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# SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVOLUTION OF VARIOUS NOVEL HETEROCYCLIC COMPOUNDS OF HYDANTOIN AND PIPERAZINE

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**Abstract:** In the present article we have prepared novel 3,5-substituted imidazolidine-2,4-dione **(3a-f)** and **(4a-f)** via Mannich reaction between piperazine derivatives and hydantoin derivatives **(2a and 2b)**. For all compounds NOE (Nuclear Overhauser Effect) NMR spectra were measured in order to prove additionally the position of the substituents in the imidazolidine-2,4-dione ring. Some physiochemical and electronic properties of the compounds were determined in order to establish the similarity between the synthesized and reference compounds. All the compounds were also characterized by $^{13}C$ NMR, FT-IR and LC/MS mass spectrum. All the newly synthesized compounds were screened for their in vitro antimicrobial activity and many of them found to show comparable activity to the standard drug with different microorganisms.

**Keywords:** Hydantoin; Piprazine; Mannich Reaction; Antimicrobial Activity.

## Introduction

Nowadays, there is an incessant search for biological functional compounds suitable for treating diverse illnesses. The development of more efficient and less toxic products often involves the study of new synthetic routes or structural modifications of existing molecules and medicinal drugs are often manufactured by modification or molecular variation using bioisosterism [I]. The synthesis of heterocyclic 2,4-imidazolidinones or hydantoins has been studied intensively for their important pharmacological properties [II]. Substances that contain these heterocyclic moieties present significant biological activities as antifungal [III], antibacterial and anti-inflammatory [IV] drugs, for the treatment of hypoglycemia [V], or as plant growth inhibitors [VI], among other properties. 2-Thiohydantoins have been widely evaluated due to their applications as hypolipidemic, anticarcinogenic, antiviral (e.g., herpes virus, HSV, HIV and tuberculosis), antimicrobial, anti-ulcer and anti-inflammatory agents [VII]. Several studies [VIII-X] have described the synthesis of amino acid compounds, their importance and applications as intermediates for the synthesis of heterocyclics [XI,XII]. The hydantoin nucleus [XIII] has many

pharmacological effects1 and is found in several clinically important medicines (e.g., nilutamide [XIV], phenytoin [XV]). Hydantoins also serve as useful intermediates for the preparation of non-natural amino acids via chemical1 or enzymatic hydrolysis [XVI]. Of existing methods to hydantoins,[XIII, XVII-XXIV] the Bucherer–Bergs reaction provides perhaps the best method for their preparation [XXV-XXXIII].

Recently, other aqueous solutions of diamines such as piperazine became of interest to scientists due to their fast reaction rate with $CO_2$. Studies show that piperazine has a much faster reaction rate compared to MEA (the most commonly used solvent in $CO_2$ capture technology) [XXXIV]. Diamines (for example, piperazine) are also known to have a higher capacity (solubility) for $CO_2$ absorption than monoamines and can reach very high loading (higher than 3 mol $CO_2$/mol piperazine) at very high $CO_2$ partial pressures. However, the absence of a hydroxyl group in piperazine makes it less soluble in water at high concentrations. Piperazine derivative have shown to posses diverse biological properties including anthelminstic, antihistamine, anti-ketonic, anticonvulsant, anti HIV and as potential cocaineabuse therapeutic agent [XXXV-XXXVIII].

Thus, looking to the wide applications of both these moieties, the present communication comprises the mild one-pot conversion of hydantoin **(2a and 2b)** to the corresponding 3,5-disubstituted imidazolidine-2,4-dione **(3a-f)** and **(4a-f)** with high yields. Such a transformation would be particularly useful for medicinal chemists since it would give them direct access to a useful bioisostere of the ester in a single chemical transformation.

**Experimental**

The elemental analyses were performed by Vario EL CHN elemental analyzer. The FT-IR spectra were recorded on Perkin Elmer Spectrum GX spectrophotometer using KBr pellets. The $^{1}H$ and $^{13}C$ NMR spectra were recorded on Bruker 400 MHz instrument using DMSO-$d_6$ as solvent. The MS-CI spectrum of were recorded on Shimadzu LC–MS 2010 eV spectrometer in acetonitrile. The melting points were checked by standard open capillary method and are uncorrected.

**Synthesis of imidazolidine-2,4-dione (2a, 2b)**

Cyclocondensation reaction of various acetophenone with potassium cyanide and ammonium carbonate in the presence of ethanol at reflux temperature for 6-7 hr gives imidazolidine-2,4-dione **(2a, 2b)** derivatives. The progress of the reaction was monitored on TLC plate. After completion of reaction, obtained reaction mass was recrytallized from methanol.

**Synthesis of 5-alky-3-((4-alkylpiperazin-1-yl)methyl)-5-phenylimidazolidine-2,4-dione(3a-f)**

Compound 2a (2gm, 0.01mol) were dissolved in ethanol as per required quantity then formaldehyde (0.45gm, 0.015mol) was added with constant stirring. After completion of addition various derivatives of piprazine (0.01mole) were added and then few drops of hydrochloric acid was added as catalyst and whole reaction mixture was refluxed for 6-7 hr, entire reaction was governed by TLC. After completion of reaction, mixture was made acidic (pH, 3-4) by adding hydrochloric acid then solvent was evaporating to get off white product which was purified by column chromatography and recrytalize from methanol.

**Synthesis of 5-alky-3-((4-alkylpiperazin-1-yl)methyl)-5,5-diphenylimidazolidine-2,4-dione(4a-f)**

Compound 2a (2gm, 0.01mol) / b (2.52gm, 0.01mol) were dissolved in ethanol as per required quantity then formaldehyde (0.45gm, 0.015mol) was added with constant stirring. After

compellation of addition various derivatives of piprazine (0.01mole) were added and then few drops of hydrochloric acid was added as catalyst and whole reaction mixture was refluxed for 6-7 hr, entire reaction was governed by TLC. After completion of reaction, mixture was made acidic (pH, 3-4) by adding hydrochloric acid then solvent was evaporating to get off white product which was purified by column chromatography and recrytalize from methanol.

**Antimicrobial Activity**

All the synthesized compounds were tested in concentrations of 0.1 g/ml using dimethylformamide (DMF) as a solvent. The microorganisms used were as follows: Gram-negative bacteria, E. coli, P. aeruginosa; Gram-positive bacteria, B. subtilis, S. aureus, and Fungi, P. piricola, F. oxysporum.

**Medium:**

The cap-assay method containing (g/l) peptone (6.0), yeast extract (3.0), meat extract (1.5), glucose (1.0), and agar (20.0) were used. The medium was sterilized and divided while hot (50-60 °C) into 15-ml portions among sterile Petri dishes 9 cm in diameter. One ml of the spore suspension of each microorganism was spread all over the surface of the cold solid medium placed in the Petri dish.

**Method:**

Portions of 0.5 g of each tested compound were dissolved in 5ml of DMF. An amount of 0.1ml of the test solution was placed on Whatman paper disc, 9 mm in diameter, and the solvent was left to evaporate. These saturated discs were placed carefully on the surface of the inoculated solid medium; each Petri dish contained at least three discs. The Petri dishes were incubated at 5 °C for an hour to permit good diffusion, then transferred to an incubator at 85 °C overnight, and then examined. The results were recorded by measuring the inhibition zone diameters and are presented in **Table 2**.

**Spectral Analysis Data**

***5-methyl-3-((4-methylpiperazin-1-yl)methyl)-5-phenyzimidazolidine-2,4-dione(3a)***

mp 153°C ; yield 70 %; FTIR (KBr/cm$^{-1}$) : 1517 (C=C, Ar), 1716 (C=O, amide), 2900, 2950 (C-H, aliphatic), 3110 (C-H, Ar), 3250 (NH, amide); $^{1}$H NMR (DMSO, δ): 1.73 (s, 3H, -$CH_3$), 2.52 (t, 4H, N-$CH_2$), 2.77 (s, 3H, N-$CH_3$), 3.17 (t, 4H, N-$CH_2$), 5.05 (s, 2H, -$CH_2$-exocyclic), 7.25-7.52 (m, 5H, Ar-H), 8.32 (brs, 1H, NH); $^{13}$C NMR (DMSO, δ): 25.6, 46.6, 51.8, 57.3, 63.8, 69.3, 127.6, 129.2, 129.6, 140.7, 156.6, 175.5; m/z: 302.17 (M+).

***3-((4-ethylpiperazin-1-yl)methyl)-5-methyl-5-phenylimidazolidine-2,4-dione(3b)***

mp 185°C; yield 74 %; FTIR (KBr/cm$^{-1}$) : 1524 (C=C, Ar), 1711 (C=O, amide), 2918, 2965 (C-H, aliphatic), 3102 (C-H, Ar), 3262 (NH, amide); $^{1}$H NMR (DMSO, δ): 0.98 (t, 3H, -$CH_2CH_3$), 1.71 (s, 3H, -$CH_3$), 2.08 (q, 2H,-$CH_2CH_3$), 2.53 (t, 4H, N-$CH_2$), 3.15 (t, 4H, N-$CH_2$), 5.07 (s, 2H, -$CH_2$-exocyclic), 7.18-7.59 (m, 5H, Ar-H), 8.34 (brs, 1H, NH); $^{13}$C NMR (DMSO, δ): 13.3, 25.6, 49.6, 52.1, 57.6, 63.8, 69.3, 127.6, 129.2, 129.6, 140.7, 156.6, 175.5; m/z: 316.18 (M+).

***5-methyl-5-phenyl-3-((4-phenylpiperazin-1-yl)methyl)imidazolidine-2,4-dione(3c)***

mp 191°C ; yield 77 %; FTIR (KBr/cm$^{-1}$) : 1520 (C=C, Ar), 1724 (C=O, amide), 2911, 2962 (C-H, aliphatic), 3114 (C-H, Ar), 3260 (NH, amide); $^{1}$H NMR (DMSO, δ): 1.73 (s, 3H, -$CH_3$), 2.49 (t, 4H, N-$CH_2$), 3.19 (t, 4H, N-$CH_2$), 5.05 (s, 2H, -$CH_2$-exocyclic), 6.95-7.77 (m, 10H, Ar-H), 8.29 (brs, 1H, NH); $^{13}$C NMR (DMSO, δ): 25.6, 51.7, 52.0, 63.8, 69.3, 114.3, 121.9, 127.6, 129.2, 129.6, 140.7, 149.6, 156.6, 175.5; m/z: 364.18 (M+).

***3-((4-benzylpiperazin-1-yl)methyl)-5-methyl-5-phenylimidazolidine-2,4-dione(3d)***

mp 182° ; yield 69 %; FTIR (KBr/cm$^{-1}$) : 1515 (C=C, Ar), 1728 (C=O, amide), 2913, 2957 (C-H, aliphatic), 3110 (C-H, Ar), 3252 (NH, amide); $^{1}$H NMR (DMSO, δ): 1.77 (s, 3H, -$CH_3$), 2.52

(t, 4H, N-$CH_2$), 2.77 (s, 3H, N-$CH_3$), 3.17 (t, 4H, N-$CH_2$), 4.48 (s, 2H, benzyl $CH_2$), 5.05 (s, 2H, -$CH_2$-exocyclic), 7.20-7.92 (m, 10H, Ar-H), 8.32 (brs, 1H, NH); $^{13}$C NMR (DMSO, δ): 25.6, 52.1, 54.7, 63.8, 64.4, 69.3, 127.2, 127.6, 128.4, 128.8, 129.2, 129.6, 138.6, 140.7, 156.6, 175.5; m/z: 378.20 (M+).

***3-((4-(2,3-dichlorophenyl)piperazin-1-yl)methyl)-5-methyl-5-phenylimidazolidine-2,4-dione (3e)***

mp 180°C ; yield 63% ; FTIR (KBr/cm$^{-1}$) : 1065, 1080 (C-Cl), 1510 (C=C, Ar), 1710 (C=O, amide), 2910, 2952 (C-H, aliphatic), 3119 (C-H, Ar), 3246 (NH, amide); $^1$H NMR (DMSO, δ): 1.69 (s, 3H, -$CH_3$), 2.55 (t, 4H, N-$CH_2$), 3.15 (t, 4H, N-$CH_2$), 5.09 (s, 2H, -$CH_2$-exocyclic), 7.12-7.84 (m, 8H, Ar-H), 8.35 (brs, 1H, NH); $^{13}$C NMR (DMSO, δ): 25.6, 51.5, 51.7, 63.8, 69.3, 117.6, 123.9, 127.2, 127.6, 129.1, 129.2, 129.6, 133.3, 140.7, 150.0, 156.6, 175.5; m/z: 432.11 (M+).

***3-((4-(2,5-dichlorophenyl)piperazin-1-yl)methyl)-5-methyl-5-phenylimidazolidine-2,4-dione (3f)***

mp 195°C ; yield 60% ;S FTIR (KBr/cm$^{-1}$) : 1060, 1083 (C-Cl), 1520 (C=C, Ar), 1719 (C=O, amide), 2916, 2961 (C-H, aliphatic), 3121 (C-H, Ar), 3251 (NH, amide); $^1$H NMR (DMSO, δ): 1.73 (s, 3H, -$CH_3$), 2.54 (t, 4H, N-$CH_2$), 3.18 (t, 4H, N-$CH_2$), 5.08 (s, 2H, -$CH_2$-exocyclic), 7.19-7.89 (m, 8H, Ar-H), 8.32 (brs, 1H, NH); $^{13}$C NMR (DMSO, δ): 25.6, 51.5, 51.7, 63.8, 69.3, 116.1, 119.7, 127.1, 127.6, 129.2, 129.6, 133.3, 140.7, 152.2, 156.6, 175.5; m/z: 432.11 (M+).

***3-((4-methylpiperazin-1-yl)methyl)-5,5-diphenylimidazolidine-2,4-dione(4a)***

mp 195°C ; yield 73%; FTIR (KBr/cm$^{-1}$) : 1516 (C=C, Ar), 1720 (C=O, amide), 2903, 2951 (C-H, aliphatic), 3112 (C-H, Ar), 3250 (NH, amide), $^1$H NMR (DMSO, δ): 1.62 (s, 3H, -$CH_3$), 2.51 (t, 4H, N-$CH_2$), 3.15 (t, 4H, N-$CH_2$), 5.06 (s, 2H, -$CH_2$-exocyclic), 7.11-7.84 (m, 10H, Ar-H), 8.31 (brs, 1H, NH); $^{13}$C NMR (DMSO, δ): 46.6, 51.8, 57.3, 63.8, 73.7, 126.2, 128.2, 129.2, 139.8, 156.6, 161.9; m/z: 364.18 (M+).

***3-((4-ethylpiperazin-1-yl)methyl)-5,5-diphenylimidazolidine-2,4-dione(4b)***

mp 203°C ; yield 64%; FTIR (KBr/cm$^{-1}$) : 1517 (C=C, Ar), 1716 (C=O, amide), 2905, 2951 (C-H, aliphatic), 3115 (C-H, Ar), 3254 (NH, amide); $^1$H NMR (DMSO, δ): 0.96 (t, 3H, -$CH_2CH_3$), 1.72 (s, 3H, -$CH_3$), 2.07 (q, 2H,-$CH_2CH_3$ ), 2.55 (t, 4H, N-$CH_2$), 3.11 (t, 4H, N-$CH_2$), 5.06 (s, 2H, -$CH_2$-exocyclic), 7.17-7.88 (m, 10H, Ar-H), 8.33 (brs, 1H, NH); $^{13}$C NMR (DMSO, δ): 13.3, 49.6, 52.1, 57.6, 63.8, 73.7, 126.2, 128.2, 129.2, 139.8, 156.6, 161.9 m/z: 378.20 (M+).

***5,5-diphenyl-3-((4-phenylpiperazin-1-yl)methyl)imidazolidine-2,4-dione(4c)***

mp 189°C ; yield 59%; FTIR (KBr/cm$^{-1}$) : 1512 (C=C, Ar), 1715 (C=O, amide), 2915, 2963 (C-H, aliphatic), 3119 (C-H, Ar), 3250 (NH, amide), $^1$H NMR (DMSO, δ): 1.69 (s, 3H, -$CH_3$), 2.55 (t, 4H, N-$CH_2$), 3.19 (t, 4H, N-$CH_2$), 5.02 (s, 2H, -$CH_2$-exocyclic), 7.05-7.87 (m, 10H, Ar-H), 8.35 (brs, 1H, NH); $^{13}$C NMR (DMSO, δ): 51.7, 52.0, 63.8, 73.7, 114.3, 121.9, 126.2, 128.2, 129.2, 129.6, 139.8, 156.6, 161.9; m/z: 426.20 (M+).

***3-((4-benzylpiperazin-1-yl)methyl)-5,5-diphenylimidazolidine-2,4-dione(4d)***

mp 149°C; yield 68%; FTIR (KBr/cm$^{-1}$) : 1517 (C=C, Ar), 1721 (C=O, amide), 2901, 2947 (C-H, aliphatic), 3112 (C-H, Ar), 3247 (NH, amide), $^1$H NMR (DMSO, δ): 1.74 (s, 3H, -$CH_3$), 2.50 (t, 4H, N-$CH_2$), 3.14 (t, 4H, N-$CH_2$), 4.62 (s, 2H, benzyl $CH_2$), 5.05 (s, 2H, -$CH_2$-exocyclic), 7.09-7.82 (m, 10H, Ar-H), 8.36 (brs, 1H, NH); $^{13}$C NMR (DMSO, δ): 52.1, 54.7, 63.8, 64.4, 73.7, 126.2, 127.2, 128.2, 128.4, 128.8, 129.2, 138.6, 139.8, 156.6 161.; m/z: 440.221 (M+).

***3-((4-(2,3-dichlorophenyl)piperazin-1-yl)methyl)-5,5-diphenylimidazolidine-2,4-dione(4e)***

mp 147°C; yield 63%; FTIR (KBr/cm$^{-1}$) : 1062, 1088 (C-Cl), 1518 (C=C, Ar), 1720 (C=O, amide), 2921, 2964 (C-H, aliphatic), 3116 (C-H, Ar), 3250 (NH, amide), $^1$H NMR (DMSO, δ):

1.74 (s, 3H, -$CH_3$), 2.50 (t, 4H, N-$CH_2$), 3.16 (t, 4H, N-$CH_2$), 5.08 (s, 2H, -$CH_2$-exocyclic), 7.15-7.74 (m, 10H, Ar-H), 8.31 (brs, 1H, NH); $^{13}$C NMR (DMSO, δ): 51.5, 51.7, 63.8, 73.7, 117.6, 123.9, 126.2, 127.2, 129.1, 129.2, 133.3, 139.8, 156.6, 161.9; m/z: 494.12 (M+).

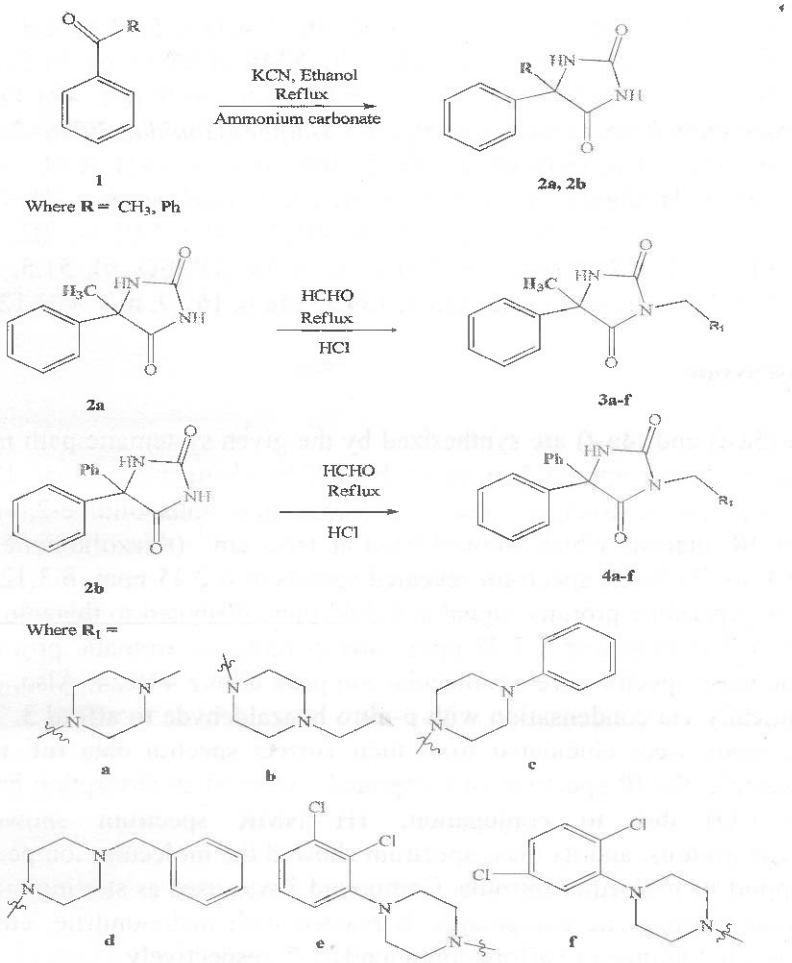
***3-((4-(2,5-dichlorophenyl)piperazin-1-yl)methyl)-5,5-diphenylimidazolidine-2,4-dione(4f)***

mp 210°C; yield 71%; FTIR (KBr/cm$^{-1}$) : 1072, 1081 (C-Cl), 1521 (C=C, Ar), 1724 (C=O, amide), 2910, 2955 (C-H, aliphatic), 3110 (C-H, Ar), 3258 (NH, amide), $^1$H NMR (DMSO, δ): 1.72 (s, 3H, -$CH_3$), 2.55 (t, 4H, N-$CH_2$), 3.15 (t, 4H, N-$CH_2$), 5.03 (s, 2H, -$CH_2$-exocyclic), 7.11-7.79 (m, 10H, Ar-H), 8.33 (brs, 1H, NH); $^{13}$C NMR (DMSO, δ): 51.5, 51.7, 63.8, 73.7, 116.1, 119.7, 126.2, 127.1, 128.2, 129.2, 133.3, 139.8, 156.6, 161.9; m/z: 494.12 (M+).

## Results and discussion

### Chemistry

The compound (**3a-f**) and (**4a-f**) are synthesized by the given systematic path in **Scheme 1**. The structures of the resulting compounds were established by elemental analysis, IR, NMR and MS spectral data. The proposed structure given to 3,5-substituted imidazolidine-2,4-dione derivatives were support by IR analysis which showed band at 1695 cm$^{-1}$ (thiazolidinone, CO) and 1338-1142 cm$^{-1}$ ($SO_2$). Its $^1$H NMR spectrum revealed signals at δ 2.45 ppm, δ 3.12 ppm and δ 3.71 ppm attributed to piperidine protons, signal at δ 3.62 ppm attributed to thiazole ring protons and two doublets at δ 7.48 ppm and δ 7.78 ppm corresponding to aromatic protons of thiophene. Furthermore, the mass spectra gave a molecular ion peak at m/z 448.24. Also, compound 2 was confirmed chemically via condensation with p-nitro benzaldehyde to afford 3. The structures of the latter compounds were elucidated from their correct spectral data (cf. the Experimental section). For example, the IR spectrum of compound 3 showed an absorption band at 1698 cm-1 (thiazolidinone CO) due to conjugation, 1H NMR spectrum showed absence of thiazolomethylene protons, and its mass spectrum showed the molecular ion peak at m/z 581.73, all of which support its molecular formula. Compound 3 was used as starting material for further synthesis of other heterocyclic compounds. It reacted with malononitrile, ethyl cyanoacetate, phenyle hydrazine and thiourea to afford compounds 4-7, respectively.




**Scheme 1. Systematic path of synthesis of compounds (3a-f) and (4a-f)**

The structures of these compounds were confirmed from their correct spectral data (cf. the Experimental section). For example, the IR spectrum of compound 7 showed the absence of the band characteristic for (thiazolidinone CO) and the presence of absorption bands at 3170, 3120 cm-1(NH), and 1213 cm-1(CS). Also, it's 1H NMR spectrum revealed signals at δ 4.58 ppm characteristic of the pyrimidine ring and at δ 8.87 ppm and δ 11.18 ppm for 2NH protons that are D2O exchangeable. Mass spectra showed M+ peak at m/z 639.83, which supports its molecular formula.

On the other hand, compound 7 was allowed to react with acrylonitrile via Michael addition to afford 8 and halo compound, namely dichloroacetone to afford compound 9. Also, compound 7 was reacted with hydrazine hydrate to afforded hydrazine pyrimidine derivative 10 (Scheme 1). The structures of all the synthesised compounds were confirmed by their correct spectral data (cf. the Experimental section).

**Table 1. Analytical & physicochemical data of the synthesized compounds (3a-f) and (4a-f)**

| Comp. | M. F. | M. W. | M. P. ◦ C | Yield % | Elementary analysis Calculated (Found) | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | C | H | N | X |
| 3a | $C_{16}H_{22}N_4O_2$ | 302.17 | 153 | 70 | 63.57 (63.45) | 7.31 | 18.55 | |
| 3b | $C_{17}H_{24}N_4O_2$ | 316.18 | 185 | 74 | 64.54 | 7.62 | 17.69 | |
| 3c | $C_{21}H_{24}N_4O_2$ | 364.18 | 191 | 77 | 69.18 | 6.62 | 15.39 | |
| 3d | $C_{22}H_{26}N_4O_2$ | 378.20 | 182 | 69 | 69.85 | 6.91 | 14.82 | |
| 3e | $C_{21}H_{22}Cl_2N_4O_2$ | 432.11 | 180 | 63 | 58.18 | 5.13 | 12.95 | 16.33 |
| 3f | $C_{21}H_{22}Cl_2N_4O_2$ | 432.11 | 195 | 60 | 58.22 | 5.15 | 12.95 | 16.35 |
| 4a | $C_{21}H_{24}N_4O_2$ | 364.18 | 195 | 73 | 69.22 | 6.65 | 15.38 | |
| 4b | $C_{22}H_{26}N_4O_2$ | 378.20 | 203 | 64 | 69.86 | 6.95 | 14.83 | |
| 4c | $C_{26}H_{26}N_4O_2$ | 426.20 | 189 | 59 | 73.19 | 6.15 | 13.15 | |
| 4d | $C_{27}H_{22}N_4O_2$ | 440.221 | 149 | 68 | 73.63 | 6.40 | 12.75 | |
| 4e | $C_{26}H_{24}Cl_2N_4O_2$ | 494.12 | 147 | 63 | 63.06 | 4.90 | 11.35 | 14.35 |
| 4f | $C_{26}H_{24}Cl_2N_4O_2$ | 494.12 | 210 | 71 | 63.08 | 4.89 | 11.32 | 14.32 |

**Antimicrobial studies**

All the newly synthesized compounds were screened for their antibacterial and antifungal activity. For antibacterial studies microorganisms employed were S. aureus, B.Subtillis, Escherichia coil and Ps.Aeruginosa. For antifungal, P. piricola and F. oxysporum were used as microorganisms. Both antimicrobial studies were assessed by minimum inhibitory concentration (MIC). The data are summarized in Table I and show that all compounds display certain activity against the tested microorganisms.

From SAR we can see that the antibacterial and antifungal activity of the synthesized compounds may be due the presence of the versatile pharmacophore which might increase the lipophilic character of the molecules, which facilitate the crossing through the biological membrane of the microorganism and thereby inhibit their growth.

| Compound | Zone of Inhibition (in mm) | | | | | |
|---|---|---|---|---|---|---|
| | Gram positive | | Gram negative | | Antifungal | |
| | B.Subtillis | S.Aureus | E.Coli | Ps.Aeruginosa | P. piricola | F. oxysporum |
| **3a** | 12 | 14 | 13 | 11 | 24 | 18 |
| **3b** | 11 | 15 | 11 | 09 | 13 | 07 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **3c** | 12 | 12 | 11 | 11 | 12 | 11 |
| **3d** | 10 | 10 | 09 | 10 | 19 | 14 |
| **3e** | 12 | 11 | 08 | 14 | 17 | 14 |
| **3f** | 17 | 16 | 11 | 18 | 14 | 09 |
| **4a** | 18 | 20 | 12 | 16 | 12 | 13 |
| **4b** | 12 | 11 | 09 | 13 | 21 | 16 |
| **4c** | 15 | 14 | 16 | 17 | 18 | 14 |
| **4d** | 16 | 08 | 13 | 12 | 25 | 17 |
| **4e** | 12 | 10 | 09 | 11 | 14 | 15 |
| **4f** | 10 | 09 | 11 | 10 | 22 | 20 |

## Conclusion

The preparation procedure follow in this work for synthesis of the title compounds offers reduction in the reaction time, operation simplicity, cleaner reaction, easy work-up and improved yields. All spectroscopic analysis confirmed the proposed structures of these compounds. Biological activity data have shown that the synthesized compounds have a significant biological activity against the tested microorganisms.

In conclusion, a series of novel 4-(4-(6,7-dihydrothieno[3,2-c]pyridin-5(4H)-ylsulfonyl) phenyl)-1-thia-4-azaspiro[4.5]decan-3-one 5 derivatives have been synthesized and evaluated for their antibacterial(MIC) activity and antifungal (MIC) activity against various bacteria and fungi. Many of the synthesized compounds showed good activity against the test bacteria and fungi.

Results of present study shows that, a new class of different dibenzothiazepine synthesized from 2-chloro substituted phenylacetamide, evaluated for antibacterial and antifungal activities. Among the **tested 3c, 3f, 4a, 4c and 4d** compounds showed better antibacterial activity and said to be the most proficient member of the series and for future scope.

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