Heterocyclic Letters
Vol. 6| No.2|185-194| Feb-April| 2016
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

ULTRASOUND PROMOTED EFFICIENT SYNTHESIS OF NEW TETRAZOLO[1,5-*A*]QUINOLINE DERIVATIVES AND THEIR COMPARATIVE ANTI MICROBIAL AND ANTI TUBERCULAR STUDY

Ankit J. Patel, Manish P. Patel*

Department of Chemistry, Sardar Patel University, Vallabh Vidyanagar 388120, Gujarat, India
E-mail: patelmanish1069@yahoo.com

Abstract:
A new series of tetrazolo[1,5-*a*]quinoline derivatives have been synthesized by 4-(chloromethyl)-7-substitueted tetrazolo[1,5-*a*]quinoline on treatment with substituted aromatic amines/phenols in the presence of DMF, K_2CO_3 under ultrasound and conventional method. Ultrasound approach offers vital improvement for the synthesis of the target compounds with regards to simplicity in operation, yield of product. All synthesized compounds were characterized by ^{1}H NMR, Mass, ^{13}C NMR spectra and evaluated for biological activities. Also effect of C-N and C-O linkage on biological activity was study.

Keywords: Tetrazolo[1,5-*a*]quinoline, Ultrasound irradiation, Antimicrobial and antitubercular activity.

Introduction

The increasing clinical importance of drug resistant bacterial and fungal pathogens has lent additional urgency to antibacterial research and development of new antibacterial compounds. The search for new antimicrobial agents will consequently always remain as an important and challenging task for medicinal chemists. In medicinal chemistry there has been a widespread use of heterocyclic compounds which is increasing day by day because this kind of compounds are explored in many of the structures of bioactive molecules which are essential for life. So heterocyclic compounds have to provide a platform for the rapid exchange of research in the areas of organic, pharmaceutical, analytical and medicinal chemistry.

Quinoline has received considerable attention in recent years, due to its occurrence in various natural products and is often used for the design of many synthetic compounds with diverse pharmacological properties such as anti-inflammatory, antimicrobial agents, cytotoxic, antitumor, antimalarial, anti-cancer, antifungal, antihypertensive, antiulcer activities[i-ix] etc. Because of these advantages of quinoline and its derivatives have always attracted both synthetic and biological chemist. Tetrazole and its derivatives exhibit a wide range of applications in medicinal as well as synthetic chemistry. Several substituted tetrazole have been shown to possess anti-inflammatory, antibacterial, anti-aids, anticancer, antifungal and anticonvulsant activities[x-xv]. The fusion of quinoline with tetrazole ring is known to increase the biological activity[xvi] and play a vital role in biology such as antifungal, anti-inflammatory, antibacterial, HCV inhibitor, antimicrobial, anticancer and anticonvulsant activities[xvii-xxiii].

"Sonochemistry" is a new trend in organic chemistry, offering a versatile and facile pathway for a large variety of syntheses. A large number of organic reactions can be carried out under ultrasonic irradiation, using cavitations as an energy source to promote molecular interactions resulted in shorter reaction times [xxiv-xxvi] high yields, and mild condition[xxvii-xxxi].
In the present study we synthesized new tetrazolo[1,5-*a*] quinoline derivatives incorporated with aromatic amines or phenols via ultrasound irradiation method using K_2CO_3 as base. In addition way we examined antibacterial and antitubercular activity of all synthesized compounds and compared effect of C-O and C-N linkage on biological activity.

Results and Discussion

Reactions outlined in **Fig.1** were adopted to synthesize the desired compounds. The key intermediate tetrazolo[1,5-*a*] quinoline-4-carboxaldehyde **1a-c** was prepared by the reaction of substituted 2-chloroquinoline-3-carboxaldehyde with sodium azide, acetic acid in ethanol[xxxii,xxxiii]. Compounds **1a-c** further react with sodium borohydride in methanol afforded (7-substituted tetrazolo[1,5-a]quinolin-4-yl)methanol which on subsequent chlorination with thionyl chloride in dichloromethane gave 4-(chloromethyl)-7-substituted tetrazolo[1,5-*a*]quinoline **2a-c** as solid. The title compounds were prepared via ultrasound and conventional method by taking equimolar amounts of compounds **2a-c** and substituted aromatic amines/phenols in DMF using K_2CO_3 as base[xxxiv].
During the course of reaction for the synthesis of compounds **3a-r**, we examined the reaction time and yield by conventional heating method and ultrasound irradiation method which are mention in **Table 1**. It was clear that ultrasound method took a shorter reaction time and higher yield than the conventional route of synthesis. Compound **3o** found in higher yield.

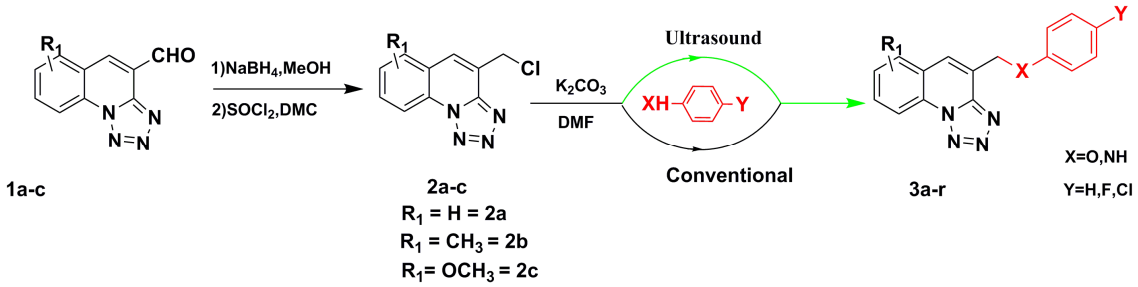

Fig. 1 Synthetic route of the title compounds **3a-r**.

According to Beistein's test of **2a**, **3a** and **3d**, we conformed that chlorine was replace by hydrogen of aromatic amines/phenols. Regarding the structure of **3a-r** the assignment of **3a** and **3d** were described. In the ^{1}H-NMR spectrum of compound **3d** the signal due to CH_2-O- was observed as singlet integrating for two protons at 5.55 ppm and for **3a** the signal due to CH_2-NH- was observed as singlet at 5.4 ppm for -NH. All the aromatic carbons of compounds **3a** showed signals around δ 105.1–157.3 ppm in the ^{13}C NMR spectra. Mass spectra of compound **3a** gave molecular ion peak at m/z 276(M+1) corresponding to molecular formula $C_{16}H_{13}N_5$. The elemental analysis values are in good agreement with theoretical data.

Table 1 Comparison of ultrasound and conventional method for the synthesis of compounds **3a-r**

Compound code	R_1	X	Y	Molecular weight	Ultrasound Method		Conventional method	
					Time(min)	% Yield	Time(h)	% Yield
3a	H	NH	H	275.308	44	88	6.7	69
3b	H	NH	F	293.298	29	87	6.4	76
3c	H	NH	Cl	309.73	23	89	6.1	75
3d	H	O	H	276.293	33	92	6	72
3e	H	O	F	294.283	30	89	5.8	70
3f	H	O	Cl	310.738	25	90	5.5	71
3g	CH_3	NH	H	289.334	40	83	6.6	65
3h	CH_3	NH	F	307.325	28	92	6.5	67
3i	CH_3	NH	Cl	323.780	27	90	6.1	79
3j	CH_3	O	H	290.319	32	87	5.3	69
3k	CH_3	O	F	308.310	30	91	5.4	73
3l	CH_3	O	Cl	324.764	26	92	5	81
3m	OCH_3	NH	H	305.334	41	92	6.3	76
3n	OCH_3	NH	F	323.324	36	94	5.7	80
3o	OCH_3	NH	Cl	339.779	39	95	6.2	78
3p	OCH_3	O	H	306.319	31	93	4.9	80
3q	OCH_3	O	F	324.309	24	86	4.3	78
3r	OCH_3	O	Cl	340.764	26	91	5.2	77

Antimicrobial activity

The *in vitro* antimicrobial activity of all the synthesized compounds was carried out by broth microdilution method[xxxv]. Mueller Hinton broth was used as nutrient medium to grow and dilute the compound suspension for the test bacteria and Sabouraud Dextrose broth used for fungal nutrition. Inoculums size for test strain was adjusted to 10^8 CFU [Colony Forming Unit] per milliliter by comparing the turbidity. The strains employed for the activity were procured from [MTCC – Micro Type Culture Collection] Institute of Microbial Technology, Chandigarh, India. The compounds **3a-r** were screened for their antibacterial activity against *Clostridium tetani* (MTCC 449), *Bacillus subtilis* (MTCC 441), *Streptococcus pneumonia* (MTCC 1936), *Escherichia coli* (MTCC 443), *Salmonella typhi* (MTCC 98), and *Vibrio cholerae* (MTCC 3906) as well as antifungal activity against *Aspergillus fumigatus* (MTCC 3008) and *Candida albicans* (MTCC 227). DMSO was used as vehicle to get desired concentration of compounds to test upon microbial strains. The lowest concentration, which showed no visible growth after spot subculture was considered as MIC for each compound. The standard antibiotics used for comparison in the present study were ampicillin, chloramphenicol and ciprofloxacin for evaluating antibacterial activity as well as griseofulvin and nystatin for antifungal activity. The protocols are summarized in **Table 2**.

Table 2 The *in vitro* antimicrobial activity of compounds **3a-r**

Minimum inhibitory concentration in µg/Ml								
Compound	Gram negative bacteria			Gram positive bacteria			Fungi	
	EC MTCC 443	ST MTCC 98	VC MTCC 3906	BS MTCC 441	CT MTCC 449	SP MTC 1936	CA MTCC 227	AF MTCC 3008
3a	**100**	**100**	**250**	**200**	**200**	200	**500**	1000
3b	250	250	**125**	**125**	**200**	125	**500**	200
3c	**62.5**	**100**	**200**	**200**	**250**	**100**	**250**	500
3d	200	250	**250**	500	500	500	1000	>1000
3e	250	250	**200**	500	500	500	1000	1000
3f	125	500	**250**	**250**	500	200	1000	1000
3g	**100**	125	**250**	**62.5**	**125**	125	**250**	500
3h	**100**	**100**	**125**	**200**	**125**	250	**500**	1000
3i	200	500	**200**	500	**200**	**100**	1000	>1000
3j	**100**	250	**250**	**250**	**200**	200	**500**	1000
3k	250	200	500	500	**100**	500	**500**	1000
3l	500	500	500	500	**250**	125	**500**	>1000
3m	200	200	**100**	**200**	**125**	125	**250**	1000
3n	250	250	**200**	**200**	**100**	200	**250**	1000
3o	**62.5**	**100**	**250**	**250**	**200**	250	**250**	250
3p	250	200	**250**	500	**200**	200	1000	1000
3q	250	250	**200**	**250**	**250**	200	1000	>1000
3r	250	250	**250**	**250**	**200**	500	**500**	1000
Ampi.	100	100	250	250	250	100	-	-
Chlo.	50	50	50	50	50	50	-	-
Cipro.	25	25	25	50	100	50	-	-
Nyst.	-	-	-	-	-	-	100	100
Gri.	-	-	-	-	-	-	500	100

SP: *Streptococcus pneumoniae*, CT: *Clostridium tetani,* BS: *Bacillus subtilis* , ST: *Salmonella typhi*, VC: *Vibrio cholera* , EC: *Escherichia coli*, CA: *Candida albicans*, AF: *Aspergillus fumigatus*, Ampi.: Ampicillin; Cipr.: Ciprofloxacin; Chlo.: Chloramphenicol; Norf.: Norfloxacin; Gres.: Griseofulvin; Nyst.: Nystatin. MTCC: Microbial Type Culture Collection Bolt value indicates compounds are more or equally potent as standard drug. Under line value indicate more activity of C-N linkage than C-O linkage.

By analysis of **Table 2** data compounds **3c** and **3o** exhibited excellent activity against gram negative bacteria *Escherichia coli* than the standard drug ampicillin. Compound **3g** is highly activated towards gram positive bacteria *Bacillus subtilis* than standard drug ampicillin. By comparing antibacterial activity of **3a, 3b, 3c** with **3d, 3e, 3f** respectively we can says that C-N linkage compounds are more or equally potent than compounds bearing C-O linkage. This type of result also obtained by comparing **3g, 3h, 3i** with **3j, 3k, 3l** and **3m, 3n, 3o** with **3p,3q,3r** respectively. We concluded that C-N linkage compounds are more potent than compounds bearing C-O linkage. Compounds **3c, 3g, 3m, 3n** and **3o** are more potent for *C.albicans* than standard drug Griseofulvin. Most of the compounds were not found sufficiently potent to inhibit *Aspergillus fumigatus*. **3c** and **3o** are more biological active than other compounds and open up a new door to optimize this series as a new class of antibacterial agents.

Antituberculosis activity

Primary screening of targeted compounds **3a–r** was performed at 250 mg mL^{-1} against the *Mycobacterium tuberculosis* $H_{37}Rv$ strain using Lowenstein Jensen medium (the conventional method) as described by Rattan[xxxvi-xxxviii]. The acquired results are presented in **Table 3** in the form of % inhibition. Rifampicin and Isoniazid were used as the reference drugs. From these results the compounds **3h, 3i, 3o** were found to possess good activity

against M. tuberculosis $H_{37}Rv$. Compound **3f, 3q** are less potent members of the series. In addition we also observe that compounds containing C-N linkage (i.e-**3a, 3b, 3c, 3g, 3h, 3i, 3m, 3n, 3o**) are more potent than compounds containing C-O linkage (i.e-**3d, 3e, 3f, 3j, 3k, 3l, 3p, 3q, 3r**).

Table 3 Antituberculosis activity of compounds **3a-r**

METHOD	L.J.MEDIUM(CONVETIONAL METHOD)		
BECTERIA	M.tuberculosis $H_{37}RV$		
CONCENTRATION	250 µg/ml		
Compound	% Inhibition	Compound	% Inhibition
3a	60%	**3k**	63%
3b	58%	**3l**	72%
3c	55%	**3m**	88%
3d	56%	**3n**	74%
3e	52%	**3o**	95%
3f	43%	**3p**	56%
3g	65%	**3q**	44%
3h	94%	**3r**	56%
3i	97%	ISONIAZIDE	99%
3j	58%	REFAMPICINE	98%

Conclusions

A series of some new tetrazolo[1,5-*a*]quinoline derivatives has been synthesized through ultrasound irradiation method. This green approach takes minimum reaction time with higher yield. It can be concluded that compounds having C-N linkage are more biologically active than compounds having C-O linkage in this series. Compounds **3c**, **3o** are highly active toward antimicrobial bacteria than rest of the series compounds. Compound **3i** is highly active towards *M.tuberculosis* $H_{37}RV$ than the other members of the series.

Experimental Section

General

All the reagents were obtained commercially and used with further purification. All melting points were taken in open capillaries and are uncorrected. The monitoring of the progress of all reactions and homogeneity of the synthesized compounds was carried out by TLC. TLC was run using TLC aluminum sheets silica gel 60 F254 (Merck). Elemental analysis (% C, H, N) was carried out by Perkin Elmer 2400 CHN elemental analyzer at Sophisticated Instrumentation Centre for Applied Research & Training (SICART), Vallabh Vidyanagar. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer using solvent peak as internal standard. Mass spectra were scanned on a Shimadzu LCMS 2010 spectrometer.

General procedure for the synthesis of 7-Substitute-4[(4-substituted phenoxy/aniline)]tetrazolo[1,5-a]quinoline (3a-r)

Conventional method

In a 100ml rounded bottom flask take substituted aromatic aniline/phenol (0.01 mol), K_2CO_3 (0.02 mol), 4-(chloromethyl)-7-substituted tetrazolo[1,5-*a*]quinoline **(2a-c)** (0.01 mol) and 30Ml DMF as solvent. This mixture was refluxed for 4-7 h. Completion of reaction progress was monitored by TLC (Ethyl acetate: n-Hexane). After completion of reaction cool it, pour in crush ice and filter to give the crude product. The obtained product was recrystallized from methanol.

Ultrasound method

To a solution of substituted aromatic aniline/phenol (0.01 mol) and K_2CO_3 (0.02 mol) in 30mL of DMF, 4-(chloromethyl)-7-substituted tetrazolo[1,5-*a*]quinoline (0.01 mol) **(2a-c)** was added and the mixture was ultrasound irradiated for 23-45 min at 50^oC.Completion of reaction progress was monitored by TLC (Ethyl acetate: n-Hexane). The reaction mixture pours in crush ice and filter to give the crude product. The obtained product was recrystallized from methanol.

N-(tetrazolo[1,5-*a*]quinoline-4-ylmethyl)aniline (3a)

Mp: 230^oC; ^1H NMR (400MHz, DMSO d_6) δ/ppm 5.3(s, 1H, NH), 4.74 (s, 2H, CH_2), 6.8-8.6 (m, 10H, Ar-H),.^{13}C NMR ($CDCl_3$, 75MHz) δ: 43.1(CH_2), 114.6, 117.5, 121.7, 127.1, 128.7, 129.1, 129.9, 130.3, 131.4, 135.6, 147.3, 150.3, 153.2. LC-MS: 276$(M)^+$. Anal. Calcd for $C_{16}H_{13}N_5$: C, 69.80; H, 4.76; N, 25.44. Found: C, 69.56; H, 4.66; N, 25.2%.

4-floro-N-(tetrazolo[1,5-*a*]quinoline-4-ylmethyl)aniline (3b)

Mp: 245^oC; ^1H NMR (400MHz, DMSO d_6) δ/ppm 5.3(s, 1H, NH), 4.74 (s, 2H, CH_2), 7.01-8.602 (m, 9H, Ar-H). ^{13}C NMR ($CDCl_3$, 75MHz) δ: 43.5(CH_2), 115.2, 115.4, 117.9, 119.4, 126.4, 127.7, 128.6, 129.6, 130.1, 131.7, 148.1, 153.8, 154.5. LC-MS: 294$(M)^+$. Anal. Calcd for $C_{16}H_{12}N_5F$: C, 65.52; H, 4.12; N, 23.88. Found: C, 65.30; H, 3.82; N, 23.60%.

4-chloro-N-(tetrazolo[1,5-*a*]quinoline-4-ylmethyl)aniline (3c)

Mp: 239^oC; ^1H NMR (400MHz, DMSO d_6) δ/ppm 5.3 (s, 1H, NH), 4.74 (s, 2H, CH_2), 6.79-8.6 (m, 9H, Ar-H). ^{13}CNMR ($CDCl_3$, 75MHz) δ: 43.4(CH_2), 115.7, 116.6, 117.3, 125.8, 126.9, 127.4, 128.3, 128.9, 129.8, 130.6, 131.2, 149.3, 153.3. LC-MS: 311$(M)^+$. Anal. Calcd for $C_{16}H_{12}N_5Cl$: C, 62.04; H, 3.90; N, 22.61. Found: C, 61.95; H, 3.62; N, 22.45 %.

4-(phenoxymethyl)tetrazolo[1,5-*a*]quinoline (3d)

Mp: 260^oC; ^1H NMR (400MHz, DMSO d_6) δ/ppm 5.55 (s, 2H, CH_2), 6.99-8.50 (m, 10H, Ar-H). ^{13}C NMR (100 MHz DMSO-d_6) δ: 67.03(CH_2), 115.44, 117.40, 120.07, 125.80, 127.70, 129.02, 129.49, 130.67, 132.05, 134.7, 144.6, 151.09, 158.03. LC-MS: 277$(M)^+$. Anal. Calcd for $C_{16}H_{12}N_4O$: C, 69.45; H, 4.36; N, 20.28. Found: C, 69.45; H, 4.46; N, 20.14%.

4-((florophenoxy)methyl)tetrazolo[1,5-*a*]quinoline (3e)

Mp: 265°C; ^{1}H NMR (400MHz, DMSO d_6) δ/ppm 5.55 (s, 2H, CH_2), 7.10-8.60 (m, 9H, Ar-H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 68.2 (CH_2), 114.6, 116.7, 117.2, 117.4, 127.3, 128.6, 129.2, 130.1, 131.3, 146.4, 153.5, 155.4, 155.8. LC-MS: 295$(M)^+$. Anal. Calcd for $C_{16}H_{11}N_4OF$: C, 65.30; H, 3.77; N, 19.04. Found: C, 65.25; H, 3.62; N, 18.82%.

4-((chlorophenoxy)methyl)tetrazolo[1,5-*a*]quinoline (3f)

Mp: 234°C; ^{1}H NMR (400MHz, DMSO d_6) δ/ppm 5.56 (s, 2H, CH_2), 6.90-8.60 (m, 9H, Ar-H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 68.4 (CH_2), 117.3, 118.2, 127.3, 127.2, 128.5, 129.4, 129.7, 131.3, 148.7, 153.5, 159.1. LC-MS: 312$(M)^+$. Anal. Calcd for $C_{16}H_{11}N_4OCl$: C, 61.84; H, 3.57; N, 18.03. Found: C, 61.39; H, 3.57; N, 17.95 %.

N-(7-methyltetrazolo[1,5-*a*]quinoline-4-ylmethyl)aniline (3g)

Mp: 242°C; ^{1}H NMR (400 MHz, DMSO d_6) δ/ppm 5.7 (s, 1H, NH), 4.70 (s, 2H, CH_2), 2.543 (S, 3H, CH_3), 6.8-8.514 (m, 9H, Ar-H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 23.5(CH_3), 43.4(CH_2), 114.3, 121.9, 127.1, 127.9, 128.6, 129.3, 129.9, 130.2, 131.2, 137.2, 144.7, 150.4, 151.6. LC-MS: 290$(M)^+$. Anal. Calcd for $C_{17}H_{15}N_5$: C, 70.57; H, 5.23; N, 24.21. Found: C, 70.77; H, 4.98; N, 23.99%.

4-floro-N-(7-methyltetrazolo[1,5-*a*]quinoline-4-ylmethyl)aniline (3h)

Mp: 251°C; ^{1}H NMR (400MHz, DMSO d_6) δ/ppm 5.8 (s, 1H, NH), 4.45 (s, 2H, CH_2), 2.543 (S, 3H, CH_3), 7.28-8.51 (m, 8H, Ar-H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 23.4(CH_3), 43.2(CH_2), 115.4, 119.5, 125.8, 127.2, 127.5, 128.7, 130.1, 131.4, 137.3, 144.3, 148.3, 151.8, 154.6. LC-MS: 308$(M)^+$. Anal. Calcd for $C_{17}H_{14}N_5F$: C, 66.44; H, 4.59; N, 22.79. Found: C, 66.65; H, 4.37; N, 23.53 %.

4-chloro-N-(7-methyltetrazolo[1,5-*a*]quinoline-4-ylmethyl)aniline (3i)

Mp: 235°C; ^{1}H NMR (400MHz, DMSO d_6) δ/ppm 5.8 (s, 1H, NH), 4.43 (s, 2H, CH_2), 2.54 (s, 3H, CH_3), 6.6-8.51 (m, 8H, Ar-H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 23.4(CH_3), 43.2(CH_2), 115.7, 125.4, 126.7, 127.3, 127.6, 128.6, 130.5, 130.6, 131.4, 137.4, 144.2, 149.1, 151.7. LC-MS: 325$(M)^+$. Anal. Calcd for $C_{17}H_{14}N_5Cl$: C, 63.06; H, 4.36; N, 21.63. Found: C, 63.21; H, 4.64; N, 21.43 %.

7-methyl-4-(phenoxymethyl)tetrazolo[1,5-*a*]quinoline (3j)

Mp: 255°C; ^{1}H NMR (400MHz, DMSO d_6) δ/ppm, 5.55 (s, 2H, CH_2), 2.54 (s, 3H, CH_3), 6.99-8.5 (m, 9H, Ar-H).^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 23.2(CH_3), 68.4(CH_2), 115.2, 122.3, 127.2, 127.5, 128.6, 129.5, 130.6, 130.7, 131.5, 137.5, 144.3, 151.8, 157.5 LC-MS: 291$(M)^+$. Anal. Calcd for $C_{17}H_{14}N_4O$: C, 70.33; H, 4.86; N, 19.30. Found: C, 70.45; H, 4.85; N, 19.12 %.

7-methyl-4-((florophenoxy)methyl)tetrazolo[1,5-*a*]quinoline (3k)

Mp: 262°C; ^{1}H NMR (400MHz, DMSO d_6) δ/ppm, 5.54 (s, 2H, CH_2), 2.54 (s, 3H, CH_3), 7.160-8.514 (m, 8H, Ar-H).^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 23.2(CH_3), 68.4(CH_2), 115.8, 117.3, 127.2, 127.5, 128.6, 130.7, 131.5, 137.5, 144.3, 151.8, 155.6, 155.8, 159.3. LC-MS: 309$(M)^+$. Anal. Calcd for $C_{17}H_{13}N_4OF$: C, 66.23; H, 4.25; N, 18.17. Found: C, 66.13; H, 4.12; N, 18.01 %.

7-methyl-4-((chlorophenoxy)methyl)tetrazolo[1,5-*a*]quinoline (3l)

Mp: 230°C; ^{1}H NMR (400MHz, DMSO d_6) δ/ppm, 5.55 (s, 2H, CH_2), 2.543 (s, 3H, CH_3), 6.99-8.514 (m, 8H, Ar-H).^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 23.2(CH_3), 68.4(CH_2), 115.4, 118.2, 127.2, 127.5, 128.6, 130.7, 131.3, 131.5, 137.5, 144.3, 151.8, 158.6. LC-MS: 326$(M)^+$. Anal. Calcd for $C_{17}H_{13}N_4OCl$: C, 62.67; H, 4.03; Cl, 10.92; N, 17.25. Found: C, 62.34; H, 3.85; N, 16.84 %.

N-(7-methoxytetrazolo[1,5-*a*]quinoline-4-ylmethyl)aniline (3m)

Mp: 225°C; ^{1}H NMR (400MHz, DMSO d_6) δ/ppm 5.4 (S, 1H, NH), 4.6 (S, 2H, CH_2), 3.53 (s, 3H, OCH_3), 6.7-7.8 (m, 9H, Ar-H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 43.2(CH_2), 54.9(OCH_3), 106.2, 114.6, 121.3, 121.7, 129.8, 130.2, 130.3, 131.2, 135.7, 142.4, 150.3, 150.7, 158.3. LC-MS: 306$(M)^+$. Anal. Calcd for $C_{17}H_{15}N_5O$: C, 66.87; H, 4.95; N, 22.94. Found: C, 66.51; H, 4.89; N, 22.79%.

4-floro-N-(7-methoxytetrazolo[1,5-*a*]quinoline-4-ylmethyl)aniline (3n)

Mp: 232°C;^{1}H NMR (400MHz, DMSO d_6) δ/ppm 5.4 (s, 1H, NH), 4.5 (s, 2H, CH_2), 3.53 (s, 3H, OCH_3), 6.92-7.8 (m, 8H, Ar-H).^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 43.2(CH_2), 54.9(OCH_3), 106.2, 115.2, 119.4, 121.3, 129.8, 130.2, 131.2, 135.7, 142.4, 148.1, 150.7, 154.5, 158.2. LC-MS: 324$(M)^+$. Anal. Calcd for $C_{17}H_{14}N_5OF$: C, 63.15; H, 4.36; N, 21.66. Found: C, 62.97; H, 4.21; N, 21.35 %.

4-chloro-N-(7-methoxytetrazolo[1,5-*a*]quinoline-4-ylmethyl)aniline (3o)

Mp: 229°C; ^{1}H NMR (400MHz, DMSO d_6) δ/ppm 5.3 (s, 1H, NH), 4.6 (s, 2H, CH_2), 3.53 (s, 3H, OCH_3), 6.5-7.8 (m, 8H, Ar-H).^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 43.2(CH_2), 54.9(OCH_3), 106.2, 115.7, 121.3, 125.8, 129.8, 130.2, 130.6, 131.2, 135.7, 142.4, 149.3, 150.7, 158.3, LC-MS: 389$(M)^+$. Anal. Calcd for $C_{17}H_{14}N_5OCl$: C, 60.0 H, 4.15; N, 20.61. Found: C, 59.65; H, 3.93; N, 20.37 %.

7-methoxy-4-(phenoxymethyl)tetrazolo[1,5-*a*]quinoline (3p)

Mp: 253°C; ^{1}H NMR (400MHz, DMSO d_6) δ/ppm, 5.6 (s, 2H, CH_2), 3.51 (s, 3H, OCH_3), 6.8-7.9(9H, m, Ar-H).^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 54.9(OCH_3), 68.7(CH_2), 106.2, 115.2, 119.4, 121.3, 129.8, 130.2, 131.2, 135.7, 142.4, 148.1, 150.7, 154.5, 158.4. LC-MS: 307$(M)^+$. Anal. Calcd for $C_{17}H_{14}N_4O_2$: C, 66.66; H, 4.61; N, 18.29. Found: C, 66.45; H, 4.49; N, 18.06 %.

7-methoxy-4-((florophenoxy)methyl)tetrazolo[1,5-*a*]quinoline (3q)

Mp: 259^{o}C; ^{1}H NMR (400MHz, DMSO d_6) δ/ppm, 5.5 (s, 2H, CH_2), 3.51 (s, 3H, OCH_3), 7.01-7.9(m, 8H, Ar-H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 54.9(OCH_3), 68.7(CH_2), 158.3, 106.2, 115.2, 121.3, 122.3, 129.8, 130.2, 130.6, 142.4, 131.2, 135.7, 150.7, 159.5. LC-MS: 325$(M)^{+}$. Anal. Calcd for $C_{17}H_{13}N_4O_2F$: C, 62.96; H, 4.04; N, 17.28. Found: C, 62.76; H, 3.89; N, 17.11 %.

7-methoxy-4-((chlorophenoxy)methyl)tetrazolo[1,5-*a*]quinoline (3r)

Mp: 227^{o}C; ^{1}H NMR (400MHz, DMSO d_6) δ/ppm, 5.5(s, 2H, CH_2), 3.51 (s, 3H, OCH_3), 6.7-7.9(m, 8H, Ar-H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 54.9(OCH_3), 68.7(CH_2), 106.2, 115.7, 121.3, 130.2, 125.8, 129.8, 130.6, 131.2, 135.7, 142.4, 149.3, 150.7, 158.3. LC-MS: 342$(M)^{+}$. Anal. Calcd for $C_{17}H_{13}N_4O_2Cl$: C, 59.92; H, 3.85; N, 16.44. Found: C, 59.91; H, 3.75; N, 16.36 %.

Acknowledgements

The authors express their sincere thanks to the Department of Chemistry, S P University for providing research facilities. We are also thankful to Microcare Laboratory, Surat for antimicrobial and antitubercular activity.

References

i. **a)** A. Mohammad, R. Agarwal. Indian J Heterocyclic Chem. 8, 225(1998).
b) C. C. Tzeng, Y. L. Chen,Y. L. Zhao, C. M. Lu & J. P. Wang. Bio Org Med Chem.14, 4373(2006).
ii. **a)** M. A. Abd-Alla, A.H.N. Ahmed, M.F. El-zohry and F.A.Omar. Collection Czechoslovak Chemical Communication. 57,1547-1552(1992).
b) G. Sarkozy. Vet Med Czech. 46,257(2001).
c) R. C. Tripathi, M. Saxena, S. Chandra. Ind J Chem. 34,164-166(1995).
iii. S. C. Kuo et al. J Med Chem. 36,1146-1156(1993).
iv. **a)** N. Hamdi, C. Lidrissi, M. Saoud, A.R. Nievas, H. Zarrouk. Chem Hetero Comp. 42(3),320-325(2006).
b) H. Lee, S. Hong, S. Yang et al. Arch Pharm Res. 23,450-454(2000).
v. **a)** A. R. Gholap, K. S. Toti, F. Shirazi, R. Kumari, M. K. Bhat , M. V. Deshpande, K. V.Srinivasan. Bioorg Med Chem.15, 6705-6715(2007).
b) R.G. Ridley. Nature. 415, 686(2002).
vi. H.S. Fazlul, A. Shreelekha, B. Vivek, A.Fakhara & P.Subhash. J Med Chem.49, 7242(2006).
vii. T.Suresh, R. Kumar, S. Magesh et al. Ind J Chem. 42, 2133-2135(2003).
viii. K. Suresh, B. Sandhya, G. Himanshu. Mini Rev Med Chem. 9,1648-1654(2009)
ix. H. Cheon, H. Kim, S. Kim. Arzneimittel-Forschung. 48,1168-1171(1998)
x. A. Bekhit, H.T.Fahmy. Pharm. Med. Chem, Weinheim.336(2), 111-118(2003).
xi. D.C. Mungra, M. P. Patel, R.G. Patel. General Papers.14,64-74(2009).
xii. C. Benard, F. Zouhiri, M. Normand, M. Danet, D. Desmaele, H. Leh. Bioorg Med Chem Lett. 14,2473-2476(2004).
xiii. V. L. Dalla, V. Gasparotto, M. G. Ferlin. Eur J Med Chem. 43(2),429-434(2008).
xiv. R. Gupta, M. Gupta, S. Paul. Ind J Chem. 42B Apr, 475-481(2010).
xv. Z. Zie, K.Y. Chai, H. Piao, K. Kwak, Z. Quan. Bioorg Med Chem Lett.15,4803-

4805(2005).
xvi. R. Gupta, A. K. Gupta, S. Paul. Ind. J. Chem. 39B, 847(2000).
xvii. A. Mukharjee, M. S. Akhtar, V. L. Sharma, M. Seth, A. P. Bhadur, A. Agnihotri, V. P. Mehtrotrapk and Kamboj. J Med Chem 32, 2297(1989).
xviii. A.D.Barry . US Patent. 3,764-681(1973).
xix. A. B. Adhan, A. E. Ola, A. Elsayed, Y. P. Ji . European J Med Chem. 39,249-255(2004).
xx. T. Sambaiah, A. Ankush, S. Rajinder, H.L.Henty and H. Peiyong. US Patent. 7,358-259(2008).
xxi. A. H. Kategaonkar, R. U. Pokalwar, S. S. Sonar, V. U. Gawali. Eur J Med Chem. 45,1128-1132(2010).
xxii. S. Bawa, S. Kumar. Ind J Chem. 48B, 142-145(2009).
xxiii. A. A. Bekhit, A. K. Talal, Al-Allaf, Aboul-Enein, M. Kunhi, S.M. Pulicat, K. Hussain. Eur J Med Chem. 39, 499-505(2004).
xxiv. R. M. Srivastava, R. A. W. N. Filho, C. A. Silva, A. Bortoluzzi. Ultrason. Sonochem.16,737(2009).
xxv. A. Duarte, W. Cunico, C. M. P. Pereira, A. F. C. Flores, R. A. Freitag, G. M. Siqueira. Ultrason.Sonochem. 17,281(2010)
xxvi. H. A. Stefani, C. M. P. Pereira, R. B. Almeida, R. C. Braga, K. P. Guzenb, R. Cella. Tetrahedron Lett. 46, 6833(2005).
xxvii. G. Cravotto, V.V. Fokin, D. Garella, A. Binello, L. Boffa, A. Barge. J. Comb. Chem.12, 13(2010).
xxviii. G. Cravotto, P. Cintas. Chem. Soc. Rev. 35, 180(2006).
xxix. L. Pizzuti, P.L.G. Martins, B.A. Ribeiro, F.H. Quina, E. Pinto A.F.C. Flores, V.D. Pereira, C.M.P. Ultrason. Sonochem. 17, 34(2010).
xxx. Z. Fu, H.Shao. Ultrason. Sonochem.18, 520(2011).
xxxi. Q. Liu, H. Ai, Z. Li. Ultrason. Sonochem.18, 477(2011).
xxxii. N.K. Ladani, M.P. Patel, R.G. Patel. Arkivoc. 2,292(2009).
xxxiii. D.C. Mungra. European journal of medicinal chemistry. 46.9,4192- 4200(2011).
xxxiv. G.G. Ladani, and M.P. Patel. New Journal of Chemistry. 39.12,9848- 9857(2015).
xxxv. NCCLS (National Committee for Clinical Laboratory Stan-dards), Performance Standards for Antimicrobial Susceptibility Testing: Twelfth Informational Supplement, ISBN 1-56238-454-6 M100-S12 (M7)(2002).
xxxvi. H. H. Jardosh and M. P. Patel. Eur. J. Med. Chem. 65,348–359(2013).
xxxvii. H. G. Kathrotiya and M. P. Patel. Eur. J. Med. Chem. 63, 675–684(2013).
xxxviii. A. Rattan, Antimicrobials in Laboratory Medicine, B.I. Churchill, Livingstone, New Delhi. 85–108 (2000).

Received on April 1, 2016.