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Laboratory Note

# Synthesis, characterization and antimicrobial activity of some substituted 1,2,3-triazoles

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**Abstract**

Two substituted 1,2,3-triazoles **4** and **6** have been synthesized by the 1,3-dipolar cycloaddition reaction of 4-azido-8-(trifluoromethyl)quinoline **2** with ethyl acetoacetate and acetylacetone, respectively. The reaction of **2** with ethyl acetoacetate afforded 1-[8-(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-1,2,3-triazole-4-carboxylic acid **3** and with acetylacetone afforded 1-{1-[8-(trifluoromethyl)-quinolin-4-yl]-5-methyl-1H-1,2,3-triazol-4-yl}ethanone **5**. Compound **3** is converted into its corresponding acid hydrazide and then condensed with different aromatic aldehydes to yield Schiff's base, *N*-[1-arylmethylene]-1-[8-(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-1,2,3-triazole-4-carbohydrazides **4**. Compound **5** is condensed with aromatic aldehydes to obtain [1-aryl-4-{1-[8-(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-1,2,3-triazol-4-yl}prop-2-en-1-ones **6**. The newly prepared 1,2,3-triazole derivatives **4** and **6** have been characterized by IR, NMR and mass spectral data. These compounds were screened for their antimicrobial activity.


*Keywords:* 1,3-Dipolar cycloaddition; 4-azido-8-(trifluoromethyl)quinoline; Antibacterial activity; Antifungal activity

## 1. Introduction

1,2,3-Triazole and its derivatives enhanced considerable attention for the past few decades due to their chemotherapeutical value [1]. Many 1,2,3-triazoles are found to be potent antimicrobial [2,3], analgesic [4], anti-inflammatory, local anesthetic [5], anticonvulsant [6], antineoplastic [7], antimalarial [8], antiviral agents [9], some of them exhibited antiproliferative [10] and anticancer activity [11].

Some 1,2,3-triazoles are used as DNA cleaving agents [10] and potassium channel activators [12]. Introduction of fluorine atom in these compounds could alter the course and as well as pharmacological activity [4,8]. In particular, introduction of $CF_3$ group in the moiety immensely increases the pharmacological as well as liphophilicity. Prompted by the chemotherapeutic importance of 1,2,3-triazoles and a view to synthesize compounds containing $CF_3$ substituent in quinoline moiety and synthesis of novel series of 1,2,3-triazolyl quinolines was undertaken. Biological activity results of such novel heterocyclic compounds are also discussed.

## 2. Chemistry

4-Chloro-8-trifluoromethylquinoline **1** was prepared in good yield according to literature procedure [4]. The reaction of **1** with sodium azide in *N*,*N*-dimethylformamide yielded 4-azido-8-trifluoromethylquinoline **2**. The 1,3-dipolar cycloaddition of compound **2** with ethyl acetoacetate in presence of sodium methoxide in methanol at 0 °C yielded 1-[8-(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-1,2,3-triazole-4-carboxylic acid **3**. The triazole carboxylic acid **3** was treated with thionyl chloride in dry ethylene dichloride to yield the corresponding acid chloride. Further treating the acid chloride with hydrazine hydrate at 0 °C afforded the corresponding 1-[8-(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-1,2,3-

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triazole-4-carbohydrazide in good yield. The acid hydrazide thus obtained was treated with different aromatic aldehydes to yield the corresponding Schiff bases, *N*-[1-arylmethylene]-1-[8-(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-1,2,3-triazole-4-carbohydrazide **4**. 4-Azido-8-trifluoromethyl quinoline **2** when treated with acetylacetone in presence of sodium methoxide in methanol at 0 °C yielded corresponding 1-{1-[8-(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-1,2,3-triazol-4-yl}ethanone **5** in good yield. 1-Aryl-4-{1-[8-(trifluoromethyl)quinolin-4-yl]-5-methyl-1H-1,2,3-triazol-4-yl}prop-2-en-1-one **6** was obtained in rather good yield by condensing **5** with various aromatic aldehydes.

## 3. Biological activity

### *3.1. Antibacterial studies*

The newly synthesized compounds were screened for their antibacterial activity against *Escherichia coli* (ATTC-25922), *Staphylococcus aureus* (ATTC-25923), *Psuedomonus aeruginosa* (ATTC-27853), *Bacillus subtilis* and *Klebsiella pneumoniae* (recultured) bacterial stains by disc diffusion method [13,14]. The discs measuring 6.25 mm in diameter were punched from Whatman no. 1 filter paper. Batches of 100 discs were dispensed to each screw capped bottles and sterilized by dry heat at 140 °C for an hour. The test compounds were prepared with different concentrations using dimethylformamide. 1 ml containing 100 times the amount of chemical in each disc was added to each bottle, which contains 100 discs. The discs of each concentration were placed in triplicate in nutrient agar medium seeded with fresh bacteria separately. The incubation was carried out at 37 °C for 24 h. Ciprofloxacin was used as a standard drug. Ciprofloxacin has 16–22 mm inhibition length for *E. coli* and 27–35 mm inhibition length for *S. aureus* at the concentration of 10 μg $ml^{-1}$. Solvent and growth controls were kept and zones of inhibition and minimum inhibitory concentrations (MIC) were noted. The results of such studies are given in the Table 2.

### *3.2. Antifungal studies*

Newly prepared compounds were screened for their antifungal activity against *Aspergilus flavus* (NICM No.524), *Aspergilus fumigatus* (NCIM No.902), *Candida albicans* (NCIM No.300), *Penicillium marneffei* (Recultured) and *Trichophyton mentagrophytes* (Recultured) in DMSO by serial plate dilution method [15,16]. Sabourands agar media was prepared by dissolving peptone (1 g), D-glucose (4 g) and agar (2 g) in distilled water (100 ml) and adjusting pH to 5.7. Normal saline was used to make a suspension of spore of fungal strain for lawning. A loopful of particular fungal strain was transferred to 3 ml saline to get a suspension of corresponding species. Twenty milliliters of agar media was poured in to each petricdishes. Excess of suspension was decanted and the plates were dried by placing in a incubator at 37 °C for 1 h. Using an agar punch wells were made in to each well labeled. A control was also prepared in triplicate and maintained at 37 °C for 3–4 days. Antifungal activity was determined by measuring the diameter of the inhibition zone. Activity of each compound was compared with Ciclopiroxolamine as standard.

## 4. Results and discussion

The investigation of antibacterial and antifungal screening data revealed that all the tested compounds **4a–4h** and **6a–6h** showed moderate to good inhibition at 10 μg $ml^{-1}$ in N,N-dimethylformamide . The compounds **4c, 4d, 4g, 4h, 6c** and **6e** are active against *B. subtilis, E .Coli* and among these compounds **4g** and **6e** exhibited less activity than the standard against *K. pneumoniae* bacterial strain. The most active compounds are **4c** and **4h**, which exhibited the maximum antibacterial activity against all bacterial strains almost equivalent to that of the standard.

The compounds **4e, 4h** and **6a** are active against *A. flavus* and the activity is which shows comparable with that of the standard. Compounds **4d, 4h, 6c** and **6h** showed good activity against *T. mentagrophytes*. The most active compounds are **4h** and **6h,** which exhibited the maximum anti fungal activity almost equivalent to that of standard.

## 5. Conclusions

This study reports the successful synthesis of the title compounds via 1,3-dipolar addition in good yields and antimicrobial activity of these derivatives containing quinoline moiety against wide range of bacterial and fungal stains. The antimicrobial activity study revealed that all the compounds screened showed good antibacterial and moderate antifungal activity. Among the newly synthesized compounds, compounds with 3-methyl thienyl substituents are found to increase antimicrobial activity.

## 6. Experimental protocols

### *6.1. Chemistry*

Melting points were determined by open capillary method and are uncorrected. The IR spectra (in KBr pellets) were recorded on a Shimadzu FT-IR 157 spectrophotometer. $^1$H-NMR spectra were recorded either on a Perkin–Elmer EM-390 (90 MHz) or on a Bruker WH-200 (270 MHz) spectrometer using TMS as an internal standard. The mass spectra were recorded on a Jeol JMS-D 300 mass spectrometer operating at 70 eV. The purity of the compounds was checked by thin layer chromatography (TLC) on silica gel plate using hexane and ethyl acetate (4:1, v/v).

*6.1.1. 1-[-(8-Trifluoromethyl)quinolin-4-yl]-5-methyl-1H-1,2,3-triazole-4-carboxylic acid (**3**)*

4-Azido-8-trifluoromethyl quinoline (15 g) was treated with ethyl acetoacetate (8.3 g) in methanol (75 ml) and the mixture was cooled to 0 °C. Sodium methoxide (3.5 g) was added under inert atmosphere to the above mixture and stirred at ambient temperature for 8 h. Progress of the reaction was monitored by TLC (ethyl acetate/n-hexane, 2:3, v/v). After completion of the reaction, the mixture was poured on to ice-cold water and neutralized with acetic acid. The precipitated solid was filtered, washed with water and recrystallized from methanol. (12.5 g, 61% yield), m.p. 190–191 °C, IR (KBr) $\nu$/cm$^{-1}$: 3300(OH), 3320, 3060 (Ar–H), 1720 (C=O), 980(C–F). $^1$H-NMR(DMSO-d$_6$) $\delta$: 2.48(s, 3H, CH$_3$), 7.58–7.61 (d, 2H, $J$ = 8.5 Hz, trifluoromethyl quinoline), 7.69–7.75 (t, 1H, $J$ = 8.1 Hz, trifluoromethyl quinoline), 8.22–8.24 (d, 1H, $J$ = 7.6 Hz, trifluoromethyl quinoline), 9.31–9.32(d, 1H, $J$ = 4.5 Hz, trifluoromethyl quinoline), MS (*m*/*z*, %): 322(M$^+$, 75), 293(10), 249(65), 196(80), 169(100), 149(10), 119(10), 83(20).

*6.1.2. 1-[8-(Trifluoromethyl) quinolin-4-yl]-5-methyl-1H-1, 2,3-triazole-4-carbohydrazide (**3a**)*

Compound **3** (12 g) was taken in dry ethylene dichloride (60 ml) and treated with thionyl chloride (6.5 g) and 1 ml of *N,N*-dimethylformamide. The mixture was heated under reflux for 5 h and then cooled to room temperature. It was then slowly added into the mixture containing 100% hydrazine hydrate (6.3 g) in 10 ml of ethylene dichloride at 0 °C and stirred for 3 h. The reaction mixture was brought to room temperature and stirred for 1 h. Ethylene dichloride was distilled out completely under reduced pressure and the residue was treated with ice-cold water. The precipitated solid was filtered, washed with dilute solution of sodium bicarbonate and then with water. The crude sample was recrystallized from methanol. (11.2 g, 89% yield), m.p 248-250 °C, IR (KBr) $\nu$/cm$^{-1}$ : 3365(N–H), 1678(C=O), 902(C–F), $^1$H-NMR-(DMSO-d$_6$) $\delta$: 2.56(s, 3H, CH$_3$), 7.57–7.59 (d, 2H, $J$ = 8.5 Hz, trifluoromethyl quinoline), 7.68–7.74 (t, 1H, $J$ = 8.1 Hz, trifluoromethyl quinoline), 8.22–8.25 (d, 1H, $J$ = 7.2 Hz, trifluorometyl quinoline), 9.31–9.32 (d, 1H, $J$ = 4.5 Hz, trifluoromethyl quinoline), 9.84(s, 1H, NH).

*6.1.3. General procedure for the preparation of N-[1-arylmethylene]-1-[8-(trifluoro-methyl)quinolin-4-yl]-5-methyl-1H-1,2,3-triazole-4-carbohydrazide (**4**)*

Compound **3** (0.5 g) was treated with equimolar quantity of aromatic aldehydes in methanol. The resulting mixture was heated under reflux for 2–3 h by adding 1 ml of glacial acetic acid. After cooling to 0 °C, the resulting crystals were filtered and washed with cold methanol.

**4a** IR(KBr) $\nu$/cm$^{-1}$: 3345(NH), 3323, 3074(Ar–H), 1695(C=O), 978(C–F), $^1$H-NMR(DMSO-d$_6$) $\delta$: 2.50(s, 3H, CH$_3$), 7.27–7.37(t, 1H, $J$ = 8.8 Hz, 4-fluorophenyl), 7.72–7.92(2 d, t, 5H, $J$ = 9.6 and 8.2 Hz, trifluoromethyl quinoline and 4-fluorophenyl), 8.05–8.13(d, 1H, $J$ = 7.2 Hz, p-fluorophenyl), 8.32–8.42(d, 1H, $J$ = 7.2 Hz, trifluoromethyl quinoline), 8.63(s, 1H, = CH), 9.33–9.42(d, 1H, $J$ = 4.5, trifluoromethyl quinoline), 12.32(s, 1H, NH), MS (*m*/*z*, %): 443(M$^+$, 15), 254(10), 237(20), 204(5), 194(20), 167(100), 136(22), 108(30), 91(20), 69(25).

**4b** IR(KBr) $\nu$/cm$^{-1}$: 3346 (N–H), 3123, 3030(Ar–H), 1690(C=O), 990(C–F),$^1$H-NMR(DMSO-d$_6$) $\delta$: 1.97(s, 3H, CH$_3$), 2.51(s, 3H, CH$_3$), 6.80–7.21(2 d, 4H, 4-methylphenyl), 7.23–7.26(d, 1H, $J$ = 7.8 Hz, trifluoromethylquinoline), 7.56–7.61(t, 1H, $J$ = 8.1 Hz,trifluoromethylquinoline),8.09–8.12(d, 1H, $J$ = 7.2 Hz, trifluoromethylquinoline), 8.27–8.30(d, 1H, $J$ = 8.4 Hz, trifluoromethylquinoline), 8.65(s, 1H, =CH), 8.87–8.99(d, 1H, $J$ = 4.5 Hz, trifluoromethylquinoline, 12.30(s, 1H, NH), MS (*m*/*z*, %): 438 (M$^+$, 15), 293(10), 254(5), 249(5), 196(10), 167(40), 133(10), 111(20), 83(50), 57(100).

**4c** IR (KBr) $\nu$/cm$^{-1}$: 3336 (N–H), 3121, 3030(Ar–H), 1692(C=O), 990(C–F), 813(C–Cl), $^1$H-NMR(DMSO-d$_6$) $\delta$: 2.58(s, 3H, CH$_3$), 7.43–7.40(d, 2H, $J$ = 8.4 Hz, 4-chlorophenyl), 7.59–7.57(d, 2H, $J$ = 7.5 Hz, trifluoromethylquinoline), 7.79–7.70(t, d, 4H, $J$ = 8.1 and 8.6 Hz, trifluoromethylquinoline and 4-chlorophenyl), 8.26(s, 1H, =CH), 9.33–9.32(d, 1H, $J$ = 4.5 Hz, trifluoromethylquinoline), 10.3(s, 1H, NH), MS (*m*/*z*, %): 459 (M$^+$, 10), 321(5), 293(60), 250(20), 237(60), 207(20), 196(80), 169(50), 139(35), 118(30), 91(50), 55(100).

**4d** IR (KBr) $\nu$/cm$^{-1}$: 3360(NH), 3015, 3090(Ar–H),1682(C=O),946(C–F),$^1$H-NMR(DMSO-d$_6$) $\delta$: 2.5(s, 3H,CH$_3$), 3.85(s, 3H, OCH$_3$), 7.04–7.06(d, 2H, $J$ = 8.6 Hz, 4-methoxylphenyl), 7.68–7.70(d, 2H, $J$ = 8.5 Hz, 4-methoxyphenyl), 7.86–7.87(d, 2H, $J$ = 7.5 Hz, trifluoromethylquinoline), 7.87–7.89(t, 1H, $J$ = 8.2 Hz, trifluoromethylquinoline), 8.09–8.11(d, 1H, $J$ = 7.2 Hz,trifluoromethylquinoline), 8.28–8.31(d, 1H, $J$ = 8.4 Hz, trifluoromethylquinoline), 8.66(s, 1H, =CH), 9.34–9.36(d, 1H, $J$ = 4.5 Hz, trifluoromethylquinoline) 12.31(s, 1H, NH), MS (*m*/*z*, %) : 454(M$^+$, 20), 254(18), 240(10), 233(10), 183(25), 169(20), 127(30), 105(40), 77(60), 69(100).

**4e** IR (KBr) $\nu$/cm$^{-1}$: 3340(N–H), 3125, 3028(Ar–H), 1688(C=O), 1340,1530(NO$_2$, sym. and asym. str.), 940(C–F), $^1$H-NMR(DMSO-d$_6$) $\delta$: 2.51(s, 3H, CH$_3$), 7.40–7.42(d, 2H, $J$ = 8.2 Hz, 4-nitrophenyl), 7.57–7.60(d, 1H, $J$ = 7.8 Hz, trifluoromethylquinoline), 7.71–7.79(t, d, 3H, $J$ = 8.1 and 8.6 Hz, trifluoromethylquinoline & 4-nitrophenyl), 8.09–8.10(d, 1H, $J$ = 7.2 Hz, trifluoromethylquinoline), 8.27–8.30(d, 1H, $J$ = 8.4 Hz, trifluoromethylquinoline), 8.65(s, 1H, =CH), 8.98–9.00(d, 1H, $J$ = 4.5 Hz, trifluoromethylquinoline), 12.31(s, 1H, NH), MS (*m*/*z*, %): 470 (M$^+$, 10), 277(10), 254(5), 246(6), 219(15), 178(20), 173(10), 125(20), 105(22), 91(100), 51(23).

**4h** IR (KBr) $\nu$/cm$^{-1}$: 3350(N–H), 3130–3041(Ar–H), 1687(C=O), 939(C–F),$^1$H-NMR(DMSO-d$_6$) $\delta$: 2.21(s, 3H, CH$_3$), 2.50(s, 3H, CH$_3$), 6.99(s, 1H, thienyl), 7.22–7.26(d, 1H, $J$ = 7.8Hz, trifluoromethylquinoline), 7.55–7.60(t, 1H, $J$ = 8.1 Hz, trifluoromethylquinoline), 7.95(s, 1H, thienyl), 8.09–8.93(d, 1H, 7.2 Hz, trifluoromethylquinoline), 8.27–

8.31(d, 1H, $J$ = 8.4 Hz, trifluoromethylquinoline), 8.64(s, 1H, =CH), 8.98–9.00(d, 1H, $J$ = 4.5 Hz, trifluoromethylquinoline), 12.31(s, 1H, NH).

*6.1.4. 1-{1-[8-(Trifluoromethyl)quinolin-4-yl]-5-methyl-1H-1,2,3-triazol-4-yl} ethanone (**5**)*

This compound was also prepared as per the above procedure by adding acetyl acetone instead of ethyl acetoacetate (75% yield), m.p.185–187 °C, IR (KBr) $\nu$/cm$^{-1}$: 3128, 3030(Ar–H), 1685(C=O), 1010(C–F). $^1$H-NMR(DMSO-d$_6$) $\delta$: 2.49(s, 3H, $CH_3$), 2.83(s, 3H, $COCH_3$), 7.57–7.60 (d, 2H, $J$ = 8.7 Hz, trifluoromethylquinoline), 7.60–7.74 (t, 1H, $J$ = 8.3 Hz, trifluoromethyl quinoline), 8.22–8.24 (d, 1H, $J$ = 7.2 Hz, trifluoromethyl quinoline), 9.30–9.32 (d, 1H, $J$ = 4.5,Hz trifluoromethyl quinoline), MS ($m/z$, %): 320(M$^+$, 20), 292(12), 277(45), 250(95), 230(25), 196(70), 169(100), 119(15).

*6.1.5. General procedure for preparation of 1-aryl-4-{1-[8-(trifluoromethyl)quinolin -4-yl]-5-methyl-1H-1,2,3-triazol-4-yl}prop-2-en-1-one (**6**)*

Compound **5** (0.5 g) was treated with equimolar quantity of aromatic aldehyde in methanol. The mixture was cooled to 10 °C, sodium hydroxide (0.25 g) in 5 ml water was added and then stirred for 24 h at room temperature. After the completion of the reaction, it was poured on to ice-cold water. The separated solid was filtered, washed with water and recrystallized from methanol.

**6a** IR (KBr) $\nu$/cm$^{-1}$: 3133, 3301(Ar–H), 1688(C=O), 1617(C=C), 970(C–F), $^1$H-NMR(DMSO-d$_6$) $\delta$: 2.57(s, 3H, $CH_3$), 7.17–7.12(t, 2H, $J$ = 8.6 Hz, 4-fluorophenyl), 7.62–7.57(d, 1H, $J$ = 7.6 Hz, trifluoromethylquinoline), 7.77–7.69 (t, d, 4H, $J$ = 8.7 and 6.5 Hz, trifluoromethylquinoline and 4-fluorophenyl), 8.09–7.92 (2d, 2H, $J$ = 15.9 Hz, CH=CH), 8.25–8.23 (d, 1H, $J$ = 7.1 Hz, trifluoromethylquinoline), 9.33–9.32(d, 1H, $J$ = 4.5 Hz, trifluoromethylquinoline).

**6b** IR (KBr) $\nu$/cm$^{-1}$: 3132, 3313 (Ar–H), 1697.2 (C=O), 1615(C=C), 990(C–F), $^1$H-NMR(DMSO-d$_6$) $\delta$: 1.98(s, 3H, $CH_3$), 2.50(s, 3H, $CH_3$), 6.81–7.20(2 d, 4H, 4-methylphenyl), 7.24–7.27(d, 1H, $J$ = 7.9 Hz, trifluoromethylquinoline), 7.55–7.60 (t, 1H), $J$ = 8.2 Hz, trifluoromethylquinoline), 7.93–8.09(2 d, 2H, $J$ = 15.9 Hz, CH=CH), 8.1–8.13(d, 1H, $J$ = 7.2 Hz,trifluoromethylquinoline), 8.27–8.30(d, 1H, $J$ = 8.4 Hz, trifluoromethylquinoline), 9.30–9.31(d, 1H, $J$ = 4.5 Hz, trifluoromethylquinoline), MS ($m/z$, %): 422 (M$^+$, 10), 196(60), 151(20), 133(25), 105(62), 77(70), 55(100). (Fig. 1, Tables 1,3)

**6c** IR (KBr) $\nu$/cm$^{-1}$: 3122, 3303(Ar–H), 1692(C=O), 1625(C=C), 990(C–F). 814(C–Cl), $^1$H-NMR (DMSO-d$_6$) $\delta$: 2.54 (s,3H,$CH_3$), 7.62–7.58 (d,2H, $J$ = 8.4 Hz, trifluoromethylquinoline), 7.75–7.69(t, 1H, $J$ = 8.1 Hz, trifluoromethylquinoline), 7.78–7.83(d, 2H, $J$ = 8.3 Hz, 4-chlorophenyl), 7.90–7.99(d, 2H, $J$ = 8.4 Hz, 4-chlorophenyl), 8.20–8.22(d, 1H, $J$ = 7.1 Hz, trifluoromethylquinoline), 9.39–9.38(d, 1H, $J$ = 4.5 Hz, trifluoromethyl quinoline), 7.94–8.25 (2 d, 2H, CH=CH, $J$ = 16 Hz).

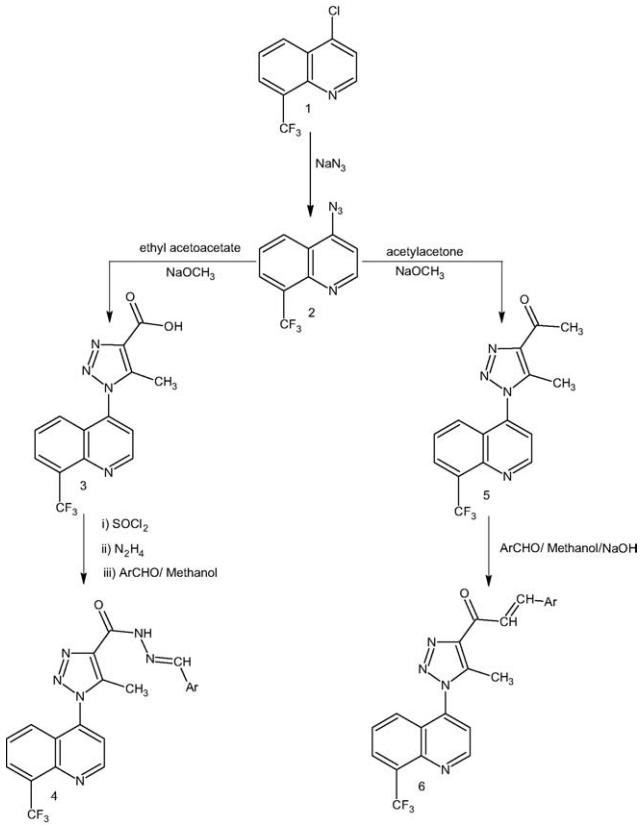


Fig. 1. Synthesis of *N*-[1-arylmethylene]-1-[8-(trifluoromethyl) quinolin-4-yl]-5-methyl-1H-1,2,3-triazole-4-carbohydrazides **4** and 1-aryl-4-{1-[8-(trifluoromethyl) quinolin-4-yl]-5-methyl-1H-1,2,3-triazol-4-yl}prop-2-en-1-ones **6**.

**6d** IR(KBr) $\nu$/cm$^{-1}$: 3130, 3315(Ar–H), 1677(C=O), 1620(C=C), 997(C–F), $^1$H-NMR(DMSO-d$_6$) $\delta$: 2.50(s, 3H, $CH_3$), 3.91(s, 3H, $OCH_3$), 7.03–7.05(d, 2H, $J$ = 8.6 Hz, 4-methoxyphenyl), 7.68–7.70(d, 2H, $J$ = 8.5 Hz, 4-methoxyphenyl), 7.85–7.86(d, 1H, $J$ = 7.5 Hz, trifluoromethylquinoline),7.87–7.89(t, 1H, $J$ = 8.1 Hz, trifluoromethylquinoline), 7.93–8.10(2 d, 2H, $J$ = 15.9 Hz, CH=CH), 8.23–8.25(d, 1H, $J$ = 7.2 Hz, trifluoromethylquinoline), 8.28–8.31(d, 1H, $J$ = 8.4 Hz, trifluoromethylquinoline), 9.30–9.31(d, 1H, $J$ = 4.5 Hz, trifluoromethylquinoline), MS ($m/z$, %): 438(M$^+$, 25), 196(60), 167(20), 133(25), 105(44), 91(65), 55(100).

**6e** IR (KBr) $\nu$/cm$^{-1}$: 3126, 3313(Ar–H), 1682(C=O), 1620(C=C), 990(C–F), $^1$H-NMR(DMSO-d$_6$) $\delta$: 2.58(s, 3H, $CH_3$), 7.61–7.57(d, 2H, $J$ = 8.5 Hz, trifluoromethylquinoline), 7.75–7.69(t, 1H, $J$ = 8.2, trifluoromethylquinoline), 7.88–7.83(d, 2H,$J$ = 4.5 Hz, 4-nitrophenyl), 8.24–7.92(2 d, 2H, $J$ = 15.9 Hz, CH=CH), 8.32–8.29(d, 1H, $J$ = 7.2 Hz, trifluoromethylquinoline), 8.33–8.32(d, 2H, $J$ = 2 Hz, 4-nitrophenyl), 9.34–9.32(d, 1H, $J$ = 4.5 Hz, trifluoromethylquinoline), MS ($m/z$, %): 453(M$^+$, 15), 151(20), 125(18), 105(80), 77(100), 71(85).

**6h** IR (KBr) $\nu$/cm$^{-1}$: 3130, 3316(Ar–H), 1666(C=O), 1614(C=C), 990(C–F), $^1$H-NMR(DMSO-d$_6$) $\delta$: 2.21(s, 3H, $CH_3$), 2.50(s, 3H, $CH_3$), 6.99(s, 1H, thienyl), 7.22–7.26(d, 1H, $J$ = 7.8 Hz,trifluoromethylquinoline), 7.80–7.82(t, 1H,

Table 1
Characterization data of compounds **4** and **6**

| Compound | Ar | Molecular formula | Molecular weight | M.p. (°C) | Yield (%) | Analysis % Found (Calc.) | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N |
| **2** | – | $C_{10}H_5F_3N_4$ | 238 | 130–131 | 80 | – | – | – |
| **4a** | 4-F–$C_6H_4$ | $C_{21}H_{15}F_4N_6O$ | 443 | 270–271 | 60 | 56.85 (56.88) | 3.40 (3.40) | 18.94 (18.95) |
| **4b** | 4-$CH_3$–$C_6H_4$ | $C_{22}H_{17}F_3N_6O$ | 438 | 290–291 | 65 | 60.25 (60.27) | 3.88 (3.90) | 19.16 (19.17) |
| **4c** | 4-Cl–$C_6H_4$ | $C_{21}H_{15}ClF_3N_6O$ | 459.5 | 257–258 | 62 | 54.86 (54.85) | 3.27 (3.28) | 18.28 (18.27) |
| **4d** | 4-$OCH_3$–$C_6H_4$ | $C_{22}H_{17}F_3N_6O_2$ | 454 | 260–262 | 65 | 58.15 (58.15) | 3.76 (3.77) | 18.45 (18.49) |
| **4e** | 4-$NO_2$–$C_6H_4$ | $C_{21}H_{15}F_3N_7O_3$ | 470 | 284–285 | 60 | 53.62 (53.62) | 3.21 (3.20) | 20.84 (20.80) |
| **4f** | 4,5-$(OCH_3)_2$-2-$NO_2$–$C_6H_2$ | $C_{23}H_{15}F_3N_7O_5$ | 526 | 248–250 | 65 | 56.01 (56.03) | 4.09 (4.11) | 16.34 (16.33) |
| **4g** | Furanyl | $C_{19}H_{13}F_3N_6O_2$ | 414 | 216–217 | 63 | 55.07 (55.07) | 3.14 (3.16) | 20.30 (20.28) |
| **4h** | 3-methyl-thienyl | $C_{20}H_{15}F_3N_6SO$ | 444 | 209–210 | 65 | 54.05 (54.04) | 3.40 (3.40) | 18.90 (18.90) |
| **6a** | 4-F–$C_6H_4$ | $C_{22}H_{14}F_4N_4O$ | 426 | 260–261 | 62 | 61.981 (61.97) | 3.32 (3.30) | 3.10 (13.14) |
| **6b** | 4-$CH_3$–$C_6H_4$ | $C_{23}H_{17}F_3N_4O$ | 422 | 256–257 | 67 | 65.38 (65.39) | 4.05 (4.05) | 13.25 (13.26) |
| **6c** | 4-Cl–$C_6H_4$ | $C_{22}H_{14}ClF_3N_4O$ | 442.5 | 227–228 | 61 | 59.65 (59.67) | 3.17 (3.18) | 12.65 (12.65) |
| **6d** | 4-$OCH_3$–$C_6H_4$ | $C_{23}H_{17}F_3N_4O_2$ | 438 | 240–241 | 64 | 63.02 (63.01) | 3.08 (3.90) | 13.00 (12.77) |
| **6e** | 4-$NO_2$–$C_6H_4$ | $C_{22}H_{14}F_3N_5O_3$ | 453 | 250–251 | 60 | 58.27 (58.28) | 3.10 (3.11) | 15.42 (15.44) |
| **6f** | 4,5-$(OCH_3)_2$-2-$NO_2$–$C_6H_2$ | $C_{24}H_{18}F_3N_5O_5$ | 513 | 230–233 | 62 | 57.13 (57.14) | 3.44 (3.45) | 13.32 (13.32) |
| **6g** | Furanyl | $C_{20}H_{13}F_3N_4O_2$ | 398 | 138–140 | 58 | 60.32 (60.30) | 3.26 (3.28) | 14.04 (14.06) |
| **6h** | 3-methyl-thienyl | $C_{21}H_{15}F_3N_4OS$ | 428 | 220–222 | 67 | 57.66 (57.68) | 3.60 (3.63) | 13.46 (13.45) |

Table 2
Antibacterial activity of the compounds 4a–h and 6a–h

| Compound | *B. subtilis* | *E. coli* | *P. aeruginosa* | *S. aureus* | *K. pneumoniae* |
|---|---|---|---|---|---|
| **4a** | 10(25) | 12(25) | 16(12.5) | 10(25) | 15(12.5) |
| **4b** | 15(12.5) | 18(12.5) | 14(12.5) | 14(12.5) | 19(12.5) |
| **4c** | 18(12.5) | 19(12.5) | 19(12.5) | 20(6) | 21(6) |
| **4d** | 20(6) | 19(12.5) | 10(25) | 15(12.5) | 26(6) |
| **4e** | 10(25) | 15(12.5) | 16(12.5) | 14(25) | 16(12.5) |
| **4f** | 15(12.5) | 16(12.5) | 22(6) | 18(12.5) | 12(25) |
| **4g** | 18(12.5) | 18(12.5) | 15(12.5) | 12(25) | 14(25) |
| **4h** | 18(12.5) | 22(6) | 25(6) | 21(6) | 22(6) |
| **6a** | 13(25) | 15(12.5) | 16(12.5) | 17(12.5) | 9(25) |
| **6b** | 17(12.5) | 12(25) | 18(12.5) | 11(25) | 14(25) |
| **6c** | 18(12.5) | 15(12.5) | 17(12.5) | 18(12.5) | 20(6) |
| **6d** | 20(6) | 16(12.5) | 22(6) | 16(12.5) | 18(12.5) |
| **6e** | 22(6) | 18(12.5) | 13(25) | 10(25) | 10(25) |
| **6f** | 15(12.5) | 14(25) | 20(6) | 14(12.5) | 12(25) |
| **6g** | 16(12.5) | 18(12.5) | 22(6) | 18(12.5) | 21(6) |
| **6h** | 20(6) | 17(12.5) | 24(6) | 19(12.5) | 20(6) |
| Standard | 20(6) | 18(12.5) | 25(6) | 19(12.5) | 20(6) |

Values in bracket are MIC values.

Table 3
Antifungal activity of the compounds **4a–h** and **6a–h** at 10 μg ml$^{-1}$

| Compound | *A. flavus* | *A. fumigatus* | *C. albicans* | *P. marneffei* | *T. mentagrophytes* |
|---|---|---|---|---|---|
| **4a** | 11(25) | 12(25) | 10(25) | 10(25) | 15(12.5) |
| **4b** | 15(12.5) | 17(12.5) | 13(25) | 15(12.5) | 19(12.5) |
| **4c** | 12(25) | 15(12.5) | 15(12.5) | 20(6) | 21(6) |
| **4d** | 14(25) | 18(12.5) | 20(6) | 15(12.5) | 26(6) |
| **4e** | 18(12.5) | 20(6) | 14(25) | 14(25) | 16(12.5) |
| **4f** | 16(12.5) | 17(12.5) | 19(12.5) | 17(12.5) | 14(25) |
| **4g** | 13(25) | 11(25) | 16(12.5) | 14(25) | 14(25) |
| **4h** | 17(12.5) | 21(6) | 20(6) | 21(6) | 22(6) |
| **6a** | 18(12.5) | 13(25) | 11(25) | 17(12.5) | 10(25) |
| **6b** | 11(25) | 10(25) | 9(25) | 12(25) | 13(25) |
| **6c** | 10(25) | 15(12.5) | 18(12.5) | 18(12.5) | 20(6) |
| **6d** | 17(12.5) | 11(25) | 13(25) | 16(12.5) | 18(12.5) |
| **6e** | 15(12.5) | 10(25) | 15(12.5) | 12(25) | 10(25) |
| **6f** | 10(25) | 15(12.5) | 11(25) | 14(25) | 13(25) |
| **6g** | 15(12.5) | 11(25) | 17(12.5) | 18(12.5) | 19(12.5) |
| **6h** | 17(12.5) | 22(6) | 22(6) | 19(12.5) | 20(6) |
| Standard | 18(12.5) | 22(6) | 20(6) | 20(6) | 20(6) |

Values in bracket are MIC values.

$J$ = 8.1 Hz, trifluoromethylquinoline), 7.91(s, 1H, thienyl), 7.95–8.30(2 d, 2H, $J$ = 16 Hz, CH=CH), 8.31–8.33(d, 1H, $J$ = 7.2 Hz, trifluoromethylquinoline), 8.34–8.36(d, 1H, $J$ = 8.4 Hz, trifluoromethylquinoline), 9.31–9.32(d, 1H, $J$ = 4.5 Hz, trifluoromethylquinoline), MS ($m/z$, %): 428 ($M^+$, 46), 400(5), 371(20), 277(5), 236(60), 196(100), 151(35), 123(35), 79(18), 53(9).

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## References

[1] Y.S. Sanghvi, B.K. Bhattacharya, G.D. Kini, S.S. Matsumoto, S.B. Larson, W.B. Jolley, R.K. Robins, G.R. Revankar, J. Med. Chem. 33 (1990) 336.
[2] M.D. Chen, S.J. Lu, G.P. Yuag, S.Y. Yang, X.L. Du, Heterocyclic Comm 6 (2000) 421–426.
[3] E.A. Sherement, R.I. Tomanov, E.V. Trukhin, V.M. Berestovitskaya, Russ. J. Org. Chem. 40 (2004) 594–595.
[4] Allais, André, Meier, Jean (Roussel–UCLAF) Ger. Offen, 1815467, 24 July 1969.
[5] K.M. Banu, A. Dinakar, C. Ananthanarayanan, Indian J. Pharm. Sci. 4 (1999) 202–205.
[6] R. Meier, EP, 199262; eidem, US, 4789680, 1986.
[7] A. Passannanti, P. Diana, P. Barraja, F. Mingoia, A. Lauria, G. Cirrincione, Heterocycles 48 (1998) 1229–1235.
[8] M. Jilino and Malcom, F.G. Stevens, J. Chem. Soc, Perkin Trans 1 (1998) 1677–1684.
[9] G.D. Diana, J.J. Nitz, EP 566199, 1993.
[10] S. Manfredini, C.B. Vicentini, M. Manfrini, N. Bianchi, C. Rutigliano, C. Mischiati, R. Gambari, Bioorg. Med. Chem. 8 (2000) 2343–2346.
[11] S. Danoun, G. Baziard-Mouysset, J. Stigliani, M. Payard, M. Selkti, B. Viossat, A. Tomas, Heterocyclic Commun. 4 (1998) 45–51.
[12] G. Biagi, V. Calderone, I. Giorgi, O. Livi, E. Martinotti, A. Martelli, A. Nardi, Farmaco 59 (2004) 397–404.
[13] R. Cruickshank, J.P. Duguid, B.P. Marion, R.H.A. Swain, in: Medicinal Microbiology, 12th Ed., vol. II, Churchil Livingstone, London, 1975, pp. 196–202.
[14] A.H. Collins, Microbiological Methods, Ed-II Butterworth, London, 1976.
[15] Z.K. Khan, in: In vitro and vivo screening techniques for bioactivity screening and evaluation, Proceeding Int. workshop UNIDO-CDRI, 1997, pp. 210–211.
[16] Antifungal Agents, in: R.S. Varma (Ed.), Past, Present and Future Prospects, National Academy of Chemistry and Biology, India, Lucknow, 1998.