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# Synthesis and Characterization of 4-chloro-N'-2-(3,3-dimethyl-1,3-dihydro-2H-benzo[f]indol-2-ylidene)-3-oxopropylidene) benzohydrazonamide and 3-(4-chlorophenyl)-1H-1,2,4-triazole

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## Abstract

Six derivatives of 4-Chlorobenzohydrazonamide have been successfully synthesized. The synthesis pathway was divided in two parts, the first part including synthesis of two starting materials 4-Chlorobenzohydrazonamide (3) and 2-(3,3-dimethyl-1,3-dihydro-2H-benzo[f]indol-2-ylidene) malonaldehyde (4). The second part is the synthesis of of indole Schiff base (4) and 3-(4-chlorophenyl)-1H-1,2,4-triazole (6) from (3). The structures of these compounds were characterized by their spectroscopic techniques such as, FT-IR, 1HNMR and 13CNMR.

**Keywords:** Heterocyclic, Indole, Schiff bases, Vilsmeier-Haack.

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# تخليق وتشخيص 4-كلورو -2-'N- (3،3-ثنائي ميثيل-1،3-ثنائي هيدرو-2H-بنزو [و] إندول-2-إيليدين) -3-أوكسوبروبليدين) بنزوهيدرازوناميد و 3- (4- الكلوروفينيل) -1 1-H،2،4-تريازول

**زهراء علي ناصر و لمى سلمان عبد**

قسم الكيمياء - كلية العلوم - جامعة ديالى

## الخلاصة

تم تحضير ستة من مشتقات 4-كلورو بنزوهيدرازوناميد بنجاح. تم تقسيم المركبات المحضرة إلى جزأين ، الجزء الأول تحضير مادتين ابتدائيتين كلوروبنزوهيدرازوناميد (3) و2- (3،3-ثنائي ميثيل-1،3-ثنائي هيدرو-2H-بنزو [و] إندول-2-إيليدين ) مالونالدهيد (4). تضمن الجزء الثاني تحضير قاعدة شيف إندول من (4) و 3- (4-كلوروفينيل) -1H-11،2،4-تريازول (6) من (3). تم تشخيص بنية هذه المركبات بواسطة خصائصها الفيزيائية وبواسطة تقنيات التحليل الطيفي مثل FTIR و1 HNMR و 13CNMR.

**الكلمات المفتاحية :** حلقية غير متجانسة و اندول و قواعد شف و تفاعل فلسماير هاك

## Introduction

Heterocyclic compounds are the most numerous and diverse group of organic compounds which play an important function in a variety of domains, including Medical applications.Indole is an example of a heterocyclic organic compound with the chemical formula (C8H7N) that has one atom in its structure other than carbon atoms, indole contains a nitrogen atom in its pyrrole ring [1]. Indole and many of its derivatives are the most interesting heterocycles class containing nitrogen due to their variety of biological actions, which include antitumor, [2,3] antiviral, [4] anxiolytic, [5,6] and anti-inflammatory [7] properties. They can also be effective in the treatment of cancer and immune-related illnesses [8].

Schiff bases are organic compounds contain the imine chemical group (azomethine) of the formula (R-CH=NR'), where R' ≠ H, which belongs to an imine subclass. Schiff bases are mainly made by condensation of primary amines with active carbonyl groups. This chemical family has also been demonstrated to have a variety of biological effects, such as antimicrobial properties. Imine or azomethine groups can be found in a wide range of natural, naturally

derived, and non-natural compounds [9, 10]. They are utilized as intermediates in the synthesis of oxazoles, thiadiazolines, and thiazolidones [11, 12]

The indole Schiff bases Are known as a significant class of heterocyclic organic compounds which have wide applications in many fields for examples anti-inflammatory activity [13], antimicrobial activity [14], antibacterial, antifungal, antitumor activity [15] and antioxidant [16]

Since 1927, the discovery of Vilsmeier-Haack reagent (e.g. POCl3+DMF) has piqued the interest of synthetic organic chemists. Because it is one of the most prevalent functional groups for carbon-carbon bond formation, it is most commonly employed to introduce the aldehyde group into aromatic rings. DMF, POCl3 serves as both a reagent and a solvent in the Vilsmeier-Haack reaction. [17] The Vilsmeier reaction was originally developed to formylate Substrates with activated aromaticity and carbonyl compounds; nevertheless, right now widely used to synthesize heterocyclic compounds such as quinolines, indoles, quinozolines, and pyridines. Vilsmeier reaction-based synthesis of different substituted chloronicotinaldehydes has received its tack a lot of attention in the literature. Under Vilsmeier reaction conditions, Meth-Cohn and Westwood synthesized 2-chloropyridines, pyridones, and quinolines utilizing enamides. [18]

## Materials and Methods

### Chemical and Solvents

Chemical, solvent and reagents used in experiments curried out in this study were from different sources and used without any further purification.

### Spectrophotometry

Purification and verification of the final derivatives were performed by spectroscopic ways such as 1H and 13C NMR (Avance Neo Neo 400, Iran), FT-IR spectrophotometer Perkin-Elmer Spectrum version 10.02 at the Department of Chemistry, Faculty of Science, Diyala University.

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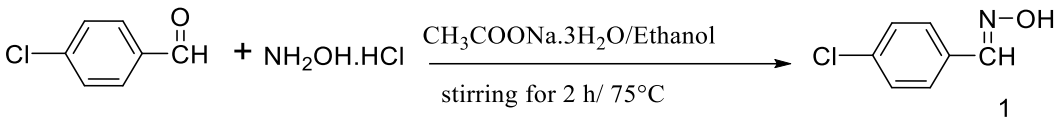
**Tools and Instruments**

The reactions follow up was achieved through thin layer chromatography (TLC) using alumina plates (size 20×20 cm) percolated with silica gel and Fluorescence Analysis Cabinet Model CM-10 as a detector. The Stuart SMP10 electronic apparatus used to calculate the melting point of the final products ((Department of Chemistry, Faculty of Sciences, and University of Diyala).

**General Methods**

**Synthesis of 4-chlorobenzaldoxime**

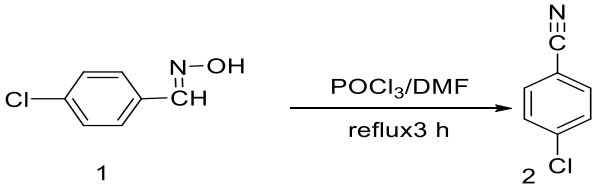



**Scheme 1:** Synthesis of 4-chlorobenzaldoxime

Hydroxyl aminehydrochloride (1.0g, 0.014 mol) and (2g, 0.014mol) of sodium acetate tri-hydrate in distilled water (5mL) at room temperature was added to a solution of 4-Chlorobenzaldehyde (0.5g 0.004mol) in ethanol (20 mL). After constant stirring in a water bath at 75°C for 2h. The resulting mixture was cooled in ice bath, bright white precipitate was formed direct, filtered off, and recrystallized from ethanol to give 1. Yield: (90%); white precipitate; m.p. 201-203 °C.

IR (KBr) νmax/cm-1: 3302, 3055, 2997, 1655, 1595, 1572, 1493, 1398, 1317, 1299, 973, 822, 825

**Synthesis of 4-chloro benzonitrile**

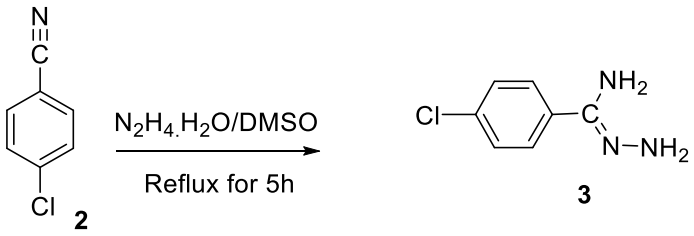



**Scheme 2:** Synthesis of 4-chloro benzonitrile

In a round bottom flask mixture of 4-chlorobenzaldoxime (0.5g, 0.0032mol) and DMF (10 mL) was stirred in ice bath for 15 min and then POCl3(0.33 mL) was added. The resultant mixture was agitated for 30 minutes at -5°C, followed by 30 minutes at room temperature and 3 hours inside an oil bath with reflux. H2O (10 mL) was then gradually added once the reaction cooled to room temperature during the course of the previous night. The resulting precipitate was collected by filtration, dried oven to furnish 2.Yield: (94%); White precipitate; m.p. 232-234 °C

IR (KBr) νmax/cm-1: 3091, 2925, 2226, 1915, 1593 and1089. 1H-NMR (400 MHz, DMSO-d6, ppm): δ = 7.91 (d, 2H,Ar-H), 7.70 (d, 2H, Ar-H); 13C-NMR (400 MHz, DMSO-d6, ppm):δ =138.94, 134.60, 130.22, , 118.51, 110.65.

**Synthesis of 4-Chlorobenzohydrazonamide**




**Scheme 3:** Synthesis of 4-Chlorobenzohydrazonamide

To a round bottom flask was added 4-chloro benzonitrile

(0.9 g, 0.0065mol), N2H4.H2O 80% (10 mL) and DMSO (20 mL). The solution was stirred under reflux for 5h. The mixture was added to ice water (10 mL). The resultant precipitate was filtered and rinsed with cool water after collection, and dried in oven to afford 3.Yield: (98%); light pink precipitate; m.p. 207-209 °C

IR (KBr) νmax/cm-1:3297, 3130, 2921, 1648, 1599, 1495, and 835. 1H-NMR (400 MHz, DMSO-d6, ppm): δ = 8.08 (d, 2H, Ar-H), 7.65 (d, 2H, Ar-H), 6.34(s, 2H, NH2), 6.18(s, 2H, NH2);13C-NMR (400 MHz, DMSO-d6, ppm):δ =153.97, 135.01, 130.44, 129.12, 126.40

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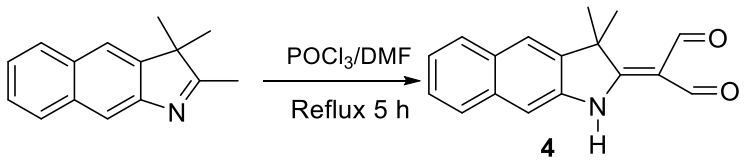
Synthesis of 2-(3,3-dimethyl-1,3-dihydro-2H-benzo[f]indol-2-ylidene)malonaldehyde

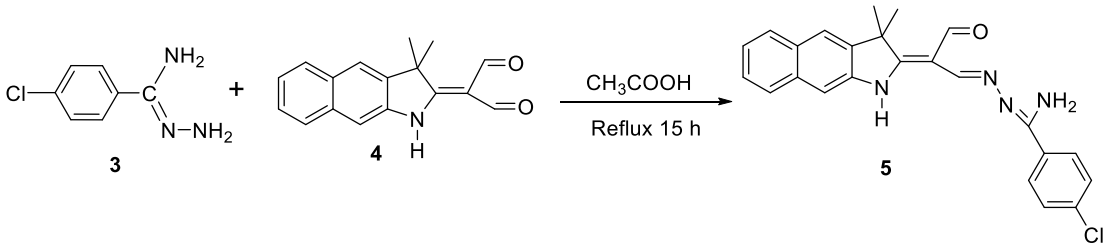



**Scheme 4:** Synthesis of 2-(3,3-dimethyl-1,3-dihydro-2H-benzo[f]indol-2-ylidene)malonaldehyde

An ice bath was used to chill a solution of 1,1,2-Trimethyl-1H-benzo[e]indole (5 g, 0.023 mol) in DMF (15 mL) for 30 minutes. A previously cooled solution of POCl3 (8.78 mL) in DMF (15 mL) in an ice bath was added dropwise while stirring to the first solution for 30 minutes at a temperature below 5 °C. The reaction mixture was placed under reflux for 5 hours after the cooling bath was removed. The resultant mixture was placed into ice water, where aqueous NaOH (35%) was added to bring the pH level down to 8.0. The solid product was then precipitated, filtered, and washed in hot water., dried in oven and recrystallized from ethanol to give 4.Yield: (92%); yellow crystals; m.p 200-201 °C

IR (KBr) νmax/cm-1:3133, 2924, 2853,2772, 1681, 1609, 1510, 1456, 1416, 1399, and 1211. 1H-NMR (400 MHz, DMSO-d6, ppm): δ =13.47 (s,1H, NH), 9.79 (s, 2H, CHO), 8.20 (d, 1H, Ar-H), 8.04 (d, H, Ar-H), 7.99 (q, 1H, Ar-H) 7.66 (t, 1H, Ar-H), 7.53 (t,1H, Ar-H), 1.94 (s, 6H, 2x CH3) .13C-NMR (400 MHz, DMSO-d6, ppm):δ 190.17 (2xCHO), 179.66(N-C= C), 137.91-114.69 (Ar-H), 109.13 (C= C-C=O), 52.93 (CH3-C-CH3) and 22.23(2x CH3).

**Synthesis of 4-chloro-N'-2-(3,3-dimethyl-1,3-dihydro-2H-benzo[f]indol-2-ylidene)-3-oxopropylidene)benzohydrazonamide**

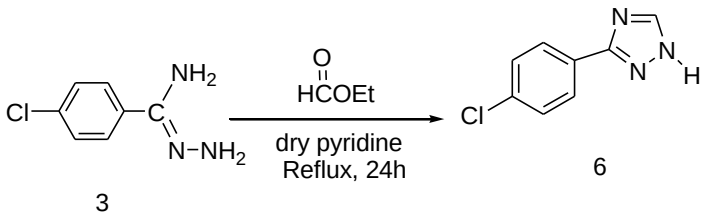



**Scheme 5:** Synthesis of 4-chloro-N'-2-(3,3-dimethyl-1,3-dihydro-2H-benzo[f]indol-2-ylidene)-3-oxopropylidene)benzohydrazonamide

Two equivalents of 2-(3,3-dimethyl-1,3-dihydro-2H-benzo[f]indol-2-ylidene)malonaldehyde 4 (0.15g, 0.00056 mol) were dissolved in acetic acid along with one equivalent of 3 (0.05 g, 0.00029 mol) (20 mL). For 15 hours, the reaction mixture was refluxed. The precipitate was filtered, washed with cold water, and recrystallized from ethanol to yield 5. The solvent was evaporated after cooling for 24 hours. Yield: (87%); light yellow precipitate; m.p. 209-211 °C

IR (KBr) νmax/cm-1: 3360, 3098, 2960, 2923, 2858, 2734, 2698, 1980, 1654, 1618, 1512, 1458, 1400, 1399, and 810. 1H-NMR (400 MHz, DMSO-d6, ppm): δ =13.47 (s,1H, NH), 9.79 (s, 1H, CHO), 8.20-7.49 (Ar-H + 1H, CH=N), 6.35 (s, 2H, NH2), 1.94 (s, 6H, 2x CH3) .13C-NMR (400 MHz, DMSO-d6, ppm): δ 190.17 (CHO), 179.65 (N-C= C), 153.98 (CH=N), 137.89-114.69 (Ar-H), 109.13 (C= C-C=O), 52.94 (CH3-C-CH3) and 22.24(2x CH3).

**Synthesis of 3-(4-chlorophenyl)-1H-1,2,4-triazole**




**Scheme 6:** Synthesis of 3-(4-chlorophenyl)-1H-1,2,4-triazole

Compound 3 (0.1 g, 0.000589 mol) and ethyl formate (1 mL) were combined and refluxed for 24 hours in dry pyridine. The produced solid was filtered, multiple times washed in water, then crystallized from acetone after cooling to produce 6. Yield: (81%); light brown precipitate; m.p 220-221

IR (KBr) νmax/cm-1: 3435, 3130, 3058, 2987, 2855, 1731, 1644, 1608, 1538, 1488, 1393, 1269, and 834; 1H-NMR (400 MHz, DMSO-d6, ppm): δ = 9.22 (1H, NH), 8.95 (2H, Ar-H), 7.73(2H, Ar-H),

,6.84 (s, 2 H, NH2).

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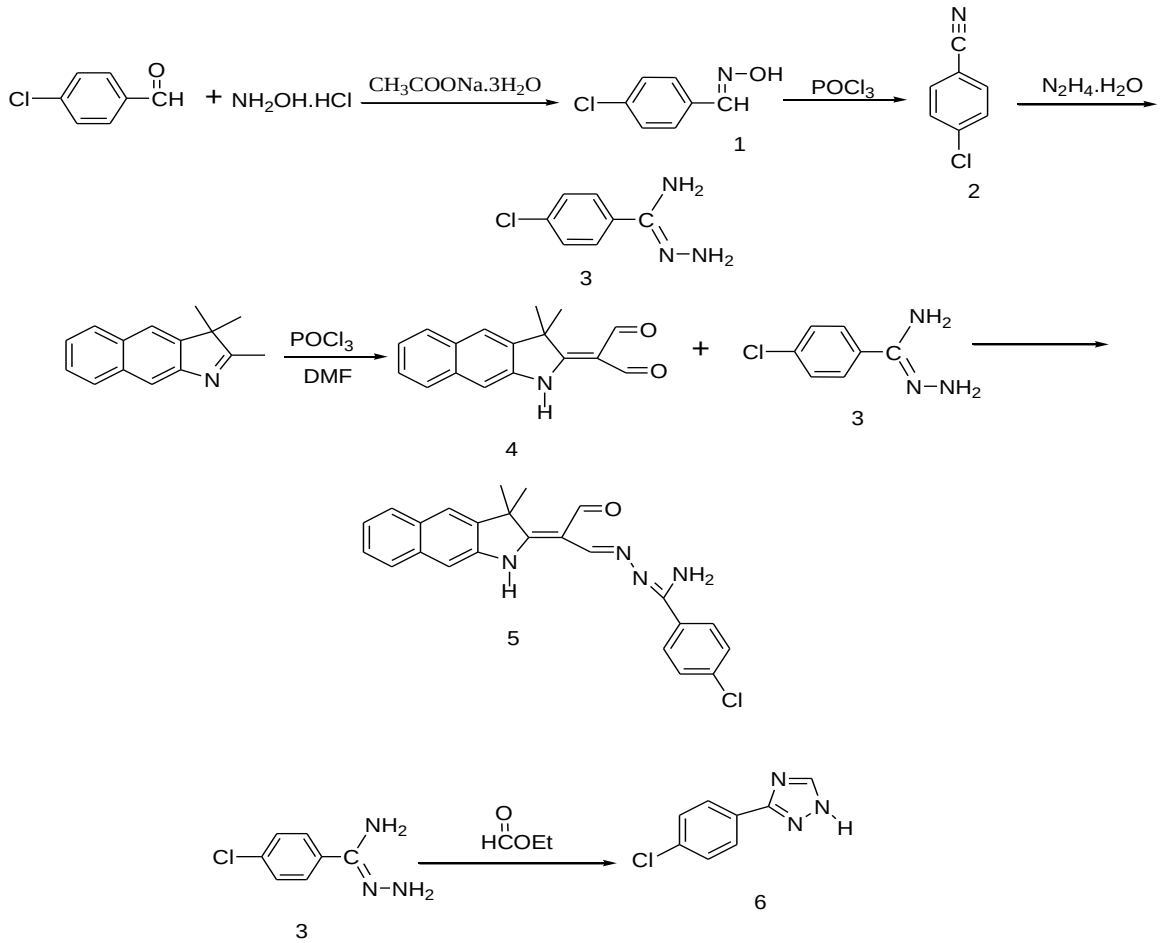
## Results and Discussion




**Scheme 7:** synthesis of compounds 1-6

The Vilsmier-Haack reaction was used to prepare the indolyl molecule, which was then created through a reaction between commercially available 1,1,2-Trimethyl-1H-benzo[e]indole, dimethylformamide, and phosphorus trichloride 1H NMR spectra Fig (1). The (N-H) group of the indole ring was ascribed to the exhibited signal at 13.47 ppm. At 9.79 ppm, a singlet signal was observed that was attributed to the two protons in the aldehyde group. Additionally, a signal at 1.95 ppm ascribed to the six proton atoms in each of the two methyl groups was seen.

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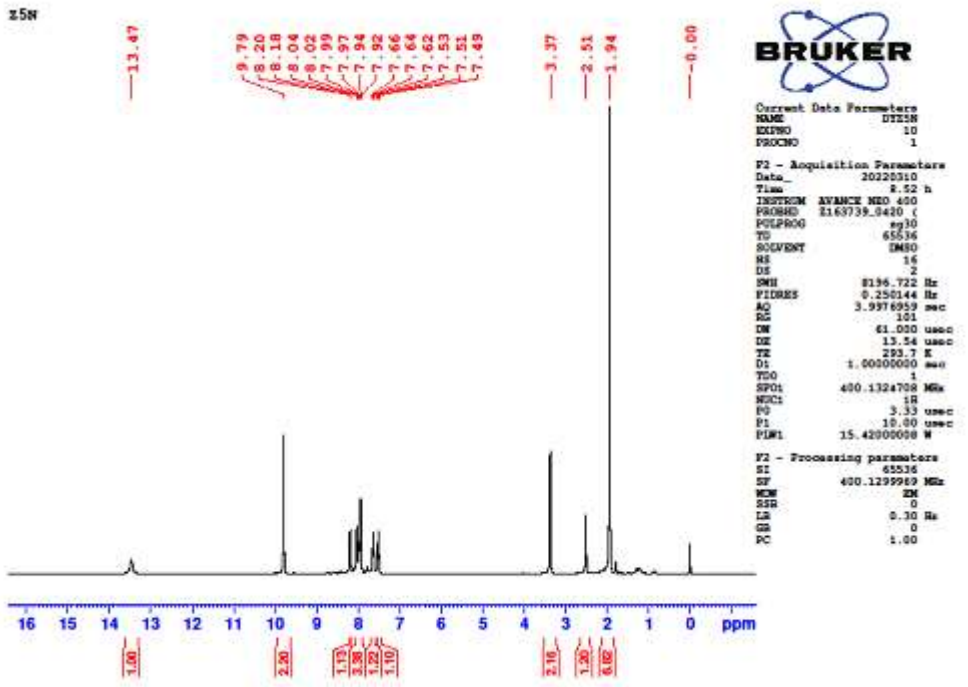


**Figure 1:** [1]HNMR spectrum of compound 4

In addition, 13 CNMR results Fig (2) confirmed the 1HNMR spectral results. A signal appeared at δ 190.17 ppm which attributed to C= O carbonyl groups. In addition, three signals at δ 109.13, 52.93 and 22.23 ppm which attributed to aliphatic carbon atoms. IR spectra also provide starching corresponding to the CO group of aldehyde group at 1681 cm-1 Fig (3)

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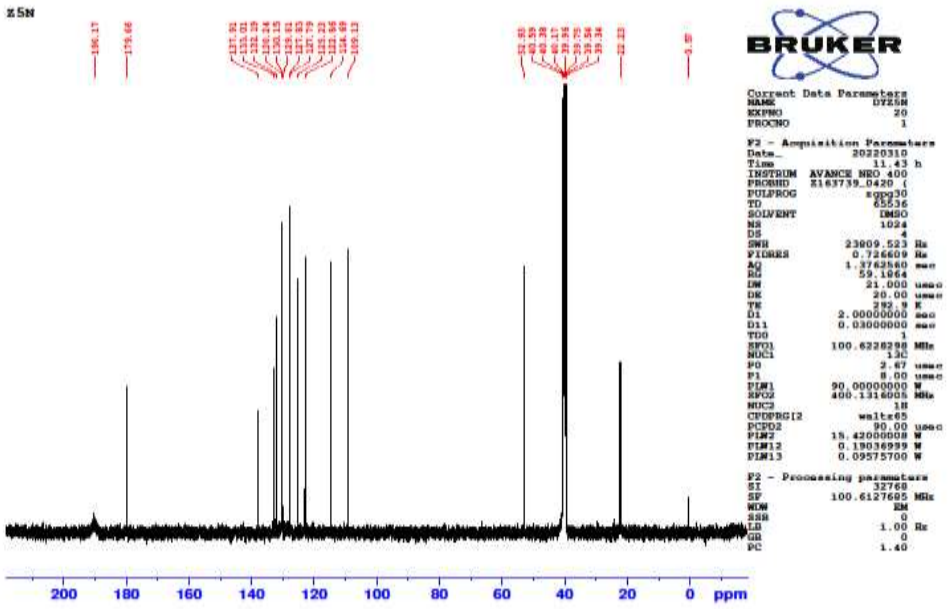


**Figure 2:** $^{13}$ CNMR spectrum of compound 4

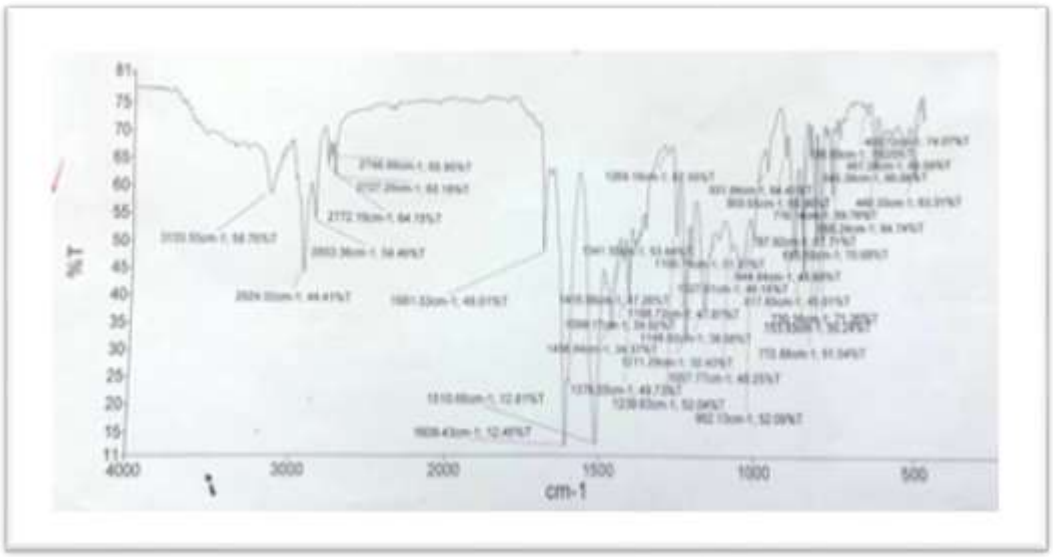


**Fig (3) IR spectra of compound 4**

Synthesis of Schiff base was performed by reaction Indolyl molecule with hydrazone amide in acetic acid. 1HNMR spectra Fig (4) shown single signals at 13.47 ppm was belonged to protone of NH of indol ring. A singlet signal at δ 9.79 ppm was referred to proton of carbonyl group.

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Disappear one signal of NH2 of hydrazon amide which normal appear at δ 6.18 ppm associated with appear a new signal at δ 153.98 ppm for azomethine group in the 13CNMR spectrum confirm the propose structure. Fig (5)

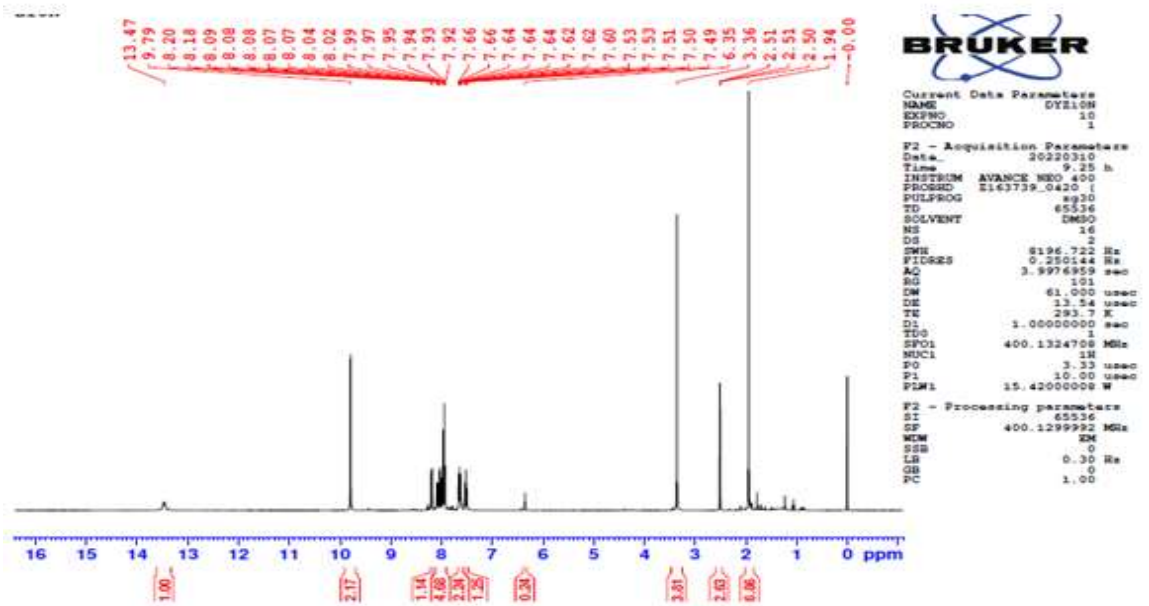

**Figure 4: $^{1}$H NMR spectrum ofcompound (5)**

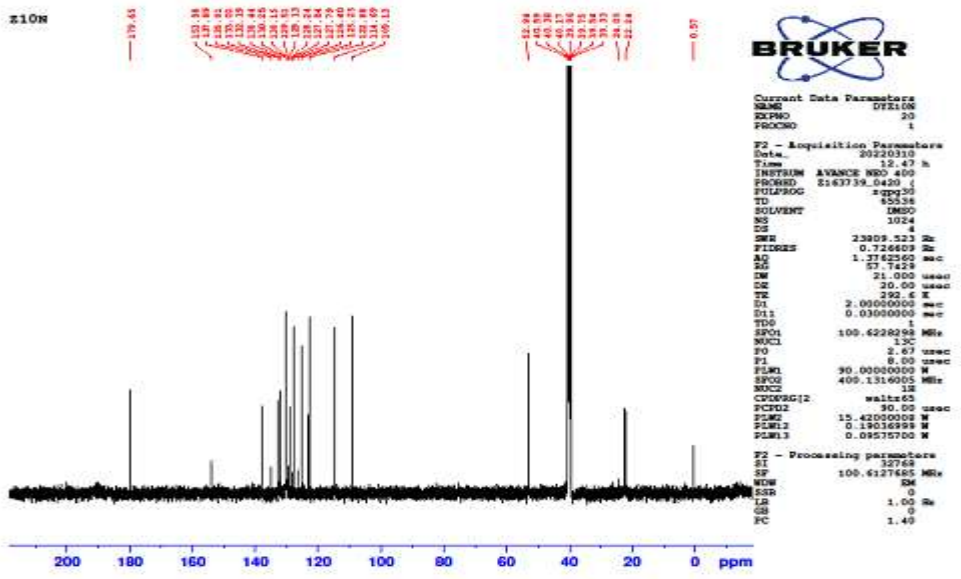

**Figure 5: $^{13}$CNMR spectrum ofcompound (5)**

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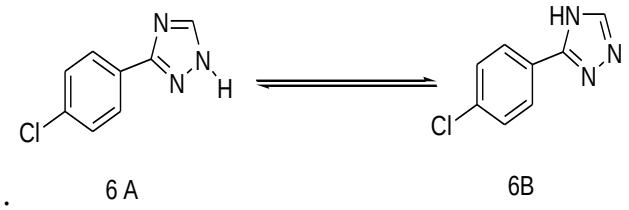
Compound 6 was produced through the heterocyclization of compound 3 with ethyl formate. Compound 6's IR display revealed NH2 and NH group-related absorption bands at 3435 and 3130 cm-1, respectively. Its 1H NMR spectrum (Fig. 6) revealed three signals at 9.22 and 8.96 ppm that correspond to two NH hydrogens, demonstrating that the product 6 exists in two tautomeric forms (6 A and 6B), as well as a singlet peak at 6.87 ppm that corresponds to the CH of the triazole ring.




6 A 6B

**Scheme 8 :**Tautomeric forms (6 A and 6B)

Extra peaks was also observed in the same spectra probably returned to rest of ethylformate as we used extra of the reagent ranging from 20-21 equivalent.

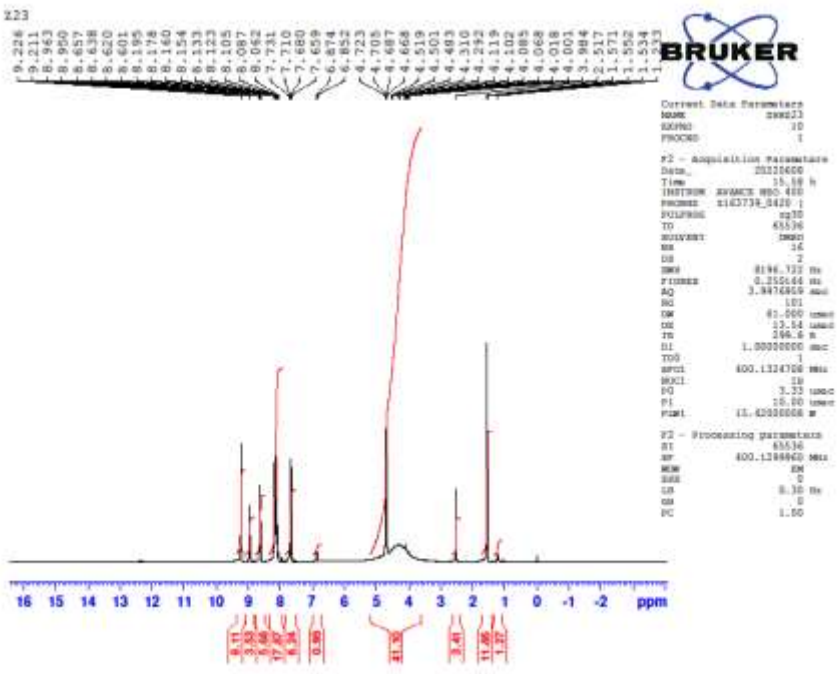



**Figure 6: $^{1}$H NMR spectrum ofcompound (6)**

## Conclusion

The synthesis of both 4-Chlorobenzohydrazonamide (3) and 2-(3,3-dimethyl-1,3-dihydro-2H-benzo[f]indol-2-ylidene)malonaldehyde (4) were achieved in 2 steps (98% yield ) and 2 step (87%) yield) respectively. Synthesis of (4) was achieved according to procedure reported by Hussin A. Rothan and et al [19] and the later product's structure was validated by its 1HNMR analysis, and all of the product's peaks agreed with information available in the literature. [19]

**Acknowledgments**

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