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. Heterocycles 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 heterocyclic 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 in 1834. 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.

1. As density of electrons is low for carbons so oxadiazole ring shows high resistance towards electrophilic substitution reactions.
2. Attack of electrophile substitution may happens on nitrogen if a change takes place in electron releasing groups.
3. 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.
4. 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-inflammatory, analgesic, anti-tumor, anti-convulsant, anti-oxidant herbicidal and anti-fungal activities. Two basic approaches are adapted by chemists for developing novel drugs:

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

For this purpose oxadiazoles and their derivatives are considered as important antinflammatory, 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 heterocycle. 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

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Biological activity</th>
<th>Reference</th>
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<tr>
<td>2-arylaminosulfonylmethyl-5-aryl-1,3,4-oxadiazole</td>
<td>Anti-bacterial activity</td>
<td>(Padmavathi et al., 2010)</td>
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<td>2,5-Disubstituted-1,3,4-oxadiazole derivatives</td>
<td>Anti-bacterial activity</td>
<td>(Jha et al., 2010)</td>
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<td>2-(Biphenyl-4-yl)-5-aryl-1,3,4-oxadiazole derivatives</td>
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<td>(Kumar et al., 2013)</td>
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<td>5-(2-amino-3-pyridyl)-2-thioxo-1,3,4-oxadiazole derivatives</td>
<td>Anti-cancer activity</td>
<td>(Liszkiewicz et al., 2003)</td>
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<tr>
<td>2-(1,3,4-triphenylpyrazol-5-yl)-5-phenyl-1,3,4-oxadiazole</td>
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<td>(Mansour et al., 2003)</td>
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<td>2-(4-chlorophenyl)-5-aryl-1,3,4-oxadiazole derivatives</td>
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<td>(Ahsan et al., 2013)</td>
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<td>5-pyridyl-1,3,4-oxadiazole-2-thiol</td>
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<td>(Khan et al., 2004)</td>
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<td>2,4-dichlorophenyl-5-(2,4,6-trichlorophenoxy)methyl1,3,4-oxadiazole</td>
<td>Anti-inflammatory activity</td>
<td>(Amir et al., 2007)</td>
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<td>2,substituted-5-(2-benzylthiophenyl)-1,3,4-oxadiazoles</td>
<td>Anti-convulsant activity</td>
<td>(Almasirad et al., 2004)</td>
</tr>
<tr>
<td>2,substituted-5-[2-(2-fluorophenoxy)phenyl]-1,3,4-oxadiazoles</td>
<td>Anti-convulsant activity</td>
<td>(Zarghi et al., 2005)</td>
</tr>
<tr>
<td>Aryl sulfonamido-5-[2′-(benzimidazol-2′′-yl)]-1,3,4-oxadiazoles</td>
<td>Anti-tubercular activity</td>
<td>(Kagthara et al., 1999)</td>
</tr>
</tbody>
</table>
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 aniline 2-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 78°C.

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 for 7-8 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-fluorobenzoate 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.
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 formed is an amide of respective aniline and is dried. Purity of product was checked by TLC.

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 ppt 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 of 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 250 ml. 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 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)

0.05 g 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-(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 250 ml. 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

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. 10 ml 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 of 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.
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 acetamide**

**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 mixed evenly. 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]N-phenyl 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 & 0.1g 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 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.

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 37°C 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 35-37°C. For checking antimicrobial 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

![Chemical structure of 4-fluoro benzoate]

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<tr>
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<th>Value</th>
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<tbody>
<tr>
<td>Color</td>
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<td>TLC spot</td>
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<td>% yield</td>
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</table>

IR Analysis

The characteristic peaks of 4-fluorobenzoate were obtained at 1601.78 cm⁻¹ for N-H, 3014.97 cm⁻¹ of alkane stretching, at 3195.52 for O-H str. and C-O at 1240.16 cm⁻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

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<td>% yield</td>
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</table>

IR Analysis

The characteristic peaks were obtained at 2945.12 cm⁻¹ for C-H methylene, for C=C at 830.37 cm⁻¹, O-H at 2766.37 cm⁻¹ and N-O at 1511 cm⁻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-fluorophenyl)-1,3,4-oxadiazole-2-ylsulfanyl)-N-(2,3-dimethylphenyl)acetamide

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%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-fluorophenyl)-1,3,4-oxadiazole-2-yl-sulfanyl)-N-(2-methylphenyl)acetamide**

<table>
<thead>
<tr>
<th>Colour</th>
<th>Light pinkish</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC spot</td>
<td>Single</td>
</tr>
<tr>
<td>Molecular wt.</td>
<td>370</td>
</tr>
<tr>
<td>Molecular formula</td>
<td>C₁₉H₁₈FN₃O₂S</td>
</tr>
<tr>
<td>Melting point</td>
<td>290-293</td>
</tr>
<tr>
<td>%yield</td>
<td>78%</td>
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</table>

**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-fluorophenyl)-1,3,4-oxadiazole-2-yl-sulfanyl)-N-(2-methyl,6-ethylphenyl)acetamide**

<table>
<thead>
<tr>
<th>Colour</th>
<th>Off white</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC spot</td>
<td>Single</td>
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<tr>
<td>Molecular formula</td>
<td>C₂₀H₂₀FN₃O₂S</td>
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<tr>
<td>Molecular wt.</td>
<td>384</td>
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<td>Melting point</td>
<td>320-328</td>
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**IR Analysis**
The characteristics peaks for 2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-sulfanyl)-N-(2-methyl,6-ethylenyl)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-oxadiazole-2-sulfanyl)-N-(2-methyl,6-ethylenyl)acetamide was awarded to it.

**2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-yl-sulfanyl)-N-(2-methyl,6-ethylenyl)acetamide**

<table>
<thead>
<tr>
<th>Colour</th>
<th>Ash white</th>
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<tbody>
<tr>
<td>TLC spot</td>
<td>Single</td>
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<tr>
<td>Molecular formula</td>
<td>C₁₇H₁₄FN₃O₂S</td>
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<tr>
<td>Molecular wt.</td>
<td>422</td>
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</table>

**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-yl-sulfanyl)-N-(2-bromophenyl)acetamide was awarded to it.
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

<table>
<thead>
<tr>
<th>Colour</th>
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</thead>
<tbody>
<tr>
<td>TLC spot</td>
<td>Single</td>
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<tr>
<td>Molecular wt.</td>
<td>370</td>
</tr>
<tr>
<td>Molecular formula</td>
<td>C19H18FN3O2S</td>
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<tr>
<td>Melting point</td>
<td>269-271</td>
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</table>

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 3071 cm\(^{-1}\) for C-H, for C=O at 1731 cm\(^{-1}\), for C-F at 1499 cm\(^{-1}\). 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-oxadiazole-2-yl-sulfanyl)-N-(3,5-dimethylphenyl)acetamide was awarded to it.

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

<table>
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<tbody>
<tr>
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<tr>
<td>Molecular wt.</td>
<td>356</td>
</tr>
<tr>
<td>Molecular formula</td>
<td>C18H16FN3O2S</td>
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<td>206-208</td>
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<tr>
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</table>

IR Analysis
IR analysis revealed the presence of characteristic peaks at 2366.58 for 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-fluorophenyl)-1,3,4-oxadiazole-2-yl-sulfanyl)-N-(2ethoxyphenyl)acetamide.

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

<table>
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<tbody>
<tr>
<td>TLC spot</td>
<td>Single</td>
</tr>
<tr>
<td>Molecular wt.</td>
<td>377</td>
</tr>
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<td>Molecular formula</td>
<td>C17H14FCIN3O2S</td>
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<tr>
<td>Melting point</td>
<td>291-293</td>
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<td>80%</td>
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</table>

IR Analysis
The characteristics peaks for 2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-sulfanyl)-N-(3-chlorophenyl)acetamide were observed at 3068 cm\(^{-1}\) for C-H, 2359 cm\(^{-1}\) for C-N, for N-H at 3266 cm\(^{-1}\) and for C-Br at 823 cm\(^{-1}\). 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-oxadiazole-2-yl-sulfanyl)-N-(3-chlorophenyl)acetamide was awarded to it.

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

<table>
<thead>
<tr>
<th>Colour</th>
<th>Light yellow</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC spot</td>
<td>Single</td>
</tr>
<tr>
<td>Molecular wt.</td>
<td>356</td>
</tr>
<tr>
<td>Molecular formula</td>
<td>C18H20FN3O2S</td>
</tr>
<tr>
<td>Melting point</td>
<td>201-203</td>
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</table>

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 O-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-
fluorophenyl)-1,3,4-oxadiazole-2-yl-sulfanyl)-N-(2-ethylphenyl)acetamide.

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

<table>
<thead>
<tr>
<th>Colour</th>
<th>Light yellow</th>
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</thead>
<tbody>
<tr>
<td>TLC spot</td>
<td>Single</td>
</tr>
<tr>
<td>Molecular wt.</td>
<td>356</td>
</tr>
<tr>
<td>Molecular formula</td>
<td>C_{18}H_{20}FN_{3}O_{2}S</td>
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<tr>
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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-fluorophenyl)-1,3,4-oxadiazole-2-yl-sulfanyl)-N-(4-ethylphenyl)acetamide.

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

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>TLC spot</td>
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<tr>
<td>Molecular formula</td>
<td>C_{18}H_{15}FN_{3}O_{2}S</td>
</tr>
<tr>
<td>Molecular wt.</td>
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</tr>
<tr>
<td>Melting point</td>
<td>298-300</td>
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<tr>
<td>% yield</td>
<td>79%</td>
</tr>
</tbody>
</table>

IR Analysis

The characteristics peaks for 2-(5-(4-fluorophenyl)-1,3,4-oxadiazole-2-sulfanyl)-N-(3-methylphenyl)acetamide were observed at 2708 cm\(^{-1}\) for C-H, 1667 of C=N cm\(^{-1}\), for O-H at 3242, for C-N str. at 1310 cm\(^{-1}\) and for C-Cl at 813 cm\(^{-1}\). 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.

REFERENCES

