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Synthesis of some new isatin derivatives of expected biological activities

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Abstract

Acetylation of isatin with acetic anhydride lead to the formation of N-acetyl isatin 1 which then reacted with semicarbazide in acetic acid to give semicarbazone derivative 2. Which then reacted with different monosaccharide such as glucose, galactose and mannose to give the corresponding azomethine sugar derivatives 3a-c. Reaction of semicarbazone derivatives with aromatic aldehydes such as benzaldehyde and p-chlorobenzaldehyde gave the corresponding Schiff bases 5a,b. Semicarbazone derivatives undergo condensation reaction with different carbonyl groups such as isatin and acetophenone it give the Schiff bases derivatives 6a,b. Also semicarabside derivative 2 reacted with different anhydride namely maleic anhydride, succinic anhydride, and phthalic anhydride in acetic acid to give the corresponding imide 7a-c. Reaction of schiff's bases derivatives 3a-c and 4 of different sugars with acetic anhydride lead to acetylation of the OH groups to give compounds 8a-c, all newly synthesized compounds were confirmed by elemental and spectral (IR, NMR, and mass) analyses. Some of the synthesized compounds were evaluated in vitro for their anti-bacterial and fungal Activity.
keywords : Isatien ,aldehydosugar , phathlic anhydride.
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1. Introduction

Isatin and most of its derivatives are important in medical chemistry [1-10]. Where they have been used as starting materials for the synthesis of variety of some drugs [11]. Isatin moiety showed some biological activities such as antioxidant, anti-inflammatory [12], antimicrobial [13,14,15,16], antitubercular [17 ,18] , anticancer [19], antiviral [20, 21] and anticonvulsant [22, 23] activities. Owin to the above facts and in continuation of our interest in attachment of carbohydrate residues compound searching for potent leads to antimicrobial agent and also valuable in design a facile synthesis of new isatin derivatives [24,25].

2. Experimental

All melting points are uncorrected and measured on a Fisher-John apparatus. Elemental analysis was determined on an Elementary Analysens system GmbH-VarioEL V.3 micro-analyzer in the central lab of Assiut University. Their results were found to be in good agreement (±0.2%) with the calculated values." IR spectra were recorded on a Pye-Unicam Sp-100 spectrophotometer using KBr wafer technique. ^{1}H NMR spectra were obtained on BRUKER 400 MHz spectrometers in a suitable deuterated solvent using tetramethylsilane as an internal standard (chemical shifts in ppm), otherwise stated. Mass spectra were obtained on JEOL JMS-600 apparatus. Preparative and analytical TLC were carried out on silica gel plates (Fluka 70643-50EA. SIGMA-ALDRICH, Germany) using UV light All reactions were carried out under an air atmosphere.

Synthesis of 2-(1-acetyl-2-oxoindolin-3-ylidene) hydrazine-1-carboxamide

A mixture of compound 1[(24)] (10m mol) and semicarbazide (10m mol) were refluxed in acetic acid for 3 h the mixture was allowed to cool.

The precipitate formed after cooling was filtered, washed, dried and recrystallized from ethanol as yellow crystals in yield (80%) m.p 226-228 ^{o}C. Analysis calculated for $C_{11}H_{10}N_4O_3$ (246); C, 53.66; H, 4.09; N, 22.75. Found; C, 53.68; H, 4.19; N, 22.85.

General procedure for the synthesis of compounds 3a-c

Hydrazide derivatives 2 (10 m mol) in absolute ethanol (10 ml) was added to a well-stirred solution of the respective monosaccharides (Glucose, Mannose, Galactose and Ascorbic acid) (10 mmol) in water (2 ml) and glacial acetic acid (1 ml). The mixture was heated under refluxed for 5 h and the resulting solution was concentration under reduced pressure and left to cool. The formed precipitate was filtered off, washed with water and cold ethanol, dried, and recrystallized from the corresponding sugar hydrazones in 80-85 % yields

Reaction of (2) with D (+) glucose: synthesis of 2-((Z)-1-acetyl-2-oxoindolin-3-ylidene)-N-((2S,3R,4R,5R)-2,3,4,5,6-pentahydroxy-3-

Resulted using glucose gave compound 3a as brown crystals; m.p 200-202 ^{o}C yield (82%). Analysis calculated for $C_{17}H_{20}N_4O_8$ (408); C, 50.11; H, 4.94; N, 13.72. Found: C, 50.21; H, 4.84; N, 13.61.

Reaction of (2) with D (+) galactose, synthesis of 2-((Z)-1-acetyl-2-oxoindolin-3-ylidene)-N-((2S,3R,4S,5R)-2,3,4,5,6-pentahydroxy-3-methylhexylidene) hydrazine-1-carboxamide 3b

Resulted using mannose and gave compound 3b as pale-yellow crystals; m.p.210-212^{o}C yield (82%). Analysis

calculated for $C_{18}H_{22}N_4O_8$ (408); C, 50.00; H, 4.94; N, 13.72. Found: C, 50.13; H, 4.89; N, 13.62.

Reaction of (2) with mannose, synthesis of 2-((Z)-1-acetyl-2-oxoindolin-3-ylidene)-N-((2R,3R,4R,5R)-2,3,4, 5,6-pentahydroxyhexylidene) hydrazine-1-carboxamide 3c.

Resulted using galactose and gave compound 3c as dark brown crystals; m.p. 208-210ºC yield (82%). Analysis calculated for $C_{17}H_{20}N_4O_8$ (408) ; C, 50.00; H, 4.94; N, 13.72. Found. C, 50.11; H, 4.84; N, 13.62.

Reaction of (2) with ascorbic acid, synthesis of 2-((Z)-1-acetyl-2-oxoindolin-3-ylidene)-N-((4R,5R)-2,3,4,5,6-pentahydroxy-2l5-hex-2-en-1-ylidene) hydrazine-1-carboxamide 4.

Resulted using ascorbic acid and Recrystallized from ethanol to give compound (4) as brown crystals; m.p.210-212ºC yield (82%). Analysis calculated for $C_{17}H_{16}N_4O_8$ (404); C, 50.56; H, 3.96; N, 11.11. Found. C, 60.32; H, 3.19; N, 13.86.

Reaction of compound 2 with different benzaldehyde

The Schiff base derivative was synthesized by refluxing an ethanolic solution of compound 2 (10m mol) with different benzaldehyde (2.78 mmol) in 1:1 molar ratio for 5 h in the presence of catalytic amount of piperidine. (1ml) the precipitate obtained after concentration of the reaction mixture was filtered, dried and was recrystallized from ethanol. The product obtained recrystallized from ethanol

Synthesis of 2-((Z)-1-acetyl-2-oxoindolin-3-ylidene)-N-benzylidenehydrazine-1-carboxamide 5a

The product obtained a pale-yellow crystal in 85% yield, m.p.110-112ºC. Analysis calculated for $C_{18}H_{14}N_4O_3$ (334); C, 64.67; H, 4.22; N, 16.76. Found. C, 64.79; H, 4.21; N, 16.66.

Synthesis of 2-((Z)-1-acetyl-2-oxoindolin-3-yliden)-N-(chlorobenzylidene)hydrazine-1-carboxamide 5b

The product obtained was a yellow crystal in 89% yield, m.p.151-153ºC. Analysis calculated for $C_{18}H_{13}ClN_4O_3$ C, 58.63; H, 3.55; N, 15.19. Found. C, 58.63; H, 3.58;N, 15.20.

Reaction of (2) with acetophenone, synthesis of 2-((Z)-1-acetyl-2-oxoindolin-3-ylidene)-N-(1-phenylethylidene) hydrazine-1-carboxamide 6a

Compound (2) (10mmol) and acetophenone (1ml) in ethanol was refluxed for 3 h in the presence of catalytic amount of piperidine (1ml) the precipitate formed after cooling was filtered, washed and recrystallized from ethanol to give compound 6a as brown crystals in yield 90% m.p.175-177ºC. Analysis calculated for $C_{19}H_{16}N_4O_3$ C, 65.51; H, 4.63; N, 16.08. Found. C, 65.55; H, 4.53; N, 16.18.

Reaction of compound 2 with isatine, synthesis of 2-((Z)-1-acetyl-2-oxoindolin-3-ylidene)-N-(2-oxoindolin-3-ylidene) hydrazine-1-carboxamide 6b

Compound 2 (10mmol,1 gm) and isatin (10mmol) in ethanol was refluxed for 3 h in the presence of catalytic amount of piperidine (1ml) the precipitate formed after cooling was filtered, washed and recrystallized from ethanol to give compound 6b as brown crystals in yield 90% m.p.220-222ºC. Analysis calculated for $C_{19}H_{13}N_5O_4$ C, 58.63; H, 3.55; N, 15.19. Found. C, 58.68; H, 3.58; N, 15.20.

Reaction of compounds 2 with anhydride

General procedure: Anhydrides (namely maleic anhydride, succinic anhydride, and phthalic anhydride). (2 mmol) in (15 ml) acetic acid was refluxed with compound 2 for 20 hr . The formed precipitate was filtered and crystallized from ethanol to give 7a - c.

Reaction of compound 2 with maleic

Formation of (Z)-*N*-(1-acetyl-2-oxoindolin-3-ylidene)-2,5-dioxo-2,5 dihydro- 1H-pyrrole-1-carbohydrazide 7a

White crystal, m.p = 210 – 212 Cº, yield (80%) , Analysis calculated for $C_{15}H_{10}N_4O_5$ (326) ; C: 55.31 ; H :3.07 , N:17.18 . Found C: 55.33, H: 3.10, N:17.15

Reaction of compound 2 with succinic anhydride: Formation of (Z)-N-(1-acetyl-2-oxoindolin-3-ylidene)-2,5-dioxopyrrolidine-1-carbohydrazide

White crystal, m.p 262 – 264 Cº, yield (65%), Analysis calculated for $C_{15}H_{112}N_4O_5$ (328); C: 54.88, H: 3.66, N: 17.07, Found C: 54.82, H: 3.64, N: 17.10.

Reaction of compound 2 with phthalic anhydride: Formation of (Z)-N'-(1-acetyl-2-oxoindolin-3-ylidene)-1,3-dioxoisoindoline-2-carbohydrazide

White crystal, m.p 255-257Cº (70%) analysis for $C_{19}H_{12}N_4O_5$ (376), calculated C: 60.64, H: 3.19, N: 14.89. Found, C: 6.66, H: 3.17, N: 14.80.

General procedure for the synthesis of acetyl derivative compounds (O- acetyle sugar derivatives 8a-c.

Acetic anhydride 3ml (10m.mol) was added to a solution of sugar imide (1 mmol) in pyridine (1ml) with stirring at room temperature for 45 h. The resulting solution was poured onto crushed-ice and the product that separated out was filtered off, washed with a saturated solution of sodium hydrogen carbonate followed by water, and then dried. The products were recrystallized from ethanol in 80-90 % yield

Reaction of with sugar imide (glucose) with acetic anhydride formation of (2R,3R,4R,5S)-6-((2-((Z)-1-acetyl-2-oxoindolin-3-ylidene) hydrazine-1-carbonyl)imino) hexane-1,2,3,4,5-pentayl pentaacetate 8a.

A solution of sugar imide 3a with acetic anhydride in pyridine

Compound 8a as brown crystals in yield 85% m.p.230-232ºC. Analysis calculated for $C_{27}H_{30}N_4O_{13}$ C, 52.43; H, 4.89; N, 9.06. Found. C, 52.40; H, 4.79; N, 9.16.

Reaction of with sugar imide (galactose) with acetic anhydride formation of (2R,3S,4R,5S)-6-((2-((Z)-1-acetyl-2-oxoindolin-3-ylidene) hydrazine-1-carbonyl) imino) hexane-1,2,3,4,5-pentayl pentaacetate 8b.

A solution of sugar hydrazone 3b with acetic anhydride in pyridine

Compound 8b pall yellow crystals in yield 90% m.p.211-213ºC. Analysis calculated for $C_{27}H_{30}N_4O_{13}$ C, 52.43; H, 4.89; N, 9.06. Found. C, 52.39; H, 4.82; N, 9.07.

Reaction of with sugar imide (mannose) with acetic anhydride formation of (2R,3R,4R,5R)-6-((2-((Z)-1-acetyl-2-oxoindolin-3-ylidene) hydrazine-1-carbonyl) imino) hexane-1,2,3,4,5-pentayl pentaacetate 8c

A solution of sugar hydrazone 3c with acetic anhydride in pyridine

Compound 8b as brown crystals in yield 90% m.p.199-201ºC. Analysis calculated for $C_{27}H_{30}N_4O_{13}$ C, 52.43; H, 4.89; N, 9.06. Found. C, 51.41; H, 4.85; N, 9.11.

Reaction of with sugar imide (mannose) with acetic anhydride formation of (2R,3R)-6-((2-((Z)-1-acetyl-2-oxoindolin-3-ylidene) hydrazine-1-carbonyl) imino)-5l5-hex-4-ene-1,2,3,4,5-pentayl pentaacetate 9.

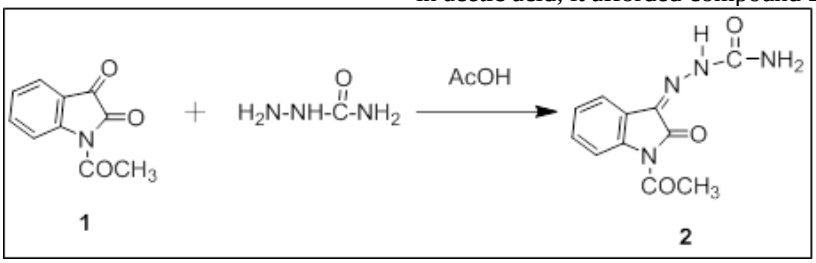
Compound 9 as brown crystals; m.p.250-253ºC yield (82%).

Analysis calculated for $C_{27}H_{29}N_4O_{13}$ C, 52.51; H, 4.73; N, 9.07. Found. C, 52.48; H, 4.52; N, 9.05.

3. Result and discussion

3.1-Synthesis of 2-(1-acetyl – 2 - oxoindolin – 3 – ylidene) hydrazine – 1 – carboximide (2)

When N- acetyl isatin 1 was refluxed with semicarbazide in acetic acid, it afforded compound 2.

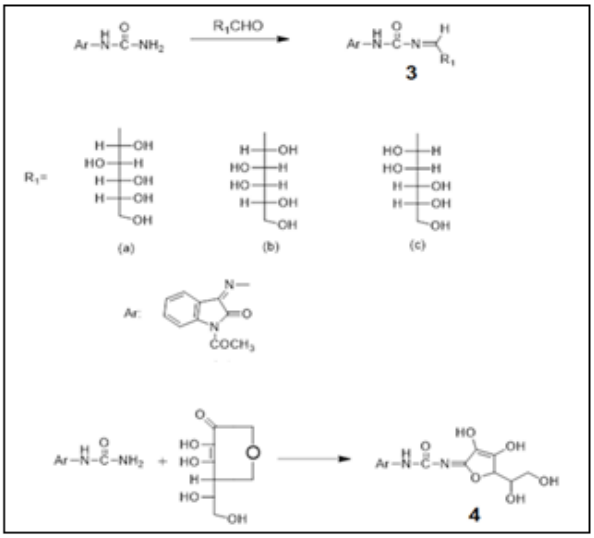


The structure of compound 2 was confirmed from Correct elemental analysis, IR spectrum displayed broad band at 3400 – 2500 cm $^{-1}$ for NH, strong band at 1725 cm $^{-1}$ and 1680 cm $^{-1}$ for CO and 1610 cm $^{-1}$ due to C = N, and mass spectrum showed molecular ion peak at m/z = 246 (30%) and base peak at m/z = 78

3.2- Reaction of compound 2 with monosaccharides

Isatin and most of its derivatives are important in medical chemistry [1-10] Also due to the fact that Schiff based considered a versatile regent for the preparation of heterocyclic compounds. in addition, Schiff based have wide spectrum of antibacterial activity. Also, many of some derivatives of Schiff bases have the ability to injure or kill an invading microorganism without the host because of their selective toxicity [26, 27].

Thus, refluxing a mixture of compound 2 with different monosaccharide (aldehydosugar) namely; glucose, galactose, mannose, and ascorbic acid in absolute ethanol containing catalytic amount of glacial acetic acid furnished the corresponding glycoside derivatives 3a - c and 4 respectively.



The structure of glycoside was confirmed from their correct elemental analysis data, IR, HNMR mass spectrum. the IR spectra of 3a showed bands at 3420 cm $^{-1}$ (broad) for OH , 3106 cm $^{-1}$ for NH , 3060 cm $^{-1}$ for aromatic CH , 2941 cm $^{-1}$ for aliphatic CH , 1739 cm $^{-1}$, 1686 cm $^{-1}$, 1666 cm $^{-1}$, for (CO) groups and 1624 cm $^{-1}$ for C=N Mass spectrum of 2a showed molecular ion peak at m/z = 408 (100%)

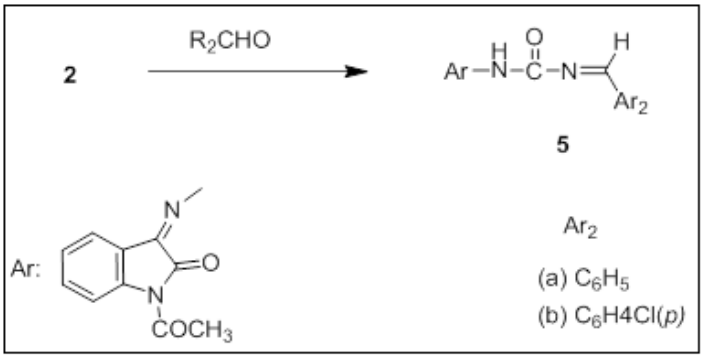
While the IR of 3b showed bands at 3410 cm $^{-1}$ (broad) for OH, NH groups,

3167 cm $^{-1}$ for aromatic CH, 2942 cm $^{-1}$ for aliphatic CH, 1686 cm $^{-1}$, 1663 cm $^{-1}$

1653 cm $^{-1}$ for CO groups and 1619 cm $^{-1}$ for C=N , Also IR spectrum of compound 3C displayed bands at 3440 cm $^{-1}$ (broad) for OH and NH groups , 3059 cm $^{-1}$ for aromatic CH , 2983 cm $^{-1}$ for aliphatic CH , 1710 cm $^{-1}$, 1666 cm $^{-1}$, 1606 cm $^{-1}$ for CO groups and 1573 cm $^{-1}$ for C=N ,The structure of compound 4 was established from ; its correct elemental analysis , it IR spectrum displayed bands at 3398 cm -^{1} for OH , 3317 cm $^{-1}$ for NH , 3057 cm $^{-1}$ for aliphatic CH , 1670 cm $^{-1}$, 1622 cm $^{-1}$ for CO groups , 1580 cm $^{-1}$ For C=N , and 1496 cm $^{-1}$ for (C=C) Mass spectra of compound 4 showed molecular ion peak at m/z = 404 (17 %).

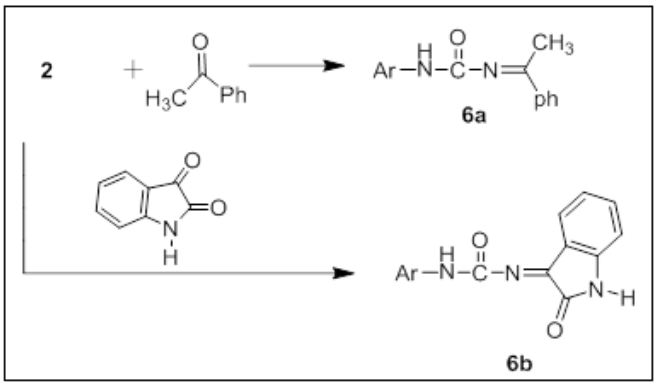
3.3- Reaction of compound 2 with aldehyde

On the other hand, when compound 2 refluxed with aromatic aldehyde namely benzaldehyde and or p-chlorobenzaldehyde in ethanol and few drops of piperidine to, furnished Schiff base derivative 5a and 5b respectively.



The structure of compounds 5a and 5b were confirmed from their correct elemental analysis, IR, HNMR and mass spectrum.

IR of compound 5a showed bands at 3380 cm $^{-1}$ (broad) for NH , 3030 cm $^{-1}$ for aromatic CH , 2994 cm $^{-1}$ for aliphatic CH , 1746 cm $^{-1}$, 1630 cm $^{-1}$, 1610 cm $^{-1}$ for CO groups and 1598 cm $^{-1}$1550cm $^{-1}$ for C=N. HNMR spectrum (DMSO – d_6 , 400MHz) of compound 5a , revealed signals at δ(ppm) 2.99 (s , 3H , CH3) , 6.5 – 7.8 (m , 9H , aromatic protons) 8.8 (s , 1H , NH , exchangeable) and 9.7 (s , 1H , NH , exchangeable) , Mass spectrum of compound 5a showed molecular ion peak at m/z = 334 (100% , base peak).



3.4- Reaction of compound 2 with ketones:

The present investigation deals with the reaction of compound 2 with ketones namely acetophenone, isatine to synthesize the corresponding imide derivatives 6a and 6b.

Thus, when compound 2 was refluxed with acetophenone and or isatine in ethanol in the presence of catalytic amount of piperdine it afforded the corresponding imide 6a and 6b respectively.

The structure of compounds 6a and 6b were confirmed from their correct elemental analysis, IR and HNMR spectrum. IR of 6a showed bands at 3464 cm $^{-1}$ for NH , 3055cm $^{-1}$ for aromatic CH , 2985 cm $^{-1}$ for aliphatic CH , 1739 cm $^{-1}$, 1663 cm $^{-1}$, 1614 cm $^{-1}$ for CO groups and 1571 cm $^{-1}$ 1560 $^{cm-1}$ for C=N .^{1}HNMR spectrum (DMSO - d_6 ,400 MHz) of 6a revealed signals at δ (ppm) 2.81 (s , 3H , $COCH_3$) , 2.80 (s , 3H , CH_3) , 7-7.7 (m , 8H , aromatic protons) and 10 (s , 1H , NH , exchangeable),While the IR of 6b showed bands at 3442 cm $^{-1}$ for NH , 3050 cm $^{-1}$ for aromatic CH , 2950 cm $^{-1}$ for aliphatic CH , 1774 cm $^{-1}$, 1691 cm $^{-1}$, 1691 cm $^{-1}$, 1609 cm $^{-1}$ for CO groups and 1597 cm $^{-1}$ for C=N, HNMR spectrum (DMSO -d_6 ,400 MHz) of 6b showed signals at δ(ppm) 2.97 (s , 3H , CH3) , 7.2 – 7.6 (m , 8H , aromatic protons) , 9.6 (s , 1H , NH , exchangeable) , 9.9 (s , 1H , NH , exchangeable)

3.5- Reaction of compound 2 with anhydride.

In the present investigation, the reaction of compound 2 with different anhydride namely maleic anhydride, succinic anhydride and phthalic anhydride was studied. Thus, compound 2 reacted with maleic anhydride, succinic anhydride and phthalic anhydride in acetic acid gave the corresponding imide derivatives 7a – c respectively.

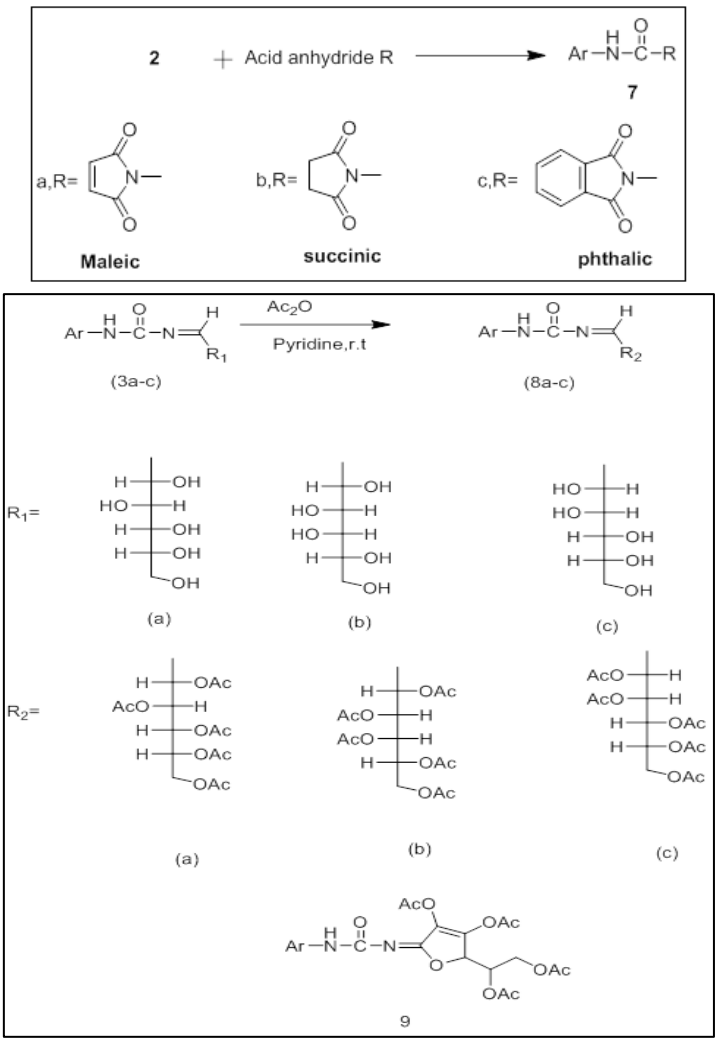
The structure of 7a- c were confirmed from their correct element analysis , IR and mass spectrum .IR of compound 7a showed bands at 3220 cm $^{-1}$ for NH , 3050 cm $^{-1}$ for aromatic CH , 2950 cm $^{-1}$ for aliphatic CH , 1720 cm $^{-1}$, 1710 cm $^{-1}$, 1680 cm $^{-1}$ 1630 cm $^{-1}$, for CO groups and 1590 cm $^{-1}$ for C=N, 1550 cm $^{-1}$ for C=C , Mass spectrum for compound 7a showed molecular ion peak at m/z = 326 (18%)

IR of compound 7b showed band at 3250 cm $^{-1}$ for NH , 3030 cm $^{-1}$ for aromatic CH , 2990 cm $^{-1}$, for aliphatic CH , 1730 cm $^{-1}$, 1680 cm $^{-1}$, 1650 cm $^{-1}$, 1610 cm $^{-1}$ for CO groups and 1590 cm $^{-1}$ for C=N, Mass spectrum for compound 7b showed molecular ion peak at m/z = 328 (30%).

Also the IR of 7c showed ands at 3300 cm $^{-1}$ for NH, 2995 cm $^{-1}$ for aliphatic CH, 1730 cm $^{-1}$, 1710 cm $^{-1}$, 1665 cm $^{-1}$, 1600 cm $^{-1}$ for CO groups and 1580 cm $^{-1}$ for compound 7c showed molecular ion peak at m/z =376 (15%).

3.6- Reaction of compounds 3a – c and 4 with acetic anhydride: formation of O–acetyl sugar derivative 8a- c

Treatment of compounds 3a - c and / or 4 with acetic anhydride in (1m) pyridine with steering at room temperature afforded the acetyl derivatives in good yields 8a - c and or 9.



The structure of 8a-c was confirmed from their correct chemical analysis and spectral data. IR of the acetyl glycoside derivative 8a showed no OH but it showed bands at 3106 cm^{-1} (sharp) for NH, 3030 cm^{-1} for aromatic CH, 1739 cm^{-1} ,1686 cm^{-1}, 1624 cm^{-1}, 1598 cm^{-1}, 1574 cm^{-1} for CO groups and 1507 cm^{-1} for C=N. Also. IR of the acetyl lacto side derivative 8b not showed any frequency (band) of OH but it showed band at 3320 cm^{-1} (broad) for NH and aromatic CH , 2942 cm^{-1} , 2843 cm^{-1} for aliphatic CH , 1686 cm^{-1} , 1663 cm^{-1} , 1653 cm^{-1} , 1619 cm^{-1} , 1597 cm^{-1} for CO groups and 1574 cm^{-1} for C=N. IR of acetyl mannose derivative 8c showed no bands for OH , but it showed bands at 3300 cm^{-1} (broad) for NH , 3059 cm^{-1} for aromatic CH , 2983 cm^{-1} , 2938 cm^{-1} , for CH aliphatic , 1750 cm^{-1} , 1666 cm^{-1} , 1606 cm^{-1} , 1573 cm^{-1} for CO groups and 1517 cm^{-1} for C=N. I.R of acetyl derivative of compound **9**(ascorbic acid) showed no bands for OH but it showed bands at 3317 cm^{-1} for NH , 3057 cm^{-1} for aromatic CH , 2920 cm^{-1} for aliphatic CH , 1666 cm^{-1} , 1622 cm^{-1} , 1580 cm^{-1} , 1596 cm^{-1} for CO groups and 1596 cm^{-1} for C=N.

Biological study

Anti-Bacterial and Fungal Activity

Some of the new synthesized compounds listed in table (1), were screened in vitro for their antimicrobial activity against model Gram positive (*Staphylococcus aureus, Streptococcus pneumonia, B.Cereus and Bacillus subtilis*) and Gram negative bacteria (*Escherichia coli, Pseudomonas sp, Haemophilus influenza, Aspergillus niger and Klebsiella pneumoniae*), including multidrug-resistant species, yeasts and mould. The MICs are compared with the results obtained for standard antibacterial ciprofloxacin, levofloxacin, moxifloxacin, Clindamycin, Streptomycin, Gentamycin, Clindamycin and Gemifloxacin, And their antifungal activity against six fungal strains (*Candida albicans, Trichophyton rubrum, Aspergillus flavus, Fusarium oxysporum, Scopulariopsis brevicaulis, Geotrichum candidum*). The antimicrobial activities of the tested compounds were evaluated by the reported method [28] using 0.005% (50 µg/mL) concentration of selected compounds in DMSO as a solvent. The inhibition zone (mm) was compared with clotrimazole as standard for antifungal. In the case of antibacterial activity, the inhibition zone (mm) was compared with a series of antibiotics according to the sensitivity of each type of bacteria to the most effective antibiotic for it as a standard. The biological activity as expressed by the growth inhibition zone of the tested microorganism listed in Tables (1, 2). Table (1) shows that All the investigated compounds presented remarkable antibacterial properties against Gram positive bacteria and compound 9 is the highest antibacterial activity against all.

Table (1): Antibacterial activity of the tested compounds (mm)

Bacteria / Compound	Staphylococcus aureus	Streptococcus pneumoniae	B.Cereus (BC)	Bacillus subtilis	Haemophilus influenza	Escherichia Coli	Aspergillus niger	Pseudomonas sp
1	28	12	27	15	13	11	12	28
2	18	19	20	18	19	15	26	27
3a	24	19	24	23	16	24	22	15
4	17	13	13	22	19	25	27	29
5a	9	10	18	15	21	25	26	24
6b	11	15	11	14	18	22	27	17
7a	24	17	24	13	14	25	22	15
7b	26	20	25	24	26	12	26	17
7c	27	25	27	24	19	20	27	28
9	22	18	22	26	16	26	27	22
Ref.	25	20	28	25	20	26	28	30
	Ciprofloxecin	Levofoxacin	moxifloxacin	gemifloxacin	Clindamycin	Strptomycin	Gentamycin	Clindamycin

Notes:the amount added in each pore, 50µL. (+) indicates gram positive, (-) indicates gram-negative bacteria, (inhibition zone, mm)

Table (2): Antifungal activity (inhibition zone, mm)

Fungi / Compound	Penicillium sp	Candida albicans	Geotrichum candidum	Aspergillus fumigatus	Syncephalastrum racemosum	Geotrichum candidum
1	15	19	17	16	16	16
2	11	16	16	14	17	19
3a	17	18	16	15	13	17
4	18	10	14	18	16	17
5a	17	20	17	21	17	22
6b	16	11	14	14	19	15
7a	12	17	14	22	12	14
7b	14	18	19	17	13	15
7c	19	14	14	16	17	17
9	15	19	18	14	19	12
Ref. Ketoconazole	18	21	18	22	19	23

Notes: The amount added in each pore, 50µL

4. Conclusion

In the present work we use 2-(1-acetyl–2-oxoindolin–3–ylidene) hydrazine – 1 – carboximide (2)) to synthesis new compounds such as azomethine sugar derivatives 3a-c, Schiff bases derivatives 5a-b and 6a-b by reaction with different carbonyl compounds with compound 2. All new synthesized compounds were found to exhibited anti-bacterial and fungal activities.

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