



Synthesis and Characterization of Some Tetrazole Derivatives from 5-Amino Salicylic Acid

Hayder Ghanim Chfat* & Hasan Thamer Ghanim

Master's, Department of Chemistry, College of Education for Girls, Kufa University.

ABSTRACT

In this research, some of Tetrazole's derivatives were composed throughout different tracks. The first track included preparing Azo using the (5-Amino Salicylic acid) with (2 – Naphthol). Whereas the second track involved the chemical reaction of the Azocompound with the Benzaldehydederivatives(4-Br , 4-Cl and 4- OH) in order to prepare Schiff's bases and in the final track, the chemical reaction of Sodium azaid with Schiff's bases in order to finally get the Tetrazole compounds. The melting point of the prepared compounds were carefully measured, and then characterized using FT-IR, ¹HNMR and ¹³CNMR Spectra.

Key words: 5-AminoSalicylic acid,Schiff bases, tetrazole,azo compound.

INTRODUCTION

The Salicylic acid is one of the naturally extracted from willow bark, and therefore is called Willow Acid. It belongs to the Phenol family, and is largely common in the manufacturing of drugs that are used as painkillers and antipyretics that are associated with childbirth[1-3]. As for the 5-Amino Salicylic acid, it is one of the components of organic compounds which possess a biological effect against numerous types of Bacteria [4-5]. However, the Azo compounds, which include the effective group (N=N) discovered by Griess, Johann Peter in 1860, they enter a wide variety of industries such as Dyestuffs industry, antibiotics, Colon drugs, and Cosmetics [6-9].

Schiff's bases are organic compounds that include Azomethine (C=N). These compounds are known as "Schiff's bases", named after the German scientist (Hugo Schiff), and which are famous for their biological importance and for its uses as anti-dioxides, anti-viruses, and for the curing of tumors as well [10-11]. The Tetrazole compound, however, is considered a quintet heterogeneous cyclical compounds which includes one Carbon atom and four Nitrogen atoms along with one Hydrogen atom, which has the chemical formula (CN₄H), and is of both biological and pharmaceutical importance [12-13].

EXPERIMENTAL

Materials

Chemicals used during the present work are manufactured from Merck and BDH company.

Instrumentation

Un recorded melting point by hat stage GalenKamp. To ensure the purity of the resulting derivatives used technique thin layer chromatography (TLC).FTIR spectroscopy was used KBr disc. ¹HNMR and ¹³CNMR spectra was used CDCl₃ and DMSO-d₆ as solvents.

Synthesis of azo compound [S][14]

This compound was prepared in two steps.

The first step: 5-Amino salicylic acid was dissolved in (HCl) (3ml) and (10ml) distilled water, then cooled in ice bath ($0-5\text{ C}^0$), Sodium nitrite (0.13g, 0.01mo) was dissolved in (10ml) distilled water and cooled in ice bath ($0-5\text{ C}^0$), then slowly mix solution together.

The second step: The 2-Naphthol (0.19g, 0.01mol) was dissolved in NaOH solution (15ml, 10%) stirred the solution in the first step then added slowly to the solution with stirring. leaving the reaction solution for a period 4hrs. Then filtered and collected the solid product.

Synthesis ester derivative (S₁)

Taking (0.5g, 0.01mol) of azo compound is dissolved in (30ml) of ethanol absolute. Then added 6 drops of H₂SO₄ concentrat. Esterfication for (9hrs), follow up the reaction by (TLC). After cooling the mixture was neutralized. The titled product was achieved by evaporating the solution under reduced pressure.

The physical properties in table (1).

Synthesis of hydrazide derivative (S₂).

Compound (S₁) (0.5g, 0.01mol) was dissolved in refluxed ethanol (30ml), hydrazine hydrate (0.5g, 0.01mol) was slowly added to the mixture. The solution was refluxed for (10hrs) the solvent was removed by evaporating, the residue was cooled in an ice bath forming a precipitate. The product was recrystallized from absolute ethanol to give titled compound.

Synthesis of Schiff bases (S₃-S₅).

A mixture of (0.01mol) of aromatic benzaldehyde derivatives and compound (S₂) was refluxed for (3-8)hrs in (30ml) of absolute ethanol. The reaction mixture was cooled and kept for (24hrs). The crystals found were filtered, dried and recrystallized from absolute ethanol to give derivatives (S₃-S₅).

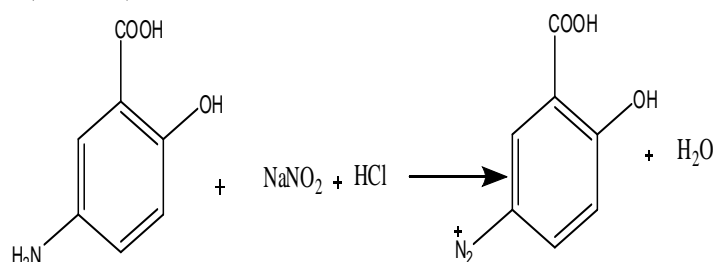
Synthesis of Tetrazole derivatives (S₆-S₈).

A mixture of Schiff bases (S₃-S₅) (0.3g, 0.004mol) dissolved in THF (15ml) and sodium azide (0.3g, 0.004mol) was dissolved in THF (15ml) and refluxed for (8-10)hrs. The reaction was then cooled and the resulting final (S₆-S₈), recrystallized from ethanol.

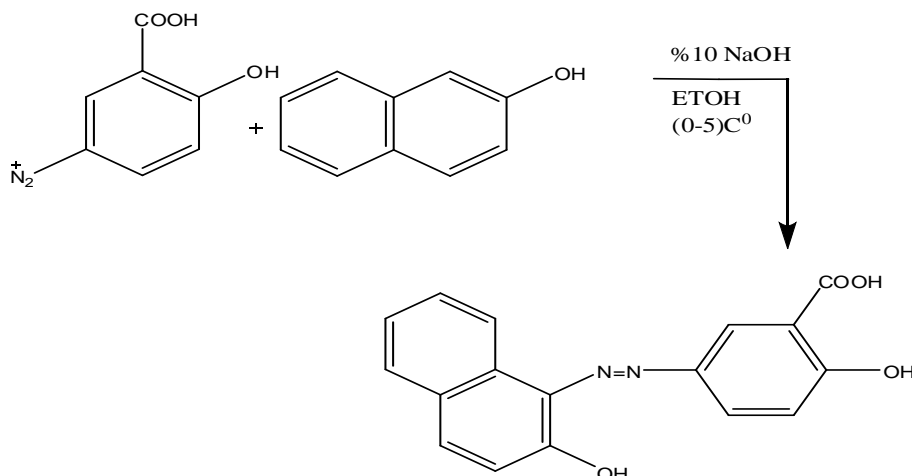
RESULTS AND DISCUSSION

Synthesis of azo compound (S)[14]

5-Amino salicylic acid (5-ASA) is react with nitrite to form the diazonium salt.



After (15) minutes diazonium salt formation is completed with 2-naphthol at ($0-5\text{ C}^0$) to form azo dye.

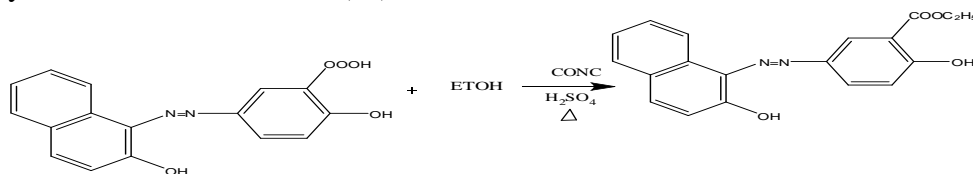


Scheme (1): preparation of azo compound

The FTIR spectrum of azo compound (S) fig(1), show of (OH) phenolic group at $(3433)\text{cm}^{-1}$, and (OH) group of carboxylic acid is broad at $(2400-3500)\text{cm}^{-1}$, The (N=N) group occur at $(1490)\text{cm}^{-1}$, and the bands of NH_2 group are disappeared.

Synthesis of ester derivative (S₁)

The reaction between azo compound (S) with absolute ethanol in the presence conc. H_2SO_4 as catalyst to synthesize ester derivative (S₁).



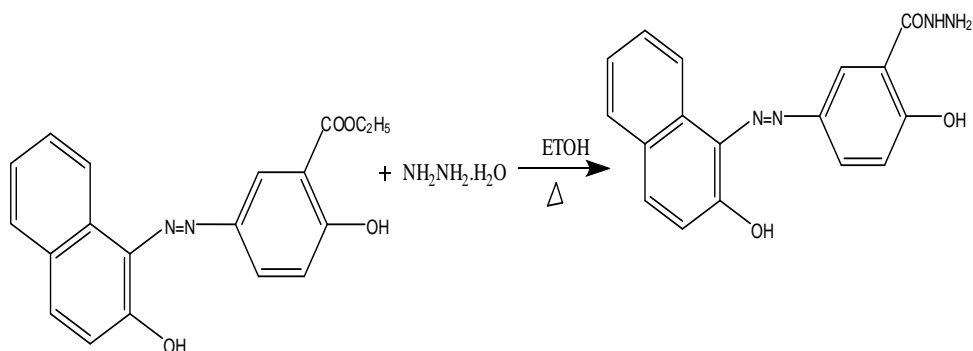
Scheme (2): preparation of ester derivative (S₁)

In the FT-IR spectrum fig (2), show band at $(3431)\text{cm}^{-1}$ due to stretching vibration of OH phenolic group, The band at $(1676)\text{cm}^{-1}$ due to $(\text{O}=\text{C}-\text{OC}_2\text{H}_5)$ ester group compound (S₁).

¹HNMR spectra fig (3) compound (S₁) appeared that (14.7 ppm, s, OH naphthol) (8.6 ppm, s, OH phenol) (7-8.2 ppm, m, CH_{arom}) (4.7 ppm, d, CH₂), (1.4 ppm, m, CH₃)

Synthesis of hydrazine derivative (S₂)

The reaction between ester derivative (S₁) with hydrazine hydrate in the presence absolute ethanol as solvent at 70°C to prepare the hydrazine derivative (S₂)

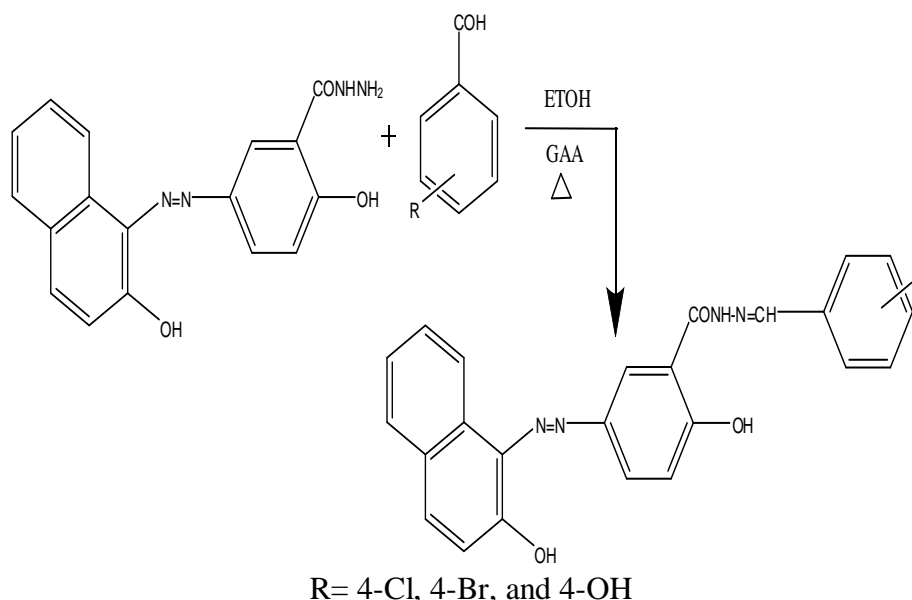


Scheme (3): preparation of hydrazine derivative (S₂)

In FT-IR spectrum, show bands at $(3450-3200)\text{cm}^{-1}$ due to stretching vibration of $(\text{NHNH}_2$ and OH) group, the band of $(\text{C}=\text{O})$ group amide occur at $(1604)\text{cm}^{-1}$ and the $(\text{N}=\text{N})$ group of azo occur at $(1514)\text{cm}^{-1}$.

Synthesis of Schiff bases derivative (S_3 - S_5)

The reaction between hydrazine derivative (S_2) with benzaldehyde derivatives (4-Cl, 4-Br and 4-OH) respectively in the presence absolute ethanol as solvent and 2 drops from (GAA) as catalyst to synthesize Schiff bases derivatives (S_3 - S_5).



Scheme (4): preparation of Schiff bases derivative (S_3 - S_5)

In the FT-IR spectra show bands at $(1664-1676)\text{cm}^{-1}$ due to $(\text{C}=\text{O})$ group of amide, the bands of Schiff bases occur at 1624cm^{-1} .

^1H NMR spectra compound (S_3) appeared that (14.7 ppm,s, OH naphthol) (8.7 ppm,s NHamide) (8.5 ppm,s, CH Schiff base), (7.4-7.9 ppm ,m, CH arom) (6.6 ppm,s, OH phenol).

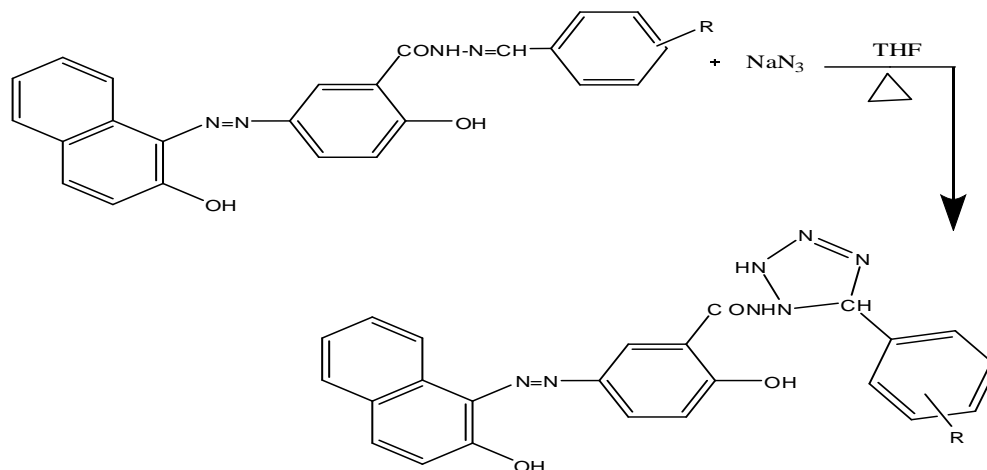
^{13}C NMR spectra appeared that (171 ppm,s, $\text{C}=\text{O}$ amide) (162 ppm,s, $\text{C}-\text{OH}$) (157 ppm ,s, CH Schiff base) (114-141 ppm,m, $\text{C}-\text{C}$ arom).

^1H NMR spectra compound (S_4) appeared that (14.7 ppm,s, OH) (8.7 ppm,s, NHamide), (8.6 ppm,s, CH Schiff base), (7.1-8.3 ppm,m, CH arom) (6.7 ppm,s, OH phenol).

^{13}C NMR spectra, compound (S_4) appeared that (171 ppm,s, $\text{C}=\text{O}$ amide), (163 ppm,s, $\text{C}-\text{OH}$ phenol and naphthol) (157 ppm,s, CH Schiff base) (114-141 ppm,m, $\text{C}-\text{C}$ arom).

Synthesis of titrazole derivatives (S_6 - S_8)

The reaction between Schiff bases (S_3 - S_5) with sodium azide in the presence (THF) as solvent to synthesize titrazole derivatives (S_6 - S_8).



Scheme (5): preparation of Tetrazole derivatives (S₆-S₈)

These derivatives were characterized by their melting point, FT-IR, ¹HNMR, spectra and checked by TLC.

The FT-IR spectra Show band of NH group at (3347-3323) cm⁻¹, and the (N=N) group occur at (1479-1492) cm⁻¹.

The ¹HNMR spectra, Show (14.9 ppm,s,OH) (8.8ppm,s,NH), (7.3-7.6 ppm,m,CH_{arom}), (3.3ppm,s, CHtetrazole) (2ppm,s,NHtetrazole)

Table(1):Physical properties and characteristics for the synthesis compounds(S-S₈)

NO	Molecular formula	M.wt	M.P	Yield%	Color	R _f	Solvent
S	C ₁₇ H ₁₁ N ₂ O ₄	307	285-287	85	Red	0.54	Ethanol
S ₁	C ₁₉ H ₁₆ N ₂ O ₄	336	289	66	Dark red	0.45	Ethanol
S ₂	C ₁₇ H ₁₄ N ₄ O ₃	322	266	77	Pale red	0.47	Ethanol
S ₃	C ₂₄ H ₁₇ N ₄ O ₃ Cl	444.5	222-224	75	Pale red	0.49	Ethanol
S ₄	C ₂₄ H ₁₇ N ₄ O ₃ Br	490	231-233	78	Red	0.50	Ethanol
S ₅	C ₂₄ H ₁₈ N ₄ O ₄	426	247-249	65	Dark red	0.49	Ethanol
S ₆	C ₂₄ H ₁₇ N ₇ O ₃ Cl	486.5	202	88	Pink	0.43	THF
S ₇	C ₂₄ H ₁₇ N ₇ O ₃ Br	532	216	85	Pink	0.45	THF
S ₈	C ₂₄ H ₁₈ N ₇ O ₄	460	242	64	Dark red	0.48	THF

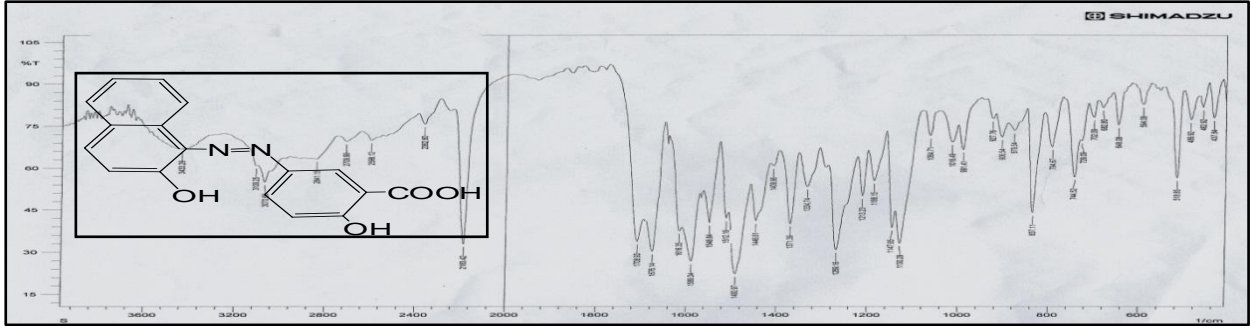


Fig (1) FT-IR spectrum of azo compound (S)

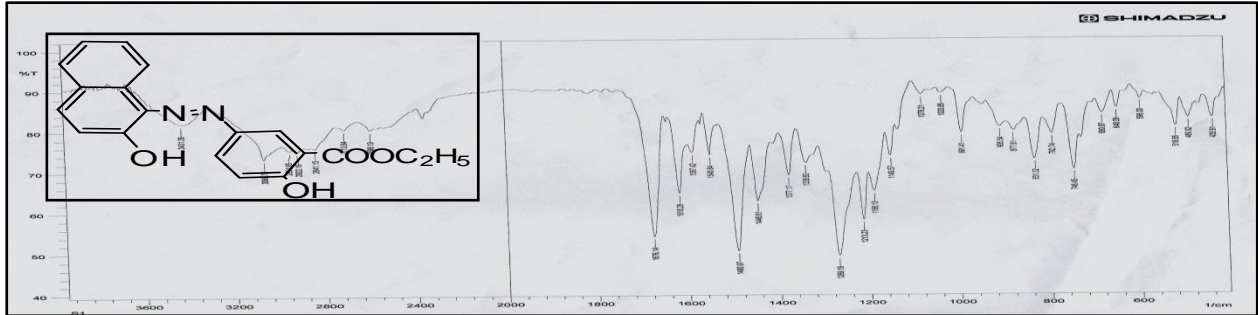


Fig (2) FT-IR spectrum of azo compound (S₁)

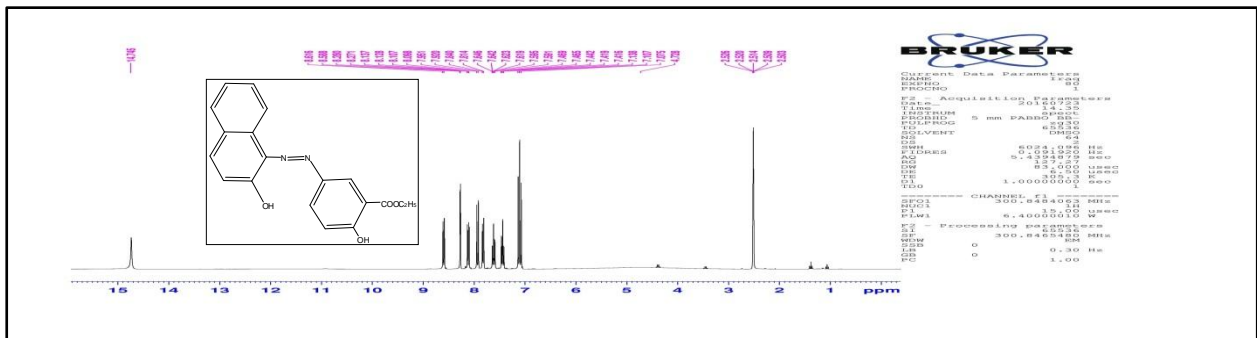


Fig (3) ¹H NMR spectrum of tetrazole compound (S₁)

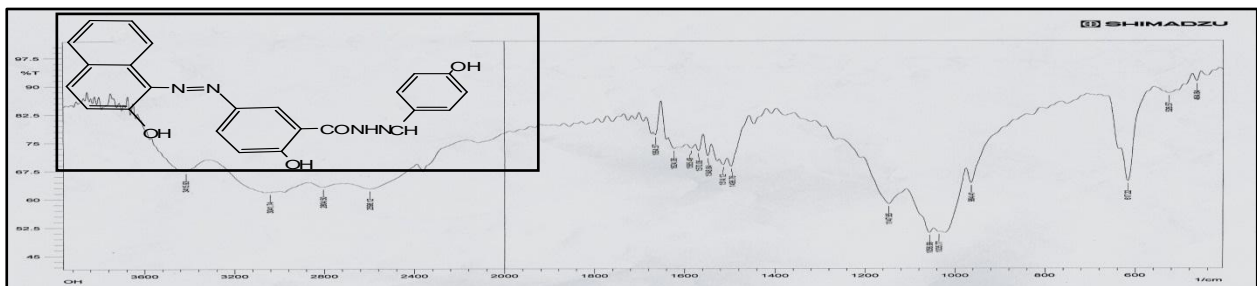


Fig (4) FT-IR spectrum of Schiff bases compound (S₅)

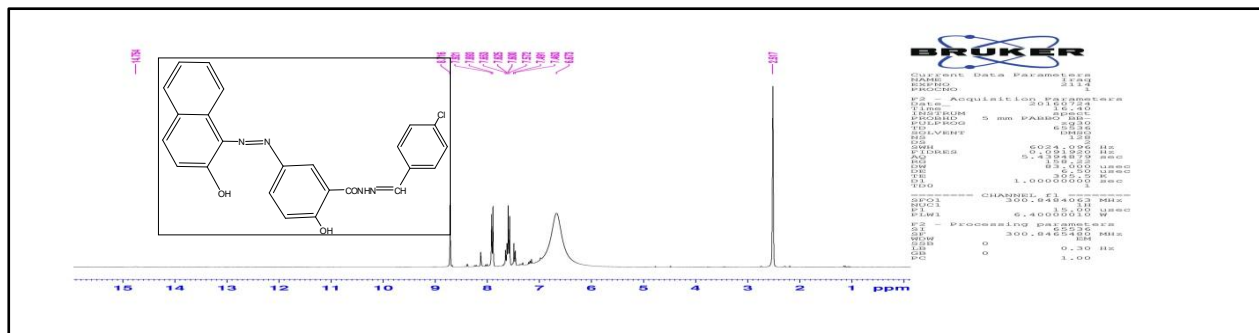


Fig (5) ¹H NMR spectrum of Schiff bases compound (S₃)

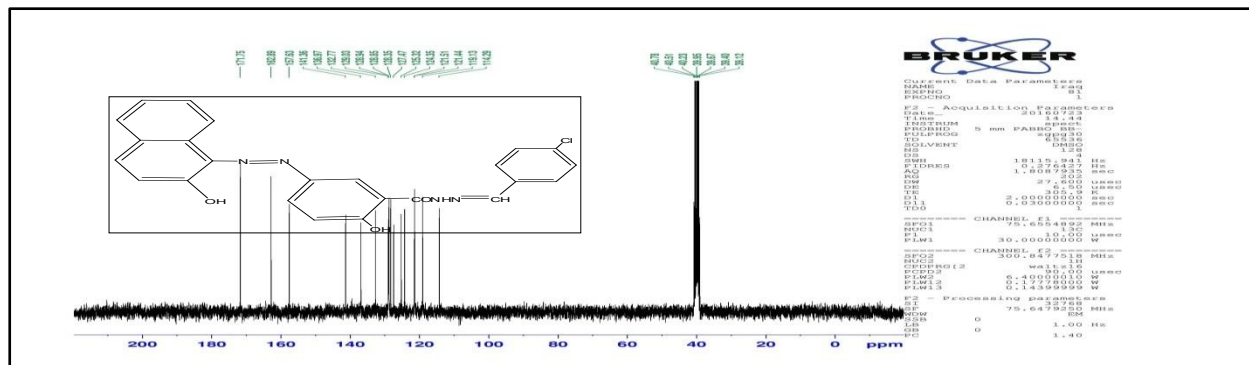


Fig (6) ¹³C NMR spectrum of Schiff bases compound (S₃)

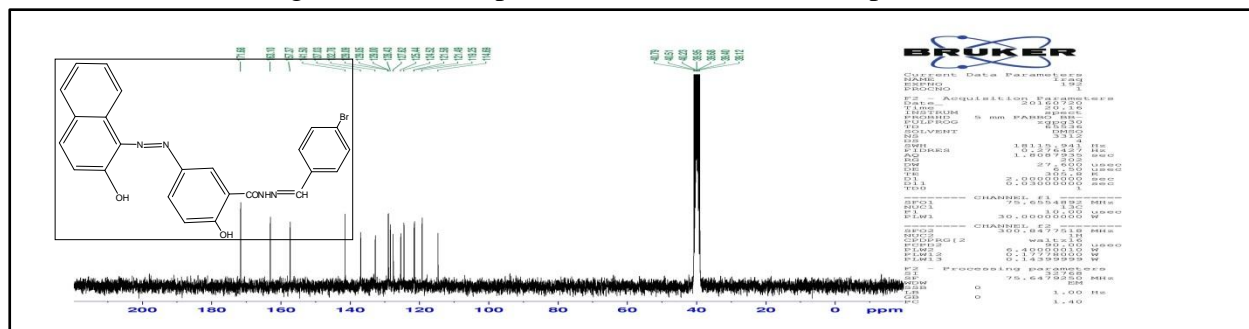


Fig (7) ¹³C NMR spectrum of Schiff bases compound (S₄)

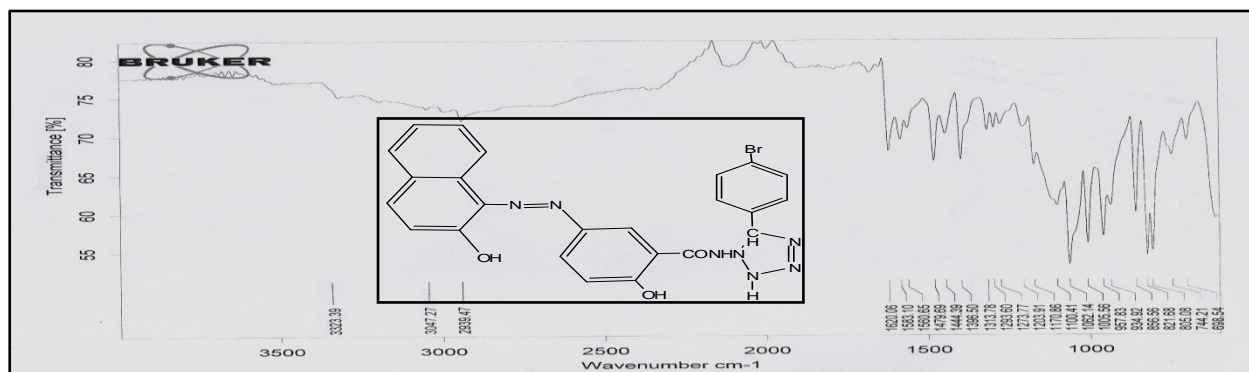


Fig (8) FT-IR spectrum of tetrazole compound (S₇)

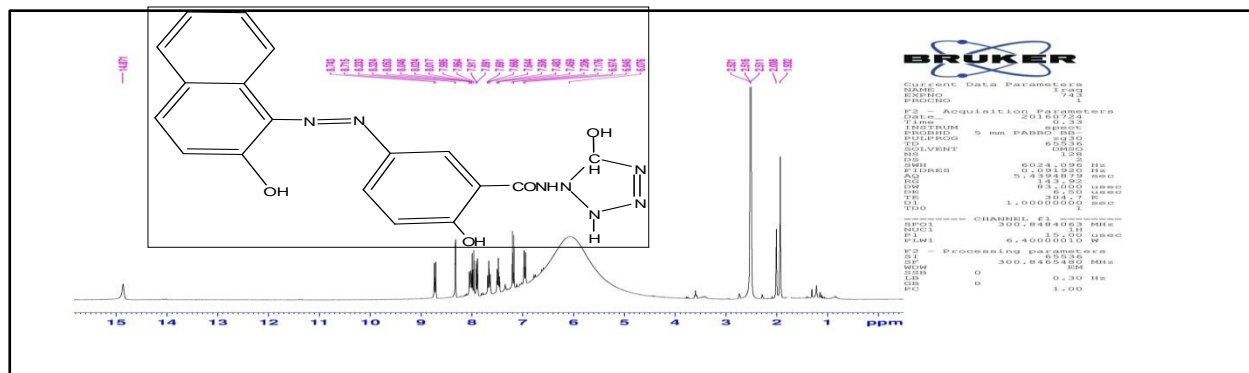


Fig (9) ^1H NMR spectrum of tetrazole compound (S_8)

CONCLUSIONS

Azo compound prepare at PH= 6.5-7 also preparation derivatives Schiff 's bases at different periods of time For a reason different substitutes totals.

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