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SYNTHESIS OF Fe METAL COMPLEX BASED ON A TRIAZAPENTADIENE-TYPE LIGAND DERIVED FROM A PYRAZOLE SUBSTRUCTURE

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ABSTRACT

Three-component reactions are often characterized by complex mechanistic pathways, and the identification of intermediate species is essential for understanding their progression. In this study, a pyrazole-based ligand was synthesized, and its reaction with malononitrile and o-tolualdehyde was examined with the aim of obtaining triazine-containing heterocycles. Two products were detected by TLC and their structures were confirmed by single-crystal X-ray diffraction. The desired triazine derivative was successfully obtained; however, the formation of (2-methylbenzylidene) propanedinitrile—arising from a Knoevenagel condensation between malononitrile and o-tolualdehyde—was also observed. Although initially detected as an unexpected by-product of the three-component reaction, its appearance is fully consistent with the well-known propensity of malononitrile to readily condense with aromatic aldehydes. The reduced reactivity of the imine functionality, attributed to the ligand being present in its salt form, was identified as the key factor limiting full conversion toward the triazine scaffold. Considering the coordination ability of triazapentadiene-type ligands, an Fe(III) complex of the pyrazole-derived ligand was also synthesized within the scope of this work.

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1. Introduction

Determining the course of three-component reactions is one of the major challenges in modern organic synthesis. These types of reactions are generally studied using DFT methods. However, in some cases, elucidating the structures of intermediates formed at early stages can greatly facilitate understanding the direction in which the reaction proceeds. The reaction between dicyandiamide and pyrazole has been shown to afford (E) 1-(amino(1H-pyrazol-1-yl) methylene) guanidine [1], demonstrating that this transformation can occur under typical condensation conditions. Recent studies have emphasized that pyrazole-based aza-heterocycles are highly

versatile pharmacophores with broad therapeutic relevance, extensive reactivity, and widespread applications in synthetic and medicinal chemistry. Biguanides are a versatile class of compounds with broad applications in catalysis, metal complexation, organic synthesis, and medicinal chemistry, including well-known examples such as metformin and chlorhexidine, highlighting both their historical importance and renewed interest in developing new synthetic methodologies to expand their chemical diversity [2]. Efficient and environmentally friendly methods have been established for synthesizing monosubstituted biguanides from amines, utilizing high-yielding, chromatography-free, and water-compatible protocols, which are particularly effective for challenging aliphatic amines [3]. Incorporation of guanidine and biguanidine groups into chlorin derivatives enables the design of targeted photosensitizers with high photodynamic efficiency, offering a versatile platform for multifunctional drug development and improved selectivity in cancer therapy [4]. Comprehensive reviews further demonstrate that modern methodologies enable the efficient preparation of functionalized pyrazole derivatives from numerous precursors while revealing their notable anti-cancer, anti-inflammatory, anti-bacterial, and anti-viral activities [5]. Metal complexes of pyrazoles and other nitrogen-based heterocycles have attracted growing attention due to their diverse bioactivities, and understanding the relationship between their structural features and biological effects is essential for designing more effective and less toxic therapeutic agents [6]. Recent findings on azo dye–based pyrazole ligands and their transition-metal complexes demonstrate that such systems can be synthesized and structurally validated through comprehensive spectroscopic, thermal, and computational analyses, typically forming paramagnetic octahedral geometries. Moreover, these studies show that both the free ligands and their metal complexes exhibit notable antimicrobial and cytotoxic activities, with certain Fe(II) and Co(II) complexes displaying particularly enhanced biological efficacy [7]. Computational analyses, including NBO, QTAIM, and molecular docking, have additionally shown that pyrazole-based systems often possess favorable electronic distributions and strong biomolecular interactions, supporting their therapeutic potential [8]. In parallel, biguanide derivatives have demonstrated promising applications as organic linkers in coordination polymers and metal–organic frameworks, facilitating structural tunability and selective gas adsorption [9]. Recent mechanistic investigations revealed that substituent effects, solvent polarity, and acid–base properties strongly influence the reactivity of dicyandiamide-based condensation systems, enabling controlled access to structurally diverse heterocycles [10]. Advances in catalyst-assisted synthetic strategies, including transition-metal catalysis and organocatalysis, have further expanded the chemical space of pyrazole-containing frameworks under milder and more sustainable reaction conditions [11]. The pharmaceutical relevance of pyrazole derivatives continues to grow, with several compounds progressing into clinical evaluation for metabolic, neurological, and inflammatory disorders [12]. Additionally, multi-component reactions involving amidines, malononitrile, and aromatic aldehydes have emerged as powerful tools for rapidly constructing nitrogen-rich scaffolds with high atom economy and structural diversity [13]. Structure–activity relationship (SAR) studies have shown that introducing electron-withdrawing substituents or heteroaromatic fragments into pyrazole or biguanide cores can significantly enhance antimicrobial, antioxidant, and enzyme-inhibitory properties [14]. Recent studies demonstrated that pyrazole-based thiocarbohydrazide Schiff bases exhibit strong COX-2 binding affinity, supported by spectroscopic characterization and molecular docking analyses, suggesting their potential as promising anti-inflammatory agents. [15].

2. Experimental part

Materials and methods

All reagents — including the pyrazole derivatives, malononitrile, *o*-tolualdehyde, and iron (III) chloride hydrate — were purchased from commercial suppliers and used without further purification unless otherwise stated. The solvents were of analytical grade and employed as received. Infrared spectra were recorded using a standard FT-IR spectrometer, and elemental analyses were carried out at an accredited analytical laboratory. Single-crystal X-ray diffraction data were collected on a modern diffractometer equipped with a CCD detector.

2.1 Synthesis of pyrazole-based ligand ((E)-1-[amino(1H-pyrazol-1-yl)methylene]guanidinium chloride)

The ligand derived from pyrazole was synthesized by heating a mixture of pyrazole (12 mmol), cyanoguanidine (12 mmol), hydrochloric acid (12 mmol), and 3 ml of deionized water at 80 °C for 30 minutes. After the reaction mixture was cooled to room temperature, white crystalline products formed, which were subsequently filtered and collected. The obtained ligand was characterized using various analytical techniques, including FT-IR spectroscopy and single-crystal X-ray diffraction.

2.2 Three-component reaction

A mixture of (E)-1-[amino(1H-pyrazol-1-yl)methylene]guanidinium chloride (188 mg, 1 mmol), o-tolualdehyde (120 mg, 1 mmol) and malononitrile (66 mg, 1 mmol) was refluxed in methanol for 5 h. The solvent was subsequently removed in vacuo, and the residue was recrystallized from methanol using charcoal.Although the main goal was to obtain a triazine-based product, the reaction did not proceed through a single, clean pathway.

Alongside the expected heterocyclic compound, we also detected a second product**-(2-methylbenzylidene) propanedinitrile**. This by-product formed independently through a typical **Knoevenagel condensation** between malononitrile and *o*-tolualdehyde. Its appearance can be explained by the high reactivity of malononitrile toward aldehydes and by the fact that the ligand, present in its salt form, shows reduced nucleophilicity, limiting its involvement in the cyclization process.

As a result, the three-component reaction produced both the desired triazine-containing compound and the Knoevenagel condensation product, providing additional insight into the competitive pathways operating within the reaction mixture.

2.3 Synthesis of (2-methylbenzylidene)propanedinitrile via Knoevenagel Condensation

The compound (2-methylbenzylidene) propanedinitrile was formed through a classical Knoevenagel condensation between malononitrile and o-tolualdehyde. Although it first emerged as an unexpected side product during the three-component reaction, its appearance is fully in line with the well-known tendency of malononitrile to readily condense with aromatic aldehydes. During purification, the compound was isolated in a stable, crystalline form, and **high-quality single crystals suitable for X-ray diffraction were successfully obtained**, enabling precise structural verification. The identification of this product not only confirmed the presence of competing reaction pathways under the applied conditions but also provided a clearer picture of how these parallel processes influence the overall product distribution.

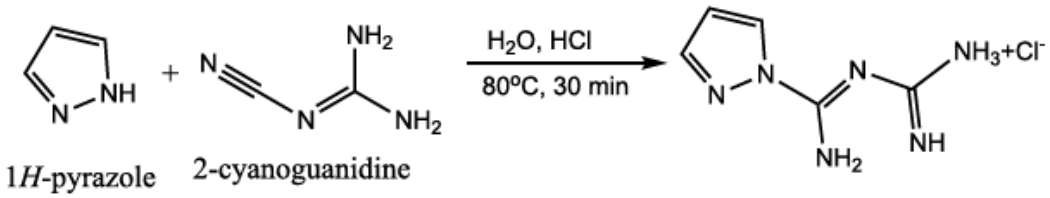
2.4 *Synthesis of Fe (III) Complex of a Pyrazole-Based Ligand*

The ligand and metal salt were separately dissolved in 3–4 ml of methanol and then combined at room temperature. Afterward, an additional small portion of the metal salt was dissolved in methanol (3–4 ml) and added to the mixture. Once the reaction had finished, 2–3 drops of sodium hydroxide were introduced, and the solution was allowed to recrystallize from methanol. The resulting metal complex was thoroughly characterized using infrared spectroscopy and elemental analysis.

3. Result and discussion

3.1 *Reaction and X-ray images of (E)-N`-(diaminomethyl)-1H-pyrazole-carboximidamide*

Considering the biological importance of pyrazole and its derivatives, we prepared pyrazole-based ligands derived from cyanoguanidine and pyrazole, as outlined in Scheme 1.



Scheme 1. Synthesis of pyrazole-based ((E)-N′-(diaminomethyl) 1H-pyrazole-1-carboximidamide).

The ligand (E)-1-(amino(1H-pyrazol-1-yl)methylene) guanidinium chloride was synthesized through a nucleophilic addition reaction, in which the amine nitrogen of pyrazole attacks the cyano group of dicyandiamide under acidic conditions. When the same transformation is attempted under basic conditions—using sodium hydroxide instead of hydrochloric acid—the reaction yields complex product mixtures that are difficult to isolate and characterize. Owing to continuous protonation, all five nitrogen atoms within the (E)-1-(amino(1H-pyrazol-1-yl)methylene) guanidinium chloride framework are capable of coordinating to metal centers. The cationic structure of the (E)-1-(amino(1H-pyrazol-1-yl)methylene) guanidine unit is illustrated in Figure 1.

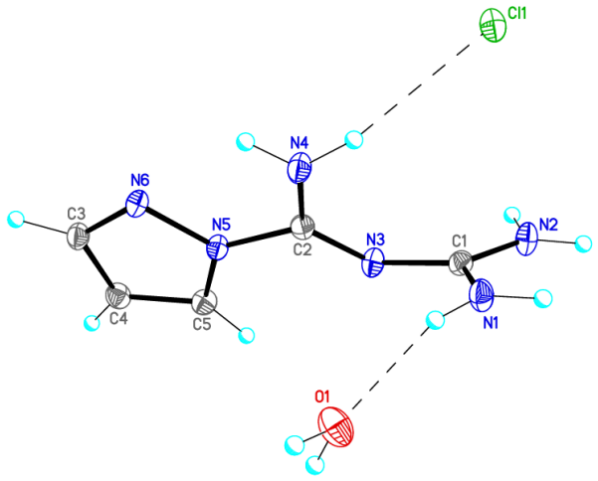


Figure 1. X-ray images of (E)-1-(amino(1H-pyrazol-1-yl)methylene)guanidine.

3.2 **X-ray images** *of (2-methylbenzylidene)propanedinitrile*

As shown in **Figure 2,** single-crystal X-ray analysis confirms that the (2-methylbenzylidene) propanedinitrile molecule adopts the expected E-configuration around the C=C double bond. The dinitrile fragment (C1–C10–N1 and C1–C11–N2) is almost linear relative to the benzylidene moiety, which is typical for C≡N groups. The aromatic ring (C3–C9) is planar, with the o-methyl substituent (C8–C7–C6 direction) causing a slight, noticeable deviation from the ring plane. The geometry around C2 supports effective π-conjugation across the molecule, consistent with the electron-withdrawing nature of the cyano groups. Overall, **Figure 2** illustrates the structural integrity and electronic characteristics of the synthesized compound.

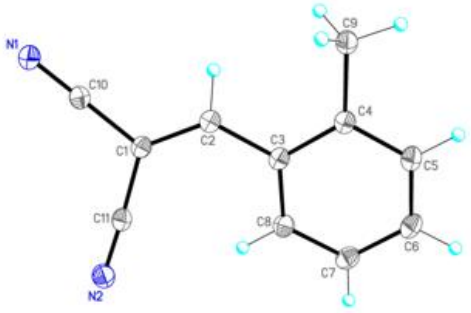
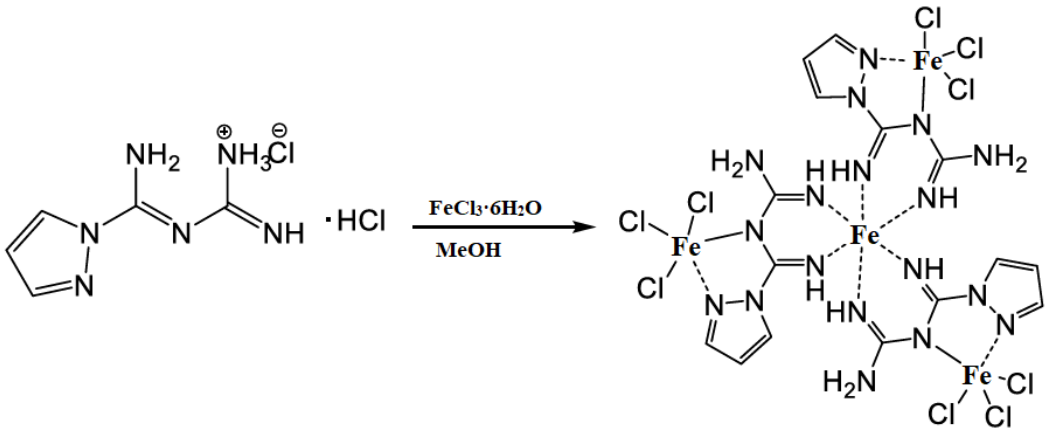


Figure 2. X-ray images of (2-methylbenzylidene) propanedinitrile.

3.3 Synthesis reaction of Fe(III) complex of a Pyrazole-Based Ligand

As illustrated in **Scheme 2**, the complex with the formula ($C_{36}H_{81}Cl_9Fe_8N_{36}O_{21}$) was prepared by reacting the $H_5L•HCl$ ligand with $FeCl_3·6H_2O$ in methanol.



Scheme 2. Synthesis of Fe (III) metal complex of pyrazole-based ligand.

Yield of the reaction 85,7 per cent, conversion 90 percent and analytic values given below.

The average atomic masses employed in the calculations were: C 12.011, H 1.008, N 14.007, O 15.999, Cl 35.453, and Fe 55.845. Based on these values, the molecular weight of the complex was calculated as M_r = 2120.112 g·mol^{-1} (36×12.011 + 81×1.008 + 9×35.453 + 8×55.845 + 36×14.007 + 21×15.999 = 2120.112).

The calculated elemental composition of the complex is as follows:
C 20.39 %, H 3.85 %, N 23.78 %, Cl 15.05 %, Fe 21.07 %, and O 15.85 %.

FT-IR analysis reveals that the characteristic ligand-based vibrational modes—ν(O–H), ν(N–H), ν(C=O), and ν(C=N)—are retained upon coordination, appearing in their typical regions (approximately 3270–3380, 2950, 1620, and 1585 cm^{-1}, respectively). In contrast, metal-centered vibrations attributable to Fe–Cl and Fe–N bonding emerge in the lower-frequency domain (ca. 250–600 cm^{-1}), consistent with the formation of the corresponding coordination environment.

4. Conclusion

Pyrazole-based ligands were successfully synthesized from pyrazole and cyanoguanidine and fully characterized using single-crystal X-ray diffraction. The three-component reaction with o-tolualdehyde and malononitrile produced both the target triazine compound and the Knoevenagel condensation by-product, (2-methylbenzylidene) propanedinitrile, revealing competing reaction pathways. The Fe(III) complex of the pyrazole-based ligand was prepared in methanol and confirmed by elemental analysis. Overall, these results demonstrate that the ligand efficiently forms stable metal complexes with precise molecular architectures. This study provides a clear foundation for exploring the biological activity of these complexes, including their potential as enzyme inhibitors.

It is easy to transfer electron bridge between Fe-S in the natural proteins and electron and magnetic interaction via bridges between Fe-Fe. The value of metal Fe is increase because of its amount, price and eco- friendly last and catalytic and electrochemistry usage. Same complex has various properties like magnetic, catalytic and electrochemical and it is possible use multiple areas. Pyrazole based ligand carry out easy electron and steric change properties and it makes easy to control magnet changes around it.

Potential application Fe based pyrazole ligand is also possible to make oxidation reduction processes, various magnet materials, for enzyme change reaction and also specific bridge interaction.

REFERENCES

1. Mahmudov, I., Atioğlu, Z., Akkurt, M., Abdullayev, Y., Sujayev, A., & Bhattarai, A. (2022). *Crystal structure and Hirshfeld surface analysis of 2-(4-amino-6-phenyl-1,2,5,6-tetrahydro-1,3,5-triazin-2-ylidene) malononitrile dimethylformamide hemisolvate*. *Acta Crystallographica Section E: Crystallographic Communications, 78*, 691–695. https://doi.org/10.1107/S2056989022006910
2. *Grytsai, O., Ronco, C., & Benhida, R. (2021). Synthetic accesses to biguanide compounds. Organic & Biomolecular Chemistry, 19(20), 4441–4458.* https://doi.org/10.*3762/bjoc.17.82*
3. *Bardovskyi, R., Fabre, M., Ronco, C., & Benhida, R. (2021). Mild Biamidine-Transfer Conditions for the Synthesis of Aliphatic Biguanides. SynOpen, 5(4), 314–320.* https://doi.org/10.1055/a-1681-4544
4. Ostroverkhov, P. V., Kirin, N. S., Tikhonov, S. I., Usachev, M. N., Abramova, O. B., Kaplan, M. A., Mironov, A. F., & Grina, M. A. (2021). *Guanidine and biguanidine derivatives of natural chlorins: Synthesis and biological assessment*. **Journal of Porphyrins and Phthalocyanines, 25**(12), 1390–1403. https://doi.org/10.6060/mhc224071o
5. Moussa, Z., Ramanathan, M., Alharmoozi, S. M., Alkaabi, S. A. S., Al Aryani, S. H. M., Ahmed, S. A., & Al-Masri, H. T. (2024). *Recent highlights in the synthesis and biological significance of pyrazole derivatives*. *Heliyon, 10*(20), e38894. https://doi.org/10.1016/j.heliyon.2024.e38894
6. Malinowska, K., Lorenz, I.–P., Sadowska, B., & Mucha, P. (2019). *Metal ion complexes with pyrazoles, aziridines and diaziridines – synthesis and biological activity*. *Current Medicinal Chemistry, 26*(4), 648–663. https://doi.org/10.2174/0929867325666180221124447
7. Alkurdi, A. F., AlJahdali, M. Sh., & Alshehri, A. A. (2022). *Synthesis, characterization, DFT calculation, and biological activity of pyrazole-based azo-metal(II) complexes*. *Results in Chemistry, 4*, Article 100457. https://doi.org/10.1016/j.rechem.2022.100566

8. Ebenezer, O., Singh-Pillay, A., Koorbanally, N. A., & Singh, P. (2020). *Antibacterial evaluation and molecular docking studies of pyrazole-thiosemicarbazones and their pyrazole-thiazolidinone conjugates*. **Medicinal Chemistry Research**. Advance online publication. https://doi.org/10.1007/s11030-020-10046-w
9. Veisi, H., Abrifam, M., Kamangar, S. A., Pirhayati, M., Saremi, S. G., Noroozi, M., … & Karmakar, B. (2021). Pd immobilization on biguanidine-modified Zr-UiO-66 MOF: synthesis, characterization, and application as a reusable heterogeneous catalyst. *Scientific Reports, 11*, 21883. https://doi.org/10.1038/s41598-021-00991-3
10. Kunishima, M., Kitamura, M., Tanaka, H., Nakakura, I., Moriya, T., & Hioki, K. (2013). Study of 1,3,5-triazine-based catalytic amide-forming reactions: Effect of solvents and basicity of reactants. *Chemical & Pharmaceutical Bulletin, 61*(8), 882–886. https://doi.org/10.1248/cpb.c13-00368
11. Lin, W.-S., & Kuwata, S. (2023). Recent developments in reactions and catalysis of protic pyrazole complexes. *Molecules, 28*(8), 3529. https://doi.org/10.3390/molecules28083529
12. Ahmed, A., Zaib, S., Bhat, M. A., Saeed, A., Altaf, M. Z., Zahra, F. T., Shabir, G., Rana, N., & Khan, I. (2024). Acyl pyrazole sulfonamides as new antidiabetic agents: Synthesis, glucosidase inhibition studies, and molecular docking analysis. *Frontiers in Chemistry, 12*, Article 1380523. https://doi.org/10.3389/fchem.2024.1380523
13. Liu, Y., & Wheeler, S. E. (2024). Impact of solvent dielectric and protonation state on rotational barriers in protonated 1,3,5-triazines. *Journal of Organic Chemistry, 89*(8), 5480–5484. https://doi.org/10.1021/acs.joc.3c02918
14. Bhagwat, S. K., Pawar, T. J., Kulkarni, S. A., Patil, A. A., More, R. A., Jimenez-Halla, J. O. C., Alvarado-Salazar, J. A., Olivares-Romero, J. L., Muteeb, G., Delgado-Alvarado, E., & Patil, S. V. (2024). *Synthesis, characterization, biological activities, and computational studies of pyrazolyl–thiazole derivatives of thiophene*. *RSC Advances, 14*, 39004–39016. https://doi.org/10.1039/D4RA06228K
15. Abdul-Malik, M. A., Abdou, A., Fouad, M. R., Alkamali, A. S. N., & Abdel-Rahee, S. A. A. (2024). Synthesis, spectral characterization and molecular docking studies of some thiocarbohydrazide-based Schiff bases with pyrazole moiety as potential anti-inflammatory agents. *Current Chemistry Letters, 13*(4), 683–694. https://doi.org/10.5267/j.ccl.2024.5.002