

SYNTHESIS OF LIGAND PARA-DI-2-(1-PHENYL-3-PYRIDYL-4,5-DIHYDRO-1H-PYRAZOL-5-YL) BENZENE BY ALDOL CONDENSATION METHOD

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Abstract

Synthesis of pyrazoline derivative ligand para-di-2-(1-phenyl-3-pyridyl-4,5-dihydro-1H-pyrazol-5-yl)benzene has been successfully carried out by aldol condensation method using 2-acetyl pyridine and terephthalaldehyde in ethanol solution. The synthesis results are then reacted with excess phenyl hydrazine. The yield of ligand obtained was 63.10% of a yellow solid. The ligand was characterized using ¹H-NMR spectroscopy, ultraviolet-visible (UV-Vis) spectroscopy, fourier transform infra-red (FTIR) spectroscopy and spectrofluorometer. The characterization with UV-Vis spectrophotometer results shows ligand has a large value of molar absorptivity (ϵ) at wavelength 236 nm and concentration 5×10^{-5} M. The results indicate that the ligand has a strong fluorescence intensity. It proved by peak emission at 467.5 nm ($I = 4055$ a.u).

Keywords: aldol condensation method; chalcone; fluorosensor; organic fluorophore.

1. INTRODUCTION

Organic compound relating with electron donating and electron accepting group via delocalized π -bond conjugated linker have involved escalating consideration since they can serve as photoactive and electro-active material in various filed of material science, one example is as fluorescence chemosensor. Many reactions have been reported to synthesize organic compounds for use as ligand such as aldol condensation, Suzuki coupling reaction, Claisen-Schmidt condensation and other reaction [1]. Aldol condensation reactions have been used extensively in the formation of carbon-carbon bonds, due to their simple reaction with raw materials that are easily obtained and very safe for the environment. Among the widely used ligands as a fluorosensor, pyrazoline and its derivatives have been studied extensively [2,3]. The pyrazoline is a dihydroproduct of pyrazole [4]. Pyrazoline derivatives have drawn much attention because of their excellent blue fluorescence property, high fluorescence quantum yield, the rigid flat structure and high hole-transport efficiency [5].

Pyrazolines are also used as optical brighteners and whiteners [6]. Qun *et al* have managed to synthesize and characterize a pyrazoline derivative, namely 5-aryl-3-benzimidazolyl-1-phenyl-pyrazoline, then examined the optical properties of the compound. In this research, the compound of 5-aryl-3-benzimidazolyl-1-phenyl-pyrazoline shows strong fluorescence intensity [3]. Bremer *et al* also have managed to synthesize, characterize, and examine the optical properties of a pyrazoline derivative compound of 2,6-Bis(5-(2,2-dimethylpropyl)-1H-pyrazol-3-yl)pyridine, and the results show that this compound also gives a strong

fluorescence intensity and is efficient to be applied as ligands for metal separation of lanthanides(III) and actinides(III) [2]. Bozkurt *et al* have managed to synthesize a new derived pyrazoline which is applied as pH sensors [7].

This study aims to produce para-di-2-(1-phenyl-3-pyridyl-4,5-dihydro-1H-pyrazol-5-yl)benzene ligand which is a derivatives of pyrazoline compounds with aldol condensation method. Synthesis of pyrazolin derivative ligands which have advantages such as having good photophysical properties and ease of synthesis. Adding the aromatic system to pyridine, and cyclic pyrazolin in the para position is expected to increase the intensity of ligand fluorescence. However, to the best of authors' knowledge, up to now there have not been reports on ligand para-di-2-(1-phenyl-3-pyridyl-4,5-dihydro-1H-pyrazol-5-yl)benzene as new material. The study results are expected to contribute to the advancement of science, especially the synthesis of organic compounds that can be used as ligands and its application as fluorosensor.

2. METHODS

2.1 Equipment and Materials

The chemicals used for the synthesis of the ligand is 2-acetylpyridine (Sigma-Aldrich A21002 99%), sodium hydroxide p.a (Merck), phenyl hydrazine (Sigma-Aldrich 97%), terephthalaldehyde (Sigma-Aldrich T2207 99%), ethanol p.a (Merck), methanol p.a (Merck), n-hexane p.a (Merck), ethyl acetate p.a (Merck), dichloromethane p.a (Merck), acetonitrile p.a (Merck), and sodium sulfate anhydrous p.a (Merck).

Equipment used includes magnetic stirrer hotplate, analytical balance, spatula, measuring pipette, TLC plate, rotary evaporator, and a variety of equipment such as erlenmeyer glass, stir bar, beaker glass, columns, and volumetric flask. The instrument used in this study are $^1\text{H-NMR}$ (Agilent Varian DDR2), FTIR (Shimadzu IR 8400 S), UV-Vis (Thermo Scientific Genesys 10uv), and a fluorescence spectrophotometer (Shimadzu RF-540).

2.2 Experiment

Synthesis procedure of ligand para-di-2-(1-methyl-3-pyridyl-4,5-dihydro-1H-pyrazol-5-yl)benzene is following procedure that previously reported from the authors in Ref. [8], 2-acetylpyridine (8 mmol in 20 ml of anhydrous ethanol and 2 mmol NaOH) with terephthalaldehyde (4 mmol), until reddish yellow solution is formed. This solution is stirred with a magnetic stirrer for 24 hour at room temperature and pressure. After 24 hours, the solution changes color to brownish red. The precipitate that formed is then filtered and washed with cold ethanol. The solid obtained chalcones dried, and then weighed. Furthermore, chalcone (2 mmol is dissolved in 10 ml of anhydrous ethanol) and is stirred for 10 minutes at room temperature, and then 4 mmol of phenyl hydrazine is added and the mixture was refluxed to 80°C for 24 hours. The solvent was filtrated and crude orange solid was purified by column chromatography with silica gel using n-hexane : ethyl acetate (3:2) to afford the desired ligand as a yellow solid. The ligand obtained is then characterized by FTIR, $^1\text{H-NMR}$ and UV-Vis spectroscopy.

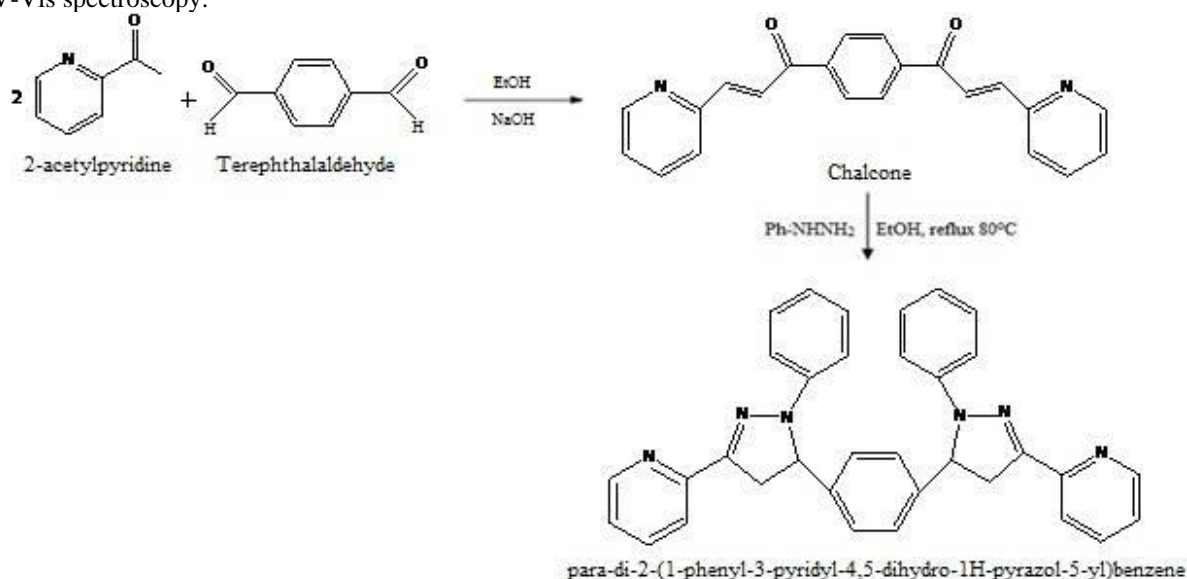


Figure 1. Reaction pathway of ligand

The structure of ligand was identified by FTIR spectroscopy and the result can be seen in Figure 2. FTIR spectrum of the ligand shows the absorption in the wave numbers of (cm^{-1}) 3053.52 is due to the cyclic amine

2.3 Fluorescent Experiment

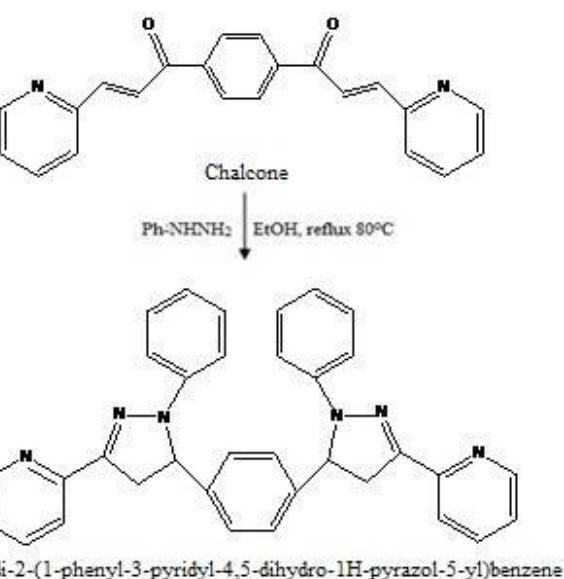
The synthesized ligand was measured for fluorescence intensity using a spectrofluorometer. The solutions of ligand (5.0×10^{-5} M) were prepared by dissolving 0.26 mg of solid in 100 ml of acetonitrile. Before measuring emissions, scanning is done first to find the appropriate maximum emission wavelength. Measurements were carried out at a wavelength range of 220-550 nm.

3. RESULTS AND DISCUSSION

3.1 Synthesis and Characterization of Ligand

Ligand synthesis reaction can be seen in Figure 1. The ligand is synthesized by the aldol condensation method and its structure was identified by using FTIR, $^1\text{H-NMR}$ and UV-Vis spectroscopy.

The synthesis of ligand carried out in two stages. In the first stage it produces an α , β -unsaturated compound called chalcone with a yield of 90.01% (yellow solid). The solids obtained are deposits resulting from the mixing process of a mixture of 2-acetylpyridine, NaOH, terephthalaldehyde and ethanol for 24 hours at room temperature. Then in the second stage, the chalcone compound obtained was reacted with excess phenyl hydrazine in ethanol media and reflux for 24 hours at 80°C of temperature and produced a crude orange precipitate and then purified by column chromatography. The yield of ligand obtained was 63.10% of a yellow solid.



pyrazoline [8]. The absorption in the wave numbers of 2922.31 cm^{-1} which indicates an aromatic C-H stretching on the pyridine and phenyl ring, which generally is in the range of $3077\text{-}3003 \text{ cm}^{-1}$ [9]. The presence of aromatic C-

H stretching is also found in the region of 1140.97-986.94 cm^{-1} . The emergence of absorption bands in the region of 1671.52-1496.10 cm^{-1} is caused by the vibration of the C=C in the aromatic rings [10].

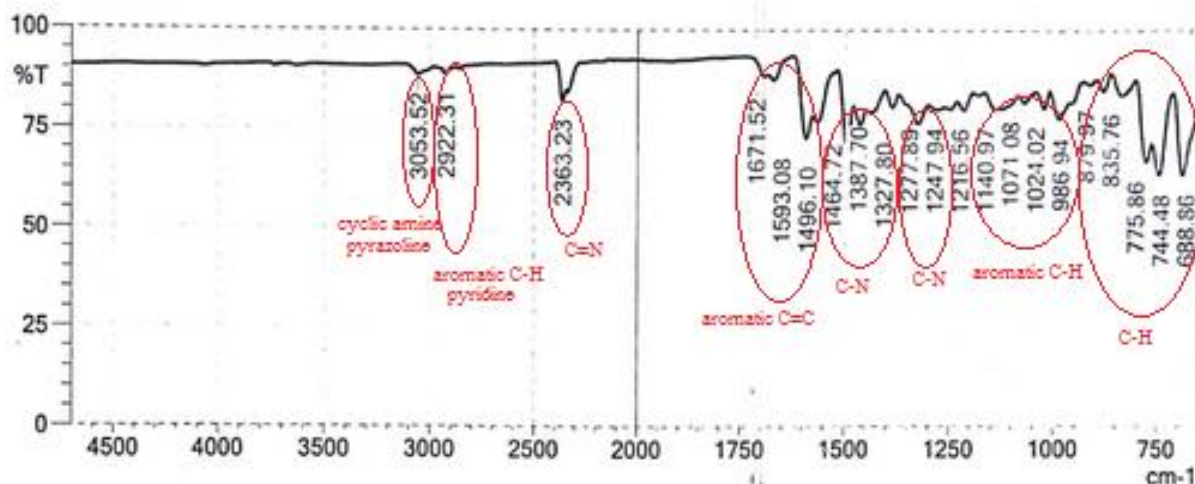


Figure 2. FTIR spectrum of ligand

The existence of absorption band in the region of 879.79-688.86 cm^{-1} is due to the bending vibration (out-of-plane bending) in C-H bonds [11]. The emergence of absorption bands in the area in 1464.72-1247.94 cm^{-1} is due to the C-N bonds in the ring [8].

The further structural identification was confirmed by $^1\text{H-NMR}$ spectrum. Based on the results of characterization by $^1\text{H-NMR}$ (500 MHz, CDCl_3) showed: δ 8.62 (m, 1H), 8.0 (m, 1H), 7.89 to 7.62 (m, 2H), 7.28 to 7.21 (m, 2H), 7.09 to 6.81 (m, 5H), 4.01 to 4.04 (m, 1H), and 3.39 to 3.38 (m, 2H). The

downfield-shifted multiple signals at 4.01-4.04 ppm was assigned to single proton of pyrazole's carbon that attached to benzene. For the first phenyl ring that bonded to nitrogen atom of pyrazoline (N-N-Ph), multiples at 6.81-7.09 ppm were attributed to five protons of each phenyl carbons. This is in accordance with the research conducted by the authors in Ref. [8].

Aromatic compounds provide several absorption bands [12]. UV-Vis spectrum of the free ligand shows one absorption peaks (Figure 3).

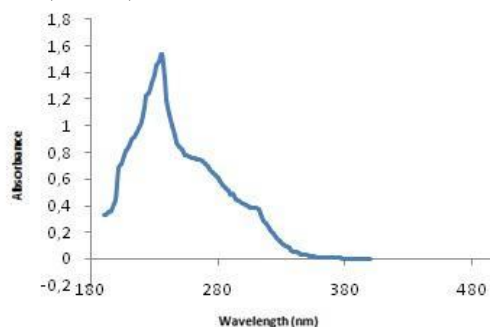


Figure 3. UV-Vis spectrum of ligand

The electron transition of $\pi \rightarrow \pi^*$ marked by the value of molar absorptivity (ϵ) that is relatively large and is seen in absorption peaks (Table 1). Molar absorptivity (ϵ) value that is relatively large also indicates that this compound has a strong fluorescence intensity.

Table 1. The UV-Vis Absorption Peak of Ligand

λ max, nm (ϵ , $\text{M}^{-1} \text{cm}^{-1}$)	Absorption
236 nm (30800000)	1.540

The peak wavelength results obtained are different from the authors in Ref. [8] with a difference of 210 nm to 236 nm so that the shift towards visible is due to the increase in the auxochrome group with the bathochromic shift where the maximum wavelength towards the greater.

3.2 Fluorescence Studies

A compound which can produce a fluorescence phenomenon is generally a polyaromatic compound which contains many conjugated π ions [11]. Based on Figure 4, there are two peaks excitation in the area of

256.5 nm (I = 3560 a.u) and 365.0 nm (I = 4527 a.u) 4055 a.u) with a similar pattern. and there are peak emission in the area 467.5 nm (I =

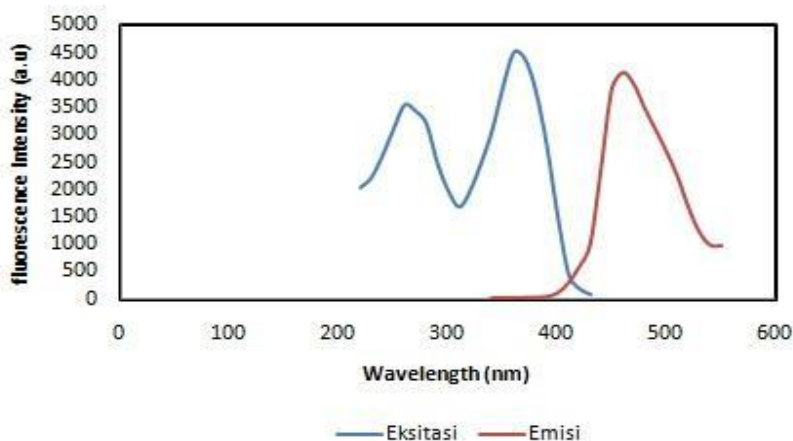


Figure 4. Fluorescence spectra of ligand

Emission of a compound is the opposite of its excitation. Because the path taken by the electrons at the time of excitation and emission are identical, then the emission and excitation spectra should be a mirror image. This is in accordance with the characteristics of the emission spectra which is a shift in wavelength towards a larger shape similar to the excitation spectra. This shift, known as a stoke shift, is caused by the loss of energy in the excited state caused by the decay of the electron flash to the ground state of the excited state [11].

4. CONCLUSIONS

Preparation of ligand para-di-2-(1-phenyl-3-pyridyl-4,5-dihydro-1H-pyrazol-5-yl)benzene using aldol condensation method has been successfully carried out with a result of 63.10 % yield. The success of the synthesis of the ligand can be seen from the structure characterization data of FTIR and ¹H-NMR, and powered by UV-Vis spectroscopy data. Large value of the molar absorptivity (ϵ) on UV-Vis spectrum shows that the ligand has a strong fluorescence intensity, which can be seen from the spectrofluorescence data.

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REFERENCES

[1] Asiri, A. M., Najat S. M., Al-Ghamdi., Huriya D. C., Parveen K., Salman A. K. Physicochemical and Photophysical Investigation of Newly Synthesized

Carbazole Containing Pyrazoline-Benzothiazole as Fluorescent Chemosensor for The Detection of Cu²⁺, Fe³⁺& Fe²⁺Metal Ion. *Journal of Molecular Structure*. **2019**, 1195 : 670-680. <https://doi.org/10.1016/j.molstruc.2019.05.088>.

- [2] Bremer, A., Ru, C. M., Girnt, D., Mu, U., Rothe, J., Roesky, P. W., Panak, P. J., Karpov, A., Mu, T. J. J., Denecke, M. A., Geist, A. 2,6-Bis(5-(2,2-dimethylpropyl)-1H-pyrazol-3-yl)pyridine as a Ligand for Efficient Actinide(III)/ Lantanide(III) Separation. *ACS Publications Inorganic Chemistry* 51, **2012**, 5199-5207. [dx.doi.org/10.1021/ic30005261](https://doi.org/10.1021/ic30005261). *Inorg. Chem*, 51, 5199-5207.
- [3] Qun, X., Hui, X., Zhu, Y., Qing, Y., & Wu, J. Synthesis and Characterization of novel 5-aryl-3-benzimidazolyl-1-phenyl-pyrazoline Derivatives. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, **2012**, 98, 76–80. <https://doi.org/10.1016/j.saa.2012.08.036>.
- [4] Velmurugan, V., Surya, S.P., Kalvikkarasi, S., Shanmugapriya, S., Vijey, A.M. Synthesis, Characterisation And Evaluation of Analgesic Activity of 3,5-Disubstituted Pyrazoline Derivatives. *International Journal of Pharmacy and Pharmaceutical Science*, **2012**, Vol 4, Issue 2, 189-191.
- [5] Zhang, Y. P., Qing, H. Z., Yung-Sang, Y., Xiao-Yu, L., Chun, M. M., Jia, X. R., Hui, C. G. (2018). A chromene pyrazoline derivatives fluorescent probe for Zn²⁺ detection in aqueous solution and living cells. *Inorganica Chimica Acta*. **2018**, 479 : 128-134. <https://doi.org/10.1016/j.ica.2018.04.020>.
- [6] Sid, A., Kaddour, L., Mahieddine, M., Nouara, Z., Paul, M. Synthesis and Characterization of 1-formyl-3-phenyl-5-aryl-2-pyrazolines. *European Journal of Chemistry* 2(3), **2011**, 311-313. DOI:10.5155/eurjchem.2.3.313.414.

- [7] Bozkurt, E., Gul, H. I., & Ozgun, D. O. Pyrazoline derived new “ off-on-off ” fluorescent pH sensors. *Optical Materials*, 84(February), **2018**, 550–555. <https://doi.org/10.1016/j.optmat.2018.07.052>.
- [8] Hakim, Y. Z., & Zulys, A. A Fluorescence Study of Pyrazole Derivative 2-(1,5-diphenyl-4,5-dihydro-1H-pyrazole-3-yl)pyridine Upon Addition of La^{3+} and Eu^{3+} Ions. *International Conference on Materials, Manufacturing and Mechanical Engineering*, **2016**, pp. 362–366.
- [9] Kosela, S. Determiation of Molecular Structure Based on theSpectra Data, Issuing Faculty of Economics.,University of Indonesia.**2010**.
- [10] Lakowicz, J.R. Principles of Fluorescence Spectroscopy,.first ed. Springer 1-382. Singapore. **2006**.
- [11] Ciupa, A., Mahon, M. F., Bank, A. De, & Caggiano, L. Simple Pyrazoline and Pyrazole “turn on” Fluorescent Sensors Selective for Cd^{2+} and Zn^{2+} in MeCN. *Organic & Biomolecular Chemistry*. *i*,2012,pp. 8753–8757. <https://doi.org/10.1039/c2ob26608c>.
- [12] Mulja, H. M & Suharman. *Analisis Instrumental*. Surabaya: Airlangga University Press. **1995**.