New bis Schiff base of isatin derivatives: syntheses, characterization, and biological activity

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Abstract:

In the current study, imesatin (A) was condensed with various aromatic aldehydes to create a number of new Schiff bases of isatin [B1-B6]. The imesatin were created by combining isatin and O-phenylenediamine. Utilizing FT- IR and 1H-NMR and 13CNMR techniques, the chemical structures of the produced compounds were verified. *Staphylococcus aureus*, a gram positive bacteria, and *Klebsiella pneumonia*, a gram negative bacteria, were used to evaluate the biological study at concentrations of 50 and 100 µg/mL. Derivatives were discovered to have biological activity against these bacterial growths.

Keywords: Isatin, Schiff Base, Biological activity.

Introduction:

Isatin figure (1) commonly referred to as tribulin, is an indole-derived chemical molecule having the formula $C_8H_5NO_2$. Otto Linné Erdman and Auguste Laurent produced the chemical for the first time about 1840 as a result of the nitric acid and chromic acid oxidation of indigo dye .

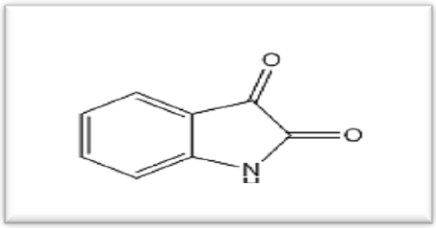


Figure (1): Chemical structure of Isatin

Isatin is a well-known organic compound. that occurs in humans as a metabolic byproduct of adrenaline, as well as in Isatis and Couroupita guianensis plants [1]. It resembles a powder that is orange-red and is frequently used as a component in the synthesis of several different biologically active chemicals, such as antitumorals[2] antivirals,[3] anti-HIVs,[4] and antituberculars [5].The "Maya blue" and "Maya yellow" dyes' colors are also a result of the isatin core [6]. Isatin is a very reactive substance that the past employed in synthetic chemistry as a nucleophile as well as an electrophile. Recently, the science of organic products has found that spiro molecules have important pharmacological effects. There have been a number of studies published regarding the synthesis isatin at the C-3 position associates [7]. One of the earliest and most popular processes for creating isatin and its derivatives [8].is the Sandmeyer synthesis. But it only functions with straightforward analogs. The metalation of anilide derivatives and other [9] synthetic techniques like Martinet, Stolle, and Gassman have also been discussed previously. The first scientist to describe the byproducts of the reaction between primary amines and carbonyl compounds was a German named Hugo Schiff figure (2) , giving rise to the nickname (Schiff's base) in 1864 [10]. It is a substance with the generic formula R1R2C = NR3, where R3 = aryl or alkyl but a hydrogen not atom). [11-15]. Depending on how they are built makeup, they fall into one of two categories: secondary ketimines or secondary aldimines This falls under the imine class. The word is frequently used interchangeably with the word azomethine, which particularly refers to secondary aldimines (i.e., RCH=NR' where R' H).

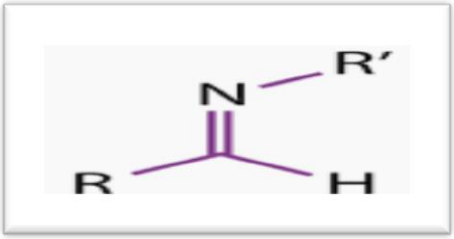


Figure (2): Chemical structure of Schiff base

We completed this study, which involved making various isatin derivatives, then examining their biological function. Many antibiotic-resistant bacteria are strongly associated with the growth in the mortality rate of infectious diseases. The key contributing factor to this problem is an absence of effective treatments [16-17]. Undoubtedly, there is a critical medical need for the development of novel

antibacterial medications with creative and more efficient mechanisms of action. [18].

Material and Methods:

General procedure:

The Synthetic chemicals were used to record all measurements by in open capillary tubes, melting points were calculated. in electro thermal apparatus 9300, melting point engineering LTD, FT-IR spectra, Fourier transform infrared shimadzu (8400), ,1HNMR, and 13CNMR spectra in (ppm) in DMSO solvent by Bruker-300MHZ, Iran.

Experimental:

Preparation Schiff bases imesatin (A).

By reaction, derivatives of Schiff bases were created between equimolar amounts of 0.01 mol of o-phenylenediamine and isatin were eliminated from 30 ml of ethanol in the presence 1 ml of glacial acetic acid, refluxed for 60 minutes, and then held at room temperature for two hours (37° C), producing imesatin (A).

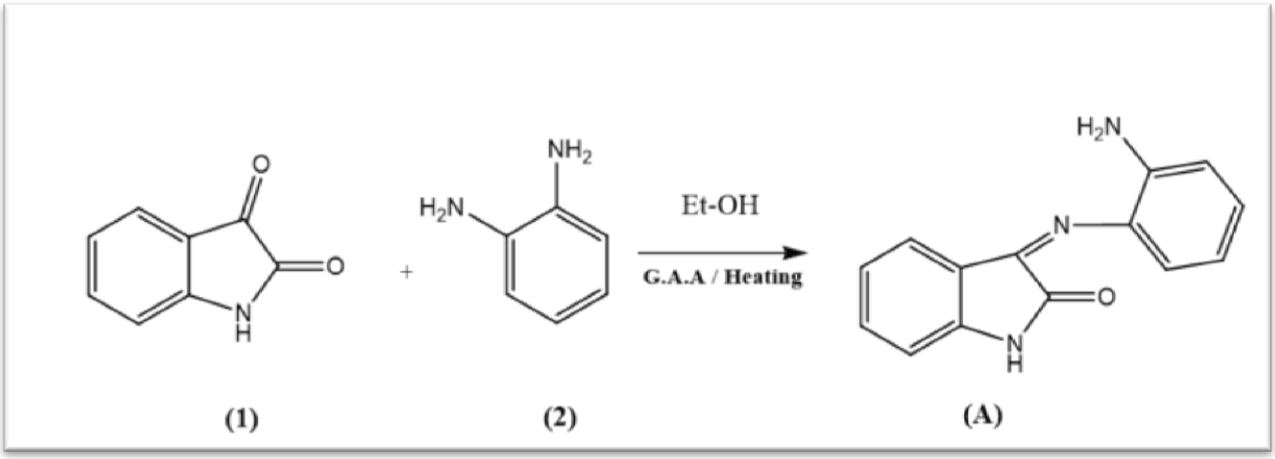
preparation of derivatives of Schiff bases (B1-B6):

By reaction, derivatives of Schiff bases were created between equimolar amounts was mixed 0.01 mol of imesatin (A) with different aromatic aldehydes, at 70° C, and addition ethanol (10 ml) and the mixture was refluxed to five hours.

.Result and discussion:

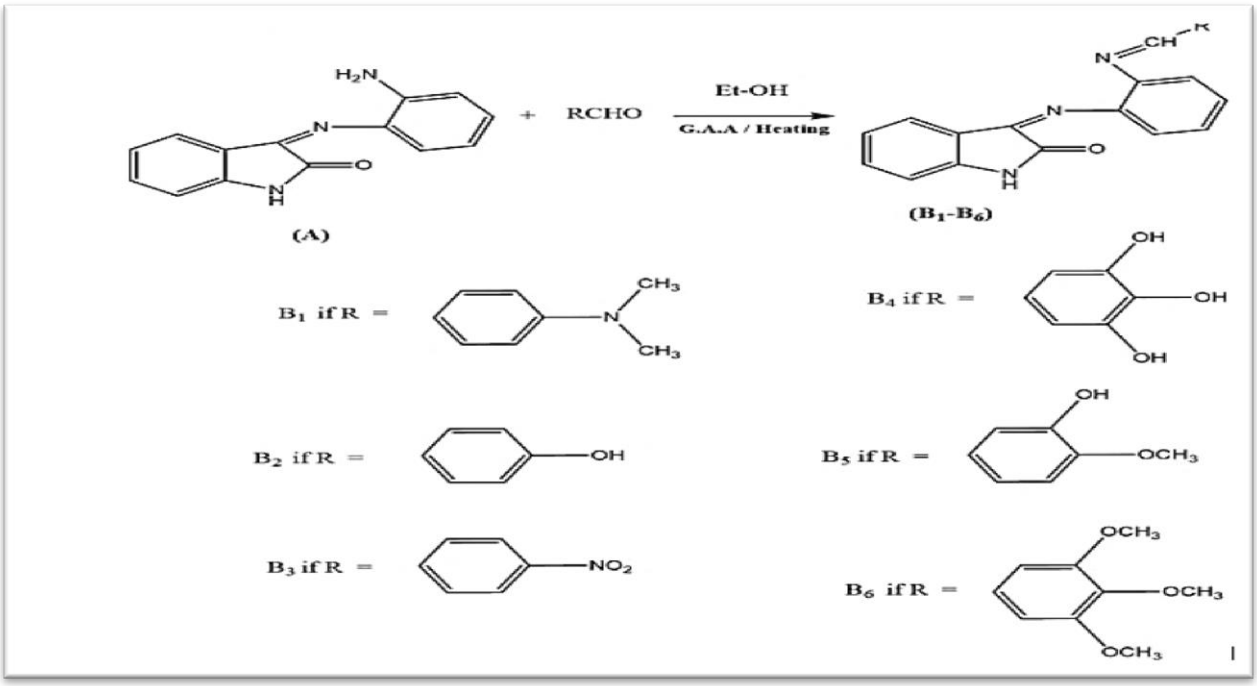
A unique set of different compounds with substituted isatin were created in the current effort. Schiff bases of substituted isatin are produced by reaction of condensation from the intermediate imesatin. The isatin ring's carbonyl group at position is the only group on which the condensation is focused. Imesatin has been subjected to reactions with various aromatic Aldehydes with glacial acetic acid present in ethanol, and a range of derivatives of schiff bases obtained in accordance with the synthetic method. scheme (1). Their spectral analyses show this the technique used to manufacture and separate the compounds generated materials with good purity. The outcome of various substituted isatin derivatives (B1-B6) divided dry and recrystallized from ethanol pure standing for a while one to three at room temperature for days.

Imesatin (A) were prepared by condensation reaction between Isatine with o-phenylenediamine This reaction was done by using absolute ethanol as solvent and glacial acetic acid 1 ml as catalyst scheme (1)



Scheme (1): preparation of imesatin

Then the reaction completed by equimolar amounts was mixed 0.01 mol of imesatin (A) with different aromatic aldehydes (N,N-Dimethyl amino benzaldehyde,4-hydroxy benzaldehyde,4-nitro benzaldehyde 3,4,5-tri hydroxy benzaldehyde,3-hydroxy-4-methoxy benzaldehyde ,3,4,5-tri-methoxy benzaldehyde) respectively at 70° C, and addition ethanol(10 ml) and it was a blend refluxed to five hours. Scheme (2).



Scheme (2): preparation of prepared Shiff´s bases derivatives

Identification of Shiff base derivatives: A

(z)-3-((2-amiophenyl)imino)indolin-2-one.

FT-IR (KBr, Cm^{-1}), Figure (3): 3194 (C-H Ar.str.); 1616 (C=N str.); 1460 (C=C str.); 1149 (C-N str.); 667(C-H Ar.oop); 3446(N-H str.);815(N-H. oop) ;1734 (C=O str.).

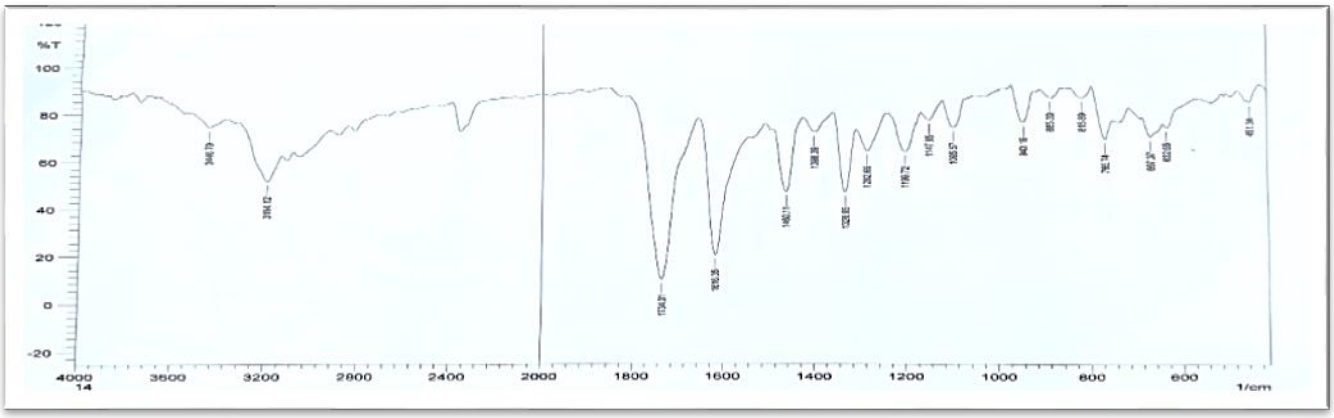


Figure 3: FT-IR for derivative (A)

Identification of Shiff base derivatives: B1

(3Z)-3-((2-((4-(dimethylamino)benzylidene)amino)phenyl)imino)indolin-2-one.

FT-IR(KBr)cm^{-1},Figure(4): 3194 and 3007 (C-H Ar.str.); 1591 (C=N str.); 1454 a (C=C str.); 667(C-H Ar.oop); 3415(N-H str.);817(N-H. oop) ;1730 (C=O str.),**1H-NMR(DMSO-*d6*)** ,**Figure(5):** δ 8.33 (s, 1H,-N=CH-), 8.30(s, 1H,-NH-)$_{\text{Isatine group}}$, 3.1(s,6H,-[CH3]2),7.5 (2H,H-2 ″ and H-6 ″ Ar-H ,7.1-7.3(m,8H,H-4,H-5,H-6,H-7,H-2′,H-3′,H-5′,H-6′ Ar-H) ,6.5 (2H,H-3 ″,H-5 ″ Ar-H).

13 CNMR(DMSO) Figure(6): δ 133 (C, C=N)Imine group ,δ143(C, C=O)Isatine ring, δ 102-128(C of phenyl group).

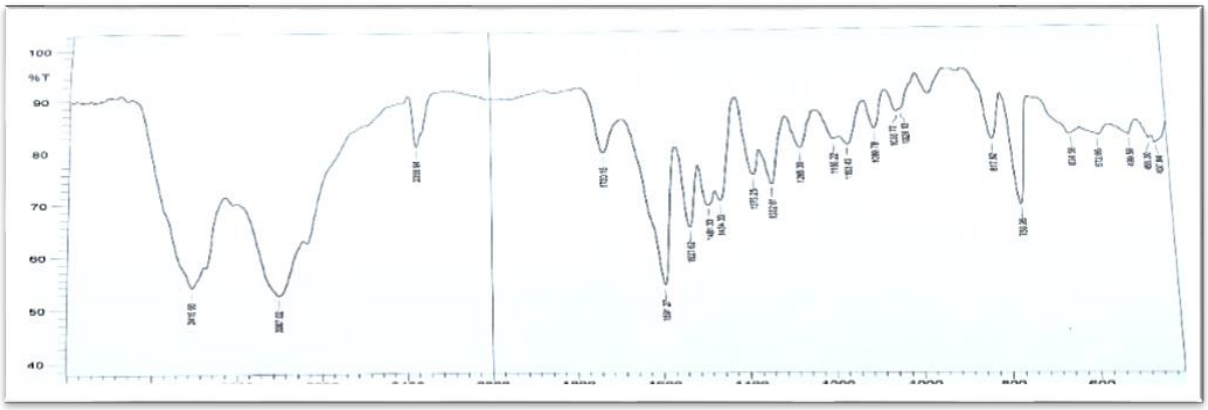


Figure 4: FT-IR for derivative (B1)

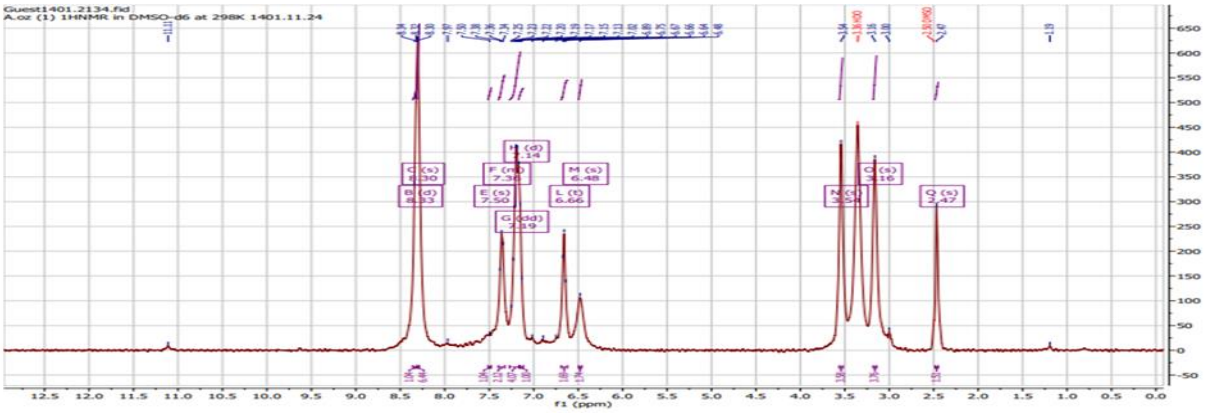


Figure (5) 1HNMR spectrum of derivative (B1)

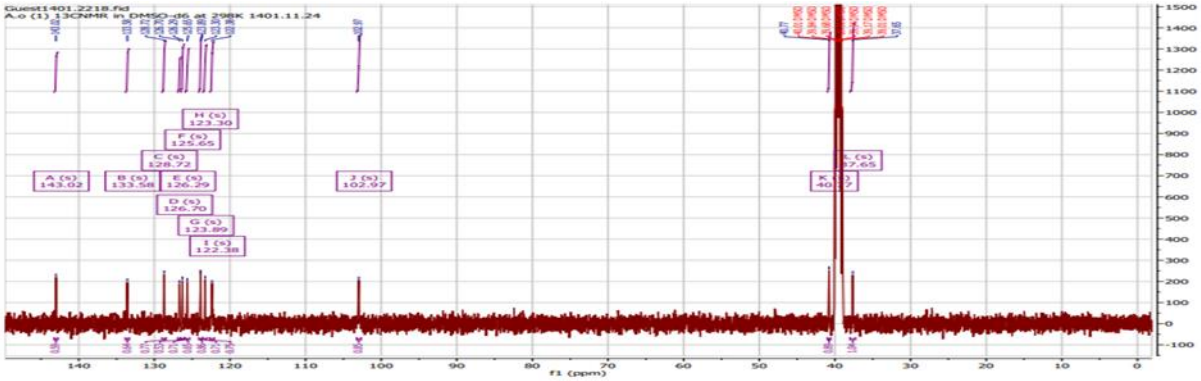


Figure (6) 13CNMR spectrum of (B1)

Identification of Shiff base derivatives: B2

(3Z)-3-((2-((4-hydroxybenzylidene)amino)phenyl)imino)indolin-2-one.

FT-IR(KBr)cm^{-1},Figure(7): 3047(C-H Ar.str.); 1616 (C=N str.); 1460 (C=C str.); 3415(O-H str.);817(N-H. oop) ;1735 (C=O str.),**1H-NMR(DMSO-*d6*), Figure(8):** δ8.29(s,1H,-N=CH-), 7.19-7.35(m,8H,H-4,H-5,H-6,H-7,H-2′,H-3′,H-5′,H-6′Ar-H), 8.33(s,1H,-NH-)Isatine group ,6.66(1H,C-6″Ar-H), 6.48(1H,C-3″ Ar-H), 7.45(1H,C-2″Ar-H),6.89(1H,C-5″Ar-H),6.48(s,1H,Ar-OH),**13CNMR(DMSO) Figure(9)**: δ 159 (C, C=N)Imine group ,δ184(C, C=O)Isatine ring, δ 103-150(C of phenyl group).

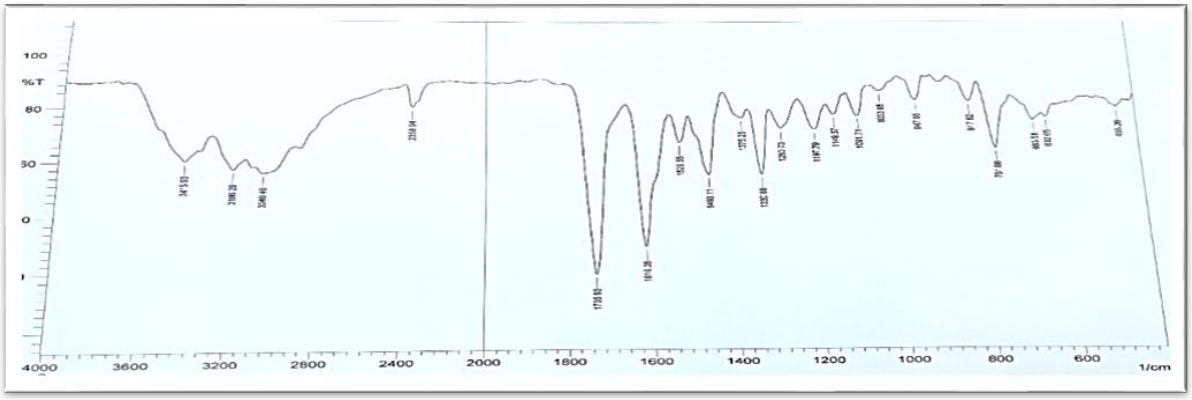


Figure 7: FT-IR for derivative (B2)

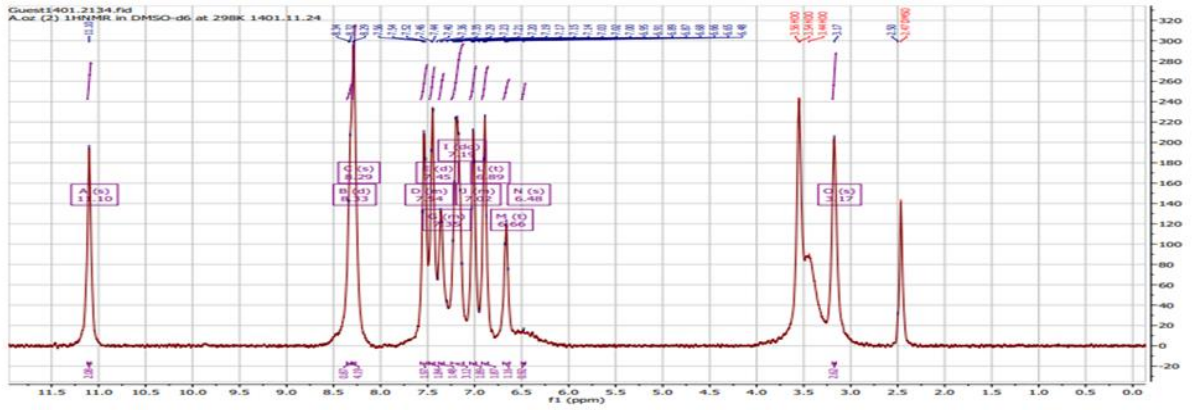


Figure (8) 1HNMR spectrum of derivative (B2)

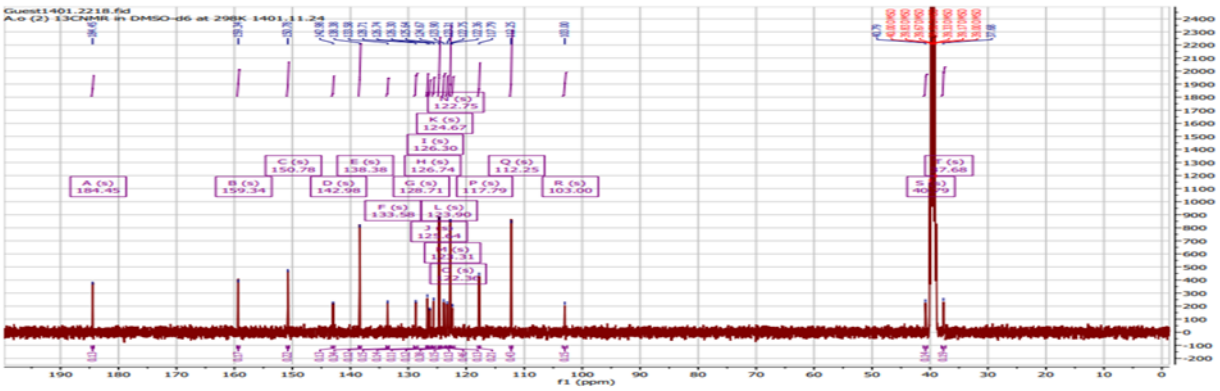


Figure (9) 13CNMR spectrum of (B2)

Identification of Shiff base derivatives: B3

(3Z)-3-((2-((4-nitrobenzylidene)amino)phenyl)imino)indolin-2-one.

FT-IR(KBr)cm^{-1},Figure(10): 3415 and 33049 (C-H Ar.str.); 1616 (C=N str.); 1460 (C=C str.); 632(C-H Ar.oop); 3415(N-H str.);817(N-H. oop) ;1735 (C=O str.);1330(NO_2 Ar. sym. St.),(1500-1560)NO_2 Ar asym.str.,**1H-NMR(DMSO-*d6*), Figure(11):** δ 8.33 (s, 1H,-N=CH-), , (8.2 (1H,H-5″ Ar-H), 8.33(s, 1H,-NH-) Isatine group ,6.9-7.35(m,8H,H-4,H-5,H-6,H-7,H-2 ′,H-3 ′,H-5 ′,H-7 ′ Ar-H),**13 CNMR(DMSO-*d6*) Figure(12)**: δ 159 (C, C=N)Imine group ,δ184(C, C=O)Isatine ring, δ 103-150(C of phenyl group).

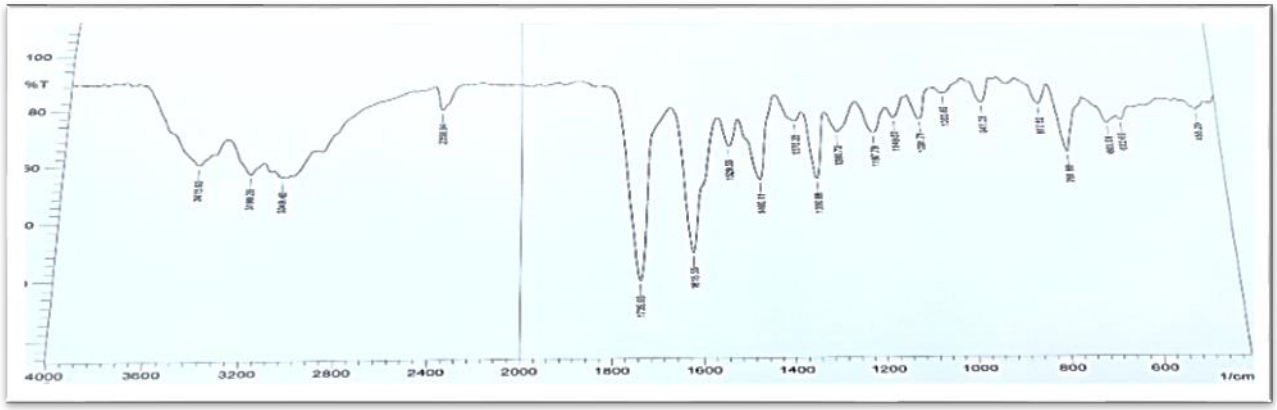


Figure 10: FT-IR for derivative (B3)

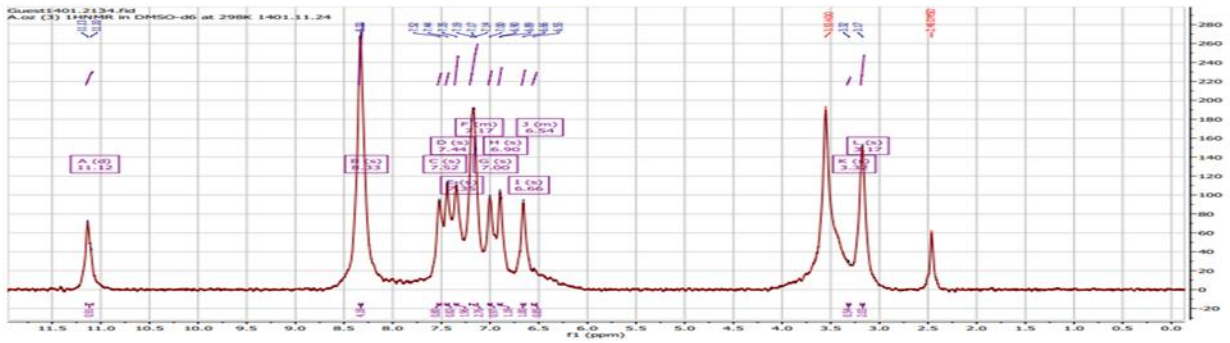


Figure (11) 1HNMR spectrum of derivative (B3)

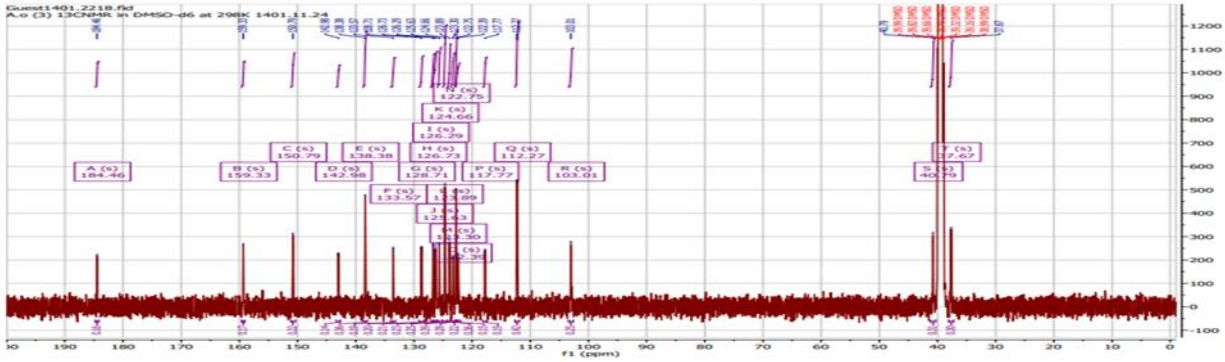


Figure (12) 13CNMR spectrum of (B3)

Identification of Shiff base derivatives: B4

(3Z)-3-((2-((3,4,5-trihydroxybenzylidene)amino)phenyl)imino)indolin-2-one .

FT-IR(KBr)$^{cm-1}$,Figure(13):3049(C-H Ar.str.); 1616 (C=N str.); 1460(C=C str.); 667(C-H Ar.oop);817(N-H. oop) ;1734 (C=O str.);3415(O-H str.) ,**1H-NMR(DMSO-*d6*), Figure(14):** δ 11.8(s,3 H,-[OH]3), 8.32 (s, 1H,-N=CH-), 8.26(s, 1H,-NH-) Isatine group , (7.54-6.90) Ar-CH , , 7.02(m,8H,H-4,H-5,H-6,H-7,H-2′,H-3′,H-5′,H-6′Ar-H), ,6.90(s,1H,H-2″Ar-H),6.67(1H,H-5″Ar-H), 7.19(1H,H-6″ Ar-H),**13 CNMR(DMSO) Figure(15)**: δ 159 (C, C=N)Imine ,δ184(C, C=O)Isatine ring group, δ 102-150(C of phenyl group).

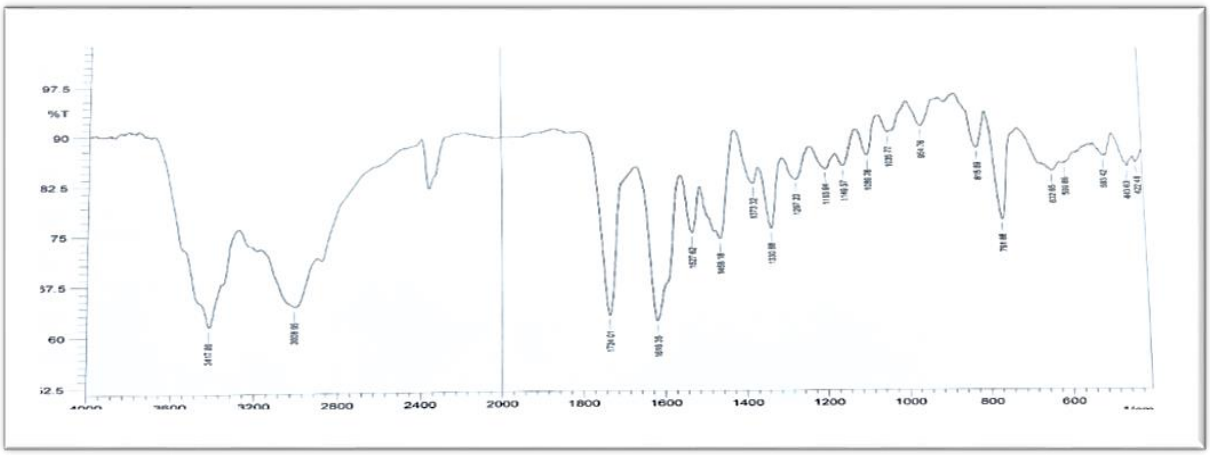


Figure13: FT-IR for derivative (B4)

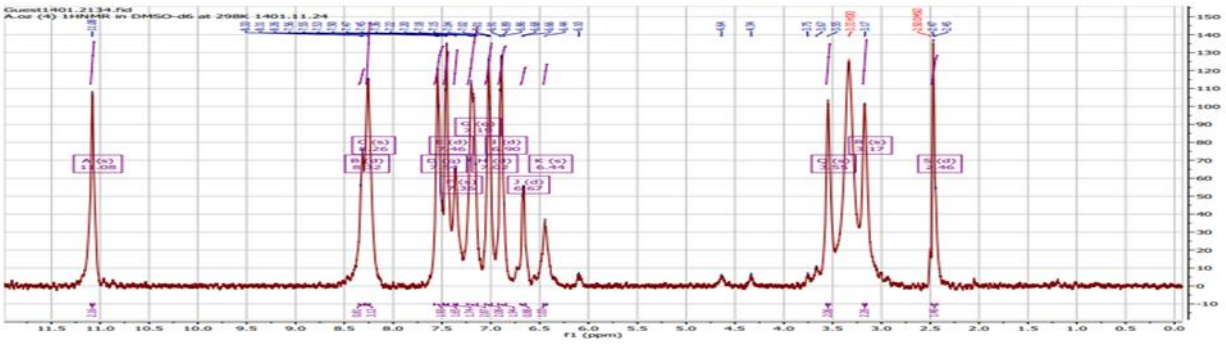


Figure (14)1HNMR spectrum of derivative (B4)

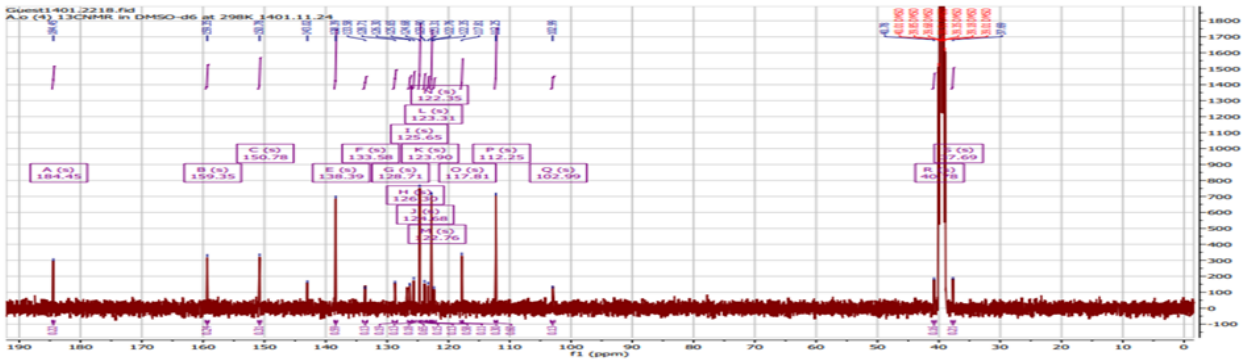


Figure (15) 13CNMR spectrum of (B4)

Identification of Shiff base derivatives: B5

(3Z)-3-((2-((3-hydroxy-4-methoxybenzylidene)amino)phenyl)imino)indolin-2-one.

FT-IR(KBr)cm^{-1},Figure(16): 3003 (C-H Ar.str.); 1616 (C=N str.); 1458 (C=C str.); 667(C-H Ar.oop); 3415(N-H str.);815(N-H. oop) ;1734 (C=O str.);1149(C-O Ether) ;3346(O-H str.);1373(C-H ben. Methyl), **1H-NMR(DMSO-*d6*), Figure(17)::** 8.27(s,1H,-NH-)$_{\text{Isatine group}}$, δ 8.33 (s,1H,-N=CH-), 7.19(1H,H-6″ Ar-H),6.89(s,1H,H-2″Ar-H),6.67(1H,H-5″Ar-H),6.45(s,1H,Ar-OH),3.55(s-3H-OCH_3).7.03(m,8H,H-4,H-5,H-6,H-7,H-2′,H-3′,H-5′,H-6′Ar-H),

13 CNMR(DMSO) Figure(18) : δ 159 (C, C=N)Imine ,δ184(C, C=O)Isatine ring, group, δ 102-138(C of phenyl group).

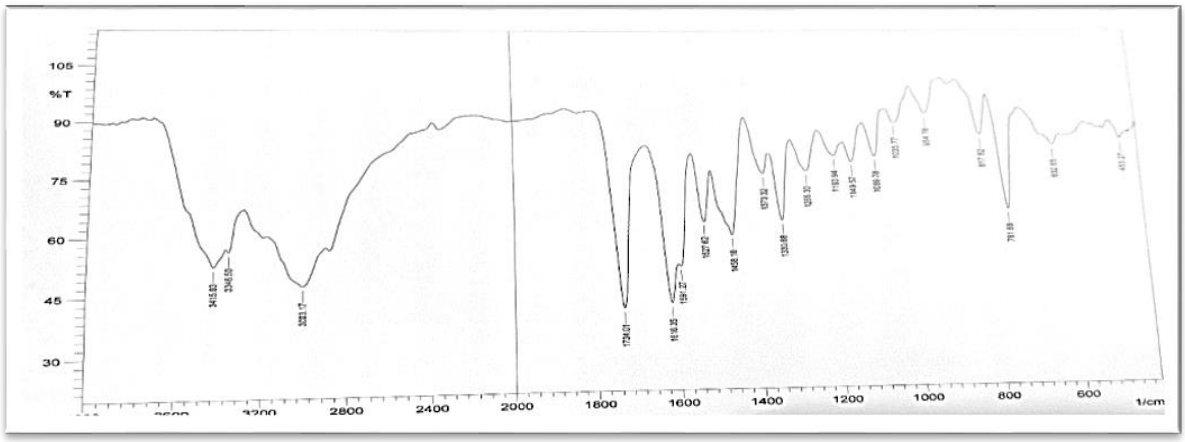


Figure16: FT-IR for derivative (B5)

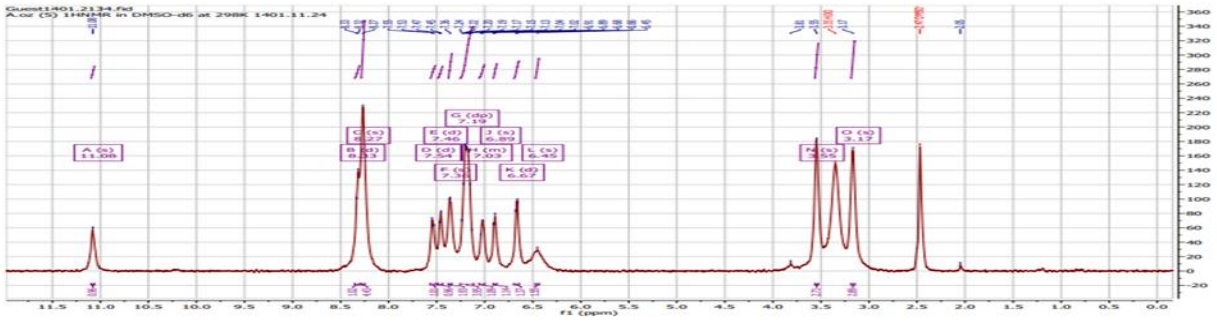


Figure (17) 1HNMR spectrum of derivative (B5)

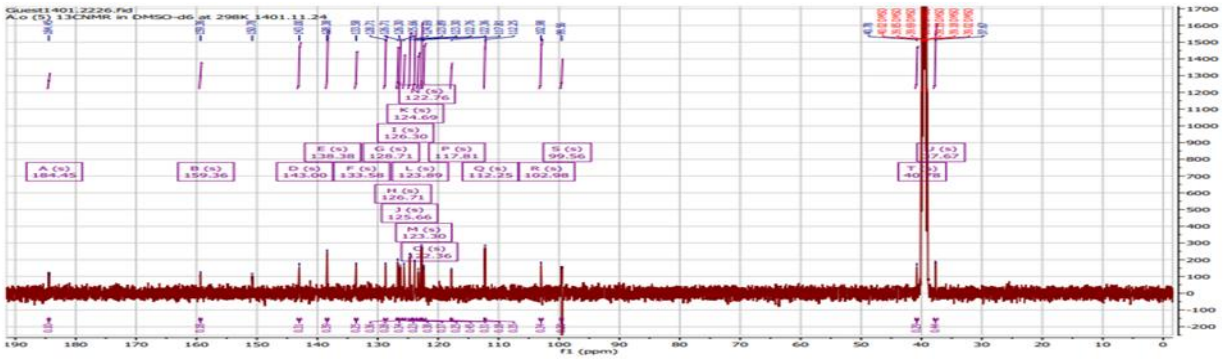


Figure (18) 13CNMR spectrum of (B5)

Identification of Shiff base derivatives: B6

(3Z)-3-((2-((3,4,5-trimethoxybenzylidene)amino)phenyl)imino)indolin-2-one.

FT-IR(KBr)cm^{-1},Figure(19): 3008 (C-H Ar.str.); 1616 (C=N str.); 1458 (C=C str.); 632(C-H Ar.oop); 3417(N-H str.);815(N-H. oop) ;1734 (C=O str.);1193 and 1267 (C-O Ether) ;1373(C-H ben. Methyl),1149(C-Nstr.). **1H-NMR(DMSO), Figure(20):** 7.63(s, 1H,-NH-) Isatine group ,δ 8.33 (s,1H,-N=CH-), , 6.50 (s,1H,H-2″ArH), ,3.16(s,9H,-[OCH_3]$_3$), 7.19(m,8H,H-4 , H-5,H-6,H-7,H-2′,H-3 ′ ,H-5 ′,H-6 ′ Ar-H),**13 CNMR(DMSO-*d6*) Figure(21)** :, δ 138 (C, C=N)Imine group, δ 102-133(C of phenyl group), δ143(C, C=O)Isatine ring

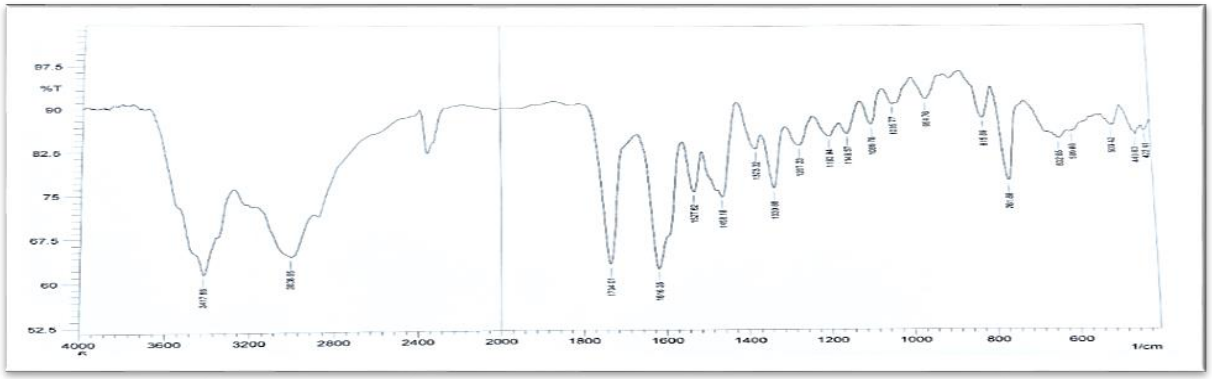


Figure19: FT-IR for derivative (B6)

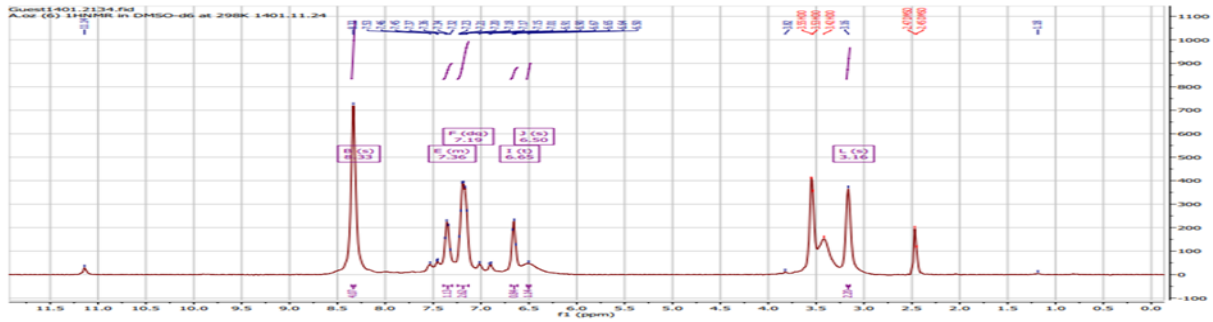


Figure (20) 1HNMR spectrum of derivative (B6)

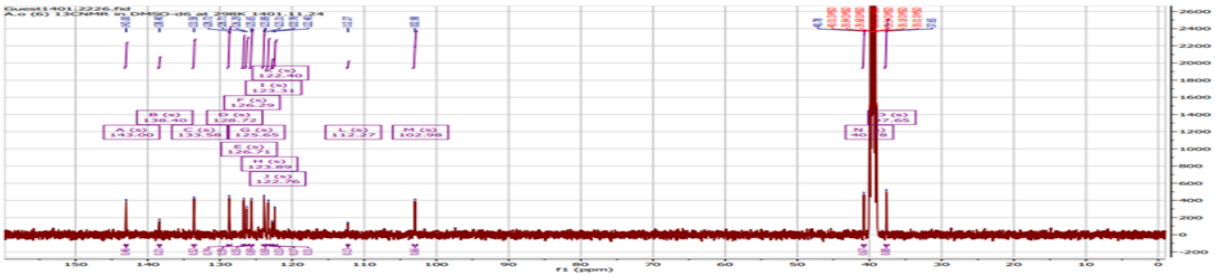


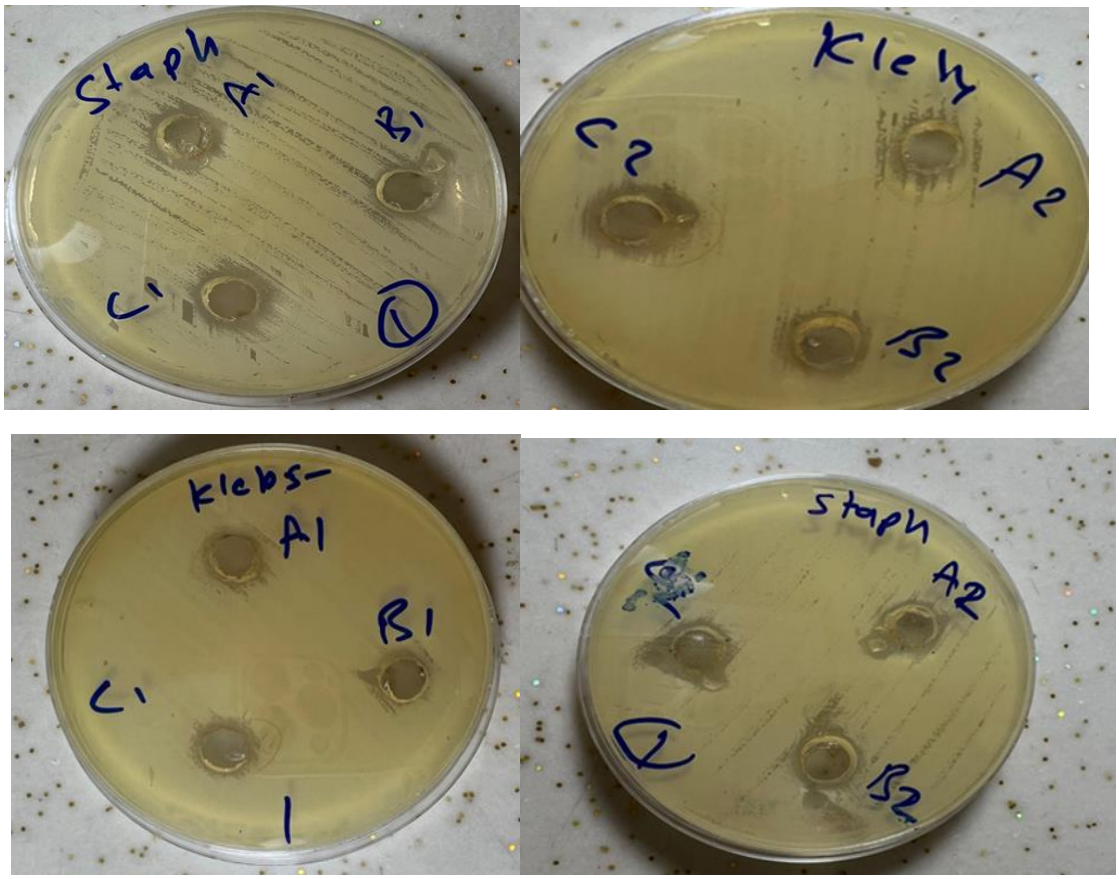
Figure (21) 13CNMR spectrum of (B6)

Table (1): physical properties of isatin derivatives

No.	M.F	M.Wt	m.p	color	%yield	Solvent
A	$C_{14}H_{11}N_3O$	237.13	183	deep brown	70%	Ethanol and DMSO
B1	$C_{23}H_{20}N_4O$	367.99	180	deep green	73%	Ethanol and DMSO
B2	$C_{21}H_{15}N_3O_2$	340.98	178	deep brown	65%	Ethanol and DMSO
B3	$C_{21}H_{14}N_4O_3$	369.97	187	greenish brown	68%	Ethanol and DMSO
B4	$C_{21}H_{15}N_3O_4$	532.86	179	brown	74%	Ethanol and DMSO
B5	$C_{22}H_{17}N_3O_2$	336.98	174	greenish brown	78%	Ethanol and DMSO
B6	$C_{24}H_{21}N_3O_4$	574.86	182	greenish brown	77%	Ethanol and DMSO

Table 2: Antibacterial activity of some synthesized compounds

	Gram positive Bacterial		*Gram negative Bacterial*	
	Staphylococcus spp		*Klebsiella spp*	
Compound	*50 µg/mL*	*100 µg/mL*	*50 µg/mL*	*100 µg/mL*
B_1	No bacterial growth	No bacterial growth	Bacterial growth	No bacterial growth
B_2	Bacterial growth	No bacterial growth	No bacterial growth	No bacterial growth
B_3	No bacterial growth	No bacterial growth	No bacterial growth	No bacterial growth



Figure(3):Inhibition zone of *Staphylococcus spp* and *Klebsiella spp*

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