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# Synthesis and characterization of 4-amino-4H-1,2,4-triazole derivatives: Anticonvulsant activity

**Mallesha Lingappa[a*], Vinay Guruswamy[a] and Veeresh Bantal[b]**

[a]*PG Department of Chemistry, JSS College of Arts, Commerce and Science, Ooty Road, Mysuru 570 025, India*
[b]*Department of Pharmacology, G Pulla Reddy College of Pharmacy, Mehdipatnam, Hyderabad 500 028, India*

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**A B S T R A C T**

A new series of 4-amino-4H-1,2,4-triazole derivatives, **3a-f** and **5a-f** were synthesized by using various aryl aldehydes and ketones. FT-IR, $^{1}$H NMR, $^{13}$C NMR and mass spectral studies were characteristic of the synthesized compounds. These new compounds were screened in male wistar rats and compared with the standard drug for their anticonvulsant activity against maximal electroshock seizure (MES) model. Compounds **3b** and **5d** of this sequence were found to be the most active. The same compound did not demonstrate neurotoxicity at the administered maximum dose (100 mg / kg) and these compounds showed good protection compared to other compounds.

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## 1. Introduction

The heterocyclic compounds usually don't easily get depolymerized or hydrolyzed contain a firm ring configuration. Heterocycles with three-atoms in the ring structure posses ring strain due to which they are more reactive. In general, those which contain one heteroatom are stable. Due to the biological importance and structural diversity of N-containing heterocycles for synthesis they are the most gorgeous targets over many years. N-heterocycles are utilized for food flavorings, medicines, dyes, rubber chemicals and adhesives.[1]Searching for the new agent is the most difficult tasks for the medicinal chemist. Due to their usefulness in a variety of applications, the synthesis of high N-containing heterocyclic systems has attracted growing interest in the last decade, applications like explosives, propellants, pyrotechnics and particularly chemotherapy. Due to its wide range of activities,[2] low toxicity, strong pharmacokinetic and pharmacodynamic profiles, 1,2,4-triazole has drawn considerable interest from the 1,2,4-triazole to medicinal chemists of two decades. The first 1,2,4-triazole is 3-amino-1,2,4-triazole and it was manufactured from aminoguanidine format on large scale, useful as herbicides.[3] *N*-substituted triazole with another substituent and it showed biological activity such as anti-inflammatory,[4] anticonvulsant,[5] anticancer,[6] antimycobacterial,[7] antioxidant[8] and antimalarial.[9]

* Corresponding author.
E-mail address: mallesha83@gmail.com (M. Lingappa)
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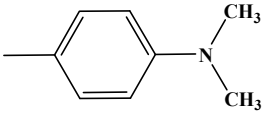
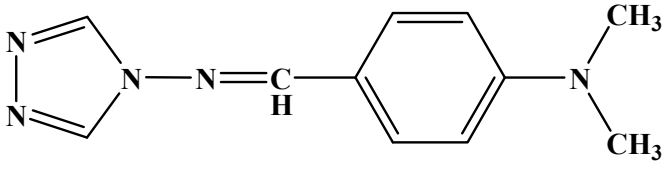
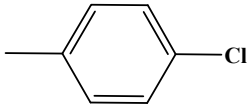
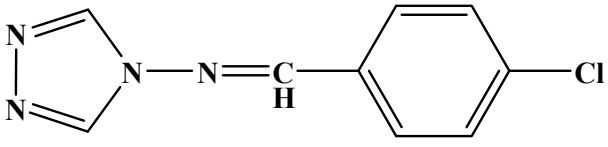
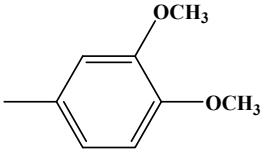
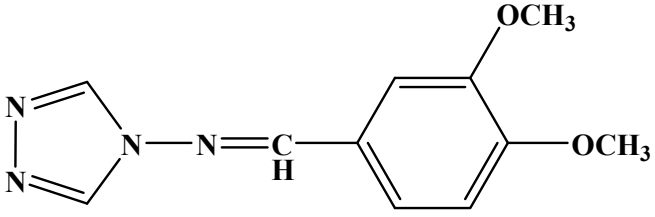
Imines act as backbones for the various heterocyclic compound syntheses. This is responsible for the biological activity is due to the presence of functional groups of sulfonamides and azomethine and this can be altered according to the form of substituent present on the aromatic rings. It is used in replacement reactions and cycloaddition.[10] Schiff bases with the nitro- and halo-derivatives showed biological activity.[11] Several researchers studied to certain Schiff bases that bear aryl groups or heterocyclic residues that have had excellent biological activity in recent years.[12] Particularly in 1,2,4-triazole and their heterocyclic derivatives have been testified to be used as drugs and to have significant activities properties.[13] Therefore, it was thought meaningful to produce Schiff base substituted 1,2,4-triazoles derivatives.

The pharmacological approaches for treating epilepsy are intended to inhibit the initiation or spread of seizures rather than the underlying mechanisms leading to epilepsy. Some epileptic patients are unresponsive to current antiepileptic drug treatment, and for this reason the major goal in epilepsy research has been to develop drugs with greater anticonvulsant efficacy and less toxicity than existing drugs.[14] There is an experimentally-induced seizure and leads to the increased susceptibility to seizures found in certain genetically-prone animals.[15] The vast number of chemicals in industrial use not worked including animal health concerns to resolve problems associated with growing costs and time needed for neurotoxicity testing. Several *in vitro* models have been commonly used in neurotoxicity assessments, including synaptic fractions, rat astrocyte cultures and murine spinal cord cultures[16] as neurotoxicity studies. The present paper reports in view of these findings, on the 1,2,4-triazole derivatives synthesis and distinguished by specific spectral studies. It was also confirmed that all the compounds had anticonvulsant activity.

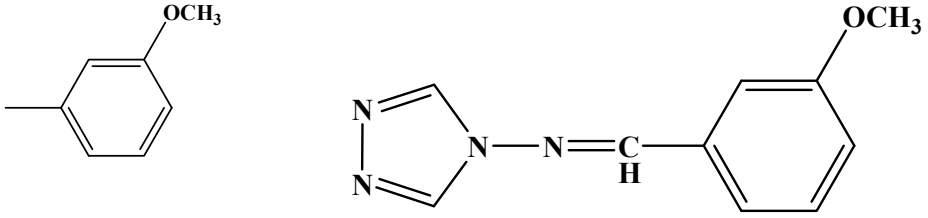
## 2. Results and Discussion

The synthesized molecules (**3a-f**) and (**5a-f**) were identified using $^{13}C$ NMR, $^{1}H$ NMR, mass and infrared study. **Table 1** showed structure of new molecules. The system outlined in the scheme was used to synthesize the Schiff bases. The physical details and UV-visible absorption spectra of **3a-f** and **5a-f** values are explained in experimental section. The reactants show in the ultraviolet absorption spectrum. Bathochromic shift occurs in products with the absorption band being located above 320 nm.

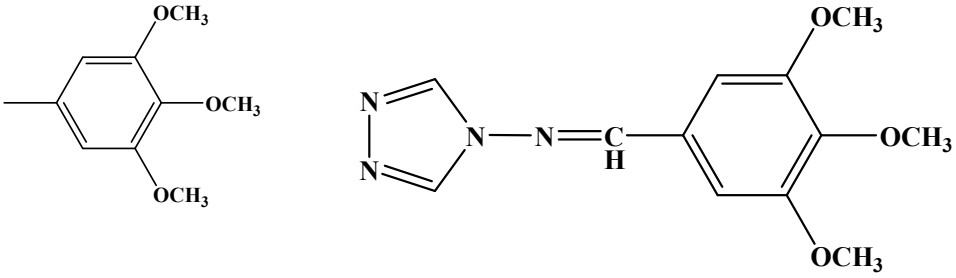
**Table 1.** Chemical structure of imines compound.

| Compound | R/R[1] | Structure |
|---|---|---|
| **3a** |  |  |
| **3b** |  |  |
| **3c** |  |  |

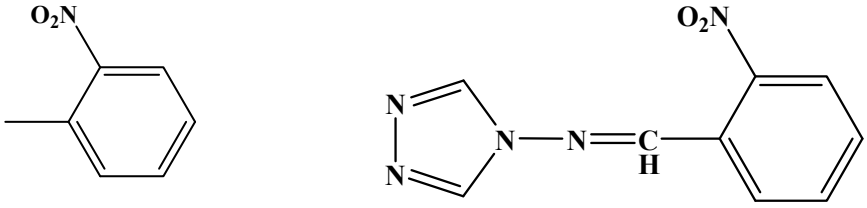
**3d**



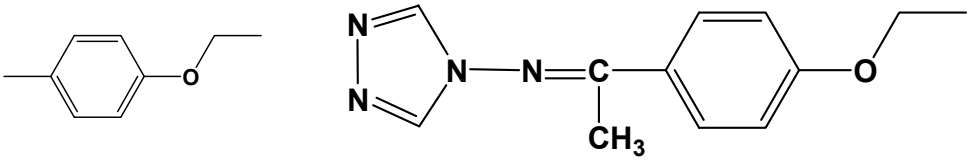
**3e**



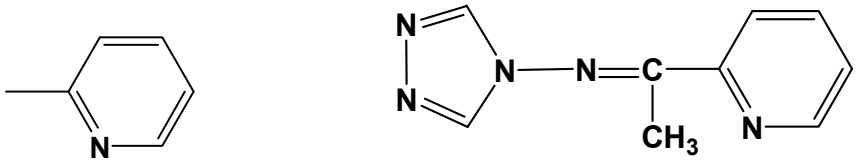
**3f**



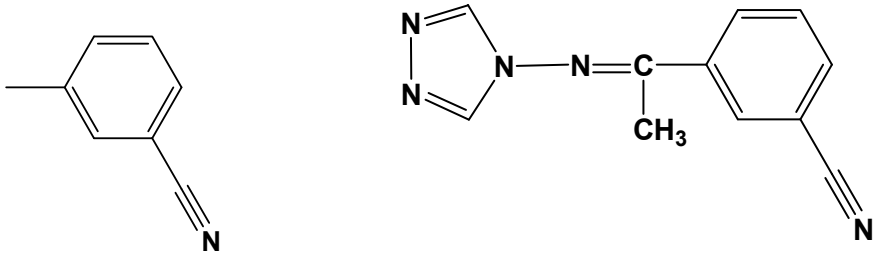
**5a**



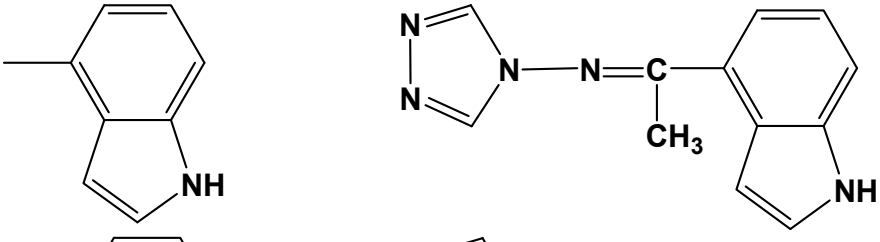
**5b**



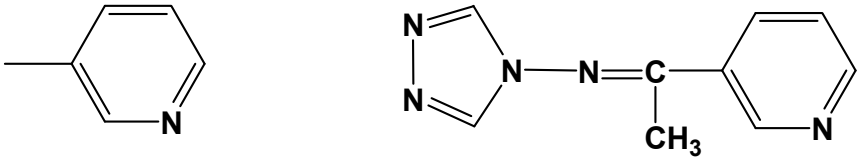
**5c**



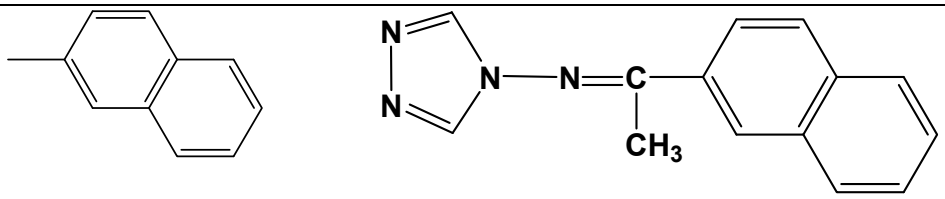
**5d**



**5e**



**5f**




The spectra of FT-IR run in FT-IR spectroscopy. The absorption of 1655-1600 $cm^{-1}$ due to C=N function. All the compounds give an absorption in 3097-3032 $cm^{-1}$ due to aromatic vibration peaks. The absence of amine and carbonyl group in FT-IR range supported the condensation of the new compounds. The changes in integral intensities and bandwidths, however, particularly of the bands originating from stretching vibrations of $NH_2$ did not show in products (**Fig. 1 and Fig. 2**).

New compounds exhibited a singlet in δ = 8.75-8.20 ppm region due to triazole proton in the $^1H$ NMR spectra. The aromatic doublet protons appeared between δ = 7.95-6.10 (Ar-H). A singlet was observed at δ = 8.40 to 8.10 ppm due to imines protons in **3a-f**. A singlet was observed at δ = 0.95-0.90 ppm due to $CH_3$ protons in **5a-f**.$^{13}C$ NMR is a commanding instrument to characterize new compounds. In products spectra one value for chemical shift is obtained, about 164.7-156 ppm for imines. The aromatic carbons represent the carbon atoms exact numeral at the appropriate chemical shift values at 160 to 106 ppm. Triazole carbons in the products appeared at 149 to 147 ppm. $CH_3$ carbons in **5a-f** showed chemical shift values at 16.8 to 13.0 ppm. The mass spectra showed molecular ion peak, which are concorded with molecular formula.

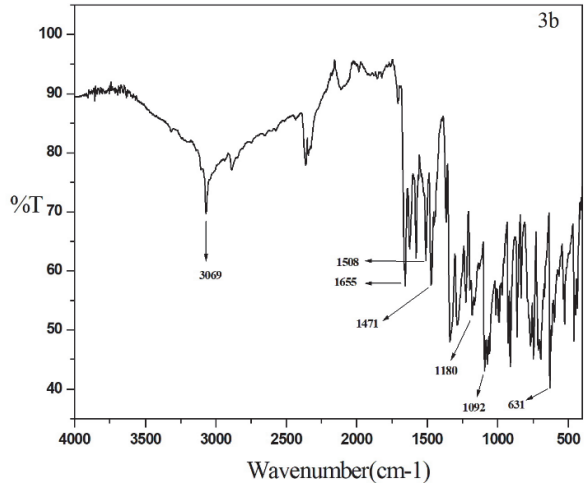



**Fig. 1**. FT-IR spectrum of **3b**

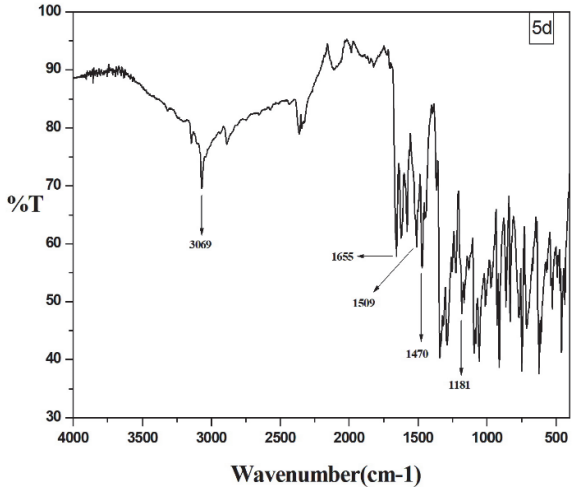



**Fig. 2**. FT-IR spectrum of **5d**

All the analogues of the synthesized triazoles were screened at 100 mg/kg dose for their anticonvulsant potential via MES model. For many decades, anti-epileptic drug research has focused on discovering new potential medicines based on their anticonvulsant action against single acute seizures that are triggered by multiple stimulators, typically in mice and rats. In MES model, all known antiepileptic drugs have anticonvulsant activity.[19] It was shown that compounds **3b** and **5d** had a major protective effect on MES-induced and it was close to that of normal (phenytoin). Similarly, other compounds displayed modest protective effect and a substantial difference in safety relative to the standard group was observed. (**Table 2**, **Fig. 3**). Neurotoxicity was used for compounds **3a-f** and **5a-f** using a rotarod method given in 100 mg / kg dose. Both molecules did not exhibit toxicity although **3a** and **5f** demonstrated 25 percent toxicity according to the normal at 2 hours of oral administration (**Table 3**). The structure of standard drug phenytoin contains imidazole group with diphenyl ring and it exhibited 75.80 % protection in the anticonvulsant activity. The electron withdrawing halogen groups in **3b** produces enhanced anticonvulsant activity against the tested rats. This indicates the positional

requirement of halogen groups on phenyl ring for enhanced activity. The indole group of **5d** showed good anticonvulsant activity and these structural activity relationship studies reveal that, the nature of the functional groups is crucial for anticonvulsant activity.

**Table 2.** *In vivo* anticonvulsant activity of compounds (**3a-f**) and (**5a-f**).

| Compound | E/F | % Protection |
|---|---|---|
| **3a** | 3.76 | 20.10 |
| **3b** | 1.67 | 64.42 |
| **3c** | 3.39 | 28.00 |
| **3d** | 3.19 | 32.36 |
| **3e** | 3.20 | 32.20 |
| **3f** | 3.29 | 30.15 |
| **5a** | 3.22 | 31.80 |
| **5b** | 3.06 | 35.30 |
| **5c** | 3.19 | 32.10 |
| **5d** | 1.63 | 65.43 |
| **5e** | 3.06 | 35.30 |
| **5f** | 3.29 | 31.15 |
| **Standard** | 1.14 | 75.80 |
| **Control (Vehicle)** | 4.71 | – |

Values are articulated in mean ± SE. n = 6 animals in each group E/F = Extension/Flexion [Decrease in ratio of extension phase (in seconds)/flexion phase (in seconds)], % Protection = (Control-test)/(Control) x 100

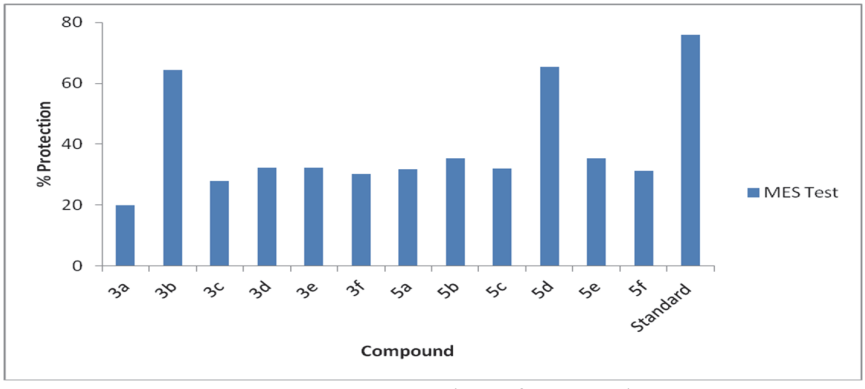



**Fig. 3**. Percentage protection of **3a-f** and **5a-f**.

**Table 3.** Neurotoxicity screening of the compounds

| Compound | Neurotoxicity screen | | | |
|---|---|---|---|---|
| | **0.5 h** | **1 h** | **2 h** | **4 h** |
| **3a** | 0/4 | 0/4 | 1/4 | 1/4 |
| **3b** | 0/4 | 0/4 | 0/4 | 0/4 |
| **3c** | 0/4 | 0/4 | 0/4 | 0/4 |
| **3d** | 0/4 | 0/4 | 0/4 | 0/4 |
| **3e** | 0/4 | 0/4 | 0/4 | 0/4 |
| **3f** | 0/4 | 0/4 | 0/4 | 0/4 |
| **5a** | 0/4 | 0/4 | 0/4 | 0/4 |
| **5b** | 0/4 | 0/4 | 0/4 | 0/4 |
| **5c** | 0/4 | 0/4 | 0/4 | 0/4 |
| **5d** | 0/4 | 0/4 | 0/4 | 0/4 |
| **5e** | 0/4 | 0/4 | 0/4 | 0/4 |
| **5f** | 0/4 | 0/4 | 1/4 | 1/4 |
| **Standard** | 0/4 | 0/4 | 0/4 | 0/4 |

The data in the table indicates the ratio of the no. of animals exhibiting neurotoxicity to the no. of animals tested.

## 3. Conclusions

In conclusion, synthesis of 1,2,4-triazole derivatives in good yield, characterized by spectral data. They were screened for anticonvulsant activity. Compounds **3b** and **5d** demonstrated good anticonvulsant activity without the significant neurological toxicity. The substituent on phenyl ring

influence on an anticonvulsant activity of tested 1,2,4-triazole derivatives. The additional modification and diversification of functional groups in order to improve the activity is currently in progress.

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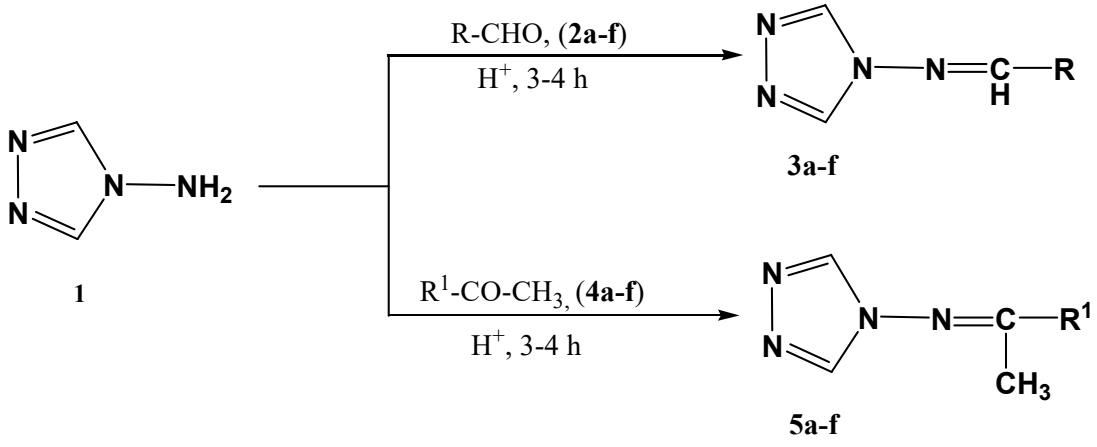
## 4. Experimental

### *4.1. Materials and methods*

Sigma Aldrich Chemicals limited bought all of the solvents and reagents. VMP III-Veego Melting Point apparatus had determined the melting range. The FT-IR spectra on Agilent FT-IR ATR Cary 630 using the spectral range of 7000–350 $cm^{-1}$. $^{1}H$ NMR spectra were registered using DMSO-$d_6$ and internal standard as TMS on Bruker DRX -500 spectrometer at 400 MHz. $^{13}C$ NMR spectra have been reported using DMSO-$d_6$ and internal standard as TMS at 100 MHz Bruker DRX 500 spectrometer. The LC-MSD-Trap-XCT instrument was used for mass spectra.

### *4.2. General procedure for **3a-f** and **5a-f** synthesis*

A mixture of 4-amino-4H-1,2,4-triazole (**1**) and substituted aldehydes (**2a-f**) and ketones (**4a-f**) in mortar mixed well. To the mixture, added a few drops of $CH_3COOH$. Using mortar and pestle, completely grounded the reaction mixture. The grinding continued for 3-4 hours (TLC controlled). For enough time at room temperature before moisture was extracted and eventually converted to dry powder. The resulting dry powdered yield was further transferred to water (25 mL) and diluted with HCl. Product was separated using filtration method and washed systematically with $H_2O$, dried, finally purification of unfinished product by crystallization from methanol and imines were obtained. Synthetic pathway imines of **3a-f** and **5a-f** are summarized in **Scheme 1** under solvent free condition.




**Scheme 1.** Synthetic pathway for the 1,2,4-triazole derivatives **3a-f** and **5a-f**.

### *4.3. Physical and spectral data*

*Synthesis of 4-((4H-1,2,4-triazol-4-ylimino)methyl)-N,N-dimethylbenzenamine **(3a)***

This compound was prepared using 4-amino-4H-1,2,4-triazole (**1**, 0.28 g, 0.003 mol) and 4-(dimethylamino)benzaldehyde (**2a**, 0.50 g, 0.003 mol). Mol. Formula: $C_{11}H_{13}N_5$, Mol. Wt.:215.2, Yield (%):66, UV-visible ($\lambda_{max}$): 420, Melting Point: 170 ˚C, Colour: Violet, Solubility: Methanol. FT-IR: ν 3097 (Ar-H), 1640 (HC=N), 1529 (C=C), 1433 (N-N), 1159 (C-N). $^1$H NMR (DMSO-$d_6$, ppm) δ: 8.25 (s, 2H, Tri-H), 8.10 (s, 1H, CH), 7.35-7.34 (d, 2H, Ar-H, *J* = 4.0 Hz), 6.50-6.49 (d, 2H, Ar-H, *J* = 4.0 Hz), 2.80 (s, 6H, 2$CH_3$). $^{13}$C NMR (DMSO-$d_6$, ppm): 158.0 (N=CH), 150.9 (Ar-C), 147 (Tri-C), 130.0, 123, 113.2 (Ar-C), 40.2 (N-$CH_3$). MS ($M^+$) m/z: 215.

*Synthesis of (4-chlorophenyl)-N-(4H-1,2,4-triazol-4-yl)methanimine (**3b**)*

This compound was prepared using 4-amino-4H-1,2,4-triazole (**1**, 0.30 g, 0.003 mol) and 4-chlorobenzaldehyde (**2b**, 0.50 g, 0.003 mol). Mol. Formula: $C_9H_7N_4Cl$, Mol. Wt.: 206.6, Yield (%):73, UV-visible ($\lambda_{max}$): 390, Melting Point: 210 ˚C, Colour: Off white, Solubility: Methanol. FT-IR: ν 3069 (Ar-H), 1655 (HC=N), 1508 (C=C), 1471 (N-N), 1180 (C-N), 631 (C-Cl). $^1$H NMR (DMSO-$d_6$, ppm) δ: 8.75 (s, 2H, Tri-H), 8.40 (s, 1H, CH), 7.60-7.59 (d, 2H, Ar-H, *J* = 4.0 Hz), 7.30 (d, 2H, Ar-H, *J* = 4.0 Hz).$^{13}$C NMR (DMSO-$d_6$, ppm): 157.5 (N=CH), 148.5 (Tri-C), 136.0, 131.5, 130.0, 128.5 (Ar-C). MS ($M^+$) m/z: 206.

*Synthesis of (3,4-dimethoxyphenyl)-N-(4H-1,2,4-triazol-4-yl)methanimine (**3c**)*

This compound was prepared using 4-amino-4H-1,2,4-triazole (**1**, 0.25 g, 0.003 mol) and 3,4-dimethoxybenzaldehyde (**2c**, 0.50 g, 0.003 mol). Mol. Formula: $C_{11}H_{12}N_4O_2$, Mol. Wt.: 232.2, Yield (%):50, UV-visible ($\lambda_{max}$): 320, Melting Point: 165 ˚C, Colour: Off white, Solubility: Methanol. FT-IR: ν 3032 (Ar-H), 1620 (HC=N), 1496 (N-N), 1483 (C=C), 1375 (C-O), 1143 (C-N). $^1$H NMR (DMSO-$d_6$, ppm) δ: 8.30 (s, 2H, Tri-H), 8.15 (s, 1H, CH), 7.10-7.09 (d, 2H, Ar-H, *J* = 4.0 Hz), 6.70-6.69 (d, 1H, Ar-H, *J* = 4.0 Hz), 3.80 (s, 6H, 2$OCH_3$). $^{13}$C NMR (DMSO-$d_6$, ppm): 157.0 (N=CH), 151.9 (Ar-C), 149.0 (Tri-C), 148.5, 127.0, 122.5, 115.0, 114.5 (Ar-C), 55.0 ($OCH_3$). MS ($M^+$) m/z: 232.

*Synthesis of (3-methoxyphenyl)-N-(4H-1,2,4-triazol-4-yl)methanimine (**3d**)*

This compound was prepared using 4-amino-4H-1,2,4-triazole (**1**, 0.30 g, 0.003 mol) and 3-methoxybenzaldehyde (**2d**, 0.50 g, 0.003 mol). Mol. Formula: $C_{10}H_{10}N_4O$, Mol. Wt.: 202.0, Yield (%):76, UV-visible ($\lambda_{max}$): 420, Melting Point: 122 ˚C, Colour: Violet, Solubility: Methanol. FT-IR: ν 3097 (Ar-H), 1600 (HC=N), 1550 (N-N), 1529 (C=C), 1378 (C-$OCH_3$), 1153 (C-N). $^1$H NMR (DMSO-$d_6$, ppm) δ: 8.30 (s, 2H, Tri-H), 8.10 (s, 1H, CH), 7.20-6.90 (m, 3H, Ar-H), 6.80 (s, 1H, Ar-H), 3.75 (s, 3H, $OCH_3$). $^{13}$C NMR (DMSO-$d_6$, ppm): 160.0 (Ar-C), 157.0 (N=CH), 148.0 (Tri-C), 138.0, 134.5, 129.5, 121.0, 116.5, 113.0 (Ar-C), 55.5 ($OCH_3$). MS ($M^+$) m/z: 202.

*Synthesis of (3,4,5-trimethoxyphenyl)-N-(4H-1,2,4-triazol-4-yl)methanimine (**3e**)*

This compound was prepared using 4-amino-4H-1,2,4-triazole (**1**, 0.25 g, 0.003 mol) and 3,4,5-methoxybenzaldehyde (**2e**, 0.50 g, 0.003 mol). Mol. Formula: $C_{12}H_{14}N_4O_3$, Mol. Wt.: 262.0, Yield (%):68, UV-visible ($\lambda_{max}$): 390, Melting Point: 143 ˚C, Colour: Off white, Solubility: Methanol. FT-IR: ν 3032 (Ar-H), 1640 (HC=N), 1550 (N-N), 1483 (C=C), 1378 (C-$OCH_3$), 1153 (C-N). $^1$H NMR (DMSO-$d_6$, ppm) δ: 8.35 (s, 2H, Tri-H), 8.15 (s, 1H, CH), 6.65 (s, 2H, Ar-H), 3.75 (s, 9H, 3$OCH_3$). $^{13}$C NMR (DMSO-$d_6$, ppm): 156.0 (N=CH), 150.5 (Ar-C), 148.0 (Tri-C), 141.0, 128.0, 106.0 (Ar-C), 56.5 ($OCH_3$). MS ($M^+$) m/z: 262.

*Synthesis of (2-nitrophenyl)-N-(4H-1,2,4-triazol-4-yl)methanimine (**3f**)*

This compound was prepared using 4-amino-4H-1,2,4-triazole (**1**, 0.28 g, 0.003 mol) and 2-nitro benzaldehyde (**2f**, 0.50 g, 0.003 mol). Mol. Formula: $C_9H_7N_5O_2$, Mol. Wt.: 217.5, Yield (%):61, UV-visible ($\lambda_{max}$): 320, Melting Point: 110 ˚C, Colour: Off white, Solubility: Methanol. FT-IR: ν 3097 (Ar-H), 1620 (HC=N), 1550 (N-N), 1529 (C=C), 1500 (C-$NO_2$), 1153 (C-N). $^1$H NMR (DMSO-$d_6$, ppm) δ:

8.30 (s, 2H, Tri-H), 8.10 (s, 1H, CH), 8.20-7.60 (m, 4H, Ar-H). $^{13}$C NMR (DMSO-$d_6$, ppm): 157.0 (N=CH), 148.0 (Tri-C), 147.0, 135.5, 132.0, 130.0, 121.5 (Ar-C). MS ($M^+$) m/z: 217.

*Synthesis of 1-(4-ethoxyphenyl)-N-(4H-1,2,4-triazol-4-yl)ethanimine (**5a**)*

This compound was prepared using 4-amino-4H-1,2,4-triazole (**1**, 0.26 g, 0.003 mol) and 1-(4-ethoxyphenyl)ethanone (**4a**, 0.50 g, 0.003 mol). Mol. Formula: $C_{12}H_{14}N_4O$, Mol. Wt.: 230.2, Yield (%):65, UV-visible ($\lambda_{max}$): 460, Melting Point: 174 ˚C, Colour: Light blue, Solubility: Methanol. FT-IR: ν 3090 (Ar-H), 1630 (HC=N), 1529 (C=C), 1430 (N-N), 1159 (C-N), 1050 (C-O). $^1$H NMR (DMSO-$d_6$, ppm) δ: 8.30 (s, 2H, Tri-H), 7.50-7.49 (d, 2H, Ar-H, *J* = 4.0 Hz), 6.80-6.79 (d, 2H, Ar-H, *J* = 4.0 Hz), 3.95 (q, 2H, $CH_2$), 1.30-1.28 (t, 3H, $CH_3$, *J* = 8.0 Hz), 0.95 (s, 3H, $CH_3$). $^{13}$C NMR (DMSO-$d_6$, ppm): 164.7 (C=N), 159.8 (Ar-C), 148.0 (Tri-C), 128.8, 125.6, 114.2 (Ar-C), 64.7 ($CH_2$), 19.5 ($CH_3$), 14.8 ($CH_3$). MS ($M^+$) m/z: 230.

*Synthesis of 1-(pyridin-2-yl)-N-(4H-1,2,4-triazol-4-yl)ethanimine (**5b**)*

This compound was prepared using 4-amino-4H-1,2,4-triazole (**1**, 0.34 g, 0.004 mol) and 1-(pyridin-2-yl)ethanone (**4b**, 0.50 g, 0.004 mol). Mol. Formula: $C_9H_9N_5$, Mol. Wt.: 187.3, Yield (%):65, UV-visible ($\lambda_{max}$): 480, Melting Point: 152 ˚C, Colour: Light blue, Solubility: Methanol. FT-IR: ν 3090 (Ar-H), 1620 (HC=N), 1529 (C=C), 1491 (Pyr C=N), 1430 (N-N), 1158 (C-N). $^1$H NMR (DMSO-$d_6$, ppm) δ: 8.80 (d, 1H, Pyr-H, *J* = 4.0 Hz), 8.35 (s, 2H, Tri-H), 8.00 (d, 1H, Pyr-H, *J* = 4.0 Hz), 7.90-7.62 (m, 2H, Pyr-H), 0.90 (s, 3H, $CH_3$). $^{13}$C NMR (DMSO-$d_6$, ppm): 164.0 (C=N), 154.0, 149.1 (Ar-C), 148.5 (Tri-C), 136.1, 126.2, 123.9 (Ar-C), 13.5 ($CH_3$). MS ($M^+$) m/z: 187.

*Synthesis of 3-(1-(4H-1,2,4-triazol-4-ylimino)ethyl)benzonitrile (**5c**)*

This compound was prepared using 4-amino-4H-1,2,4-triazole (**1**, 0.29 g, 0.003 mol) and 3-acetylbenzonitrile (**4c**, 0.50 g, 0.003 mol). Mol. Formula: $C_{11}H_9N_5$, Mol. Wt.: 211.2, Yield (%):55, UV-visible ($\lambda_{max}$): 500, Melting Point: 160 ˚C, Colour: Green, Solubility: Methanol. FT-IR: ν 3095 (Ar-H), 2360 (C≡N), 1625 (HC=N), 1529 (C=C), 1430 (N-N), 1150 (C-N). $^1$H NMR (DMSO-$d_6$, ppm) δ: 8.20 (s, 2H, Tri-H), 7.90 (s, 1H, Ar-H), 7.85-7.50 (m, 3H, Ar-H), 0.90 (s, 3H, $CH_3$). $^{13}$C NMR (DMSO-$d_6$, ppm): 163.0 (C=N), 147.5 (Tri-C), 134.5, 133.5, 131.5, 129.6, 112.7 (Ar-C), 115.8 (C≡N), 13.0 ($CH_3$). MS ($M^+$) m/z: 211.

*Synthesis of 1-(1H-indol-4-yl)-N-(4H-1,2,4-triazol-4-yl)ethanimine (**5d**)*

This compound was prepared using 4-amino-4H-1,2,4-triazole (**1**, 0.26 g, 0.003 mol) and 1-(1H-indol-3-yl)ethanone (**4d**, 0.50 g, 0.003 mol). Mol. Formula: $C_{12}H_{11}N_5$, Mol. Wt.: 225.3, Yield (%):67, UV-visible ($\lambda_{max}$): 490, Melting Point: 157 ˚C, Colour: Light blue, Solubility: Methanol. FT-IR: ν 3069 (Ar-H), 1655 (HC=N), 1509 (C=C), 1470 (N-N), 1181 (C-N). $^1$H NMR (DMSO-$d_6$, ppm) δ: 10.80 (s, 1H, NH), 8.29 (s, 2H, Tri-H), 7.50-7.49 (d, 1H, Ar-H, *J* = 4.0 Hz), 7.23-7.22 (d, 1H, Ar-H, *J* = 4.0 Hz), 6.95 (t, 1H, Ar-H), 6.40-6.38 (d, 1H, Indole-H, *J* = 8.0 Hz), 6.10-6.08 (d, 1H, Indole-H, , *J* = 8.0 Hz ), 0.95 (s, 3H, $CH_3$). $^{13}$C NMR (DMSO-$d_6$, ppm): 162.0 (C=N), 149.0 (Tri-C), 135.0, 126.6, 123.0, 120.0, 115.0, 113.4 (Ar-C), 101.5 (Indole-C), 14.0 ($CH_3$). MS ($M^+$) m/z: 225.

*Synthesis of 1-(pyridin-3-yl)-N-(4H-1,2,4-triazol-4-yl)ethanimine (**5e**)*

This compound was prepared using 4-amino-4H-1,2,4-triazole (**1**, 0.34 g, 0.004 mol) and 1-(pyridin-3-yl)ethanone (**4e**, 0.50 g, 0.004 mol). Mol. Formula: $C_9H_9N_5$, Mol. Wt.: 187.2, Yield (%):65, UV-visible ($\lambda_{max}$): 480, Melting Point: 152 ˚C, Colour: Light blue, Solubility: Methanol. FT-IR: ν 3090 (Ar-H), 1620 (HC=N), 1529 (C=C), 1491 (Pyr C=N), 1430 (N-N), 1158 (C-N). $^1$H NMR (DMSO-$d_6$, ppm) δ: 9.20 (s, 1H, Pyr-H), 8.80-8.79 (d, 1H, Pyr-H, *J* = 4.0 Hz), 8.35-8.34 (d, 1H, Pyr-H, *J* = 4.0 Hz), 8.25 (s, 2H, Tri-H), 7.65-7.63 (t, 1H, Pyr-H, *J* = 8.0 Hz), 0.95 (s, 3H, $CH_3$). $^{13}$C NMR (DMSO-$d_6$, ppm):

164.0 (C=N), 154.0, 149.1 (Ar-C), 148.0 (Tri-C), 136.5, 126.1, 123.8 (Ar-C), 13.5 ($CH_3$). MS ($M^+$) m/z: 187.

*Synthesis of 1-(naphthalen-2-yl)-N-(4H-1,2,4-triazol-4-yl)ethanimine (**5f**)*

This compound was prepared using 4-amino-4H-1,2,4-triazole (**1**, 0.25 g, 0.003 mol) and 1-(naphthalen-2-yl)ethanone (**4f**, 0.50 g, 0.003 mol). Mol. Formula: $C_{14}H_{12}N_4$, Mol. Wt.: 236.3, Yield (%):62, UV-visible ($\lambda_{max}$): 440, Melting Point: 140 ˚C, Colour: Light blue, Solubility: Methanol. FT-IR: ν 3080 (Ar-H), 1625 (HC=N), 1528 (C=C), 1430 (N-N), 1158 (C-N). $^1$H NMR (DMSO-$d_6$, ppm) δ: 8.35 (s, 1H, Ar-H), 8.25 (s, 2H, Tri-H), 7.95-7.94 (d, 1H, Ar-H, *J* = 4.0 Hz), 7.85-7.84 (d, 1H, Ar-H, *J* = 4.0 Hz), 7.60-7.30 (m, 4H, Ar-H), 0.90 (s, 3H, $CH_3$). $^{13}$C NMR (DMSO-$d_6$, ppm): 163.0 (C=N), 148.0 (Tri-C), 136.1, 133.5, 128.6, 128.2, 128.1, 126.9, 127.3, 126.2, 126.1 (Ar-C), 16.5 ($CH_3$). MS ($M^+$) m/z: 236.

*4.4. Anticonvulsant activity*

Male Wistar rats (190-220 g) and mice (19-20 g) procured from National Institute of Nutrition, Hyderabad (190-220 g) were used in the present study. The animals were kept in individual cages for 1 week to acclimatize for the laboratory conditions. They were allowed to free access of water and food. All the experimental procedures were carried out in accordance with Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines. The study was reviewed and approved by the Institutional Animal Ethics Committee, G Pulla Reddy College of Pharmacy, Hyderabad, India.

*Maximal electroshock seizure model (MES)*

MES seizure model was used in the present study to evaluate the anticonvulsant activity of the compounds on male Wistar rats.[19] Seizures were induced in rats by delivering electro shock of 150mA for 0.2 s by means of a convulsiometer through a pair of ear clip electrodes. The test compounds (100 mg/kg) were administered by oral route in the form of solution (the compounds were dissolved in 1% sodium carboxy methyl cellulose), 30 min before the MES seizure test. The animals were observed closely for 2 min (noted tonic flexion (F) and extension (E) phases in seconds). The percentage of inhibition of seizure relative to control was recorded and calculated. Phenytoin (100 mg/kg) was used as a standard drug.

*Neurotoxicity screening*

The minimal motor impairment was measured in mice by the rotorod test.[19] The mice were trained to stay on the accelerating rotorod that rotates at 10 revolutions per minute. The rod diameter was 3.2 cm. Trained animals were administered with the test compounds at a dose of 100 mg/kg by oral route. Neurotoxicity was indicated by the inability of the animal to maintain equilibrium on the rod for at least 1 min in each of the three trails. Phenytoin was used as a standard drug.

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