



ISSN 0975-413X  
CODEN (USA): PCHHAX

Der Pharma Chemica, 2018, 10(8): 7-12  
(<http://www.derpharmachemica.com/archive.html>)

## Microwave Assisted Synthesis and Evaluation for Anticonvulsant Activity of Some 1,4 Dihydropyridine Derivatives

Dinesh Rishipathak\*, Luketa Alai, Kanchan Somase, Sanjay Kshirsagar

Department of Pharmaceutical Chemistry, Savitribai Phule Pune University, MET's Institute of Pharmacy, Bhujbal Knowledge City Adgaon, Nashik. Maharashtra, India

### ABSTRACT

Several new promising bioactive derivatives of 3,3'-(2, 6-dimethyl-4-substituted aryl-1, 4-dihydropyridine-3,5-diyl)-bis-(N-benzylidene-1H-1,2,4-triazol-5-amine) were synthesized under microwave irradiations. The compounds were obtained in excellent yields. All the titled compounds were characterized by Infrared Radiation (IR), Proton Nuclear Magnetic Resonance ( $^1\text{H-NMR}$ ), and mass spectral analysis. Synthesized compounds were evaluated for their anticonvulsant effect using PTZ induced convulsion studies. The pharmacological evaluation of the compounds showed increase in latency (onset time) to induce convulsions; decrease in the number of convulsions and increase in latency of death compared to control. The compounds A-I and I-II showed highest percentage of protection (80%) at the dose of 20 mg/kg among the evaluated compounds compared to control. The analysis of structural features revealed that substitution of Chloro group and methoxy group enhanced the anticonvulsant potential of the synthesized compounds.

**Keywords:** 1,4-Dihydropyridines, 1,2,4-Triazole, Anticonvulsant, Microwave

### INTRODUCTION

Microwave assisted organic synthesis (MAOS) has emerged as a new "lead" in organic synthesis. The technique offers simple, clean, fast, efficient, and economic for the synthesis of a large number of organic molecules. Important advantage of this technology include highly accelerated rate of the reaction, Reduction in reaction time with an improvement in the yield and quality of the product. Now day's technique is considered as an important approach toward green chemistry, because this technique is more environmentally friendly [1].

Epilepsy is the most common neurological disorder in humans, affecting 1%-2% of the global population. According to World Health Organization data, approximately 50 million people worldwide, a prevalence of 50 per 100 000 of the general population, suffer from epilepsy [2]. Despite the availability of the conventional AEDs and the development of several new anticonvulsants, the treatments of epilepsy still remain inadequate since loss of effectiveness (resistance) occurs after prolonged drug exposure.

1,4-Dihydropyridine (DHP) is a molecule based upon pyridine, and the molecules that have been semi-saturated with two substituents replacing one double bond. They are particularly well known in pharmacology as L-type calcium channel blockers. Five isomeric DHPs are capable of existence, but in fact most of the known DHPs have either the 1,2-dihydro structure or the 1,4-dihydro structure. DHPs have a broad range of pharmacological actions as agents in vasodilation, bronchodilation, hepatoprotection and geroprotection and as antiatherosclerosis, antidiabetes, antitumor, antimutagenic, antioxidant, anticonvulsant and antiradical agents [3].

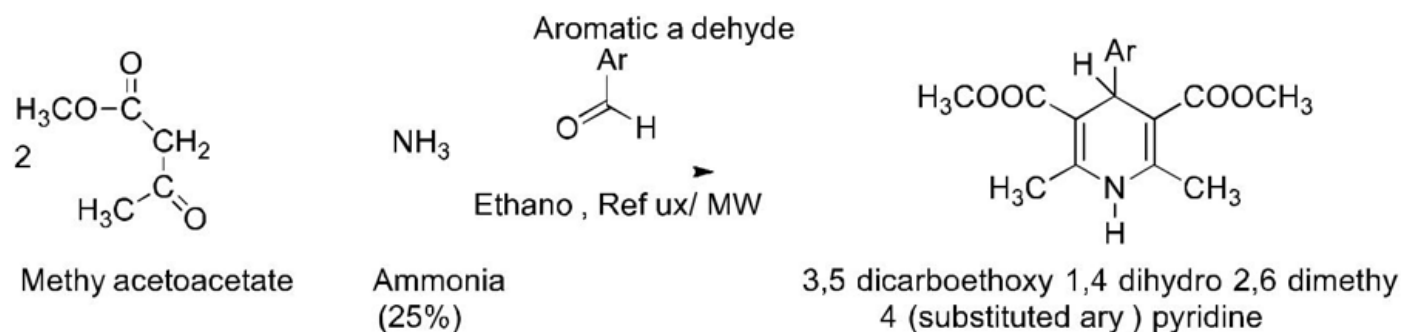
1,2,4-Triazoles, are five membered heterocycle with three nitrogen atoms in the ring. Triazole exists as two isomers, 1,2,3-triazoles and 1,2,4-triazoles. 1,2,4-triazoles consist wide variety of pharmacological activities such as Antimicrobial, Antiinflammatory, Hypoglycemic activity, Anticonvulsant, Antifungal, Antitubercular and Antidepressant.

### MATERIALS AND METHODS

All the chemicals and solvents used were purchased either from Thomas Baker, LobaChemie and Sigma-Aldrich. Reagents used were of analytical grade. Thin Layer Chromatography (TLC) was performed on 60 F254 silica gel plates (Merck) and visualized under UV light. Infrared (IR) spectra were recorded on DRS on a shimadzu 1000 Fourier-transform infrared (FTIR) spectrometer in the range of  $4000-200\text{ cm}^{-1}$  and only intense peaks are reported [4-6]. Proton Nuclear Magnetic Resonance ( $^1\text{H-NMR}$ ) spectra were recorded with a Bruker Avance II 400 NMR Spectrophotometer using  $\text{CDCl}_3$  solvent, at SAIF, Punjab University, Chandigarh. Tetramethylsilane (TMS) is used as an internal standard. All the chemical shifts were reported in  $\delta$  (ppm). The Proton Nuclear Magnetic Resonance ( $^1\text{H-NMR}$ ) chemical shifts and coupling constants were determined assuming first-order behavior. Mass spectra were recorded with a PE Sciex model API 3000 instrument.

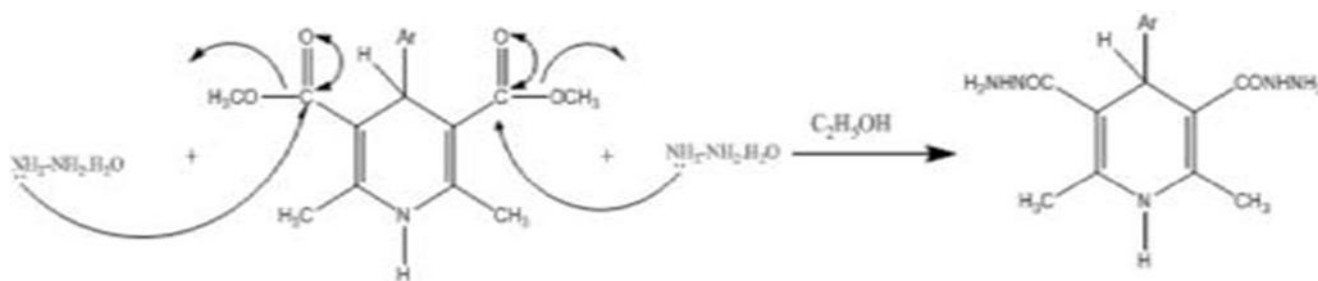
## Synthetic scheme

Synthesis of 3,5-di-carbo-methoxy-1,4-di-hydro-2,6-dimethyl-4-(substituted aryl)-pyridine (Hantzsch-dihydropyridine synthesis)[4]



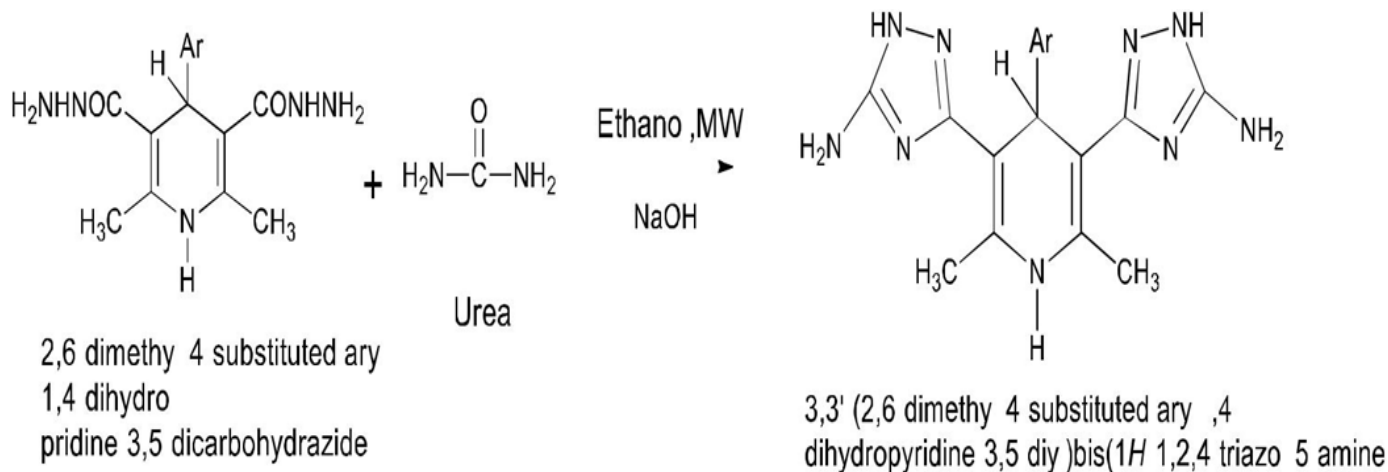
**Synthesis of 1,4-dihydropyridine derivatives:** A mixture of methyl acetoacetate, concentrated ammonia and substituted aldehyde (2: 1: 1 mole) in ethanol was irradiated under microwave. To the resulting mixture crushed ice was added and stirred vigorously, and filtered. The crude solid product obtained was air dried and recrystallized from ethanol. Purity of the product was checked by TLC.

Synthesis of 2,6-dimethyl-4-substituted aryl-1,4-dihydropyridine-3,5-dicarbohydrazide



**Synthesis of 2,6-dimethyl-4-substituted aryl-1,4-dihydropyridine-3,5-dicarbohydrazide:** A mixture of 3,5-dicarboethoxy-1,4-dihydro-2,6-dimethyl-4-(substituted phenyl)-pyridines were irradiated with hydrazine hydrate (99%) (1: 2) in ethanol under microwave at 15-20 min for 590 W. The reaction mixture was cooled to room temperature, poured into crushed ice & stirred vigorously. Solid thus obtained was filtered, air dried and recrystallized from Ethanol. Purity of the product was checked by TLC.

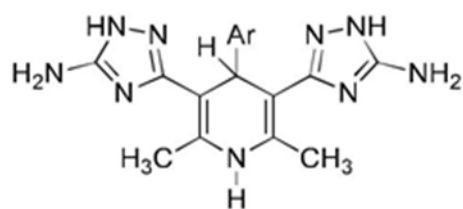
Synthesis of 3,3'-(2,6-dimethyl-4-substituted aryl-1,4-dihydropyridine-3,5-diyl)-bis-(1H-1,2,4-triazol-5-amine)



**Synthesis of 3,3'-(2,6-dimethyl-4-substituted aryl-1,4-dihydropyridine-3,5-diyl)-bis-(1H-1,2,4-triazol-5-amine):** A mixture of 1 mole of hydrazide of 1,4-DHP and 2 mole of urea in ethanol was irradiated under microwave for 20-25 min at power 490 W. 15 ml of 4% NaOH solution was added to the above solution. Then it was acidified with conc. HCl to obtain the product as precipitate. The solid thus obtained was filtered, air dried and recrystallized using ethanol. Purity of the product was checked by TLC.

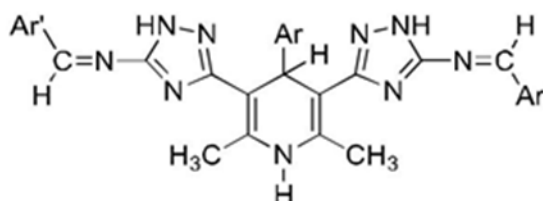
Synthesis of 3,3'-(2,6-dimethyl-4-substituted aryl-1,4-dihydropyridine-3,5-diyl) bis-(N-benzylidene-1H-1,2,4-triazol-5-amine)

Reaction-



3,3'-(2,6 dimethyl 4 substituted aryl ,4 dihydropyridine 3,5 diyl)bis (1H 1,2,4 triazo 5 amine)

Ar' CHO  
Ethano



3,3'-(2,6 dimethyl 4 substituted aryl 1,4 dihydropyridine 3,5 diyl)bis (N benzy lidene 1H 1,2,4 triazo 5 amine)

#### Synthesis of 3,3'-(2,6-dimethyl-4-substituted aryl)-1,4-dihydropyridine-3,5-diyl-bis-(N-benzylidene-1H-1,2,4-triazol-5-amine)

A mixture of 1 mole of triazoles of 1,4-dihydropyridines and 2 mole of substituted aldehydes in ethanol was irradiated under microwave for 25-35 min at power 420 W. The reaction mixture was cooled to room temperature, poured into crushed ice and stirred vigorously. Solid thus obtained was filtered, air dried and recrystallized from Ethanol. Purity of the product was checked by TLC.

**Pharmacological evaluation:** All the experiments were conducted according to the guidelines of Committee for Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Environments and Forests, Government of India with their procedures and protocols reviewed and approved by the Institutional Animal Ethical Committee (IAEC), constituted under CPCSEA. Swiss Albino male mice, weighing 22-30 g were used for the study. The animals were purchased from Hafkine's Institute, at Parel, Mumbai, India. Animals were housed in registered animal house of MET's Institute of Pharmacy, Nashik (Registration no.1344/ac/10/CPCSEA). Ambient temperature of  $25 \pm 1^\circ\text{C}$ , relative humidity of 45%-55% and 12 h light: 12 h dark cycles were maintained in the animal house. The animals had free access to water and standard pelleted diet except during experimentation food and water was withheld.

**Acute toxicity studies:** OECD guidelines (no. 425) were followed for acute toxicity studies. Acute intraperitoneal (i.p.) toxicity test was carried out for determining median Lethal Dose (LD50). Animals were dosed two at a time at a minimum of 48 h intervals. Doses were selected from the sequence 2000, 550, 175, 55, 17.5, 5.5, 1.75 mg/kg with 5 animals per group. Each animal was observed carefully for the signs of toxicity as well as for mortality in the first 30 min after dosing and then occasionally for further 4 hours and daily thereafter for a period of 14 days. The number of mice dying during 48 hours period was recorded.

**Anticonvulsant activity (PTZ induced convulsion method) (Table 1):** The drugs were freshly prepared. Pentylenetetrazole (Dose: 80 mg/kg, i.p.), a stock solution containing 8 mg/ml was prepared by dissolving it in distilled water. Diazepam (Dose: 2 mg/kg, i.p.), a stock solution containing 0.2 mg/ml was prepared by dissolving it in distilled water. All the test compounds were insoluble in water hence they were dissolved in DMSO. The doses of test compounds were 20 mg/kg, i.p. and 40 mg/kg, i.p. of Step III (Figure 1) derivatives and 1 mg/kg i.p. and 2 mg/kg i.p. of Step IV (Figure 2) derivatives respectively. The injection volume was 1 ml/100 g of body weight of animal.

Group of six mice were used. One group was used for studying the effects of Pentylenetetrazole alone (Control) and the other one for studying the protective effects of Diazepam (Standard). PTZ (80 mg/kg, i.p.) was administered half an hour after the administration of Diazepam and the test compounds. The test group animals were observed for onset of convulsions, number of convulsions and percentage of protection [7-11].

## RESULTS AND DISCUSSION

#### Synthesis of 3,5-dicarbomethoxy-1,4-dihydro-2,6-dimethyl-4-(substituted aryl)-pyridine (Hantzsch dihydropyridine synthesis) [4]

##### 3,5-dicarbomethoxy-1,4-dihydro-2,6-dimethyl-4-(p-methoxyphenyl)-pyridine

Reaction condition- Microwave at power 420 W and irradiation time was for 55 min. Mol. Formula-  $\text{C}_{18}\text{H}_{21}\text{NO}_5$ , Mol.wt-331.36, M.P.-185-188°C, Yield: 84%; IR (KBr)  $\text{cm}^{-1}$ -1255 (C—O—C str) 1686 (C=O str) 3342 (N-H) 1656 (secondary amine) 1609, 1485 (C=C).

##### 3,5-dicarbomethoxy-1,4-dihydro-2,6-dimethyl-4-phenyl-pyridine

Reaction condition: Microwave at power 490 W and irradiation time was for 20 min. Mol. Formula-  $\text{C}_{17}\text{H}_{19}\text{NO}_4$ , Mol.wt-301.34, M.P.-182-185°C, Yield: 66%; IR (KBr)  $\text{cm}^{-1}$ -1730 (C=O str) 3344 (N-H) 1648 (secondary amine) 1616, 1473 (C=C).

##### 3,5-dicarbomethoxy-1,4-dihydro-2,6-dimethyl-4-(o-chlorophenyl)-pyridine

Reaction condition-Microwave at power 490 W for 35 min, Mol. Formula  $\text{C}_{17}\text{H}_{18}\text{ClNO}_4$ , Mol. Wt 335.78, M.P.-140-142°C, Yield:-96%; IR (KBr)  $\text{cm}^{-1}$ -1732 (C=O str) 3327 (N-H) 1556 (secondary amine) 1651, 1492 (C=C) 1095 (Ar-Cl).

##### 3,5-dicarbomethoxy-1,4-dihydro-2,6-dimethyl-4-(p-chlorophenyl)-pyridine

Reaction condition-Microwave at power 420 W and irradiation time was for 35 min. Mol. Formula- $\text{C}_{17}\text{H}_{18}\text{ClNO}_4$  Mol. wt-335.78, M.P.-138-140°C, Yield: 62%; IR (KBr)  $\text{cm}^{-1}$ -1687 (C=O str) 3483 (N-H) 1647 (secondary amine) 1624, 1498 (C=C) 1052 (Ar-Cl).

*3,5-dicarbomethoxy-1,4-dihydro-2,6-dimethyl-4-(furan-2-yl)-pyridine*

Reaction condition-Microwave at power 490 W and irradiation time was for 20 min. Mol. Formula- C<sub>15</sub>H<sub>17</sub>NO<sub>5</sub>, Mol.wt 291.3, M.P.-182-185°C, Yield: 72%; IR (KBr) cm<sup>-1</sup>-1696 (C=O str) 3346 (N-H) 1653 (secondary amine) 1617, 1490 (C=C) 1147 (C-O-C).

**Synthesis of 2,6-dimethyl-4-substitutedaryl-1,4-dihydropyridine-3,5-dicarbohydrazide***4-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbohydrazide*

Mol. Formula- C<sub>16</sub>H<sub>21</sub>N<sub>5</sub>O<sub>3</sub> Mol.wt-331.37; M.P.-177-179°C Yield: 95%; IR (KBr) cm<sup>-1</sup>-1668 (C=O amide) 1251 (C—O—C str) 3320 (N-H) 1607 (secondary amine) 1607, 1472 (C=C).

*2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3,5-dicarbohydrazide*

Mol. Formula C<sub>15</sub>H<sub>19</sub>N<sub>5</sub>O<sub>2</sub>, (C=Oamide) 3344, Mol.wt-301.34, M.P.-170-173°C, (N-H) 1651 (secondary) Yield: 78%; IR (KBr) cm<sup>-1</sup>-1699 (amine) 1625, 1435 (C=C).

*4-(2-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbohydrazide*

Mol. Formula- C<sub>15</sub>H<sub>18</sub>ClN<sub>5</sub>O<sub>2</sub>, Mol.wt-335.79, M.P. 182-184°C, Yield: 93%; IR (KBr) cm<sup>-1</sup>-1683 (C=O amide) 3325 (N-H) 1623 (secondary amine) 1623, 1472 (C=C) 1096 (Ar-Cl).

*4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbohydrazide*

Mol. Formula- C<sub>15</sub>H<sub>18</sub>ClN<sub>5</sub>O<sub>2</sub>, Mol.wt-335.79, M.P. 190-192°C, Yield:-81%; IR (KBr) cm<sup>-1</sup>-1697 (C=O amide) 3336 (N-H) 1627 (secondary amine) 1651, 1487 (C=C) 1099 (Ar-Cl).

*4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbohydrazide*

Mol. Formula-C<sub>17</sub>H<sub>17</sub>N<sub>5</sub>O<sub>3</sub> Mol.wt-291.31, M.P. 190-191°C, Yield : 72%; IR (KBr) cm<sup>-1</sup>-1696 (C=O amide), 3351 (N-H), 1653 (secondary amine) 1627, 1491 (C=C), 1147 (C-O-C).

**Synthesis of 3,3'-(2,6-dimethyl-4-substituted aryl-1,4-dihydropyridine-3,5-diyl)-bis-(1H-1,2,4-triazol-5-amine)***3,3'-(4-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(1H-1,2,4-triazol-5-amine) (A-I)*

Mol. Formula- C<sub>18</sub>H<sub>21</sub>N<sub>9</sub>O, Mol.wt-379.42 M.P. 168-170°C Yield:-83%. IR (KBr) cm<sup>-1</sup>-1251 (Ar-O-R), 3295 (N-H), 1695 (=C=N), 2950 (C-H); <sup>1</sup>H-NMR (400MHZ CDCl<sub>3</sub>) δ (ppm)=5.18 (pyridine N-H), 2.32 (-CH<sub>3</sub>), 6.77(-NH<sub>2</sub>), 10.3 (triazole), 4.95 (pyridine), 7.19 (Ar-H), 7.16 (AR-H), 3.82(-OCH<sub>3</sub>).

*3,3'-(2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3,5-diyl)bis(1H-1,2,4-triazol-5-amine) (B-I)*

Mol. Formula-C<sub>17</sub>H<sub>19</sub>N<sub>9</sub>, Mol.wt-349.39, M.P.-180-182°C, Yield: 76%; IR (KBr) cm<sup>-1</sup>-3344(N-H), 1695 (=C=N), 2951(C-H).

*3,3'-(4-(2-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(1H-1,2,4-triazol-5-amine) (C-I)*

Mol. Formula-C<sub>17</sub>H<sub>18</sub>ClN<sub>9</sub>, Mol.wt-383.84, M.P. 166-170°C Yield: 80%; IR (KBr) cm<sup>-1</sup>-3244 (N-H), 1696 (=C=N), 2952 (C-H) 1119 (Ar-Cl); <sup>1</sup>H-NMR (300MHZ CDCl<sub>3</sub>) δ (ppm)=5.39 (pyridine N-H), 2.17 (-CH<sub>3</sub>), 5.67 (-NH<sub>2</sub>), 9.95 (triazole), 3.61 (pyridine), 7.03 (Ar-H), 7.13 (AR-H), 7.26 (AR-H); MS (ESI) m/z (M+H) +384.3 (C<sub>17</sub>H<sub>18</sub>ClN<sub>9</sub>), 353.2 (C<sub>15</sub>H<sub>12</sub>ClN<sub>9</sub>), 300.2 (C<sub>15</sub>H<sub>15</sub>ClN<sub>9</sub>), 272.2 (C<sub>11</sub>H<sub>14</sub>N<sub>9</sub>), 112.2 (C<sub>6</sub>H<sub>4</sub>Cl).

*3,3'-(4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(1H-1,2,4-triazol-5-amine) (D-I)*

Mol. Formula- C<sub>17</sub>H<sub>18</sub>ClN<sub>9</sub>, Mol.wt-383.84, M.P.184-186°C, Yield: 95%; IR (KBr) cm<sup>-1</sup>-3344 (N-H), 1695 (=C=N), 2951 (C-H) 1099 (Ar-Cl).

*3,3'-(4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(1H-1,2,4-triazol-5-amine) (F-I)*

Mol. Formula-C<sub>15</sub>H<sub>17</sub>N<sub>9</sub>O, Mol.wt-339.36, M.P.-180-182°C, Yield: 94%; IR (KBr) cm<sup>-1</sup>-3346 (N-H), 1696 (=C=N), 2952 (C-H) 1148 (C-O-C).

**Synthesis of 3,3'-(2,6-dimethyl-4-substituted aryl-1,4-dihydropyridine-3,5-diyl) bis-(N-benzylidene-1H-1,2,4-triazol-5-amine)***3,3'-(4-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(N-benzylidene-1H-1,2,4-triazol-5-amine) (A-II)*

Mol. Formula-C<sub>32</sub>H<sub>29</sub>N<sub>9</sub>O, Mol.wt-555.63, M.P.-180-181°C, Yield: 70%; IR (KBr) cm<sup>-1</sup>-1250 (Ar-O-R), 3350 (-NH), 1684 (C=N).

*3,3'-(4-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(N-(2-chlorobenzylidene)-1H-1,2,4-triazol-5-amine) (B-II)*

Mol. Formula-C<sub>32</sub>H<sub>27</sub>Cl<sub>2</sub>N<sub>9</sub>O, Mol.wt- 624.52, M.P.-150-154°C; Yield: 55%; IR (KBr) cm<sup>-1</sup>-1251 (Ar-O-R), 3310 (-NH), 1685 (C=N), 1049 (Ar-Cl).

*3,3'-(4-(4-methoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(N-(4-chlorobenzylidene)-1H-1,2,4-triazol-5-amine) (C-II)*

Mol. Formula-C<sub>32</sub>H<sub>27</sub>Cl<sub>2</sub>N<sub>9</sub>O Mol.wt-624.52, M.P.-150-152°C, Yield:-79%.%; IR (KBr) cm<sup>-1</sup>-1251 (Ar-O-R), 3348 (-NH), 1693 (C=N), 1095 (Ar-Cl).

*3,3'-(2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3,5-diyl)bis(N-benzylidene-1H-1,2,4-triazol-5-amine) (D-II)*

Mol. Formula-C<sub>31</sub>H<sub>27</sub>N<sub>9</sub> Mol.wt-525.61 M.P.-192-194°C Yield: 72%.%; IR (KBr) cm<sup>-1</sup>-3344 (-NH), 1684 (C=N), 3027 (C-H); <sup>1</sup>H-NMR (400 MHZ CDCl<sub>3</sub>) δ (ppm)=5.00 (pyridine-N), 2.35 (pyridine -CH<sub>3</sub>), 6.68 (-NH<sub>2</sub>), 9.87 (NH- triazole), 8.21 (C=N), 3.82 (pyridine), 7.21 (multiplet Ar-H).

*3,3'-(4-(2-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(N-benzylidene-1H-1,2,4-triazol-5-amine) (E-II)*

Mol. Formula-C<sub>31</sub>H<sub>26</sub>ClN<sub>9</sub>O Mol.wt-560.05 M.P.-220-225°C Yield:-52%.%. IR (KBr) cm<sup>-1</sup>-3302 (-NH), 1701 (C=N), 1118 (Ar-Cl); <sup>1</sup>H-NMR (400 MHZ CDCl<sub>3</sub>) δ (ppm)=5.40 (pyridine-N), 2.30 (pyridine -CH<sub>3</sub>), 9.10 (NH- triazole), 8.23 (C=N), 3.61 (pyridine), 7.22s (multiplet Ar-H).

*3,3'-(4-(4-chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(N-benzylidene-1H-1,2,4-triazol-5-amine) (F-II)*

Mol. Formula-C<sub>31</sub>H<sub>26</sub>ClN<sub>9</sub>O, Mol.wt-560.05, M.P.-176-178°C; Yield: 69%.%; IR (KBr) cm<sup>-1</sup>-3336 (-NH), 1697 (C=N), 1087 (Ar-Cl).

3,3'-(4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)-bis-(N-benzylidene-1H-1,2,4-triazol-5-amine) (G-II)

Mol. Formula-C<sub>29</sub>H<sub>25</sub>N<sub>9</sub>O Mol.wt-515.57 M.P.-186-188°C Yield: 72%.%; IR (KBr) cm<sup>-1</sup>-3347 (-NH), 1686 (C=N), 1122 (C-O-C).

3,3'-(4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(N-(4-methoxybenzylidene)-1H-1,2,4-triazol-5-amine) (H-II)

Mol. Formula-C<sub>29</sub>H<sub>25</sub>N<sub>9</sub>O<sub>3</sub>, Mol.wt-575.62, M.P.-168-170°C, Yield:-60%.%; IR (KBr) cm<sup>-1</sup>-3350(-NH), 1693(C=N), 1151(C-O-C).

3,3'-(4-(furan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-diyl)bis(N-2-chlorobenzylidene)-1H-1,2,4-triazol-5-amine) (I-II)

Mol. Formula- C<sub>29</sub>H<sub>23</sub>Cl<sub>2</sub>N<sub>9</sub>O, Mol.wt-584.46, M.P.-168-170°C, Yield: 60%.%; IR (KBr) cm<sup>-1</sup>-3350(-NH), 1643(C=N), 1257(C-O-C); <sup>1</sup>H-NMR (400 MHZ CDCl<sub>3</sub>) δ (ppm)=5.19 (pyridine-N), 2.34 (pyridine-CH<sub>3</sub>), 9.82 (NH- triazole), 8.78 (C=N), 3.94 (pyridine), 7.22 (multiplet Ar-H); MS (ESI) m/z (M+H) +. 583.5 (C<sub>29</sub>H<sub>23</sub>Cl<sub>2</sub>N<sub>9</sub>O), 473.2 (C<sub>23</sub>H<sub>19</sub>ClN<sub>9</sub>O), 378.2 (C<sub>20</sub>H<sub>17</sub>ClN<sub>5</sub>O), 204.2 (C<sub>9</sub>H<sub>6</sub>ClN<sub>4</sub>).

### Pharmacological Evaluation

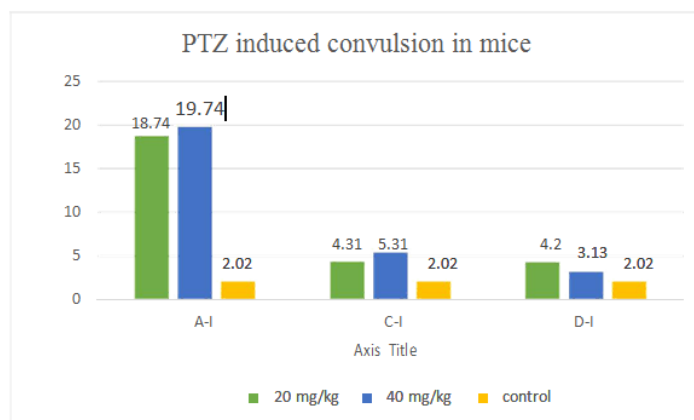
**Table 1: Anticonvulsant effect of some synthesized 1,4-dihydropyridines containing 1,2,4-triazoles in mice using PTZ induced convulsion method**

Code	Dose (mg/Kg, i.p.)	Latency to induce convulsions (Min)	No. of convulsions	% Protection
PTZ (Control)	80	2.02 ± 1.131	5	0
Diazepam	2	-	0	100
A-I	20	18.742 ± 4.798**	2	60
	40	14.074 ± 3.493*	2	60
C-I	20	4.315 ± 0.6903 <sup>NS</sup>	1	80
	40	3.18 ± 0.4979 <sup>NS</sup>	3	40
D-I	20	4.201 ± 0.263 <sup>NS</sup>	3	40
	40	3.13 ± 0.402 <sup>NS</sup>	3	40
B-II	1	3.79 ± 267 <sup>NS</sup>	2	40
	2	7.45 ± 5.112 <sup>NS</sup>	2	40
C-II	1	3.68 ± 0.7656 <sup>NS</sup>	3	40
	2	8.44 ± 2.651 <sup>NS</sup>	2	60
I-II	1	11.766 ± 6.189 <sup>NS</sup>	3	40
	2	16.36 ± 3.819*	2	60

N=5, in each group; \*: P < 0.05; \*\*: P < 0.01; NS: Non significant; One Way ANOVA followed by Dunnett's test. Values expressed as Mean ± SEM

Formula of percentage protection [8]:

$$\% \text{ protection} = \frac{\text{Number of convulsions of control} - \text{Number of convulsions of test}}{\text{Number of convulsions of control}} \times 100$$



**Figure 1: Graphical representation of some anticonvulsant effect of some Step III synthesized derivatives in mice using PTZ induced convulsion method**

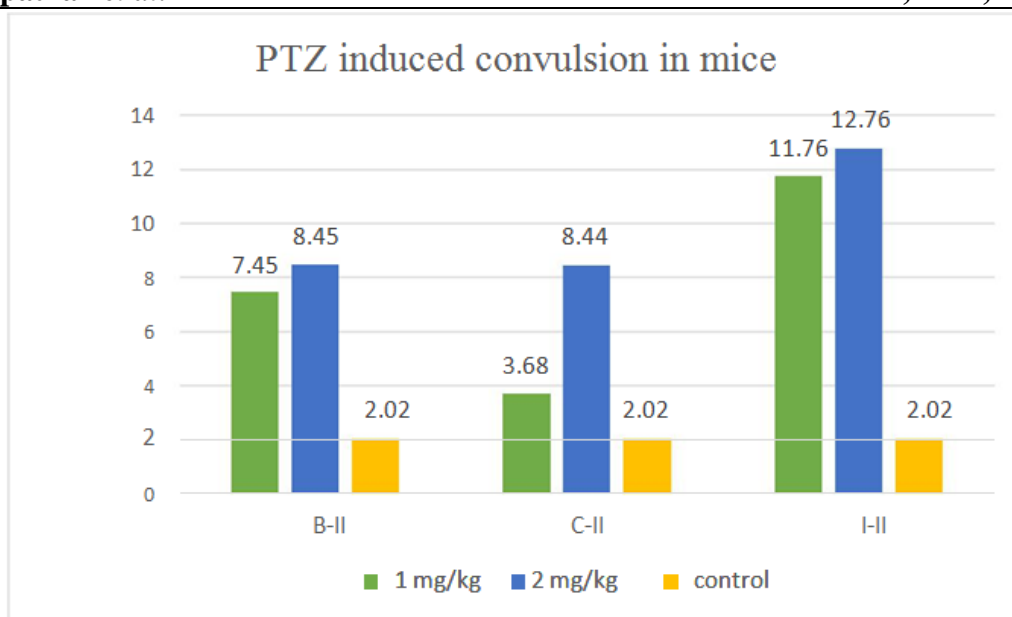


Figure 2: Graphical representation of some anticonvulsant effect of some Step IV synthesize derivatives in mice using PTZ induced convulsion method

### CONCLUSION

The 3,3'-(2,6-dimethyl-4-substituted aryl-1,4-dihydropyridine-3,5-diyl) bis-(*N*-benzylidene-1*H*-1,2,4-triazol-5-amine) derivatives was synthesize using microwave for 25-35 min at power 420 W. The structures of the compounds were confirmed on the basis of IR, <sup>1</sup>H-NMR, and Mass analyses. The analysis of structural features revealed that substitution of Chloro group and methoxy group enhanced the anticonvulsant potential of the synthesized compounds.

Acute toxicity study was done for determining LD<sub>50</sub>. The LD<sub>50</sub> was found to be 310.2 mg/Kg for Step III derivatives and 17.5 mg/Kg for Step IV derivatives. Two doses were selected for the anticonvulsant evaluation of the compounds, 20 and 40 mg/kg for Step III derivatives and 1 and 2 mg/kg for Step IV derivatives.

The anticonvulsant activity (PTZ induced convulsion method) of the compounds showed increase in latency (onset time) to induce convulsions; decrease in the number of convulsions. The compounds A-I and I-II showed highest percentage of protection (80%) at the dose of 20 mg/kg among the evaluated compounds compared to control.

### ACKNOWLEDGEMENT

The authors are very thankful to the Management and Principal of MET's Institute of Pharmacy, Bhujbal Knowledge City, Nashik, Maharashtra for providing infrastructural facilities to carry out the research work.

### REFERENCES

- [1] F. Mavandadi, A. Pilotti, *Drug Discovery Today*, **2006**, 11(3/4), 165-174.
- [2] J.B. Taylor, D.J. Triggle, (Edi.), *Comprehensive Medicinal Chemistry II*, Elsevier Ltd, **2006**, 6, 279-294.
- [3] N. Edraki, *Drug Discovery Today*, 14 (November), 2009, 058-1066.
- [4] J. Clayden, *Organic Chemistry*, New York: Oxford University Press, **2006**, 1191-1193.
- [5] J.R. DYER, *Applications of absorption spectroscopy of organic compounds*, New Delhi, Prentice Hall of India. Pvt. Ltd., **2007**, 33-38.
- [6] D.L. Pavia, *Spectroscopy*, New Delhi, Cengage Learning India Pvt. Ltd., **2010**, 37-91, 390-451, 644, 648.
- [7] S.K. Kulkarni, *Handbook of Experimental Pharmacology*, New Delhi, Vallabh prakashan, **2009**, 131-134.
- [8] M. Abdel-Aziz, G.A. Abuo-Rahma, A.A. Hassan, *Eur. J. Med. Chem.*, **2009**, 44, 3480-3487.
- [9] P. Zapater, *Brain Res.*, **1998**, 796, 311-314.
- [10] B.K. Shoichet, I.D. Kuntz, D.L. Bodian, *J. Comput. Chem.*, **2004**, 13(3), 380-397.
- [11] B.B. Subudhi, P.K. Panda, S.P. Swain, P. Sarangi, *Acta Poloniae Pharmaceutica—Drug Research.*, **2009**, 66(2), 147-153.