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Der Chemica Sinica, 2013, 4(5):46-51

Pelagia Research Library
ISSN: 0976-8505
CODEN (USA) CSHIA5

Synthesis of some 2-(aryl-methylenehydrazone)-quinazolin-5-one derivatives with potential antimicrobial activity

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ABSTRACT

*An efficient and convenient procedure has been developed for the synthesis of some 2-(aryl-methylenehydrazone)-quinazolin-5-one **(4a-d)** derivatives in good yield. We report here synthesis of 2-thioxo-quinazolines **(2a-d)** which were used as base to the synthesis of 2-hydrazino derivatives. Also 2-hydrazino derivatives gave the 2-(aryl-methylenehydrazone)-quinazolin-5-one **(4a-d)**. The structures of compounds have been evaluated on the basis of elemental analysis, FT- IR, ^{1}H NMR and ^{13}C NMR spectral data. Antimicrobial activity of compounds **2a, 2b, 4a** and **4c** are giving excellent results.*

Keywords: Quinazoline, hydrazone, benzylidene, antimicrobial activity

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INTRODUCTION

Dihydropyrimidinones (DHPMs) and their derivatives have occupied an important position in natural and synthetic organic chemistry, due to their wide range of biological activities [1], such as antibacterial, antiviral, antihypertensive, antitumor effects and calcium channel blockers. Scaffold decoration of DHPMs is highly important for creating structural diversity to produce “drug-like” molecules for biological screening. The synthesis of DHPMs was first reported by Biginelli in 1893[2] and has been reviewed recently [3]. Improved procedures and new Biginelli-like scaffolds have been reported over the past decade and a variant of the Biginelli condensation has been described for its application to the total synthesis of bioactive guanidine alkaloids [4]. Basically, these methods are all similar in the use of different lewis acid catalyst as well as protic acid under classical reflux [5]. Other studies have focused on the use of ionic liquids [6], microwave irradiation [7] and combinatorial chemistry [8]. The use of boron compounds [9], TMSCl [10] and heterogeneous catalysts, such as tangstophosphoric acid [11], Zeolite [12], montmorillonite [13], ion-exchange resins [14], grindstone technique [15] and antimony(III)chloride ($SbCl_3$) [16] have also been reported. However, to the best of our knowledge, there have been relatively few reports of the synthesis of fused DHPMs from cyclic β-diketones with high yields. More recently, the Biginelli reaction has been employed for the synthesis of DHPMs, which used cyclic ketones instead of open-chain dicarbonyl compounds using concentrated hydrochloric acid [17] and sulfuric acid [18] as the catalyst.

Quinazolines derivatives have attracted considerable attention since they exhibit potent antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* [19] and *calcium antagonist* activity [20-21].
Also, The pharmacodynamic versatility of quinazoline moiety has been documented not only in many of its synthetic derivatives but also in several naturally occurring alkaloids isolated from animals, families of plant kingdoms and from microoraganism [22–24]. These isolated quinazolines derivatives were found to have wide range

of biological properties including anti-tumor, sedative, analgesic, antidiabetic, antibacterial, anti-inflammatory, antifungal and anticancer [25–31].

The original Biginelli protocol for the preparation of the DHMPs consisted of heating a mixture of the three components (aldehyde, β-keto ester and urea) in ethanol containing a catalytic amount of hydrochloric acid. This procedure leads in one step-one pot to the desired DHPMs. The major drawback associated with this protocol is the low yields, particularly for substituted aromatic and aliphatic aldehydes [32].

We wish to report herein the advantage of using antimony(III)chloride ($SbCl_3$) [16] in the synthesis of 2-thioxo-quinazolines **(2a-d)** derivatives, which provides better results with more sterically hindered substrates with good yield. $SbCl_3$ is inexpensive, easy to handle on large scale. Antimony(III)chloride ($SbCl_3$) catalyst was significantly more effective than other acid catalyst in the Biginelli reaction of cyclic β-diketones and it provides better results with more sterically hindered substrates with good yields [16] (Scheme 1).

Synthesized compounds **(2a-d)** and **(4a-d)** were evaluated against bacterial and fungal pathogenic strains and results are summarized here (Table 2) as a MIC value.

MATERIALS AND METHODS

General: All the reagents were obtained commercially and used with further purification. All melting points were taken in open capillaries and are uncorrected. The monitoring of the progress of all reactions and homogeneity of the synthesized compounds was carried out by TLC. TLC was run using TLC aluminum sheets silica gel 60F254 (Merck). Elemental analysis (% C, H, N) was carried out by Perkins Elmer 2400 CHN elemental analyzer. IR spectra were recorded on a shimadzu FTIR 8401 spectrophotometer in KBR. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer using TMS as internal standard. Mass spectra were scanned on a shimadzu LCMS 2010 spectrometer.

General procedure for preparation of 2-thioxo-quinazolines (2a-d): To a mixture of 1,3-cyclohexanedione (1mmol), thiourea (1.5 mmol), aldehydes (**1a-d)** (1mmol) and antimony(III)chloride (20 mol %), acetonitrile (5ml) was added and content was refluxed for 8 hours. After completion of the reaction as monitored by TLC, the reaction mixture is poured into ice-cold water and stirred for 10-15 minutes. The content of the flask were then filtered and washed with cold water (20 ml) to remove excess thiourea. The solid so obtained was the corresponding 2-thioxo-quinazolines (**2a-d).** It was then recrystallized by hot methanol to get the pure product (Scheme 1).

4-(4-Chloro-phenyl)-2-thioxo-2,3,4,6,7,8-hexahydro-1H-quinazolin-5-one (2a): White solid, (from methanol), (yield 92%), m.p. 256-257°C, Anal.Calcd for $C_{14}H_{13}ClN_2OS$: C 57.43, H 4.48, N 9.57% Found: C 57.41, H 4.45, N 9.51%. IR (KBr, cm^{-1}): 3311 (br, NH's), 3040, 3010 (ArC-H), 2960 (alkyl C-H), 1614 (C=C), 1705 (C=O), 1177 (C=S), 735 (C-Cl). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.72-1.8 (m, 2H, CH_2), 1.95-2.0 (m, 2H, CH_2), 2.18-2.28 (m, 2H, CH_2), 5.42 (bs, 1H, CH), 7.2 (dd, 2H, Ar-H), 7.35 (dd, 2H, Ar-H), 8.90 (bs, 1H, NH), 10 (bs, 1H, NH), ^{13}C NMR (400 MHz, DMSO-d_6) δ: 20.45 (CH_2), 26.2 (CH_2), 38.8 (CH_2), 49.22 (CH), 111.7, 126.3, 127.2, 128.3, 128.8, 133.5, 142.1, 155.2 (Ar-C), 173.9 (C=S), 194.8 (C=O), MS: (M+1) 293.04.

4-(4-Fluoro-phenyl)-2-thioxo-2,3,4,6,7,8-hexahydro-1H-quinazolin-5-one (2b): Cream solid, (from methanol), (yield 90%), m.p. 276-278°C, Anal.Calcd for $C_{14}H_{13}FN_2OS$: C 60.85, H 4.74, N 10.14% Found: C 60.78, H 4.70, N 10.09%. IR (KBr, cm^{-1}): 3305 (br, NH's), 3040, 3010 (ArC-H), 2960 (alkyl C-H), 1617 (C=C), 1686 (C=O), 1174 (C=S), ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.73-1.81 (m, 2H, CH_2), 1.93-1.98 (m, 2H, CH_2), 2.13-2.23 (m, 2H, CH_2), 5.46 (bs, 1H, CH), 7.19 (dd, 2H, Ar-H), 7.31 (dd, 2H, Ar-H), 8.85 (bs, 1H, NH), 9.89 (bs, 1H, NH), ^{13}C NMR (400 MHz, DMSO-d_6) δ: 20.45 (CH_2), 26.2 (CH_2), 38.18 (CH_2), 49.4 (CH), 111.7, 126.3, 127.2, 128.3, 128.8, 133.5, 142.1, 155.2 (Ar-C), 173.7 (C=S), 192.8 (C=O), MS: (M+1) 277.2

4-(2-Chloro-phenyl)-2-thioxo-2,3,4,6,7,8-hexahydro-1H-quinazolin-5-one (2c): Off-white solid, (from methanol), (yield 94%), m.p. 239-241°C, Anal.Calcd for $C_{14}H_{13}ClN_2OS$: C 57.43, H 4.48, N 9.57% Found: C 57.49, H 4.45, N 9.51%. IR (KBr, cm^{-1}): 3310, 3229 (br, NH's), 3040, 3010 (ArC-H), 2960 (aliphatic C-H), 1614 (C=C), 1698 (C=O), 1179 (C=S), 735 (C-Cl). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.72-1.8 (m, 2H, CH_2), 1.95-2.0 (m, 2H, CH_2), 2.2-2.3 (m, 2H, CH_2), 5.32 (bs, 1H, CH), 7.10-7.39 (m, 4H, Ar-H), 7.90 (bs, 1H, NH), 9.89 (bs, 1H, NH), ^{13}C

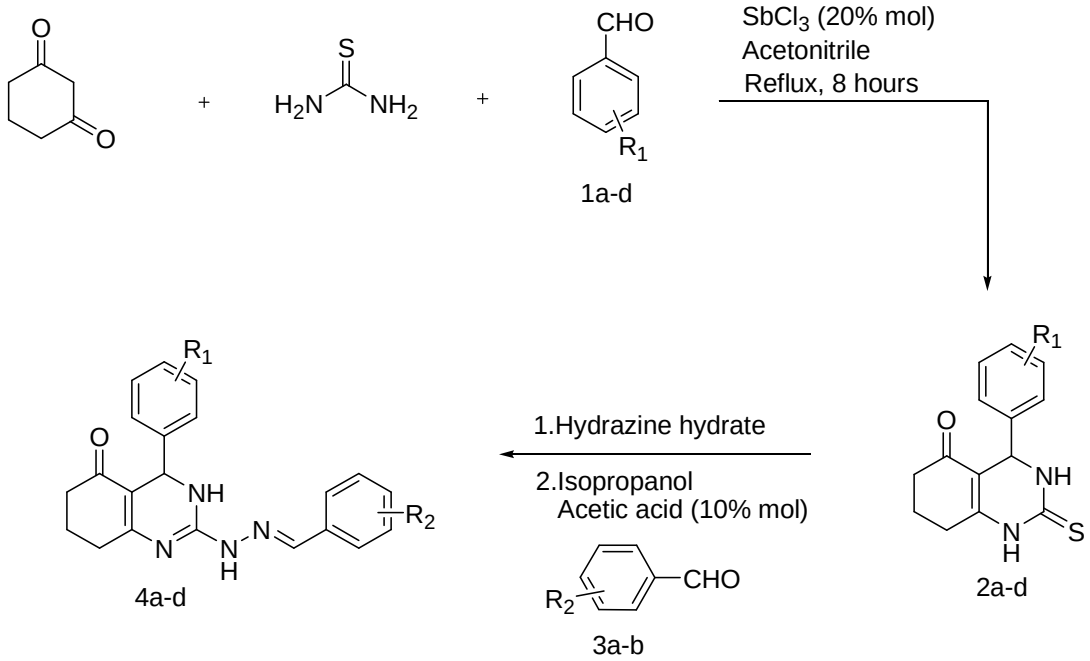
NMR (400 MHz, DMSO-d_6) δ: 20.45 (CH_2), 26.2 (CH_2), 38.8 (CH_2), 49.4 (CH), 111.7, 126.3, 127.2, 128.3, 128.8, 133.5, 142.1, 155.2 (Ar-C), 173.8 (C=S), 192.8 (C=O), MS: (M+1) 293.04.

4-Phenyl-2-thioxo-2,3,4,6,7,8-hexahydro-1H-quinazolin-5-one (2d): Light yellow solid, (from methanol), (yield 92%), m.p. 220-223 °C, Anal.Calcd for $C_{14}H_{14}N_2OS$: C 65.09, H 5.46, N 10.84% Found: C 65.11, H 5.55, N 10.89%. IR (KBr, cm^{-1}): 3300 (br, NH's), 3010, 3024 (ArC-H), 2960 (aliphatic C-H), 1692 (C=O), 1611 (C=C), 1185 (C=S). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.83-1.9 (m, 2H, CH_2), 2.1-2.2 (m, 2H, CH_2), 2.4-2.5 (m, 2H, CH_2), 5.34 (bs, 1H, CH), 7.10-7.39 (m, 5H, Ar-H), 7.80 (bs, 1H, NH), 9.69 (bs, 1H, NH), ^{13}C NMR (400 MHz, DMSO-d_6) δ: 19.3 (CH_2), 27.6 (CH_2), 29.8 (CH_2), 53.4 (CH), 111.9, 126.7, 127.1, 128.3, 143.4, 156.2 (Ar-C), 174.4 (C=S), 193.9 (C=O), MS: (M+1) 259.09.

Table 1. Analytical IR spectral data of 4-aryl-2-thioxo-2,3,4,6,7,8-hexahydro-1H-quinazolin-5-ones (2a-d) and 2-(aryl-methylene hydrazone)-quinazolin-5-one (4a-d)

Sr.No	R_1	R_2	m.p. (°C)	Yield (%)	Mol.Formula*	IR (KBr, cm^{-1})
2a	4-Cl	-	256-257	92	$C_{14}H_{13}ClN_2OS$	3311, 1705, 1177
2b	4-F	-	276-278	90	$C_{14}H_{13}FN_2OS$	3305, 1686, 1174
2c	2-Cl	-	239-241	94	$C_{14}H_{13}ClN_2OS$	3310, 1698, 1179
2d	H	-	220-223	92	$C_{14}H_{14}N_2OS$	3300, 1692, 1185
4a	4-Cl	4-Cl	170-173	90	$C_{21}H_{18}Cl_2N_4O$	3345, 1689
4b	4-Cl	2-Cl	177-179	92	$C_{21}H_{18}Cl_2N_4O$	3334, 1692
4c	2-Cl	4-Cl	189-191	89	$C_{21}H_{18}Cl_2N_4O$	3340, 1695
4d	2-Cl	2-Cl	197-199	93	$C_{21}H_{18}Cl_2N_4O$	3340, 1698

**All compounds gave analysis for C, H and N in the range of ±0.4.*



Scheme 1. Synthesis of 4-aryl-2-thioxo-2,3,4,6,7,8-hexahydro-1H-quinazolin-5-ones (2a-d) and 2-(aryl-methylenehydrazone)-quinazolin-5-one (4a-d)

General procedure for preparation of 2-(aryl-methylenehydrazone)-quinazolin-5-one (4a-d): To a corresponding compound (**2a-d)** (1 mmol), hydrazine hydrate (1.1 mmol) was added, content was refluxed for 10 hours. After completion of the reaction as monitored by TLC, isopropanol (5ml) was added followed by corresponding aldehydes (**3a-b)** (1 mmol) and acetic acid (10 mol %), content was refluxed for 12-18 hours. After completion of the reaction as monitored by TLC, the reaction mixture was filtered and washed with isopropanol (5 ml). The solid so obtained was the corresponding (**4a-e**). It was then recrystallized by hot isopropanol to get the pure product (Scheme 1).

2-[N'-(4-Chloro-benzylidene)-hydrazino]-4-(4-chloro-phenyl)-4,6,7,8-tetrahydro-3H-quinazolin-5-one (4a): Yellow solid (from isopropanol) (Yield 90%), m.p. 170-173°C, Anal.Calcd for $C_{21}H_{18}Cl_2N_4O$: C 61.03, H 4.39, N 13.56% Found: C 61.01, H 4. 34, N 13.50%. IR (KBr, cm^{-1}): 3345, (br, NH's), 2965 (ArC-H), 1689 (C=O), 1602 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.7-1.9 (m, 2H, CH_2), 2.2-2.3 (m, 2H, CH_2), 2.4-2.5 (m, 2H, CH_2), 5.3 (d, 1H, CH), 7.3 (dd, 2H, Ar-H), 7.36 (dd, 2H, Ar-H), 7.42 (dd, 2H, Ar-H), 7.8 (dd, 2H, Ar-H), 8.05 (bs, 1H, NH), 8.12 (s, 1H, azomethine proton), 10.1 (bs, 1H, NH), ^{13}C NMR (400 MHz, DMSO-d_6) δ: 20.59 (CH_2), 26.19 (CH_2), 36.18 (CH_2), 49.23 (CH), 108.76, 128.0, 128.18, 128.37, 128.54, 131.4, 133.1, 134.7, 144.0, 147.0, 152.3 (Ar-C), 192.63 (C=O), MS: (M+Na) 435.1.

2-[N'-(2-Chloro-benzylidene)-hydrazino]-4-(4-chloro-phenyl)-4,6,7,8-tetrahydro-3H-quinazolin-5-one (4b): Light yellow solid (from isopropanol) (Yield 92%), m.p. 177-179°C, Anal.Calcd for $C_{21}H_{18}Cl_2N_4O$: C 61.03, H 4.39, N 13.56% Found: C 61.07, H 4. 44, N 13.60%. IR (KBr, cm^{-1}): 3334, (br, NH's), 2965 (ArC-H), 1692 (C=O), 1607 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.7-1.87 (m, 2H, CH_2), 2.18-2.28 (m, 2H, CH_2), 2.3-2.4 (m, 2H, CH_2), 5.31 (d, 1H, CH), 7.1 (dd, 2H, Ar-H), 7.15 (dd, 2H, Ar-H), 7.3-7.5 (m, 4H, Ar-H), 7.95 (bs, 1H, NH), 8.07 (s, 1H, azomethine proton), 10.0 (bs, 1H, NH), ^{13}C NMR (400 MHz, DMSO-d_6) δ: 20.57 (CH_2), 26.09 (CH_2), 36.08 (CH_2), 49.3 (CH), 108.2, 128.3, 128.1, 128.39, 128.54, 131.46, 133.15, 134.75, 144.4, 147.2, 152.31 (Ar-C), 192.9 (C=O), MS: (M+Na) 435.1.

2-[N'-(4-Chloro-benzylidene)-hydrazino]-4-(2-chloro-phenyl)-4,6,7,8-tetrahydro-3H-quinazolin-5-one (4c): Light brown solid (from isopropanol) (yield 89%), m.p. 189-191°C, Anal.Calcd for $C_{21}H_{18}Cl_2N_4O$: C 61.03, H 4.39, N 13.56% Found: C 60.98, H 4.33, N 13.55%. IR (KBr, cm^{-1}): 3340, (br, NH's), 2970 (ArC-H), 1695(C=O), 1600 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.67-1.77 (m, 2H, CH_2), 2.11-2.22 (m, 2H, CH_2), 2.25-2.37 (m, 2H, CH_2), 5.3 (d, 1H, CH), 7.05-7.22 (m, 4H, Ar-H), 7.4 (dd, 2H, Ar-H), 7.5 (m, 2H, Ar-H), 7.99 (bs, 1H, NH), 8.13 (s, 1H, azomethine proton), 10.07 (bs, 1H, NH), ^{13}C NMR (400 MHz, DMSO-d_6) δ: 20.50 (CH_2), 26.11 (CH_2), 36.17 (CH_2), 49.0 (CH), 108.7, 128.0, 128.1, 128.33, 128.59, 131.8, 133.0, 134.99, 144.07, 147.99, 152.13 (Ar-C), 192.66 (C=O), MS: (M+Na) 435.1.

2-[N'-(2-Chloro-benzylidene)-hydrazino]-4-(2-chloro-phenyl)-4,6,7,8-tetrahydro-3H-quinazolin-5-one (4d): Brown solid (from isopropanol) (yield 93%), m.p. 197-199°C, Anal.Calcd for $C_{21}H_{18}Cl_2N_4O$: C 61.03, H 4.39, N 13.56% Found: C 60.98, H 4.33, N 13.55%. IR (KBr, cm^{-1}): 3340, (br, NH's), 2987 (ArC-H), 1698 (C=O), 1601 (C=C). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.76-1.84 (m, 2H, CH_2), 2.02-2.14 (m, 2H, CH_2), 2.31-2.39 (m, 2H, CH_2), 5.34 (d, 1H, CH), 7.1-7.24 (m, 4H, Ar-H), 7.4-7.7 (m, 4H, Ar-H), 8.12 (bs, 1H, NH), 8.03 (s, 1H, azomethine proton), 9.98 (bs, 1H, NH), ^{13}C NMR (400 MHz, DMSO-d_6) δ: 20.37 (CH_2), 26.26 (CH_2), 36.27 (CH_2), 49.13 (CH), 108.17, 128.02, 128.21, 128.38, 128.53, 131.44, 133.12, 134.77, 144.02, 147.03, 152.15 (Ar-C), 192.4 (C=O), MS: (M+Na) 435.1.

Antimicrobial activity

The *in vitro* antimicrobial activity of all the synthesized compounds was carried out by broth microdilution method. Mueller Hinton broth was used as nutrient medium to grow and dilute the compound suspension for the test bacteria and Sabouraud Dextrose broth used for fungal nutrition. Inoculum size for test strain was adjusted to 10^8 CFU [Colony Forming Unit] per milliliter by comparing the turbidity. The strains employed for the activity were procured from [MTCC – Micro Type Culture Collection] Institute of Microbial Technology, Chandigarh.

The compounds **(2a-d)** and **(4a-d)** were screened for their antibacterial activity against *Escherichia coli (E.coli)*, *Pseudomonas aeruginosa (P.aeruginosa)*, *Staphylococcus aureus (S.aureus)*, *Streptococcus pyogenes (S.pyogenes)* as well as antifungal activity against and *Candida albicans (C.albicans)*. DMSO was used as vehicle to get desired concentration of compounds to test upon microbial strains. The lowest concentration, which showed no visible growth after spot subculture was considered as MIC for each compound. The standard antibiotics used for comparison in the present study were ampicillin for evaluating antibacterial activity as well as griseofulvin for antifungal activity. The protocols are summarized in (Table 2).

An examination of the data (Table 2) reveals that amongst all the synthesized compounds **(2a-d)** and **(4a-d),** compounds **4a** and **4c** exhibited excellent activity against Gram positive bacteria *Staphylococcus aureus (S.aureus)*. Compounds **2a** and **4a** exhibited excellent activity against Gram negative bacteria *Escherichia coli (E.coli)* as compared to standard antibiotic ampicillin.

Antifungal study revealed that compounds **2a**, **2b** and **4a** are more potent as compared to standard fungicidal griseofulvin against *Candida albicans (C.albicans)*.

Table 2: Antimicrobial activity of compounds 2a-d and 4a-d

Comp.No.	Minimal inhibitory concentration µg/ml				
	Gram-negative bacteria		Gram-positive bacteria		Fungi
	E.coli	***P.aeruginosa***	***S.aureus***	***S.pyogenus***	***C.albicans***
2a	62.5	250	200	250	**250**
2b	200	100	250	200	**250**
2c	100	100	200	125	500
2d	200	250	250	200	1000
4a	62.5	250	62.5	100	**250**
4b	200	100	200	200	>1000
4c	100	100	62.5	125	1000
4d	200	250	250	200	1000
Ampicillin	100	--	250	100	--
Griseofulvin	--	--	--	--	500

(--) No inhibition zone.

RESULTS AND DISCUSSION

The key intermediates for the synthesis of 2-(aryl-methylenehydrazone)-quinazolin-5-one **(4a-d)** are shown in the (scheme 1). 4-aryl-2-thioxo-2,3,4,6,7,8-hexahydro-1H-quinazolin-5-ones **(2a-d)** were prepared by Biginelli reaction of 1,3-cyclohexandione, thiourea and aldehydes **(1a-d)** in acetonitrile in the presence of antimony(III)chloride as acid catalyst. Antimony(III)chloride gave us excellent yield compare to other acid catalysts such as concentrated hydrochloric acid, sulfuric acid and TMSCl. The best results were obtained with a 0.2:1:1:1.5 ratio of antimony(III)chloride, aldehydes **(1a-d)**, cyclic ketone and thiourea for the synthesis of compounds **(2a-d)**. Compounds **(2a-d)** on reflux with hydrazine hydrate for 10 hours formed the hydrazides which were reacted *insitu* with the aldehydes **(3a-b)** in isopropanol and acetic acid as catalyst yielded the desired 2-(aryl-methylenehydrazone)-quinazolin-5-one **(4a-d)**.

Compound **2a** show intense peaks at 3311 cm^{-1} in IR spectra for (NH), 1705 cm^{-1} for carbonyl (C=O) and 1177 for thioxo (C=S) streatching. In the mass spectra molecular ion peak is in agreement with the molecular weight of the compound. Elemental analysis data have been found to be in conformity with the assigned structure. ^{1}H NMR spectrum of **2a** showed a double doublet at δ 7.2 and 7.35 ppm for aromatic (4H) protons and two broad singlet at δ 8.9 and 10 ppm for two NHs. Furthermore, the ^{13}C NMR of compound **2a** showed the signal at δ 173.9 ppm which is corresponding to C-2 (C=S group).

Also, compounds **(4a-d)** can be prepared in excellent yield from compounds **(2a-d)** via 2-hydrazino derivatives of compounds **(2a-d**) (Scheme 1).We have observed that *insitu* formation of compounds **(4a-d)** gave excellent isolated yield. The IR spectra of compound **4a** show intense peak at around 3345 cm^{-1} for (NHs), 1689 cm^{-1} for (C=O). ^{1}H NMR spectra of **4a** showed double doublets at δ 7.3, 7.36, 7.42 and 7.8 ppm for two pera substituted aromatic (8H) protons and two broad singlet at δ 8.05 and 10.1 ppm indicating the presence of two NH protons, in addition to the signals corresponding to six methylene protons at δ 1.7-2.5 ppm. Singlet at around δ 8.12 ppm indicates for azomethine proton, and at around δ 5.3 ppm indicates for C-5 proton. Data from the elemental analysis and mass spectrum is also in agreement with the assigned structure. The ^{13}C NMR of compound **4a** revealed that the signal corresponding to the thione was absent and a resonance of –N=**C**-N- carbon atom (C-2) at δ 152.34 ppm was indicated to the chemical shift of the corresponding carbon atom. The signal at δ 192.63 corresponding to the (C=O) and at δ 147 ppm corresponds to azomethine carbon. The signal at δ 49.23 ppm indicates for C-5 carbon.

Similarly, all these compounds were characterized on the basis of spectral studies. All the compounds were screened for their antibacterial and antifungal activities using ampicillin and griseofulvin as standard drugs.

CONCLUSION

A series of some derivatives **(4a-d)** have been synthesized with high yield via *insitu* approach from compounds **(2a-d)**. Also, compounds **(2a-d)** can be prepared by multicomponent reaction between 1,3-cyclohexanedione, thiourea and aldehydes with high yield using antimony(III)chloride as a catalyst.

It can be concluded from (Table 2) that compound **4a** and **4c** is highly active against Gram positive bacteria *Staphylococcus aureus (S.aureus)*, compounds **2a** and **4a** exhibited excellent activity against Gram negative bacteria *Escherichia coli (E.coli)* as compared to standard antibiotic ampicillin. Antifungal study revealed that compounds **2a**, **2b** and **4a** are more potent as compared to standard fungicidal griseofulvin against *Candida albicans (C.albicans)*.

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