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# SYNTHESIS OF NOVEL 4-SUBSTITUTED-1, 2, 3-TRIAZOLE TAGGED 1-PHENYL-3-(TRIFLUOROMETHYL)-1*H*-PYRAZOLE-4-CARBALDEHYDE DERIVATIVES

**V. Rajashakar[1]*, G. Babu[1], K. Naveen Kumar[1] and M. Chinna Eswaraiah[2]**

[1]Pharmaceutical Chemistry.

[2]Pharmacognosy, Anurag Pharmacy College, Ananthagiri, Kodad.

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***Corresponding Author**
**V. Rajashakar**
Pharmaceutical Chemistry.

## ABSTRACT

Eleven derivatives of 1-phenyl-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-3-(trifluoromethyl)-1*H*-pyrazole-4-carbaldehydes were synthesized from the key intermediate 5-azido-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole-4-carbaldehyde (5). In the final step the reaction of 5 with substituted acetylenes was carried out by employing click chemistry approach. The structures of the synthesized compounds were confirmed by means of $^{1}$H NMR, IR, and Mass spectra. The synthesized compounds were screened for anti-inflammatory and antimicrobial activities. Among the compound tested 6b, 6c and 6j exhibited significant anti-inflammatory activity while the other compounds 6a and 6k showed moderate activity. None of the synthesized compounds showed any significant antimicrobial activity even at the concentration of 1000 µg/ml.

**KEYWORDS:** Trifluoromethylpyrazole, 1,2,3-triazole, 5-azido-1-phenyl-3-(trifluoromethyl) -1*H*-pyrazole-4-carbaldehyde, anti-inflammatory and antimicrobial activity.

## INTRODUCTION

Pyrazoles including their fluorinated derivatives have demonstrated a broad spectrum of biological activities and represented an important structural class in pharmaceuticals. Much work has been done on the design and the synthesis of complex pyrazoles. Incorporation of trifluoromethyl groups into pyrazole ring can lead to profound changes in its physical, chemical, and especially biological properties. Accordingly, an increasing number of trifluoromethyl-substituted derivatives of nitrogen containing heterocycles have been

prepared, which has led to the discovery of novel bioactive products. mono- and bis-(trifluoromethyl) containing pyrazole motifs, in particular, are present in numerous pharmacologically relevant compounds, including Selective COX-2 inhibitors celecoxib and mavacoxib, factor Xa inhibitor razaxaban, and fungicide penthiopyrad are representative examples of the successfully commercialized trifluoromethyl containing pyrazoles.[1,6]

Triazoles are the class of heterocyclic compounds which are under study since many a years. Its diversity in showing the pharmacological activities is mind blowingly identified by the medicinal chemists. Triazole, with many compounds as incorporating with other heterocyclic nucleus, hydrazides, substituted triazoles, β-agonist or incorporated with antibiotics has some of great uses which fascinates the chemists to continue research on it and find out more hidden potentials of this nucleus. The pharmacological properties shown by this moiety includes, Antidepressant (etoperidone) (9), antitumor (Mubritinib) (10), β-lactamase inhibitors (Tazobactam) (12), anticonvulsant (Rufinamide)(13).[3,4]

Literature survey reveals that the trifluoromethylpyrazole and 1,2,3-triazole derivatives have various biological activities and this prompted us to combine these two scaffolds into a single molecular frame work and evaluate this scaffolds for antimicrobial and anti-inflammatory activity.

## MATERIALS AND METHODS

All the required chemicals used were obtained from sigma Aldrich and Sd-fine chemicals. All the solvents used were of laboratory grade. Each reaction was monitored by TLC by using appropriate solvent system, which was selected by trial and error method. Precoated TLC plates (0.25mm silica gel) were obtained from E. Merck. All the synthesized compounds were purified by column chromatography. Melting points were determined on CINTEX programmable melting point apparatus and they were uncorrected. Infrared spectra were recorded on Perkin Elmer Model 283 B and Nicolet-740 FT-IR instrument and values are given in $cm^{-1}$. Proton magnetic resonance spectra were recorded on Varian unity 500 and Avance 300 MHz BrukerUx-NMR instrument. The samples were made in chloroform-dusing tetramethylsilane ($Me_4Si$) as the internal standard and were given in the scale. Mass spectra were recorded on VG Micromass 7070 H (EI-ESI), VG Autospec (FAB) using $CS^+$ ion gun, m-nitrobenzylalcohol (MNBA) as a matrix and were given in mass units (m/z). Analytical thin layer chromatography (TLC) was performed on precoated silica gel-60 $F_{254}$ (0.5 mm) glass plates. Visualization of the spots on TLC plates was achieved by exposure to U.V. light.

**Procedure for synthesis of 1-Phenyl-3-(trifluoromethyl)-1H pyrazol-5(4H)-one,** (**3**)

A mixture of ethyl 4,4,4-trifluoro-3-oxobutanoate (5 g, 0.1 mmol) and phenyl hydrazine (2.9 g, 0.1 mmol) in acetic acid, in a roundbottom flask was heated to reflux till the completion of the reaction (monitored by TLC). Then the neat reaction mass was allowed to come to room temperature, acetic acid was removed by rotary evaporator and the leftover residual solid mass was washed with water and hexane to obtain the pure solid (3).

**TLC Solvent System**

**EtOAc:** hexane (10:90).

**Procedure for synthesis of 5-chloro-1-phenyl-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde,** (**4**)

A mixture of compound (4) 2g (7.1 mmol), sodium azide 0.7g (10.7 mmol) and tetrabutyl ammonium bromide 0.38g (1.18 mmol) was dissolved in DMSO (22 mL) and stirred at room temperature for 12 hr. The progress of the reaction was monitored by TLC. After completion of the reaction, the compound was extracted into ethyl acetate, dried over $Na_2SO_4$ and concentrated in vacuo. The crude material was purified by column chromatography.

**TLC Solvent System**

**EtOAc:** hexane (10:90).

**Procedure for synthesis of 5-azido-1-phenyl-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde,** (**5**)

A mixture of compound (4) 2g (7.1 mmol), sodium azide 0.7g (10.7 mmol) and tetrabutyl ammonium bromide 0.38g (1.18 mmol) was dissolved in DMSO (22 mL) and stirred at room temperature for 12 hr. The progress of the reaction was monitored by TLC. After completion of the reaction, the compound was extracted into ethyl acetate, dried over $Na_2SO_4$ and concentrated in vacuo. The crude material was purified by column chromatography.

**TLC Solvent System**

**EtOAc:** hexane (10:90).

**Synthesis of various triazole derivatives by click chemistry approach**

The mixture of 0.2 g (0.7 mmol) of compound (5) and 0.04 g (0.4 mmol) of phenyl acetylene were dissolved in tertiary butanol : water (1:1) and to this was added copper sulphate 0.08 g (0.4 mmol) , sodium ascorbate (catalytic amounts). Then the reaction mixture was allowed to

stir for 3 to 4 hr at room temperature. The mixture was diluted with ethyl acetate (40 mL) and washed with water (20 mL). The organic phase was dried over sodium sulphate and concentrated under reduced pressure. The residue was purified by column chromatography to afford pure compound.

**TLC Solvent System**

**EtOAc:** hexane (10:90).

**Spectral analysis**

**6a.1-phenyl-5-(4-phenyl-1H-1,2,3-triazol-1-yl)-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde:** $C_{19}H_{12}F_3N_5O$, 63% yield, mp: 169-171$^0$C. $^1$H-NMR ($CDCl_3$, 300MHz): δ = 10.04 (s, 1H), 8.11 (s, 1H), 7.85 (d, J=8.3 Hz, 2H), 7.52-7.35 (m, 6H), 7.34-7.22 (m, 2H). IR (KBr cm$^{-1}$): 3142, 2925(C-H), 1695(-C=O), 1487, 1293, 1197, 959,807,761 cm$^{-1}$ . MASS (ESI-MS): *m/z* 381 $[M+H]^+$.

**6b.5-(4-(4-(tert-butyl)phenyl)-1H-1,2,3-triazol-1-yl)-1-phenyl-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde:** $C_{23}H_{20}F_3N_5O$, 67% yield, mp: 135-137 $^0$C. $^1$H-NMR ($CDCl_3$, 300MHz**):** δ = 10.01 (s, 1H), 8.06 (s, 1H), 7.77 (d, J=8.2 Hz, 2H), 7.53-7.35 (m, 5H), 7.27 (t, J=7.6 Hz, 2H), 1.35 (s, 9H). IR (KBr cm$^{-1}$): 3124, 2925 (C-H), 1697 (-C=O), 1486, 1293, 1171, 959 , 807, 767 cm$^{-1}$. MASS (ESI-MS): *m/z* 440 $[M+H]^+$.

**6c.1-phenyl-5-(4-p-tolyl-1H-1,2,3-triazol-1-yl)-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde:** $C_{20}H_{14}F_3N_5O$, 65% yield, mp: 135-137 $^0$C. $^1$H-NMR ($CDCl_3$, 300MHz**):** δ = 10.02 (s, 1H), 8.05 (s, 1H), 7.73 (d, J=7.5 Hz, 2H), 7.51-7.35 (m, 3H), 7.34-7.16 (m, 4H), 2.42 (s, 3H). IR (KBr cm$^{-1}$): 3136, 2925(C-H), 1697(-C=O), 1488, 1293, 1193, 960, 808,762 cm$^{-1}$ .MASS (ESI-MS): *m/z* 398 $[M+H]^+$ .

**6d.5-(4-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)-1-phenyl-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde:** $C_{20}H_{14}F_3N_5O_2$, 68% yield, mp: 139-142 $^0$C. $^1$H-NMR ($CDCl_3$, 300MHz**):** δ = 10.03 (s, 1H), 8.00 (s, 1H), 7.77 (d, J=8.3 Hz, 2H), 7.58-7.26 (m, 6H), 6.98 (d, J=9.0 Hz, 2H), 3.85 (s, 3H). IR (KBr cm$^{-1}$): 2923, 2953(C-H), 1695(-C=O), 1460, 1249, 1141, 1019, 768, cm$^{-1}$ ·MASS (ESI-MS): *m/z* 414 $[M+H]^+$.

**6e.5-(4-cyclopropyl-1H-1,2,3-triazol-1-yl)-1-phenyl-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde:** $C_{20}H_{14}F_3N_5O_2$, 69% yield, mp: 131-133$^0$C. $^1$H-NMR ($CDCl_3$, 300MHz**):** δ = 9.96 (s, 1H), 7.54 (s, 1H), 7.50-7.37 (m, 3H), 7.31-7.18 (m, 2H), 2.04-1.97 (m, 2H), 1.08-

0.96 (m, 2H), 0.96-0.85 (m, 2H). IR (KBr $cm^{-1}$): 3102, 2923 (C-H), 1698 (-C=O), 1468, 1302, 1182, 963, 806, 767 $cm^{-1}$. MASS (ESI-MS): *m/z* 348 [M+H].

**6f.ethyl1-(4-formyl-1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)-1H-1,2,3-triazole-4-carbaldehyde:** $C_{16}H_{12}F_3N_5O_3$, 68% yield, mp: 162-165$^0$C. $^1$H-NMR ($CDCl_3$, 300MHz**):** δ =10.05 (s, 1H), 8.49 (s, 1H), 7.64-7.30 (m, 5H), 4.45 (q, J=7.17 Hz, 2H), 1.42 (t, J=7.17 Hz, 3H). IR (KBr $cm^{-1}$): 3138, 2927(C-H), 1699(-C=O), 1508, 1281, 1186, 966, 857, 764, $cm^{-1}$ MASS (ESI-MS): *m/z* 380 $[M+H]^+$.

**6g.5-(4-(4-methoxy-2-methylphenyl)-1H-1,2,3-triazol-1-yl)-1-phenyl-3-(trifluoromethyl) -1H-pyrazole-4-carbaldehyde:** $C_{21}H_{16}F_3N_5O_2$, 68% yield, mp: 162-165$^0$C. $^1$H-NMR ($CDCl_3$, 300MHz**):** δ = 10.05 (s, 1H), 7.88 (s, 1H), 7.73 (d, J=8.30 Hz, 1H), 7.56-7.37 (m, 3H), 7.35-7.21 (m, 2H), 6.91-6.76 (m, 2H), 3.84 (s, 3H), 2.36 (s, 3H). IR (KBr $cm^{-1}$): 3083, 2927 (C-H), 1702 (C=O) , 1507, 1292, 1199, 961, 807, 767 $cm^{-1}$. MASS (ESI-MS): *m/z* 428 $[M+H]^+$.

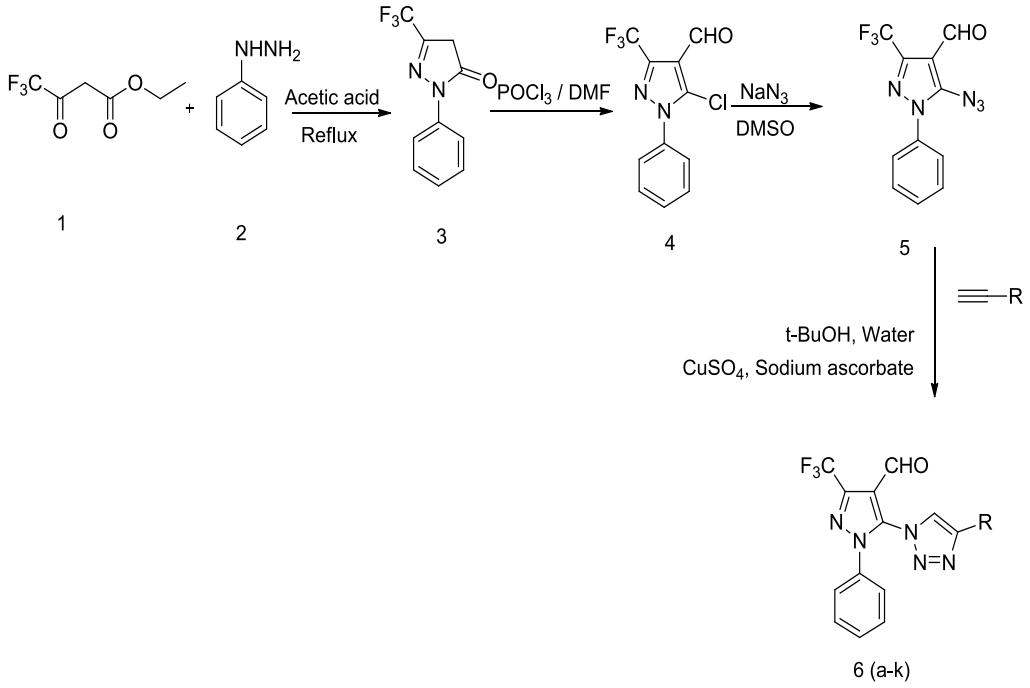
**6h.5-(4-octyl-1H-1,2,3-triazol-1-yl)-1-phenyl-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde:** $C_{21}H_{24}F_3N_5O$, 68% yield, mp: 83-85 $^0$C . $^1$H-NMR ($CDCl_3$, 300MHz**):** δ = 9.96 (s, 1H), 7.56 (s, 1H), 7.51-7.34 (m, 3H), 7.31-7.18 (m, 2H), 2.76 (t, J=7.5 Hz, 2H), 1.79-1.57 (m, 2H), 1.40-1.16 (m, 10H), 0.97-0.80 (m, 3H). IR (KBr $cm^{-1}$): 3150, 2924 (C-H), 1697 (-C=O),1412, 1294, 1183, 961 809, 766 $cm^{-1}$.MASS (ESI-MS): *m/z* 420 $[M+H]^+$.

**6i.5-(4-hexyl-1H-1,2,3-triazol-1-yl)-1-phenyl-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde:** $C_{19}H_{20}F_3N_5O$, 70% yield, mp: 82-85 $^0$C . $^1$H-NMR ($CDCl_3$, 300MHz**):** δ = 9.95 (s, 1H), 7.56 (s, 1H), 7.47-7.35 (m, 3H), 7.30-7.18 (m, 2H), 2.76 (t, J=7.3 Hz, 2H), 1.76-1.58 (m, 7.18 (m, 2H), 2.76 (t, J=7.3 Hz, 2H), 1.76-1.58 (m, 2H), 1.37-1.21 (m, 6H), 0.94-0.82 (m, 3H). IR (KBr $cm^{-1}$): 3144, 2926 (C-H), 1702 (-C=O), 1503, 1285, 1187, 959, 811, 767 $cm^{-1}$. MASS (ESI-MS): *m/z* 392 $[M+H]^+$.

**6j.5-(4-(4-pentylphenyl)-1H-1,2,3-triazol-1-yl)-1-phenyl-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde:** $C_{24}H_{22}F_3N_5O$, 67% yield, mp: 152-154$^0$C . $^1$H-NMR ($CDCl_3$, 300MHz**):** δ = 10.02 (s, 1H), 8.04 (s, 1H), 7.75 (d, J=8.12 Hz, J=7.5 Hz, 2H), 1.71-1.55 (m, 2H), 1.44-1.22 (m, 4H), 2H), 7.49-7.34 (m, 3H), 7.33-7.18 (m, 4H), 2,64 (t, 0.96-0.81 (m, 3H). IR (KBr $cm^{-1}$): 3145, 2926 (C-H), 1689 (-C=O), 1487, 1293, 1178, 961 , 807, 765 $cm^{-1}$.MASS (ESI-MS): *m/z* 454 $[M+H]^+$ .

**6k.1-phenyl-5-(4-((phenylamino)methyl)-1H-1,2,3-triazol-1-yl)-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde:** $C_{20}H_{15}F_3N_6O$, 67% yield, mp: 142-146$^0$C . $^1$H-NMR ($CDCl_3$, 300MHz**):** δ = 9.93 (s, 1H), 7.71 (s, 1H), 7.48-7.23 (m, 3H) 7.2-7.04 (m, 2H), 6.73 (t, J=7.1 Hz, 1H), 6.65 (d, J=7.7 Hz, 2H) 4.49 (s, 2H). IR (KBr cm$^{-1}$): 3105, 2869 (C-H), 1694 (-C=O), 1487, 1259, 1189, 964, 861, 770 cm$^-$. MASS (ESI-MS): *m/z* 413 $[M+H]^+$.

**Scheme 1**




R=Phenyl acetylene, 4-ome,2me Phenylacetylene, t-butyl Phenyl acetylene, Cyclopropylacetylene, Ethyl propiolate, 4-ome phenylacetylene, 4-me phenylacetyline, 1-Octylene, 1Decylene, 4-Pentylphenyl acetylene, Anilineacetylene

**Synthesis of a series of novel 4-substituted-1,2,3-triazole tagged 1-phenyl-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde derivatives (6a-k).**

**Anti-inflammatory activity**

**Procedure**

In the present investigation, the anti-inflammatory activities of eleven derivatives were tested by (chemical) carrageenan induced rat paw edema method using Diclofenac as standard. Young adult male wistar rats weighing 150-180 gm were used, which were acclimatized to the laboratory conditions and maintained on standard laboratory rat feed and clean water. Rats were fasted for 12 hrs prior to experiment, while allowing free access to water throughout the experiment.

The rats were divided into the groups of 3 animals each, one group served as the control and received only the vehicle i.e. the CMC. In the other groups, the test (100mg/kg) and standard drug (10 mg/kg) were administered orally in a dose of (0.5 ml of 20 mg/ml test and 2mg/ml standard drug solutions per 200 g body weight). A mark was made on both the hind paws just beyond the tibiotarsal junction, so that every time the paw was dipped in the mercury column up to the marked level to ensure constant paw volume. After 1 hr of administration of the test and standard samples, 0.1 ml of freshly prepared 1% carrageenan suspension was injected into dorsal region of sub-plantar surface of hind paw of rat subcutaneously with the help of 26G needle.

The paw volume was measured using the plethysmometer at 0, 60,120.180, 240 min after the carrageenan challenge. The average value of edema was calculated by taking the average of each group at different hours. Percentage reduction of edema was calculated for each group with respect to the control group.

Inflammation was expressed as the change in paw volume

Edema = $T_t - T_0$

Where $T_0$ = Volume at '0' hr

$T_t$ = Volume at't' hr

Percentage reduction = $(V_0 - V_t)/V_0 \times 100$

Where, $V_0$ = Volume of the paw of control at time't'

$V_t$ = Volume of the paw of drug treated at time't'

From the data obtained, the mean edema volume and percentage reduction in edema was calculated.

**Anti-microbial activity**

**Determination of Minimum Inhibitory Concentration**[32]

The minimum inhibitory concentrations (MIC) of various synthetic compounds were tested against three representative Gram-positive organisms viz. *Bacillus subtilis* (MTCC 441), *Staphylococcus aureus* (MTCC 96), *Micrococcus luteus* MTCC 2470, and Gram-negative organisms viz *Escherichia coli* (MTCC 443), *Pseudomonas aeruginosa* (MTCC 741), by Microdilution method recommended by CLSI Standard Protocol (1) in liquid medium (Nutrient agar) distributed in 96-well plates, serial dilutions of the tested compounds were performed (concentrations from 1000 µg/mL, 500 µg/mL, 250 µg/mL, 150 µg/mL to 0.97 µg/mL) in a 200 µL culture medium final volume, afterwards each well was seeded with a 50

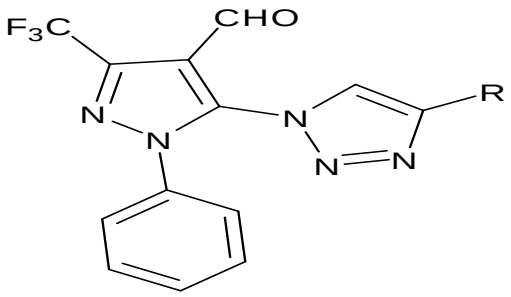
μL microbial suspension of 0.5 MacFarland density. In each test a microbial culture control and a sterility control (negative) were performed. The plates were incubated for 24 hours at $37^{O}$C. The lowest concentration which inhibited the visible microbial growth was considered the MIC (μg/mL) value for the tested compound. Ciprofloxacin were used as standard drugs.

## RESULTS AND DISCUSSION

Eleven derivatives of 1-phenyl-5-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-3-(trifluoromethyl)-1*H*-pyrazole-4-carbaldehydes were synthesized from the key intermediate 5-azido-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazole-4-carbaldehyde (**5**). In the final step the reaction of **5** with substituted acetylenes was carried out by employing click chemistry approach. The structures of the synthesized compounds were confirmed on the basis of physical and spectral data.

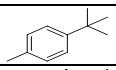
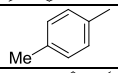
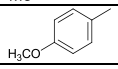
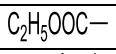
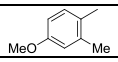
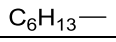
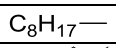
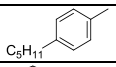
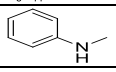
### Anti-inflammatory activity

All the synthesized compounds were screened for anti-inflammatory activity by using Carrageenan–induced paw edema method. The percentage inhibition of paw volume was taken as a parameter for anti-inflammatory activity. The percentage reduction in edema of test compounds is compared with that of the standard drug Diclofenac.




**(6a-k)**

**Table 1: Anti –Inflammatory data of 1-phenyl-5-(4-phenyl-1H-1,2,3-triazol-1-yl)-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde**

| Treatment | R | Dose mg/kg | Mean edema volume(ml) | | | |
|---|---|---|---|---|---|---|
| | | | 1hr | 2hr | 3hr | 4hr |
| **Control** | | | **0.26±0.03** | **0.31±0.045** | **0.48±0.021** | **0.33±0.056** |
| Diclofenac (standard) | | 10 | 0.20±0.01 | 0.20±0.011 | 0.15±0.01 | 0.18±0.018 |
| 6a |  | 100 | 0.22±0.01 | 0.25±0.011 | 0.26±0.01 | 0.22±0.017 |
| 6b |  | 100 | 0.21±0.17 | 0.22±0.019 | 0.17±0.018 | 0.20±0.019 |
| 6c |  | 100 | 0.22±0.15 | 0.23±0.018 | 0.22±0.016 | 0.23±0.017 |
| 6d |  | 100 | 0.24±0.11 | 0.27±0.015 | 0.38±0.019 | 0.29±0.010 |
| 6e |  | 100 | 0.23±0.16 | 0.26±0.018 | 0.30±0.016 | 0.26±0.017 |
| 6f |  | 100 | 0.23±0.15 | 0.27±0.018 | 0.39±0.019 | 0.28±0.010 |
| 6g |  | 100 | 0.23 ±0.14 | 0.27±0.17 | 0.34±0.16 | 0.28±0.19 |
| 6h |  | 100 | 0.24±0.16 | 0.28±0.19 | 0.36±0.14 | 0.29±0.13 |
| 6i |  | 100 | 0.24±0.19 | 0.28±0.14 | 0.36±0.17 | 0.29±0.15 |
| 6j |  | 100 | 0.22±0.15 | 0.23±0.13 | 0.19±0.12 | 0.22±0.16 |
| 6k |  | 100 | 0.23±0.13 | 0.26±0.16 | 0.28±0.13 | 0.26±0.15 |

**Edema volume = (mean ± SEM)**

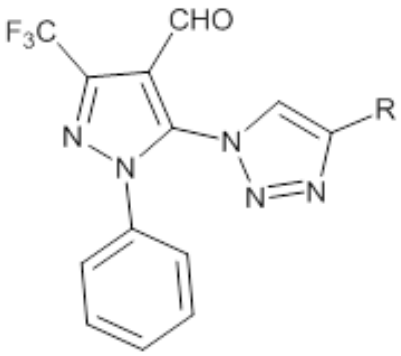
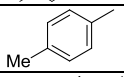
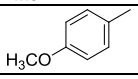
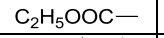
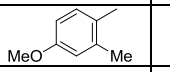
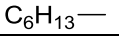
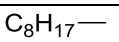
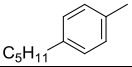
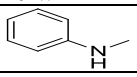


**Table 2: Percentage protection against edema formation (6a-k)**

| Treatment | R | Dose mg/kg | % protection 1hr | 2hr | 3hr | 4hr |
|---|---|---|---|---|---|---|
| Diclofenac (standard) | | 10 | 24 | 36 | 68 | 45 |
| 6a |  | 100 | 14 | 20 | 46 | 30 |
| 6b |  | 100 | 19 | 29 | 65 | 39 |
| 6c |  | 100 | 16 | 25 | 54 | 30 |
| 6d |  | 100 | 8 | 14 | 22 | 12 |
| 6e |  | 100 | 11 | 16 | 30 | 20 |
| 6f |  | 100 | 9 | 13 | 22 | 14 |
| 6g |  | 100 | 10 | 12 | 30 | 15 |
| 6h |  | 100 | 8 | 10 | 26 | 11 |
| 6i |  | 100 | 8 | 8 | 26 | 10 |
| 6j |  | 100 | 14 | 25 | 60 | 33 |
| 6k |  | 100 | 12 | 16 | 41 | 20 |

All synthesized compounds were screened for anti-inflammatory activity by carrageenan induced paw edema method, among the compound screened 6b, 6c and 6j exhibited significant anti-inflammatory activity while the other compounds 6a and 6k showed moderate activity. From the data obtained, the mean edema volume and percentage reduction in edema was calculated and the results are comparable to the standard drug Diclofenac.

**Anti-bacterial activity**

All the synthesized compounds were screened for antibacterial activity at a concentration of 1000µg/ml, 500µg/ml, 250µg/ml, 150µg/ml by cup plate method using 24-hr old cultures of gram-positive bacteria (*Staphylococcus aureus and Bacillus subtilis)* and two gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa).* Ciprofloxacin was used as a standard drug. DMSO was used as a control. Zone of inhibition was measured in mm.

None of the synthesized compounds were found to possess inhibitory activity towards cultures of *Staphylococcus aureus, Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa* compared to that of standard ciprofloxacin.

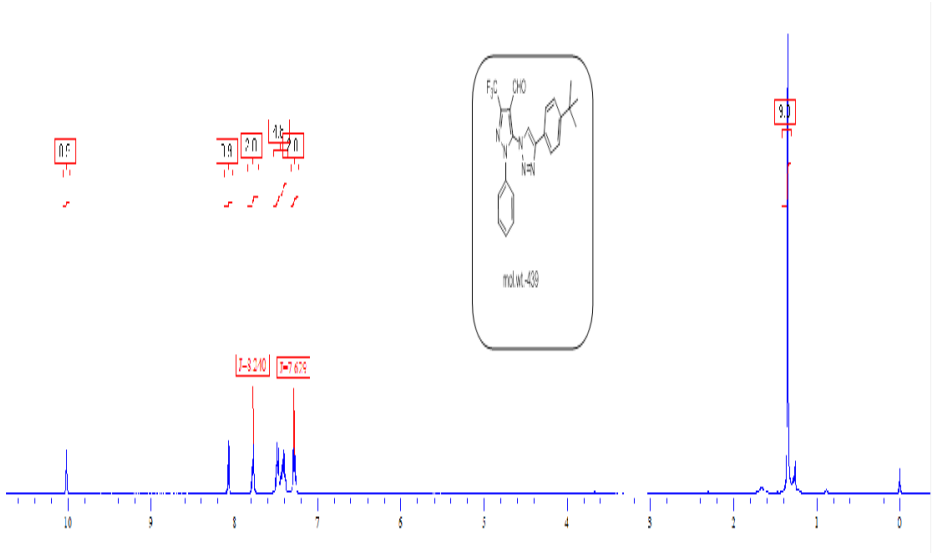



**Figure 1; $^{1}$HNMR spectrum of 5-(4-(4-tert-butylphenyl)-1H-1,2,3-triazol-1-yl)-1-phenyl-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde**

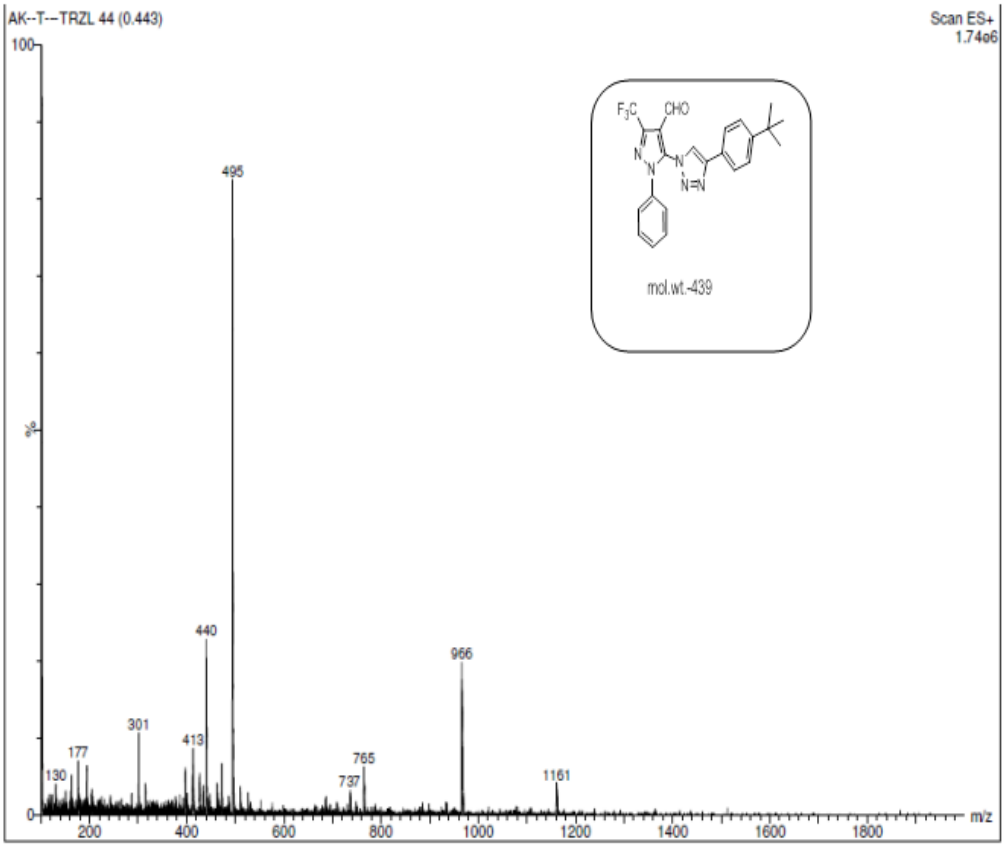



**Figure 2: Mass spectrum of 5-(4-(4-tert-butylphenyl)-1H-1,2,3-triazol-1-yl)-1-phenyl-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde.**

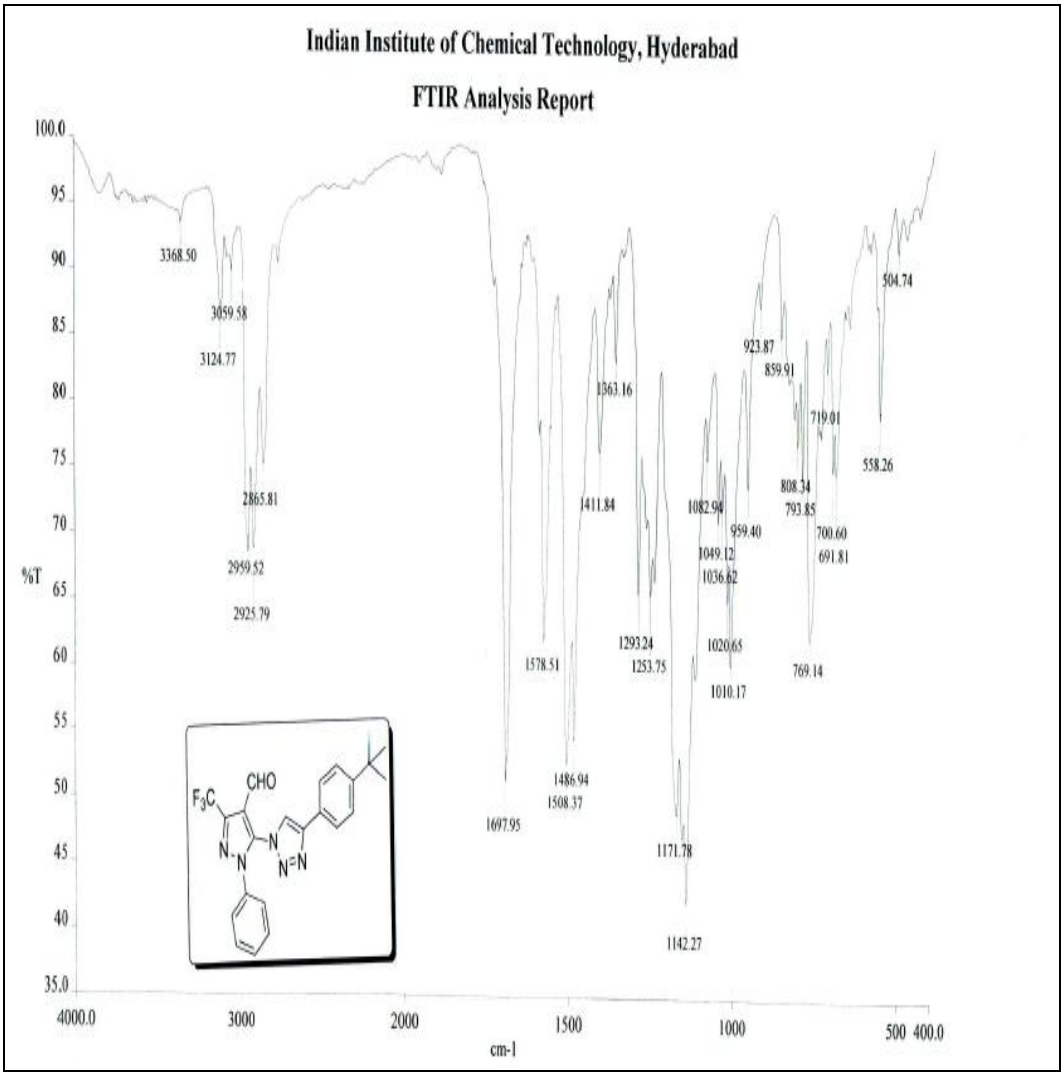



**Figure 3: IR spectrum of 5-(4-(4-tert-butylphenyl)-1H-1,2,3-triazol-1-yl)-1-phenyl-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde.**

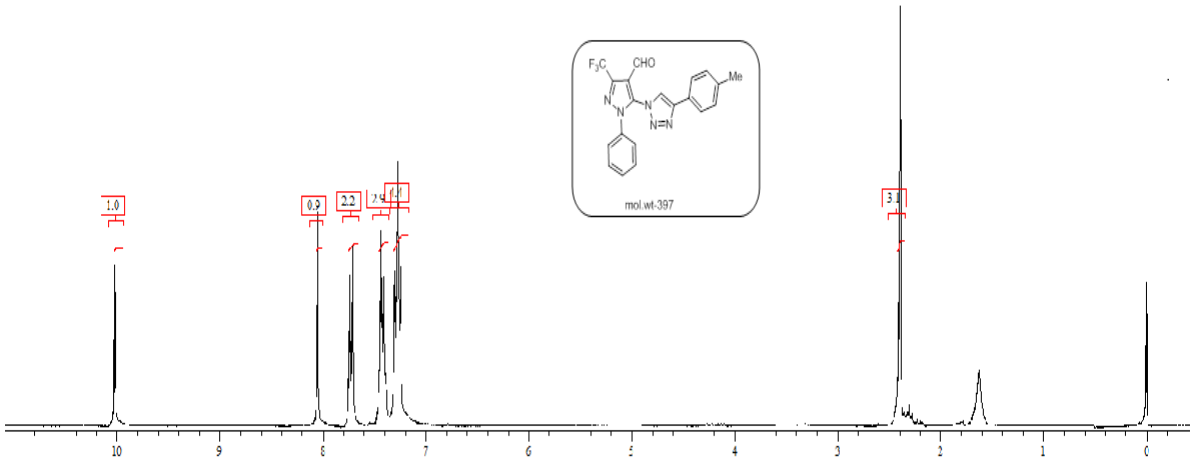



**Figure 4: $^{1}$HNMR spectrum of 1-phenyl-5-(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)-3-(trifluoromethyl)-1H- pyrazole-4-carbaldehyde.**

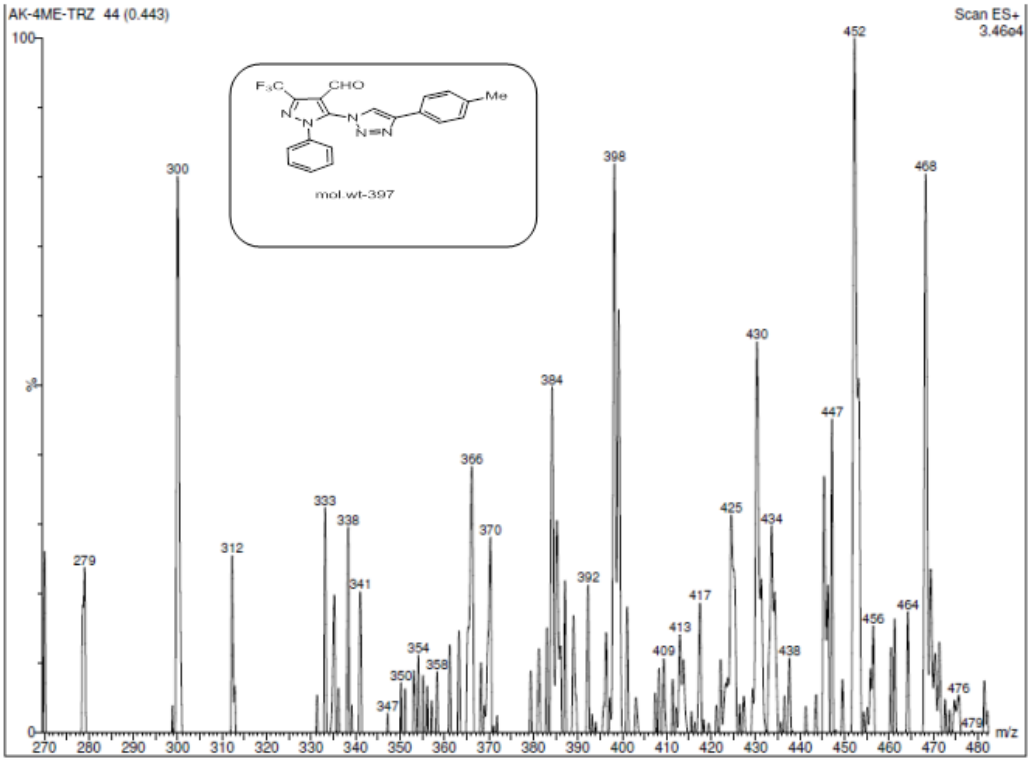



**Figure 5: Mass spectrum of 1-phenyl-5-(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde.**

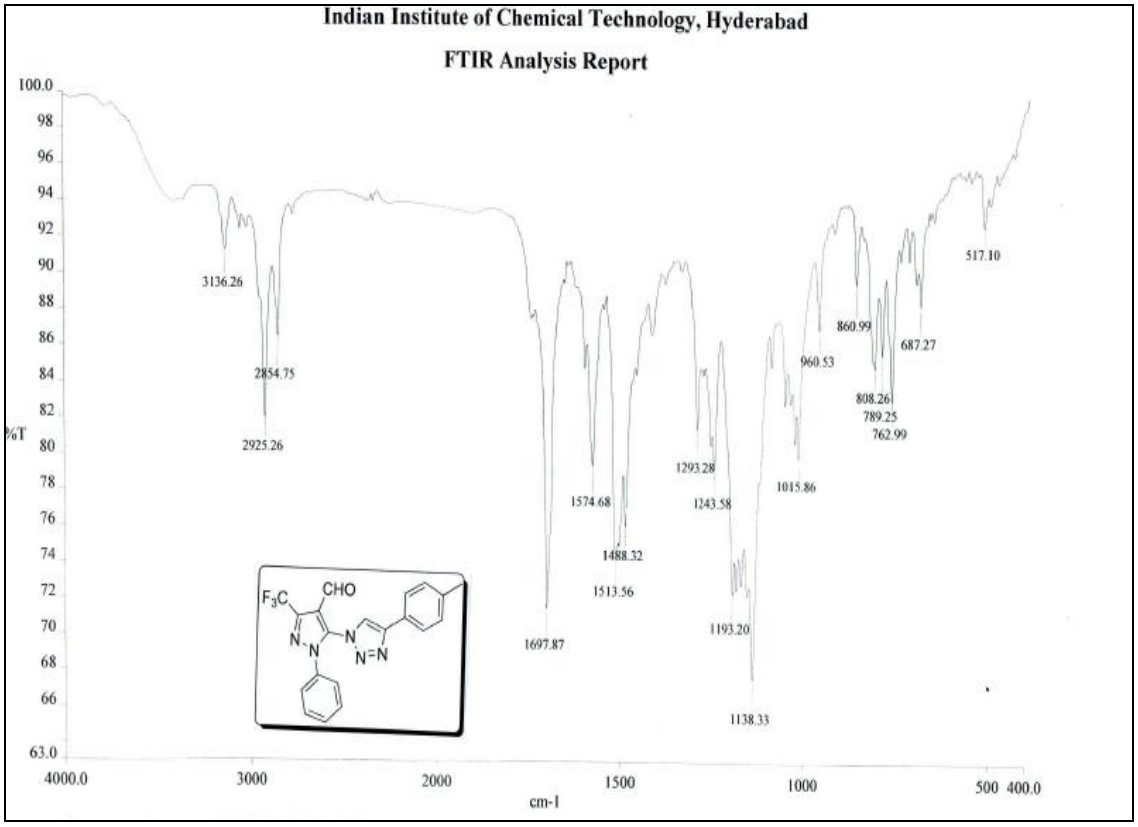



**Figure 6: IR spectrum of 1-phenyl-5-(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)-3-(trifluoromethyl)-1H-pyrazole-4-carbaldehyde.**

## CONCLUSION

The present study was aimed at synthesis of trifuoromethyl substituted heterocycles and evaluation of their biological activity. Eleven derivatives of 1-phenyl-5-(4-phenyl-1*H*-1, 2, 3-triazol-1-yl)-3-(trifluoromethyl)-1*H*-pyrazole-4-carbaldehyde (6a-k) were synthesized and screened for anti- inflammatory and anti- microbial activities. All the synthesized compounds were characterized by spectral data. In anti-inflammatory and anti-microbial studies, none of the compounds showed any significant anti-microbial activity even at concentration of 1000µg/ml using ciprofloxacin as standard.

However the compounds 6b, 6c and 6j exhibited good anti-inflammatory activity while the other 6a and 6k showed moderate activity against the edema formation at a concentration of 100 mg/kg and the results are comparable with the standard drug, Diclofenac (10 mg/kg).

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