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SYNTHESIS AND BIOLOGICAL ACTIVITIES OF 2-(FUROYL AMINO)-5-(SUBSTITUTED ARYL)-1,3,4-THIADIAZOLE AND 2-(SUBSTITUTED BENZOYL AMINO)-5-(FURYL)-1,3,4-THIADIAZOLE

Vijay V Dabholkar* and Bharat M Parmar

Organic Research Laboratory, Department of Chemistry,
K C College, Churchgate, Mumbai-400 020. India.
E-mail: bparmar1976@rediffmail.com
vijaydabholkar@gmail.com

Abstract

1-(substituted aroyl)-4-furoyl- thiosemicarbazides **3(a-e)** / 1-furoyl-4-(substituted benzoyl)-thiosemicarbazides **7(a-f)** are synthesized under phase transfer catalysis, which on cyclisation with perchloric acid in acetic anhydride furnish perchloric acid salt of 2-(furoylamino)-5-(substituted aryl)-1,3,4-thiadiazoles **4(a-e)**/ 2-(substituted benzoylamino)-5-(furyl)-1,3,4-thiadiazoles **8(a-f)** respectively. The sulphur and nitrogen containing compounds were screened for anti-microbial activity showed convincing inhibition against *E. coli, S. typhi*, *S. aureus,* and *B.Substilus* bacteria.

Keywords : 1-(substituted aroyl)-4-furoyl- thiosemicarbazides, PTC, 2-(furoylamino)-5-(substituted aryl)-1,3,4-thiadiazoles

INTRODUCTION

Substituted 1,3,4-thiadiazole have attracted much attention due to their anti microbial[1,2,3], anti bacterial[4], animitotic[5], anti inflammatory[6,7], psychotropic[8], antiafloxigenic[9], anti convulsant[10], plant growth regulating[11] and mono amine oxidase inhibiting activities[12]. The wide range of therapeutic value of the above ring system prompted us to synthesize several new 2-(furoylamino)-5-(substituted aryl)-1,3,4-thiadiazoles **4(a-e)** / 2-(substituted benzoylamino)-5-(furyl)-1,3,4-thiadiazoles **8(a-f)**. The structures of the products were confirmed by elemental analysis, IR, ^{1}H, ^{13}C NMR and mass spectral analysis. The anti-microbial activities of the newly synthesized compounds were also investigated. In the present invention perchloric acid was used for cyclisation of 1-(substituted aroyl)-4-furoyl- thiosemicarbazides **3(a-e)** / 1-furoyl-4-(substituted benzoyl)-thiosemicarbazides **7(a-f)** to yield **4(a-e) / 8(a-f)** respectively**.**

RESULT AND DISSUCION

Interaction of furoyl chloride/ substituted benzoyl chloride with ammonium thiocyanate at room temperature catalysed by polyethyleneglycol (PEG-400) yielded substituted furoyl thiocyanate **1/** Substituted benzoyl thiocyanate **2** as an intermediate. Which on treatment with Furoic acid hydrazide/ Substituted benzoic acid hydrazide[13] in *situ* at room temperature affords 1-(substituted aroyl)-4-furoyl- thiosemicarbazides **3(a-e)** / 1-furoyl-4-(substituted benzoyl)-

thiosemicarbazides **7(a-f)** in excellent yields, further, cyclisation was achieved with perchloric acid in acetic anhydride to furnish perchloric acid salt of 2-(furoylamino)-5-(substituted aryl)-1,3,4-thiadiazoles **4(a-e)** / 2-(substituted benzoylamino)-5-(furyl)-1,3,4-thiadiazoles **8(a-f)**. **(Scheme A and B).** The NMR Spectrum of **3(a-e)** and **7(a-f)** showed three singlate in the range of 10.5 to 12.5 for 3 –NH group, Where as spectrum of **4(a-e)** and **8(a-f)** showed singlet for one –NH group. More over the IR spectra of **3** and **7** also showed band in the region 1230 to 1280 cm^{-1} for –C=S group , which was found absent in the IR spectra of **4(a-f)** and **8(a-f)**. Also the prominent bands in the region of 1465-1470 for C-S-C group and 1540-1560 for –C=N group had confirmed the structure of **4 / 8**.

BIOLOGICAL ACTIVITY

The antibacterial activity was determined in vitro by filter paper disc diffusion method[16,17] by measuring inhibition zone in mm. All the tested compounds with standard drug were screened for antibacterial activity against bacterial strain at concentration of 250µg/ml. Nutrient agar was used as culture medium. Some of compounds exhibited noticeable antibacterial activity. (**table- III**)

Experimental

IR spectra (KBr in cm^{-1}) were recorded on Perkin-Elmer spectrum One FTIR spectrophotometer in the range of 4000-400 cm^{-1}. Melting points of all the compounds were determined in soft glass open capillaries on an electrothermal apparatus and are uncorrected. ^{1}H NMR spectra as well as ^{13}C NMR spectra were recorded on Bruker Amx 500 MHz NMR spectrophotometer using DMSO-d_6 as solvent and TMS as an internal standard (chemical shifts in δ ppm). Mass spectra were recorded on 1100 series LC/MSD trap, Agilent. C,H,N estimation were recorded on Carlo Erba 1108 (CHN) Elemental Analyser. The substiuted benzoyl chlorides, furoyl chloride, Substituted benzoic acid hydrazide and furoic acid hydrazide were prepared according to the literature procedure[13,14,15]. Commercial sample of ammonium thiocyanate, poly ethylene glycol (PEG-400) and all the solvents were used.

Scheme A

1-benzoyl-4-furoyl- thiosemicarbazides 3a

To the solution of furoyl chloride (3.2 gms, 0.024 mole) in acetonitrile (25 cm^3), ammonium thiocyanate (2.80 gms, 0.0368 mole) and polyethylene glycol (PEG-400) (0.2 gm) were added. The mixture was stirred for 1 hr at room temperature and then benzoic acid hydrazide (3.10 gms, 0.022 mole) was added to it. The reaction mixture was further stirred for two hrs. To the resulting mixture, water (50 cm^3) was added to dissolve inorganic salt. The slurry was filtered and the solid obtained was washed with water and acetonitrile (1:1)(30 cm^3). The product was recrystallised from DMF:Ethanol:Water (4:3:3) to yield **3a** (85 %).

The compounds **3b-e** were prepared in a similar manner and their analytical data are reported in **table-I**.

3a) This compound was obtained as off white crystal in yield 87%, m.p. 143-145°C, [found : C, 53.98; H, 3.79; N, 14.54; S, 11.06. $C_{13}H_{11}N_3O_3S$ requires C, 53.97; H, 3.80; N, 14.53; S, 11.07 %];.υ_{max} /cm^{-1}: 1247 (C=S), 1693 (C=O), 3018-3246 (NH), δ_H 6.75-8.08 (m, 7H, ArH), 11.13 (s,1H,NH^c), 11.58 (s,1H,NH^b), 12.10 (s,1H,NH^a), δ_c 112.7,118.8, 127.7, 128.6, 132.1, 144.6, 148.6, 157.2(Ar-C), 164.6 (C=O), 178.3 (C=O), 180.6 (C=S), MS (m/z): 290

3b) This compound was obtained as white crystal in yield 83%, m.p. 191-193°C, [found : C, 55.43; H, 4.30; N, 13.87; S, 10.55. $C_{14}H_{13}N_3O_3S$ requires C, 55.44; H, 4.29; N, 13.86; S, 10.56 %]; υ_{max} /cm^{-1} 1280 (C=S), 3010-3203 (NH), 1674 (C=O), δ_H 2.37 (s, 3H, CH_3), 6.69-7.99 (m, 7H, ArH), 10.99(s, 1H, NH^c), 11.48 (s,1H, NH^b), 12.21 (s, 1H, NH^a), δ_c 21.1 (-CH_3), 112.5,118.6, 127.6, 128.8, 129.1, 142.0, 144.5, 148.2 (Ar-C), 157.2 (C=O), 164.3 (C=O), 179.9 (C=S), MS (m/z): 304.1

3c) This compound was obtained as white crystal in yield 85%, m.p. 206-213°C, [found : C, 51.33; H, 3.93; N, 13.82; S, 10.52. $C_{13}H_{12}N_4O_3S$ requires C, 51.31; H, 3.95; N, 13.81; S, 10.53 %]; δ_H 5.80 (s, 2H, NH_2), 6.75-8.07 (m, 7H, ArH), 10.60 (s, 1H, NH^c), 11.52 (s, 1H, NH^b), 12.50 (s, 1H, NH^a), δ_c 112.6, 112.7, 117.9, 118.6, 128.2, 129.4, 144.5, 148.5 (Ar-C), 152.5 (C=O), 157.3 (C=O), 164.3 (C=S), MS (m/z): 304.9

3d) This compound was obtained as white crystal in yield 90 %, m.p. 183-185°C, [found : C, 52.65; H, 4.08; N, 13.16; S, 10.05. $C_{14}H_{13}N_3O_4S$ requires C, 52.66; H, 4.07; N, 13.17; S, 10.03 %]; δ_H 3.81 (s, 3H, OCH_3), 6.75-8.07 (m, 7H, ArH), 10.96 (s, 1H, NH^c), 11.55 (s, 1H, NH^b), 12.14 (s, 1H, NH^a), δ_c 55.5 (-OCH_3), 112.7, 113.8, 118.8, 124.1, 129.6, 144.6, 148.6, 157.2 (Ar-C), 162.3 (C=O), 164.0 (C=O), 180.3 (C=S), MS (m/z): 320

3e) This compound was obtained as white crystal in yield 89%, m.p. 164-166°C, [found : C, 47.32; H, 3.21; N, 15.04; S, 11.47. $C_{11}H_9N_3O_4S$ requires C, 47.31; H, 3.22; N, 15.05; S, 11.46 %]; δ_H 6.70-7.93 (m, 6H, ArH), 10.93 (s, 1H, NH^c), 11.51(s, 1H, NH^b), 12.02(s, 1H, NH^a), δ_c 112.0, 112.7, 115.3, 118.8, 144.5, 145.7, 146.1, 148.5 (Ar-C), 155.8 (C=O), 157.1(C=O), 180.7 (C=S), MS (m/z): 281.5

2-(furoylamino)-5-(phenyl)-1,3,4-thiadiazoles perchloric acid salt 4a

To the 14 ml acetic anhydride, charged 1.4 gms of 1-(benzoyl)-4-furoyl- thiosemicarbazides **3a** and stirred the reaction mass for 5 mins. Droppwise addition of 1.4 ml of perchloric acid was carried out maintaining the temperature of reaction below 50°C. Clear solution was observed initially then the solution became Hazy and finally product started precipitating out. Cooled the reaction mass to 25-30°C and stirred the reaction mass for 30 mins at same temperature. Filtered the product and washed with 10 ml of acetic acid. Dried the product at R.T. for 10-12 hrs to give **4a** (66 %).
The compounds **4b-e** were prepared in a similar manner and their analytical data are reported in **table-I**.

4a) This compound was obtained as cream coloured solid in yield 83%, m.p. 253-254°C, [found : C, 41.98; H, 2.68; N, 11.31; S, 8.62. $C_{13}H_{10}N_3O_6SCl$ requires C, 41.99; H, 2.69; N, 11.30; S, 8.61 %]; υ_{max} /cm^{-1} 1465 (C-S-C), 1555 (-C=N), 1697 (C=O), 3149 (NH), δ_H 6.77-8.06 (m, 8H, ArH), 13.18 (s, 1H, NH), δ_c 112.6, 117.6, 127.0, 129.4, 130.1, 130.7, 147.9, 150.2, (Ar-C), 150.6 (C=N), 170.1 (C=N), 179.9 (C=O), MS (m/z): 272.1

4b) This compound was obtained as cream coloured solid in yield 82%, m.p. 249-251°C, [found : C, 43.56; H, 3.13; N, 10,88; S, 8.31. $C_{14}H_{12}N_3O_6SCl$ requires C, 43.58; H, 3.11; N, 10.89; S, 8.30 %]; υ_{max} /cm^{-1} 1492 (C-S-C), 1558 (-C=N), 1697 (C=O), 3151 (NH), δ_H 2.34 (s, 3H, CH_3),

6.75-8.03 (m, 7H, ArH), 11.00 (s, 1H, NH), δ_c 21.4 (CH_3), 113.0, 117.9, 127.3, 127.8, 130.4, 141.1, 145.7, 148.3 (Ar-C), 156.2 (C=N), 158.9 (C=N), 162.6 (C=O), MS (m/z): 286.2

4c) This compound was obtained as cream coloured solid in yield 85%, m.p. 180-184°C, [found : C, 42.01; H, 3.02; N, 13.06; S, 7.48. $C_{15}H_{13}N_4O_7SCl$ requires C, 42.00; H, 3.03; N, 13.07; S, 7.47 %]; δ_H 2.06 (s, 3H, CH_3), 5.4 (s, 1H, NH), 6.73-8.02 (m, 7H, ArH), 10.20 (s, 1H, NH), δ_c 24.2 (CH_3), 112.6, 117.5, 119.3, 124.6, 127.7, 128.0, 141.5, 145.4 (Ar-C), 147.8 (C=N), 155.4 (C=N), 161.9 (C=O), 168.9 (C=O), MS (m/z): 329.2

4d) This compound was obtained as cream coloured solid in yield 90%, m.p. 243-246°C, [found : C, 41.83; H, 2.98; N, 10.47; S, 7.98. $C_{14}H_{12}N_3O_7SCl$ requires C, 41.84; H, 2.99; N, 10.46; S, 7.97 %];δ_H 3.81 (s, 3H, OCH_3), 6.73-8.11 (m, 7H, ArH), 12.1 (s, 1H, NH), δ_c 55.4 (CH_3), 112.4, 114.7, 117.3, 122.7, 128.5, 129.6, 145.4, 147.5 (Ar-C), 155.7 (C=N), 161.1 (C=N), 161.9 (S-C=N), MS (m/z): 302.1

4e) This compound was obtained as cream coloured solid in yield 87%, m.p. 240-245°C, [found : C, 36.52; H, 2.64; N, 11.61; S, 8.86. $C_{11}H_8N_3O_7SCl$ requires C, 36.51; H, 2.65; N, 11.62; S, 8.85 %];δ_H 6.75-8.00 (m, 6H, ArH), 13.29 (s, 1H, NH), δ_c 111.1, 112.6, 112.7, 117.7, 117.9, 145.1, 145.2, 145.5 (Ar-C), 148.1 (C=N), 147.9 (C=N), 152.9 (C=O), MS (m/z): 262.4

Scheme B

1- furoyl-4-benzoyl- thiosemicarbazides 7a

To the solution of benzoyl chloride (3.4 gms, 0.024 mole) in acetonitile (25cm^3), ammonium thiocyanate (2.80 gms, 0.0368 mole) and polyethylene glycol (PEG-400) (0.3 gm) were added. The mixture was stirred for 1 hr at room temperature and then furoic acid hydrazide (3.0 gms, 0.024 mole) was added to it. The reaction mixture was further stirred for two hrs. To the resulting mixture, water (50 cm^3) was added so that inorganic salt was dissolved. The slurry was filtered and the solid obtained was washed with water and acetonitrile (1:1) (30 cm^3). The product was recrystallised by DMF:Ethanol:Water (4:3:3) to yield **7a** (85%).
The compounds **7b-e** was prepared in a similar manner and their analytical data are reported in **table II**.

7a) This compound was obtained as white crystal in yield 85%, m.p. 199-201°C, [found : C, 53.96; H, 3.81; N, 14.52; S, 11.08. $C_{13}H_{11}N_3O_3S$ requires C, 53.97; H, 3.80; N, 14.53; S, 11.07 %]; υ_{max} /cm^{-1} 1247 (C=S), 1660 (C=O), 3269 (NH), δ_H 6.68-7.96 (m, 8H, ArH), 11.00 (s, 1H, NH^c), 11.79 (s, 1H, NH^b), 12.28 (s, 1H, NH^a), δ_c 112.1, 115.3, 128.5, 128.8, 131.9, 133.2, 145.7, 146.1 (Ar-C), 155.8 (C=O), 167.8 (C=O), 180.9 (C=S), MS (m/z): 290.2

7b) This compound was obtained as white coloured solid in yield 81%, m.p. 219°C, [found : C, 46.68; H, 3.01; N, 16.77; S, 9.57. $C_{13}H_{10}N_4O_5S$ requires C, 46.70; H, 2.99; N, 16.76; S, 9.58 %]; δ_H 6.69-8.32 (m, 7H, ArH), 11.02 (s, 1H, NH^c), 12.14 (s, 2H, NH^a and NH^b), δ_c 112.1, 115.3, 123.4, 130.4, 137.8, 145.7, 146.2, 149.9 (Ar-C), 155.8 (C=O), 166.2 (C=O), 180.6 (C=S), MS (m/z): 335.1

7c) This compound was obtained as off white crystal in yield 83%, m.p. 193-194°C, [found : C, 55.42; H, 4.28; N, 13.87; S, 10.57. $C_{14}H_{13}N_3O_3S$ requires C, 55.44; H, 4.29; N, 13.86; S, 10.56 %]; δ_H 2.37 (s, 3H, CH_3), 6.68-7.91(m, 7H, ArH), 10.98 (s, 1H, NH^c), 11.69 (s, 1H, NH^b), 12.30 (s, 1H, NH^a), δ_c 21.2 (-CH_3), 112.1, 115.3, 128.9, 128.9, 129.1, 143.7, 145.7, 146.1 (Ar-C), 155.8 (C=O), 167.8 (C=O), 181.0 (C=S), MS (m/z): 304.1

7d) This compound was obtained as white crystal in yield 86%, m.p. 209-211°C, [found : C, 52.64; H, 4.08; N, 13.18; S, 10.03. $C_{14}H_{13}N_3O_4S$ requires C, 52.66; H, 4.07; N, 13.17; S, 10.03 %];υ_{max} /cm^{-1} 1238 (C=S), 1681 (C=O), 3300 (NH), δ_H 3.84 (s, 3H, OCH_3), 6.69-8.00 (m, 7H, ArH), 10.96 (s, 1H, NH^c), 11.60 (s, 1H, NH^b), 12.32 (s, 1H, NH^a), δ_c 55.6 (-OCH_3), 112.1, 113.8, 115.3, 123.6, 131.1, 145.7, 146.1, 155.8 (Ar-C), 163.3 (C=O), 167.0 (C=O), 181.1 (C=S), MS (m/z): 320.1

7e) This compound was obtained as white crystal in yield 88%, m.p. 160-162°C, [found : C, 52.67; H, 4.08; N, 13.16; S, 10.02. $C_{14}H_{13}N_3O_4S$ requires C, 52.66; H, 4.07; N, 13.17; S, 10.03 %]; δ_H 3.84 (s, 3H, OCH_3), 6.69-7.94 (m, 7H, ArH), 10.99 (s, 1H, NH^c), 11.78 (s, 1H, NH^b), 12.28 (s, 1H, NH^a), δ_c 55.5 (-OCH_3), 112.1, 113.3, 115.3, 119.6, 121.1, 129.7, 133.2, 145.7, 146.1, 155.8 (Ar-C), 159.1 (C=O), 167.5 (C=O), 180.9 (C=S), MS (m/z): 320.1

7f) This compound was obtained as white crystal in yield 89%, m.p. 175-177°C, [found : C, 52.68; H, 4.05; N, 13.18; S, 10.01. $C_{14}H_{13}N_3O_4S$ requires C, 52.66; H, 4.07; N, 13.17; S, 10.03 %]; υ_{max} /cm^{-1} 1249 (C=S), 1666 (C=O), 3290 (NH), δ_H 3.97 (s, 3H, OCH_3), 6.69-7.94 (m, 7H, ArH), 11.03 (s, 1H, NH^c), 11.30 (s, 1H, NH^b), 12.06 (s, 1H, NH^a), δ_c 56.6 (-OCH_3), 112.1, 112.7, 115.3, 119.7, 121.2, 131.1, 134.9, 145.7, 146.1, 155.9 (Ar-C), 157.4 (C=O), 164.9 (C=O), 180.3 (C=S), MS (m/z): 320.1

2-(benzoyl amino)-5-(furyl)-1,3,4-thiadiazoles perchloric acid salt 8a

To the 14 ml acetic anhydride, charged 1.4 gms of 1- furoyl-4-benzoyl-thiosemicarbazides **3a** and stirred the reaction mass for 5 mins. Droppwise addition of 1.4 ml of perchloric acid was done maintaining the temperature of reaction mass below 50°C. Clear solution was observed initially then the solution become Hazy and finally product started precipitating out. Cooled the reaction mass to 25-30°C and stirred the reaction mass for 30 mins at same temperature. Filtered the product and washed with 10 ml of acetic acid. Dried the product at R.T. for 10-12 hrs to give **8a** (66 %).
The compounds **8b-e** were prepared in a similar manner and their analytical data are reported in **table II**.

8a) This compound was obtained as cream coloured solid in yield 85%, m.p. 210-214°C, [found : C, 41.98; H, 2.70; N, 11.29; S, 8.62. $C_{13}H_{10}N_3O_6SCl$ requires C, 41.99; H, 2.69; N, 11.30; S, 8.61 %];υ_{max} /cm^{-1} 1467 (C-S-C), 1543 (-C=N), 1660 (C=O), 3298 (NH), δ_H 6.73-7.95 (m, 8H, ArH), 12.0 (s, 1H, NH), δ_c 111.1, 112.7, 128.5, 128.8, 131.4, 133.2, 145.2, 145.6 (Ar-C), 153.0 (C=N), 158.7 (C=N), 165.3 (C=O), MS (m/z): 272.1

8b) This compound was obtained as cream coloured solid in yield 81%, m.p. 233-236°C, [found : C, 37.46; H, 2.17; N, 13.43; S, 7.67. $C_{13}H_9N_4O_8SCl$ requires C, 37.45; H, 2.16; N, 13.44; S, 7.68 %];MS (m/z): 317.0

8c) This compound was obtained as cream coloured solid in yield 83%, m.p. 214-218°C, [found : C, 43.59; H, 3.12; N, 10.88; S, 8.29. $C_{14}H_{12}N_3O_6SCl$ requires C, 43.58; H, 3.11; N, 10.89; S, 8.30 %]; δ_H 2.38 (s, 3H, CH_3), 6.73-7.95 (m, 7H, ArH), 13.1 (s, 1H, NH). δ_c 21.1 (CH_3), 110.9, 112.6, 120.3, 128.5, 129.3, 143.5, 143.7, 145.2 (Ar-C), 155.5 (C=N), 156.3 (C=N), 168.0 (C=O), MS (m/z): 286.1

8d) This compound was obtained as cream coloured solid in yield 90%, m.p. 236-238°C, [found : C, 41.82; H, 3.00; N, 10.47; S, 7.96. $C_{14}H_{12}N_3O_7SCl$ requires C, 41.84; H, 2.99; N, 10.46; S, 7.97 %]; υ_{max} /cm^{-1} 1469 (C-S-C), 1548 (-C=N), 1658 (C=O), 3273 (NH), δ_H 3.83 (s, 3H, OCH_3), 6.72-8.12 (m, 7H, ArH), 12.5 (s, 1H, NH), δ_c 55.6 (OCH_3), 110.9, 112.7, 114.1, 123.3, 130.6, 145.3, 145.5, 152.4 (Ar-C), 158.8 (C=N), 163.2 (C=N), 164.3 (C=O), MS (m/z): 302.1

8e) This compound was obtained as cream coloured solid in yield 88%, m.p. 194-198°C, [found : C, 41.85; H, 2.99; N, 10.47; S, 7.95. $C_{14}H_{12}N_3O_7SCl$ requires C, 41.84; H, 2.99; N, 10.46; S, 7.97 %]; δ_H 3.80 (s, 3H, OCH_3), 6.75-7.99 (m, 7H, ArH), 13.2 (s, 1H, NH), δ_c 55.4 (OCH_3), 110.9, 112.4, 112.6, 112.9, 119.5, 120.8, 129.9, 132.5, 145.2, 145.5 (Ar-C), 152.4 (C=N), 159.3 (C=N), 167.8 (C=O) MS (m/z): 302.1

8f) This compound was obtained as cream coloured solid in yield 86%, m.p. 252-253°C, [found : C, 41.83; H, 3.01; N, 10.45; S, 7.96. $C_{14}H_{12}N_3O_7SCl$ requires C, 41.84; H, 2.99; N, 10.46; S, 7.97 %]; υ_{max} /cm^{-1} 1469(C-S-C), 1566 (-C=N), 1681 (C=O), 3188(NH), δ_H 3.90 (s, 3H, OCH_3), 6.73-7.95 (m, 7H, ArH), 12.5 (s, 1H, NH), δ_c 56.1 (OCH_3), 111.1, 112.3, 112.7, 120.6, 121.4, 130.3, 133.8, 145.1, 145.6, 152.9 (Ar-C), 157.3 (C=N), 164.6 (C=N), 172.1(C=O), MS (m/z): 302

Conclusion:

Thiosemicarbazide derivatives are synthesized using phase transfer catalyst to increase the yield which on cyclisation using perchloric acid in acetic anhydride furnish perchloric acid salt of 1,3,4-thiadiazoles derivatives. The sulphur and nitrogen containing compounds were screened for anti-microbial activity showed convincing inhibition against *E. coli, S. typhi*, *S. aureus,* and *B.Substilus* bacteria.

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Table –I characterization of synthesized compounds 3,4 of scheme A

Scheme A

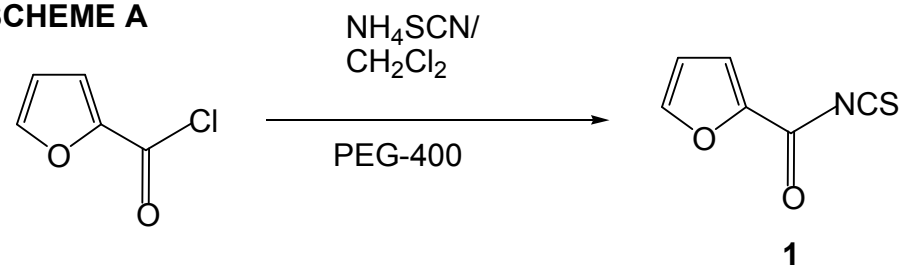
Comps	Ar	Molecular Formula	Molecular Weight	M.P.	Yield (%)
3a	$-C_6H_5$	$C_{13}H_{11}N_3O_3S$	289	143-145°C	87 %
3b	p-$C_6H_4CH_3$	$C_{14}H_{13}N_3O_3S$	303	191-193°C	83 %
3c	p -$C_6H_4NH_2$	$C_{13}H_{12}N_4O_3S$	304	206-213°C	85 %
3d	p-$C_6H_4OCH_3$	$C_{14}H_{13}N_3O_4S$	319	183-185°C	90 %
3e	$-C_4H_3O$	$C_{11}H_9N_3O_4S$	279	164-166°C	89 %
4a	$-C_6H_5$	$C_{13}H_{10}N_3O_6SCl$	371.5	253-254°C	83 %
4b	p -$C_6H_4CH_3$	$C_{14}H_{12}N_3O_6SCl$	385.5	249-251°C	82 %
4c	p-$C_6H_4NHCOCH_3$	$C_{15}H_{13}N_4O_7SCl$	428.5	180-184°C	85 %
4d	p -$C_6H_4OCH_3$	$C_{14}H_{12}N_3O_7SCl$	401.5	243-246°C	90 %
4e	$-C_4H_3O$	$C_{11}H_8N_3O_7SCl$	361.5	240-245°C	87 %

Table –II characterization of synthesized compounds 3,4 of scheme B

Scheme B

7a	$-C_6H_5$	$C_{13}H_{11}N_3O_3S$	289	199-201°C	85 %
7b	*p* $-C_6H_4NO_2$	$C_{13}H_{10}N_4O_5S$	334	219°C	81 %
7c	*p* $-C_6H_4CH_3$	$C_{14}H_{13}N_3O_3S$	303	193-194°**C**	83 %
7d	*p*-$C_6H_4OCH_3$	$C_{14}H_{13}N_3O_4S$	319	209-211°**C**	86 %
7e	*m*-$C_6H_4OCH_3$	$C_{14}H_{13}N_3O_4S$	319	160-162°**C**	88 %
7f	*o*-$C_6H_4OCH_3$	$C_{14}H_{13}N_3O_4S$	319	175-177°**C**	89 %
8a	$-C_6H_5$	$C_{13}H_{10}N_3O_6SCl$	371.5	210-214°**C**	85 %
8b	*p* $-C_6H_4NO_2$	$C_{13}H_9N_4O_8SCl$	416.5	233-236°**C**	81 %
8c	*p* $-C_6H_4CH_3$	$C_{14}H_{12}N_3O_6SCl$	385.5	214-218°**C**	83 %
8d	*p*-$C_6H_4OCH_3$	$C_{14}H_{12}N_3O_7SCl$	401.5	236-238°**C**	90 %
8e	*m*-$C_6H_4OCH_3$	$C_{14}H_{12}N_3O_7SCl$	401.5	194-198°**C**	88 %
8f	*o*-$C_6H_4OCH_3$	$C_{14}H_{12}N_3O_7SCl$	401.5	252-253°**C**	86 %

SCHEME A



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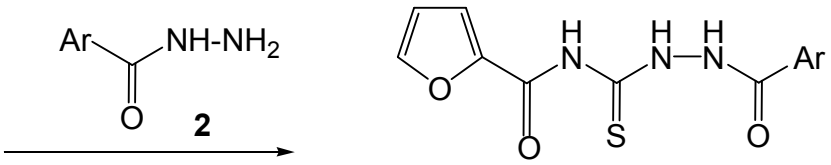
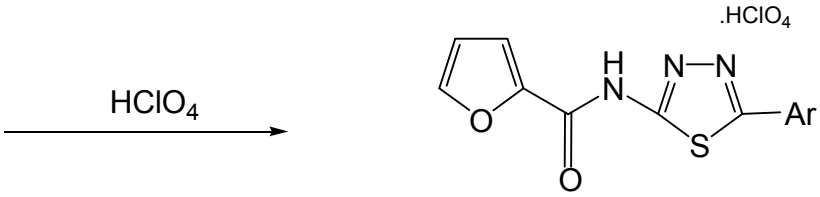
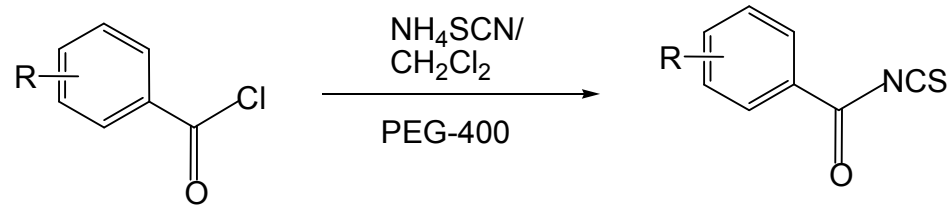


3(a-e)



4(a-e)

SCHEME B



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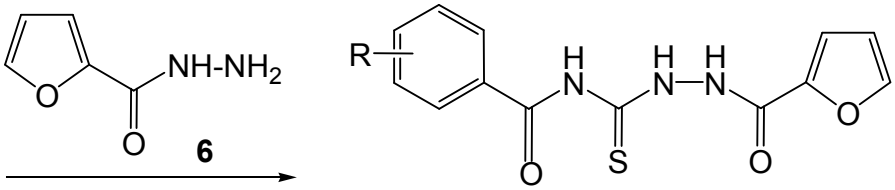
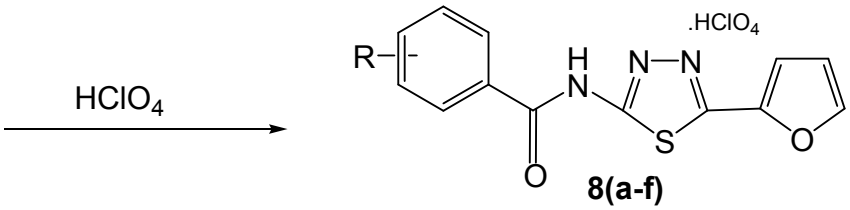


7(a-f)



8(a-f)

Table III Antibacterial activity of compound 4a,4b & 8a, 8d

Compound	Zone of Inhibition (in mm)			
	Gram Positive		Gram Negative	
	S. aureus	*S.typhi*	*E.coli*	*B.Substilus*
4a	++	---	---	++
4b	++	---	---	++
8a	++	---	---	++
8d	++	---	---	++
Ampicillin	++++	++++	++++	++++

*** Diameter of the hole was 6mm**

*** Zone of inhibition: (-) 6mm, (+) 6-10mm, (++) 10-15mm, (+++) 15-20, (++++) 20-25.**