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Preparation; Characterization and Investigation of the Biological Activity of Novel (Thiadiazol-Diazo) Compounds from 4-methoxy-2-nitroaniline

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Abstract

Aim of the study is synthesis Diazo-compounds via multi-step pathway. Initially step react (4-methoxy-((2-nitroaniline)) was coupled via 4-hydroxy-benzoic acid for yield the azo-derivative (1) . in the subsequent steps compound (1) was treated with (Thiosemicarbazide) to ob-tain thiadiazol (2) . Lastly; (Thiadiazol-Diazo) derivatives (3-6) were prepared by react compound (2) with pyrogallol; Salicylaldehyde; 1-Methylimidazole and 1-Naphthol to get. The structure of the prepared compounds were confirmed via (FT-IR and 1H_NMR) Spectroscopy. Additional; they were screened for antibacterial and antifungal activities .

Keywords: *[Diazo; Thiadiazol; Anticancer; Antibacterial]*

Introduction

The Azo compound's containing functional groups) R'-N = N-R. (; R' ;R. may be the aryl-groups or alkyl-groups; it were wide-ly used in fields of antibacterial ; pharmacy ; medicine and as anti-viral; anti-fungal; cytotoxic and anti-cancer agents [1;2]. It has applications in a wide range of fields; including: thermal transfer printers ; lasers ; and fuel cells; as well as a sensor for solar cells; dyeing textiles; leather; paper; food;

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cosmetics and pharmaceuticals [3-5]. Dyes that carry it have attracted heterocy-clic compounds very wide attention because of the diversity of its colors and simplicity in manufacturing and performance of good dyeing ; and the ability to bio-activity because they contain different atoms such as oxygen; nitrogen and sulfur; which helps them to bind with various elements [6-8]. Acquired organic molecules containing sulfur special attention in the field of medical chemistry. That is; replacing the oxygen atom in oxadiazole with a sulfur atom gives the thiadiazole derivatives. Used heterocyclic compounds with sulfur and nitrogen in the structures in the design of medical chemistry drugs [9;10]. The synthe-sis of many derivatives of 4;3;1-thiazole; as has been observed these derivatives display many pharmacological activity's such as antimicrobial; anti-tuberculosis; analgesics; anti_cancer; antioxidant and antidiabetic [11;12].

Instruments

Fourier-transform infra-red spectra recorded range about (4000-400 1/cm) on ((8400S); ((Shimadzu spectrophotometer)) using KBr pellets. 1HNMR analyses were preformed at (500 MHz) Brucker FT-spectrometer in (DMSO-d6) University of Teh-ran; Iran.

Materials and Methods

In this work all chemicals compounds are high purity and obtained from commercial source include : Potassium Hydroxide ; 4-Methoxy-(2-nitroaniline) ; 1-Methylimidazole ; Sodium- Hydroxide (from Sigma-Aldrich company by Germany) ; 4-hydroxybenzoic acid (Riedel de Haen; Germany) ; Concentration Hydrochloric acid (from Himedia company by India) ; high purity Ethanol (from Scharlau by Spain) ; pyrogallol ; Sodium Nitrite ; Phosphorous oxychloride (B.D.H; England) ; Thiosemi-carbazide ; Salicylaldehyde (Thomas Baker ; India) and 1-Naphthol (SCR ; China) .

1. Azo_compound (1) [13]

Compound (1):

I- Prepare of diazonium: (0.0059mol;1g) of 4-Methoxy-2-nitroaniline was getting and dissolve with mix from (30 ml) of H2O and (4ml) of conc. Hydrochloric acid. (10ml) of solution's (0.0059mol;0.4071g) of sodium-nitrite (NaNO2) with added some drop by drop with stir to (20 min) at a temperature from (zero -5°C) .

II - Prepare of Azo-dye:

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(0.0059mol;0.8412g) from 4-hydroxybenzoic acid was dissolve in (30 ml) ethanol with (20 ml) from (5% ;NaOH) ; then the generated diazonium-salt in the (I) step was added to mixture with sustained stir ; at (0-5°C) ; and the pH of the mixture was brought to 6 followed by constant agitation for (1 h) ; Following a 24-hours aging period; the precipitate underwent successive distilled water rinses and subsequent recrystallization from ethanol. in table 1 shown the physics properties; and in Scheme 1 show general reaction of compounds (1) prepare.

2.prepare of thiadiazol derivative (2) [14]

In a circular flask with two holes equipped with a magnetic stirrer and a condenser; react (1:1) moles of compound (1) (0.0031mol;1g) and (Thiosemicarbazide) (0.0031mol;0.2872g) dissolved in (10 ml) of (phosphorous oxychloride) with continu-ous stirring for 3 hrs.; then it left the mixture to cooling and then add (40 ml) from distilled water slowly and gradually and after completing the addition process the mixture was ascended to (4 h.) ; Then the product mixture is filtration prod-uct treated with (KOH solution) until they became neutral ; then the precipitate collected after filtering ; Wash with water and dried and re-crystallized ethanol . Thin-layer chromatography (TLC) was employed to track the reaction with mixture ethanol and benzene (1:4; v/v) serving as the mobile phase. The process resulted in the formation of a dark brown precipitate (Rf = 0.34). The corresponding physical properties are documented in Table 1. In Scheme 1 show general reaction to preparing of thiadiazol derivative compound (2).

3.Prepare diazo derivatives (3-6)[15]

"In the third line: the diazo compounds was prepared by dissolved (0.0013mol;0.5g) of thiadiazol derivative (2) in a solution consisted of 4ml of hydrochloric acid and (30ml) of distilled water and the solution was cooled to 0-5°C; then the prepared so-dium nitrite solution was added by dissolved (0.0013mol) of sodium nitrite in (10ml) of distilled water; and then the Diazoni-um salts solution was added drop by drop with stirring noting that the temperature did not rise above 0-5°C; after which the solution was kept with cooled and stirring for (20 min) ; during addition; temperature of each the reaction mixture was main-tained up to 0-5 oC. Then this solution was added drop by drop to the solution consisting of (0.0013mol) of each of (1-Methylimidazole; pyrogallol; 1-Naphthol; Salicylaldehyde) and (1g) of sodium hydroxide dissolved in (30ml) of distilled water cooled to 0-5°C and (5ml) of absolute ethyl alcohol; pH = 6 was made for the mixture and stirring for (1h) at the same tempera-ture; and the solution was kept for (24h); then

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the precipitate was filtered off and washing by distilled water and recrystallized with absolute ethyl alcohol. The physical properties were shown in table 1" .

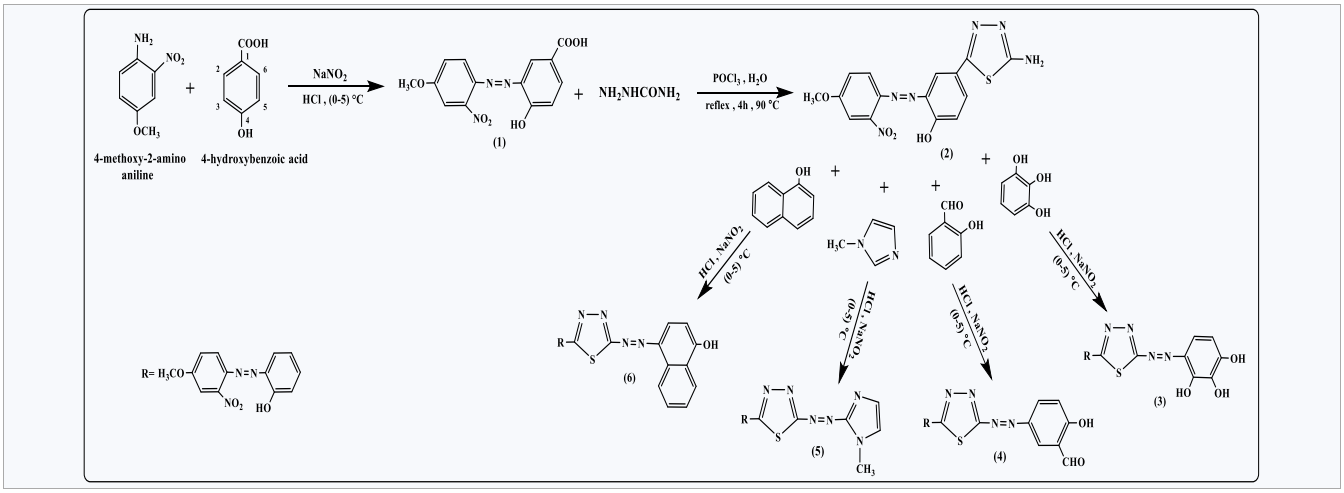

Figure 1. Show prepare compounds (1-6)

Results and Discussion

1. Compound (1) (4-hydroxy-3-((4-methoxy-2-nitrophenyl)-diazenyl) benzoic acid)

Fourier-transform infra-red show at 3406 1/cm to (OH) carboxylic acid; 3415 1/cm to (OH) phenol ; 2949 1/cm; to (C-H) aliphatic; 3091 1/cm; to (C-H) aromatic; 1450 1/cm;to (N=N); 1525 and 1330 1/cm; to NO2 ; 1652 1/cm; to (C=O) group; 1525 1/cm to (C=C) aromatic ; 1244 1/cm; to C-O. 1H-NMR for (1) show δ : (11.35 (S; 1H; OH)) carboxylic ; 10.4 ((S; 1H; OH)) phenol ; 6.7-8.6 ((M; 6H; Ar-H)) and 4.07 (S; 3H;OCH3) .

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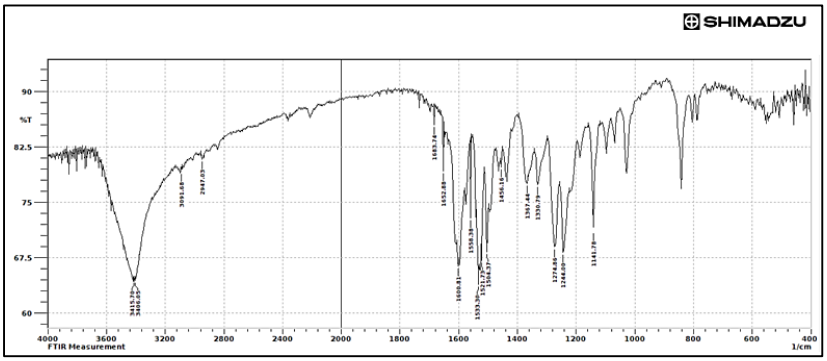
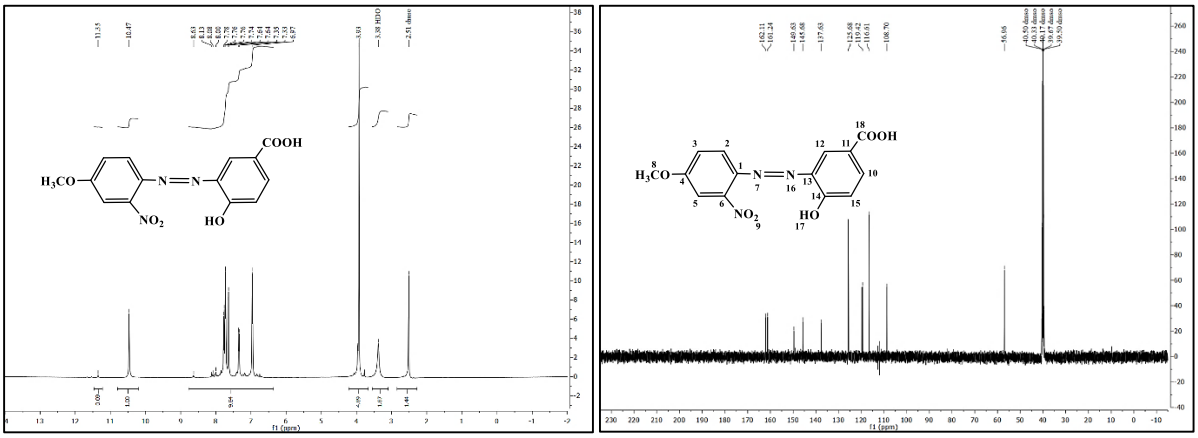


(a)



(b) (c)

Fig. 1. a) Fourier-transform infra-red Spectrum Comp. (1); b)^{1}H-NMR Spectrum Comp. (1); c) ^{13}C-NMR Spectrum Comp. (1)

2. Compound (2) {4-(5-amino-(1;3;4thiadiazol-2-yl))-2-((4-methoxy-2-nitrophenyl) diazenyl) phenol}

FT-IR show band on3420 1/cm to (OH); 3487 and 3371 1/cm; to (NH2); 2930 1/cm; to (C-H) aliphatic; 3090 1/cm; to (C-H) aro-matic; 1419 1/cm; to (N=N) ; 1643 1/cm; to (C=N) ; 1525 1/cm; to (C=C) aromatic; 1512 and 1350 1/cm; to (NO2) and 1211 1/cm; to (C-O). 1H-NMR of compound (2) show δ : at 4.7 for (S; 2H; NH2) ; 10.4 (S; 1H; OH) ; 6.2-8.04 (M ;6H; Ar-H) ; 3.37 (S; 3H ; OCH3).

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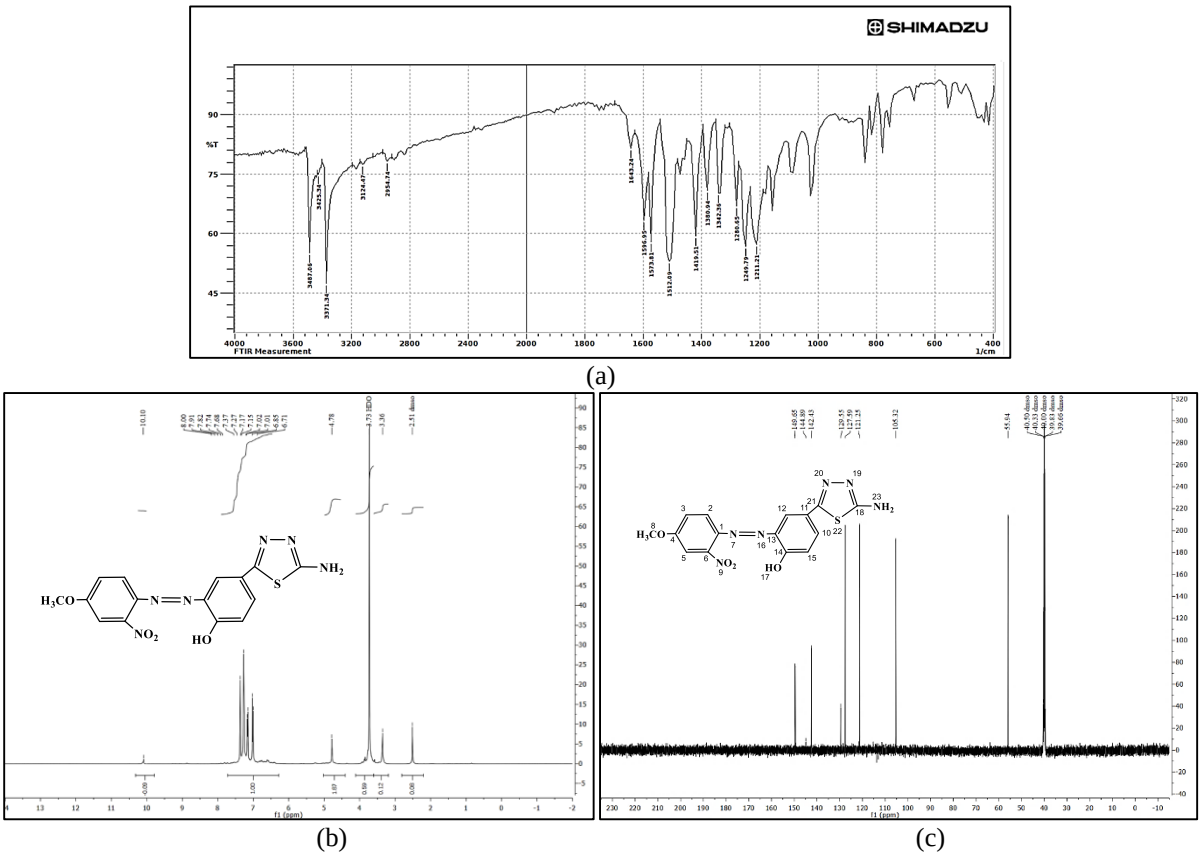

(a) (b) (c)

Fig. 2. a) Fourier-transform infra-red of Comp. (2) ; b)^{1}H-NMR of the Comp. (2); c)^{13}C-NMR of the Comp. (2)

3. Compound (3) {4-((5-(4-hydroxy-3-((4-methoxy-2-nitrophenyl)diazenyl)phenyl)-1;3;4-thiadiazol-2-yl)diazenyl)benzene-1;2;3-triol}

FT-IR show clear band in 3402 1/cm to OH group; 3101 1/cm to (C-H) aromatic; 2924 and 2854 1/cm to (C-H) aliphatic; (1465 1/cm to (N=N); 1620 1/cm to (C=N) ; 1527 1/cm to (C=C) aromatic; 1234 1/cm to (C-O) ; 1350 1/cm to NO2 and 1280 1/cm to C-S. 1H-NMR of compound (3) showing δ : 9.07 ; 9.2 to (S; 4H; OH) ; 6.91 -7.91 (M ; 8H;Ar-H); 3.3 (S; 3H; CH3) .

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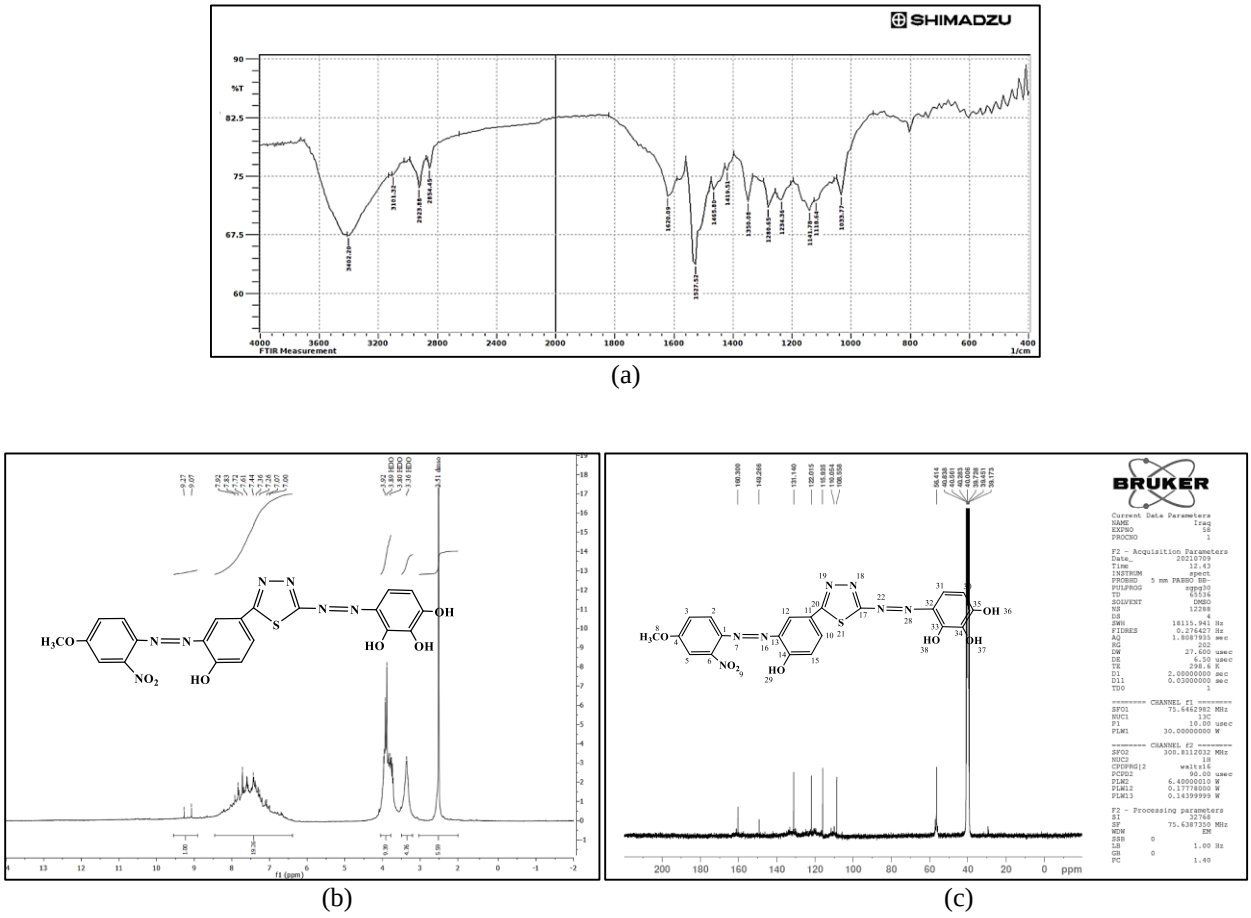

(a)

(b) (c)

Fig. 3. a) Fourier-transform infra-red of Comp. (3) ; b)^{1}H-NMR of the Comp. (3); c)^{13}C-NMR of the Comp. (3)

4. Compound(4){2-hydroxy-5-((5-(4-hydroxy-3-((4-methoxy-2-nitrophenyl) diazenyl)phenyl)-1;3;4-thiadiazol-2-yl)diazenyl)benzaldehyde}

Fourier-transform infra-red appear clear band on 3440 1/cm; to (OH) aldehyde ; 3379 1/cm; to OH phenol; 3101 1/cm to (C-H) aromatic; 2923 and 2854 1/cm; to C-H aliphatic; 1720 1/cm; to C=O; 1604 1/cm ; to (C=N); 1458 1/cm; to (N=N); 1536 1/cm for (C=C) aromatic; 1350 1/cm to NO2; 1234 1/cm; to C-O and 1242 1/cm; to C-S. 1H-NMR of compound (4) show δ : 10.3 (S;1H;CH aldehyde) ; 9.2 ; 10.0 (S;2H; OH); 6-8.1 (M; 9H; Ar-H); 3.3 (S; 3H; OCH3) ; 1.2 (S; 3H; N=CH3) .

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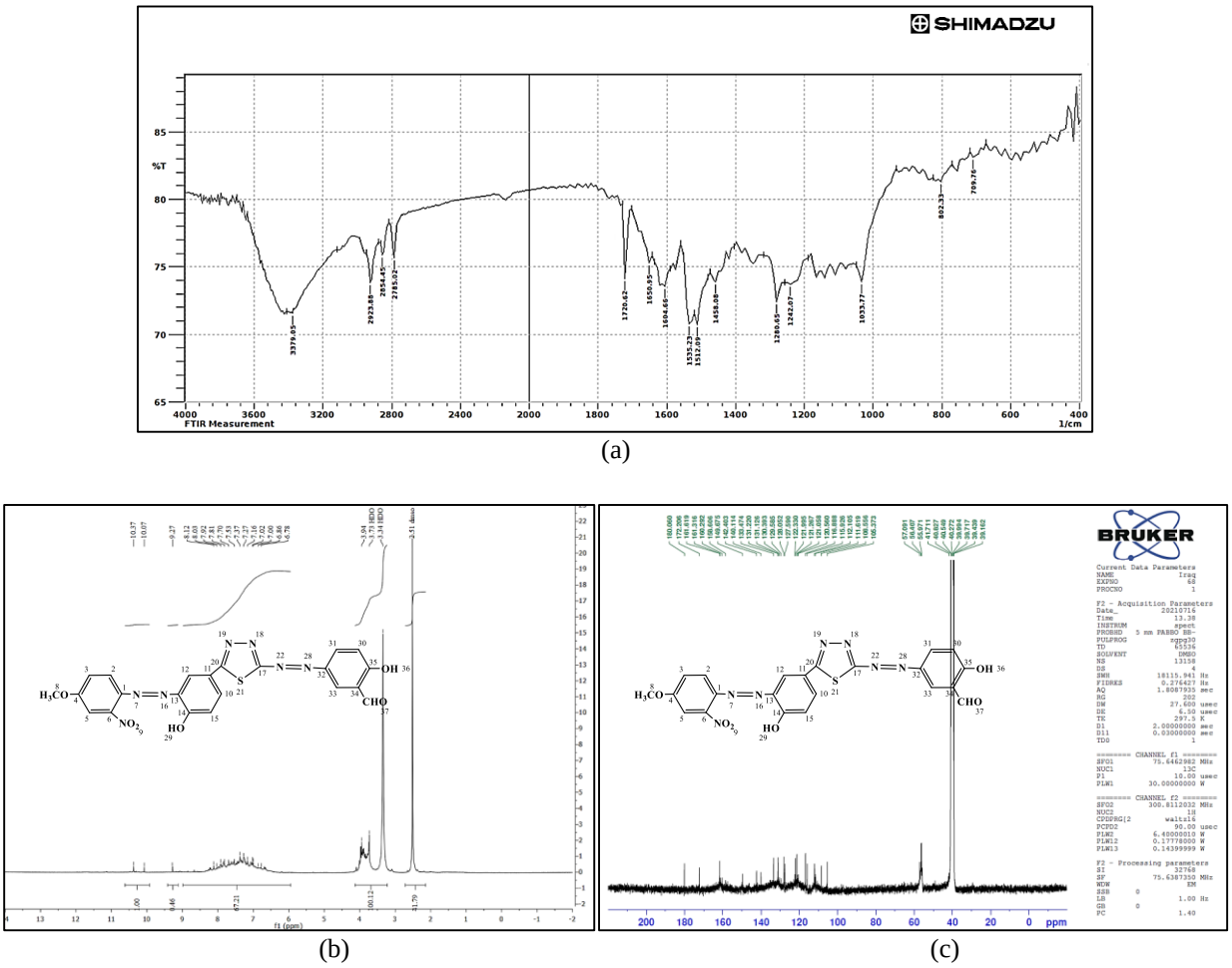

(a)

(b) (c)

Fig. 4. a) Fourier-transform infra-red of Comp. (4) ; b)^{1}H-NMR of the Comp. (4); c)^{13}C-NMR of the Comp. (4)

5. Compound (5) 2-((4-methoxy-2-nitrophenyl)diazenyl)-4-(5-((1-methyl-1H-imidazol-2-yl)diazenyl)-1;3;4-thiadiazol-2-yl)phenol

FT-IR show clear band on 3394 1/cm; to OH group; 3101 1/cm to C-H aromatic; 2923 and 2854 1/cm; to C-H aliphatic; 1604 1/cm; to C=N group; 1458 1/cm; to N=N group; 1535 1/cm; to C=C aromatic; 1350 1/cm; to NO2 group; 1234 1/cm; to C-O group and 1242 1/cm; to C-S group. 1H-NMR of compound (5) show δ : 9.2 for (S;1H;OH); 6-8.1 for (M; 9H; Ar-H); 3.3 for (S; 3H; OCH3); 1.2 (S; 3H; N-CH3).

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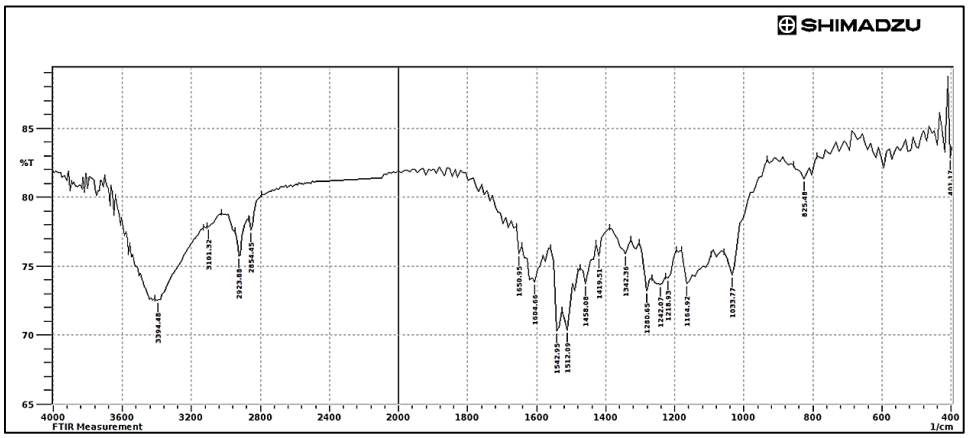
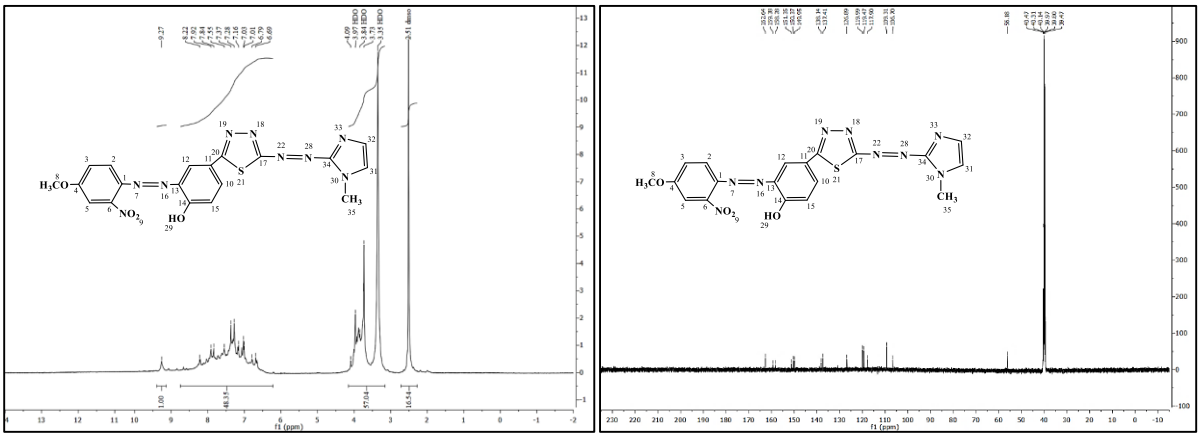


(a)



(b) (c)

Fig. 5. a) Fourier-transform infra-red of Comp. (5) ; b)^{1}H-NMR of the Comp. (5); c)^{13}C-NMR of the Comp. (5)

6. Compound (6) {4-((5-(4-hydroxy-3-((4-methoxy-2-nitrophenyl)diazenyl)phenyl)-1;3;4-thiadiazol-2-yl)diazenyl)naphthalen-1-ol}

Fourier-transform infra-red show at 3417 ; 3301 1/cm; to OH group; 3101 1/cm; to C-H aromatic; 2931 1/cm; to C-H aliphatic; 1650 1/cm; to C=N; 1596 1/cm to C=C aromatic; 1458 1/cm to N=N and 1350 1/cm; to NO2. 1H-NMR of compound (6) show δ : 10.3 for (S;1H;CH Aldehyde) ; 11.4 ; 13.3 for (S;2H;OH) ; 6.6-8.8 for (M;12H;Ar-H) ; 3.4 for (S;3H;OCH3) .

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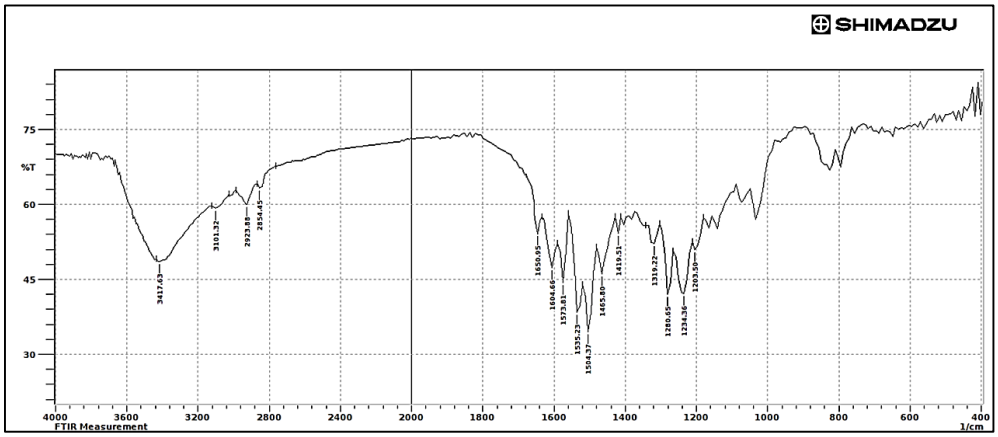
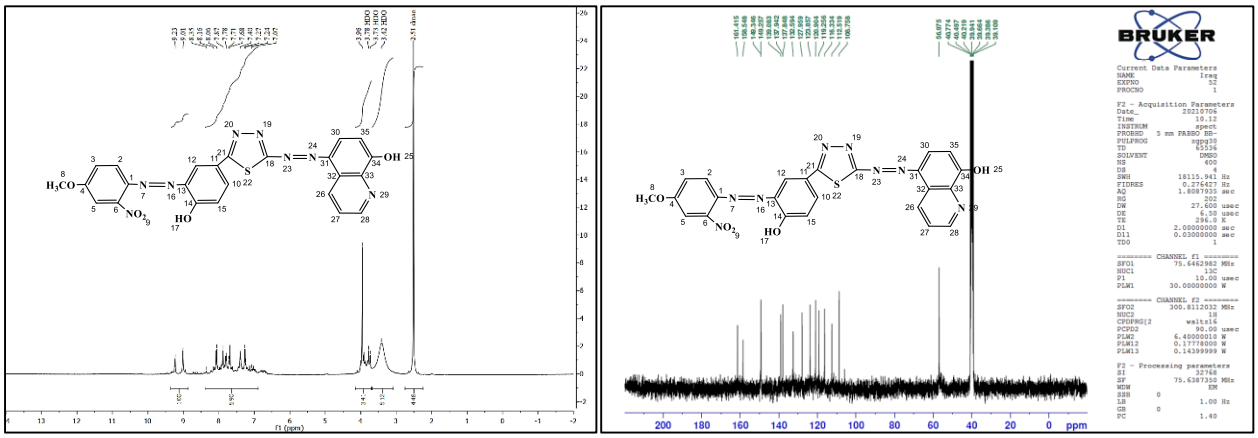


(a)



(b) (c)

Fig. 6. a) Fourier-transform infra-red of Comp. (6) ; b)^{1}H-NMR of the Comp. (6); c)^{13}C-NMR of the Comp. (6)

Table 1. Showing Physical properties for compounds (1-6)

Compounds	Colour	Melting point (ºC)	Molecular weight (g/mol)
1	Orange	143-146	317.26
2	Brown	124-127	372.36
3	Dark Brown	155-157	509.45
4	Brown	144-146	505.47
5	Dark Brown	141-143	465.45
6	Black	145-147	527.52

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Biological Study

The antibacterial activity and Antifungal activity of synthesized derivatives (3-6) was studied it is based on the method of spreading agar [16]. Tested derivatives synthesized against Staphylococcus aureus (Gram Positive) and E- Coli (Gram nega-tive); and Aspergillus Niger-fungicide. compounds were dissolved in DMSO-d6; to get conc. 0.003M. The zones for suppression formed were measured in centimeter. The table 2 show the zones of suppression of the derivatives (3-6).

Table 2. Show The antibacterial & antifungal activities of synthesized comp. (1-6)

	Antibacterial-Activity		Antifungal-Activity	
Comp.	**Conc. (M)**	**Escherichia coli (cm)**	**Staphylococcus aureus (cm)**	**Aspergillus Niger (cm)**
3	0.003	1.3	2	6
4	0.003	3.3	2.4	6
5	0.003	3	4.6	7
6	0.003	1.7	2.5	5

Conclusions

Ability prepares the compounds in their stable form and have high biological activity.

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