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# Synthesis and Evaluation Antibacterial Activity of Some New Substituted 5-Bromoisatin Containing Five, Six Heterocyclic Ring

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## Abstract:

This research includes the synthesis of some new different heterocyclic derivatives of 5-Bromoisatin. New sulfonylamide, diazine, oxazole, thiazole and 1,2,3-triazole derivatives of 5-Bromoisatin have been synthesized. The synthesis process started by the reaction of 5-Bromoisatin with different reagents to obtain schiff bases of 5-Bromoisatin intermediate compounds(1, 8, 19) by using glacial acetic acid as a catalyst in three routes. The first route, 5-Bromoisatin reacted with *p*-aminosulfonylchloride to product compound(1), then converted to sulfonyl amide derivatives(2-7) by the reaction of compound(1) with different substituted primary aromatic amine in absolute ethanol. The second route includes the reaction of 5-Bromoisatin reacted with ethyl glycinate to give 5-bromo-3-(Ethyl imino acetate)-2-oxo indole(8), which undergo react with hydrazine hydrate 80% to obtain hydrazine derivatives(9) that react with different acid anhydrides to obtain diazine derivatives(10-14). Also compound(8) reacts with urea and thiourea to give compounds(15,16) which undergo cyclization with *p*-bromophenacylbromide in absolute ethanol as a solvent to obtain oxazole (17) and thiazole (18), respectively. The third route included the reaction of 5-Bromoisatin with *p*-phenylenediamine in ethanol to obtain compound(19) which is converted to new substitutes 1,2,3-triazole derivatives(22,23) by diazotation of compound(19) and treating the resulted salt(20) with sodium azid, then acetylaceton or ethylacetoacetate, respectively. Newly synthesized compounds were identified by spectral methods. (FTIR, $^{1}$H-NMR, $^{13}$C-NMR) and measurements of some of its physical properties and also some specific reactions. Furthermore the effects of the synthesized compounds were studied on some strains of bacteria.

**Key words:** 5-Bromoisatin, Sulfonylamide, Diazine, Oxazole, Thiazole, 1,2,3-Triazole, antibacterial.

## Introduction

Isatin and its derivatives have a broad range of important biological, pharmacological and medicinal properties. It has discontinuous and

distinct distribution of peripheral tissue and body fluid and isatin conjoint site that are widely distributed and widely used as starting materials for the synthesis of broad range of heterocyclic compounds and as substrates for drug synthesis[1-3]. Sulfonamides are one of the oldest groups of the drugs; they have been in clinical use for over 70 years. It plays an important role in medicinal chemistry and it is used as anticancer drugs because it contains the sulfonamide subunit[4]. Owing to its wide application as antimicrobial[5], antibacterial[6], antioxidant[7], anticonvulsant, antipsychotic, antihypertensive, anti-inflammatory, diuretic, hypo-glycemic[8-10]. Sulfonamides are an essential class of antibacterial drugs used in medicine and veterinary practice[11]. Sulfa drugs are widely used in the treatment of infections, especially for patients intolerant to antibiotics. The vast commercial success of these medicinal agents has made the chemistry of sulfonamides become important in pharmaceutical sciences[12]. Pyridazine nucleus has been extensively studied as new and selective medicinal agents and as drugs acting on the system of cardiovascular; its derivatives can be used in the prostate cancer[13]. The biological activities of Its derivatives are antibacterial[14], antimicrobial[15], antifungal[16], antiinflammato-ry activities[17]antimala, analgesic and antipyretic[18]. Also developed newly pyridazine derivatives for the treatment of chronic lower back pain, chromic inflammatory pain associated with csteo arthritis and rheumatoid arthritis[19]. Oxazole and its derivatives used in industrial purposes and increased interest in their application of chemistry[20]. Thiazole derivatives are used as sedative, cardiotonic, anesthetic and many other applications of thiazole derivatives like cosmetics (sunscreens) or in liquid crystals[21]. 1,2,3-Triazoles are mainly useful in synthetic organic chemistry due to their variety of interesting biological activities like antibacterial, anticancer, antiviral,analgesic, fungicidal activity[22]. Triazoles have also a wide variety of interesting drugs[23].

# Materials and Methods

## Materials and Instruments

Chemicals used in this work are supplied from BDH, Fluka, Merck and Sigma Aldrich companies and used without further purification. Melting points were uncorrected and registered via digital Stuart scientific SMP3 melting point device .Thin layer chromatography (TLC) used to check purity and homogeneity of synthesis compounds. FTIR spectra of the compounds in the (4000-600) $cm^{-1}$ spectral range were recorded on SHIMAZU FTIR-8400 Fourier transform Infrared spectrophotometer using KBr discs. $^{1}$HNMR and $^{13}$CNMR spectra were recorded on Bruker 600MHz in Germany, instrument using TMS as internal reference and DMSO-$d_6$ as a solvent.

**Synthesis of 5-bromo-3-(*p*-iminophenyl enesulfonylchloride)-2-oxo indole(1)[24]**

In round bottomed flask were placed (2g, 0.0088mol) of 5-Bromoisatin-(Indole-2,3-dione) were placed with (1.70g, 0.0088mol) *p*-anilinesulphonylchloride in (9ml) dimethylformamide and 4-5 drops of glacial acetic acid, refluxed the mixture for (12 hrs.). The precipitate was filtered off, washed with water, dried and recrystallized from ethanol. Physical properties and FTIR spectral data of compound (1) are listed in Table (1).

**Synthesis of 5-bromo- 3- [*p*-imino( phenylenesulfonyl subutituted amine)]-2-oxo indole(2-7)[25]**

substituted primary aromatic amines (0.0025mol) are dissolved in ( 7 ml ) absolute ethanol, place this solution in 50 ml round bottomed flask then (1g, 0.0025 mol.) of compound (1) was added in partition with stirring and trying to keep the temperature below 40°C. The mixture was refluxed for (3 hrs.) with continuous stirring after that the mixture was cooled to room temperature and poured into excess cold water with stirring; the obtained precipitate was filtered, washed with water for several times and dried. The product was purified by recrystallization from methanol. Physical properties and FTIR spectral data of the products are listed in Table (1).

**Synthesis of 5-bromo-3-(Ethyl imino acetate)-2-oxo indole(8)[24]**

A solution of 5-Bromoisatin(Indole-2,3-dione) (2g, 0.0088mol) with (1.175g, 0.0088mol) ethyl glycinate in (10ml) (DMF) dimethylformamide and 4-5 drops of glacial acetic acid. The mixture was refluxed for (12 hrs.), trying to keep the heat of the range at (50-60)°C The formed precipitate may be cooled off before pouring into crushed ice, filtered with recrystalization from ethanol-water. Physical properties and FTIR spectral data of compound (8) are listed in Table (2).

**Synthesis of 5-bromo-3-(imino acetohydrazide)-2-oxo indole(9)[26]**

In round bottomed flask 50 ml was placed (2g, 0.0061mol) of compound (8), dissolved in (10ml) dimethylformamide then added excess of hydrazine hydrate 80% (0.007mol) with continuous stirring, the solution was refluxed for (7 hrs.). The resulted, cooled off before pouring into crushed ice. The precipitate was filtered, washed by distilled water and dried then was purified by recrystallization from ethanol. Physical properties and FTIR spectral data are listed in Table (2).

**Synthesis of 5-bromo-3-[imino aceto (hexahydrodiazepine-3,7-dione)]-2-oxo indole(10), 5-bromo-3-[iminoaceto(tetra hydropyridazin-3,6-dione)]-2-oxo indole (11), 5-bromo-3-[iminoaceto (6-nitro- 1,2-dihydrophtalazin-3,10-dione)]-2-oxo indole(12), 5-bromo-3-[iminoaceto(1,2-dichloro pyridiazin-3,6-dione)]-2-oxo indole(13) and 5-bromo-3-[imino aceto(1,2-dihydro itaconic-3,6-dione)]-2-oxo indole(14)[27]**

A mixture of hydrized derivative(9) (0.5 g, 0.0017 mol.) with (Glutaric anhydride, succinic anhydride, 4-nitrophthalic anhydride, 2,3dichloro malic anhydride and itaconic anhydride) respectively (0.0017 mol.) in (10 ml) of glacial acetic acid was refluxed for ( 6-8 hrs), then cooling mixture by adding it to ice bath product the obtain precipitate which was filtered and recrystallized from suitable solvent. Physical properties and FTIR spectral data of compounds (10-14) are listed in Table (2).

**Synthesis of 5-bromo-3-[(imino aceto) urea]-2-oxo indole-[15] and 5-bromo-3-[( imino aceto ) thiourea ]-2-oxo indole(16)[27]**

In 50 ml round bottomed flask, a mixture (1 g, 0.0031 mol) of compound (8) with (urea, thiourea) were placed respectively (0.0031 mol) and (0.25 g ,0.0031 mol) of sodium acetate in (8 ml) absolute ethanol, refluxed for (10-12 hrs.).The reaction mixture was filtered, poured on ice water, dried and recrystallized the precipitate from ethanol-water to give crystals. Physical properties are listed in Table (3).

**Synthesis of 5-bromo-3-[imino (acet amide)-N-4-*p*-bromo phenyloxazol-2-yl]-2-oxo indole(17) and 5-bromo-3-[(imino acetamide)-N-4-*p*-bromophenylthiazol-2-yl]-2-oxo indole(18)[27]**

The mixture compounds (15, 16) (0.003mol) with (0.83g, 0.003mol) *p*-bromophenacyl bromide in (10ml)

absolute ethanol was refluxed for (6-7 hrs.). Cooled, neutralized via solution of ammonium hydroxide. A solid product was filtered, washed with water and dried under vacuum. The product was recrystallized from ethanol. Physical properties and FTIR spectral data of these compounds are listed in Table (3).

**Synthesis of 5-bromo-3-[imino(*p*-phenyleneamine)]-2-oxo indole (19) [24]**

A mixture of 5-Bromoisatin(Indole-2,3-dione) (1g, 0.0044mol) with *p*-phenylenediamine (0.48g, 0.0044mol) in (10ml) DMF and 4-5 drops of glacial acetic acid, the mixture was refluxed for 12 hrs. The formed precipitate may be cooled off at room temperature before pouring into crushed ice, filtered with recrystalization from ethanol. Physical properties and FTIR spectral data of compound (19) are listed in Table (4).

**Synthesis of 5-bromo-3-[imino(*p*-phenyl diazonium salt)]-2-oxo indole(20)[25]**

A solution of compound (19) (0.6 g, 0.0019 mol) in (1.5 ml) concentration HCl was cooled to (0-5)°C. A Cooled solution of sodium nitrite (0.13g, 0.0019 mol) in (5ml) of water was added drop wise during 10min., then the reaction mixture was stirred for 30 min. Physical properties and FTIR spectral data of the product are listed in Table (4).

**Synthesis of 5-bromo-3-[imino(*p*-phenyl eneazido)]-2-oxo indole (21)[25]**

An aqueous solution of sodium azid (1.5ml) (0.3g, 0.0017 mol) was added drop wise to an aqueous solution of diazonium salt (20). The reaction mixture was stirred for 20 minutes to give an oily compound (21). Physical properties and FTIR spectral data are listed in Table (4).

**Synthesis of 5-bromo-3-[imino(*p*-phenyl ene-4-acetyl-5-methyl-1H-1,2,3-triazole)] -2-oxo indole(22)[25]**

A cold solution of (3ml.) sodium ethoxide, (0.15 g, 0.0015 mol) acetyl acetone and (0.5 g, 0.0015 mol) compound (21) was gradually added. Refluxing the mixture for 3 hours. The resulting precipitate was separated and recrystallized by drying ether. Physical properties and FTIR spectral data of dry product are listed in Table (4).

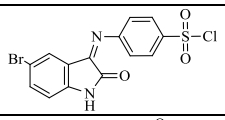
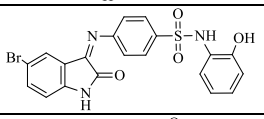
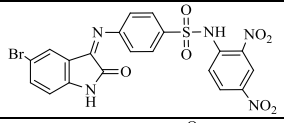
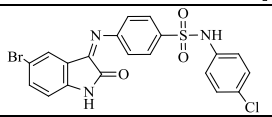
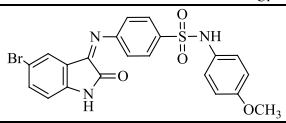
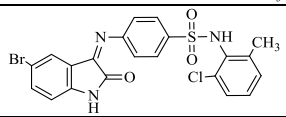
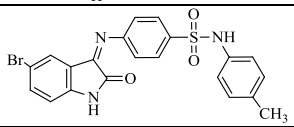
**Synthesis of 5-bromo-3-[imino(*p*-pheny lene-4-carboxylicacid-5-methyl-1H-1,2,3 -triazole)]-2-oxo indole(23)[25]**

Dissolving the mixture of compound (21) (0.5 g, 0.0015 mol) with ethyl acetoacetate (0.195 g, 0,0015 mol) in (5ml.) methanol was cooled to 0°C. Sodium methoxide (0.0015mol) in (3ml) methanol was added cautiously to the mixture and refluxed for 6 hours. The crude product was recrystallized from aceton. Physical properties and FTIR spectral data of dry product are listed in Table (4).

## Anti-bactrial activity test[28]

The test was performed according to the disk diffusion method. Some of the synthesized compounds were tested against two strain –ve bacteria (*Escherichia coli* and *pseudoman acruginosa*) and two strain gram +ve (*Bacilles* and *Staphylococcus aura*). Whattman no.1, 5mm diameter of filter paper disk were sterilized via autoclaving for 15 min. at 121°C. The sterile disks were impregnated with different compounds (800µg /disk). Agar plates were surface inoculated uniformly in 100°µL from both culture of tested microorganism. The impregnated disk was placed on the medium suitably spaced a part and the plates incubated at 5 °C for 1 hr. to permit good diffusion ,then transferred to an incubator at 37°C for 24 hrs. . The inhibition zones caused by various compounds on the microorganisms were examined.

## Table (1): Physical properties and FTIR spectral data $cm^{-1}$ of compounds(1-7)

| Com.No. | Physical Properties | | | | Major FTIR Absorption $cm^{-1}$ | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Structures | M.P. C° | Yield % | Color | ν(N-H) | ν(C-H) arom. | ν(C=O) amide | ν(C=N) | ν($SO_2$) | Others |
| **1** |  | 225-226 | 90 | orange | 3348 | 3068 3045 | 1706 | 1614 | Sym. 1164 Asym. 1315 | - |
| **2** |  | 184-187 | 87 | orange | 3218 3201 | 3074 3062 | 1716 | 1612 | Sym. 1157 Asym. 1375 | ν(O-H) 3398 |
| **3** |  | 176-178 | 88 | orange | 3338 | 3095 3045 | 1703 | 1625 | Sym. 1163 Asym. 1332 | ν($NO_2$) Sym. 1521 Asym.1388 |
| **4** |  | 282-284 | 87 | orange | 3271 | 3085 | 1720 | 1608 | Sym. 1197 Asym. 1388 | ν(C-Cl) 1091 |
| **5** |  | 269-271 | 84 | orange | 3234 3205 | 3049 | 1722 | 1610 | Sym. 1166 Asym. 1389 | ν*P*-Position 821 |
| **6** |  | 194-196 | 85 | orange | 3180 3168 | 3055 | 1733 | 1610 | Sym. 1161 Asym. 1305 | ν(C-Cl) 1078 ν*O*-Position 721 |
| **7** |  | 295-297 | 87 | orange | 3249 | 3039 | 1722 | 1610 | Sym. 1174 Asym. 1305 | ν(C-H) aliph. 2991 ν *P*-Position 823 |

## Table (2): Physical properties and FTIR spectral data $cm^{-1}$ of compounds(8-14)

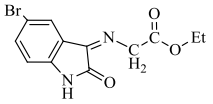
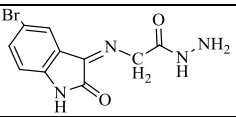
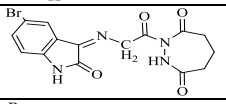
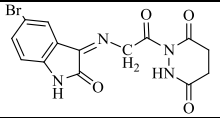
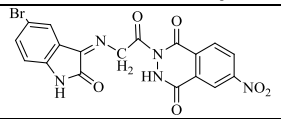
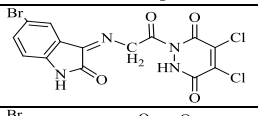
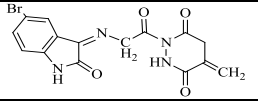
| Com.No. | Physical Properties | | | | Major FTIR Absorption $cm^{-1}$ | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Structures | M.P.° C | Yield % | Color | ν(N-H) | ν(C-H) arom. | ν(C-H) aliph. | ν(C=O) amide | ν(C=N) | Others |
| **8** |  | 112-115 | 91 | Pale orange | 3298 | 3088 | 2981 2937 | 1730 Ester Over Lap with amide | 1616 | ν (C-O-C) Asym. 1247 Sym. 1191 |
| **9** |  | 164-166 | 60 | Pale brown | 3240 3215 | 3076 3026 | 2937 2848 | 1685 amide | 1618 | ν($NH_2$) asym. 3446 Sym. 3361 |
| **10** |  | 166-169 | 87 | Off white | 3249 | 3085 | 2921 2850 | 1711 1699 1683 | 1616 | ν(C-Br) 698 |
| **11** |  | 183-185 | 85 | brown | 3203 | 3038 3031 | 2956 2921 | 1714 1697 1685 | 1616 | ν(C-Br) 698 |
| **12** |  | 237-239 | 81 | Pale orange | 3230 | 3083 3051 | 2954 2920 | 1718 1699 1681 | 1616 | ν($NO_2$) Asym. 1541 Sym. 1369 |
| **13** |  | 183-184 | 70 | brown | 3211 | 3085 | 2925 2852 | 1757 1714 1683 | 1616 | ν(C-Cl) 1057 |
| **14** |  | 230-231 | 65 | Pale grey | 3238 | 3085 | 2923 | 1716 1683 | 1616 | (=$CH_2$) 1539 |

**Table (3): Physical properties and FTIR spectral data $cm^{-1}$ of compounds(15-18)**

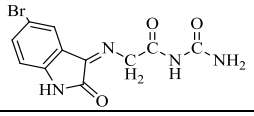
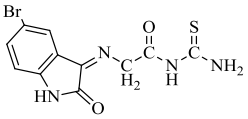
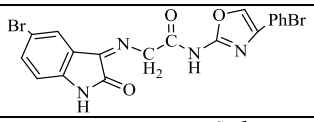
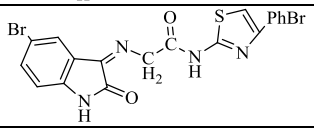
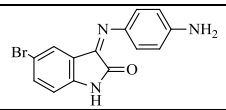
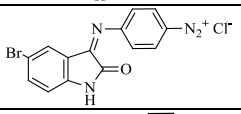
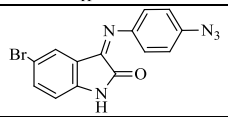
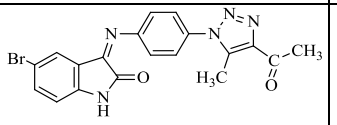
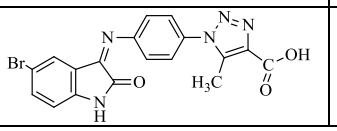
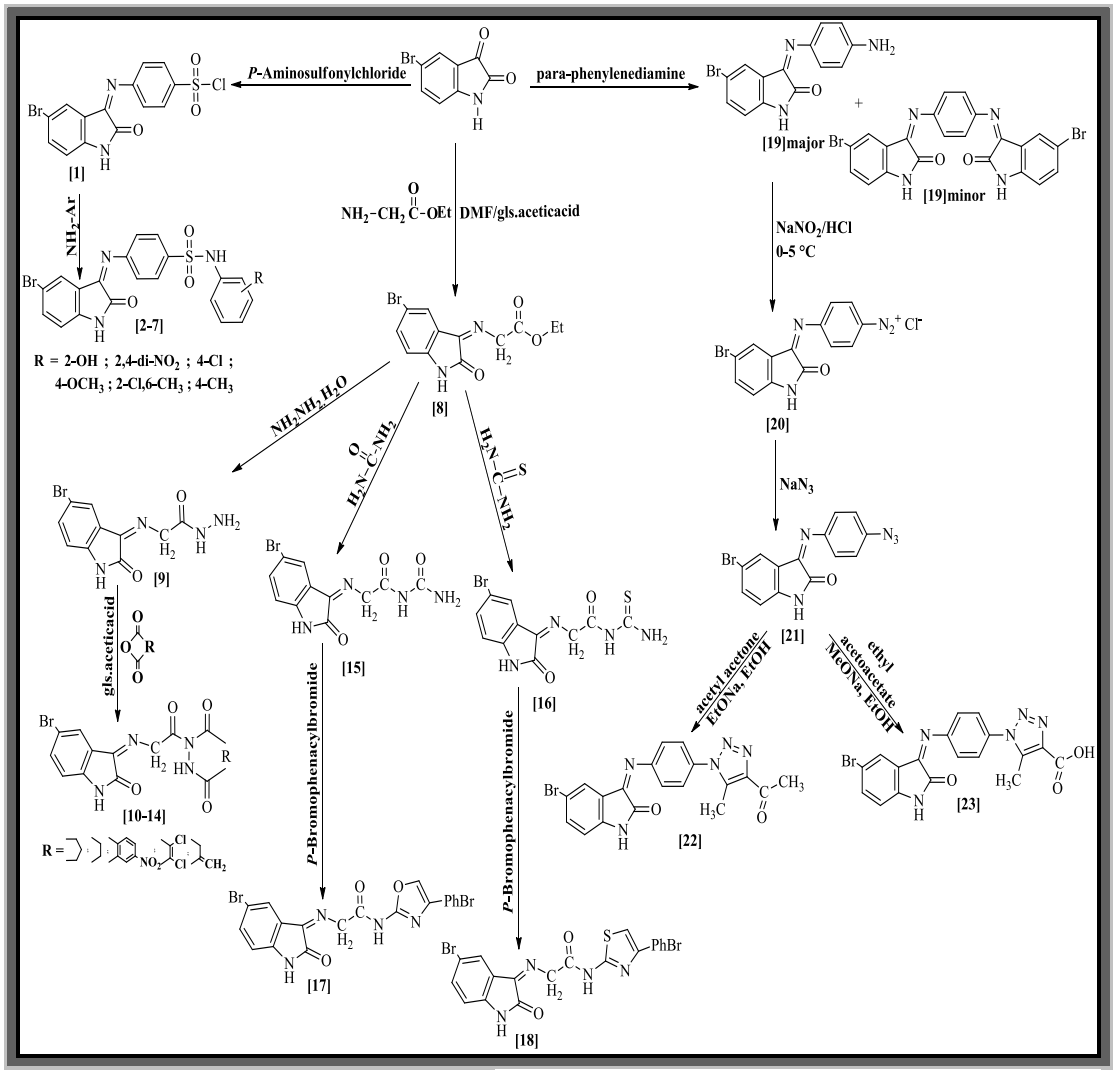
| Com.No. | Physical Properties | | | | Major FTIR Absorption $cm^{-1}$ | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Structures | M.P. ° C | Yield % | Color | ν(N-H) | ν(C-H) arom. | ν(C-H) aliph. | ν(C=O) amide | ν(C=N) | Others |
| **15** |  | 148-150 | 85 | Pale grey | 3245 | 3045 | 2981 2848 | 1728 1718 | 1616 | ν($NH_2$) asym. 3465 Sym. 3340 |
| **16** |  | 139-141 | 80 | Pale gray | 3298 | 3031 | 2908 2852 | 1733 | 1618 | ν($NH_2$) asym. 3432 Sym. 3313 ν(C=S) 1242 |
| **17** |  | 98-100 | 84 | gray | 3259 | 3056 3033 | 2906 2854 | 1731 1695 | 1616 | ν(C-O-C) 1197,1070 ν *P*-Position 808 |
| **18** |  | 98-99 | 80 | Pale gray | 3367 | 3055 3033 | 2906 2854 | 1731 1695 | 1616 | ν(C-S-C) 1290,1197 ν*P*-Position 808 |

**Table 4 - Physical properties and FTIR spectral data $cm^{-1}$ of compounds(19-23)**

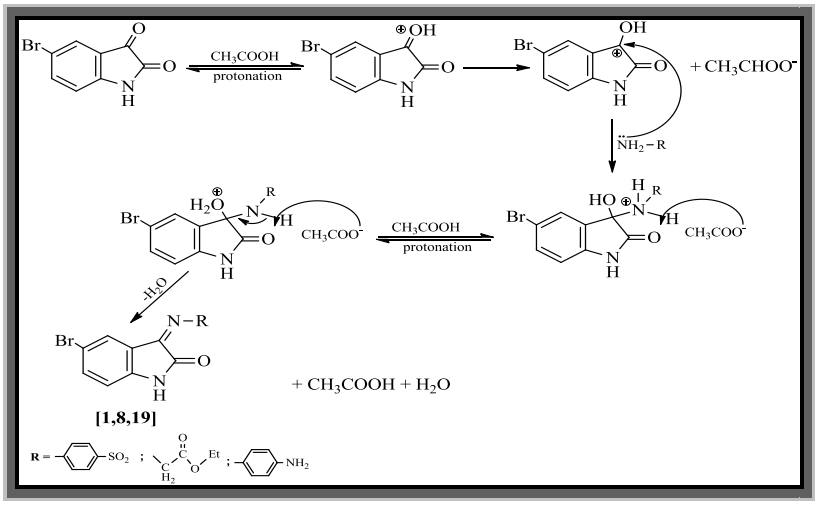
| Com. No. | Physical Properties | | | | Major FTIR Absorption $cm^{-1}$ | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Structures | M.P. °C | Yield % | Color | ν(N-H) | ν(C-H) arom. | ν(C=O) amide | ν(C=N) | Others |
| **19** |  | 178-180 | 93 | Deep red | 3228 | 3062 | 1730 | 1610 | ν($NH_2$) 3413,3342 ν*P*-Position. 821 |
| **20** |  | oily | 79 | Brown | - | - | - | - | - |
| **21** |  | 252-254 | 80 | Deep Gray | 3226 | 3068 3045 | 1710 | 1616 | ν N≡N—N 2123 ν*P*-Position 844 |
| **22** |  | 307-310 | 65 | Brown | 3371 | 3039 | 1726 | 1614 | ν(N=N) 956 ν*P*-Position 823 |
| **23** |  | 269-270 | 63 | Brown | 3371 | 3045 | 1720 | 1614 | ν(O-H) (3463-2800)brod ν(N=N) 977 ν*P*-Position 819 |

## Results and Discussion:

The synthetic sequences for synthesis of series of new 5-Bromoisatin linked to sulfonylamide, diazine, oxazole, thiazole and 1,2,3-triazole moieties as in Scheme(1). Compound (1) was synthesized by reaction of 5-bromoisatin with *p*-aminosulfonylchloride and dropes of glacial acetic acid in DMF to give schiff's bases compound(1). The mechanism involved two steps, the first step in condensation reaction involved nucleophilic addition while the second stepinclude eliminate water moleculeas to obtain Schiff base compounds(1,8,19) by using glacial acetic acid as catalyst, the mechanism[24] as shown in Scheme(2).




**Scheme(1): Synthesis series of new sulfonylamide, diazine, oxazole, thiazole and 1,2,3-triazole derivatives of 5-Bromoisatin**




**Scheme(2): Mechanism of synthesized compounds[1,8,19]**

FTIR spectrum show absorption band (3348)$cm^{-1}$ for υ(N-H); (3068,3045) $cm^{-1}$ for υ(C-H)arom.; (1706) $cm^{-1}$ for υ(C=O)amide; (1614) $cm^{-1}$ for υ(C=N); (1315) $cm^{-1}$ for $\upsilon SO_2$ asym.;1164 for $\upsilon SO_2$ sym. of compound(1) is listed in Table (1). Also sodium fusion test confirmed the presence of chlorine group[29]. Compound(2-7) was prepared by the reaction of compound(1) with different substituted primary aromatic amine in absolute ethanol. FTIR spectral showed absorption band (3398)$cm^{-1}$ for υ(O-H); (3218,3201)$cm^{-1}$ for υ(N-H); (3074,3062) $cm^{-1}$ for υ(C-H)arom.; (1716) $cm^{-1}$ for υ(C=O)amide; ; (1612) $cm^{-1}$ for υ(C=N); (1375) $cm^{-1}$ for $\upsilon SO_2$ asym.;1157 for $\upsilon SO_2$ sym. of compound(2). And (3338)$cm^{-1}$ for υ(N-H); (3095,3045) $cm^{-1}$ for υ(C-H)arom.; (1703) $cm^{-1}$ for υ(C=O)amide; (1625) $cm^{-1}$ for υ(C=N); (1521) $cm^{-1}$ for $\upsilon NO_2$ sym.;1388 for $\upsilon NO_2$ asym.; (1332) $cm^{-1}$ for $\upsilon SO_2$ asym.;1163 for $\upsilon SO_2$ sym of compound(3). Besides (3217)$cm^{-1}$ for υ(N-H); (3085) $cm^{-1}$ for υ(C-H)arom.; (1720) $cm^{-1}$ for υ(C=O)amide; (1608) $cm^{-1}$ for υ(C=N); (1388) $cm^{-1}$ for $\upsilon SO_2$ asym.;1197 for $\upsilon SO_2$ sym; (1091) $cm^{-1}$ for υ(C-Cl) of compound(4). (3234,3205)$cm^{-1}$ for υ(N-H); (3049) $cm^{-1}$ for υ(C-H)arom.; (1722) $cm^{-1}$ for υ(C=O)amide; (1610) $cm^{-1}$ for υ(C=N); (1389) $cm^{-1}$ for $\upsilon SO_2$ asym.;1166 for $\upsilon SO_2$ sym; (821) $cm^{-1}$ υ*P*-position of compound(5). (3180,3168)$cm^{-1}$ for υ(N-H); (3055) $cm^{-1}$ for υ(C-H)arom.; (1733) $cm^{-1}$ for υ(C=O)amide; (1610) $cm^{-1}$ for υ(C=N); (1305) $cm^{-1}$ for $\upsilon SO_2$ asym.;1161 for $\upsilon SO_2$ sym; (1078) $cm^{-1}$ for υ(C-Cl); (721) $cm^{-1}$ υ*O*-position of compound(6). And (3249)$cm^{-1}$ for υ(N-H); (3039) $cm^{-1}$ for υ(C-H)arom.; (2991) $cm^{-1}$ for υ(C-H)aliph.; (1722) $cm^{-1}$ for υ(C=O)amide; (1610) $cm^{-1}$ for υ(C=N); (1305) $cm^{-1}$ for $\upsilon SO_2$ asym.;1174 for $\upsilon SO_2$ sym (823) $cm^{-1}$ υ*P*-position of compound(7) All details of FTIR spectral data of compounds (2-7) are listed in Table (1). $^1$H-NMR spectra data of compound(3) δppm in DMSO-$d_6$ solvent showed signal at δ= (6.82-8.16)ppm due to aromatic rings protons, singlet signal at δ= (8.35)ppm due to (S-N-H)protons and singlet signal at δ= (8.78) ppm due to (N-H indole ring) protons, as listed in Table(5) and shown in Figure(1). $^{13}$C-NMR spectrum data of compound(3) are listed in Table(6) and shown in Figure(2).

5-Bromoisatin react with ethyl glycinate to gave compound(8). FTIR spectrum of compound(8) showed the disappearance of υ(C=O) of ketone group with still appearance (3088) $cm^{-1}$ for ν(C-H) aromatic with appear new absorption band at (2981,2937) $cm^{-1}$ for (C-H)aliph.; the absorption band at 1730 for C=O (ester overlap with amide);1616 for C=N imine and appearance of characteristic absorption bands at (1247asym., 1191sym)$cm^{-1}$ for (C-O-C). hydrazide derivative(9) synthesized by reaction of compound(8) with hydrazide hydrate 80%. FTIR spectrum of synthesized compound(9) from the appearance of bands at (3446 and 3361) $cm^{-1}$ which was assigned to the asymmetric and symmetric stretching bands of ($NH_2$) and (NH) group's appearance of band at (3240,3215) $cm^{-1}$. In addition to the disappearance of C-O-C band at (1247asym., 1191sym)$cm^{-1}$ of compound(8). Diazine derivatives (10-14) were synthesized by the reaction of hydrazide derivative(9) with (Glutaric anhydride, succinic anhydride,4-nitrophthalic anhydride ,2,3 dichloro malic anhydride and itaconic anhydride) respectively. The FTIR spectra of compounds (10-14) show the disappearance of the two bands of (-$NH_2$) group of hydrazide derivative (9). FTIR spectral data of compounds (10-14) appearance of a band due to (-NH) group at the range (3249-3203) $cm^{-1}$. Two carbonyl groups of compounds(10-14) appeared at (1757-1711) $cm^{-1}$ for cyclic carbonyl and at (1699-1681) $cm^{-1}$

for the amide carbonyl. All details of FTIR Spectral data of compounds (8-14) are listed in Table(2). $^{1}$H-NMR spectrum for compound(11) showed triplet signal at δ=(3.32)ppm due to (-C<u>H</u>$_2$-C<u>H</u>$_2$-) protons, singlet signal at δ=(4.64)ppm due to (=N-C<u>H</u>$_2$-) protons, signal at δ=(6.74-7.67)ppm due to aromatic rings protons, singlet signal at δ=(8.12)ppm due to (N-N-<u>H</u>)protons, and singlet signal at δ=(9.82)ppm due to (N-<u>H</u> indole ring) protons as listed in Table (5) and shown in Figure(3).$^{13}$C-NMR spectral data are listed in Table(6) and shown in Figure(4).

The compound(8) was converted to urea(15) and thiourea(16) derivatives via reaction with (urea and thiourea) respectively. FTIR spectral date showing the absorption at (3465 cm$^{-1}$) asym. (3340 cm-1) sym. for $NH_2$, (3245 cm$^{-1}$) for NH, (1728,1718 cm$^{-1}$) for C=O amide, (1616 cm$^{-1}$) for C=N of compound(15). (3432 cm$^{-1}$) asym. (3313 cm$^{-1}$) sym. for $NH_2$, (3298 cm$^{-1}$) for NH, (1733 cm$^{-1}$) for C=O amide, (1618 cm$^{-1}$) for C=N, (1242 cm$^{-1}$) for C=S, of compound(16). FTIR spectra of these compounds that shows results are listed in Table(3). Cyclization of (urea and thiourea)derivatives compound (15,16) by *p*-bromophenacylbromide to obtain oxazole and thiazole derivatives. FTIR spectral date showing the absorption at (3259 cm$^{-1}$) for NH, (1731,1695 cm$^{-1}$) for C=O amide, (1616 cm$^{-1}$) for C=N amide, (1197 asym.,1070sym. cm$^{-1}$) for C-O-C, (808 cm$^{-1}$) for *P*-position of compound(17). (3367 cm$^{-1}$) for NH, (1731,1695 cm$^{-1}$) for C=O amide, (1616 cm$^{-1}$) for C=N amide, (1290 asym.,1197sym. cm$^{-1}$) for C-S-C, (808 cm$^{-1}$) for *P*-position of compound(18). FTIR spectra of these compounds that shows results are listed in Table(3). $^{1}$H-NMR spectrum of compound(17) showed singlet signal at δ=(4.75)ppm due to (=N-C<u>H</u>$_2$-)protons, singlet signal at δ=(7.53)ppm due to oxazole ring proton, signal at δ= (7.71-8.08) ppm due to aromatic rings protons, singlet signal at δ=(9.30)ppm due to (N-<u>H</u> oxazole ring)protons and singlet signal at δ= (9.45)ppm due to (N-<u>H</u> indole ring) as shown in Table(5).$^{13}$C-NMR spectral data are listed in Table(6).

Synthesis of 1,2,3-triazoles compounds(22,23) via condensation 5-bromoisatin with *p*-phenylenediamine in ethanol as a solvent to give the compound(19). Which the diazotation of compound(19) to obtained diazonium chloride(20)[30] . The 1,2,3-triazoles are very important organic compounds having wide spectrum of biological activities[31]. The reaction must be carried out in low temperature between (0-5)°C because the high temperature decomposition of diazonium salt(20), the obtained diazonium chloride(20) was treated with calculated amount of sodium azide to afford compound(21). FTIR spectrum of compounds(19-23) showed the absorption at ν cm$^{-1}$ (2123 for N=N-N group). The azide derivative(21) was converted to compounds(22) and (23) via the reaction with acetylacetone and ethylacetoacetate respectively. The 2+3 cycloaddition implies a reaction between 1,3-dipole 5-bromo-3-[imino(*p*-phenyleneazido)]-2-oxo indole and 1,3-diketone or β-keto ester compounds called dipolarophile [acetylactone and ethylacetoacetate] in basic solution [EtOH+EtONa]. FTIR spectral showed the disappearance of the azid group ($N_3$) band in the starting material[21] at (2123 cm$^{-1}$) which is a good indication for successful condensation. The spectrum also shows absorption bands at (1726 cm$^{-1}$ for ν C=O amide; 1614 cm$^{-1}$ for ν C=N imine; 956 cm$^{-1}$ for νN=N). For compound(22); [1720 cm$^{-1}$ for ν C=O amide; 1614 cm$^{-1}$ for ν C=N imine; 977cm$^{-1}$ for νN=N in addition appearance abrod band (3463-2800) cm$^{-1}$ for νO=C-OH] for compound(23). All details of FTIR Spectral data of compounds(19-23) are

listed in Table(4). $^{1}$H-NMR spectrum of compound (22) δppm in DMSO-$d_6$ solvent showed singlet signal at δ=(2.49)ppm due to (O=C-C<u>H</u>$_3$) protons, singlet signal at δ=(3.31)ppm due to (C<u>H</u>$_3$) protons, signal at δ=(6.77-7.76)ppm due to aromatic rings protons and singlet signal at δ=(8.21)ppm due to (N-<u>H</u> indole ring) proton, as listed in Table(5) and shown in Figure(5). $^{13}$C-NMR spectral data of compound(22) are listed in Table(6) and shown Figure(6).

**Table (5): $^{1}$H-NMR spectral data (δ ppm) for selected compounds**

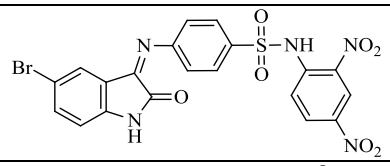
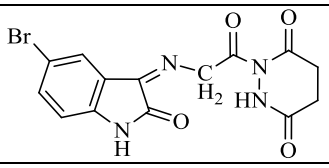
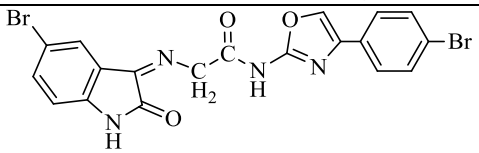
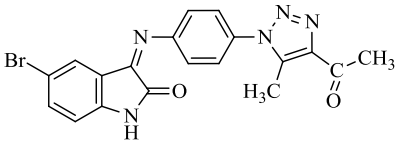
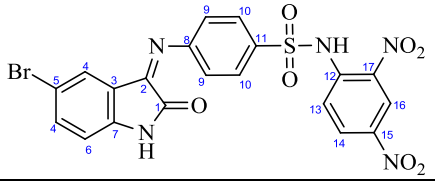
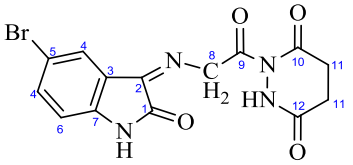
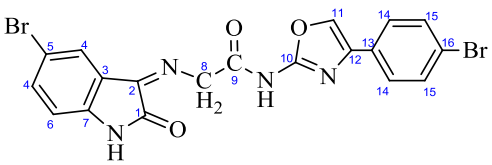
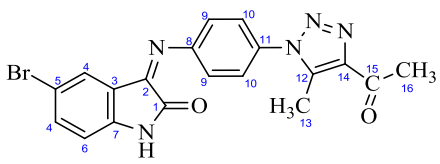
| Comp. No. | Structures | $^{1}$HNMR Spectral data(δppm) |
|---|---|---|
| 3 |  | 6.82-8.16(m,10H,Ar-<u>H</u>); 8.35(s,1H,S-N-<u>H</u>); 8.78(s,1H,N-<u>H</u> indole ring). |
| 11 |  | 3.32 (t,4H,-C<u>H</u>$_2$-C<u>H</u>$_2$-) ; 4.64(s,2H, =N-C<u>H</u>$_2$-); 6.74-7.67 (m,3H,Ar-<u>H</u>) ; 8.12(s,1H, N-N-<u>H</u>) ; 9.82(s,1H,N-<u>H</u> indole ring). |
| 17 |  | 4.75 (s,2H,=N-C<u>H</u>$_2$-) ; 7.53 (s,1H, oxazole ring); 7.71-8.08 (m,7H,Ar-<u>H</u>) ; 9.30(s,1H,N-<u>H</u> oxazole ring); 9.45 (s,1H,N-<u>H</u> indole ring). |
| 22 |  | 2.49(s,3H,O=C-C<u>H</u>$_3$);3.31(s,3H,C<u>H</u>$_3$); 6.77-7.76(m,7H,Ar-<u>H</u>); 8.21 (s,1H,N-<u>H</u> indole ring). |

**Table (6): $^{13}$CNMR spectral data (δ ppm) for selected compounds**

| Comp. No. | Compound structure | $^{13}$CNMR spectral data (δ ppm) |
|---|---|---|
| 3 |  | 112.11-143.89 ($C_{3,4,5,6,7,9,10,11,13,14,15,16,\ 17}$); 140.56($C_{12}$); 150.320($C_8$); 159.42 ($C_2$); 183.69($C_1$). |
| 11 |  | 36.31($C_{11}$) ; 43.03 ($C_8$) ; 111.30-138.18 ($C_{3,4,5,6,7}$) ; 143.38 ($C_2$) ; 162.67($C_1$);163.10($C_9$);176.32($C_{10,12}$). |
| 17 |  | 65.85($C_8$); 90.04($C_{11,12}$); 112.11-135.59 ($C_{3,4,5,6,7,9,10,13,14,15,16}$) ; 143.89($C_{10}$) ; 169.13($C_2$); 185.38($C_9$); 198.97($C_1$). |
| 22 |  | 52.13($C_{16}$) ;105.23($C_{13}$) ;110.65-136.88($C_{3,4,5,6,7,8,9,10,13,14}$); 151.18($C_2$); 167.22($C_1$,15). |

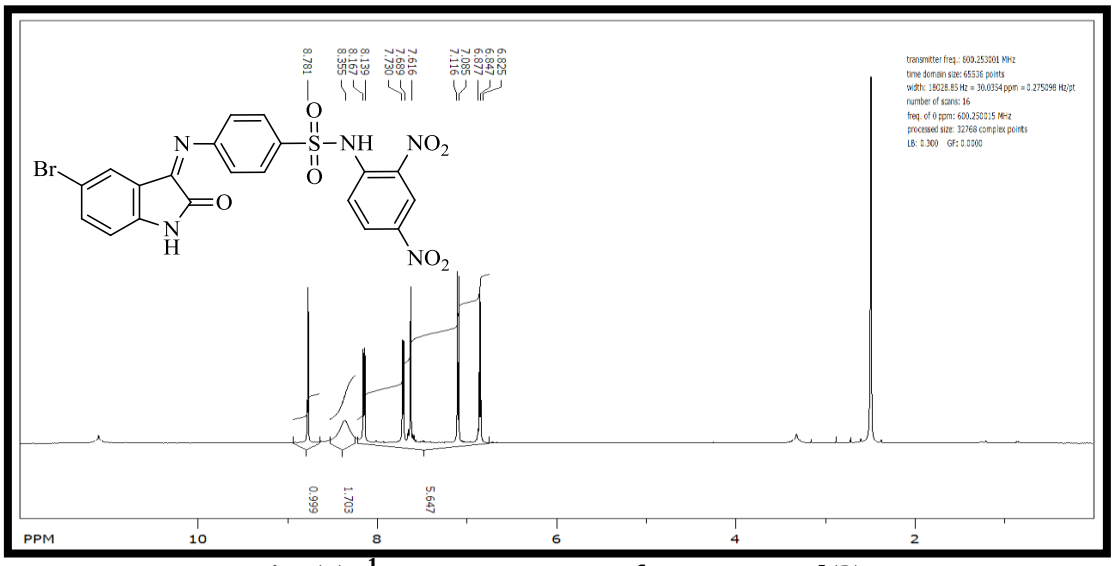



**Fig. (1): $^{1}$H-NMR spectrum for compound(3)**

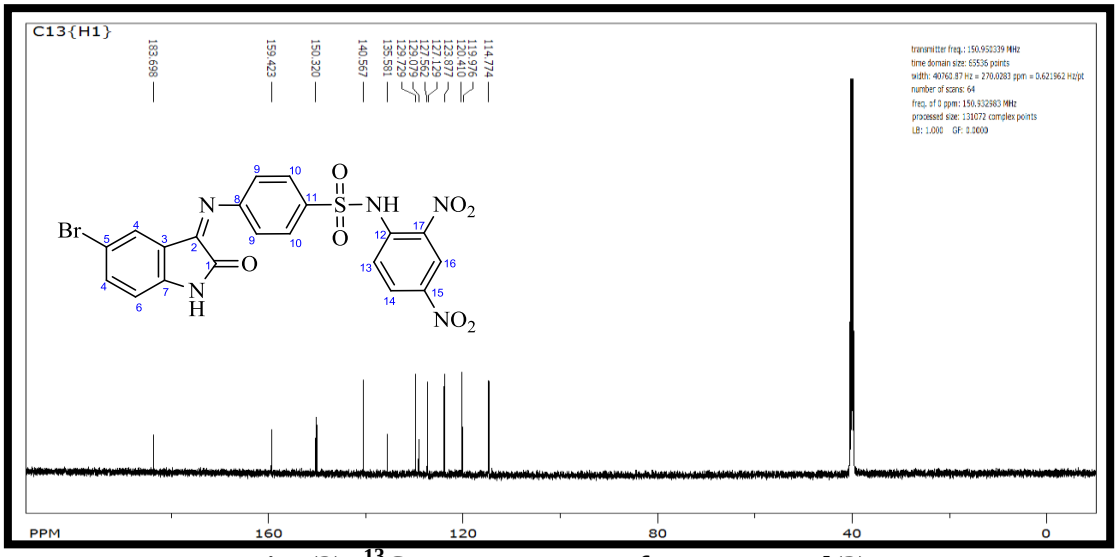



**Fig. (2): $^{13}$C-NMR spectrum for compound(3)**

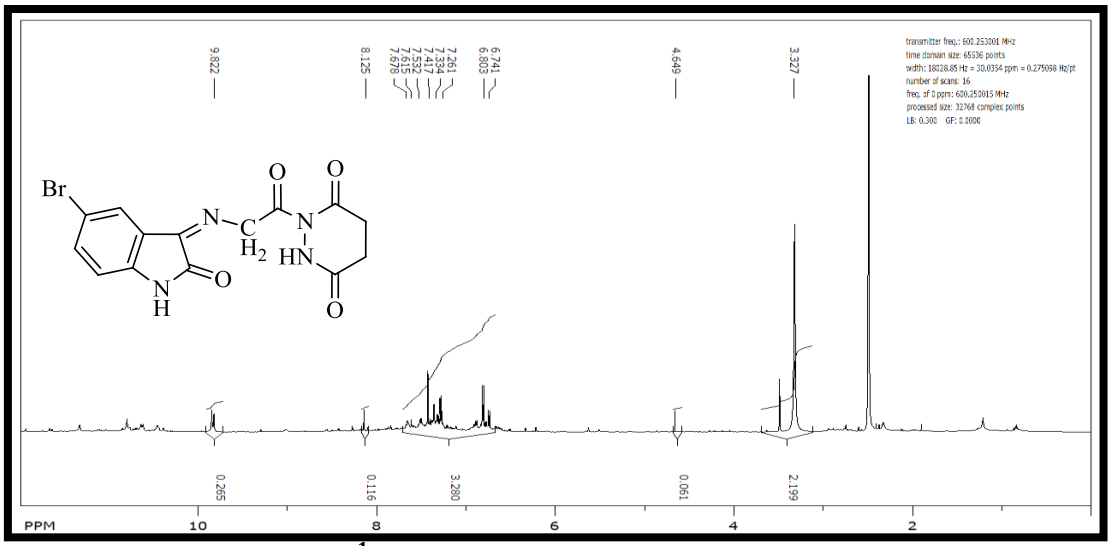



**Fig. (3): $^{1}$H-NMR spectrum for compound(11)**

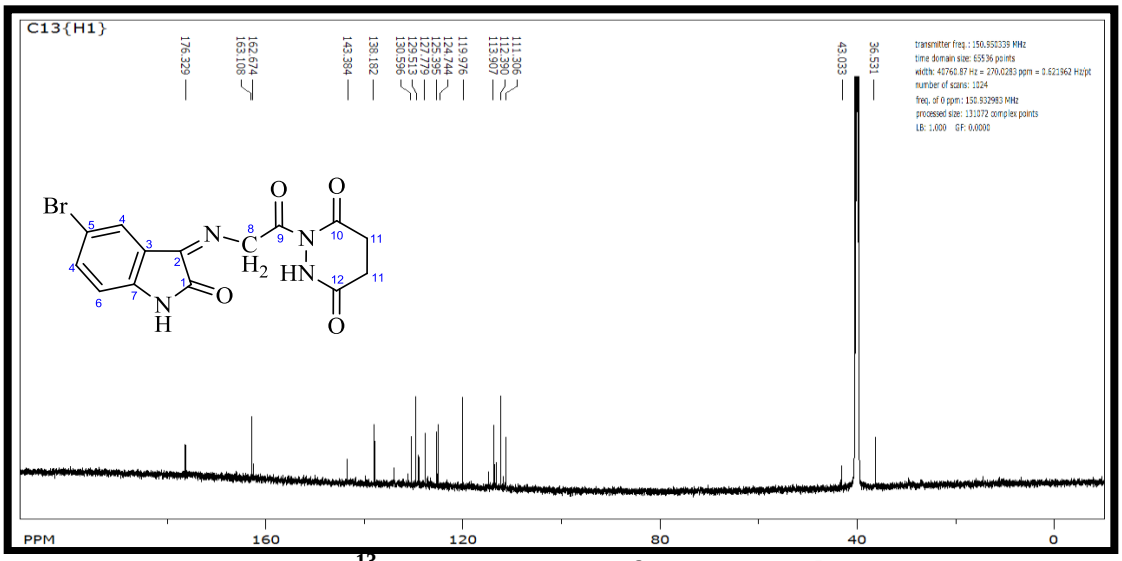



**Fig. (4): $^{13}$C-NMR spectrum for compound(11)**

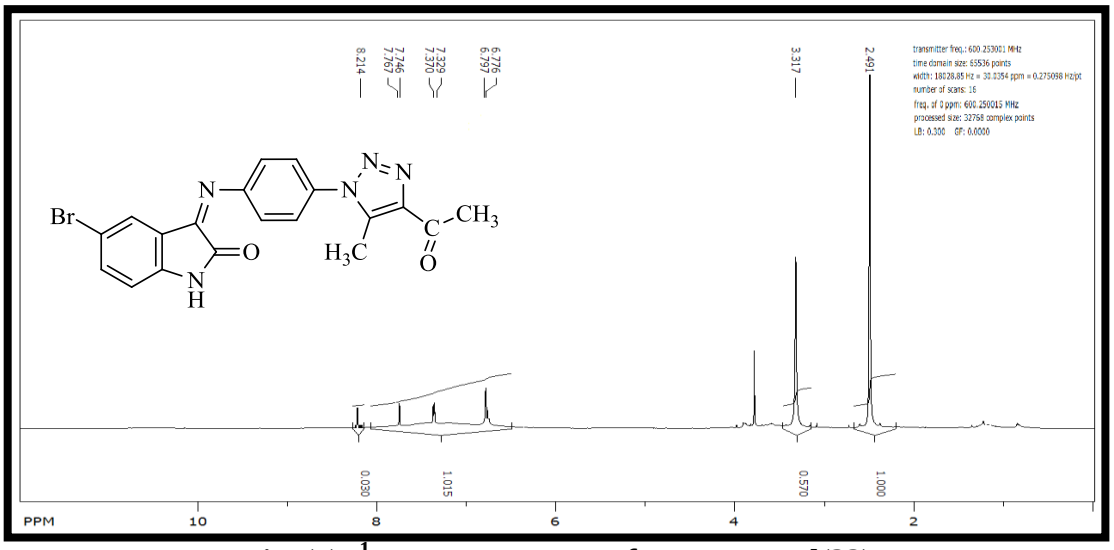



**Fig. (5): $^{1}$H-NMR spectrum for compound(22)**

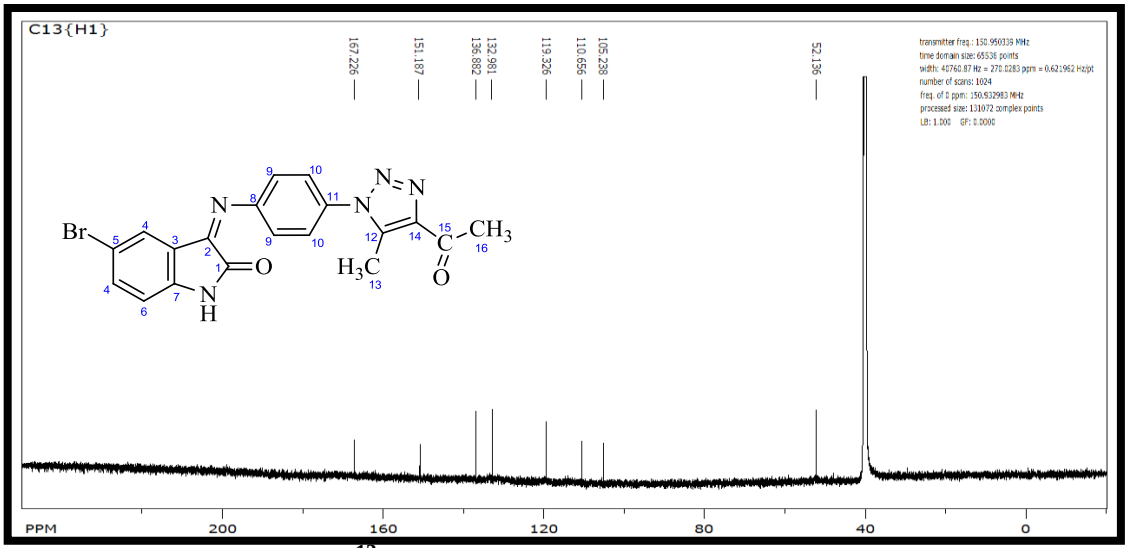



**Fig. (6): $^{13}$C-NMR spectrum for compound(22)**

## Anti-bacterial Activity Study:

The results of antibacterial activity are listed in Table(7). The results referred that all synthetic compounds possess moderate activity against certain types of bacteria. Compound (2,19) possesses moderate activity against *Staphylococcus aureus*. Compounds (8) possess a moderate activity against *Bacillies subtilus* while compounds (1,2,9,15,19,22,23) possess a moderate activity against for same bacteria. *Escherichia coli* showed weak activity by compounds(1,8,9,18) and showed moderate activity for compound(15). compound(1,2,23) possesses a good activity against *Pseudomonas aeruginosa* with a moderate activity for compound(8,9,11,19,22).

**Table (7): Anti-bacterial activity of the tested prepared compounds**

| Comp. No. | *Staphylococcus aureus* | *Bacillies subtilus* | *Escherichia coli* | *Pseudomones aerginosa* |
|---|---|---|---|---|
| **1** | 6 | 5 | 2 | 12 |
| **2** | 7 | 5 | - | 11 |
| **8** | 5 | 7 | 3 | 8 |
| **9** | 4 | 6 | 4 | 10 |
| **11** | 2 | - | - | 8 |
| **15** | 5 | 2 | 8 | - |
| **18** | - | - | 6 | - |
| **19** | 8 | 2 | - | 10 |
| **22** | 5 | 3 | - | 10 |
| **23** | 6 | 2 | - | 12 |

Solvent: DMSO **;** [C]: 800µg/ml.
Zone of inhibition: (-) no inhibition zone; (3-6) weak; (7-10) moderate; (11-15) strong.

## Conclusion:

The present research involves the synthesis of sulfonylamide, diazine, oxazole, thiazole and 1,2,3-triazole derivatives of 5-Bromoisatin to explore their antibacterial activity. Exhibited highest antibacterial activity for *staphylococcus aureus* compound(19), *Bacilliessubtilus* compound(8), *Escherichia coli* compound(15) and *Pseudomonas aeruginosa* compound (1,23). Hence, it is conculuded that there is in ample scope for further study in developing these as good lead compounds for the treatment of bacterial strain as well as fungal strain.

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# تحضير وتقدير الفعالية المضادة للبكتريا لبعض معوضات 5-بروموايساتين الجديدة الحاوية على حلقات خماسية، سداسية غير متجانسة

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**الخلاصة:**

تضمن هذا البحث تحضير بعض المشتقات الحلقية المختلفه الجديدة غير المتجانسة من 5-بروموايساتين.المشتقات الجديد من ديازين سلفونيل أمايد، اوكسازول، ثايازول،3,2,1-ترايازول من 5-بروموايساتين التي تم تحضيرها. عملية التحضير تبدأ بتفاعل 5-بروموايساتين مع كواشف مختلفة للحصول على المركبات الوسطيه قواعد شيف من 5-بروموايساتين (1، 8، 19) باستخدام حامض الخليك الثلجي كعامل مساعد في ثلاثة مسارات. المسار الأول، تفاعل 5-بروموايساتين مع بارا-امينوسلفونيل كلوراید لينتج المركب(1)، تم تحويله الى مشتقات السلفونيل امايد(2-7) من خلال تفاعل مركب(1) مع مختلف الامينات الاوليه الاروماتيه المعوضه في الايثانول المطلق. ويشمل المسار الثاني تفاعل 5-بروموايساتين مع اثيل كلايسينيت ليعطي 5-برومو-3- (اثيل إمينو استيت)-2-أوكسو اندول(8)، الذي يتفاعل مع هيدرازين المائي 80٪ للحصول على مشتقات الهيدرازين(9) التي تتفاعل مع انهدريدات اروماتيه وحلقيه مختلفه للحصول على مشتقات الديازين(10-14). كذلك يتفاعل المركب(8) مع اليوريا وثايويوريا ليعطي مركبين(15،16) التي حولقت مع بارا-بروموفيناسيل بروماید في الإيثانول المطلق كمذيب للحصول على الاوكسازول(17) والثيازول(18) على التوالي. بينما شمل المسار الثالث تفاعل 5-بروموايساتين مع بارا-فنيلين داي امين في الإيثانول للحصول على المركب(19) الذي تحول الى معوضات جديدة 3,2,1-ترايازول. مشتقات(22،23) من دايازيشن لمركب[19] ومعاملة الملح الناتج(20) مع صوديوم ازايد، ثم استيل اسيتون أو اثيل اسيتواستيت، على التوالي. تم اثبات تراكيب المركبات الجديدة المحضرة بواسطة الطرق الطيفية ($^1$H-NMR, $^{13}$C-NMR, FTIR) وقياس بعض خواصها الفيزياوية وبعض الكشوفات الخاصة. فضلا عن ذلك تمت دراسة تأثر المركبات المحضرة على بعض سلالات البكتيريا.

**الكلمات المفتاحية:** 5-بروموإيساتين، سلفونيل امايد، دايازين، اوكسازول، ثايازول، 3,2,1-ترايزول، مضاد للبكتريا.