Organic Chemistry
Current Research
ISSN: 2161-0401

Ghoneim and Assy, Organic Chem Curr Res 2015, 4:3
DOI: 10.4172/2161-0401.1000148

Research Article Open Access

Synthesis and Characterization of Antimicrobial Activity of Azoles and Azines Derivatives from Tertiary Butyl Carbazatel

Ghoneim AA* and Assy MG

Chemistry Department, Faculty of Science, Zagazig University, Zagazig, Egypt

Abstract

Backgound: We synthesized a new series of heterocyclic compounds tertiary butoxy carbazone derivatives 2a-b. The synthesized compounds 1,3,4-oxadiazole derivatives 3a, 4a, 1,3-thiazolidine (5a-b), azitidin-2-one derivative (6a), pyrrolidin-2-one (7a), were achieved by the cyclization of tertiary butoxy hydrazone derivatives 2a,b with bromine in acetic acid, acetic anhydride, thioglycollic acid, chloro acetyl chloride acid and malononitrile. Also teriary butyl carbazate was reacted with isatin to afford indolylidene acetohydrazide derivative 11 which was reacted with ammonium acetate and hydrazine hydrate to 12 and 15 to give compound respectively.

Keywords: Hydrazones; Tertiary butyl carbazate; Oxadiazoline; Thiazolidinone; Indole-2,3-dione

Introduction

Compounds with the structure of R1R2C=NNH_2 [1] are known as hydrazones, which are usually synthesized from the reaction of ketones or aldehydes with hydrazide by the replacement of the oxygen with the NNH_2 functional group [2,3]. Hydrazones and their derivatives are now well known for their importance in biological fields such as anticancer [4,5], antimicrobial [6,7], Anti-inflammatory [8,9], antituberculous, anticonvulsant [10]. Acyl hydrazones considered as important tool in organic chemistry. Acyl hydrazones are a very old class of molecules: the first example of N-acylhydrazines was mentioned in 18501, and a number of *N*-unsubstituted, mono-and di substituted acylhydrazines are now commercially available. Acyl hydrazones are a versatile class of nitrogen-substituted molecules with a high degree of chemical reactivity, used as precursors and intermediates of many important organic molecules such as heterocycles, pharmaceuticals, polymers, dyestuffs and photographic products [11]. The cyclic products of acylhydrazones are an important class of heterocyclic compounds with a wide range of biological activities [12-15] such as analgesic, anti–inflammatory, anti-microbial, anticonvulsant, anti-platelet, anti-tubercular, antiviral and anti-tumor activities [16,17].

Experimental

Melting points were determined on Electro thermal IA 9,100 series digital melting point apparatus in capillaries and are uncorrected. IR spectra were obtained in the solid state as potassium bromide discs using a Perkin-Elmer model 1430 spectrometer. ^{1}H NMR spectra were recorded on a Varian/Gemini 400 MHz spectrometer in DMSO-d_6 as a solvent and TMS as an internal standard (chemical shifts in δ, ppm). Mass spectra were measured on an instrument VG-7035 at 70 or 15 eV. Elemental analyses were performed at the Micro analytical Centre, Cairo University, and Giza, Egypt.

Tertiary butyl 2- benzylidenehydrazine carboxylate (2a)

To a solution of tert butyl carbazate (3 g, 0.01 mol) in ethanol (15 ml), benzaldehyde (1.36 g, 0.01 mol) was added. The reaction mixture was stirring at room temperature for 15 min to get the solid 1a. Then the solid was filtered and dried. The residue was recrystallized from methanol. Yield: 90%, mp 196–198°C. IR (KBr, cm^{-1}): 3251, 3025, 2962, 1374, 1712, 1608, 1132, ^{1H}-NMR (DMSO-*d*6 /ppm): 1.46 (s, 9H, CMe3), 5.39 (s, 1H, CH), 7.24 (d, 2H, C_6H_5), 7.36-7.61 (t, 3H, C_6H_5), 10.89 (s, 1H, NH). Anal. Calcd for $C_{12}H_{16}N_2O_2$ (220.27): C, 65.43; H, 7.32; N, 12.72. Found: C, 65.22; H, 7.73; N, 12.63.

Tertiary butyl 2- (4- nitrobenzylidene)hydrazinecarboxylate (2b)

To a solution of tertiary butyl carbazate (1 g, 0.01 mol) in ethanol (15 ml), 4-nitrobenzaldehyde (1.36 g, 0.01 mol) was added. The reaction mixture was kept for reflux on water bath for 2 h. Then it was poured in to ice-cold water to get the product $\mathbf{1}_b$ and the solid was filtered and dried. The residue was recrystallized from ethanol. Yield: 64%, mp 211–213°C. IR (KBr, cm^{-1}): 3151, 3125, 2962, 1474, 1353, 1558, 1132, ^{1}H-NMR (DMSO-*d*6 /ppm): 1.42 (s, 9H, CMe3), 5.67 (s, 1H, CH), 6.64-6.6.68 (d, *J*=9, 2H, C_6H_5), 7.36-7.61 (d, *J*=7.6, 2H, C_6H_5), 11.89 (s, 1H, NH). Anal. Calcd for $C_{12}H_{15}N_3O_4$ (265.27): C, 54.33; H, 5.70; N, 15.84. Found: C, 54.22; H, 5.53; N, 15.73.

Tert-butoxy-5-phenyl-1,3,4-oxadiazole (3a)

A mixture of 2a (3.93 g, 0.01 mol) and anhydrous sodium acetate (0.15 g) was mixed and dissolved in glacial acetic acid (5 ml). Bromine (1 g) in glacial acetic acid (0.25 ml) was added to the above mixture with stirring for 30 min. The color of bromine disappears. Then the mixture poured into ice-cold water (100 ml). The solid 3a was collected and recrystallized from ethanol. Yield: 64%, mp 185–187°C. IR (KBr, cm^{-1}): 3151, 3125, 2962, 1474, 1353, 1558, 1132, ^{1}H-NMR (DMSO-*d*6 /ppm): 1.42 (s, 9H, CMe3), 7.36-7.61 (m, 5H, C_6H_5). Anal. Calcd for $C_{12}H_{14}N_2O_2$ (218.25): C, 66.04; H, 6.47; N, 12.84. Found: C, 66.22; H, 6.73; N, 12.73.

(2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (4a)

A mixture of hydrazone 2a (1 mmol) and acetic anhydride (5 ml) and drop wise of pyridine was refluxed for 2 hr. the mixture was left

***Corresponding author:** Amira Atef Ghoneim, Chemistry Department, Faculty of Science, Zagazig University, Zagazig, EG-44519, Egypt, Tel: +2015420190; E-mail: Mohamed_goma59@yahoo.com

Received: July 29, 2015; **Accepted:** August 27, 2015; **Published**: September 03, 2015

Citation: Ghoneim AA, Assy MG (2015) Synthesis and Characterization of Antimicrobial Activity of Azoles and Azines Derivatives from Tertiary Butyl Carbazate. Organic Chem Curr Res 4:148. doi:10.4172/2161-0401.1000148

to cool. After cooling, the reaction mixture was poured into ice water and added drops of con hydrochloric acid with stirring until the solid coagulations, which were them filtered off and recrystallized from ethanol. Yield: 58%, mp 99–101°C IR (KBr, cm^{-1}): 3251, 2962, 1715, 1680, and 1353. ^{1}H NMR (DMSO-*d6*, *δ*, ppm): 2.62 (s, 3H, -$COCH_3$), 7.50-7.52 (m, 5H, phenyl), 8.72 (s, 1H, CH=N), 6.50-6.52 (d, J=8.3 1H, CH), $C_{10}H_{10}N_2O_2$ (190.2): C, 63.15; H, 5.30; N, 14.73; O, 16.82. Found: C, 63.37; H, 5.39; N, 14.92.

General preparation of 3-tetriary butyl acetohydrazide-2-substitutedphenyl-1,3-thiazolidine (5a-b)

A solution of hydrazone **2a-b** (0.01 mol) in in N,N-dimethylformamide(30 ml) and thioglycolic acid (0.15 mol) in presence of anhydrous zinc chloride were refluxed for 6 hr. The solvent was evaporated under reduced pressure. The solid was washed with water. The solid was recrystallized from ethanol.

Tertiary butyl (2-phenyl-4-oxothiazolidin-3-yl)carbamate (5a)

Yield: 51%, mp 128–130°C. IR (KBr, cm-^{1}): 3151, 3125, 2962, 1674, 1613, 1558, 1263, and 1211. ^{1}H-NMR (DMSO-*d6* /ppm): 1.42 (s, 9H, CMe3), 5.87 (s, 1H, CH), 7.24 (d, 2H, C_6H_5), 7.36-7.61 (t, 3H, C_6H_5), 3.32-3.26 (d, J=2H, CH_2), 8.35 (s, 1H, NH). Anal. Calcd for $C_{14}H_{18}N_2O_3S$ (294.37): C, 57.12; H, 6.16; N, 9.52; S, 10.89. Found: C, 57.24; H, 6.01; N, 9.93; S, 10.56.

Tertiary butyl (2-(4-phenyl-4-oxothiazolidin-3-yl)carbamate *(5b)*

Yield: 56%, mp 178-180°C. IR (KBr, cm-1): 3152, 3125, 2962, 1684, 1513, 1558, 1421, and 1201. ^{1}H-NMR (DMSO-*d6* /ppm): 1.47 (s, 9H, CMe3), 5.92 (s, 1H, CH), 7.84-7.86 (dd, *J=7.14,* 2H, C_6H_4), 8.23-8.26 (dd, *J=8.24,* 2H, C_6H_4), 3.62-3.42 (d, *J=2.4*, 2H, CH_2), 9.42 (s, 1H, NH). Anal. Calcd for $C_{14}H_{17}N_3O_5S$ (339.37): C, 49.55; H, 5.05; N, 12.38; S, 9.49. Found: C, 49.24; H, 5.11; N, 12.63; S, 9.56.

Tertiary butyl (3-Chloro-2-oxo-4-phenylazitidin-1-yl) carbamate (6a)

A solution of hydrazone2a (0.01 mol) and few drops of triethylamine in dioxane (20 ml) and chloro acetyl chloride (0.01 mol) was added drop wise with stirring at room temperature for 2 hr. Then the mixture was refluxed for 4 hr. the solid was collected after cooling and filtrated. The solid was recrystallization by ethanol. Yield: 75%, mp 118-120°C. IR (KBr, cm^{-1}): 3142, 3132, 2972, 1689, and 1513. Anal. Calcd for $C_{14}H_{17}ClN_2O_3$ (296.75): C, 56.66; H, 5.77; N, 9.44; Cl, 11.95. Found: C, 56.34; H, 5.42; N, 9.26; Cl, 11.52.

Tertiary butyl 5-amino-4-cyano-3-phenyl-1H-pyrazole-1-carboxylate (7a)

A solution of hydrazone 2a (0.01 mol) and few drops of piperdine in absolute ethanol (20 ml) and malonoitrile (0.01 mol) was refluxed for 7 hr. then the mixture was cooling and the solid was collected after cooling and filtrated. The solid was recrystallization by ethanol. Yield: 50%, mp 224-226°C. IR (KBr, cm^{-1}): 3242, 3032, 2952, 2235 and 1679. ^{1}H-NMR (DMSO-*d6* /ppm): 1.42 (s, 9H, CMe3), 6.23 (s, 2H, NH_2), 7.42-7.32 (m, 5H, C_6H_5). Anal. Calcd for $C_{15}H_{16}N_4O_2$ (284.31): C, 63.37; H, 5.67; N, 19.71. Found: C, 63.24; H, 5.63; N, 19.68.

Tertiary butyl 2-(4-ethoxy-4-oxobutan-2-ylidene)hydrazinecarboxylate (8)

A mixture of tertiary butyl carbazate (1g, 7.7 mmoles) and ethyl acetoacetate was added dissolved in acetic acid (25 ml) and water (5 ml). The solution was stirred for 1 hr. The product was collected as a yellow precipitate and washed with a little water followed by pet-ether. Yield: 85%, mp 110-112°C. IR (KBr, cm^{-1}): 3326, 3127, 2972, 1722, and 1669. ^{1}H-NMR (DMSO-*d6*/ppm): 1.43 (s, 9H, CMe3), 2.54 (s, 2H, CH_2), 2.14 (s, 3H, CH_3), 12.42 (s, 1H, OH). Anal. Calcd for $C_{11}H_{20}ClN_2O_4$ (244.29): C, 54.08; H, 8.25; N, 11.47. Found: C, 54.24; H, 8.15; N, 11.13.

Tertiary butyl 3-methyl-5-oxo-4,5-dihydro-1H-pyrazole-1-carboxylate (9)

A solution of hydrazone 8 (0.01 mol) was refluxed in o-dichlorobenzene (15 ml) for 7 hr. The residue was filtered and recrystallization from ethanol to give compound pyrazolone derivative **9.** Yield: 60%, mp 207-209°C. IR (KBr, cm-1): 3036, 2942, 1683, 1583, 1558, 1421, and 1230. ^{1}H-NMR (DMSO-*d6* /ppm): 1.47 (s, 9H, CMe3), 4.31 (s, 2H, CH_2), 2.30 (s, 3H, CH_3), 12.42 (s, 1H, OH). Anal. Calcd for $C_9H_{14}N_2O_3$ (198.22): C, 54.53; H, 7.12; N, 14.13. Found: C, 54.24; H, 7.01; N, 14.93.

Tertiary butyl 2-(2-oxoindolin-3-ylidene)hydrazinecarboxylate (11)

A mixture of tertiary butyl carbazate (2.16 g, 0.01 mol) and indole-2,3-dione **10** (1.47 g, 0.01 mol) in (50 ml) ethanol and catalytic amount of glacial acetic acid was added and the mixture was refluxed for 1 hr. The reaction mixture was then allowed to cool at room temperature. The separated yellow colored was formed and filtrated, washed with methanol and recrystallized from DMF. Anal. Calcd for $C_{13}H_{15}N_3O_3$ (261.28): C, 59.76; H, 5.79; N, 16.08. Found: C, 59.78; H, 5.83; N, 16.38.

3-Tertiary-butoxy-5H-[1,2,4]triazino[5,6-b]indole (12)

Compound **11** (2 g, 4.03 mmol) was fused with anhydrous ammonium acetate (0.62 g, 8.06 mmol) with an air condenser at 160°C for 2 hr. The obtained residue was dissolved in water and crystallized from water and ethanol to give compound 12 as yellow crystals; yield: 54%; mp 200-202°C. ^{1}H-NMR (DMSO-*d6*,δ, ppm): 1.43 (s, 9H, CMe3), 7.84-8.26 (m, 4H, Ph), 11.02 (s, 1H, NH). Anal. Calcd for $C_{13}H_{14}N_4O$ (242.28): C, 64.45; H, 5.82; N, 23.13. Found: C, 64.48; H, 5.85; N, 23.38.

1-(3-Tert-butoxy-5H-[1,2,4]triazino[5,6-b]indole-5-yl)-tetra-O-β acetyl glucopyranose (13)

A mixture of Compound 12 and sodium hydride was dissolved in dry *N,N*-dimethylformamide (DMF) was stirred at room temperature for some time and then the temperature was raised to 50°C. The reaction was poured into water and extracted by ethyl acetate. The solvent was evaporated under vacuum. The product was purified on a column of silica gel using chloroform: methanol (90: 10) for elution to give solid, yield: 43%; mp 190-192°C; Rf=0.53. ^{1}H-NMR (DMSO-*d6*,δ, ppm): 7.84-8.26 (m, 4H, Ph), 6.39 (d, 1H, H-1`, *J1`,2`=8.5*), 4.37(d, 2H, H-6,6`, *J6,6`=5.5*), 3.863-96 (m, 4H, H-2,3,4,5), 1.99 (4s, 12H, 4×CH_3CO)1.45 (s, 9H, CMe3), Anal. Calcd for $C_{27}H_{32}N_4O_{10}$ (572.56): C, 56.64; H, 5.63; N, 9.79. Found: C, 56.44; H, 5.69; N, 9.56.

(2R,3S,4R,5S)-2-(3-tert-butoxy-5H-[1,2,4]triazino[5,6-b]indol-5-yl)-tetrahydro-6-(hydroxymethyl)-2H-pyran-3,4,5-triol (14)

Treatment of the glycoside 13 with ammonia (63%) solution and dry methanol under reflux gave white crystals. Yield: 75.6%; ^{1}H-NMR (DMSO-*d6*,δ, ppm): 7.24-7.56 (m, 4H, Ph), 5.39 (d, 1H, H-1`

J1`,2`=7.4), 4.37(d, 2H, H-6,6`, *J6,6`=5.5*), 3.34-3.26 (m, 4H, H-2,3,4,5), 3.69 (m, 4H, OH-2,3,4,6)1.45 (s, 9H, CMe3), Anal. Calcd for $C_{19}H_{24}N_4O_6$ (404.42): C, 56.43; H, 5.98; N, 13.85. Found: C, 56.58; H, 5.95; N, 13.88.

4-Amino-3-tert-butoxy [1,2,4]triazino[5,6-b]indole (15)

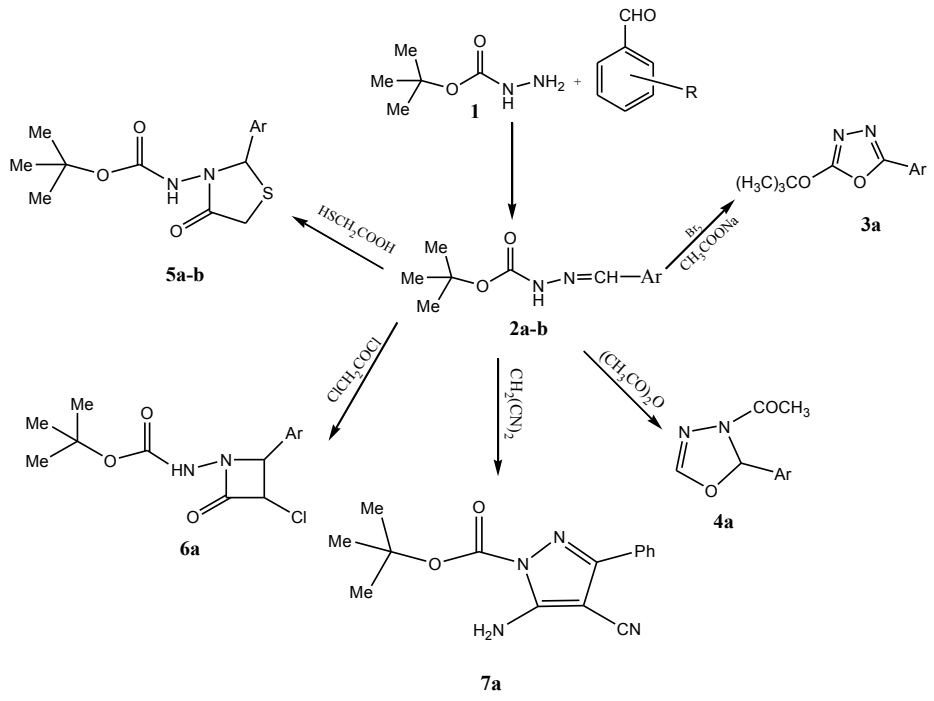
To a solution of compound **11** (2 g, 4.03 mmol) and hydrazine hydrate in (30 ml) ethanol was refluxed for 7 hr and after cooling the residue was formed. The solid was recrystallized from ethanol. Yield: 49%; mp: 218-220°C. ^{1}H-NMR (DMSO-*d*6,δ, ppm): 1.47 (s, 9H, CMe3), 7.04-7.16 (m, 4H, Ph), 4.02 (s, 2H, NH_2). Anal. Calcd for $C_{13}H_{15}N_5O$ (257.29): C, 60.69; H, 5.88; N, 27.22. Found: C, 59.96; H, 5.65; N, 27.76.

Results and Discussion

The starting material, tertiary-butyl carbazone derivatives 2a-b was prepared by the condensation of tertiary butyl carbazate with benzaldehyde derivatives in the presence of ethyl alcohol. 1,3,4-oxadiazoles derivative 3a was synthesized by oxidation of hydrazone 2a using bromine in glacial acetic acid [18] containing anhydrous sodium acetate (Scheme 1). The suggested mechanism for oxidative cyclization may be outlined according to the Gibson method [19] in Scheme 2. The synthesis of 1,3,4-Oxadiazoline 4a was achieved by the cyclization of hydrazone 2a with acetic anhydride. The IR spectrum of compound 4a showed strong absorption bands at 1715 for (C=O), and 1680 (C=N). ^{1}H NMR spectrum displayed also a singlet signal at 2.62 ppm assigned for CH_3 group and absence of a single peak at 1.42 for tertiary butoxygroup. [2+3] cycloaddition of arylidinehydrazones 2a-b with thioglycolic acid in *N,N*-dimethyl formamide and anhydrous zinc chloride gives thiazolidinone derivatives 5a-b in 56-60% yield according to Scheme 1. ^{1}H-NMR spectrum of compound 5a-b showed a singlet single beak at 3.52 was assigned to the CH_2 group located in the thiazolidine moiety. The IR spectra of 5a-b showed C=O bands in the region 1674-1684 cm^{-1}. Base induced cyclocondensation of hydrazone2a with chloroacetylchloride in the presence of triethylamine in dioxane resulted in azidine cyclization affording 3-Chloro-4-phenyl-azitidin-2-one derivative 6a. Also hydrazone 2a was reacted with malanonitrile gave compound 7a. The condensation of tertiary butyl carbazate with ethylacetoacetate in acetic acid afforded pyrazole derivative 9. Compound 9 was also obtained by intramolecular cyclization of 8 up on refluxing in *o*-dichlorobenzene (Scheme 3). The structure of 8 was confirmed from IR spectrum, show bands at 3326, 3127,1722, and 1669 cm-1 due to NH, C=O of ester and CO of amide. The ^{1}H NMR spectrum exhibit singlet at 2.1 ppm due to N=C-CH_3 and 2.5 ppm due to 2H of CH_2COOEt. The ^{1}HNMR spectrum of the compound 9 revealed the appearance of different singlet signals at δ 2.30 ppm due to CH_3.pyrazole and 4.31 ppm corresponding to NCOCH_2. Tertiary butyl carbazate was condensation with indole-2,3-dione 10 in ethanol containing catalytic amount of glacial acetic acid yielded (Z)-3-(2-(tertiary butoxylate) hydrazono)indolin-2-one 11. The compound 11 was reacted with ammonium acetate to afford 3-tert-butoxy-5H-[1,2,4] triazino [5,6-b] indole 12. Compound 12 was coupling with bromo acetyl glucose to give N-glycoside 13. The deportation was removed by ammonia in methanol yielded compound 14. Compound 11 subject to hydrazinolysis by heating with hydrazine hydrate afforded compound 15 (Scheme 4).

Antimicrobial activity

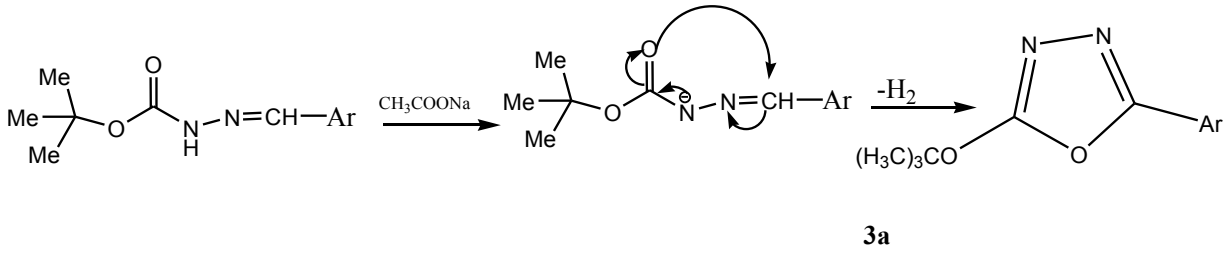
The synthesized compounds were ready to display antimicrobial activity. Antimicrobial activities were observed for all heterocyclic



Ar: a: Ph

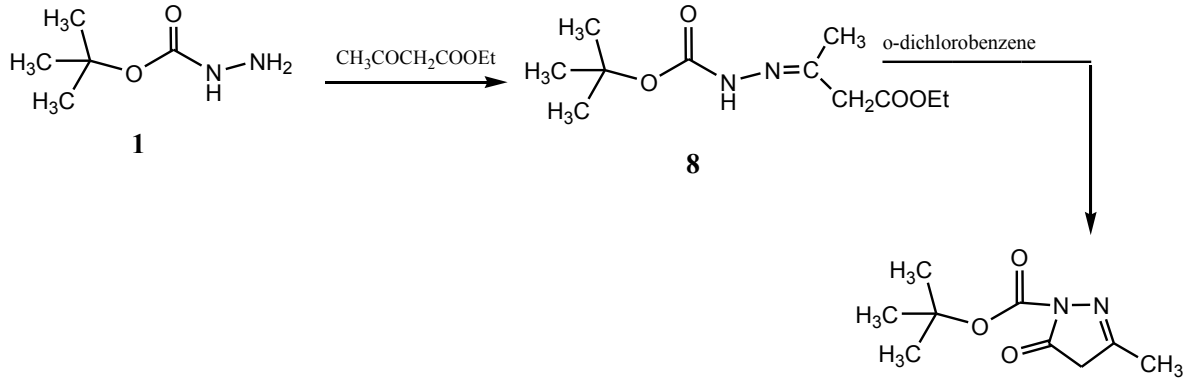
b: 4-NO_2-C_6H_4

Scheme 1: Synthesis of 1,3,4-oxadiazoles, 1,3-thiazolidine, azitidin-2-one, and pyrrolidin-2-one derivatives from hydrazones.



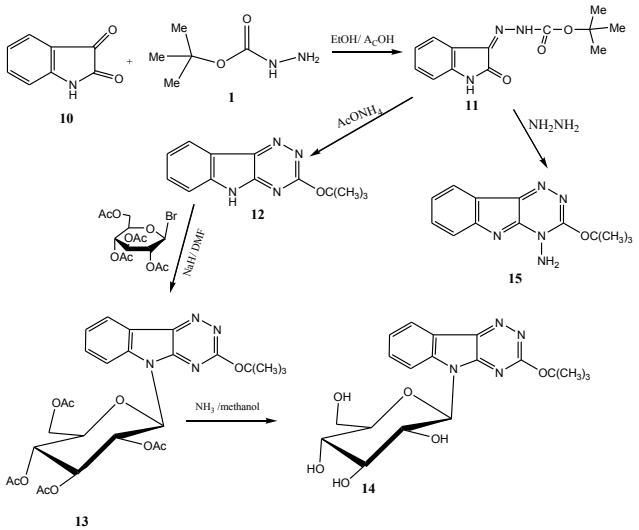
3a

Scheme 2: Mechanism for oxidative cyclization of compound 3.



1 **8** **9**

Scheme 3: Synthesis of compound 9.



Scheme 4: Synthesis of *N*-glycoside.

Comp. No	Inhibition Zone (mm)			
	Bacteria		Fungi	
	Staphylococcus aureus Gram +ve	*Escherichia coli* Gram -ve	*Pencillium chrysogenum*	*Aspergillus niger*
3a	26	17	16	13
4a	15	9	13	12
5a	17	15	16	9
7a	19	5	12	15
9	15	10	10	18
12	22	18	19	20
14	20	18	18	16
Ciprofloxacin	23	22	0	0
Ketoconazole	0	0	20	17

Table 1: Antibacterial and antifungal activities of synthesized compounds.

compounds using strains of bacteria such as Staphylococcus aureus and Escherichia coli and fungal strains of *Pencillium chrysogenum* and *Aspergillus niger*. The antimicrobial activities of the synthesized compounds were studied by cup plate method. Using a sterile cork borer of about 5 mm diameters, wells were made in each petri dish. Standard, control and test were marked on the bottom of the petri dish to identify each cup. Using sterile syringe injected 0.1 ml of standard, control and test into the cups. After injection the petri dishes were kept at room temperature for 24 hr for uniform diffusion of the agent to occur in seeded agar medium. The petri dishes incubated at 37 ± 0.5°C for 24 hr. To extent the diameter of inhibition after 24 hr was measured as the zone of inhibition in millimetres as compared with standard drug. Ciprofloxacin (100 µg/ml) used standard for bacteria and Ketoconazole (100 µg/ml) for fungi. The zone of inhibition was measured in mm to estimate the potency of the test compounds (Table 1). Compound 3a, 12 and 14 (100 µg/ml) showed maximum activity against these bacterial strains and compounds 4a and 7a (100 µg/ ml) showed moderate activity against these bacterial strains. The results of antifungal screening revealed that compound 9 (100 µg/ml) showed better activity and compounds 7a, 9 (100 µg/ml) showed moderate activity against As per gillusnigris and Pencillium chrysogenum using ketaconazole (100 µg/ ml) as standard. The investigation of antimicrobial screening data revealed that all the tested compounds shown good antimicrobial activity.

Conclusions

A synthesis of some 1,3,4-oxadiazoles, 1,3-thiazolidine, azitidin-2-one, and pyrrolidin-2-one derivatives from tertiary butyl (2-benzylidenehydrazine carboxylate derivative is described. The structures of the synthesized compounds were well characterized by elemental analyses, IR, 1H NMR, and mass spectral studies. The biological activities of these products were evaluated**.**

Acknowledgements

Authors would like to thank Zagazig University and the Faculty of Science and Department of Chemistry. They also offer thanks to the Faculty of Science and Department of Biology for their support.

References

1. March, Jerry (1985) Advanced Organic Chemistry: Reactions, Mechanisms, and Structure. 3rd edn, Wiley Publishers, New York.
2. Stork G, Benaim J (1977) Monoalkylation of α,ß-Unsaturated Ketones via Metalloenamines: 1-butyl-10-methyl-$\Delta^{1(9)}$-2-octalone. Org Synth 6: 242.
3. Day AC, Whiting MC (1970) Acetone hydrazone. Org Synth 6: 10.
4. Rollas S, Küçükgüzel SG (2007) Biological activities of hydrazone derivatives. Molecules 12: 1910-1939.
5. Chimenti F, Fioravanti R, Bolasco A, Manna F, Chimenti P, et al. Selective inhibitory activity against MAO and molecular modeling studies of 2-thiazolylhydrazone derivatives. J Med Chem 2007, 50: 707-712.
6. Mao J, Wang Y, Wan B, Kozikowski AP, Franzblau SG, et al. (2007) Design, synthesis, and pharmacological evaluation of mefloquine-based ligands as novel antituberculosis agents. Chem Med Chem 2: 1624-1630.
7. Andreani A, Burnelli S, Granaiola M, Leoni A, Locatelli A, et al. (2008) New antitumor imidazo[2,1-b]thiazole guanylhydrazones and analogues. J Med Chem 51: 809-816.
8. Noulsri E, Richardson DR, Lerdwana S, Fucharoen S, Yamagishi T, et al. (2009) Antitumor activity and mechanism of action of the iron chelator, Dp44mT, against leukemic cells. Am J Hematology 84: 170-176.
9. Vicini P, Incerti M, Doytchinova IA, La Colla P, Busonera B, et al. (2006) Synthesis and antiproliferative activity of benzo[d]isothiazole hydrazones. Eur J Med Chem 41: 624-632.
10. Chinnasamy RP, Sundararajan R, Govindaraj S (2010) Synthesis, characterization, and analgesic activity of novel schiff base of isatin derivatives. J Adv Pharm Technol Res 1: 342-347.
11. Craig C (1998) Kirk-Othmer Encyclopedia Chemical Technology. 4th edn, John Wiley and Sons, New York 26: 516-541.
12. Melnyk P, Leroux V, Sergheraert C, Grellier P (2006) Design, synthesis and in vitro antimalarial activity of an acylhydrazone library. Bioorg Med Chem Lett 16: 31-35.
13. Küçükgüzel SG, Mazi A, Sahin F, Oztürk S, Stables J (2003) Synthesis and biological activities of diflunisal hydrazide-hydrazones. Eur J Med Chem 38: 1005-1013.
14. Sriram D, Yogeeswari P, Madhu K (2005) Synthesis and in vitro and in vivo antimycobacterial activity of isonicotinoyl hydrazones. Bioorg Med Chem Lett 15: 4502-4505.
15. Küçükgüzel SG, Rollas S, Küçükgüzel I, Kiraz M (1999) Synthesis and Antimycobacterial activity of some coupling products from 4-aminobenzoic acid hydrazones. Eur J Med Chem 34: 1093-1100.
16. Abdel-Aal MT, El-Sayed WA, El-Ashry el-SH (2006) Synthesis and antiviral evaluation of some sugar arylglycinoylhydrazones and their oxadiazoline derivatives. Arch Pharm (Weinheim) 339: 656-663.
17. Friedman JF, Mital P, Kanzaria HK, Olds GR, Kurtis JD (2007) Schistosomiasis and pregnancy. Trends Parasitol 23: 159-164.
18. Bamsal R, Bhagchandani G (1982) Synthesis 2-amino-5-aroyl-. 1,3,4-Oxadiazoles. J Indian Chem soc, LIX, 277.
19. Gibson MS (1962) Hydrazones-III: Intramolecular 1,3-dipolar additions involving nitro- and carbonyl groups. Tetrahedron 18: 1377-1380.