Heterocyclic Letters
Vol. 8| No.1|95-104|Nov-Jan |2018
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

SYNTHESIS, CHARACTERIZATION AND BIOLOGICALEVALUATION OF SOME NEW ACRIDINE DERIVATIVES

Shankar Hangirgekar*, Shankar Phulwale

Department of chemistry, Shivaji University ,
Kolhapur-641006, Maharastra.
Email: hangirgekarshankar@gmail.com

Abstract
A simple, efficient and cost-effective method for the synthesis of 3, 4-dihydro-3, 3-dimethyl-9-phenylacridine-1*(2H, 9H,10H)*-one by a one-pot three component cyclo condensation of dimedone, substituted aldehydes and substituted aniline in the presence of polyethylene glycol has been developed in present work. 10 novel 3, 4-dihydro-3, 3-dimethyl-9-phenylacridine-1*(2H, 9H, 10H)*-one derivatives have been synthesized. The chemical structures were assigned by means of spectral analysis such as FT-IR, ^{1}H NMR, MS etc. Synthesized compounds were screened for in vitro antibacterial and antifungal activity against *S. aureus, E. coli, P. Aeruginosa,B. Subtilis, Protease vulgaris, Klebsieallapneumonia,Candidaalbicans*and *Candida krusei*respectively. In antifungal activity, compounds-10 showed more potent activity against *Candida albicans*and*Candida krusei.*

Keywords:
3, 4-dihydro-3, 3-dimethyl-9-phenylacridine-1*(2H, 9H, 10H)*-one, antibacterial activity, antifungal activity, multicomponent reaction.

Introduction:

Multicomponent reactions (MCRs) have emerged as efficient and powerful strategies in the modern synthetic organic chemistry because synthesis of complex organic molecules from simple and readily available substrates can be achieved in a very fast and efficient manner without the isolation of any intermediates.[I]MCRs contribute to the requirements of an environment friendly process by reducing the number of synthetic steps, energy consumption and waste production.Therefore, developing new MCRs and improvement of known MCRs are popular areas of research in the current synthetic organic chemistry.[II]Research groups have shown antimicrobial activity of different acridine analogs.[III]Acridines are an important class of organic compounds which find use as dyes, fluorescent materials for visualization of

biomolecules, and in laser technology due to their useful spectroscopic properties.[IV]Acridines have also received significant attention from many pharmaceutical and organic chemists, essentially because of the broad spectrum of their biological properties, such as:[V]antibacterial,[VI]anticancer,[VII] antifungal,[VIII]antimalerial[IX]and anti-inflammatory[X]antiproliferative[XI]antileishmanial[XII]activity.There are a few reports in the literature on the three-component Hantzsch-type condensation of aromatic aldehydes, anilines and dimedone via the traditionalorganic solventsunder microwave irradiation and in ionic liquidsleading to acridines. The main drawback of these methods is the inability[XIII] to synthesize 9-aryl-hexahydroacridine- 1, 8-diones, therefore, the development of simple, efficient, high-yielding and environment friendly methods and use of simple, readily available, recyclable, new heterogeneous catalysts for the preparation of acridines under mild conditions isindemand.[XIV]
These findings prompted us to prepare some new acridine derivatives and screen them for their antibacterial activity.[XV] By knowing the chemical and pharmacological importances of acridne derivative it was planned to synthesize some novel acridne derivative under the frame of green chemistry.[XVI] In recent years, polyethylene glycol prompted reactions have attracted the attention of organic chemists due to their solvating ability and aptitude to act as a phase transfer catalyst, negligible vapor pressure and easy recyclability, ease of work-up, eco-friendly nature and economical cost.[XVII]polyethylene glycol is non-halogenated, inexpensive potentially recyclable and water soluble which facilitate its removal from reaction product.

Experimental:

2.1 Material

The chemicals were purchased from Merck, SD fine and Himedia. The yields refer to the isolated products. The products were characterized by their physical constants, comparison with authentic samples and IR and NMR spectroscopy. The purity determination of the substrate and the reaction monitoring were accomplished by TLC silica gel 60 on Aluminium sheets.

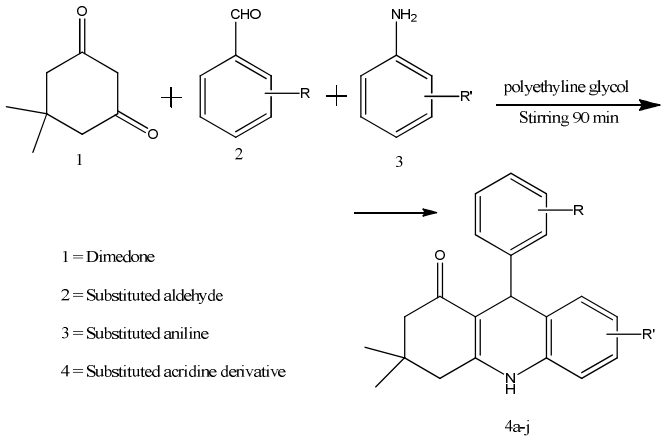
2.2 Instrumentation

FT-IR spectrawere run on an AFFINITY-1, Shimadzu Corporation, Kyoto, Japan.^{1}H NMR (400 MHz) spectra were run on aBRUKER AVANCE II 400 NMR spectrometerin DMSOd6 using TMS as a reference (ð in ppm).Mass Spectrophotometer Micromass Q-TOF Massspectrometer (LC-MS). The melting points were recorded on a DBK Programmed Melting Point Apparatus WadegatiLabequipPvt. Ltd. Mumbai, India.

2.3 General method for the preparation of substituted 3, 3-dimethyl-9-(substitutedphenyl)-3, 4, 9, 10-tetrahydro acridine-*(2H)*-one derivatives

The mixture of 5, 5-dimethylcyclohexane-1, 3-dione (1mmol), substituted aldehyde, (1mmol) and substituted aniline (1mmol) were added in polyethylene glycol and stirred for 90 min. The resulting mixture was stirred at 90 min. After completion of reaction (monitored by TLC), reaction mixture was poured in ice and neutralised with dilute Hcl. The product wasseparated by using whatmannpaper.Crude product was further purified by crystallisation from hot ethanol. The product was confirmed by melting point, IR, ^{1}H NMR and Mass spectrometer. The mobile phase used for thin layer chromatography was pet ether: ethyl acetate: methanol (1:1:0.25 v/v).[XVIII]

2.4 Reaction



Compound 4a 6, 8-dichloro-3, 4-dihydro-3, 3-dimethyl-9(nitrophenyl)acridin-1-(2H, 9H, 10H)-one;IR (KBr); v cm^{-1} 3088 (N-H Stretching), 3030 (Ar-stretching), 2958 (-CH_3stretching),1718(C=O Stretching), 1527 (-NO_2 Stretching), 1449 (C=C Stretching), 731(C-Cl Stretching); The ^{1}H NMR (DMSO) ðppm; 11.88 (S, 1H, N-H), 8.07 (d, 2H, Ar-H, J= 9.75), 7.48 (d, 2H, Ar-H, J= 5.2), 7.46 (S, 1H, Ar-H), 6.51 (S, 1H, Ar-H), 5.56 (S, 1H, C-H), 2.45 (q, 4H, CH_2, J= 14.28), 1.14 (S, 6H, CH_3); Mass Spectrum shows the formation of molecular ion peak at m/z = 417.1. The reaction provided 58 % yield.The mobile phase used forthin layer chromatography was pet ether: ethyl acetate: methanol (1:1:0.25 v/v).

Compound 4b 7-chloro-3, 4-dihydro-3, 3-dimethyl-6-nitro-9-(4-nitrophenyl)acridine-1(2H, 9H, 10H)-one;IR (KBr); v cm^{-1} 3090 (N-H Stretching), 3040 (Ar-stretching), 2956 (-CH_3stretching), 1718 (C=O Stretching), 1533 (-NO_2 Stretching), 1517 (C=C Stretching), 736 (C-Cl Stretching); The ^{1}H NMR (DMSO) ðppm; 8.35 (d, 2H, Ar-H, J= 11.05), 7.92 (d, 2H, Ar-H, J= 15), 7.36 (S, 1H, Ar-H), 6.81 (S, 1H, Ar-H), 5.56 (S, 1H, C-H), 2.44 (q, 4H, CH_2, J= 17.8), 1.13 (S, 6H, CH_3); Mass Spectrum shows the formation of molecular ion peak at m/z = 427.1. The reaction provided 55 % yield.The mobile phase used forthin layer chromatography was pet ether: ethyl acetate: methanol (1:1:0.25 v/v).

Compound 4c 8, 9-dihydro-2, 8, 8-trimethyl-5-(4-nitrophenyl)benzo[1, 8]naphthyridin-6(5H, 7H, *10H)*-one;IR (KBr); v cm^{-1} 3076 (N-H Stretching), 2958 (CH_3stretching),1718 (C=O Stretching), 1527 (-NO_2 Stretching), 1471 (C=C Stretching); The ^{1}H NMR (DMSO) ðppm; of 11.88 (S, 1H, N-H), 8.07 (d, 2H, Ar-H, J= 1.3), 8.03 (S, 1H, Ar-H), 7.43 (d, 2H, Ar-H, J= 9.75), 7.14 (S, 1H, Ar-H), 5.57 (S, 1H, C-H), 2.43 (q, 4H, CH_2 ,J= 24.6), 1.79 (S, 3H, CH_3), 1.14 (S, 6H, CH_3); Mass Spectrum shows the formation of molecular ion peak at m/z = 364.2. The reaction provided 50 % yield.The mobile phase used forthin layer chromatography was pet ether: ethyl acetate: methanol (1:1:0.25 v/v).

Compound-4d 9-(4-chlorophenyl)-3, 3-dimethyl-6-nitroacridin-1(2H, 9H, 10H)-One: IR (KBr); v cm^{-1}3078 (N-H Stretching), 3032 (Ar-stretching), 2956 (-CH_3stretching),1718 (C=O Stretching), 1527 (-NO_2 Stretching), 1489 (C=C Stretching), 721(C-Cl Stretching); The^{1}HNMR (DMSO) ðppm; 11.88 (S, 1H, N-H), 8.00 (S, 1H, Ar-H), 7.36 (S, 1H, Ar-H), 7.28 (d, 2H, Ar-H, J= 11.15), 7.04 (d, 2H, Ar-H, J= 10.4), 7.02 (S, 1H, Ar-H), 5.49 (S, 1H, C-H), 2.39 (q, 4H, CH_2, J= 40.5), 1.12 (S, 6H, CH_3); Mass Spectrum shows the formation of molecular ion peak at m/z = 383.0. The reaction provided 67 % yield. The mobile phase used forthin layer chromatography was pet ether: ethyl acetate: methanol (1:1:0.25 v/v).

Compound-4e3, 4-dihydro-3, 3-dimethyl-6-nitro-9-(3-nitrophenyl)acridin-1(2H, 9H, 10H)-one: IR (KBr); v cm^{-1}3088 (N-H Stretching), 3039 (Ar-stretching), 2960 (-CH_3stretching),1718 (C=O Stretching), 1525 (-NO_2 Stretching), 1469 (C=C Stretching)The ^{1}HNMR (DMSO) ðppm; of 11.88 (S, 1H, N-H), 8.41 (S, 1H, Ar-H), 8.39 (S, 1H,; Ar-H), 7.60 (d, 2H, Ar-H, J= 9.9), 7.56 (d, 2H, Ar-H, J= 9.7), 7.46 (S, 1H, Ar-H), 5.56 (S, 1H, C-H), 2.40 (q, 4H, CH_2, J= 19.8), 1.14 (S, 6H, CH_3); Mass Spectrum shows the formation of molecular ion peak at m/z = 393.2. The reaction provided 45 % yield.The mobile phase used forthin layer chromatography was pet ether: ethyl acetate: methanol (1:1:0.25 v/v).

Compound-4f5, 8-dichloro-9-(4-chlorophenyl)-3, 4-dihydro-3, 3-dimethylacridin-1(2H, 9H, 10H)-one;IR (KBr); v cm^{-1} 3078 (N-H Stretching), 2956 (Ar-Strech)2926 (-CH_3 stretching), 1718 (C=O Stretching), 1449 (C=C Stretching), 788 (C-Cl Stretching); The ^{1}HNMR (DMSO) ðppm; 8.07 (d, 2H, Ar-H, J= 47.6), 6.76 (S, 1H, Ar-H), 6.65 (S, 1H, Ar-H), 5.56 (S, 1H, C-H), 2.45 (q, 4H, CH_2, J= 12.6), 1.11 (S, 6H, CH_3); Mass Spectrum shows the formation of molecular ion peak at m/z = 407.8. The reaction provided 62 % yield.The mobile phase used forthin layer chromatography was pet ether: ethyl acetate: methanol (1:1:0.25 v/v).

Compound-4g 5, 8-dichloro-3, 4-dihydro-3, 3-dimethyl-9-(3-nitrophenyl)acridin-1-(2H, 9H, 10H)-one:IR (KBr); v cm^{-1} 3080 (N-H Stretching), 2956 (-CH_3stretching),1718 (C=O Stretching), 1527 (-NO_2 Stretching), 1500 (C=C Stretching), 732 (C-Cl Stretching); The ^{1}H NMR (DMSO) ðppm; 11.88 (S, 1H, N-H), 8.11 (d, 2H, Ar-H, J= 9.75), 7.58 (S, 1H, Ar-H), 7.17 (S, 1H, Ar-H),6.76 (S, 1H, Ar-H),6.66 (S, 1H, Ar-H), 5.56 (S, 1H, C-H), 2.45 (q, 4H, CH_2, J= 17.6), 1.14 (S, 6H, CH_3); Mass Spectrum shows the formation of molecular ion peak at m/z = 417.1. The reaction provided 56 % yield.The mobile phase used forthin layer chromatography was pet ether: ethyl acetate:methanol (1:1:0.25 v/v). The mobile phase used forthin layer chromatography was pet ether: ethyl acetate: methanol (1:1:0.25 v/v).

Compound-4h 5-(4-chlorophenyl)-8, 9-dihydro-2, 8, 8-trimethylbenzo [b] [1, 8]naphtha-ridin-6(5H, 7H, 10H)-one:IR (KBr); v cm^{-1} 3030 (Ar-H Stretching), 2956 (-CH_3 stretching), 1714 (C=O Stretching), 1489 (C=C Stretching), 721 (C-Cl Stretching); The ^{1}H NMR (DMSO)ðppm; 11.88 (S, 1H, N-H),7.58 (S, 1H, Ar-H), 7.25 (d, 2H, Ar-H, J= 12.5), 7.04 (d, 2H, Ar-H, J= 9.75), 6.900 (S, 1H, Ar-H), 5.50 (S, 1H, C-H), 2.40 (q, 4H, CH_2, J= 11.2), 1.54 (S, 3H, CH_2), 1.11 (S, 6H, CH_3); Mass Spectrum shows the formation of molecular ion peak at m/z = 352.1. The reaction provided 52 % yield.The mobile phase used forthin layer chromatography was pet ether: ethyl acetate: methanol (1:1:0.25 v/v).

Compound-4i6, 7-dihloro-3, 4-dihydro-3, 3-dimethyl-9-(3-nitrophenyl)acridine-1*(2H, 9H, 10H)*-one:IR (KBr); v cm^{-1} 3076 (N-H Stretching), 2958 (-CH_3stretching), 1718 (C=O Stretching), 1529 (-NO_2 Stretching), 1498 (C=C Stretching), 732 (C-Cl Stretching); The reaction provided 47 % yield. The mobile phase used forthin layer chromatography was pet ether: ethyl acetate: methanol (1:1:0.25 v/v).

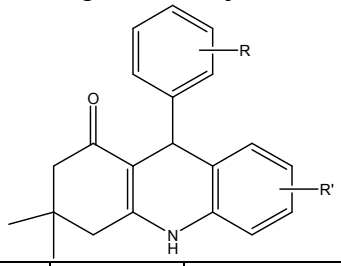
Compound-4j: 3,4-dihydro-3,3-dimethyl-6-nitro-9(4-nitrophenyl)acridine-1*(2H, 9H, 10H)*-one: IR (KBr); v cm^{-1} 3076 (Ar-H Stretching), 2958 (-CH_3 stretching), 1718 (C=O Stretching), 1525 (-NO_2 Stretching), 1490 (C=C Stretching); The reaction 1718 (C=O Stretching), 1525 (-NO_2 Stretching), 1490 (C=C Stretching); The reaction provided 61 % yield. The mobile phase used forthin layer chromatography was pet ether: ethyl acetate: methanol (1:1:0.25 v/v).

2.5 Results and Discussion

2.5.1 Chemistry

The general procedure for the synthesis of compounds **1-3**and the compound substituted 3, 3-dimethyl-9-(substitutedphenyl)-3, 4, 9, 10-tetrahydro acridine-*(2H)*-one was prepared from the Claisen-Schimidt reaction. Firstly base abstract acidic proton of dimedone to carbanion formed on carbonyl carbon of substituted aldehyde to formed ά, β, unsaturated system by means of Claisen-Schimidt reaction. This intermediate formed, ά, β, unsaturated compound react with substituted aniline by Michacel addition followed aromatization to form desired product. The yields of synthesized compounds were found to be in range of 35-65 % and the characterization was done by melting point and TLC. Characteristic IR bands show several functional vibration modes, which confirm by structure of synthesized compounds, some structures were also confirmed by IR, ^{1}H NMR and MASS spectral studies. The reaction sequence is outlined in **Scheme 1.** Physicochemical data of compounds-**4a-j**are summarized in Table 1. The formation of compound-**4a**is confirmed from the spectroscopic and physicochemical data observed as the vibrational modes in IR spectrum (cm^{-1}) showed N-H Stretching at 3088, Ar-stretching at 3030, CH_3 stretching at 2958, C=O Stretching at 1718, NO_2 Stretching at 1527, C=C Stretching at 1449 , C-Cl Stretching at 731. Then ^{1}H NMR (DMSO) spectrum displayed ðppm at 11.88 for 1H of N-H at C-10 position, 8.07 for 2H of Ar-H at C-11 and C15 position, J= 9.75 Hz, 7.48 for 2H of Ar-H at C-12 and C-14 position, J= 5.2 Hz , 7.46 for 1H of Ar-H at C-5 position of acridine nucleus, 5.56 for 1H of C-H at C-9 position of acridine nucleus, 2.45 for the 4H of CH_2 group of cyclohexanone ring at C-2 and C-4 position, J= 14.28, 1.14 for 6H of two methyl group at C-3 of cyclohexanone ring. Mass Spectrum shows the formation of molecular ion peak at m/z = 417. Which is equal to the calculated molecular weight and hence compound **4a** is confirmed. The yield of compound was found to be 58%.

Table-1 Physicochemical data of the compounds-4a-j



Compound code	R	R'	Time (min)	Yields (%)	M. F	M. W	Rf value	M.P (^{o}C)
4a	4-NO_2	6-CL 8-CL	90	58	$C_{21}H_{18}Cl_2N_2O_3$	417.23	2.5	240
4b	4-NO_2	7-CL 6- NO_2	120	55	$C_{21}H_{18}ClN3O5$	427.89	2.4	267
4c	4-NO_2	7-CH_3	90	50	$C_{21}H_{21}N_3O_3$	363.76	3.2	198
4d	4-Cl	6-NO_2	120	67	$C_{21}H_{19}ClN_2O_3$	382.76	3.6	310
4e	3-NO_2	6-NO_2	90	45	$C_{21}H_{19}N_3O_5$	393.65	2.5	290

4f	4-Cl	5-Cl 8-Cl	90	62	$C_{21}H_{18}Cl_3NO$	406.32	2.1	298
4g	3-NO_2	5-Cl 8-Cl	150	56	$C_{21}H_{18}Cl_2N_2O_3$	417.43	1.2	210
4h	4-Cl	6-CH_3	140	52	$C_{21}H_{21}ClN_2O$	352.45	1.2	204
4i	3-NO_2	6-Cl 7-Cl	90	52	$C_{21}H_{18}Cl_2N_2O_3$	417.32	1.6	189
4j	4-NO_2	6-NO_2	120	61	$C_{21}H_{19}N_3O_5$	393.54	0.5	214

3. Biological activities

3.1 Antibacterial activity

Antibacterial activity of the synthesized compounds wasdetermined by the disc diffusion method against *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumonia, Protease vulgaris, Salmonella typhi*and *Staphylococcus aureus*at 100µg/ml concentration.The bacteria were subcultured on nutrient agar medium. Thepetridishes were incubated at 37ºC for 24hr. Streptomycin (100 µg/disc) were used as standards. The results are presented in Table2

Table 2.Antibacterial data of the synthesized compounds

Compound code	**Zone of inhibition (mm)**					
	E. coli	***P. aeruginosa***	***B. subtilis***	***S. aureus***	***K. pneumonia***	***P. vulgaris***
4a	24	23	19	23	18	18
4b	26	18	21	21	27	24
4c	25	20	20	19	24	22
4d	22	22	-ve	21	17	23
4e	22	20	30	21	23	20
4f	24	-ve	21	23	24	24
4g	22	19	-ve	21	18	22
4h	21	20	30	24	25	-ve
4i	-ve	18	-ve	-ve	20	22
4j	19	22	22	23	23	-ve
DMSO (controller)	-ve	17	16	16	18	-ve
Streptomycin-(Standard)	27	26	30	21	30	20

3.1.1 Graphical representation of antibacterial activity (compound-4a-j)

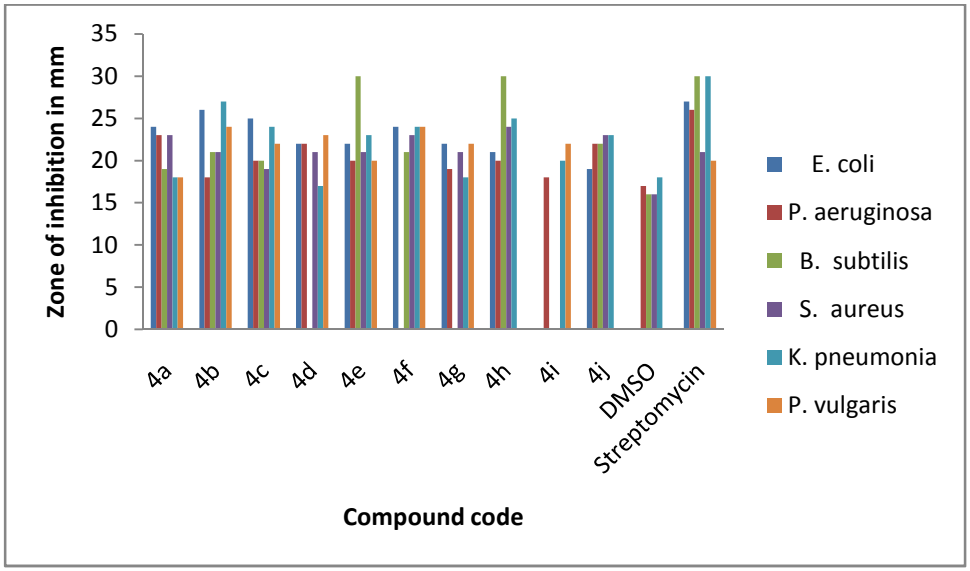


Fig.No. 1 Comparison of antibacterial activity of substituted 3, 3-dimethyl-9-(substi-tutedphenyl) 3, 4, 9, 10-tetrahydroacridine-1*(2H)*-one derivatives.

3.2 Antifungal activity

Antifungal activity of the synthesized compounds was determined by the poison plate method against*Candida albicans, Candida krusei* at 100µg/ml concentration. The fungi were subcultured on potato dextrose agar. Thepetridishes were incubated at 28ºC for 24hr. Gresiofulvin(100 µg/disc) were used as standards. The results are presented in Table 3

Table 3.Antifungal data of the synthesized compounds.

Compound Code	**Zone of Inhibition in millimetre (mm)**	
	Candida albicans	***Candida krusei***
4a	21mm	24mm
4b	-ve	23mm
4c	-ve	25mm
4d	27mm	20mm
4e	28mm	22mm
4f	27mm	21mm
4g	22mm	22mm
4h	20mm	27mm

4i	23mm	22mm
4j	22mm	26mm
DMSO (Controller)	20mm	20mm
Gresiofulvin	25mm	21mm

3.2.1 Graphical representation of antibacterial activity

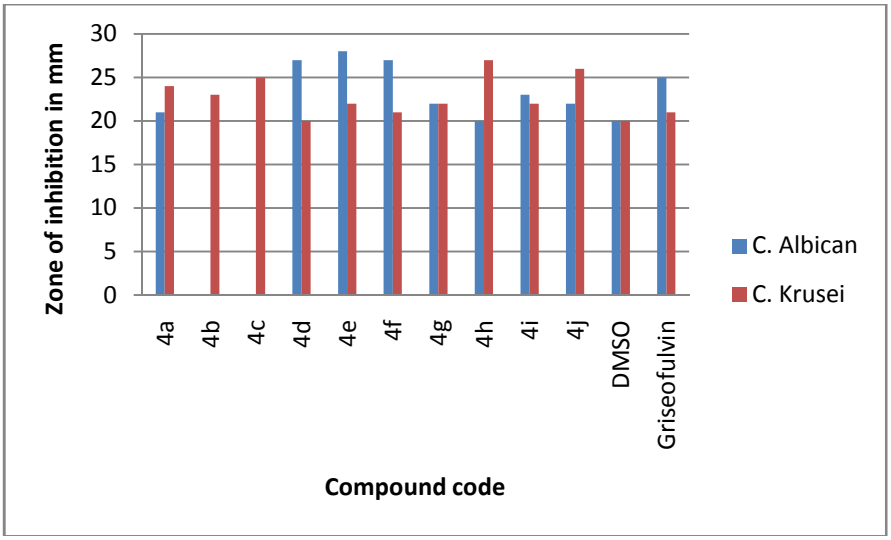


Fig. No. 2 Comparison of antifungal activity of substituted 3, 3-dimethyl-9-(substitut-edphenyl) 3, 4, 9, 10-tetrahydroacridine-1*(2H)*-one derivatives

3.3 Result and Discussion

The antibacterial activities of synthesized compounds were evaluated against*Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, P. vulgaris. K. pneumonia*and *Bacillus subtilis* using disc diffusion method and results are shown in Table no. 8.1.5 and zone of inhibition in mm. Streptomycin was used as standard for synthesised compounds.

The compound-**4a**(23mm) showed more potent activity against *Staphylococcusaureus*where as showed equipotent activity (24mm and 23mm)against *Escherichia coli* and *Pseudomonas aeruginosa* and weaker activityagainst*P. Vulgaris*. Compound-**4a** (19mm and 18mm) showed low activity against*Bacillus subtilis* and*K.pneumonia* as compared to standard streptomycin-(27mm, 26mm, 30mm, 21mm,30mm and 20mm).

The compound-**4b**(24mm) showed more potent activity against *P. vulgaris* where as showed equipotent activity (26mm and 21mm) against *Escherichia coli* and *Staphylococcus aureus*and showed weaker activity (27mm) against*K. Pneumonia*. Compound-**4b** (18mm and 21mm) showed low activity against*Pseudomonas aeruginosa* and*Bacillus subtilis* as compared to standard streptomycin-(27mm, 26mm, 30mm, 21mm, 30mm and 20mm).The compound-**4c**(22mm) showed more potent activity against *P. vulgaris* where as showed weaker activity (25mm, 20mm, 19mm, and 24 mm) against*Escherichia coli, Pseudomonas*

*aeruginosa,Staphylococcus aureus*and *K. Pneumonia* respectively. Compound-**4c** (20mm) showed low activity against*Bacillus subtilis* as compared tostandard streptomycin-(27mm, 26mm, 30mm, 21mm, 30mm and 20mm).

The compound-**4d**(23mm) showed more potent activity against *P. vulgaris* where as showed equipotent activity (21mm) against *Staphylococcus aureus*and showed weaker activity (22mm, 22mm, and 17mm)against*Escherichia coli, Pseudomonas aeruginosa andK. Pneumonia* respectively. Compound-**4d** showed no activity against*Bacillus subtilis* as compared to standard streptomycin-(27mm, 26mm, 30mm, 21mm, 30mm and 20mm). The compound-**4e**(30mm, 21mm, and 20mm)showed equipotent activity against*Bacillus subtilis,Staphylococcus aureus*and*P. vulgaris*where as showed weaker activity (22mm, 20mm, and 23mm)against*Escherichia coli, Pseudomonas aeruginosa andK. Pneumonia* as compared to standard streptomycin-(27mm, 26mm, 30mm, 21mm, 30mm and 20mm).

The compound-**4f**(24mm and 23mm) showed more potent activity against *P. vulgaris* and *Staphylococcus aureus* and showed weaker activity (24mm, 21mm and 24mm) against*Escherichia coli, Pseudomonas aeruginosa*and*Bacillus subtilis.* Compound-**4f** showed no activity against*K. Pneumonia* as compared to standardstreptomycin-(27mm, 26mm, 30mm, 21mm, 30mm and 20mm).

The compound-**4g**(22mm) showed more potent activity against *P. vulgaris* where as showed equipotent activity (21mm)against *Staphylococcus aureus*where as showed weaker activity (22mm, 19mm, and 18mm)against*Escherichia coli, Pseudomonas aeruginosa andK. Pneumonia.* Compound-**4g** showed no activity against*Bacillussubtilis* as compared to standard streptomycin-(27mm, 26mm, 30mm, 21mm, 30mm and 20mm).

The compound-**4h**(24) showed more potent activity against*Staphylococcus aureus*where as showed equipotent activity (30mm)against*Bacillus subtilis* and showed weaker activity (21mm, 20mm, and 25mm) against*Escherichia coli, Pseudomonas aeruginosa andK. Pneumonia* respectively. Compound-**4g** showed no activity against*P. vulgaris* as compared to standard streptomycin-(27mm, 26mm, 30mm, 21mm, 30mm and 20mm).

The compound-**4i**(24) showed more potent activity against*P. vulgaris* where as showed weaker activity (18mm and 20mm)against*Pseudomonas aeruginosa andK. Pneumonia* and showed no activity against*Escherichia coli,Bacillus subtilis* and *Staphylococcus aureus*as compared to standard streptomycin-(27mm, 26mm, 30mm, 21mm, 30mm and 20mm).

The compound-**4j**(23) showed more potent activity against*Staphylococcus aureus*where as showed weaker activity (19mm, 22mm, 22mm and 23mm)against*Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis* and *K. Pneumonia* respectively. Compound-**4j** showed no activity against*P. vulgaris* as compared tostandard streptomycin-(27mm, 26mm, 30mm, 21mm, 30mm and 20mm).

The antifungal activities of synthesized compounds were evaluated against*Candida krusei* and *Candida albicans*using poison plate method and results are shown in table no. 8.2.7 and zone of inhibition (in mm). Gresiofulvin was used as standard forsynthesized compound.

The compound-**4e** (28mm and 22mm) showed more potent activity against*Candida krusei*and *Candida albicans* amongst all synthesized compounds. The compound-**4f**(21mm) showed equipotent activity against *Candida krusei* and compound-**4d** (20mm)showed weaker activity against *Candida krusei* but compound **4b** and **4c** showed no activity against*Candida albicans*as compared to standard *Gresiofulvin*-(25mm and 21mm).

Acknowledgement

Author is thankful to School of Pharmacy, SRTM University Nanded for providing necessary facilities for theresearch work.

Referance

I. R. G. VagheiandS.M. Malaekehpoor,J. Iran. Chem. Soc.7, 957(2010).
II. D.J.Ramon and M.Yus, Angew. Chem., Int. Ed.44, 1602 (2005).
III. I. Gazi, G.E. Bahrim, R. DinicaandM.Demeunynck,Roumanian Biotechnological Letters. 13,87 (2008).
IV. M.N. Esfahani, M. Montazerozohori,T.Abdizadeh,C. R. Chimie, 18, 547(2015).
V. El S. H. Ashry, L.F. Awada, El S.I. Ibrahim and O.Kh. Bdeewy, ARKIVOC. (ii), 178(2006).
VI. B.M. Shaikh, S.G. Konda, A.V. Mehare, G.G.Mandawad,S.S.ChobeandB.S. Dawane, Der PharmaChemica. 2(4) , 25(2010).
VII. G. Cholewiñski, K. Dzierzbicka, and A.M.Koodziejczyk,Pharmacological reports. 63,305(2011).
VIII. B.B. Patel, R.G. Patel and M.P. Patel,J. Serb. Chem. Soc.71 (10), 1015(2006).
IX. A.F.C. Valdés, The Open Medicinal Chemistry Journal. 5, 11(2011).
X. Y.L.Chen,I.Li. Chen, C.M. Lu, C.C. Tzeng, Lo.Ti.Tsao and J.P.Wang, Bioorganic & Medicinal Chemistry.11, 3921(2003).
XI. R. Ferreira, A. Aviñó, S.Mazzini and R.Eritja, Molecules,17, 7067(2012).
XII. N. Chauhan, A.S. Vidyarthi and R.Poddar, IJIRSET.2, 11(2013).
XIII. S. SudhaandM.A. Pasha, The ScientificWorld Journal, 2013,1(2013).
XIV. F. Farhadi,IJISET, 1,10 (2014).
XV. I. Gazi, G.E. Bahrim, R.Dinica and M.Demeunynck,Roumanian Biotechnological Letters,13, 87 (2008).
XVI. M. Himaja, D. Poppy and K.Asif, IJRAP. 2(4),1079(2011).
XVII. R. Tayebee, M. Jomei, B. Maleki, M. Razi, H.Veisi and M. Bakherad, Journal of Molecular Liquids, 206, 119(2015).
XVIII. A. Rajendran,C. Karthikeyan, S. Ramu and D.Ragupathy, Journal of Advanced Chemical Sciences , 1(2), 49(2015).

Received on January 8, 2018.