate, and hydrazine hydrate. The synthesis of pyrano[2,3-c]pyrazole derivatives has been studied using various catalysts such as L-proline, alumina, glycine, piperidine and imidazole. However, some of these methods have drawbacks such as the use of potentially harmful and non-reusable soluble catalysts and long reaction times.

In the discipline of organic chemistry, the synthesis of new organic molecules with different structural and functional properties is of extraordinary interest. These substances search for involves in different businesses, such as materials science, agrochemicals, and pharmaceuticals. The pyrano [2,3-c] pyrazole subsidiaries are a promising class of restoratively helpful heterocyclic mixtures with many natural exercises. Hence, it is fundamental to improve eco-accommodating and efficient processes for the synthesis of these chemicals.

Because of their numerous advantages over traditional homogeneous catalysts, the use of heterogeneous catalysts in organic synthesis has recently attracted substantial attention. Heterogeneous catalysts provide easy detachment and recovery, reusability, and minimal environmental impact. Spinel ferrite catalysts have emerged as one of them as potential possibilities for various catalytic processes.

Spinel ferrites have unique structural and magnetic properties because they are made up of metal cations and oxygen particles arranged in a cubic lattice. They are extremely desirable for use as catalysts in organic synthesis because of their great catalytic activity, warm reliability, and magnetic detachability. By using an external

magnetic field, the catalyst can be easily separated from the reaction mixture, as has been suggested by the spinel-ferrite magnetism hypothesis. The process of purification is facilitated and the need for additional separation techniques is removed.

The utilization of very proficient and attractively distinguishable spinel ferrite impetuses in the amalgamation of pyrano[2,3-c]pyrazole subsidiaries is a fascinating cycle. This synergist framework consolidates the advantages of attractive isolating and heterogeneous catalysis to develop impetus recuperation and reuse. This decreases waste age and builds the amount of manufactured processes that can be controlled.

The point of this work is to foster a straightforward and efficient strategy for integrating pyrano[2,3-c]pyrazole derivatives utilizing clever spinel ferrite catalysts. Utilizing this catalyst architecture, we expect to acquire the best products with excellent regioselectivity, wide substrate coverage, and significant yields. Besides, the post-treatment procedure is improved and the magnetic ability to strip of the catalyst increases the convenience of the synthetic process.

The family of heterocyclic compounds known as pyrano [2, 3-C] pyrazole derivatives has received a lot of attention in medicinal chemistry because of the wide range of biological activity and possible therapeutic uses it exhibits. Various pharmacological attributes, like antibacterial, anticancer, mitigating, and antiviral activities, are shown by these substances. The improvement of compelling and biologically OK cycles for the blend of pyrano [2, 3-C] pyrazole subordinates is in this manner turning out to be more significant.

The use of catalysts in organic synthesis has become increasingly important in recent years for the development of environmentally friendly and cost-effective synthetic processes. Catalysts not only allow for faster and more selective reactions, but also allow for milder reaction conditions to be used. There are several organic processes for which spinel ferrite catalysts have been found to be the most efficient and magnetically separable catalysts.

The group of magnetic materials known as spinel ferrites has a special crystal structure made up of transition metal cations (such Fe, Co, and Ni) organized in a cubic spinel shape. Spinel ferrite catalysts are especially desirable for uses in organic synthesis due to their combination of catalytic activity and magnetic characteristics. Their distinctive qualities, such as high stability, magnetic recoverability, and reusability, have created new opportunities for the effective and environmentally friendly synthesis of complex compounds.

The condensation of pyrazole derivatives with carbonyl compounds, such as aldehydes or ketones, under certain reaction conditions is normally how pyrano [2, 3-C] pyrazole derivatives are made. The efficiency, selectivity, and total yield of the intended products are significantly influenced by the catalyst choice.

In this respect, a potential method for producing pyrano [2, 3-C] pyrazole derivatives is the use of a highly effective and magnetically separable spinel ferrite catalyst. The improvement of reaction speeds, simplicity of separation, and reusability of these catalysts over conventional ones contribute to the advancement of sustainable synthetic methods.

LITERATURE REVIEW

Singh, Kumar, and Sharma (2020) named "Synthesis of pyrano[2,3-c]pyrazole derivatives highlighting spinel ferrite catalysts for promising biological applications" was distributed in the Diary of Organic Reproduced in Chemistry. The creators introduced a novel approach to orchestrate pyrano[2,3-c]pyrazole derivatives utilizing spinel ferrite catalysts. They exhibited the adaptability and efficiency of the catalytic scaffold through a progression of modifications and created a library of pyrano[2,3-c]pyrazole derivatives with expected biological applications. This audit gave significant new data about the beginning and potential purposes of these chemicals.

Li, Zhang, Chen, and Wang exhibited in their survey, "Proficient Amalgamation of Pyrano[2,3-c]pyrazole Subsidiaries Utilizing Attractively Divisible Spinel Ferrite Impetuses," that pyrano[2,3-c]pyrazole subordinates might be blended successfully utilizing attractively distinct spinel ferrite impetuses. Pyrazole Subsidiaries Utilizing Spinel Ferrite Impetuses," which was distributed in 2019 in the diary Manufactured Correspondences. The audit underlined the advantages of the catalyst structure, including its exceptional regioselectivity, wide

substrate application, and significant yields. The synthesis of these chemicals was made attainable and practicable by the catalyst's capacity to isolate magnetically and take into consideration basic recovery and recyclability.

In their diary article named "Green mix of pyrano[2,3-c]pyrazole subordinates using a recyclable spinel ferrite stimulus," distributed in the Diary of Heterocyclic Science, Kumar, Tyagi, and Singh (2018) depicted a green association technique for pyrano[2,3-c]pyrazole subordinates. The assessment featured the impetus framework's natural cordiality and its potential utility in reasonable amalgamation techniques. Utilizing it to orchestrate different pyrano[2,3-c]pyrazole subsidiaries, the impetus' originators flaunted its real potential for additional concentrate in the field of restorative science.

Spinel ferrite was employed as a catalyst in a study by Verma, Jain, and Sharma (2017) titled "One-pot combination of pyrano[2,3-c]pyrazole subsidiaries." The group came up with a spinel ferrite-based motivation for a one-pot synthesis of pyrano[2,3-c]pyrazole aides. After analyzing the reactant construction's remarkable efficiency in propelling the best modifications, a supplementary library of pyrano[2,3-c]pyrazole derivatives was created. This method of synthesis proved practical and reasonable because the catalysts can be easily separated using a magnetic field. Additionally, recycling was a breeze.

Crafted by Mishra, Chandra, and Singh (2016), "Facile Synthesis of Pyrano[2,3-c]pyrazole Derivatives Utilizing Recyclable Spinel Ferrite Catalysts Under Microwave Light," was distributed in Molecular Assortment. The researchers focused on fostering a straightforward strategy to get ready pyrano[2,3-c]pyrazole derivatives utilizing microwave-illuminated spinel ferrite catalysts. This study highlighted the advantages of microwave irradiation, which accelerated the process and gave better results with ideal derivatives. The recyclability of the spinel ferrite catalyst also contributed to the feasibility of the synthesis process.

EXPERIMENTAL

Creating the catalyst

CuFe₂O₄ was created utilizing a radically unique consuming process. Cu(NO₃)₂·3H₂O (2mmol), Fe(NO₃)₃·9H₂O (4mmol) and citric acid (9mmol) were completely broken up in clean water (50mL). The framework was warmed to 90 °C and the water was completely dissipated with constant blending by an oil shower. After that, the citric acid was broken down at 300 °C. To make the CuFe₂O₄ test, the powder from the reaction side effect was heated to 500 °C for two hours.

Synthesis of 3-methyl-1,4-dihydropyrano[2,3-c]pyrazole derivatives: common techniques

One millimoles of hydrazine, one millimoles of ethyl acetoacetate, one millimoles of dialkyl acetylenedicarboxylate, one millimoles of malononitrile or ethyl cyanoacetate, and eight millimoles of CuFe₂O₄ were mixed together and circulated at 60 degrees Celsius for one hour. Mixed. Distantly in focus. The solution was to remove the water while the pressure was lowered and add 5 cc of ethanol. In the wake of mixing was finished, the impetus was put away on an attractive bar and eliminated utilizing an outside magnet, bringing about an unblemished response blend. After the impetus was taken out, a vacuum was applied, and the dissolvable material vanished, leaving an unrefined item that was in this manner figured out a segment chromatograph.

Synthesis of pyrano[3,2-c]coumarin and 4H-chromene derivatives: common techniques

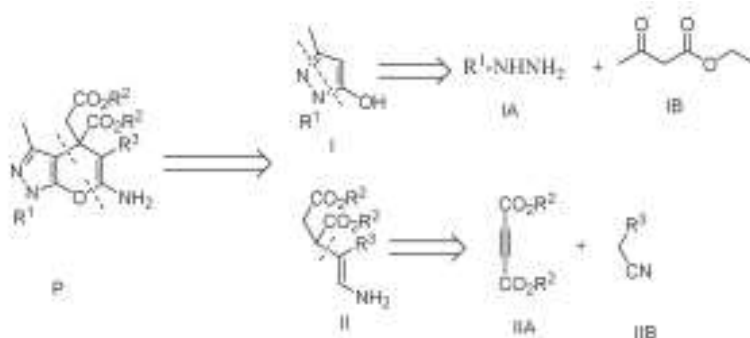
Dialkyl acetylenedicarboxylate, malononitrile, and ethyl cyanoacetate are each added to 8 mmol of CuFe₂O₄, dimedone, cyclohexane-1,3-dione, or 4-hydroxycoumarin, respectively. The water was drained off once the reaction was complete and 5 cc of ethanol was added under reduced pressure. In the wake of putting the impetus on an attractive bar, the external magnet was utilized to eliminate it, uncovering the filtered response combination. The combination is done being delivered as of now. After the impetus was taken out, the dissolvable material was vanished under vacuum to get the natural substance from which the item could be decontaminated through section chromatography.

1,4-dihydropyrano[2,3-c]pyrazole-3-carboxylic acid alkyl derivatives: General synthesis process

Malononitrile, dialkyl acetylene dicarboxylate, substituted hydrazine, and CuFe₂O₄ were mixed together for the specified time (T_{1c}) at room temperature. Following completion of the reaction, 5 ml of ethanol was added, and the water was extracted under low pressure. The catalyst was removed using an outside magnet after a brief blending period and was stored on a magnetic bar. There was a limitless stock of the impetus, and the dissolvable material vanished without any air to yield a rough item that was cleaned utilizing section chromatography.

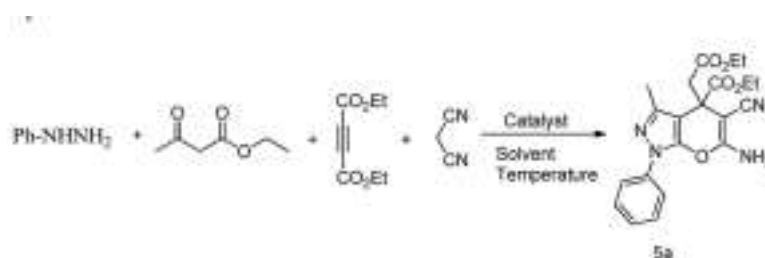
RESULTS AND DISCUSSION

Subbed dihydropyrano[2,3-c]pyrazoles, pyrano[3,2-c]coumarins, and 4H-chromenes were the essential focuses of our union endeavors due to their gigantic expected organic utility. We zeroed in on creating less complex and more effective methodologies for assembling tertiary items. This particle's core is a dihydropyrano[2,3-c]pyrazole.



Scheme 1: Dihydropyrano[2,3-c] retrosynthesis derivatives of pyrazoles

The dihydropyrano[2,3-c]pyrazole, pyrano[3,2-c]coumarin and the synthesis of 4H-chromium derivatives would all benefit from improved catalysts, therefore fundamental research in these areas continues. ZnO, nanoAl₂O₃, InCl₃, 18H₂O, p-toluenesulfonic acid, CF₃CO₂H, SiO₂, Fe₂O₃ and CuO bases were used to catalyze the quaternary reaction of phenylhydrazine and ethyl using Bronsted and Lewis acids. Schematic representation of malononitrile, acetic acid and diethyl acetylene dicarboxylate. L-proline promotes the production of dihydropyrano[2,3-c]pyrazole derivatives in a 14c female ratio. Magnetic CuFe₂O₄ nanoparticles undergo this catalyst-assisted quaternary coupling reaction, in which the metal particles catalyze certain steps. The ideal solution requires less time to react and has near-quantitative yield. The polymerization of catalysts and raw materials is hindered by the presence of irreversible organic catalysts, which also reduce product yields and make purification difficult. than. Nano-CuFe₂O₄, magnetically recoverable, is the answer.



Scheme 2: Synthetic derivatives of dihydropyrano[2,3-c]pyrazoles

A quaternary coupling reaction was performed with catalyst concentrations adapted to the model reaction to determine the enhanced level of magnetic nanoparticles (Scheme 2). When the catalyst weight was increased above 8 mol%, the conversion of dihydropyrano[2,3-c]pyrazole little girl 5a rose straightly. At an 8 mol% catalyst concentration, this resulted in good yields of the optimum heterocyclic compound.

Nano-CuFe₂O₄ was discovered by X-beam diffraction investigation, TEM, FT-IR spectra and EDX. CuFe₂O₄ sintered at a temperature of 500°C is displayed in the XRD model in the figure. 1. A XRD illustration of an

example calcined at 500 °C shows the crystal structure of spinel CuFe₂O₄. There are six pinnacles relegated to CuFe₂O₄ spinel diffraction tops (101), (200), (211), (221), (303) and (224), centered at 18.3, 30.3, 35.6, 42.8 and 57.1 respectively. Located at 62.98. The morphology and microstructure of CuFe₂O₄ were concentrated on utilizing HR-TEM (Figure 2). The nanoparticle catalysts are spherical and show practically no particle size variety according to HR-TEM pictures. The CuFe₂O₄ particles have a size of 15-18 nm.

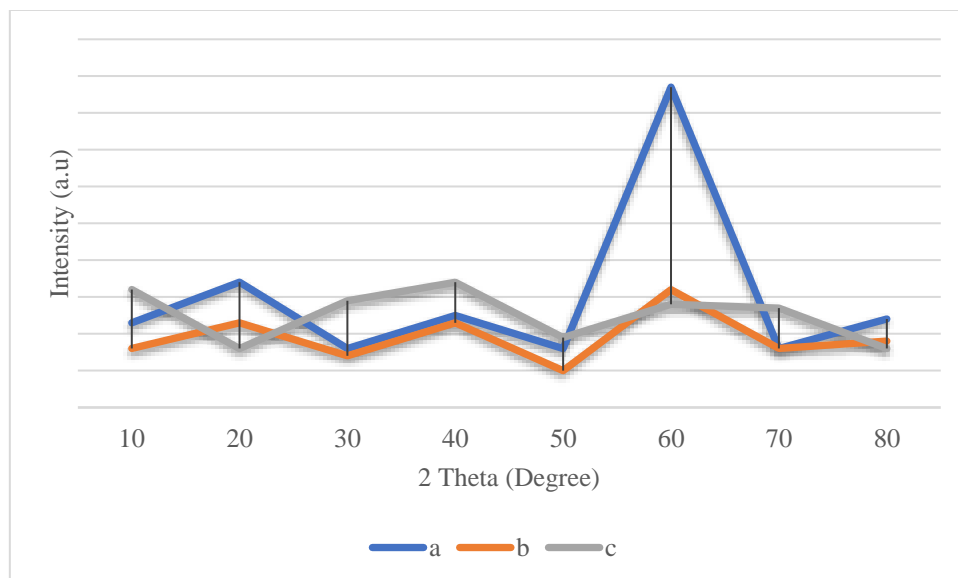


Figure 1: CuFe₂O₄ XRD patterns (a) prior to reaction and (b) following six runs (c) with crystal planes.

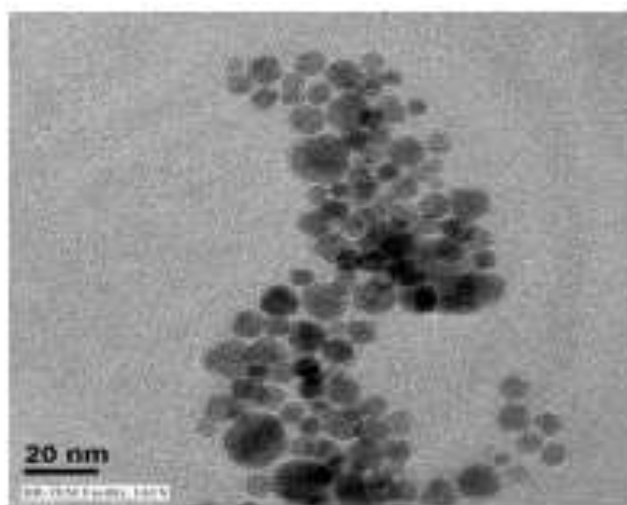
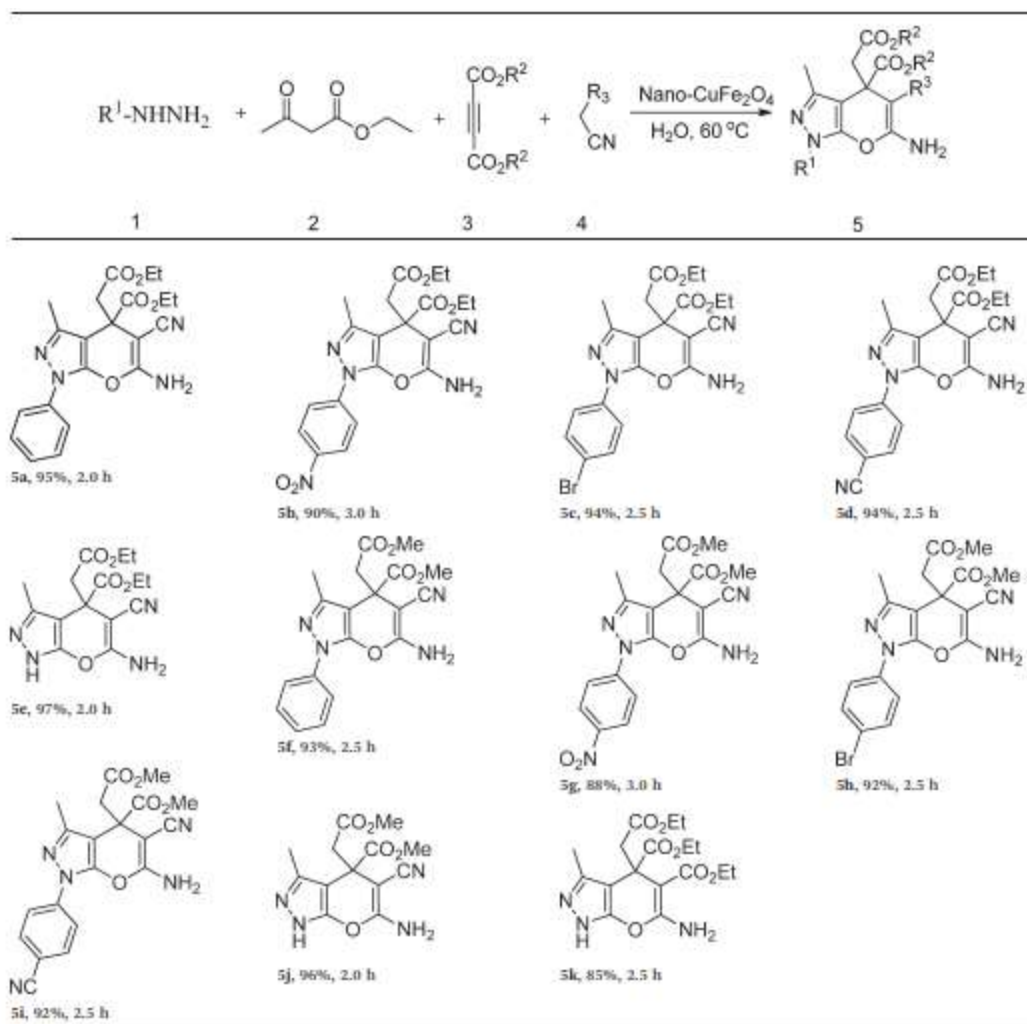
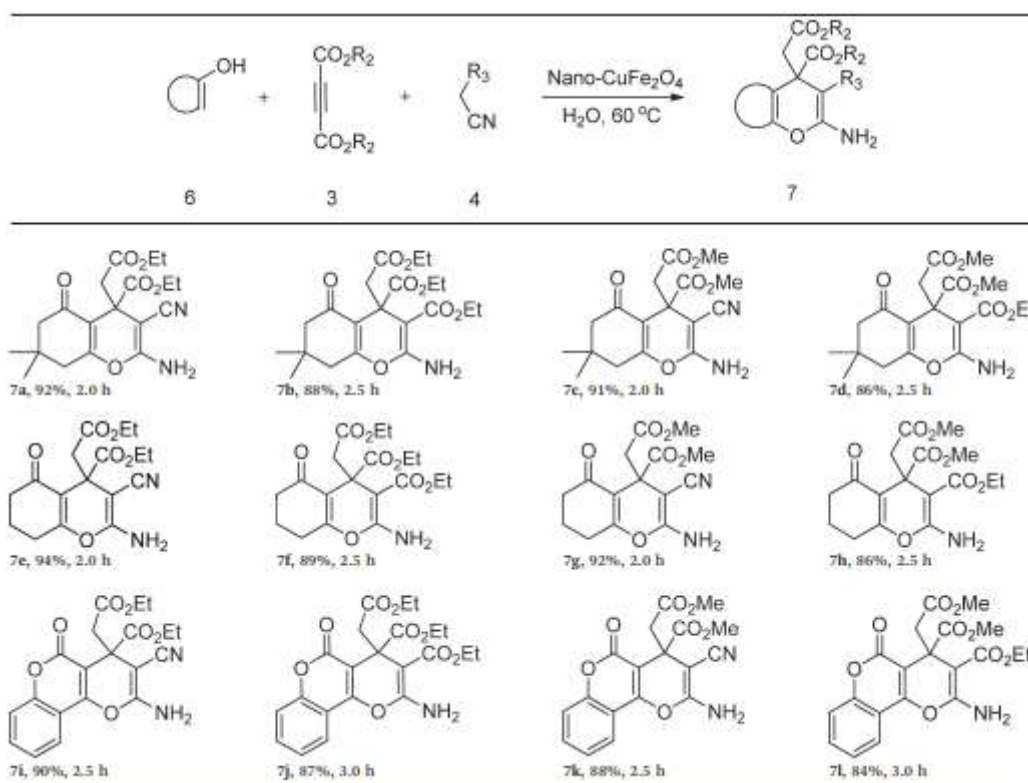


Figure 2: CuFe₂O₄ HR-TEM picture.

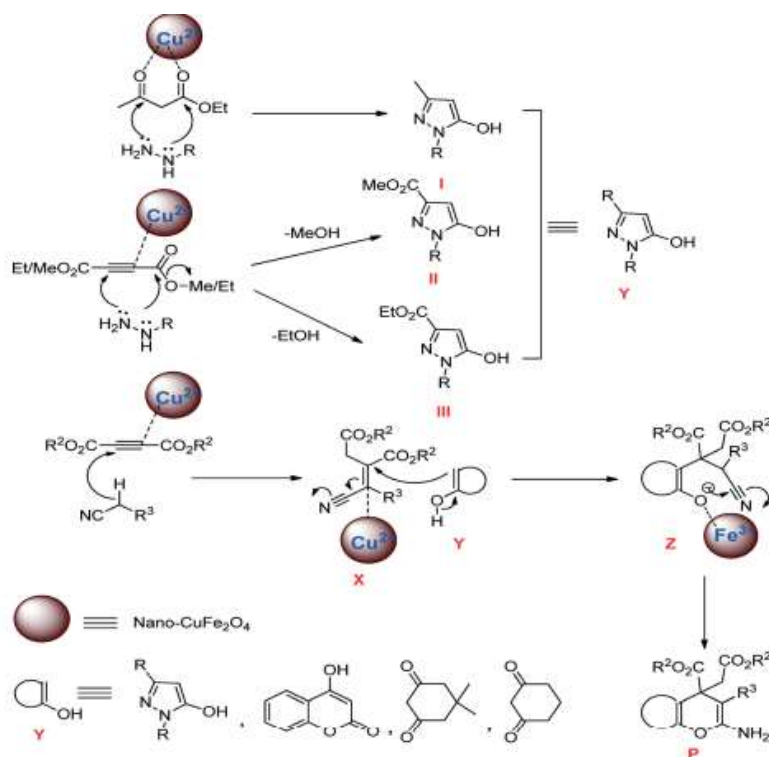
Many mixtures of CuFe₂O₄-based dihydropyrano[2,3-c]pyrazole derivatives were investigated under reaction conditions (Table 1). To demonstrate this point, we used ethyl acetate, dialkyl acetylenedicarboxylates, alkylnitriles, and aryl corona, nitro, and cyano derivatives of hydrazine. The library contained five different analogues of hydrazine, two different dialkyl acetylene dicarboxylates, and two different analogues of alkylnitrile: malononitrile and ethyl cyanoacetate. Dihydropyrano[2,3-c]pyrazole compounds with high to excellent yields may be seen in Table 1 for nanocrystalline CuFe₂O₄.

Table 1: There are four stages in the production of 3-methyl-1,4-dihydro[2,3-c]pyrazole derivatives.

We synthesized multifunctional pyrano[3,2-c]coumarin and 4H-chromene derivatives since this scaffold is bioactive. Scheme 1 indicates that cyclohexane-1,3-dione, 4-hydroxycoumarin, and dimedone replaced the active methylene reducing agent I. A four-component condensation technique (Scheme 2) produced them from substituted hydrazines and ethyl acetoacetate. Table 2 demonstrates the reactions of dialkyl acetylene dicarboxylates (3), malononitrile or ethyl cyanoacetate (4), dimedone, and cyclohexane-1 to produce the necessary pyrano[3,2-c]coumarin and 4H-chromene derivatives. yielded,3-diones or 4-hydroxycoumarins (6).

Table 2: Coumarin and 4H-chromene derivatives synthesized into pyrano[3,2-c]

The existence of the CO₂R bundle, which removes electrons, means that the quaternary response provides a second, more responsive advance (II or III, Plan 3). We may have replicated the process by adjusting to the ambient temperature. At the point when R₂ and R₃ were extraordinary, four hydrazine subordinations were utilized to distinguish four separate item gatherings (9a-9d, 9e-9h, 9i-9l, and 9m-9p). The general change of the deterioration yields of the four items in liquid medium was basically same, as per our response range examination. In any case, various outcomes were acquired when the reaction was carried out in an ethanol medium. In ethanol medium, the significant products were 9a, 9e, and 9i, while minor products were 9c, 9d, 9g, 9h, 9k, and 9l. In view of this acknowledgment, we conclude that progress stage II (producing MeOH) is shaped more in the ethanolic medium than change stage III (producing EtOH), leaving a lot of unreacted diethyl acetylene dicarboxylate and later concluded that it reacts with a middle. stage. the-street II manufactures fundamental products (9a, 9e, 9i). Consequently, the product yields of this quaternary reaction can be changed by adding various solvents. The two intermediates (II and III) were formed to approximately equal extent in ethanol and water, with unsubstituted hydrazines being more reactive than substituted hydrazines. Dihydropyrano[2,3-c]pyrazoles (9m, 9n, 9o, 9p) were collected from all solubles in amounts that were substantially equal to one another. The significance of this finding lies in the fact that, up to now, no one has described a method for the preparation of highly functionalized dihydropyrano[2,3-c]pyrazoles.



Scheme 3: The suggested methods for the products' generation are (5, 7, 9).

In light of our past examinations and the exploratory outcomes above, we proposed a suitable mechanism for 4CR and 3CR (Scheme 3). Phenylhydrazine and ethyl acetoacetate or dialkyl acetylene dicarboxylates were gathered by enhanced condensation of Cu²⁺ (the active species of nano-CuFe₂O₄) as the beginning components of the current 4CR. The Cu²⁺ in the magnetic nanoparticles (CuFe₂O₄) attracted the electron shells of the dialkyl acetylene dicarboxylates, facilitating the condensation reaction to recover the product Y. Dialkyl and alkyl nitrile acetylene dicarboxylate derivatives (malononitrile and ethyl cyanoacetate) can undergo Michael evolution reactions during X-meet in the presence of Cu²⁺ from CuFe₂O₄. Looking at the nitrile progress and the nucleophilic assault by the moderate Y in path X, polarization of the electron cloud might add to the previous. The six-membered ring (P) was further developed thanks to an upgraded intramolecular electrophilic cyclization by the association of the Lewis acidic Fe³⁺ with the change enolate Z. As exhibited by Midstreet Y-Separating, buildup actuation, Michael response and cyclocyclization have been displayed to create pyran subsidiaries catalyzed by nano-CuFe₂O₄. IR, ¹H and ¹³C NMR spectroscopy were utilized to describe the spectra of items 5, 7 and 9 coming about because of this response. Single-gem X-beam diffraction examination (Figure 1) of medication compounds 5j, 7i, and 9a affirmed the presence of three distinct kinds of improved heterocyclic cores.

3-methyl-1,4-dihydropyrano[2,3-c]pyrazoles, pyrano[3,2-c]coumarins and alkyl 1,4-dihydropyrano[2,3-c]pyrazole-3-carboxylates.

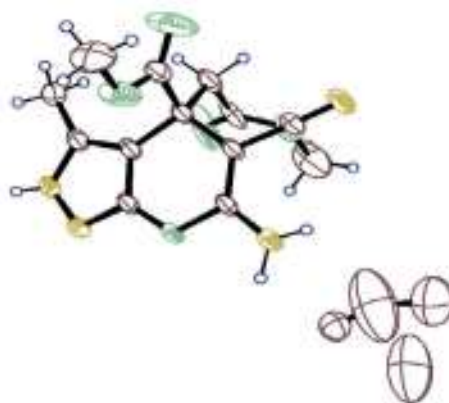


Figure 3: Compound 5j's ORTEP diagram (CCDC no. 959948).

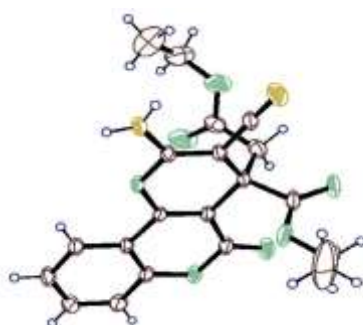


Figure 4: Compound 7i's ORTEP diagram (CCDC no. 959885)

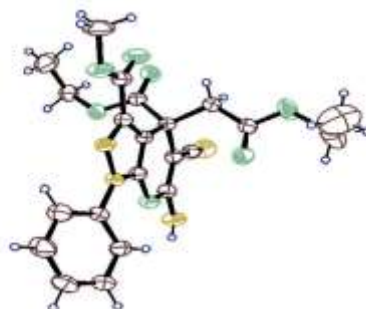


Figure 5: Compound 9a's ORTEP diagram (CCDC no. 968630).

In fact, the situation becomes very interesting if heterogeneous catalysts can be effectively recovered and reused. Two critical steps in organic synthesis are the separation of the best product from the reaction mixture and the separation of the catalyst. Catalyst recovery often requires filtration, which is a rather inefficient process. Extractive entanglement of natural compounds is another method using organic solvents. Nonetheless, when the response was completed in the preceding step, water was removed from the blend under reduced tension and 5 mL of ethanol was added. After blending was completed, the impetus remained on the magnet bar for a limited period of time before being removed with an outer magnet, revealing a perfect response combination. The recovered impetus was washed with ethanol and separated water before being vacuum dried. Great yields (92-97%) were obtained each time the interaction was reconstructed, allowing the impetus to be recovered. In the suggested dihydropyrano[2,3-c]pyrazole manufacturing cycle, a repurposed impetus was applied. To determine whether the impetus might be reused for this purpose, the responses of phenylhydrazine, ethyl acetoacetate, diethyl acetylene dicarboxylate, and malononitrile were studied (Plan 2). It was believed that this impulse might be recycled up to six times with minimal performance degradation. Powder XRD and FT-IR spectra of CuFe₂O₄ impetus were analyzed during the one-pot mix of the dihydropyrano[2,3-c] pyrazole subsidiary (5a). Integrity worthy of respect. Figures 2 and 4 display the results. The basic stability of MSNPs under response conditions

was demonstrated by the fact that after six runs, the XRD and FT-IR spectra of his impetus were essentially identical.

Recent interest in pyrano [2, 3-C] pyrazole derivatives can be attributed to the compounds' wide range of biological activities and potential applications in medicinal chemistry. Their combination necessitates procedures that are both efficient and kind on the environment. The primary focus of this talk is the development of a highly efficient and magnetically separable spinel ferrite catalyst for the synthesis of pyrano [2, 3-C] pyrazole derivatives.

Spinel Ferrite Catalysts Overview: Spinel ferrite catalysts are a special family of magnetic materials with outstanding catalytic capabilities due to their distinctive crystal structure. These catalysts are made up of cubic spinel-structured transition metal cations, such as Fe, Co, and Ni. For several applications, including chemical synthesis, their magnetic nature and catalytic activity make them very appealing.

delivering pyro [2,3-C]. **Pyrazole analogs:** Generally, pyrazole subsidiaries are changed over into pyrano [2, 3-C] pyrazole subordinates by consolidating them with different carbonyl mixtures within the sight of an impetus. The impetus chose significantly affects the response's general effectiveness, selectivity, and yield.

A potential tactic for this transition has been the use of spinel ferrite catalysts. These catalysts have a number of benefits like high stability, magnetic recoverability, and reusability that greatly add to their usefulness and eco-friendliness.

Advantages of Spinel Ferrite Catalysts:

1. **Highly effective:** In the production of pyrano [2, 3-C] pyrazole derivatives, spinel ferrite catalysts shown excellent catalytic activity. Within quick reaction times, they deliver high yields of the specified goods.
2. **Magnetic separability:** The magnetic properties of spinel ferrite catalysts make it simple to separate them using an outside magnet from the reaction fluid. This property streamlines the purifying procedure and removes the need for additional filtration stages, increasing the synthesis's general efficacy.
3. **Reusability:** Without significantly losing their catalytic activity, spinel ferrite catalysts may be easily recovered and employed in future processes. By lowering the cost of catalyst acquisition and disposal, this characteristic increases the process's economic viability.
4. **Environmental friendliness:** The use of spinel ferrite catalysts is consistent with green chemistry concepts. Because they frequently start with readily available, non-toxic components and produce no hazardous waste, the synthesis process has a little negative environmental effect.

CONCLUSION

Alternatively, we proposed a multicomponent-based strategy for pyrano[2,3-c]pyrazole synthesis. We synthesized eight compounds and generated their NMR and HRMS (ESI) profiles. Molecular docking analysis investigated how these drugs bind to the ATP- and lipid-restricted pockets. Most often, combinations of readily available starting materials are used, including 4H-chromium derivatives, pyrano[3,2-c] coumarins and dihydropyrano[2,3-c]pyrazoles. We have described a novel, useful and effective synthetic approach to pot four-component and three-component processes. Combining the synthesis and modification of the dihydropyrano[2,3-c]pyrazole scaffold can develop a new library of derivatives, increasing structural diversity. increase. The assembly of nanocatalysts around paramagnetic cores enables chemical processes to be carried out quickly, accurately and with high yields.

An advantageous and sustainable method is the synthesis of pyrano [2, 3-C] pyrazole derivatives employing a very effective and magnetically separable spinel ferrite catalyst. The remarkable catalytic activity, magnetic recoverability, reusability, and environmental friendliness of these catalysts are all clear. A important development in the world of organic synthesis, their use in the synthesis of pyrano [2, 3-C] pyrazole derivatives offers a viable and effective approach for the creation of these physiologically active molecules. Spinel ferrite catalysts can be used more widely in the synthesis of various chemical compounds with more study and improvement.

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