Global Scientific JOURNALS

GSJ: Volume 8, Issue 11, November 2020, Online: ISSN 2320-9186
www.globalscientificjournal.com

Synthesis and characterization of new derivatives of 4-fluoro benzoic acid as bioactive compound

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Abstract:

Infectious microbial diseases are a serious issue of the whole World. Medicinal chemists & biologists are paying special attention on disease causing pathogens and bacteria because risk of diseases is increasing day by day & fatal for life. A series of hydrazide hydrazones of 4-fluorobenzoic acid hydrazide were prepared and evaluated as potential antimicrobial agents. Reaction progress was checked by using pre-coated silica gel aluminium packed thin layer plates with the help of ethyl acetate & n-hexane that will serve as mobile phase. These new compounds were characterized by their physical properties (melting point, Colour, TLC spot, Molecular formula, Molecular wt, %yield, solubility), the structures were confirmed by elemental analysis, IR spectral methods.

Keywords: 4-fluoro benzoic acid, IR, Antimicrobial activity

1. INTRODUCTION

In present days, infectious microbial diseases are a serious issue of the whole World. Medicinal chemists & biologists are paying special attention on disease causing pathogens and bacteria because risk of diseases is increasing day by day & fatal for life. Literature survey reveals that resistance has been increased for existing antimicrobial drugs. So, it is necessary to design novel biologically important antimicrobial drugs with good activity profiles. These facts have made the synthesis and characterization of new drugs an ongoing process for research purposes. Two methodologies are in use for this purpose one is the use of already existing materials and second one is the use of new self created procedure. Hetero-cycles specially oxadiazoles are of great importance for this task and are in use for synthesizing new drugs from last decades**.** Organic compounds are characterized such that some or all the atoms are linked through ring structure with at least one non-carbon atom. In heterocyclic compounds the cyclic part represents the presence of at least one ring structure and the term hetero represents the one atom other than carbon in the ring. On the basis of general structure heterocyclic compounds resemble to the organic compounds but due to the hetero-

atoms they show unique physical and chemical properties (Kunied & Mustsanga, 2012).

History of hetero cyclic compounds was started with the development of organic chemistry in 1800s. In 1832, Dobereiner designed a reaction between starch and sulfuric acid to produce a furan named furfural. By using dry distillation of bones, Runge synthesized pyrrole in1834. Treibs in 1936, separated derivatives of chlorophyll from crude oil and also explained biological origin of petroleum (Arora *et al.,* 2012). Heterocyclic chemistry constitutes almost 65% of organic chemistry. It has wide range of applications. It has a vital role in carrying out enzymatic reactions necessary for life.

Large number of hetero-cyclic compounds are in clinical use & are pharmacologically very active. Heterocyclic bases like pyrimidines and purines make the genetic material DNA. Effect of induction due to hetero-atom makes oxadiazole a weak base.

- As density of electrons is low for carbons so oxadiazole ring shows high resistance towards electrophilic substitution reactions.

- Attack of electrophile substitution may happens on nitrogen if a change takes place in electron releasing groups.
- In oxadiazole ring nucleophilic substitution is difficult but if substituting agent is halogen atom then nucleophile is substituted in the ring by releasing the halogen atom.
- The ring cleavage reactions in oxadiazoles are also of great importance because of applications in pharmacological industry. As a result of these reactions compounds having ring structures and nitrogen are obtained.

For medicinal chemists, it is a challenging task to prepare novel drugs. Oxadiazoles have shown a large number of applications like anti-bacterial, anti-inflamatory, analgesic, anti-tumor, anti-convulsant, anti-oxidant herbicidal and anti-fungal activities.Two basic approaches are adapted by chemists for developing novel drugs:

- Forming analogues as well as their derivative formation gives new substituted compounds for good and developed treatment.
- Searching & preparing new compounds that bacteria and diseases has never been presented before.

For this purpose oxadiazoles and their derivatives are considered as important antiinflammatory,
anti-convulsant and anti-bacterial agents.

1-Rivera *et al*. (2006), developed a pathway of forming 2-amino-5-phenyl-1,3,4-oxadiazole by performing oxidative cyclization of different oxidizing agents like Nbromosuccinamide, H2O2 & bleach etc. NaOH was used as base & a catalyst naming potassium iodide.

2-Kiselyov *et al*. (2010) synthesized oxadiazoles by performing condensation of C3H3NS derivative through hydrazine hydrate for about 4.2 hours. Further reaction of transitional molecule was carried out and desired compound was synthesized.

3-Kamble *et al.,* (2008) used microwave for the synthesis of oxadiazoles. The microwave method is a cleaner technique which gives higher production in lesser time.

Within the sight chalcones exhibit swift hydrazine hydrate cyclization. Medium used was with formic acid and polyethylene glycol. Titled product was converted into derivatives of oxadiazole by reacting it with acetic acid.

4-Cyclization of acyl thiosemicarbazide was used to synthesize 5-aryl-2-amino-1,3,4- oxadiazoles. 1,3-dibromo-5,5-dimethylhydantoin was used as oxidizing agent. The important benefit of this method is that it is safe to use, easily available and cheap (Rivera *et al.*, 2006).

Thiophene is the most common sulfur based hetero-cycle. In physical and chemical properties it resembles benzene a lot. During the purification of benzene it was obtained for the first time. Thiophene is a common contaminant of benzene and is obtained from natural
resources. It was discovered in the late 19th century. In the furan ring, when the two methane (-CH=) groups are interchanged with two pyridine type nitrogen, oxadiazole or furadiazole is obtained with molecular representation C2H2N2O (de Oliveira et al., 2012). This replacement decreases the aromaticity of the ring
such that it starts reflecting the characteristics of conjugate diene (Bachwani & Sharma,2011). There exist four isomers of oxadiazole having nitrogen at different positions and isomerization is also due to this reason. Isomers are 1,2,5-oxadiazole, 1,2,5-oxadiazole,1,2,4-oxadiazole and 1,2,4-oxadiazole (Somani *et al*., 2011).

But 1,2,3-oxadiazole is not stable and opens readily giving diazoketone tautomer (Leite *et al.,* 2000), (Schmidt *et al*., 2003), (Salahuddin *et al.,* 2017).

Biological activities of some compounds

Compounds	Biological activity	Reference
2-arylaminosulfonylmethyl-5- aryl-1,3,4-oxadiazole	Anti-bacterial activity	(Padmavathi *et al.*, 2010)
2,5-Disubstituted-1,3,4-oxadiazole derivatives	Anti-bacterial activity	(Jha *et al.*, 2010)
2-(Biphenyl-4-yl)-5-aryl-1,3,4-oxadiazole derivatives	Anti-bacterial activity	(Kumar *et al.*, 2013)
5-(2-amino-3-pyridyl)-2-thioxo- 3H-1,3,4-oxadiazole derivatives	Anti-cancer activity	(Liszkiewicz *et al.*, 2003)
2-(1,3,4-triphenylpyrazol-5-yl)- 5-phenyl-1,3,4-oxadiazole	Anti-cancer activity	(Mansour *et al.*, 2003)
2-(4-chlorophenyl)-5-aryl-1,3,4-oxadiazole derivatives	Anti-cancer activity	(Ahsan *et al.*, 2013)
5-pyridyl-1,3,4-oxadiazole-2- thiol	Anti-inflammatory activity	(Khan *et al.*, 2004)
2,4-dichlorophenyl-5-(2,4,6-trichlorophenoxymethyl)1,3,4-oxadiazole	Anti-inflammatory activity	(Amir *et al.*, 2007)
2,substituted-5-(2-benzylthiophenyl)-1,3,4-oxadiazoles	Anti-convulsant activity	(Almasirad *et al.*, 2004)
2,substituted-5-[2-(2-fluorophenoxy)phenyl]-1,3,4-oxadiazoles	Anti-convulsant activity	(Zarghi *et al.*, 2005)
Aryl sulfonamido-5-[2’-(benzimidazol-2’’-yl)]-1,3,4-oxadiazoles	Anti-tubercular activity	(Kagthara *et al.*, 1999)

MATERIALS AND METHODS

The apparatus used for the research purpose is given below:
Measuring cylinder
Beakers
Pipettes
Iodine flask
Magnetic stirrer
Glass rod
Round bottom flask (250ml, 100ml)
Condenser
Capillaries
Funnels
Viols
Separating funnels
Reagent bottles
Spatula
TLC card
Filter paper
Aluminum foil

Chemicals and reagents

The chemicals which were used for research purpose are:
4-Fluorobenzoic acid
n-hexane
Ethyl acetate
Methanol
Absolute Ethanol
Chloroform
Diethyl Ether
Sulfuric acid (H2SO4)
Hydrazine hydrate
Carbon disulphide (CS2)
KOH
NaOH
Na2CO3
Hydrochloric acid (HCL)
DMF
LiH
Bromoacetyl bromide
Aniline
2-Ethyl aniline
2-Chloro aniline
3-Chloro aniline
4-Ethyl aniline
3-Methyl aniline
2-Ethoxy aniline
2,5-Dimethyl aniline
2,3-dimethyl aniline
2-Methyl aniline2-Bromo aniline
2-Methyl,6-Ethyl aniline
3-NO2 aniline
3,5-dimethyl aniline

Instruments used

For research work instruments that were used are given below:
Electric Balance, UV lamp, Rotary Vacuum evaporator, Microwave oven, Hot plate, FT-IR

Solvent purification

Methanol

CaO was used for purifying methanol i.e. for removing water from methanol. 1 liter of methanol was taken into a round bottom flask (500ml). CaO was added and kept it overnight. Distillation of methanol was done at 69 C.

Dry DMF

DMF was taken into a round bottom flask of required capacity & is allowed to boil by placing it on hot plate until it started evaporating. To keep the DMF water free sodium sulphate was added to the bottle after boiling DMF.

Absolute ethanol

In order to purify ethanol, CaO was used. One liter of ethanol was taken into the round bottom flask of 500 ml and was subjected to the CaO and left for night. Temperature for distillation of ethanol was set to about 78C.

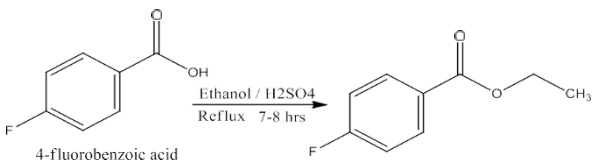
General procedure

Reaction progress was checked by using pre-coated silica gel aluminium packed thin layer plates with the help of ethyl acetate & n-hexane that will serve as mobile phase.
Melting points were checked by using melting point apparatus & open capillaries.

Synthesis of 4-fluorobenzoate from 4-fluorobenzoic acid (1)

Procedure

4-fluorobenzoic acid (15g) was taken in a round bottom flask (250ml) and dissolved in 60ml of absolute Ethanol. Then 7.5ml of H2SO4 was added and shake it well. A condenser was used to reflux it for7-8 hrs. The progress of reaction was monitored from time to time by using Ethyl acetate and n-hexane with the help of TLC. The gradual completion of reaction was checked. The final product formation i.e. 4-fluorobenzoatee and its purity was checked by TLC & observing it under UV lamp. After the completion of reaction 5ml of 10% solution of Na2CO3 was added to remove un-reacted acid. Then chilled water was added and rested it for some time to perform solvent extraction as ester of 4-fluorobenzoic acid is not solid.



4-fluorobenzoic acid

Solvent extraction procedure

10% solution of Na2CO3 was added and pH was maintained at 9. Then chloroform was added and whole solution was transferred into separating funnel. Shake it well and rest for almost 20 minutes until two layers get separated. Then denser ester layer was separated from bottom, chloroform was evaporated by rotary vacuum evaporator and liquid ester was obtained with yield 80%.

Formation of 4-fluorobenz hydrazide (2)

Procedure

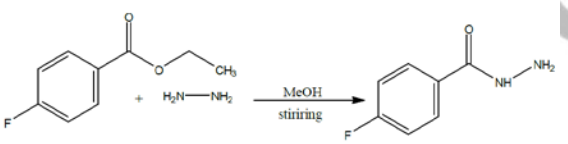
The synthesized ester (12.5ml) was taken into a round bottom flask (250ml), 50ml of absolute ethanol & 37.5ml of hydrazine hydrate was added in the flask. The ester, ethanol & hydrazine hydrate for the synthesis of hydrazide must be in following ratio:

Ester: Absolute ethanol: Hydrazine hydrate

1 : 4 : 3

Then round bottom flask was covered with aluminium foil, placed on hot plate & allowed to stir it for almost 12-15 hrs. As the solid product appeared, reaction completion was checked by performing TLC using n-hexane, ethyl acetate & TLC cards & observed under UV lamp.

After completion of reaction n-hexane was added. Solution filtered as needle like crystals appeared. Allowed it to dry & a shiny off white product was obtained that was hydrazide & product was calculated (79%).

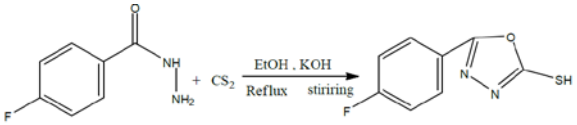


1,3,4-oxadiazole synthesis (3)

Procedure

A solution of potassium hydroxide (4 pellets) was made in absolute ethanol (40ml) & poured into a round bottom flask. 10g of prepared hydrazide and 10ml of carbon disulphide was added in the round bottom flask. Condenser was adjusted and allowed to reflux for 6-8

hours. Reaction progress was checked at regular intervals by using TLC procedure with the use of varying ratio of n-hexane & ethyl acetate. As the reaction got completed, 20ml of chilled distilled water and a very small amount of dil. Sulfuric acid (H2SO4) to maintain the pH 2-3 in order to remove un-reacted base. Solid precipitates were obtained on vigorous shaking and filtered. Product was dried, collected &calculated.



Common scheme for amide formation

Chemicals used

Aniline (0.1 ml/0.05g)

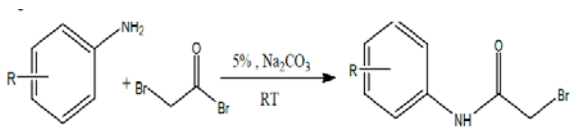
Bromoacetyl bromide (0.1 ml)

Distilled water

10% solution of sodium carbonate

Procedure

0.1ml of aniline (for liquid anilines) & 0.05g (for solid anilines) was taken in an iodine flask (250ml). Freshly prepared 10ml solution of 10% of Na2CO3 was added into the iodine flask and mixed it. Solution attains pH approximately 8-9 & becomes basic. Mix it well and acid was added slowly. Cover the flask with lid and shake it well until precipitates began to appear. Reaction was shaken for another 20 minutes to obtain fine precipitates and filtered. Product formed is an amide of respective aniline and is dried. Purity of product was checked by TLC.



Formation of 2-bromo-N-(2,3-dimethylphenyl) acetamide

Chemicals

2,3-dimethyl aniline

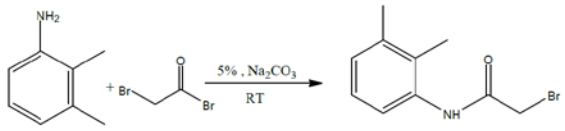
Bromoacetyl bromide

Distilled water

10% solution of Na2CO3

Procedure

A clean iodine flask of 250 ml was taken. 10ml solution of freshly prepared 10% solution of sodium carbonate was added to the flask followed by the addition of 0.1 ml of 2,3-dimethyl aniline. Shake the flask to mix it properly. Then bromoacetyl bromide was added gradually. Again shake it vigorously until ppts appeared. Precipitates were filtered and proper washing was done. Dry the precipitates and product purity was checked by TLC.



3.5.2 Preparation of 2-bromo-N-(2,5-dimethylphenyl) acetamide

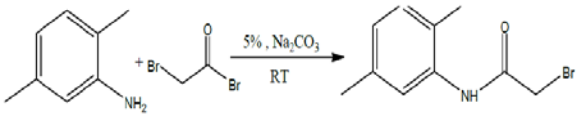
Chemicals

2,5-dimethyl aniline

Bromoacetyl bromide
Distilled water
10% solution of sodium carbonate

Procedure

Wash the round bottom flask properly and rinse with distilled water. Add 10 ml of 10%
solution of sodium carbonate in round bottom flask and 0.1 ml of 2,5-dimethyl aniline. Shake
it well to mix it evenly. Gradually add 1 ml 0f acid in the flask and shake it vigorously. Filter
the reaction as the precipitates appeared. Precipitates were dried and confirmed by
performing TLC. Amount of obtained product was calculated and saved.



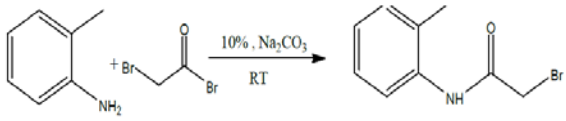
Synthesis of 2-bromo-N-(2-methylphenyl)acetamide

Chemicals used

2-methyl aniline
Bromoacetyl bromide
Distilled water
10% solution of sodium carbonate

Procedure

10 ml solution of prepared 10% sodium carbonate was added in a neat round bottom flask of 250ml. Then 0.1 ml of 2-methyl phenyl amine was added with the help of pipette and shake gently to mix it. Acid was added slowly and again shake to obtain precipitates. Filter it on getting precipitates. Dry it and check its purity. The solid product was then calculated and saved properly.



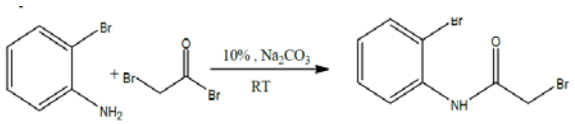
Formation of 2-bromo-N-(2-bromophenyl)acetamide

Chemicals used

2-bromo aniline
Bromoacetyl bromide
Distilled H2O
10 % solution of Na2CO3 10 ml

Procedure

A washed round bottom flask was taken and 10 ml of 10 % sodium carbonate solution was poured.0.1 ml of 2-bromo aniline was dispersed into the flask and was shaken properly. Then 1 ml of acid titled acid was added and shaken it vigorously until ppts appeared. Reaction mixture was filtered to separate the precipitates formed. Precipitates were dried and solid product obtained was calculated.



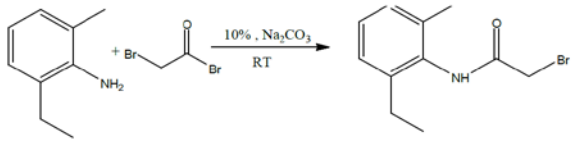
Synthesis of 2-bromo-N-(2-methyl,6-ethylphenyl) acetamide

Chemicals used

2-methyl,6-ethyl aniline
Bromoacetyl bromide
Distilled water
10% solution of sodium carbonate

Procedure

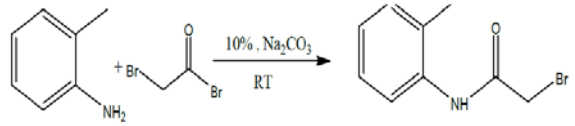
A properly cleaned iodine flask was taken and 10 ml solution of 10 % sodium carbonate was added. After that 0.1 ml of 2-methyl,6-ethyl phenyl amine was poured and shaking of reaction was done for 2-3 minutes at room temperature. Then bromoacetyl bromide was added safely and shaking was done for another 10 minutes or more according to reaction conditions. Precipitates then obtained were filtered and purity was checked. Solid precipitates were collected and weighed.



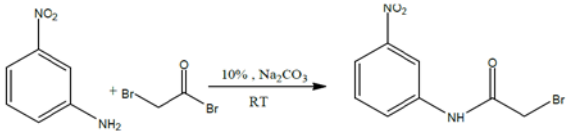
Formation of 2-bromo-N-(3-nitrophenyl)acetamide

Chemicals used

3-nitro aniline (0.05g)



0.05g of solid 3-nitro aniline was weighed on weighing balance and then transferred
to a clean iodine flask of 250 ml in which 10 ml solution of 10% sodium carbonate was already present. Mix the reaction mixture so that solid aniline got dissolved in Na2CO3 solution evenly. After that bromoacetyl bromide was added gradually and shaken vigorously for 10 minutes to prepare solid precipitates which were filtered later with proper washing. Solid precipitates were collected, weighed and saved.



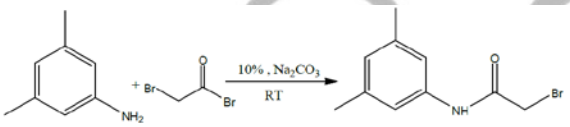
Synthesis of 2-bromo-N-(3,5-dimethylphenyl) acetamide

Chemicals used

3,5-dimethyl aniline
Bromoacetyl bromide (1 ml)
Distilled water
10 % solution of sodium carbonate

Procedure

10 ml freshly prepared solution of 10 % sodium carbonate was added in a clean round bottom flask rinsed with distilled water followed by the addition of 0.1 ml of 3,5-dimethyl aniline. Mix it properly and 1 ml of acid was added safely with the help of pipette into the flask. Shake it well so that precipitates appeared. Filter the ppts by using filter paper and wash the product with distilled water properly. Dry the ppts, collect them, weigh them and
save.



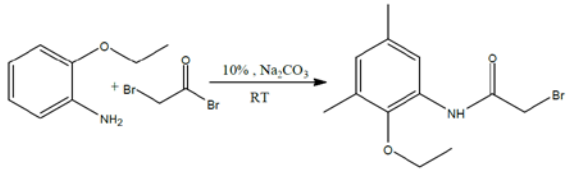
Preparation of 2-bromo-N-(2-ethoxyphenyl)acetamide

Chemicals used

2-ethoxy aniline (0.1 ml)
Bromoacetyl bromide (1 ml)
Distilled water
10 % solution of sodium carbonate

Procedure

A clean iodine flask rinsed with distilled water was taken and addition of 10 ml solution of 10 % sodium carbonate was done. Then 0.1 ml of 2-ethoxy aniline was poured and mixed evenly. Then slow and safe addition of acid was done and shaken properly until ppts of acetamide appeared. Filter it and dry the ppts. Confirmation of reaction was checked by performing TLC. Solid product then obtained was weighed and kept.



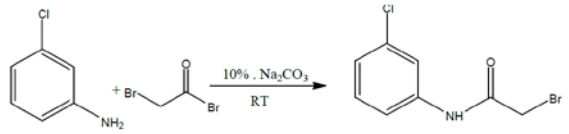
Synthesis of 2-bromo-N-(3-chlorophenyl)acetamide

Chemicals used

3-chloro aniline
Bromoacetyl bromide
Distilled water
10% solution of Na2CO3

Procedure

A clean iodine flask of 250 ml was taken. 10ml solution of freshly prepared 10% solution of sodium carbonate was added to the flask followed by the addition of 0.1 ml of 3- chloro aniline. Shake the flask to mix it properly. Then bromoacetyl bromide was added gradually. Again shake it vigorously until ppts appeared. Precipitates were filtered and proper washing was done. Dry the precipitates and product purity was checked by TLC. Amount
was calculated & packed.



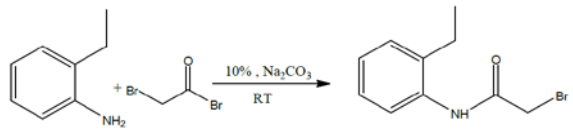
Synthesis of 2-bromo-N-(2-ethylphenyl)acetamide

Chemicals used

2-ethyl aniline
Bromoacetyl bromide
Distilled water
10% solution of sodium carbonate

Procedure

Wash the round bottom flask properly and rinse with distilled water. Add 10 ml of 10% solution of sodium carbonate in round bottom flask and 0.1 ml of 2-ethyl aniline. Shake it well to mix it evenly. Gradually add 1 ml 0f acid in the flask and shake it vigorously. Filter
the reaction as the precipitates appeared. Precipitates were dried and confirmed by performing TLC. Amount of obtained product was calculated and saved.



Synthesis of 2-bromo-N-(4-ethylphenyl)acetamide

Chemicals used

4-ethyl phenyl amine
Bromoacetyl bromide
Distilled water
10% solution of sodium carbonate

Procedure

10 ml solution of prepared 10% sodium carbonate was added in a neat round bottom flask of 250ml. Then 0.1 ml of 4-ethyl phenyl amine was added with the help of pipette and shaken gently to mix it. Acid was added

slowly and again shake to obtain precipitates. Filter it on getting precipitates. Dry it and check its purity. The solid product was then calculated and saved properly.

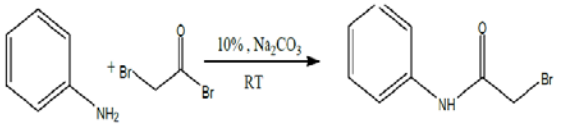
Synthesis of 2-bromo-N-phenyl aetamide

Chemicals used

Aniline
Bromoacetyl bromide
Distilled water
10% solution of sodium carbonate

Procedure

A clean iodine flask rinsed with distilled water was taken and addition of 10 ml solution of 10 % sodium carbonate was done. Then 0.05g of aniline was poured and mixedevenly. Then slow and safe addition of acid was done and shaken properly until ppts of acetamide appeared. Filtered it and dried the ppts. Confirmation of reaction was checked by performing TLC. Solid product then obtained was weighed and kept.



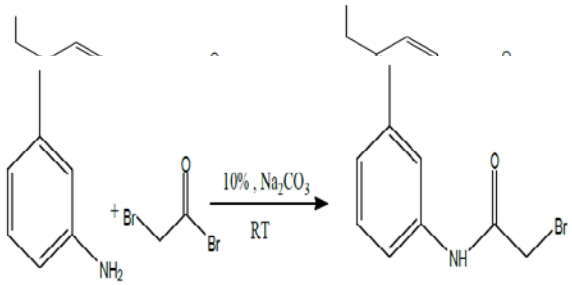
Synthesis of 2-bromo-N-(3-methylphenyl)acetamide

Chemicals used

3-methyl aniline
Bromoacetyl bromide
Distilled water
10% solution of sodium carbonate

Procedure

A properly cleaned iodine flask was taken and 10 ml solution of 10 % sodium
carbonate was added. After that 0.1 ml of 4-ethyl aniline was poured and shaking of reaction
was done for 2-3 minutes at room temperature. Then bromoacetyl bromide was added safely and shaking was done for another 10 minutes or more according to reaction conditions.
Precipitates then obtained were filtered and purity was checked. Solid precipitates were
collected and weighed.



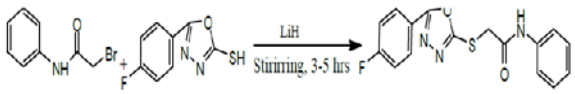
Synthesis of N-substituted 2[5-(4-fluorophenyl)1,3,4-oxadiazol-2-yl-sulfanyl]Nphenyl Acetamide

Chemicals used

5-(4-fluorophenyl)-1,3,4-oxadiazole-2-thiol (0.1g)
DMF (3-4 ml)
LiH (0.05g)
2-bromo-N-phenyl acetamide (0.09g)
Distilled water
n-hexane
Ethyl acetate

Procedure

A neat round bottom flask was taken. Synthesized and weighed 5-(4-fluorophenyl)-
1,3,4-oxadiazole-2-thiol(0.1g) was added to the round bottom flask also with the addition of
3-4 ml DMF and catalyst LiH. It was allowed to stir for about half an hour. After 30 minutes
stirring 2-bromo-N-phenyl acetamide was added and placed to continuous stirring. The reaction progress was monitored properly. After completion of reaction workup was done by
adding chilled water. Precipitates were filtered, washed properly, dried and purity was
checked. Then obtained product was saved for further analysis.



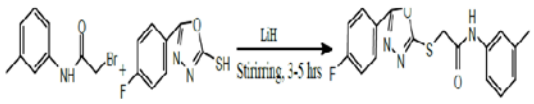
Synthesis of N-substituted 2[5-(4-fluorophenyl)1,3,4-oxadizol-2-yl-sulfanyl]-N-(3-methylphenyl) acetamide

Chemicals used

5-(4-fluorophenyl)-1,3,4-oxadiazole-2-thiol
DMF (3-4 ml)
LiH (0.05g)
2-bromo-N-(3-methylphenyl)acetamide
Distilled water
n-hexane
Ethyl acetate

Procedure

A properly washed round bottom flask of 50 ml was taken & o.1g of synthesized 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-thiol was added. Then 3-4 ml of dimethylformamide was poured into the round bottom flask followed by the addition of 0.05g of lithium hydride and allowed to stir for about 30 minutes at room temperature. LiH acts as a catalyst in this reaction. 0.09g of prepared 2-bromo-N-(3-methylphenyl) acetamide was weighed and transferred to the reaction mixture, covered the mouth of round bottom flask with aluminium foil and allowed to continuous stirring. Confirmation of reaction was checked by TLC. After completion of reaction chilled distilled water is added and placed for stirring until ppts appeared. Reaction mixture was filtered and dried. Purity is again checked by TLC. The solid product is collected, weighed and saved



Synthesis of N-substituted 2[5-(4-fluorophenyl)1,3,4-oxadizol-2-yl-sulfanyl]-N-(2-chlorophenyl) acetamide

Chemicals used

5-(4-fluorophenyl)-1,3,4-oxadiazole-2-thiol
DMF (3-4 ml)
LiH (0.05g)
2-bromo-N-(2-chlorophenyl)acetamide
Distilled water
n-hexane
Ethyl acetate

Procedure

0.1g of 5-(4-fluorophenyl)-1,3,4-oxadiazole-2-thiol was taken in a properly washed and dried round bottom flask of 50ml. Then 3-4ml of DMF was added followed by addition of lithium hydride and allowed for stirring for about 30 minutes. Then 0.09g of synthesized 2-bromo-N-(2-chlorophenyl) acetamide was added and started stirring. Progress of reaction was checked time to time by TLC with the help of n-hexane and ethyl acetate in different ratios. As reaction got completed chilled distilled water added up to neck and again started stirring until ppts became visible. Then ppts were filtered, dried, calculated and saved for further activities.

Biological activities

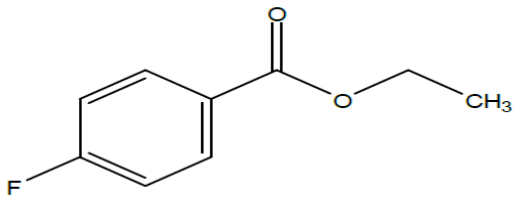
Activities of newly synthesized compounds were monitored against microbes in opposition to antibacterial and antifungal strains. All the strains used were collected from pharmaceutical institute of Lahore. Microorganisms were cultured and facilitated with a fundamental growth medium. Ager medium was rich in gelatinous material which gave the bacteria excellent medium for growth. Each bacterium was provided a suitable environment nutrient and culture medium for rapid growth. The temperature was set at 37C which is the best suitable temperature for bacterial growth and to establish long colonies.

Disk diffusion method

A well known method i.e. disk diffusion method was used to monitor the antimicrobial activity of newly synthesized compounds. In this method the body fluid of individual under study was placed onto filter paper and then placed into potato dextro medium. After that plates were placed under incubation for about 24h by maintaining temperature at 35-37C. For checking anti-microbial activity temperature was set at about 4C while for examining anti-fungal activity it was 28C for 24h. Then growth of inhibition was measured by measuring diameter.

RESULT AND DISCUSSION

4-fluoro benzoate



Color	Brownish liquid
TLC spot	Single
Molecular weight	167
Molecular formula	$C_9H_9FO_2$
Melting point	124-127C
% yield	80%

IR Analysis

The characteristic peaks of 4-fluorobenzoate were obtained at 1601.78 cm-1 for N-H bending, 2983.61cm-1 of alkane stretching, 1715.58 cm-1 of C=O, at 605.35 cm-1 for C-Br and C-O str. at 1268.55 cm-1. These peaks ensured the presence of ester with the existence of carbonyl in molecule. Analysis confirmed the structure of 4-fluorobenzoate.

4-fluorobenzo hydrazide

Colour	White shinny powder
TLC spot	Single
Molecular wt.	153
Molecular formula	$C_7H_7N_2FO$
Melting point	142-146
% yield	79%

IR Analysis

The characteristic peaks of 4-fluorobenzoate were obtained at 3300.56cm-1 for N-H, 3014.97cm-1 of alkane stretching, at 3195.52 for O-H str. and C-O at 1240.16cm-1. These peaks ensured the presence of hydrazide with the existence of carbonyl in molecule. Analysis
confirmed the structure of 4-fluorobenzo hydrazide.

5-(4-fluorobenzyl 1,3,4-oxadiazole)-2-thiol

Colour	White ppts
TLC spot	Single spot
Molecular wt.	211
Molecular formula	$C_8H_5N_2OSF$
Melting point	210-215C
% yield	80%

IR Analysis

The characteristic peaks were obtained at 2945.12cm-1 for C-H methylene, for C=C at 830.37cm-1, O-H at 2766.37cm-1 and N-O at 1511cm-1. Presence of these peaks confirmed the five membered oxadiazole ring & amidic carbonyl assembly in molecule. Considering the
fundamental analysis the structure was designed as 5-{(4-fluorobenzyl 1,3,4-oxadiazole)-2-thiol.

2-(5-(4-fluorophenyal)-1,3,4-oxadiazole-2-yl-sylfanyl)-N-(2,3-dimethylphenyl)acetamide

Colour	Off white
TLC spot	Single
Molecular formula	$C_{19}H_{18}FN_3O_2S$
Molecular wt.	370
Melting point	270-273

%yield	78%

IR Analysis
The characteristics peaks for 2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-sulfanyl)-N(2,3dimethylphenyl)acetamide were observed at 3058.71 cm-1 for C-H, at 2924cm-1 for O-H, for C-Cl at 847cm-1 and for C-O at 1208.88cm-1. These peaks and their study revealed the presence of five membered oxadiazole ring and amidic carbonyl assembly in molecule. On the basis of analysis the name 2-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl-sulfanyl)-N-(2,3-dimethylphenyl)acetamide was awarded to it.

2-(5-(4-fluorophenyal)-1,3,4-oxadiazole-2-yl-sylfanyl)-N-(2-methylphenyl)acetamide

Colour	Light pinkish
TLC spot	Single
Molecular wt.	370
Molecular formula	C19H18FN3O2S
Melting point	290-293
%yield	78%

IR Analysis
The characteristics peaks for 2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-sulfanyl)-N-(2 methylphenyl)acetamide were observed at 3281 cm-1 for N-H, at 1664.86cm-1 for C=N, 1501.52 of N-Ocm-1, for C-Cl str. at 692.58cm-1 and for C=C at 885cm-1. These peaks and their study revealed the presence of five membered oxadiazole ring and amidic carbonyl assembly in molecule. On the basis of analysis the name 2-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl-sulfanyl)-N-(2-methylphenyl)acetamide was awarded to it.

2-(5-(4-fluorophenyal)-1,3,4-oxadiazole-2-yl-sylfanyl)-N-(2-bromophenyl)acetamide

Colour	Ash white
TLC spot	Single
Molecular formula	C17H14FN3O2S
Molecular wt.	422

IR Analysis
The characteristics peaks for 2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-sulfanyl)-N-(2-bromophenyl)acetamide were observed at 3068cm-1 for C-H, 1618cm-1 of C=O, for C-N at 3266cm-1, for C-S str. at 830cm-1 and for C-Br at 823cm-1. These peaks and their study revealed the presence of five membered oxadiazole ring and amidic carbonyl assembly in molecule. On the basis of analysis the name 2-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-ylsulfanyl)-N-(2-bromophenyl)acetamide was awarded to it.

2-(5-(4-fluorophenyal)-1,3,4-oxadiazole-2-yl-sylfanyl)-N-(2-methyl,6-ethylphenyl)acetamide

Colour	Off white
TLC spot	Single
Molecular formula	C20H20FN3O2S
Molecular wt.	384
Melting point	320-328
%yield	91%

IR Analysis
The characteristics peaks for 2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-sulfanyl)-N-(2-methyl,6-ethylphenyl)acetamide were seen at 3071cm-1 for C-H, for N-H at3269 cm-1, for C-H stretching of methylene at 2931cm-1, C-N at 2361cm-1 and for C-F at 1287cm-1. These peaks and their study revealed the presence of five membered oxadiazole ring and amidic carbonyl assembly in molecule. On the basis of analysis the name 2-(5-(4-fluorophenyl)- 1,3,4-

oxadiazol-2-yl-sulfanyl)-N-(2-methyl,6-ethylphenyl)acetamide was given to it.

2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-yl-sulfanyl)-N-(3,5-dimethylphenyl)acetamide

Colour	Light pinkish
TLC spot	Single
Molecular wt.	370
Molecular formula	$C_{19}H_{18}FN_3O_2S$
Melting point	269-271
%yield	71%

IR Analysis

The characteristics peaks for 2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-sulfanyl)-N-(3,5 dimethylphenyl)acetamide were observed at 3257 cm-1 for N-H, at 3071cm-1 for C-H, for C=O at 1731cm-1, for C-F at 1499cm-1. These peaks and their study revealed the presence of five membered oxadiazole ring and amidic carbonyl assembly in molecule. On the basis of analysis the name 2-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl-sulfanyl)-N-(3,5-dimethylphenyl)acetamide was awarded to it.

2-(5-(4-fluorophenyal)-1,3,4-oxadiazole-2-yl-sylfanyl)-N-(2ethoxyphenyl)acetamide

Colour	Off white
TLC spot	Single
Molecular wt.	356
Molecular formula	$C_{18}H_{16}FN_3O_2S$
Melting point	206-208
% yield	70%

IR Analysis

IR analysis revealed the presence of characteristic peaks at 2366.58 for C=C=O stretching, at 1459.24 for O-H stretching, at 1254.11 for C-O, at 845 for C-Cl bond str., at 761.66 for C-H. These peaks confirmed the presence and structure of desired compound 2-(5-(4-fluorophenyal)-1,3,4-oxadiazole-2-yl-sylfanyl)-N-(2ethoxyphenyl)acetamide.

2-(5-(4-fluorophenyal)-1,3,4-oxadiazole-2-yl-sylfanyl)-N-(3-chlorophenyl)acetamide

Colour	Yellowish white
TLC spot	Single
Molecular formula	$C_{17}H_{14}FClN_3O_2S$
Molecular wt.	377
Melting point	291-293
%yield	80%

IR Analysis

The characteristics peaks for 2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-sulfanyl)-N-(3-chlorophenyl)acetamide were observed at 3068cm-1 for C-H, 2359cm-1 of C-N, for N-H at 3266cm-1 and for C-Br at 823cm-1. These peaks and their study revealed the presence of five membered oxadiazole ring and amidic carbonyl assembly in molecule. On the basis of analysis the name 2-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl-sulfanyl)-N-(3-chlorophenyl)acetamide was awarded to it.

2-(5-(4-fluorophenyal)-1,3,4-oxadiazole-2-yl-sylfanyl)-N-(2-ethylphenyl)acetamide

Colour	Light yellow
TLC spot	Single
Molecular wt.	356
Molecular formula	$C_{18}H_{20}FN_3O_2S$
Melting point	201-203

IR Analysis

IR analysis revealed the presence of characteristic peaks at 2876 for N-H stretching,
at 1477 for C-H bending, at 1651 for C=N, at 3258 for 0-H str., at 2051 for C=N and at 843
for C-Cl. These peaks confirmed the presence and structure of desired compound 2-(5-(4-

fluorophenyal)-1,3,4-oxadiazole-2-yl-sylfanyl)-N-(2-ethylphenyl)acetamide.

2-(5-(4-fluorophenyal)-1,3,4-oxadiazole-2-yl-sylfanyl)-N-(4-ethylphenyl)acetamide

Colour	Light yellow
TLC spot	Single
Molecular wt.	356
Molecular formula	$C_{18}H_{20}FN_3O_2S$
Melting point	201-203
% yield	75%

IR Analysis

IR analysis revealed the presence of characteristic peaks at 3387 for N-H stretching, at 2987 for C-H stretching, at 1669 for C=O, at 1292 for C-O-C bond str., at 2051 for C=N, at 823 for C-F and at 515 for C-S. These peaks confirmed the presence and structure of
desired compound 2-(5-(4-fluorophenyal)-1,3,4-oxadiazole-2-yl-sylfanyl)-N-(4-ethylphenyl)acetamide.

2-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl-sulfanyl)-N-phenyl Acetamide

Colour	Off white
TLC spot	Single
Molecular formula	$C_{18}H_{15}FN_3O_2S$
Molecular wt.	355
Melting point	298-300
%yield	79%

IR Analysis

The characteristics peaks for 2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-sulfanyl)-Nphenyl acetamide were seen at 3131cm-1 for C-H, for N-H at3388 cm-1, for C-N at 2359cm-1,
for C-O at 1288 and for C-F at 11157cm-1. These peaks and their study revealed the presence of five membered oxadiazole ring and amidic carbonyl assembly in
molecule. On the basis of analysis the name 2-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl-sulfanyl)-N-acetamide was given to it.

2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-yl-sylfanyl)-N-(3-methylphenyl)acetamide

Colour	Pinkish
TLC spot	Single
Molecular formula	$C_{18}H_{15}FN_3O_2S$
Molecular wt.	355
Melting point	275-278
%yield	77%

IR Analysis

The characteristics peaks for 2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-sulfanyl)-N-(3-methylphenyl)acetamide were observed at 2708cm-1 for C-H, 1667 of C=Ncm-1, for O-H at 3242, for C-N str. at 1310cm-1 and for C-Cl at 813cm-1. These peaks and their study revealed the presence of five membered oxadiazole ring and amidic carbonyl assembly in molecule. On the basis of analysis the name 2-(5-(4-fluorophenyl)-1,3,4-oxadiazol-2-ylsulfanyl)-N-(3-methylphenyl) acetamide was awarded to it.

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