



## Synthesis of triazine linked pyrazole heterocyclics by conventional heating and microwave irradiative cyclocondensation and evaluation of antitubercular and antimicrobial potential

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Received 29 November 2019; accepted (revised) 15 October 2020

The synthesis of (4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-(5-methyl-2-substituted phenyl/*H*-pyrazol-3-yl)-amines and (4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-(5-methyl-2-substituted benzoyl/isonicotinoyl/cinnamoyl-pyrazol-3-yl)-amines by conventional heating and microwave irradiative cyclocondensation have been achieved by the cyclisation of N-(4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-3-oxo butyramide with substituted hydrazines and acid hydrazides. The required butyramide has been synthesized by the reaction of 2,4-diamino-6-methyl-[1,3,5]-triazine with benzaldehyde followed by the condensation with ethyl acetoacetate. Structural elucidation of synthesized compounds has been performed by IR, <sup>1</sup>H NMR and mass spectral studies besides chemical transformation and elemental analysis. The title compounds have been evaluated for their antitubercular and antimicrobial potential against some selected microorganisms to establish the structure activity relationship.

**Keywords:** Triazine-pyrazole, conventional, microwave, antitubercular, antimicrobial

The synthesis of organic compounds by microwave irradiation technique has number of advantages over the conventional heating<sup>1</sup>. High density microwave irradiation technology has emerged as a reliable and useful methodology for accelerating the time consuming reactions<sup>2</sup>. It can be used for high speed parallel synthesis of number of biologically active molecules<sup>3</sup>. In synthetic organic chemistry, pyrazole is widely exploited pharmacophore having different practical applications in the medicinal and agrochemical field<sup>4,5</sup>. Pyrazole ring system has been consistently rewarded as a promising molecule, as its activity covers the domains such as antipyretic<sup>6</sup>, antimicrobial<sup>7</sup>, antitumor<sup>8</sup>, antidepressant<sup>9</sup>, antitubercular<sup>10,11</sup>, analgesic<sup>12</sup>, ulcerogenic<sup>13</sup>, antiinflammatory<sup>14</sup>, anticonvulsant<sup>15</sup>, antihistaminic<sup>16</sup> and anticancer<sup>17</sup>. Pyrazole fused heterocyclics have been widely used in pesticides and medicines<sup>18</sup>. On perusal of literature, it was observed that position N-1, C-3, C-4 are much important for the studies of structure activity relationship and C-3 should be linked to different heterocyclics for better chemotherapeutic activities<sup>19</sup>. All these observations encouraged us and developed interest in synthesizing triazine linked to pyrazoles at C-3 position. Presence

of two bioactive rings within a single molecule enhances the antimicrobial activity profile and hence synthesis of triazine linked pyrazoles has been carried out both by conventional heating and microwave irradiative cyclocondensation for the purpose of comparison.

Most explored method for synthesis of pyrazoles is the reaction of 1,3-dicarbonyl, ester, oxo-amide, hydrazine hydrate using suitable catalyst<sup>20,21</sup>. The double nucleophilic character of hydrazine for reaction with each carbonyl group of 1,3-diketone needs high temperature and long reaction time<sup>22</sup>. Therefore, we reported herein synthesis of (4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-(5-methyl-2-substituted phenyl/*H*-pyrazol-3-yl)-amines **3a-g** and (4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-(5-methyl-2-substituted benzoyl/isonicotinoyl/cinnamoyl-pyrazol-3-yl)-amines **5a-f** by conventional heating without using any catalyst and compared with the microwave irradiative cyclocondensation. So as to establish the structure activity relationship, all title compounds were evaluated for their antitubercular and antimicrobial potential against some selected microorganisms.

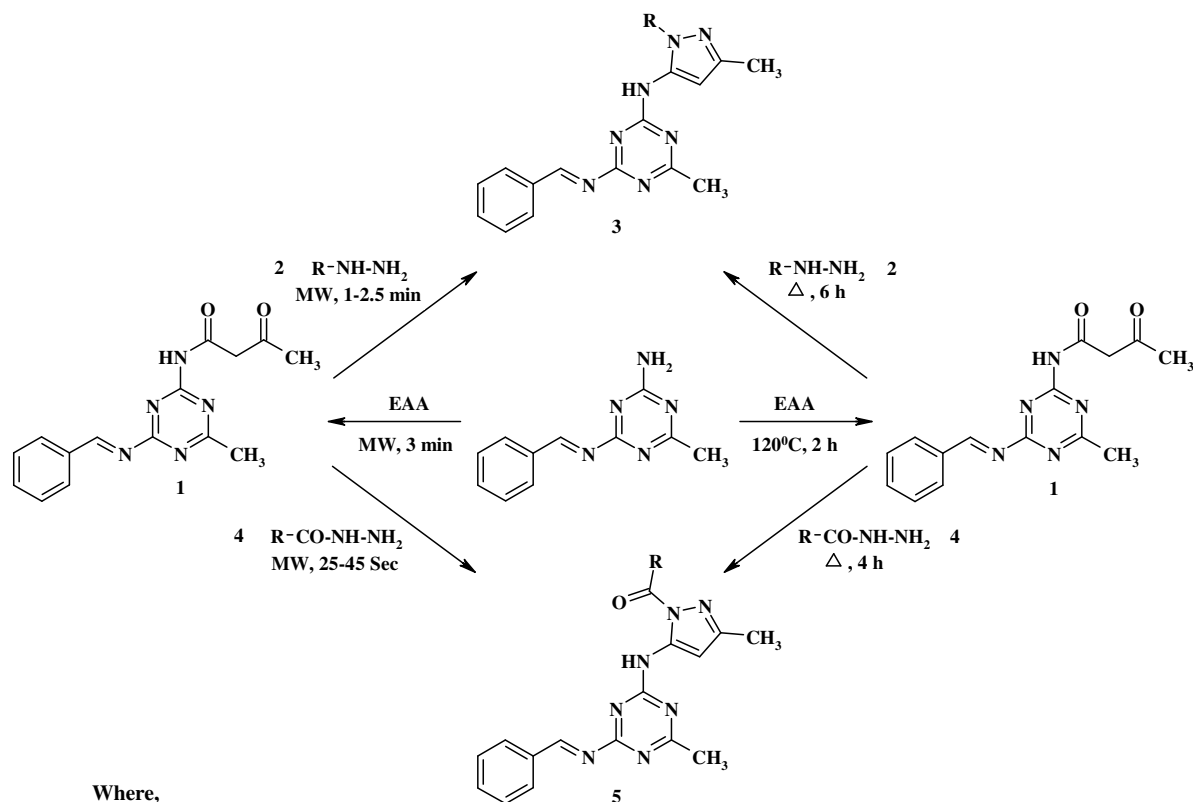
## Results and Discussion

The compound 2-amino-4-benzylideneamino-6-methyl-[1,3,5]-triazine was prepared by reacting 2,4-diamino-6-methyl-[1,3,5]-triazine (0.01 mole) with benzaldehyde (0.01 mole) in chloroform medium for 3 hr. It was then refluxed with ethyl acetoacetate (0.01 mole) for 3 hr at 120°C using oil bath to give the compound N-(4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-3-oxo butyramide **1** which on cyclocondensation with substituted hydrazines **2a-g** (0.01 mole) and substituted acid hydrazides **4a-f** (0.01 mole) in ethanolic medium afforded (4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-(5-methyl-2-substituted phenyl/H-pyrazol-3-yl)-amines **3a-g** and (4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-(5-methyl-2-substituted benzoyl/isonicotinoyl/cinnamoyl-pyrazol-3-yl)-amines **5a-f**. Alternatively, all these compounds were synthesized by irradiating the reaction mixtures under microwave conditions at 1200 W Scheme I). On comparative study, it was observed that microwave irradiative

reactions received high product yield, enhanced reaction rates and high purity than conventional heating. IR, <sup>1</sup>H NMR and mass spectral studies of synthesized compounds fully supported the structures and showed single spots in TLC.

## Antitubercular activity

The title compounds **3a-g** and **5a-f** were evaluated for their *in-vitro* antitubercular activity<sup>23</sup> by BACTEC-TB and Microplate Alamar Blue Assay (MABA) methods for direct determination of minimum inhibitory concentration (MIC) against *M. tuberculosis*. Test compounds were dissolved in 10% (v/v) DMSO at a concentration of 10 mM. For the BACTEC-TB assay, the test vial sjnhjn of 7H12 medium containing <sup>14</sup>C labelled palmitic acid were inoculated with mycobacterium and incubated at 37°C temperature. The amount of <sup>14</sup>CO<sub>2</sub> reflects the rate and amount of growth and is expressed in term of growth index (GI). On addition of compound to the test vial, suppression of growth of the test organism



Where,

2a = Phenyl hydrazine

2b = 2,4-Dinitro-phenyl hydrazine

2c = Hydrazine

2d = 2-Methyl-phenyl hydrazine

2e = 3-Methyl-phenyl hydrazine

2f = 4-Methyl-phenyl hydrazine

2g = 4-Methoxyl-phenyl hydrazine

4a = Benzoic acid hydrazide

4b = 3-Methyl-benzoic acid hydrazide

4c = 2-Hydroxy-benzoic acid hydrazide

4d = 4-Amino-benzoic acid hydrazide

4e = 4-Pyridine hydrazide

4f = 3-Phenyl-acrylic acid hydrazide

Scheme I

*M. tuberculosis* could be detected by routine observation of GI output as compared to the control and standard drug Rifampin (2 µg/mL). For MABA assay, two fold serial dilutions of compounds were made in Middle brook 7H9 medium supplemented with 10% (v/v) ADC, in well plates (Nunc) in duplicate. An inoculum of 10<sup>5</sup> CFU/mL was prepared and 200 µL was added per well. Growth controls containing no drug and a sterile control without bacteria were also prepared for each assay. The plates were incubated at 37°C for 5 days before adding 20 µL of sterile 0.01% resazurin to the wells and incubating for a further 24 hr at 37°C. A change in colour from blue (oxidized state) to pink (reduced state) indicated the growth of bacteria. The compounds showing MIC at 50 µM were further evaluated for CFU determination using agar dilution method. Serial dilutions of compounds, prepared in 0.1 mL, 10% (v/v) DMSO, added to each well of well plates (Nunc) and 1.9 mL MB7H10 agar medium supplemented with 10% (v/v) OADC were poured to respective wells and allowed to solidify at RT. For positive control, rifampin and streptomycin were dissolved in water, filtered, sterilized and used in 2 and 6 µg/mL respectively. Solution 10 µL was inoculated in each well on solidified agar medium and incubated at 37°C for four weeks and growth was recorded. The compounds **3b**, **3e**, **3g**, **5c**, **5d** and **5e** showed promising activity against *M. tuberculosis*. MIC values of compounds **3b**, **5d** and **5e** were found to be 6.25 µM and of compounds **3e**, **3g** and **5c** were found to be 50, 25 and 12.5 µM respectively (Table I).

#### Antimicrobial activity

The evaluation of antibacterial potential of synthesized compounds **3a-g** and **5a-f** was performed by using cup plate diffusion method<sup>24,25</sup>. The bacterial organisms having both gram-positive and gram-

negative strains *i.e.* *E. coli*, *S. aureus*, *S. typhi*, *B. subtilis* and *P. vulgaris* were used. Sensitivity plates were seeded with a bacterial inoculum of 1×10<sup>6</sup> CIU/mL and each well of diameter 10 mm was loaded with 0.1 mL of test compound solution (1000 µg/mL) in DMF, so that concentration of each test compound was 100 µg/mL. The zones of inhibition were recorded after incubation for 24 hr at 37°C using vernier caliper and it was observed that the compounds **3b**, **3g**, **5d** and **5e** were highly active against *E. coli* and *S. aureus* and moderately active against *S. typhi* and *P. vulgaris*. Compounds **3d**, **3f** and **5c** were moderately active against *E. coli* and *S. aureus*. Majority of the compounds were found to be inactive against *B. subtilis* (Table II). To determine the minimum inhibitory concentration (MIC), serial dilution technique<sup>26</sup> was used using nutrient broth medium. MIC values of compounds **3b**, **3g**, **5d** and **5e** were found to be 40, 55, 60 and 45 µg/mL respectively against *E. coli* and 55, 70, 50 and 65 µg/mL respectively against *S. aureus*.

The evaluation of antifungal activity of compounds **3a-g** and **5a-f** using paper disc method<sup>27,28</sup> with the concentration 1% and 2%, showed that compounds **3b** and **5d** were highly active against *A. niger*, whereas other compounds showed low to moderate activity. The zones of inhibition were recorded after incubation for 48 hr at 37°C (Table II).

#### Experimental Section

The MW assisted reactions were carried out using commercially available microwave oven (1200 W). Melting points of all synthesized compounds were recorded using the Veego, VMP-D digital melting point apparatus and are uncorrected. Chemicals used were of AR grade. <sup>1</sup>H NMR spectra were recorded with TMS as internal standard on a Bruker Avance-II 400 NMR spectrometer using CDCl<sub>3</sub> and DMSO-*d*<sub>6</sub> as solvents. IR spectra were recorded on Perkin-Elmer spectrophotometer in the range 4000-400 cm<sup>-1</sup> in Nujol mull and as KBr pellet. Mass spectral measurements were carried out by EI method on Jeol-JMC 300 spectrometer at 70 eV. Homogeneity of the compounds was checked on silica gel-G plates by TLC and spots were visualized by the iodine vapours.

The compound 2-amino-4-benzylideneamino-6-methyl-[1,3,5]-triazine was synthesized by refluxing the mixture of 2,4-diamino-6-methyl-[1,3,5]-triazine (0.01 mole) and benzaldehyde (0.01 mole) in chloroform (10 mL) for 3 h. The crude solid mass obtained was crystallized from hot ethanol (80%),

Table I — Antitubercular activity

Compd (Conc. µM)	BACTEC-TB					MABA				
	50	25	12.5	6.25	3.125	50	25	12.5	6.25	3.125
3b	+	+	+	+	-	+	+	+	+	-
3e	+	-	-	-	-	+	-	-	-	-
3g	+	+	-	-	-	+	+	-	-	-
5c	+	+	+	-	-	+	+	+	-	-
5d	+	+	+	+	-	+	+	+	+	-
5e	+	+	+	+	-	+	+	+	+	-

(+) : Active, (-) : Inactive

Table II — Antibacterial and antifungal activity

Compd	Antibacterial activity					Antifungal activity	
	<i>E. coli</i>	<i>S. aureus</i>	<i>S. typhi</i>	<i>B. subtilis</i>	<i>P. vulgaris</i>	<i>A. niger</i>	
						(Conc. 1%)	(Conc. 2%)
<b>3a</b>	+	+	+	-	+	+	+
<b>3b</b>	+++	+++	++	+	++	+++	+++
<b>3c</b>	+	+	-	-	-	+	+
<b>3d</b>	++	++	+	+	+	+	++
<b>3e</b>	+	+	+	-	+	+	+
<b>3f</b>	++	++	+	-	+	+	++
<b>3g</b>	+++	+++	++	+	++	++	+
<b>5a</b>	+	+	-	-	-	-	+
<b>5b</b>	+	+	+	-	+	+	+
<b>5c</b>	++	++	+	+	+	+	++
<b>5d</b>	+++	+++	++	+	++	+++	+++
<b>5e</b>	+++	+++	++	+	++	+	++
<b>5f</b>	+	+	+	-	+	-	+

(-): Inactive (10 mm and less); (+): Weakly active (11-15 mm)

(++): Moderately active (16-20 mm); (+++): Highly active (21 mm and above)

m.p.144-48°C. Anal. Found: C, 59.99; H, 5.17; N, 32.44. Calcd for C<sub>11</sub>H<sub>11</sub>N<sub>5</sub>: C, 61.97; H, 5.16; N, 32.86%. Alternatively, it was prepared by irradiating the above reaction mixture under microwave conditions for 3 min 30 sec, (95%), m.p. 146°C.

#### Synthesis of N-(4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-3-oxo butyramide, **1**

The compound N-(4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-3-oxo butyramide **1** was prepared by refluxing the equimolar mixture of 2-amino-4-benzylideneamino-6-methyl-[1,3,5]-triazine (0.01 mole) and ethyl acetoacetate (0.01 mole) for 3 h at 120°C using oil bath, the resulting solid was crystallized from hot ethanol, **1** (82%), m.p.122°C. Anal. Found: C, 59.71; H, 5.11; N, 23.49. Calcd for C<sub>15</sub>H<sub>15</sub>N<sub>5</sub>O<sub>2</sub>: C, 60.60; H, 5.09; N, 23.55%. IR: 3329 (NH), 1681 (C=O), 1546 (C=N), 1325 cm<sup>-1</sup> (C-N); <sup>1</sup>H NMR (CDCl<sub>3</sub>+DMSO-*d*<sub>6</sub>): 7.94 (1H, s, Ar-CH=N), 7.93 (1H, s, Trz-NH), 7.38-7.52 (5H, m, Ar-H), 3.46 (2H, s, CO-CH<sub>2</sub>-CO), 2.21 (3H, s, Trz-CH<sub>3</sub>), 2.19 (3H, s, CO-CH<sub>3</sub>)<sup>29,30</sup>. Alternatively, the above reaction mixture was irradiated under microwave conditions for 3 min to give compound, **1** (92%), m.p. 128°C. Completion of the reaction was monitored with TLC.

#### Synthesis of (4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-(5-methyl-2-phenyl-pyrazol-3-yl)-amine, **3a**

The compound (4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-(5-methyl-2-phenyl-pyrazol-3-yl)

-amine **3a** was prepared by refluxing the mixture of N-(4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-3-oxo-butyramide **1** (0.01 mole) and phenyl hydrazine **2a** (0.01 mole) in absolute ethanol (10 mL) for 6 h using water bath. The crude solid residue obtained was crystallized from hot ethanol, **3a** (80%), m.p.120°C. Anal. Found: C, 68.14; H, 5.12; N, 26.51. Calcd for C<sub>21</sub>H<sub>19</sub>N<sub>7</sub>: C, 68.28; H, 5.18; N, 26.54%. IR: 3379 (NH), 1548 (C=N), 1323 (C-N), 1168 cm<sup>-1</sup> (N-N); <sup>1</sup>H NMR (CDCl<sub>3</sub>+DMSO-*d*<sub>6</sub>): δ 7.96 (1H, s, Ar-CH=N), 6.98-7.57 (10H, m, Ar-H), 6.73 (1H, s, Pyrz-H), 4.03 (1H, s, Trz-NH), 2.14 (6H, s, Pyrz-CH<sub>3</sub>, Trz-CH<sub>3</sub>); MS: *m/z* 354 (M<sup>+</sup>-CH<sub>3</sub>), 292 (M<sup>+</sup>-C<sub>6</sub>H<sub>5</sub>), 265 (M<sup>+</sup>-C<sub>6</sub>H<sub>5</sub>.CH=N), 212 (M<sup>+</sup>-CH<sub>3</sub>.C<sub>6</sub>H<sub>5</sub>.C<sub>3</sub>HN<sub>2</sub>), 172 (CH<sub>3</sub>.C<sub>6</sub>H<sub>5</sub>.C<sub>3</sub>HN<sub>2</sub>.NH<sup>+</sup>), 157 (CH<sub>3</sub>.C<sub>6</sub>H<sub>5</sub>.C<sub>3</sub>HN<sub>2</sub><sup>+</sup>), 104 (C<sub>6</sub>H<sub>5</sub>.CH=N<sup>+</sup>), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>). This reaction was extended to synthesize other compounds **3b-g** using different substituted hydrazines **2b-g**: **3b**: (85%), m.p.116°C. Anal. Found: C, 53.93; H, 3.67; N, 27.07. Calcd for C<sub>21</sub>H<sub>17</sub>N<sub>9</sub>O<sub>4</sub>: C, 54.90; H, 3.73; N, 27.44%. IR: 3327 (NH), 1543 (C=N), 1411 (NO<sub>2</sub>), 1323 (C-N), 1170 cm<sup>-1</sup> (N-N); <sup>1</sup>H NMR (CDCl<sub>3</sub>+DMSO-*d*<sub>6</sub>): δ 7.39-8.89 (9H, m, Ar-H, Ar-CH=N), 5.88 (1H, s, Pyrz-H), 3.43 (1H, s, Trz-NH), 2.20 (6H, s, Pyrz-CH<sub>3</sub>, Trz-CH<sub>3</sub>); MS: *m/z* 459 (M<sup>+</sup>), 444 (M<sup>+</sup>-CH<sub>3</sub>), 262 (CH<sub>3</sub>.C<sub>6</sub>H<sub>3</sub>N<sub>2</sub>O<sub>4</sub>.C<sub>3</sub>HN<sub>2</sub>.NH<sup>+</sup>), 197 (M<sup>+</sup>-CH<sub>3</sub>.C<sub>6</sub>H<sub>3</sub>N<sub>2</sub>O<sub>4</sub>.C<sub>3</sub>HN<sub>2</sub>.NH), 104 (C<sub>6</sub>H<sub>5</sub>.CH=N<sup>+</sup>), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>).

**3c**: (88%), m.p. 132°C. Anal. Found: C, 61.31; H, 5.11; N, 32.89. Calcd for C<sub>15</sub>H<sub>15</sub>N<sub>7</sub>: C, 61.42; H, 5.15; N, 33.43%.

**3d:** (75%), m.p.105°C. Anal. Found: C, 68.87; H, 5.40; N, 25.19. Calcd for C<sub>22</sub>H<sub>21</sub>N<sub>7</sub>: C, 68.91; H, 5.52; N, 25.57%.

**3e:** (80%), m.p.132°C. Anal. Found: C, 68.77; H, 5.34; N, 25.53. Calcd for C<sub>22</sub>H<sub>21</sub>N<sub>7</sub>: C, 68.91; H, 5.52; N, 25.57%.

**3f:** (78%), m.p.142°C. Anal. Found: C, 67.79; H, 5.45; N, 24.95. Calcd for C<sub>22</sub>H<sub>21</sub>N<sub>7</sub>: C, 68.91; H, 5.52; N, 25.57%.

**3g:** (80%), m.p.128°C. Anal. Found: C, 65.95; H, 5.29; N, 24.46. Calcd for C<sub>22</sub>H<sub>21</sub>N<sub>7</sub>O: C, 66.15; H, 5.30; N, 24.55%.

Alternatively, compound **3a** was synthesized by irradiating the above reaction mixture under microwave conditions for 2 min 30 sec. **3a** (95%), m.p. 126°C. The reaction was monitored on silica gel-G plates by TLC and extended to synthesize the other compounds **3b-g** (89-96%).

#### Synthesis of (2-benzoyl-5-methyl-pyrazol-3-yl)-(4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-amine, **5a**

The compound (2-benzoyl-5-methyl-pyrazol-3-yl)-(4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-amine **5a** was prepared by refluxing the mixture of N-(4-benzylideneamino-6-methyl-[1,3,5]-triazin-2-yl)-3-oxo-butylamide **1** (0.01 mole) and benzoic acid hydrazide **4a** (0.01 mole) in absolute ethanol (10 mL) for 4 h using water bath. The crude solid residue obtained was crystallized from hot ethanol.

**5a:** (80%), m.p.84°C. Anal. Found: C, 65.89; H, 4.79; N, 24.11. Calcd for C<sub>22</sub>H<sub>19</sub>N<sub>7</sub>O: C, 66.49; H, 4.82; N, 24.67%. IR: 3298 (NH), 1683 (C=O), 1544 (C=N), 1323 (C-N), 1176 cm<sup>-1</sup> (N-N); <sup>1</sup>H NMR (CDCl<sub>3</sub>+DMSO-*d*<sub>6</sub>): δ 7.95 (1H, s, Ar-CH=N), 7.28-7.94 (10H, m, Ar-H), 6.56 (1H, s, Pyrzh-H), 4.24 (1H, s, Trz-NH), 2.06 (6H, s, Pyrzh-CH<sub>3</sub>, Trz-CH<sub>3</sub>); MS: *m/z* 397 (M<sup>+</sup>), 382 (M<sup>+</sup>-CH<sub>3</sub>), 293 (M<sup>+</sup>-C<sub>6</sub>H<sub>5</sub>.CH=N), 292 (M<sup>+</sup>-C<sub>6</sub>H<sub>5</sub>.CO), 212 (M<sup>+</sup>-CH<sub>3</sub>.C<sub>6</sub>H<sub>5</sub>.CO.C<sub>3</sub>HN<sub>2</sub>), 200 (CH<sub>3</sub>.C<sub>6</sub>H<sub>5</sub>.CO.C<sub>3</sub>HN<sub>2</sub>.NH<sup>+</sup>), 105 (C<sub>6</sub>H<sub>5</sub>.CO<sup>+</sup>), 77 (C<sub>6</sub>H<sub>5</sub><sup>+</sup>). This reaction was extended to synthesize other compounds **5b-f** using different substituted acid hydrazides **4b-f**.

**5b:** (82%), m.p.78°C. Anal. Found: C, 66.88; H, 4.98; N, 23.71. Calcd for C<sub>23</sub>H<sub>21</sub>N<sub>7</sub>O: C, 67.14; H, 5.14; N, 23.83%. IR: 3296 (NH), 1681 (C=O), 1541 (C=N), 1325 (C-N), 1170 cm<sup>-1</sup> (N-N); <sup>1</sup>H NMR (CDCl<sub>3</sub>+DMSO-*d*<sub>6</sub>): δ 7.94 (1H, s, Ar-CH=N), 7.07-7.83 (9H, m, Ar-H), 6.57 (1H, s, Pyrzh-H), 4.45 (1H, s, Trz-NH), 2.34 (3H, s, Ar-CH<sub>3</sub>), 2.06 (6H, s, Pyrzh-CH<sub>3</sub>, Trz-CH<sub>3</sub>); MS: *m/z* 410 (M<sup>+</sup>-H), 396 (M<sup>+</sup>-CH<sub>3</sub>),

320 (M<sup>+</sup>-CH<sub>3</sub>.C<sub>6</sub>H<sub>4</sub>), 307 (M<sup>+</sup>-C<sub>6</sub>H<sub>5</sub>.CH=N), 292 (M<sup>+</sup>-CH<sub>3</sub>.C<sub>6</sub>H<sub>4</sub>.CO), 199 (CH<sub>3</sub>.CH<sub>3</sub>.C<sub>6</sub>H<sub>4</sub>.CO.C<sub>3</sub>HN<sub>2</sub><sup>+</sup>), 119 (CH<sub>3</sub>.C<sub>6</sub>H<sub>4</sub>.CO<sup>+</sup>), 91 (CH<sub>3</sub>.C<sub>6</sub>H<sub>4</sub><sup>+</sup>).

**5c:** (85%), m.p.92°C. Anal. Found: C, 63.34; H, 4.58; N, 23.43. Calcd for C<sub>22</sub>H<sub>19</sub>N<sub>7</sub>O<sub>2</sub>: C, 63.91; H, 4.63; N, 23.71%.

**5d:** (80%), m.p.176°C. Anal. Found: C, 62.97; H, 4.77; N, 26.61. Calcd for C<sub>22</sub>H<sub>20</sub>N<sub>8</sub>O: C, 64.07; H, 4.89; N, 27.17%.

**5e:** (75%), m.p.122°C. Anal. Found: C, 62.85; H, 4.41; N, 28.03. Calcd for C<sub>21</sub>H<sub>18</sub>N<sub>8</sub>O: C, 63.31; H, 4.55; N, 28.12%.

**5f:** (78%), m.p.104°C. Anal. Found: C, 67.55; H, 4.96; N, 23.08. Calcd for C<sub>24</sub>H<sub>21</sub>N<sub>7</sub>O: C, 68.07; H, 5.00; N, 23.15%.

Alternatively, compound **5a** was synthesized by irradiating the above reaction mixture under microwave conditions for 35 sec, **5a** (92%), m.p. 86°C. The reaction was monitored on silica gel-G plates by TLC and extended to synthesize the other compounds **5b-f** (85-95%).

#### Supplementary Information

Supplementary information is available in the website <http://nopr.niscair.res.in/handle/123456789/60>.

#### Acknowledgement

Thanks are due to Director, SAIF, Punjab University, Chandigarh and CSIR-Central Drug Research Institute, Lucknow for providing analytical data, spectral facility and antitubercular evaluation. Authors are thankful to Dr. V. D. Nanoty, Principal, Shri R. L. T. College of Science, Akola for providing necessary facilities.

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