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Synthesis And Biological Evaluation of Some New Quinazoline Derivatives

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ABSTRACT

OBJECTIVE: Quinazolines have gained significant attention due to their diverse pharmacological activities, including anti-inflammatory, antimicrobial, analgesic, hypnotic, sedative, antifungal, antispasmodic, antidiabetic, anti-tubercular, CNS depressant, and anti-cancer properties. Recent studies indicate that quinazoline derivatives exhibit moderate activity against various cancer cell lines and HIV. Additionally, several research articles have documented their antihistaminic properties. Given the importance of these heterocyclic compounds in medicinal chemistry, we aim to synthesize novel substituted quinazolines, characterize the synthesized compounds using IR and ^{1}H-NMR spectral data, and evaluate their antibacterial activity.

METHODOLOGY: The synthesis involves preparing different substituted 2-methylquinazolines using various substituted anilines. Final derivatives are obtained through the condensation of these 2-methylquinazolines with substituted aromatic aldehydes. The resultant quinazoline derivatives were purified using appropriate solvents, yielding 40-65%. Thin Layer Chromatography (TLC) was performed with chloroform: ethyl acetate (7:3) as the eluent to confirm the attachment.

EXPERIMENTAL: Melting points were determined using Thiele's tube in open capillaries and are reported uncorrected. The purity of the compounds was assessed by TLC on silica gel G plates with chloroform: ethyl acetate (7:3) as the solvent system, visualized under UV light. IR spectra were recorded using KBr pellets on a Shimadzu 8000 series spectrophotometer. ^{1}H-NMR spectra were obtained on a Varian EM-200, 200 MHz spectrophotometer with DMSO as the solvent and TMS as the internal standard (chemical shift values are expressed in ppm).

INTERPRETATION:

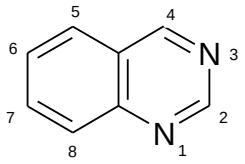
Compound HA: ^{1}H-NMR (ppm): 2.4 (s, CH_3), 3.0 (s, CH_2), 6.2 (s, NH), 7.1-8.6 (m, Ar-H).

BIOLOGICAL EVALUATION:

ANTIBACTERIAL ACTIVITY: Antibacterial activity was assessed using the disc-diffusion method against Bacillus subtilis, Bacillus pumilus, Escherichia coli, and Pseudomonas aeruginosa. The potency of the synthesized compounds was measured against the standard drug Ampicillin by determining the zone of inhibition.

RESULTS: The synthesized compounds were screened for antibacterial activity at concentrations of 50 µg/ml and 100 µg/ml, using DMF as a control against Escherichia coli, Bacillus pumilus, Bacillus subtilis, and Pseudomonas aeruginosa on nutrient agar media. Ampicillin at 50 µg/ml and 100 µg/ml was used as a standard against Gram-positive and Gram-negative bacteria. The synthesized agents demonstrated significant antibacterial activity.

INTRODUCTION: Quinazoline[1] or 1, 3-diazo naphthalene represented by structure (1) has also been given names like *phenazine, benzo-1, 3-diazine, or 5, 6-benzo pyrimidine*. It was first prepared by Gabriel in 1903.



(1)

Quinazoline is a solid, m.p. 48 C, and can be recrystallized from ether. It is soluble in water and most of the organic solvents. It is basic (pka 1.4) in nature. Generally, a suitably substituted anthranilic acid serves as a precursor of

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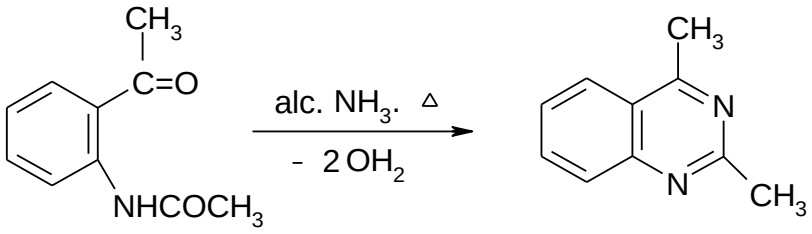
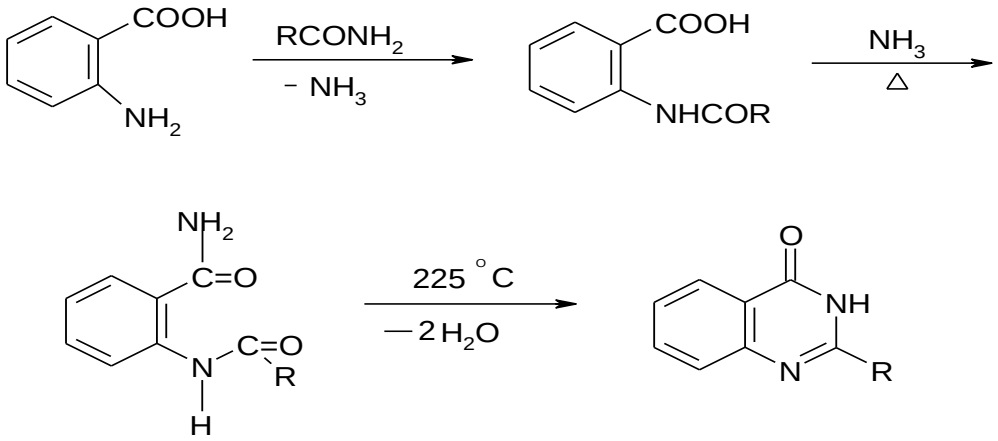
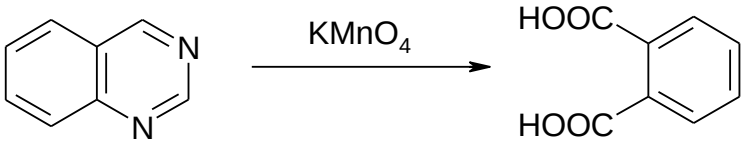
quinazolines—Schofield *et al* [2] synthesized quinazoline derivatives by heating the acyl derivative of *o*-aminoacetophenone with ammonia. The reaction is of general applicability[3]. 2,4-dimethylquinazoline can be obtained starting from o-acetamido acetophenone.



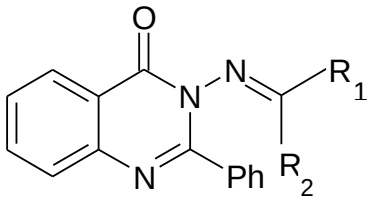
Anthranilic acid on fusion with aliphatic amide yields the 4-quinazoline derivative[4]. This is called the *Niemantowaski reaction.*



Quinazoline forms stable monobasic salts. Nitration appears to be the only known electrophilic substitution reaction of quinazolines. Nitration (fuming nitric acid, conc. H_2SO_4) gives 6-nitroquinazoline though theoretically 8-position is expected to be more reactive[5]. Quinazoline is stable to oxidation but under drastic conditions, the benzene ring is ruptured to yield 4-pyrimidine dicarboxylic acids.



Quinazoline-1-oxide is unknown although 4-substituted derivatives have been prepared. Quinazoline 3-oxide, however, has been prepared. Quinazolines on reduction (Na / CH_3OH) yield the 1,2,3,4-tetrahydro derivatives. Quinazolines are reported to have a number of biological activities. Nautiyal *et al.* [6]., has reported antiviral and hypoglycemic activities of substituted 2-phenyl-3-[2-substituted anilino thiadiazolyl –5- (N- mercaptophenyl) quinozolin-4-one.
V. Algarsamy[7] has reported the antibacterial and antifungal activities of 2, 3-disubstituted quinazolines-4(3H) (2).



(2)

R_1= CH_3
R_2= CH_2CH_3

3-[5-substituted 1, 3, 4- thiadiazole-2-yl]-2-styryl quinazoline (3) was synthesized[8] by refluxing equimolar quantities of 3-(1, 3, 4- thiadiazole-2-yl)-2- methyl quinazoline and aromatic aldehydes in GAA.

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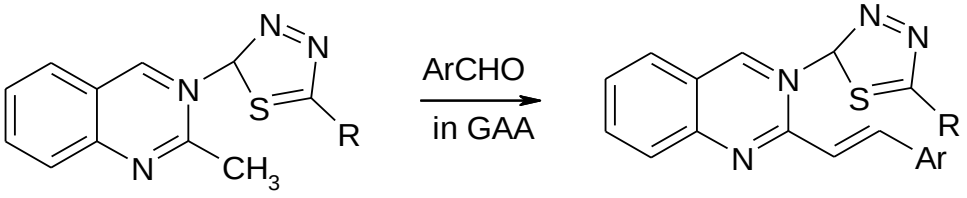
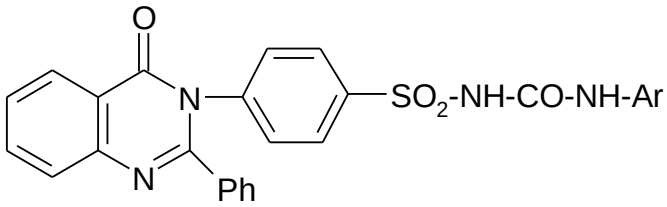


(3)

Quinazolines [9-10] and the compound containing the sulphonyl group[11-12] are known to possess hypoglycemic and antidiabetic activity respectively. Reddy *et. al*[13]., have reported hypoglycemic activity of some 1-quinazolinonyl-3-arylcyclohexylsulphonyl-2-thioureas.1-[β-(4-oxo-2-ethyl/phenyl-3-4 (H) quinazolinyl phenyl) sulphonyl] -3-aryl-2-ureas (4) were reported to have hypoglycemic activity[14] against streptrozoscine induced diabetic rats.

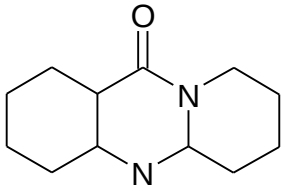


Ar = Phenyl (a)

= p-Tolyl (b)

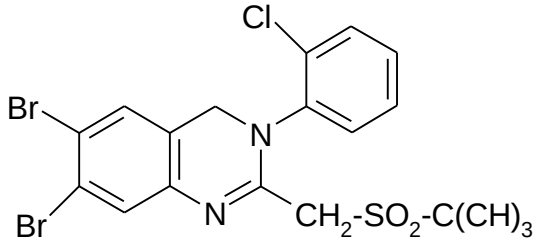
(4)

Bronchodilator activity of N-alkyl, aryl analogous of 2, 3, 4, 5-tetrahydroazepino [2,1-b] quinazoline –11-1(H)-one has been reported[15]. Mild CVS and anti-inflammatory activities of some 2-(phenyl/Chloro-methyl) -(N, N-disubstituted amino carbonyl phenyl)-8- substituted-4- (3H)-quinazoline has been reported by Srimal *et al*[16]., azepine [2,1-b]quinazolin-12-(6H) –one–7,8,9,10-tetrahydro (5) is having anti-inflammatory activity[17].



(5)

Antifungal activity of 2-(4-aryl-2-pyrazolin-3-yl)-3-aryl-4- (3H)-Quinazolines have been tested[18]. Compound 3-[4-[3-(4-hydroxyphenyl)-one-oxo- (2,3-dibromo) propane phenyl]-2-phenyl-4- 3(H)- quinazolinone was found to have pesticidal activity against H.Nana[19].6, 7-dibromo-2-(t-butylsulphono) methyl-3-ortho chlorophenyl-4-(3H) –quinazolinone (6) has been found to have potential antispasmodic activity [20].



(6)

Reddy *et. al* [21]., have reported antimicrobial activity of 3-aryl-2-[2-(chromon-3-yl) vinyl]-4-(3H)-quinazolinones.

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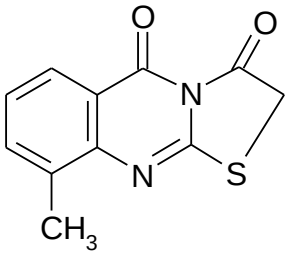
Pujari *et al* [22]., reported the synthesis of 9-methyl-thiazole [2,3-b]-quinazoline-3,5-dion (7). Similarly, compounds (8) and (9) have been synthesized.



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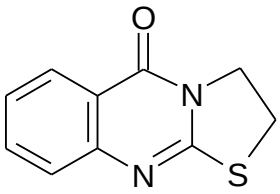

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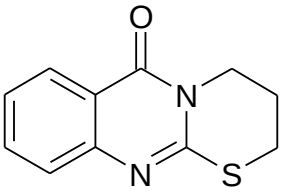
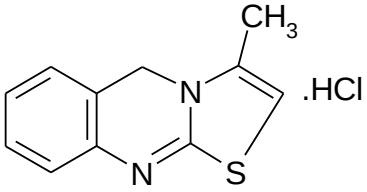


(9)

3,4-dihydroquinazolinone-2-thione obtained from the reaction of a 2-aminobenzyl amine with carbon disulfide on condensation with chloroacetone yields 5H-3-methylthiazole-[2,3-b]-quinazoline-hydrochloride (10) [23] which on basification gave a product (11) [24] this product is unstable and when kept in an oven at 80 ^{0}C for 72 hrs gave (12) [25] as light yellow crystals.



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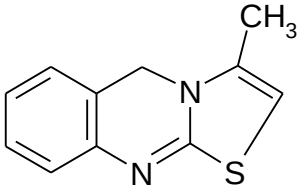

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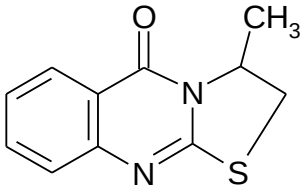

(12)

Treatment of 3,4-dihydroquinazoline-2-thione and p-methoxy-phenacyl bromide in anhydrous ethanol gave 5H-3-(p-anisyl) thiazole- [2,3-b] –quinazoline (13), while with p-nitropheacylbromide and p-bromo phenacyl bromide it gave carbinolamine compound (14).

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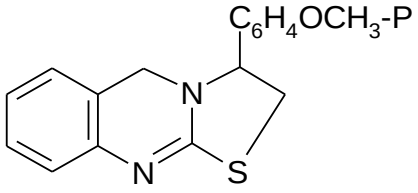

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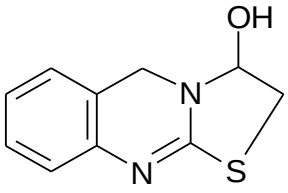
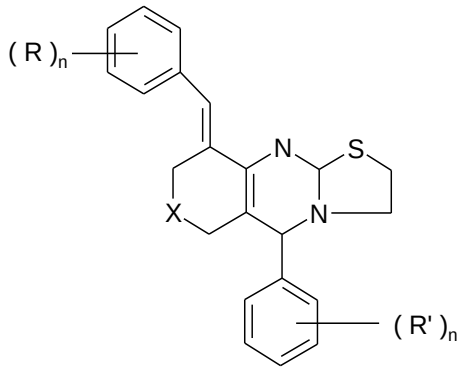


(14)

A variety of useful biological activities found in quinazoline-4-one derivatives has an impetus to the synthesis of the condensed quinazolin-4-ones-1, 3,4-thiazole- [2,3-b]-quinazoline-5-one derivatives have received proper attention.[26,27,28].

Pathak *et. al.* [29], have reported the synthesis of 3-amino-2-mercaptoquinazolin-4-one and its cyclization to thiadiazoloquinazolines by reaction with one carbon donor.

A series of tricyclic thiazole- [3,2-a]-thiopyran- [4,3-b]-pyrimidine and related taxa, azo, and carbo analogs of (15) have been reported to have anti-inflammatory activity[30].



X = S, SO_2, O, NR', CH_2

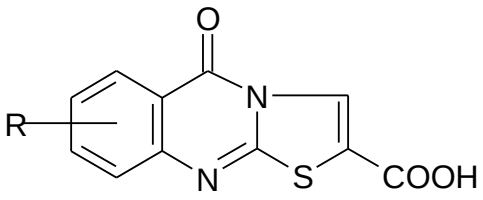
R = H, alkyl, alkoxy

R' = alkyl, acyl

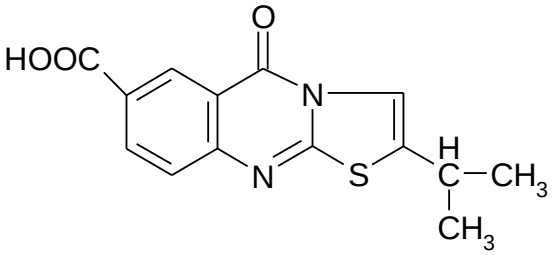
N = 1-3

(15)

A series of substituted 5-oxo-5H-thiazolo [2,3-b] quinazoline carboxylic acid were prepared[31] and reported to have antiallergic activity. Compound (16), (17), (18) and (19) were more potent ones.



16, R= 7-OCH_3
17, R = 7- S-CH_3
18, R = 7-$CH(CH_3)_2$



(19)

Some 2-substituted –2,3-dihydro-5H-thiazolo [2,3-b] quinazoline derivatives have been reported[32] to have anti-inflammatory and immunomodulatory activity in laboratory animals.

Mohammed *et. al,* [33] reported that the 3-[4'-(p-tolyl)-5'-thioxo-s-triazolidin-3'yl]-4-hydroxy-6-methyl—2[1H]-quinazoline (20) on treatment with hydrazine hydrate gave 3-hydrazino derivative (21) which on condensation with p-methoxy-Benzaldehyde in the presence of piperidine gave 3-[4'-(p-tolyl)-5'-(p-methoxy-benzalazino)s-triazolidin-3'-yl] –4-hydroxy-6-methyl-2-(1H)-quinolone (22).

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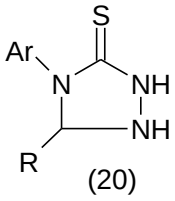

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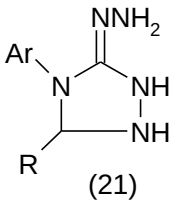

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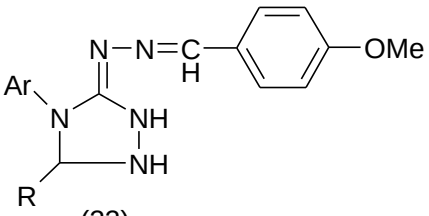

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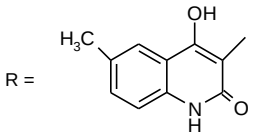
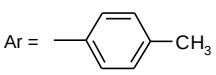
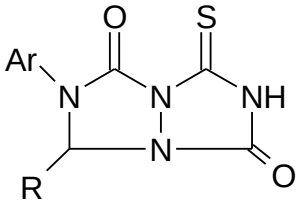




3[6'-(p-tolyl)-1', 5'-dioxo-3'thioxo-s-triazolidino [2,1-a]-s-triazolidin-7'-yl]-4-hydroxy-6-methyl-2 (1H)-quinolone (25) on treatment with hydrazine hydrate gave hydrazine derivative (23) which on condensation with formic acid gave 3[5', 9'-(7'H)-dioxo-8-(p-tolyl)-bis-s-triazolo-[2,1-a,4,3-d]-s-triazol-7'yl]-4-hydroxy-6-ethyl-2(1H)-quinolone(24).



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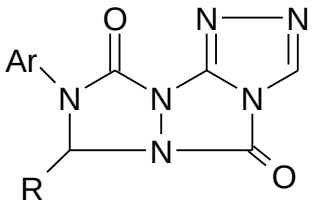

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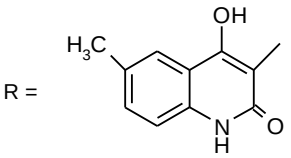
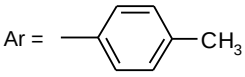
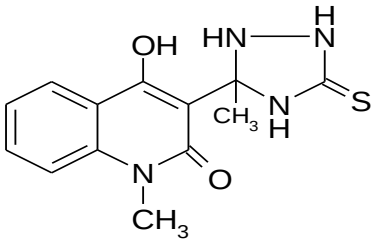




Ismail *et. al* [34]., reported the reaction of 4-hydroxy-1-methyl-3[5'-methyl-3'tjioxo-s-triazolidin-5'-yl]-2 (1H)-quinolone (26) with hydrazine hydrate gave hydrazino derivate (26) which on condensation with p-methyl Benzaldehyde afforded 3[3'-p-methylbenzalazino5'-methyl-s-triazolidin-5'-yl]-4-hydroxy-1-methyl-2(1H)-quinolone(27).



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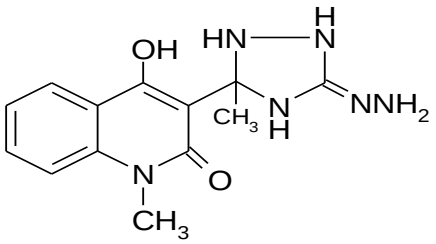

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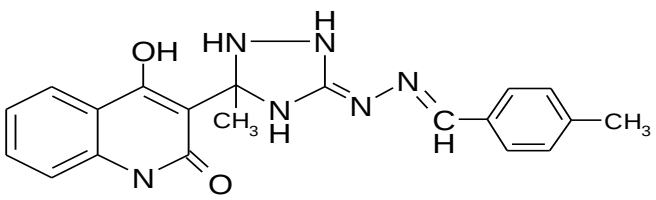

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Recorded in literature are numerous ketonic Mannich bases [35-38] prepared for pharmacological testing as antispasmodics, analgesics, chemotherapeutic agents, antibacterial agents, antifungal agents, and local anesthetics, such compounds may, in general, be prepared easily using the mannish reaction, which utilizes the appropriate ketones, formaldehyde or Paraformaldehyde and the desired amine. This may be illustrated as follows,

$$RCOCH_3 + HCHO + R_2'NH.HCL \rightarrow RCOCH_2CH_2NR_2'.HCL + H_2O$$

During the past four decades, numerous β-amino-ketones were synthesized and tested for useful therapeutic activities, promising pharmacological properties of β-amino-ketones prompted several groups of workers to continue their studies with several of the derivatives of β-amino-ketones.

METHODOLOGY

PREPARATION OF THE COMPOUND H_1: Anthranilic acid (0.01mol, 1.37g) is taken in a round bottom flask, to this acetic anhydride (0.1 mol, 10.2 ml) was added and refluxed on a gentle flame for 1 h. After that, the excess of acetic anhydride was distilled off under reduced pressure. The residue obtained was dissolved in petroleum ether and kept aside for 1 h. The obtained solid was filtered and dried. The Product is recrystallized with distilled water.
Melting point: 181 -182 ° C, Percentage yield: 85%.

PREPARATION OF THE COMPOUND H_2: n-acetylated anthranilic acid (0.01 mol, 2.3g) was taken in a round bottom flask, to this formamide (0.8 ml) was added and heated at 150ºC to 180ºC for a period of 5 h and cooled. The solid product thus obtained was broken up and dissolved in a solution of sodium bicarbonate, filtered, and dried. The product is recrystallized with distilled water. Melting point: 230ºC - 231ºC, Percentage yield: 73%.

PREPARATION OF THE COMPOUND HA: A mixture of **H_2** (0.1 mol), Aniline (0.1 mol), and paraformaldehyde (0.1 mol) was dissolved in glacial acetic acid (20 ml) taken in the round bottom flask. The reaction mixture was refluxed for about 8 hrs. After the completion of the reaction, the reaction mixture was kept overnight and poured onto a saturated solution of sodium bicarbonate. The product obtained was washed with water, dried, and recrystallized with Chloroform: alcohol (4:1).
Melting point: 242ºC -243 ºC, Percentage yields: 70%. The remaining compounds of this series **HB** and **HC** are synthesized by using different substituted amines like p-toluidine, and ranitidine, applying the compound HA procedure.

PREPARATION OF THE COMPOUND HAA: A mixture of compound **HA** (0.01 mol,), 2-chloro benzaldehyde (0.01 mol) & 20 ml of GAA is taken in a round-bottomed flask and refluxed for 16 to 20 hours. After the completion of the reaction the contents of the flask were poured on crushed ice, the separated solid was filtered and dried. The product was recrystallized with Chloroform: alcohol (1:5). Melting point: 217º-218 ºC, Percentage yield: 65%. The remaining compounds of this series, Compound HAB, and HAC are synthesized by using 3-nitro benzaldehyde and 4-hydroxy benzaldehyde, applying the compound HAA procedure.

PREPARATION OF THE COMPOUND HBA: A mixture of compound **HB** (0.01 mol,), 2-chloro benzaldehyde (0.01 mol) & 20 ml of GAA is taken in a round-bottomed flask and refluxed for 16 to 20 hours. After the completion of the reaction the contents of the flask were poured on crushed ice, and the separated solid was filtered and dried. The product was recrystallized with DMF.
Melting point: 208-209 ºC, Percentage yield: 55%. The remaining compounds of this series, Compound HBB and HBC are synthesized by using 3-nitro benzaldehyde and 4-hydroxy benzaldehyde, applying the compound HBA procedure.

PREPARATION OF THE COMPOUND HCA: A mixture of compound **HC** (0.01 mol,), 2-chloro benzaldehyde (0.01 mol) & 20 ml of GAA is taken in a round-bottomed flask and refluxed for 16 to 20 hours. After the completion of the reaction the contents of the flask were poured on crushed ice, and the separated solid was filtered and dried. The product was recrystallized with Chloroform: alcohol (1:5). Melting point: 225ºC -226ºC, Percentage yield: 60%. The remaining compounds of this series, Compound HCB, and HCC are synthesized by using 2-chloro benzaldehyde and 3-nitro benzaldehyde, applying the compound HCA procedure.

PHARMACOLOGICAL ACTIVITY

ANTIBACTERIAL ACTIVITY: All the compounds synthesized in the present investigation were screened for their anti-bacterial activity by subjecting the compounds to standard procedures. Antibacterial activities were tested on nutrient medium against *Bacillus pumilus, Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa* which are representative types of gram-positive and gram-negative organisms respectively. The antibacterial activity of the compounds was assessed by disc-diffusion method.

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PREPARATION OF NUTRIENT AGAR MEDIA:
Media Composition and Procedure:
The nutrient agar media was prepared by using the following ingredients.

1) Peptone (Bacteriological) 20.0 gm
2) Beef extract (Bacteriological) 5.0 gm
3) Sodium chloride 5.0 gm
4) Agar Agar 20.0 gm
5) Distilled water up to 1000.0 ml.

Weighed quantities of peptone and beef extract were dissolved in distilled water by gentle warming and then a specified amount of agar was dissolved by heating on a water bath. Then the pH of the solution was adjusted to 7.2 to 7.4 by adding the sodium chloride and the volume of the final solution was made up to 1000 ml with distilled water. Then it was transferred into a suitable container, plugged with non-adsorbent cotton and the media was sterilized by an autoclave at 121^0C for 20 minutes at 15 lbs pressure.

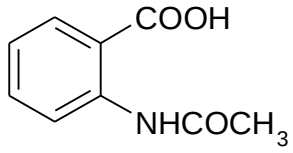
PREPARATION OF TEST SOLUTIONS: 10 mg of the compound was dissolved in 10 ml of DMSO. From this 1 ml of solution was taken and diluted up to 10 ml with DMSO. Now the concentration of the test solution was 100 µg/ml.

PREPARATION OF STANDARD ANTIBIOTIC SOLUTION: Ampicillin was used as standard antibiotics for comparison and solutions were prepared by using sterile water, as they were water-soluble. The solutions were diluted by using sterile water so that the concentrations of the solutions were 100 µg/ml.

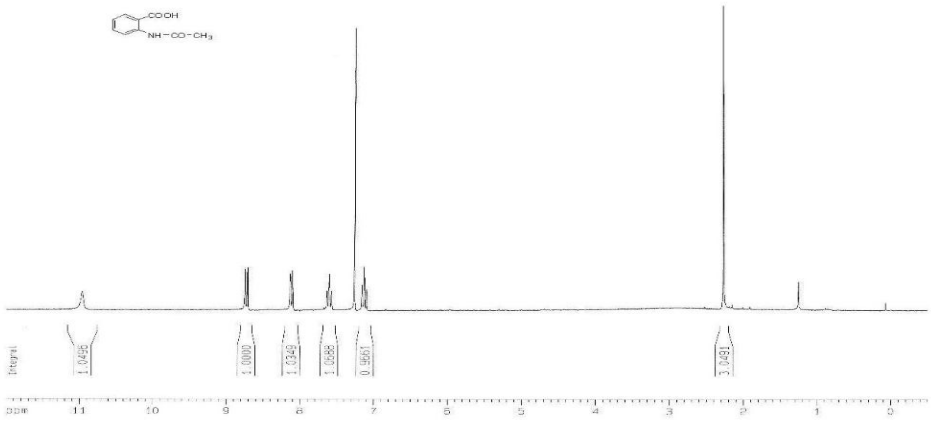
PREPARATION OF DISCS: Discs of 6-7 mm in diameter were punched from No-1 Whatman filter paper with a sterile cork borer of the same size. These discs were sterilized by keeping them in the oven at 140^0c for 60 minutes. Then standard and test solutions were added to each disc and discs were air-dried.

METHOD OF TESTING: The sterilized media was cooled to 45 ^{0}c with gentle shaking to bring about uniform cooling and then inoculated with 18-24 hrs old culture under aseptic conditions, mixed well by gentle shaking. This was poured into sterile Petri dishes (properly labeled) and allowed the medium to set. After solidification, all the Petri dishes were transferred to a laminar flow unit. Then the discs that were previously prepared were carefully kept on the solidified media by using sterilized forceps. These Petri dishes were kept as it is for one-hour diffusion at room temperature and then for incubation at 37^0c for 24 hours in an incubator. The extent diameter of inhibition after 24 hours was measured as the zone of inhibition in millimeters and the results were shown in table 2.

RESULTS
Compound H_1:



2-acetamido benzoic acid



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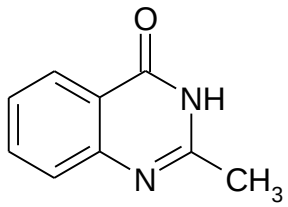
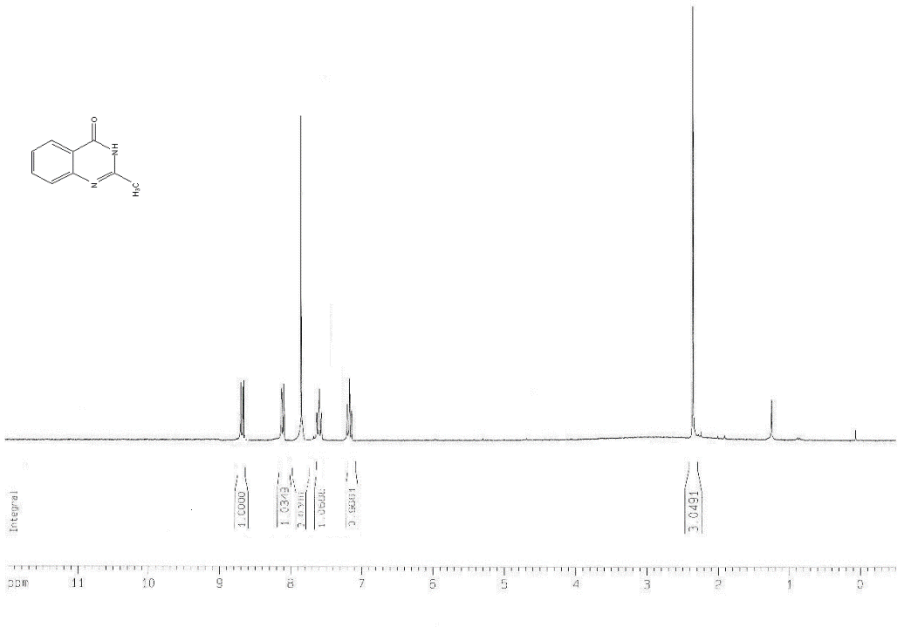
The compound under investigation has a molecular formula of $C_9H_9NO_3$ with a molecular weight of 179 g/mol. Its melting point is observed to be 181-182°C. The retention factor (Rf) value is 0.46, determined using a solvent system of chloroform and ethyl acetate in a 7:3 ratio. The ^1H NMR spectrum exhibits key signals, including a singlet at 11.0 ppm corresponding to the carboxyl hydrogen (COOH), a singlet at 7.2-7.3 ppm for the amine hydrogen (NH), and aromatic hydrogens appearing as multiplets between 7.1-8.8 ppm. Additionally, a singlet at 2.2-2.3 ppm represents the three protons of the methyl group (CH_3). The compound is soluble in acetone and alcohol when cold, and it was recrystallized using distilled water.

Compound H_2:

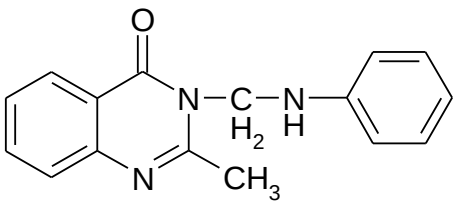


2-methyl quinazoline-4(3*H*)-one



The compound has a molecular formula of $C_9H_8N_2O$ and a molecular weight of 160 g/mol. It has a melting point of 230-231°C. The Rf value is recorded as 0.39, using a solvent system of chloroform and ethyl acetate in a 3:7 ratio. In the ^1H NMR spectrum, a singlet at 7.8-7.9 ppm corresponds to the amine hydrogen (NH), while aromatic hydrogens are observed as triplets and doublets between 7.1-8.8 ppm. The methyl group (CH_3) protons appear as a singlet at 2.2-2.3 ppm. The compound is soluble in glacial acetic acid when cold and was recrystallized using distilled water.

Compound HA:



2-methyl-3-{(phenylamino) methyl} quinazolin-4(3*H*)-one

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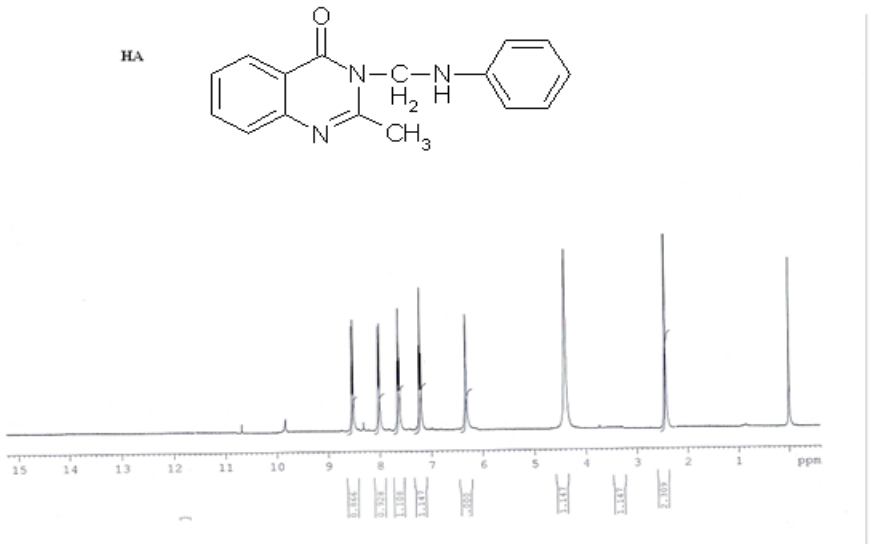
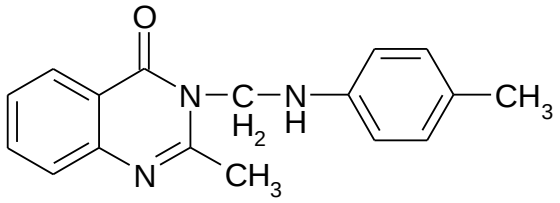
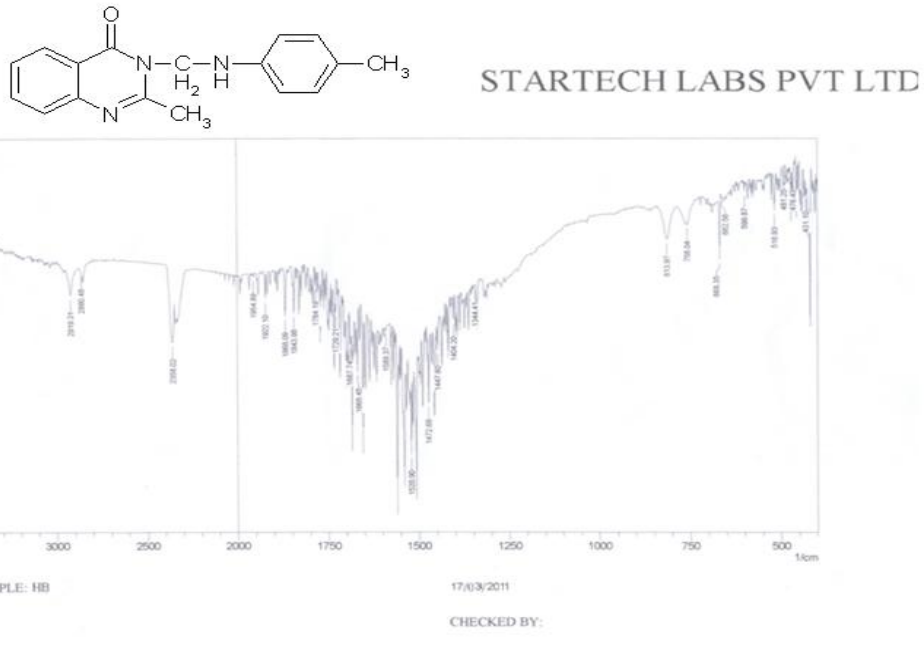


The compound has a molecular formula of $C_{16}H_{15}N_3O$ with a molecular weight of 265 g/mol. Its melting point is 242-243°C, and the Rf value is 0.60, using a solvent system of ethyl acetate and chloroform in a 3:7 ratio. The ^1H NMR spectrum shows a singlet at 2.4 ppm corresponding to the methyl group (CH_3), a singlet at 4.3 ppm for the methylene group (CH_2), and a singlet at 6.2 ppm for the amine hydrogen (NH). The aromatic hydrogens (Ar-H) are observed as a multiplet between 7.1-8.6 ppm. The LCMS analysis (70 eV) gives an m+1 peak at 266, indicating the molecular ion. The compound is soluble in glacial acetic acid when cold and was recrystallized using a mixture of chloroform and glacial acetic acid in a 4:1 ratio.

Compound HB:



2-methyl-3-{(p-tolylamino) methyl} quinazoline-4(3H)-one



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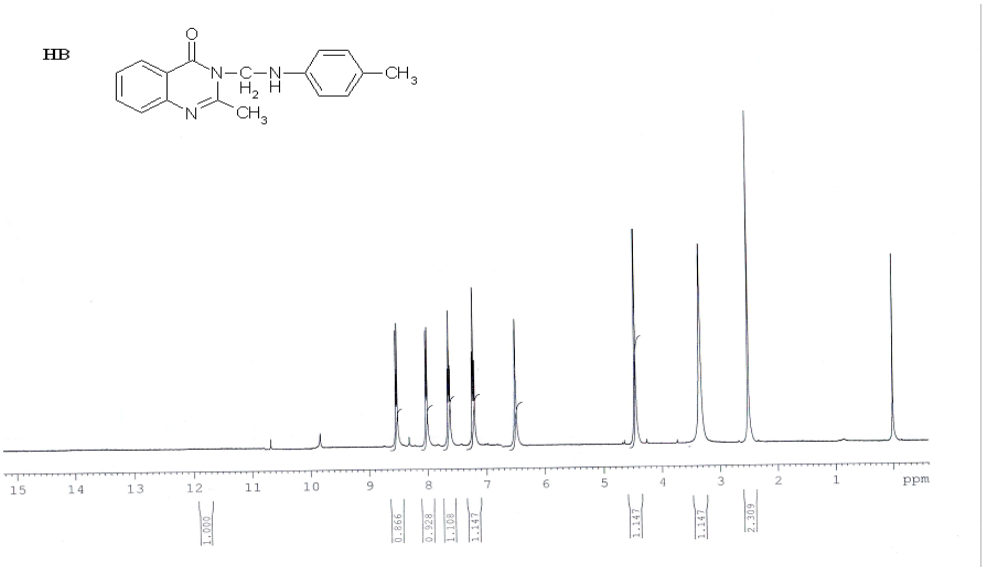
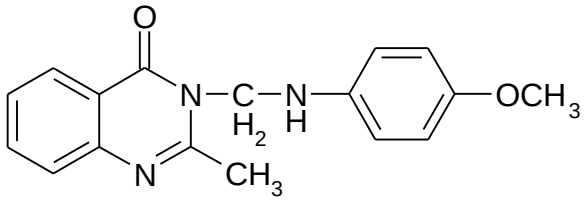
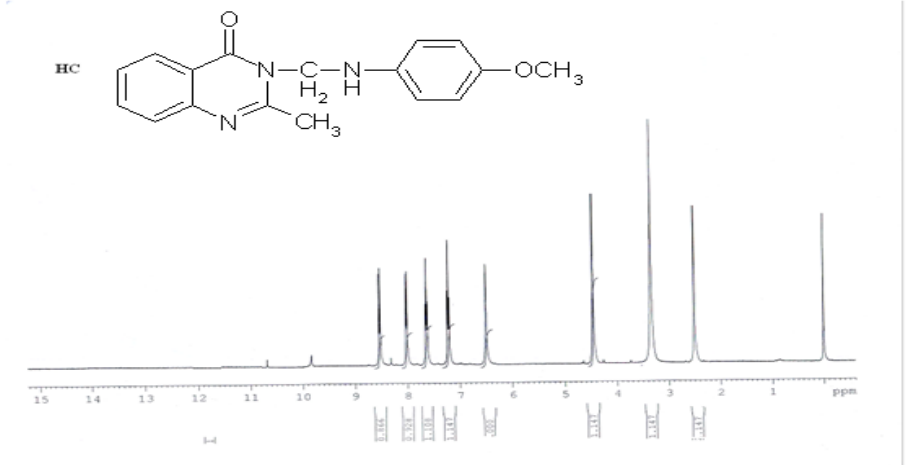


The compound has a molecular formula of $C_{17}H_{17}N_3O$ and a molecular weight of 279 g/mol. It has a melting point of 194-195°C and an Rf value of 0.63, using chloroform and ethyl acetate in a 3:7 ratio. The IR spectrum shows characteristic absorption bands at 2919 and 2860 cm^{-1} for aromatic C-H stretching, 1658 cm^{-1} for C=O stretching, 1520 and 1472 cm^{-1} for C=N stretching, and 813 and 758 cm^{-1} for 1,4-disubstituted benzene. In the ^1H NMR spectrum, singlets appear at 2.5 ppm and 3.2 ppm for two methyl groups (CH_3), 4.5 ppm for methylene (CH_2), and 6.4 ppm for the amine hydrogen (NH). Aromatic protons (Ar-H) are observed as a multiplet between 7.2-8.8 ppm. The compound is soluble in glacial acetic acid when cold and was recrystallized using dimethylformamide (DMF).

Compound HC:



3-{(4-methoxyphenylamino)methyl}-2-methyl quinazoline-4(3H)-one



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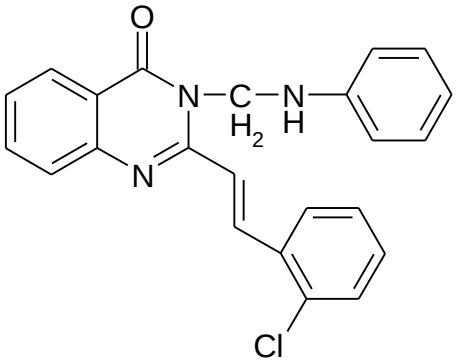
The compound has a molecular formula of $C_{17}H_{17}N_3O_2$ with a molecular weight of 295 g/mol. Its melting point is 257-258°C, and the Rf value is 0.45, determined using a solvent system of chloroform and ethyl acetate in a 3:7 ratio. The ^1H NMR spectrum exhibits a singlet at 2.6 ppm for the methyl group (CH_3), a singlet at 3.2 ppm for the methoxy group (OCH_3), and a singlet at 4.3 ppm for the methylene group (CH_2). The amine hydrogen (NH) appears as a singlet at 6.3 ppm, while aromatic protons (Ar-H) are observed as a multiplet between 7.2-8.7 ppm. The compound is soluble in glacial acetic acid (GAA) and acetone in cold conditions and was recrystallized using a mixture of chloroform and GAA in a 6:1 ratio.

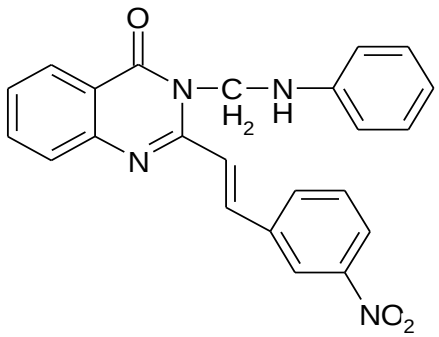
Compound HAA:



2-(2-chlorostyryl)-3-{(phenylamino) methyl} quinazoline-4(3H)-one

The compound has a molecular formula of $C_{23}H_{18}ClN_3O$ with a molecular weight of 388 g/mol. It has a melting point of 217-218°C and an Rf value of 0.48, determined using a solvent system of chloroform and ethyl acetate in a 3:7 ratio. The compound is soluble in chloroform under cold conditions and was recrystallized using a mixture of chloroform and alcohol in a 1:5 ratio.

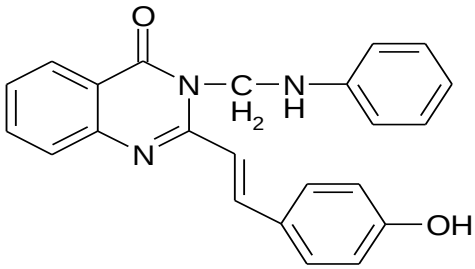
Compound HAB



2-(3-nitrostyryl)-3-{(phenylamino) methyl} quinazoline-4(3H)-one

The compound has a molecular formula of $C_{23}H_{18}N_4O_3$ with a molecular weight of 398 g/mol. Its melting point is 265-266°C, and the Rf value is 0.42, determined using a solvent system of chloroform and ethyl acetate in a 3:7 ratio. The compound is soluble in chloroform when cold and was recrystallized using a mixture of chloroform and alcohol in a 1:5 ratio.

Compound HAC:



2-(4-hydroxystyryl)-3-{(phenylamino) methyl} quinazoline-4(3H)-one

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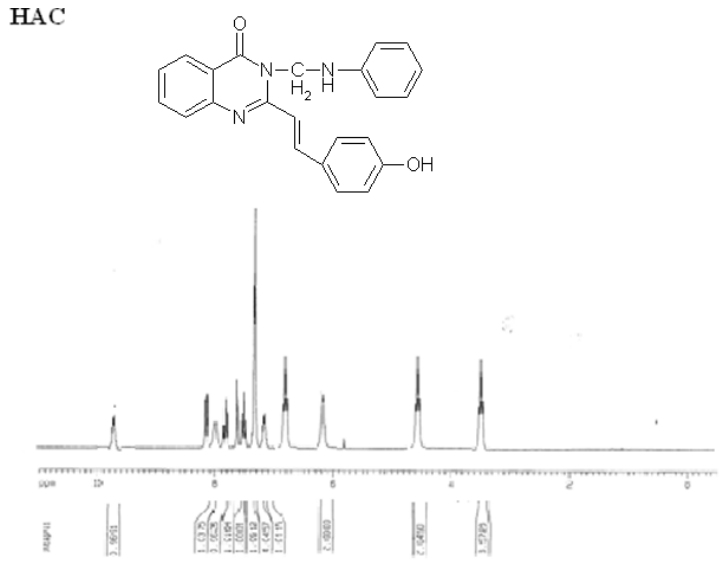
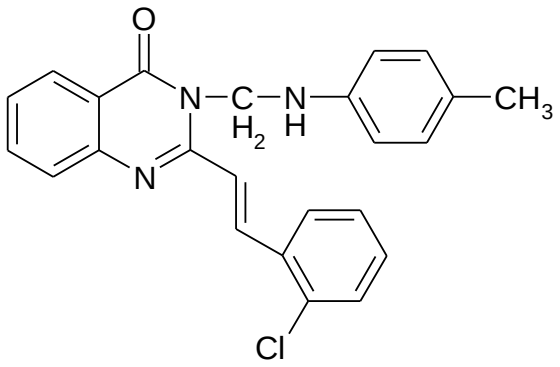
HAC

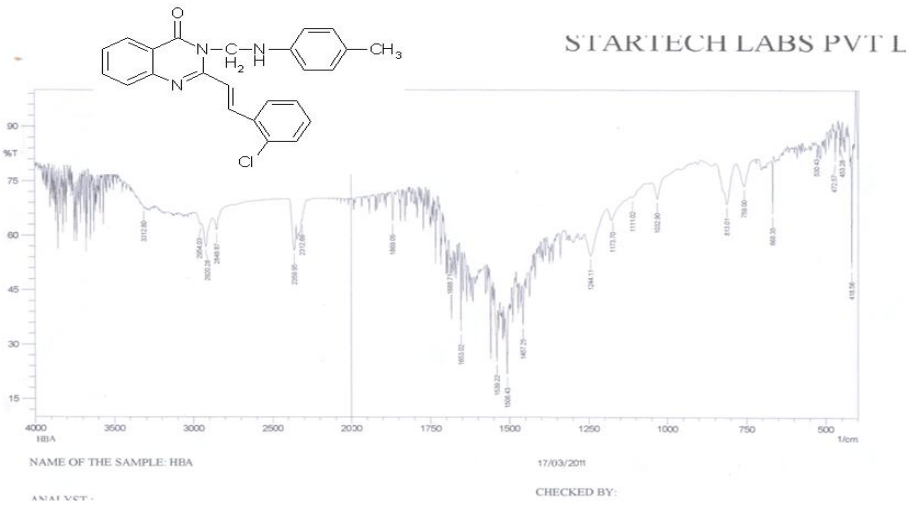


The compound has a molecular formula of $C_{23}H_{19}N_3O_2$ and a molecular weight of 369 g/mol. It has a melting point above 300°C, and the Rf value is 0.61, determined using chloroform and ethyl acetate in a 3:7 ratio. The ^1H NMR spectrum shows a singlet at 3.7 ppm for the methylene group (CH_2), a doublet at 4.6 ppm for the CH group, and another doublet at 6.7 ppm for the CH group. A singlet at 6.1 ppm corresponds to the NH group, while aromatic protons (Ar-H) are seen as a multiplet between 7.2-8.4 ppm. The OH group appears as a singlet at 9.8 ppm. The compound is soluble in chloroform when cold and was recrystallized using a mixture of chloroform and alcohol in a 1:5 ratio.

Compound HBA:



2-(2-chlorostyryl)-3-{(p-tolylamino) methyl} quinazoline-4(3H)-one



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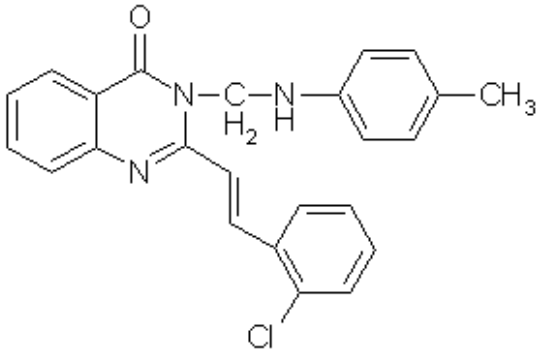
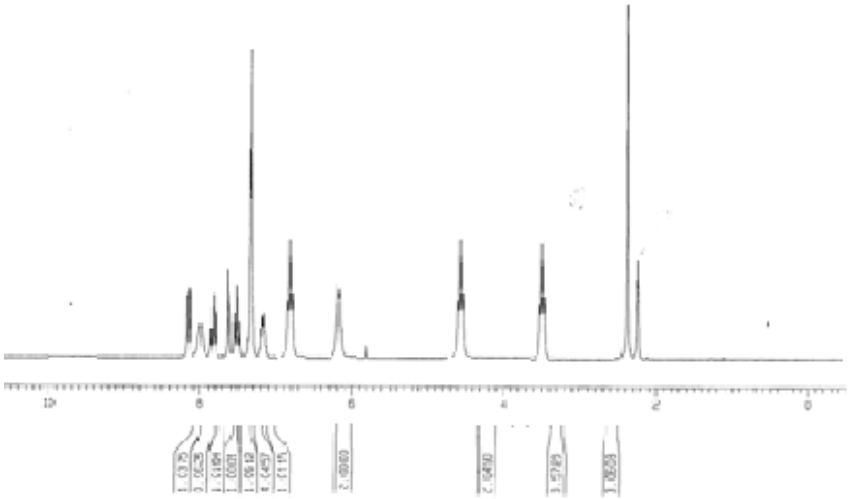
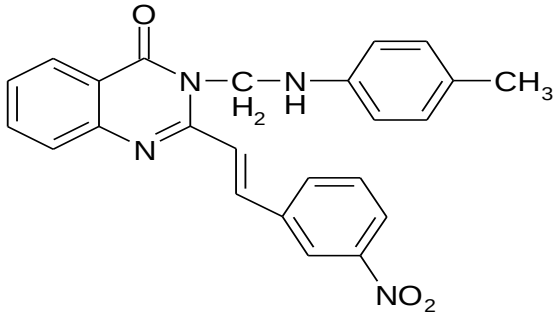




The compound has a molecular formula of $C_{24}H_{20}ClN_3O$ with a molecular weight of 401 g/mol. It exhibits a melting point of 208-209°C and an Rf value of 0.45, using a solvent system of chloroform and ethyl acetate in a 3:7 ratio. The IR spectrum shows significant absorption bands at 3312 cm^{-1} (N-H stretching), 2954 cm^{-1} (C-H stretching of ArOH), 2930 cm^{-1} (C-H stretching of CH_3), 1680 cm^{-1} (C=C stretching), 1653 cm^{-1} (C=O stretching), and bands at 1539, 1506, and 1457 cm^{-1} for C=N stretching. Additionally, absorptions at 813 and 759 cm^{-1} correspond to 1,4-disubstituted benzene.
The ^1H NMR spectrum displays a singlet at 2.1 ppm for the methyl group (CH_3), a singlet at 3.6 ppm for the methylene group (CH_2), a doublet at 4.7 ppm for the CH group, and a singlet at 6.1 ppm for the NH group. The singlet at 6.7 ppm corresponds to the CH group, while the aromatic protons (Ar-H) appear as a multiplet between 7.4-8.3 ppm.
The compound is soluble in chloroform when cold and was recrystallized using a mixture of chloroform and alcohol in a 1:5 ratio.

Compound HBB:



2-(3-nitrostyryl)-3-{(p-tolylamino) methyl} quinazoline-4(3H)-one

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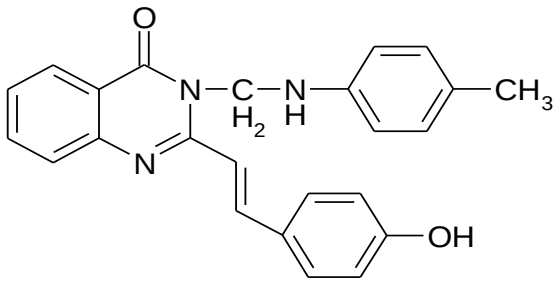
The compound has a molecular formula of $C_{24}H_{20}N_4O_3$ with a molecular weight of 412 g/mol. It has a melting point above 300°C and an Rf value of 0.42, determined using a solvent system of chloroform and ethyl acetate in a 3:7 ratio. The compound is soluble in chloroform in cold conditions and was recrystallized using a mixture of chloroform and alcohol in a 1:5 ratio.

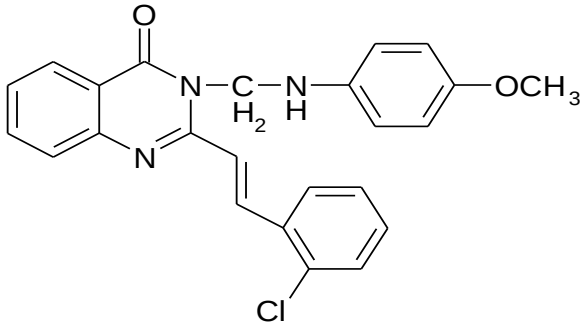
Compound HBC:



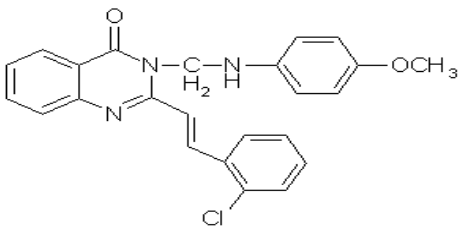
2-(4-hydroxystyryl)-3-{(p-tolylamino) methyl} quinazoline-4(3H)-one

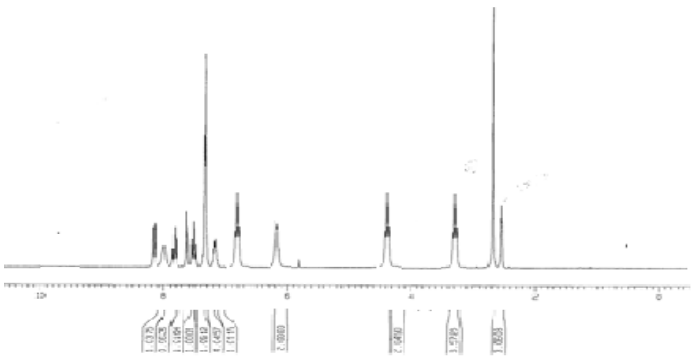
The compound has a molecular formula of $C_{24}H_{21}N_3O_2$ and a molecular weight of 383 g/mol. It has a melting point of 270-271°C, and the Rf value is 0.65, determined using a solvent system of chloroform and ethyl acetate in a 3:7 ratio. The compound is soluble in chloroform under cold conditions and was recrystallized using a mixture of chloroform and alcohol in a 1:5 ratio.

Compound HCA:



2-(2-chlorostyryl)-3-{(4-methoxyphenylamino)methyl} quinazoline-4(3H)-one





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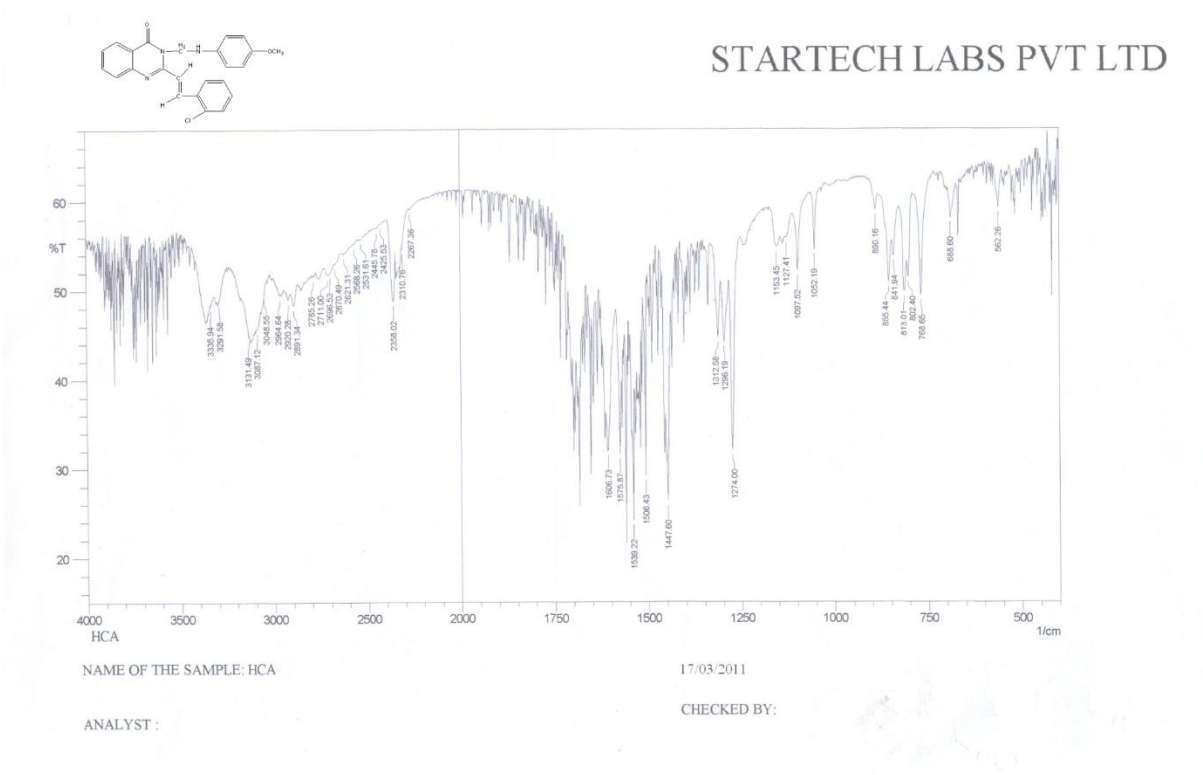
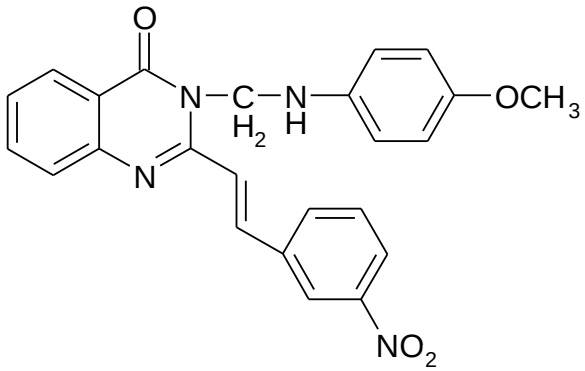


The compound has a molecular formula of $C_{24}H_{20}ClN_3O_2$ and a molecular weight of 417 g/mol. It exhibits a melting point of 225-226°C, with an Rf value of 0.62, determined using a solvent system of chloroform and ethyl acetate in a 3:7 ratio. The ^1H NMR spectrum shows characteristic signals at 2.8 ppm (singlet for OCH_3), 3.2 ppm (singlet for CH_2), 4.4 ppm (doublet for CH), 6.1 ppm (singlet for NH), 6.6 ppm (singlet for CH), and a multiplet between 7.2-8.2 ppm for aromatic protons (Ar-H). The IR spectrum presents significant peaks at 3340 cm^{-1} (N-H stretching), 2964 and 2920 cm^{-1} (C-H stretching of aromatic H), 2785 cm^{-1} (C-H stretching of CH_3), 1680 cm^{-1} (C-O stretching), 1650 cm^{-1} (C=O stretching), 1472 cm^{-1} (C-H stretching of CH_2), and 1449-1447 cm^{-1} (C-N stretching). Additionally, absorptions at 855, 803, 758 cm^{-1} correspond to 1,4-disubstituted benzene, while 686 cm^{-1} is attributed to C-H stretching. The compound is soluble in chloroform in cold conditions and was recrystallized using a chloroform-alcohol mixture in a 1:5 ratio.

Compound HCB:



2-(3-nitrostyryl)-3-{(4-methoxyphenylamino)methyl} quinazoline-4(3H)-one

The compound has a molecular formula of $C_{24}H_{20}N_4O_4$ and a molecular weight of 428 g/mol. It exhibits a melting point of 255-256°C, and the Rf value is 0.38, determined using a solvent system of chloroform and ethyl acetate in a 3:7 ratio. This compound is soluble in chloroform under cold conditions and was recrystallized using a chloroform-alcohol mixture in a 1:5 ratio.

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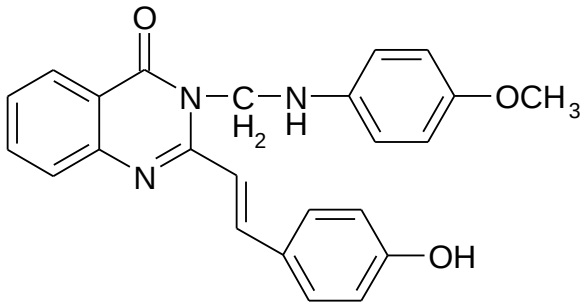
Compound HCC:



2-(4-hydroxystyryl)-3-{(4-methoxyphenylamino)methyl} quinazoline-4(3H)-one

The compound has a molecular formula of $C_{24}H_{21}N_3O_3$ and a molecular weight of 399 g/mol. It has a melting point of 236-237°C, with an Rf value of 0.40, determined using a solvent system of chloroform and ethyl acetate in a 3:7 ratio. This compound is soluble in cold chloroform and was recrystallized using a mixture of chloroform and alcohol in a 1:5 ratio.

Table no. 1: QUINAZOLINE DERIVATIVES

S.No.	Compound Code	Mol. Formula	Molecular Wt.	Rf Value	Melting Point (°C)	Yield %
1	HAA	$C_{23}H_{18}ClN_3O$	388	0.48	217-218	65
2	HAB	$C_{23}H_{18}N_4O_3$	398	0.42	265-266	60
3	HAC	$C_{23}H_{19}N_3O_2$	369	0.61	above 300	64
4	HBA	$C_{24}H_{20}ClN_3O$	401	0.45	208-209	55
5	HBB	$C_{24}H_{20}N_4O_3$	412	0.42	above 300	62
6	HBC	$C_{24}H_{21}N_3O_2$	383	0.65	270-271	66
7	HCA	$C_{24}H_{20}ClN_3O_2$	417	0.62	225-226	55
8	HCB	$C_{24}H_{20}N_4O_4$	428	0.38	255-256	52
9	HCC	$C_{24}H_{21}N_3O_3$	399	0.40	236-237	62

Re-crystallized by Chloroform: alcohol (1:5).

ANTIBACTERIAL ACTIVITY: The synthesized Quinazoline derivatives i.e 9 compounds were screened for anti bacterial activity at the concentration of 50µg/ml and 100µg/ml using DMF as a control against the *Bacillus pumilus, Bacillus substilis, Escherichia coli and Pseudomonas aeruginosa* by disc-diffusion method on nutrient agar media, The standard drug used was Ampicillin for the comparison at the concentration 50µg/ml and 100µg/ml against all the above mentioned organisms. The data in the table 2 indicates that most of the compounds found to posses moderate to good antibacterial activity against the all the above-mentioned organisms.

Table no. 2: Antibacterial activity of synthesized Quinazoline derivatives

Sample Code	*Inhibition zone diameter in mm							
	B.subtilis		*B.pumilis*		*E.coli*		*P.aeruginosa*	
	50µg	100µg	50µg	100µg	50µg	100µg	50µg	100µg
HAA	14	**24**	13	22	13	**23**	12	22
HAB	11	15	10	14	9	12	8	11
HAC	11	21	12	22	11	21	10	20
HBA	13	**25**	12	**24**	12	21	15	**23**
HBB	13	**24**	13	**24**	11	15	10	14
HBC	14	**24**	13	**23**	12	**23**	13	22
HCA	14	**24**	12	**24**	13	**23**	12	**23**
HCB	14	**23**	13	**23**	10	14	10	13
HCC	13	**25**	14	**24**	14	**24**	13	**25**
Ampicillin	20	34	21	32	21	31	20	30
DMF	-	-	-	-	-	-	-	-

*Average of triplicate ± Standard deviation

Note: -'denotes no activity, 8-12 mm poor activity, 13-17 mm moderate activity,
18-20 above good.

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DISCUSSION: From antibacterial screening against *Bacillus pumilus, Bacillus substilis, Escherichia coli and Pseudomonas aeruginosa*, it was found that compound like HAA, HBA, HCA, HBC, HCC showed significant broad spectrum activity. This may be due to the presence of side chain and Cl group, which is attached to 2nd position of styryl group (attached to quinazolines nucleus at 2nd position) and may be due to methoxy group attached to phenylaminomethyl. It was significant activity when compared to standard (Ampicilline 50 μg/ml and 100μ g/ml). Coumpounds HBB and HCB showed significant activity against Gram-positive bacteria but poor activity against Gram-negative bacteria. Compound HAB was found ineffective against all the organisms whereas compound HAC shows very poor activity. The above result established the fact that quinazolinone-4-(3H)-one substituted with styryl group can be studied further to search for antibacterial activity.

SUMMARY: The objective of the present work is to synthesize substituted quinazoline derivatives and to study their antibacterial activity in particular. Thus an attempt has been made in this direction. As expected, Quinazoline derivatives exhibited anti-bacterial activity in which some are good and moderately active like standard employed for comparison. Therefore further a detailed study of toxicity is necessary. There is no such a thing as completely safe drug. Drugs are powerful tools, which alter physiological processes for the better or for the worse. A society that wishes to benefit from them will not achieve all the benefits open to it, if it ignores the fact and seeks for impossible standards of harmlessness. The anti-bacterial activity testing showed that few compounds are promising anti-bacterial agent when compared to standard drug ie; Ampiciline. Further the detailed structural activity relationship studies are required along with the molecular manipulation i.e. molecular modeling may give better drugs. Molecules prepared for the biological testing do not always turn out as potential new drugs, but may be intended to serve as models for evaluation of hypothesis.

CONCLUSION: From the data of antibacterial activity, it is clearly concluded that the synthesized compounds are promisingly having moderate to good anti-bacterial activity. Quinazolinones moiety is an important pharmacophore showing many types of pharmacological activities. The synthesized compounds with methoxy and chloro substituent have showed more activity as compared to other compounds because these groups enhance the lipid solubility of the drugs. The presence of hydrocarbon side chain and aromatic rings also contribute to lipid solubility of the synthesized compounds. Due to good lipid solubility the synthesized drugs can penetrate the lipid membranes easily to exhibit antibacterial activity. The above results establish the fact that quinazolinone-4-(3H)-ones substitutes at 1st and 3rd position with appropriate groups could be a rich source of exploitation. Therefore, in search of new generation of active compounds, it may be worthwhile to explore the possibility in this area by attaching and substituting with different aryl, halo moieties, which may results in better pharmacological activities. Hence in the present study, quinazolinone-4-(3H)-ones were linked to other groups at 1st and 3rd position and showed potent and specific anti-bacterial activity. Such types of derivatives with further alteration in their structure may lead to development of new antibacterial drugs.

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