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Der Pharma Chemica, 2010, 2(4): 118-134
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X

Synthesis, antimicrobial and antioxidant activities of some novel cyclized naphthyl cyclohexanone derivatives

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Abstract

2-((Naphthalen-1-or-2-yl)methylene)cyclohexanone ***(1a,b)*** *were synthesized through condensation of 1- and/or 2-naphthaldehyde with cyclohexanone. The cyclization of* ***1a,b*** *with substituted hydrazines gave the corresponding hexahydroindazole derivatives* ***2a,b-6a,b****. While on condensation with hydroxylamine hydrochloride and/or thiourea gave benzoisoxazole derivative* ***7a,b*** *and quinazoline-2-thione derivative* ***8a,b****. Also condensation of* ***1a,b*** *with guanidine sulphate followed by chloroacetylation gave* ***10a,b*** *which were condensed with ortho substituted aniline gave quinazoline derivatives* ***11a,b****,* ***12a,b****. Condensation of* ***1a,b*** *with various active methylene compounds afforded the corresponding chromene derivatives* ***13a,b-15a,b****. The antimicrobial activity of the newly synthesized compounds was done against different gram positive, gram negative bacteria and fungi species. Also the antioxidant activity of these compounds was evaluated.*

Key words: Naphthaldehyde, cyclohexanone, chalcones, antimicrobial activity, antioxidant activity.

INTRODUCTION

In the recent years, antimicrobial agents have been received a great deal of attention due to their potential biological applications in different fields. The antimicrobial activity caught our attention due to the appearance of resistant strains of pathogens in the last decade [1], besides, emerging and re-emerging of bacterial infectious diseases which still cause death and disability worldwide [2]**.** Moreover, antibiotics have revolutionized the medical care in the 20th century and with their discovery, people were convinced that infectious diseases might some day be

wiped out [3]. Thus scientists are working to find new ways to defeat bacteria that are increasingly resistant to the antibiotics already available.

On the other hand, antioxidants have gained a lot of importance because of their potential prophylactic and therapeutic activities against many diseases. Free radicals are constantly formed as a result of normal organ functions or excessive oxidative stress [4]. High levels of free radicals can cause damage to biomolecules such as lipids, proteins, enzymes and DNA in cells and tissues, resulting in mutations that can lead to malignancy. The development of synthetic compounds, capable of scavenging free radicals has been of great success. In recent years, many publications have covered the antimicrobial, antioxidant and cytotoxic roles of several heterocyclic compounds [5, 6].

The available naphthalene containing drugs such as nafacillin, naftifine, tolnaftate, and terbinafine play vital roles in the control of microbial infections. In addition, many different studies demonstrated the significant antimicrobial activity of various newly synthesized naphthalene and cyclohexane-containing derivatives [7-10].

It is well known that α,β-Enones are widely used as versatile precursors for synthesis of several types of heterocyclic compounds, such as pyrazoles, isoxazoles, pyrimidines, chromenes and fused heterocyclic derivatives which are of great biological interest, especially as antimicrobials [11-17] and antioxidants [18-20].

Encouraged by these observations, the present study aimed to synthesize a new series of compounds of naphthalene-cyclohexane backbone that incorporate with the above mentioned heterocycles in order to examine their antimicrobial activities against different Gram-positive, Gram-negative bacteria and pathogenic fungi in comparison with several control drugs and also to evaluate the minimum inhibitory concentrations (MICs) of some of the prepared compounds. In addition, determinates the scavenging activity of all the newly synthesized derivatives against DPPH radicals. Structure activity relationships were also studied.

MATERIALS AND METHODS

Chemistry

All melting points are uncorrected and were recorded on an open glass capillary tubes using an Electrothermal IA 9100 digital melting point apparatus. Elemental microanalyses were carried out at Micro analytical Unit, Central Services Laboratory, National Research Center, Dokki, Cairo, Egypt, using Vario Elementar and were found within ±0.5% of the theoretical values. Infrared spectra were recorded on a Jasco FT/IR-6100, Fourier transform, Infrared spectrometer (Japan) at cm^{-1} scale using KBr disc technique at Central Services Laboratory, National Research Center, Dokki, Cairo, Egypt. ^1H NMR spectra were determined by using a JEOl EX-270 NMR spectrometer at Central Services Laboratory, National Research Center, Dokki, Cairo, Egypt. The mass spectra were measured with a Finnigan MAT SSQ-7000 mass spectrometer at Central Services Laboratory, National Research Center, Dokki,Cairo, Egypt. Follow up of the reactions and checking the purity of the compounds were made by TLC on silica gel-precoated aluminium sheets (Type 60, F 254, Merck, Darmstadt, Germany) and the spots were detected by exposure to UV lamp at λ_{254} nanometer for few seconds.

2-((Naphthalen-1-or-2-yl)methylene)cyclohexanone (1a,b)
A mixture of cyclohexanone (9.80 mL, 0.10 mole) and the appropriate aldehydes namely, 1-naphthaldehyde and/or 2-naphthaldehyde (15.60 g, 0.10 mole) in (10%) alcoholic sodium hydroxide (50 mL) was stirred for 3 h at room temperature. The reaction mixture was left overnight, filtered, washed several times with water, dried and recrystallized from the proper solvent to give compounds **1a,b** respectively.

3,3a,4,5,6,7-Hexahydro-3-(naphthalen-1-or-2-yl)-2*H*-indazole (2a,b)
A mixture of compound **1a,b** (0.48 g, 0.002 mole) and hydrazine hydrate 98% (0.20 mL, 0.004 mole) in absolute ethanol (10 mL) was refluxed for 3 h. The formed precipitate was filtered, dried and recrystallized from the proper solvent to give compounds **2a,b** respectively.

1-(3,3a,4,5,6,7-Hexahydro-3-(naphthalen-1-or-2-yl) indazol-2-yl)ethanone (3a,b)
A mixture of compound **1a,b** (0.48 g, 0.002 mole) and hydrazine hydrate 98% (0.20 mL, 0.004 mole) in glacial acetic acid (10 mL) was refluxed for 3 h. The formed precipitate was filtered, dried and recrystallized from the proper solvent to give compounds **3a,b** respectively.

3,3a,4,5,6,7-Hexahydro-2-methyl-3-(naphthalen-1-or-2-yl)-2*H*-indazole (4a,b)
A mixture of compound **1a,b** (0.48 g, 0.002 mole) and methylhydrazine (0.10 mL, 0.002 mole) in absolute ethanol (10 mL) was refluxed for 4 h. The formed precipitate was filtered, dried and recrystallized from the proper solvent to give compounds **4a,b** respectively.

3,3a,4,5,6,7-Hexahydro-3-(naphthalen-1-or-2-yl)-2-phenyl-2*H*-indazole (5a,b)
A mixture of compound **1a,b** (0.48 g, 0.002 mole) and phenylhydrazine (0.22 mL, 0.002 mole) in absolute ethanol (10 mL) was refluxed for 4 h. The formed precipitate was filtered, dried and recrystallized from the proper solvent to give compounds **5a,b** respectively

4,5,6,7-Tetrahydro-3-(naphthalen-1-or-2-yl)-1*H*-indazole-2(3*H*)-carbothioamide (6a,b)
A mixture of compound **1a,b** (0.48 g, 0.002 mole) and thiosemicarbazide (0.19 g, 0.002 mole) in (1%) alcoholic sodium hydroxide (15 mL) was refluxed for 10 h. Then the reaction solution was cooled, poured into ice/cold water and acidified by diluted hydrochloric acid. The formed precipitate was filtered, dried and recrystallized from the proper solvent to give compounds **6a,b** respectively.

1,3,4,5,6,7-Hexahydro-3-(naphthalen-1-or-2-yl)benzo[c]isoxazole (7a,b)
A mixture of compound **1a,b** (0.48 g, 0.002 mole) and hydroxylamine hydrochloride (0.14 g, 0.002 mole) in (1%) alcoholic sodium hydroxide (15 mL) was refluxed for 10 h. Then the reaction solution was cooled, poured onto ice/cold water and acidified by diluted hydrochloric acid. The formed precipitate was filtered, dried and recrystallized from the proper solvent to give compounds **7a,b** respectively.

3,4,5,6,7,8-Hexahydro-4-(naphthalen-1-or-2-yl)quinazoline-2(1*H*)-thione (8a,b)
A mixture of compound **1a,b** (0.48 g, 0.002 mole) and thiourea (0.16 g, 0.002 mole) in (1%) ethanolic sodium hydroxide (15 mL) was refluxed for 24 h. The formed precipitate was filtered, washed several times with water, dried and recrystallized from the proper solvent to give compounds **8a,b** respectively.

5,6,7,8-Tetrahydro-4-(naphthalen-1-or-2-yl)quinazolin-2-amine (9a,b)
A mixture of compound **1a,b** (0.48 g, 0.002 mole) and guanidine sulphate (0.22 g 0.001 mole) in (1%) ethanolic sodium hydroxide (20 mL) was refluxed for 10 h. After cooling, the solution was poured onto ice cold/water and acidified by diluted hydrochloric acid. The formed precipitate was filtered, washed several times with water, dried and recrystallized from the proper solvent to give compounds **9a,b** respectively.

2-Chloro-*N*-(5,6,7,8-tetrahydro-4-(naphthalen-1-or-2-yl)quinazolin-2-yl)acetamide (10a,b)
A mixture of compound **9a,b** (2.75 g, 0.01 mole) and chloroacetyl chloride (1.13 mL, 0.01 mole) in dry benzene (20 mL) was refluxed for 8 h. The formed precipitate after cooling was filtered, washed several times with petroleum ether, dried and recrystallized from the proper solvent to give compounds **10a,b** respectively.

3,4-Dihydro-*N*-(5,6,7,8-tetrahydro-4-(naphthalen-1-or-2-yl)quinazolin-2-yl)quinoxalin-2-amine (11a,b)
A mixture of compound **10a,b** (0.70 g, 0.002 mole) and o-phenylenediamine (0.22 g, 0.002 mole) in absolute ethanol (20 mL) was refluxed for 6 h. The formed precipitate was filtered, dried and recrystallized from the proper solvent to give compound**s 11a,b** respectively.

N-(2*H*-Benzo[b][1,4]oxazin-3-yl)-5,6,7,8-tetrahydro-4-(naphthalen-1-or-2-yl)quinazolin-2-amine (12a,b)
A mixture of compound **10a,b** (0.70 g, 0.002 mole) and o-aminophenol (0.22 g, 0.002 mole) in absolute ethanol (20 mL) was refluxed for 8 h. The formed precipitate was filtered, dried and recrystallized from the proper solvent to give compounds **12a,b** respectively.

2-Amino-5,6,7,8-tetrahydro-4-(naphthalen-1-or-2-yl)-4*H*-chromene-3-carbonitrile (13a,b)
A mixture of compound **1a,b** (0.48 g, 0.002 mole) and malononitrile (0.14 g, 0.002 mole) in (1%) sodium ethoxide solution (15 mL) was refluxed for 6 h. The formed precipitate was filtered, washed several times with water, dried and recrystallized from the proper solvent to give compounds **13a,b** respectively.

5,6,7,8-Tetrahydro-2-hydroxy-4-(naphthalen-1-or-2-yl)-4*H*-chromene-3-carbonitrile (14a,b)
A mixture of compound **1a,b** (0.48 g, 0.002 mole) and ethylcyanoacetate (0.23 mL, 0.002 mole) in (1%) sodium ethoxide solution (15 mL) was refluxed for 4 h. The formed precipitate was filtered, washed several times with water, dried and recrystallized from the proper solvent to give compounds **14a,b** respectively.

1-(5,6,7,8-Tetrahydro-2-hydroxy-4-(naphthalen-1-or-2-yl)-4*H*-chromen-3-yl)ethanone (15a,b)
A mixture of compound **1a,b** (0.48 g, 0.002 mole) and ethylacetoacetate (0.26 mL, 0.002 mole) in (1%) sodium ethoxide solution (20 mL) was refluxed for 6 h. The formed precipitate was filtered, washed several times with water, dried and recrystallized from the proper solvent to give compounds **15a,b** respectively.

Microorganisms

The organisms used were: Gram positive bacteria namely *Bacillus subtilus* NRRL B-543, *Staphylococcus aureus;* NRRL B-313, Gram negative bacteria *Escherichia coli;* NRRL B-210, pathogenic yeast *Candida albicans* NRRL Y-477 and fungi *Aspergillus niger* NRRL-3.These microorganisms were obtained from Northern Utilization Research and Development Division, US Department of Agriculture, Peoria, Illinois.

Test of antimicrobial activity

Thirty compounds were screened in vitro for their antimicrobial activities against five strains by the agar diffusion technique [21]. All of the newly synthesized compounds were dissolved in dimethyl sulfoxide (DMSO) to prepare chemicals of stock solutions of 10 mg/1mL. The pathogenic bacteria and fungi were maintained on nutrient agar and Czapek's-Dox agar media, respectively in Petri dishes with an inner diameter 9 cm to provide thin agar plates after solidification of thickness 3.4-3.5 mm. After solidification, hollows of 10 millimeter diameter wells were cut from the agar using a sterile cork-borer, and 0.1 mL of each of the tested solutions were poured into the wells. The Petri dishes were incubated at 5-8^{o}C for 2-3 h to permit good diffusion and then incubated for 24 h at 30°C in case of bacteria and 48 h at 28°C in case of yeast and fungi. After incubation the diameter of inhibition zone (mm) was measured. Gentamicin, ampicillin, amoxycillin, tetracyclinol, chloramphenicol, and fluconazole were purchased from Egyptian market and used in a concentration of 25 mg/mL as standard antibacterial and antifungal references.

Minimum inhibitory concentration (MIC)

The antimicrobial activities of the compounds were evaluated through the determination of the minimum inhibitory concentration (MIC) by the micro dilution method in culture broth. For both the antibacterial and the antifungal assays, the compounds were dissolved in DMSO (7 mg/mL) [22, 23]. Further dilutions of the compounds and standard drugs in the test medium were prepared at the required quantities of 200, 100, 50, 10 and 2 mg/mL concentrations. The minimum inhibitory concentration (MIC) values were determined using the method of twofold serial dilutions [24, 25]. In order to ensure that the solvent per se had no effect on bacterial growth, a control test was also performed containing inoculated broth supplemented with only DMSO at the same dilutions used in our experiments and found inactive in culture medium. All of the compounds were tested for their in vitro growth inhibitory activity against different bacteria, fungi and yeast.

B-Antioxidant activity

Determination of scavenging activity against DPPH radicals

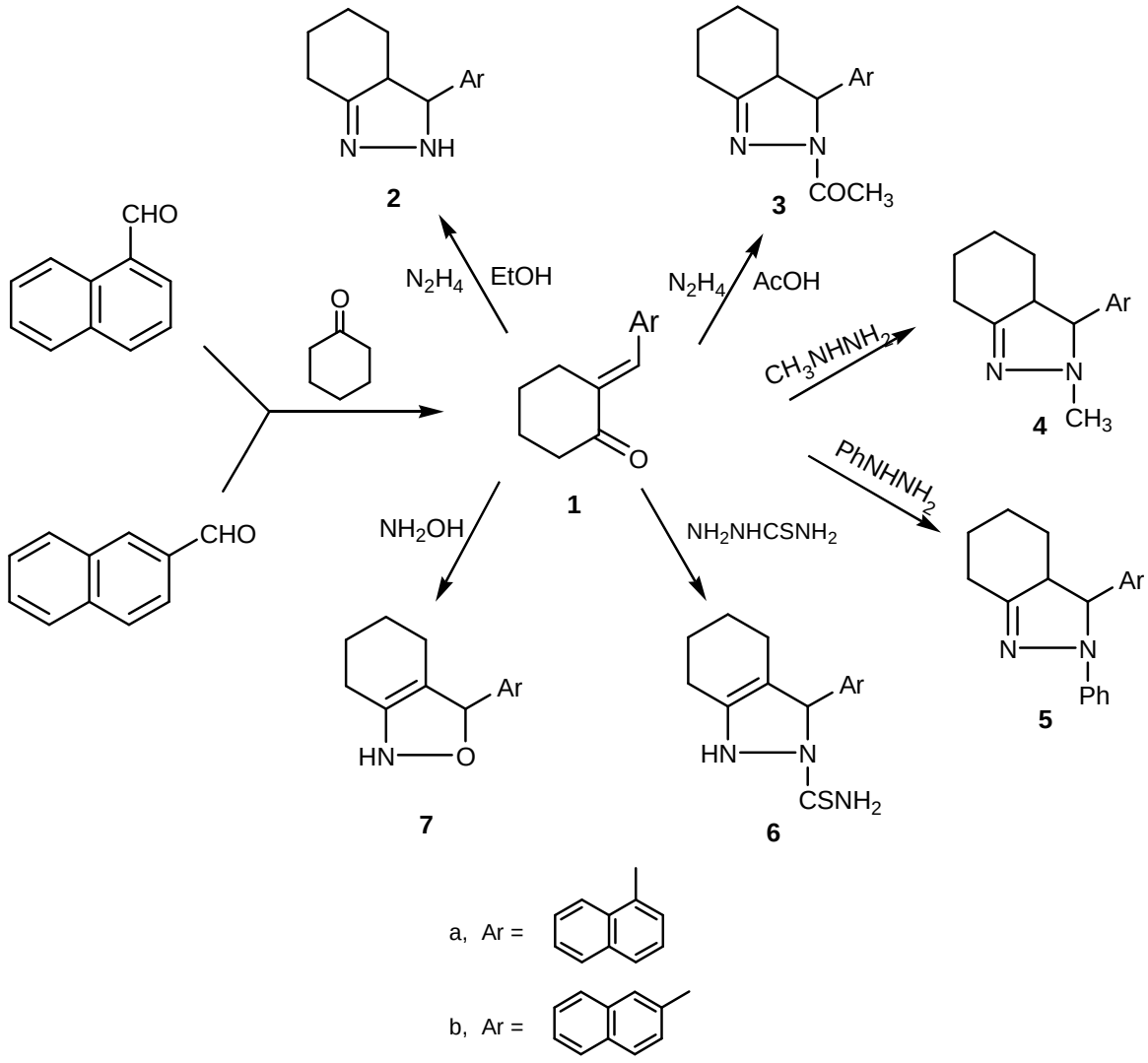
The 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical assay usually involves hydrogen atom transfer reaction but, based on kinetic data, an electron transfer mechanism has also been suggested for this assay [26, 27]. Briefly, stock solutions (10 mg/mL) of each of the synthetic compounds were prepared in methanol [28, 29]. Dilutions were made to obtain concentrations ranging from 2 to 5×10 mg/mL. Diluted solutions (1 mL each) were mixed with 1 mL of freshly prepared 80 µg/mL DPPH radical methanol solutions and allowed to stand for 30 min in the dark at room temperature for any reaction to take place. Absorbance values of these solutions were recorded on an ultraviolet and visible (UV-Vis) spectrometer at 517 nm using a blank containing

the same concentration of DPPH radicals. Inhibitions of DPPH radicals in percent (I %) was calculated as follow:

$I\ \% = [(A_{blank} - A_{sample})/A_{blank}] \times 100$

RESULTS AND DISCUSSION

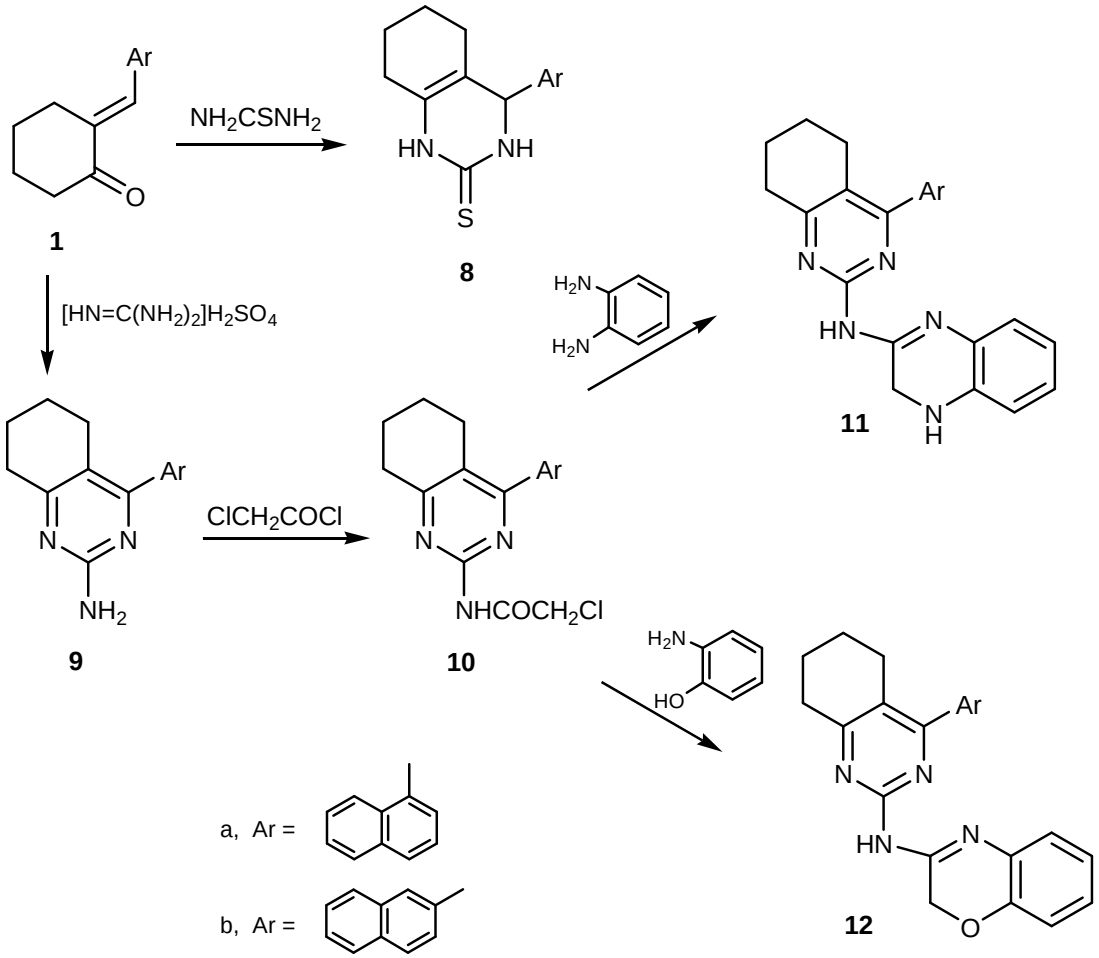
Chemistry



Scheme 1

Chalcones are well known as intermediates for synthesizing various heterocyclic compounds [30]. The desired 2-((naphthalen-1-or-2-yl)methylene)cyclohexanone (**1a,b**) were obtained by condensation of 1-naphthaldehyde and/or 2-naphthaldehyde with cyclohexanone in 5% ethanolic sodium hydroxide. Upon reaction of **1a,b** with hydrazine hydrate in refluxing ethanol gave the

corresponding 3,3a,4,5,6,7-hexahydro-3-(naphthalen-1-or-2-yl)-2*H*-indazole (**2a,b**), while their condensation with hydrazine hydrate in acetic acid afforded the corresponding acetyl indazole derivatives **3a,b** respectively. On the other hand, when cyclocondensation reaction was carried out by using different substituted hydrazines namely; methyl hydrazine and /or phenyl hydrazine in absolute ethanol yields the corresponding *N*-substituted indazole compounds **4a,b**, **5a,b** respectively. Also, the key compounds **1a,b** were allowed to react with thiosemicarbazide in ethanolic sodium hydroxide to give 3,3a,4,5,6,7-hexahydro-3-(naphthalen-1-or-2-yl)indazole-2-carbothioamide (**6a,b**) respectively. Furthermore, cyclocondensation of chalcones **1a,b** with hydroxylamine hydrochloride in alchoholic sodium hydroxide afforded 3,3a,4,5,6,7-hexahydro-3-(naphthalen-1-or-2-yl)benzo[c]isoxazole (**7a,b**) respectively. (Scheme 1)

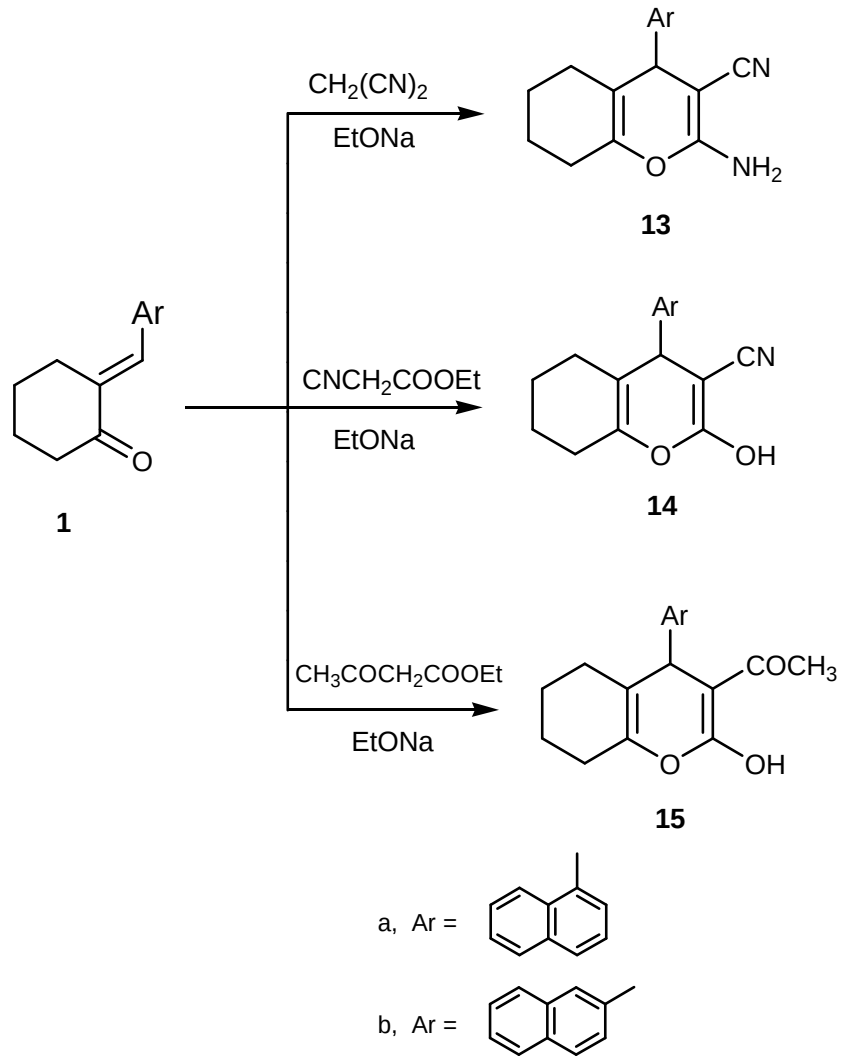


Scheme 2

In addition, reaction of **1a,b** with thiourea in ethanolic sodium hydroxide furnished 3,4,5,6,7,8-hexahydro-4-(naphthalen-1-or-2-yl)quinazoline-2(1*H*)-thione (**8a,b**). At the same time their reactions with guanidine sulphate gave the corresponding intermediates 5,6,7,8-tetrahydro-4-(naphthalen-1-or-2-yl) quinazolin-2-amine (**9a,b**) respectively, which were condensed with chloroacetyl chloride in dry benzene to afforded 2-chloro-*N*-(5,6,7,8-tetrahydro-4-(naphthalen-1-or-2-yl)quinazolin-2-yl)acetamide (**10a,b**) respectively. Further reaction of compound **10a,b**

with ortho phenylenediamine and/or ortho aminophenol in ethanol yielded 3,4-dihydro-*N*-(5,6,7,8-tetrahydro-4-(naphthalen-1-or-2-yl)quinazolin-2-yl)quinoxalin-2-amine (**11a,b**) and *N*-(2*H*-benzo[b][1,4]oxazin-3-yl)-5,6,7,8-tetrahydro-4-(naphthalen-1-or-2-yl)quinazolin-2-amine (**12a,b**) respectively. (Scheme 2)

Furthermore, cyclocondensation of α,β-unsaturated ketone **1a,b** with active methylene group compounds namely; malononitrile, ethylcyanoacetate and/or ethylacetoacetate in sodium ethoxide afforded the chromene derivatives **13a,b-15a,b** respectively. (Scheme 3)



Scheme 3

Table 1. Physical and analytical data of all new compounds 1a,b-15a,b

Comp. no.	m.p. (°C) (Cryst. solvent)	Yield %	Mol. Formula (Mol. Wt.)	Analysis (%)Calcd./ Found			
				C	H	N	S
1a	191-193 (Ethanol)	70	$C_{17}H_{16}O$ (236.31)	86.40 86.67	6.82 7.21		
1b	165-166 (Ethanol)	68	$C_{17}H_{16}O$ (236.31)	86.40 86.21	6.82 6.59		
2a	112 (Ethanol)	64	$C_{17}H_{18}N_2$ (250.34)	81.56 81.37	7.25 7.47	11.19 11.31	
2b	171-172 (Ethanol)	60	$C_{17}H_{18}N_2$ (250.34)	81.56 81.72	7.25 6.97	11.19 11.41	
3a	144-145 (Acetic acid)	71	$C_{19}H_{20}N_2O$ (292.37)	78.05 78.32	6.89 6.53	9.58 9.79	
3b	100 (Acetic acid)	75	$C_{19}H_{20}N_2O$ (292.37)	78.05 78.28	6.89 6.65	9.58 9.37	
4a	179-180 (Ethanol)	69	$C_{18}H_{20}N_2$ (264.36)	81.78 81.44	7.63 7.51	10.60 10.42	
4b	143-145 (Ethanol)	65	$C_{18}H_{20}N_2$ (264.36)	81.78 81.84	7.63 7.49	10.60 10.41	
5a	183-184 (Methanol)	58	$C_{23}H_{22}N_2$ (326.43)	84.63 84.38	6.79 6.51	8.58 8.23	
5b	193-194 (Ethanol)	70	$C_{23}H_{22}N_2$ (326.43)	84.63 84.48	6.79 6.92	8.58 8.62	
6a	159-160 (Methanol)	86	$C_{18}H_{19}N_3S$ (304.43)	69.87 69.53	6.19 6.35	13.58 13.69	10.36 10.11
6b	179-180 (Methanol)	70	$C_{18}H_{19}N_3S$ (304.43)	69.87 69.98	6.19 5.94	13.58 13.78	10.36 10.41
7a	299-300 (Acetic acid)	78	$C_{17}H_{17}NO$ (251.32)	81.24 81.46	6.82 6.61	5.57 5.39	
7b	264-265 (Acetic acid)	69	$C_{17}H_{17}NO$ (251.32)	81.24 81.52	6.82 5.60	5.57 5.78	
8a	269-270 (Methanol)	64	$C_{18}H_{18}N_2S$ (294.41)	73.43 73.66	6.16 6.27	9.51 9.34	10.89 10.64
8b	228-229 (Methanol)	63	$C_{18}H_{18}N_2S$ (294.41)	73.43 73.75	6.16 6.32	9.51 9.68	10.89 10.61
9a	152-153 (Ethanol)	83	$C_{18}H_{17}N_3$ (275.35)	78.52 78.33	6.22 6.38	15.26 15.42	
9b	157-158 (Ethanol)	55	$C_{18}H_{17}N_3$ (275.35)	78.52 78.61	6.22 6.31	15.26 15.01	
10a	169-170 (Ethyl acetate)	80	$C_{20}H_{18}ClN_3O$ (351.83)	68.28 68.41	5.16 5.32	11.94 11.75	
10b	204-205 (Ethyl acetate)	56	$C_{20}H_{18}ClN_3O$ (351.83)	68.28 68.09	5.16 4.92	11.94 11.64	
11a	219-220 (Acetic acid)	87	$C_{26}H_{23}N_5$ (405.49)	77.01 77.28	5.72 5.54	17.27 17.32	
11b	197-198 (Acetic acid)	68	$C_{26}H_{23}N_5$ (405.49)	77.01 77.25	5.72 5.61	17.27 17.10	
12a	213-214 (Acetic acid)	65	$C_{26}H_{22}N_4O$ (406.48)	76.83 76.64	5.46 5.36	13.78 13.66	
12b	180-180 (Acetic acid)	67	$C_{26}H_{22}N_4O$ (406.48)	76.83 76.95	5.46 5.59	13.78 13.91	

13a	137-138 (Ethanol)	92	$C_{20}H_{18}N_2O$ (302.37)	79.44 79.28	6.00 6.24	9.26 9.45	
13b	123-124 (Ethanol)	90	$C_{20}H_{18}N_2O$ (302.37)	79.44 79.60	6.00 6.22	9.26 9.08	
14a	>300 (Acetic acid)	72	$C_{20}H_{17}NO_2$ (303.35)	79.19 79.38	5.65 5.47	4.62 4.51	
14b	229-230 (Acetic acid)	74	$C_{20}H_{17}NO_2$ (303.35)	79.19 79.41	5.65 5.36	4.62 4.77	
15a	>300 (Acetic acid)	56	$C_{21}H_{20}O_3$ (320.38)	78.73 78.51	6.29 6.43		
15b	>300 (Acetic acid)	56	$C_{21}H_{20}O_3$ (320.38)	78.73 78.92	6.29 6.34		

Table 2. Spectral data of the newly synthesized compounds

Comp. no.		IR (KBr, cm^{-1}), ^{1}H.NMR ($CDCl_3$, δ ppm), MS [m/z (%)]
1a	IR ^{1}H.NMR MS	3047 (CH- Ar), 2930, 2864 (CH_2 cyclohexanone), 1663 (C=O, α, β unsaturated ketone). 1.25 (2H, m, CH_2 cyclohexanone), 1.69 (2H, m, CH_2 cyclohexanone), 2.79 (2H, m, CH_2-C=CH cyclohexanone), 3.72 (2H, m, CH_2-C=O cyclohexanone), 7.45-8.41 (8H, m, CH, naphthalene protons). 236 [M^+] (31), 235 [M-1] (52), 179 [$C_{13}H_7O$] (15), 127 [$C_{10}H_7$] (45), 78 [C_6H_6] (100).
1b	IR ^{1}H.NMR MS	3049 (CH- Ar), 2929, 2857 (CH_2 cyclohexanone), 1659 (C=O, α, β unsaturated ketone). 1.23 (2H, m, CH_2 cyclohexanone), 1.86 (2H, m, CH_2 cyclohexanone), 3.07 (2H, m, CH_2-C=CH cyclohexanone), 3.72 (2H, m, CH_2-C=O cyclohexanone), 7.50-7.98 (8H, m, CH, naphthalene protons). 236 [M^+] (4), 235 [M-1] (3), 178 [$C_{13}H_6O$] (5), 127 [$C_{10}H_7$] (8), 78 [C_6H_6] (93), 63 [C_5H_3] (100).
2a	IR ^{1}H.NMR MS	3329 (NH), 3048 (CH- Ar), 2928, 2858 (CH_2 2*H*-indazole). 1.23, 1.71, 2.10, 2.78 (8H, m, $H_{4,5,6,7}$ 2*H*-indazole), 3.71 (1H, m, H_{3a} 2*H*-indazole), 5.37 (1H, d, H_3 2*H*-indazole), 7.41-8.11 (7H, m, naphthalene protons), 10.41 (1H, s, NH which exchangeable by D_2O). 250 [M^+] (10), 249 [M-1] (13), 235 [M-NH] (6), 234 [235-H] (10), 194 [$C_{13}H_{10}N_2$] (3), 127 [$C_{10}H_7$] (18), 78 [C_6H_6] (30), 45 [C_3H_9] (100).
2b	IR ^{1}H.NMR MS	3289 (NH), 3048 (CH- Ar), 2923, 2852 (CH_2 2*H*-indazole). 1.13, 1.62, 1.96, 2.42 (8H, m, $H_{4,5,6,7}$ 2*H*-indazole), 3.50 (1H, m, H_{3a} 2*H*-indazole), 5.01 (1H, d, H_3 2*H*-indazole), 7.41-7.96 (7H, m, naphthalene protons), 10.01(1H, s, NH which exchangeable by D_2O). 250 [M^+] (3), 249 [M-1] (7), 234 [M-NH_2] (11), 194 [$C_{13}H_{10}N_2$] (4), 127 [$C_{10}H_7$] (56), 77 [C_6H_5] (14), 63 [C_5H_3] (100).
3a	IR ^{1}H.NMR MS	3046 (CH- Ar), 2935, 2860 (CH_2 2*H*-indazole), 1662 (C=O amide). 1.24, 1.80, 2.38, 2.80 (8H, m, $H_{4,5,6,7}$ 2*H*-indazole), 2.88 (3H, s, CH_3CO), 3.72 (1H, m, H_{3a} 2*H*-indazole), 4.31 (1H, d, H_3 2*H*-indazole), 7.50-8.14 (7H, m, naphthalene protons). 292 [M^+] (7), 291 [M-1] (3), 249 [M-$COCH_3$] (9), 194 [$C_{13}H_{10}N_2$] (2), 127 [$C_{10}H_7$] (16), 77 [C_6H_5] (5), 43 [C_3H_7] (100).
3b	IR ^{1}H.NMR MS	3049 (CH- Ar), 2932, 2860 (CH_2 2*H*-indazole), 1664 (C=O amide). 1.18, 1.71, 2.30, 2.61 (8H, m, $H_{4,5,6,7}$ 2*H*-indazole), 2.71 (3H, s, CH_3CO), 3.67 (1H, m, H_{3a} 2*H*-indazole), 4.22 (1H, d, H_3 2*H*-indazole), 7.50-7.97 (7H, m, naphthalene protons). 293 [M+1] (19), 292 [M^+] (30), 291 [M-1] (14), 250 [M-$COCH_2$] (31), 127 [$C_{10}H_7$] (100).
4a	IR ^{1}H.NMR MS	3052 (CH- Ar), 2937, 2855 (CH_2 2*H*-indazole). 1.23, 1.71, 2.46, 2.79 (8H, m, $H_{4,5,6,7}$ 2*H*-indazole), 2.53 (3H, s, CH_3), 3.70 (1H, m, H_{3a} 2*H*-indazole), 5.20 (1H, d, H_3 2*H*-indazole), 7.45-8.41 (7H, m, naphthalene protons). 264 [M^+] (5), 263 [M-1] (5), 251 [M-CH] (4), 43 [C_3H_7] (100).
4b	IR ^{1}H.NMR MS	3050 (CH- Ar), 2923, 2850 (CH_2 2*H*-indazole). 1.19, 1.69, 2.42, 2.72 (8H, m, $H_{4,5,6,7}$ 2*H*-indazole), 2.41 (3H, s, CH_3), 3.68 (1H, m, H_{3a} 2*H*-indazole), 5.10 (1H, d, H_3 2*H*-indazole), 7.45-7.98 (7H, m, naphthalene protons). 264 [M^+] (10), 263 [M-1] (8), 250 [M-CH_2] (4), 63 [C_5H_3] (100).

5a	IR	3045 (CH- Ar), 2940, 2856 (CH_2 2*H*-indazole).
	^{1}H.NMR	1.24, 1.68, 1.71, 2.79 (8H, m, $H_{4,5,6,7}$ 2*H*-indazole), 3.70 (1H, m, H_{3a} 2*H*-indazole), 4.80 (1H, d, H_3 2*H*-indazole), 7.46-8.41 (12H, m, Ar-H, naphthalene protons).
	MS	324 [M-2] (2), 250 [M-C_6H_4] (5), 127 [$C_{10}H_7$] (9), 43 [C_3H_7] (100).
5b	IR	3049 (CH- Ar), 2924, 2853 (CH_2 2*H*-indazole).
	^{1}H.NMR	1.18, 1.56, 1.62, 2.43 (8H, m, $H_{4,5,6,7}$ 2*H*-indazole), 3.51 (1H, m, H_{3a} 2*H*-indazole), 4.66 (1H, d, H_3 2*H*-indazole), 7.46-7.99 (12H, m, Ar-H, naphthalene protons).
	MS	326 [M^+] (5), 250 [M-C_6H_4] (8), 127 [$C_{10}H_7$] (12), 63 [C_5H_3] (100).
6a	IR	3437, 3264, 3145 (NH, NH_2), 3046 (CH- Ar), 2929, 2859 (CH_2 1*H*-indazole), 1165 (C=S).
	^{1}H.NMR	1.25, 1.69, 1.95, 2.60 (8H, m, $H_{4,5,6,7}$ 1*H*-indazole), 5.16 (1H, s, H_3 1*H*-indazole), 7.25-8.51 (7H, m, naphthalene protons), 9.46, 9.80 (3H, s, NH, NH_2 which exchangeable by D_2O).
	MS	305 [M+1] (2), 304 [M^+] (2), 244 [M-$CSNH_2$] (2), 151 [$C_{11}H_5N$] (100).
6b	IR	3381, 3248, 3150 (NH, NH_2), 3050 (CH- Ar), 2926, 2857 (CH_2 1*H*-indazole), 1179 (C=S).
	^{1}H.NMR	1.78, 1.64, 1.91, 2.44 (8H, m, $H_{4,5,6,7}$ 1*H*-indazole), 4.82 (1H, s, H_3 1*H*-indazole), 7.23-7.95 (7H, m, naphthalene protons), 9.30, 10.10 (3H, s, NH, NH_2 which exchangeable by D_2O).
	MS	305 [M+1] (8), 304 [M^+] (10), 244 [M-$CSNH_2$] (5), 77 [C_6H_5] (100).
7a	IR	3412 (NH), 3049 (CH- Ar) and 2927, 2859 (CH_2 benzo[c]isoxazole).
	^{1}H.NMR	1.25, 1.59, 1.75, 2.73 (8H, m, $H_{4,5,6,7}$ benzo[c]isoxazole), 5.15 (1H, s, H_3 benzo[c]isoxazole), 7.25-8.78 (7H, m, naphthalene protons), 10.41 (1H, s, NH which exchangeable by D_2O).
	MS	250 [M-1] (2), 248 [M-3] (16), 125 [$C_{10}H_5$] (100).
7b	IR	3409 (NH), 3050 (CH- Ar), 2921, 2853 (CH_2 benzo[c] isoxazole).
	^{1}H.NMR	1.21, 1.50, 1.69, 2.45 (8H, m, $H_{4,5,6,7}$ benzo[c]isoxazole), 4.83 (1H, s, H_3 benzo[c]isoxazole), 7.25-8.10 (7H, m, naphthalene protons), 11.04 (1H, s, NH which exchangeable by D_2O).
	MS	250 [M-1] (1), 249 [M-2] (5), 247 [M-4] (16), 125 [$C_{10}H_5$] (100).
8a	IR	Broad band centered at 3432 (NH), 3052 (CH- Ar), 2925, 2854 (CH_2 quinazoline-2-thione).
	^{1}H.NMR	1.22, 1.57, 1.98, 2.47 (8H, m, $H_{5,6,7,8}$ quinazoline-2-thione), 5.82 (1H, s, H_4 quinazoline-2-thione), 7.04-8.18 (7H, m, naphthalene protons).
	MS	294 [M^+] (25), 293 [M-1] (26), 219 [M-CH_3N_2S] (25), 164 [$C_8H_8N_2S$] (100).
8b	IR	3417, 3175 (NH), 3050 (CH- Ar), 2923, 2853 (CH_2 quinazoline-2-thione).
	^{1}H.NMR	1.18, 1.43, 1.97, 2.23 (8H, m, $H_{5,6,7,8}$ quinazoline-2-thione), 5.62 (1H, s, H_4 quinazoline-2-thione), 7.04-7.91 (7H, m, naphthalene protons).
	MS	294 [M^+] (30), 293 [M-1] (15), 127 [$C_{10}H_7$] (100).
9a	IR	Broad band centered at 3288 (NH_2), 3049 (CH- Ar), 2921, 2855 (CH_2 quinazolin-2-amine).
	^{1}H.NMR	1.26, 1.52, 2.35, 2.65 (8H, m, $H_{5,6,7,8}$ quinazolin-2-amine), 7.42-7.80 (7H, m, naphthalene protons), 8.63 (2H, s, NH_2 which exchangeable by D_2O).
	MS	273 [M-2] (2), 127 [$C_{10}H_7$] (12), 45 [C_3H_9] (100).
9b	IR	3293, 3167 (NH_2), 3053 (CH- Ar), 2923, 2852 (CH_2 quinazolin-2-amine).
	^{1}H.NMR	1.21, 1.48, 2.31, 2.55 (8H, m, $H_{5,6,7,8}$ quinazolin-2-amine), 7.32-7.78 (7H, m, naphthalene protons), 9.10 (2H, s, NH_2 which exchangeable by D_2O).
	MS	275 [M-2] (10), 127 [$C_{10}H_7$] (100),
10a	IR	3203 (NH), 3049 (CH- Ar), 2924, 2851 (CH_2 quinazoline), 1678 (C=O, amide).
	^{1}H.NMR	1.21, 1.48, 2.29, 2.42 (8H, m, $H_{5,6,7,8}$ quinazoline), 4.03 (2H, s, CH_2), 7.04-7.44 (7H, m, naphthalene protons), 9.86 (1H, s, NH which exchangeable by D_2O).
	MS	353, 351 [M^+] (5, 2), 127 [$C_{10}H_7$] (5), 62 [C_4H_{14}] (100).
10b	IR	3208 (NH), 3049 (CH- Ar), 2933, 2854 (CH_2 quinazoline), 1674 (C=O, amide).
	^{1}H.NMR	1.19, 1.39, 2.21, 2.35 (8H, m, $H_{5,6,7,8}$ quinazoline), 3.99 (2H, s, CH_2), 7.09-7.41 (7H, m, naphthalene protons), 10.02 (1H, s, NH which exchangeable by D_2O).
	MS	353, 351 [M^+] (10, 3), 127 [$C_{10}H_7$] (100.
11a	IR	Broad band centered at 3200 (2 NH), 3049 (CH- Ar), 2933, 2855 (CH_2 quinazoline).
	^{1}H.NMR	1.46, 1.62, 2.29, 2.39 (8H, m, $H_{5,6,7,8}$ quinazoline), 5.31 (2H, s, quinoxaline), 7.32-7.73 (11H, m, Ar-H, naphthalene protons), 8.93, 9.93 (2H, s, 2 NH which exchangeable by D_2O).
	MS	405 [M^+] (5), 127 [$C_{10}H_7$] (100).
11b	IR	Broad band centered at 3208 (2 NH), 3049 (CH- Ar), 2931, 2850 (CH_2 quinazoline).

	^{1}H.NMR	1.38, 1.51, 2.11, 2.31 (8H, m, $H_{5,6,7,8}$ quinazoline), 5.20 (2H, s, quinoxaline), 7.28-7.70 (11H, m, Ar-H, naphthalene protons), 9.12, 10.10 (2H, s, 2 NH which exchangeable by D_2O).
	MS	403 [M-2] (10), 127 [$C_{10}H_7$] (100).
12a	IR	3197 (NH), 3047 (CH- Ar), 2932, 2853 (CH_2 quinazoline).
	^{1}H.NMR	1.24, 1.45, 2.29, 2.29 (8H, m, $H_{5,6,7,8}$ quinazoline), 5.08 (2H, s, CH_2 benzoxazine), 7.40-7.80 (11H, m, Ar-H, naphthalene protons), 9.95 (1H, s, NH which exchangeable by D_2O).
	MS	406 [M^+] (6), 127 [$C_{10}H_7$] (100).
12b	IR	3203 (NH), 3049 (CH- Ar), 2933, 2854 (CH_2 quinazoline).
	^{1}H.NMR	1.18, 1.23, 2.11, 2.25 (8H, m, $H_{5,6,7,8}$ quinazoline), 4.89 (2H, s, CH_2 benzoxazine), 7.30-7.85 (11H, m, Ar-H, naphthalene protons), 9.73 (1H, s, NH which exchangeable by D_2O).
	MS	405 [M-1] (6), 77 [C_6H_5] (100).
13a	IR	Broad band centered at 3371 (NH_2), 3054 (CH- Ar), 2925, 2857 (CH_2 4*H*-chromene), 2218 (C≡N).
	^{1}H.NMR	1.45, 1.53, 1.61, 2.67 (8H, m, $H_{5,6,7,8}$ 4*H*-chromene), 4.09 (1H, s, H_4 4*H*-chromene), 7.45-7.94 (7H, m, naphthalene protons), 8.62 (2H, s, NH_2 which exchangeable by D_2O).
	MS	303 [M+1] (12), 258 [$C_{19}H_{14}O$] (25), 128 [$C_{10}H_8$] (46), 62 [C_4H_{14}] (100).
13b	IR	3340, 3218 (NH_2), 3053 (CH- Ar), 2927, 2859 (CH_2 4*H*-chromene), 2216 (C≡N).
	^{1}H.NMR	1.41, 1.49, 1.59, 2.60 (8H, m, $H_{5,6,7,8}$ 4*H*-chromene), 4.21 (1H, s, H_4 4*H*-chromene), 7.38-7.90 (7H, m, naphthalene protons), 8.88 (2H, s, NH_2 which exchangeable by D_2O).
	MS	302 [M^+] (3), 258 [$C_{19}H_{14}O$] (6), 127 [$C_{10}H_7$] (37), 43 [C_3H_7] (100).
14a	IR	Broad band centered at 3422 (OH), 3058 (CH- Ar), 2942, 2851 (CH_2 4*H*-chromene), 2194 (C≡N).
	^{1}H.NMR	1.23, 1.54, 1.70, 2.79 (8H, m, $H_{5,6,7,8}$ 4*H*-chromene), 3.70 (1H, s, H_4 4*H*-chromene), 7.45-8.41 (7H, m, naphthalene protons).
	MS	303 [M^+] (5), 302 [M-1] (8), 127 [$C_{10}H_7$] (9), 63 [C_5H_3] (100).
14b	IR	Broad band centered at 3329 (OH), 3053 (CH- Ar), 2947, 2852 (CH_2 4*H*-chromene), 2173 (C≡N).
	^{1}H.NMR	1.18, 1.50, 1.67, 2.56 (8H, m, $H_{5,6,7,8}$ 4*H*-chromene), 3.91 (1H, s, H_4 4*H*-chromene), 7.31-7.81 (7H, m, naphthalene protons).
	MS	303 [M^+] (9), 127 [$C_{10}H_7$] (25), 78 [C_6H_6] (100).
15a	IR	Broad band centered at 3424 (OH), 3055 (CH- Ar), 2931, 2859 (CH_2 4*H*-chromene), 1705 (C=O).
	^{1}H.NMR	1.24, 1.70, 2.25, 2.79 (11H, m, $H_{5,6,7,8}$ 4*H*-chromene, $COCH_3$), 3.71 (1H, s, H_4 4*H*-chromene), 7.45-8.41 (7H, m, naphthalene protons).
	MS	318 [M-2] (8), 305 [M- CH_3] (3), 277 [M-$COCH_3$] (3), 128 [$C_{10}H_8$] (62), 77 [C_6H_5] (100).
15b	IR	Broad band centered at 3408 (OH), 3053 (CH- Ar), 2932, 2854 (CH_2 4*H*-chromene), 1703 (C=O).
	^{1}H.NMR	1.19, 1.68, 2.23, 2.68 (11H, m, $H_{5,6,7,8}$ 4*H*-chromene, $COCH_3$), 3.64 (1H, s, H_4 4*H*-chromene), 7.40-7.91 (7H, m, naphthalene protons).
	MS	320 [M+] (5), 318 [M-2] (7), 127 [$C_{10}H_7$] (51), 77 [C_6H_5] (100).

Antimicrobial activity

The in vitro antimicrobial activity of the thirty synthesized compounds using agar diffusion method was represented table 3. While the data of table 4 represented MIC of the tested compounds in comparing to the reference drugs. Table 3 investigated that the compounds **1a,b-5a,b** didn't show any antimicrobial activity and this might be explained that these derivatives that contain cyclohexanone and/or indazole moieties in attachment to naphthalene ring are less lipophilic agents than the other derivatives **6a,b-15a,b** thus their diffusions through the bacterial or fungal cell membranes to induce their activities were inhibited [31].

The results of table 4 showed that the significant antibacterial activity was obtained in the presence of tetrahydroindazole-2-carbothioamide moiety **6a,b** against gram negative bacteria *E.coli* and gram positive *B.subtilus*, but the activity was lost against *S.aureus* in comparison with gentamicin, ampicillin and chloramphenicol. Hexahydrobenzoisoxazole in attachment with 1-and 2-naphthalene ring **7a,b** demonstrated significant inhibition against *B.subtilus*, moderate activity against *E.coli* and complete activity loss against *S.aureus* comparing to gentamicin, ampicillin

and chloramphenicol. The attachment of hexahydroquinazoline-2-thione moiety with 1-naphthalene ring **8a** exhibited potent antibacterial activity against *S.aureus* and gram negative *E.coli* and moderate activity against *B.subtilus* comparing to amoxycillin while its attachment to 2-naphthalene **8b** abolished the antibacterial against *E.coli* and signified the activity against *B.subtilus* to be equipotent to gentamicin, ampicillin and chloramphenicol. The replacement of the sulfur atom with amino group **9a,b** increased the activity against *E.coli* and intensified the activity against *B.subtilus* and *S.aureus* to be gentamicin, amicillin and chloramphenicol equipotent except compound **9a** which lost activity against *S.aureus.* Generally the amino group improved the antimicrobial activity.

The presence of chloracetamido group instead of the amino group **10a,b** gave approximately the same results of the amino group with significant inhibition of *S.aureus* for both derivatives comparing with gentamicin, ampicillin and chloramphenicol. Further substitution of the amino group with quinoxaline nucleus **11a,b** significantly increased the anti *E.coli* activity in addition to the tested gram positive bacteria when compared with gentamicin, amicillin and chloramphenicol. When the amino group was substituted with benzoxazine ring system **12a,b** showed gentamicin and ampicillin equipotency with respect to gram positive bacteria and amoxycillin equipotency with respect to gram negative bacteria. The presence of tetrahydrochromene-3-carbonitrile moiety in attachment to 2-naphthalene ring **14b** abolished the activity against the tested gram negative *E.coli*, while it showed potent activity against gram positive bacteria *S.aureus* and moderate activity against *B.subtilus* in comparing to amoxycillin. The replacement of the cyano group of the chromene moiety with acetyl group **15a** didn't affect the antibacterial activity against gram negative *E.coli* and gram positive *S.aureus* and increased the potency against *B.subtilus*. But the activity was highly increased against the tested gram negative bacteria in case of 2-naphthyl attachment **15b** taking amoxycillin as a reference drug.

It can be concluded that best antibacterial activity against both gram positive and gram negative bacteria was obtained in the presence of quinoxaline in attachment to aminoquinozoline moiety **11a,b**. All the derivatives showed weak antifungal effect against *C-albicans* and complete loss of activity was observed against *A-niger* in case of the derivatives **6a,b-8a,b, 9a**, **14a, 15a,b** while the derivatives **9a, 10a,b-12a,b** showed weak activity.

Table 3. Antimicrobial activity of newly synthesized compounds

Comp. No.	Inhibition zone (mm)				
	Gram-negative	Gram-positive		Fungal species	
	E. coli	***B. subtilus***	***S. aureus***	***C. albicans***	***A. niger***
1a	0	0	0	0	0
1b	0	0	0	0	0
2a	0	0	0	0	0
2b	0	0	0	0	0
3a	0	0	0	0	0
3b	0	0	0	0	0
4a	0	0	0	0	0
4b	0	0	0	0	0
5a	0	0	0	0	0
5b	0	0	0	0	0

6a	18	19	11	13	16
6b	19	22	11	17	12
7a	17	23	0	11	17
7b	14	18	0	16	12
8a	16	14	17	14	11
8b	15	16	17	12	16
9a	13	14	14	16	14
9b	23	26	18	18	16
10a	27	32	22	22	18
10b	22	17	17	21	20
11a	20	23	20	22	22
11b	19	24	17	17	21
12a	18	23	16	18	18
12b	21	21	17	14	19
13a	14	13	14	13	15
13b	12	11	11	11	14
14a	16	16	12	13	16
14b	0	14	17	11	11
15a	0	24	16	14	14
15b	17	26	17	13	14
Gentamicin	17	18	18	14	0
Ampicillin	18	18	18	17	15
Amoxycillin	18	18	18	17	15
Tetracyclinol	18	18	22	15	14
Chloramphenicol	23	20	16	15	14
Fluconazole	18	18	15	15	13
DMSO	0	0	0	0	0

The sensitivity of microorganisms to the tested compounds is identified in the following manner:
Highly sensitive = Inhibition zone 21–35 mm
Moderately sensitive = Inhibition zone: 11–20 mm
Slightly sensitive = Inhibition zone: 5–10 mm
Not sensitive = Inhibition zone: 0 mm

Table 4: Antimicrobial activity (MIC values in *µ*g/ mL) of synthesized compounds and the standard drugs used in the study

Comp. no.	Minimum inhibitory concentration in µg/mL				
	Gram-negative	Gram-positive		Fungal species	
	E. coli	***B. subtilus***	***S. aureus***	***C. albicans***	***A. niger***
6a	>50	>50	0	>200	0
6b	>50	>50	0	>150	0
7a	>100	>50	0	>200	0
7b	>200	>50	0	>200	0
8a	>100	>200	>100	>200	0
8b	0	>50	>100	>200	0
9a	>150	>50	0	>150	0
9b	>100	>50	>50	>100	>150
10a	>50	>50	>50	>100	>150
10b	>100	>50	>50	>100	>150
11a	>50	>50	>50	>150	>150
11b	>50	>50	>50	>150	>150

12a	>100	>50	>50	>100	>150
12b	>100	>50	>50	>150	>150
14b	0	>150	>100	>150	0
15a	0	>100	>100	>150	0
15b	>100	>100	>100	>150	0
Gentamicin	>50	>50	>25	0	0
Ampicillin	>50	>50	>50	0	0
Amoxycillin	>100	>100	>100	0	0
Tetracyclinol	>25	>25	>25	0	0
Chloramphenicol	>50	>50	>50	>25	>25
Fluconazole	0	0	0	>25	>100

CONCLUSION

Most of the synthesized compounds exhibited moderate to potent antibacterial activity against the tested gram negative and gram positive comparable to gentamicin, ampicillin, chloramphenicol (MIC > 50 µg/mL) and amoxicillin (>100 µg/mL) but no one of the derivatives showed tetracyclinol equipotency (MIC >25 µg/mL).
The antifungal activity of the synthesized compounds ranges from weak to complete loss of the activity against the tested fungal species in comparison with the fluconazole.

The resulted antimicrobial activity of the newly synthesized derivatives didn't be affected by either substitution at position 1 or 2 of naphthalene moiety, this mean no steric hindrance affected the activity of the derivatives.

Antioxidant activity
Table 5 presented the antioxidant activity of the novel derivatives in comparison to ascorbic acid which showed 96% of DPPH radical inhibition. The derivatives containing N-substituted (unsubstituted) indazole nucleus with acetyl, methyl and/or phenyl groups at either 1- or 2-naphthalene ring **2a,b-5a,b** didn't show any antioxidant activity. The derivatives carrying indazole carbothioamide, benzo[c]isoxazole, acetamidoquinazoline, benzo[b]oxazine, aminochromene rings at 2-naphthalene moiety (**6b**, **7b**, **10b**, **12b 13b**) and aminochromene, hydroxychromene moieties at 1-naphthalene (**13a**, **14a**) showed ≥ 20% DPPH radical inhibitory effect.

Also the figures showed that the derivatives containing 1- and 2- naphthalenyl cyclohexanone (**1a,b**), quinazoline-2-thione, aminoquinazoline, benzo[b]oxazine at 1-naphthalene (**8a**, **9a**, **12a**), aminoquinoxaline, chromene-3-carbonitrile and chromene-3-acetyl at 2-naphthalene (**11b**, **14b**, **15b**) showed ≥ 50% inhibition of DPPH radicals. Highest antioxidant activity ≥ 70% was obtained by the derivatives containing 1-naphthalenyl indazolecarbothioamide , benzo[c]isoxazole, acetamidoquinazoline, amioquinoxaline and chromene-3-acetyl (**6a**, **7a**, **10a**, **11a**, **15a**), 2-naphthalenyl quinazoline-2-thione and quinazoline-2-amine (**8b**, **9b**).

Table 5: Antioxidant activity of newly synthesized compounds

Comp. No.	% DPPH inhibition
1a	55.24
1b	50.10
2a	0
2b	0
3a	0
3b	0
4a	0
4b	0
5a	0
5b	0
6a	70.01
6b	27.90
7a	78.65
7b	24.90
8a	53.75
8b	72.47
9a	54.68
9b	70.10
10a	72.47
10b	21.16
11a	70.13
11b	64.98
12a	50.62
12b	43.63
13a	44.76
13b	27.34
14a	20.97
14b	53.37
15a	70.05
15b	50.23
Ascorbic acid	96.00

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