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# One-pot multicomponent synthesis and antibacterial evaluation of some novel acridine derivatives

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**Abstract**

*In the present communication a simple and efficient synthesis of some new acridines are described by the one-pot condensation of 3, 4, 9, 10-tetrahydroacridine-1(2H)-one, substituted aldehyde and liquior ammonia in alkaline polyethylene glycol (PEG-400) as green reaction solvent. The newly synthesized products were evaluated for their antibacterial and antifungal activity*

**Key words:** Polyethylene glycol (PEG-400), 3,4,9,10-tetrahydroacridine-1(2H)-one, substituted aldehyde, antimicrobial activity.

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## INTRODUCTION

Acridine derivatives have occupied a unique position in medicinal chemistry due to their biological activities like antitumor[1] anti-malerial[2], DNA-binding and DNA photo-damaging ability[3], antileishmanial activities[4], Antimicrobial activity[5] Most of the acridine derivatives are also used in the pigments and dyes[6-7]. These findings prompted us to prepare some new acridine derivatives and screen them for their antibacterial activity. 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. In recent years, polyethylene glycol (PEG-400) prompted reactions[8-11] 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. PEG is non-toxic, non-halogenated, inexpensive potentially recyclable and water soluble which facilitate its removal from reaction product.

## MATERIALS AND METHODS

Melting points were uncorrected determined in an open capillary tube. The purity of the products was checked by TLC on pre-coated sheets of silica gel of 0.25 mm thickness. IR spectra were recorded (KBr $cm^{-1}$) on FTIR shimadzu spectrometer. $^1H$ NMR spectra were recorded in DMSO-$d_6$ on Avance-300 MHz spectrometer using TMS as an internal standard. The mass spectra were recorded on EI-shimadzu GC- Mass spectrometer.

***General procedure for synthesis of acridine derivatives***

A mixture of 3, 4, 9, 10-tetrahydroacridine-1(2H)-one 1 and aromatic aldehyde 2 were dissolved in the alkaline polyethylene glycol (PEG-400) (20) ml solution just boil the reaction mixture then subsequently add to it 5 ml ammonia. After completion of the reaction (monitored by TLC) the content were poured in ice cold water. To furnish the pure synthesized acridines recrystalized from ethanol.

***Spectroscopic data of selected compounds: 3(a-h)***

*4-(5,6,7,8,9,10,11,16,17,18-decahydroacridino[1,2-b]benzo[1,7]phenanthrolin-8-yl)phenol (3a)*

IR (KBr): 3158, 3100; $^1H$ NMR (DMSO-$d_6$): δ 2.12-2.24(m, 12H, $CH_2$), δ8.41(s 2H -NH), δ8.50(s 1H -NH), 6.6-6.9 (m, 13H, Ar-H), δ 11.58 (s, 1H, OH) ppm; M.S. (m/z): 484[$M^+$]; Anal. Calcd for $C_{33}H_{29}ON_3$: C, 81.96; H, 6.04; N, 8.69 %. Found: C, 80.55; H, 5.95; N, 8.59%.

*(4-Chlorophenyl)(5,6,7,8,9,10,11,16,17,18-decahydroacridino[1,2-b]benzo[1,7]phenanthrolin-8-yl)phenol (3b)*

IR (KBr): 3148, 3110; $^1H$ NMR (DMSO-$d_6$): δ 2.05-2.14(m, 12H, $CH_2$), δ8.30(s 2H -NH), δ8.35(s 1H -NH), 6.5-6.8 (m, 13H, Ar-H), δ 11.30 (s, 1H, OH) ppm; M.S. (m/z): 501[$M^+$]; Anal. Calcd for $C_{33}HClN_3$: C, 78.95; H, 5.62; N, 8.37 %. Found: C, 78.80; H, 5.52; N, 8.27%.

*(4-Methoxyphenyl)(5,6,7,8,9,10,11,16,17,18-decahydroacridino[1,2-b]benzo[1,7]phenanthrolin-8-yl)phenol (3c)*

IR (KBr): 3145, 3200; $^1H$ NMR (DMSO-$d_6$): δ 2.10-2.18(m, 12H, $CH_2$), δ8.25(s 2H -NH), δ3.45(s 1H –$OCH_3$), δ8.22 (s 1H -NH), 6.8-6.9(m, 13H, Ar-H), δ 11.45 (s, 1H, OH) ppm; M.S. (m/z): 498[$M^+$]; Anal. Calcd for $C_{33}H_{31}ON_3$: C, 82.06; H, 6.28; N, 8.44%. Found: C, 82.00; H, 6.25; N, 8.40%.

*Antimicrobial activity*:

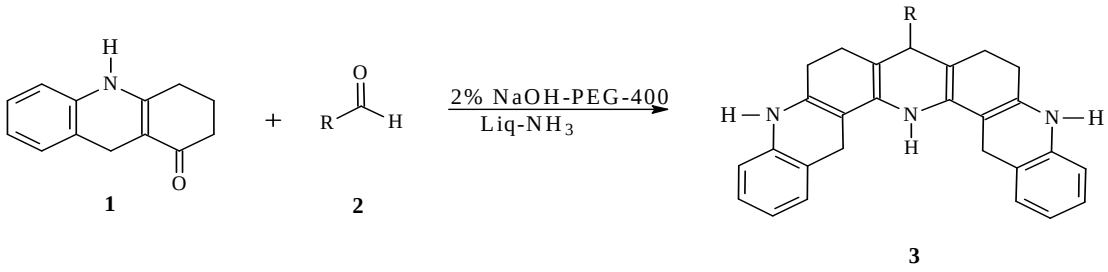
The antimicrobial activities of the synthesized compounds **3(a-h)** were determined by agar diffusion method[16]. The compounds were evaluated for antibacterial activity against *Bacillus subtilis* (MTCC 1789), *Proteus vulgaris* (MTCC 1771), *Staphylococcus aureus* (MTCC 96) and *Escherichia coli* (MTCC 2939), were procured from Institute of Microbial technology (IMTech), Chandigarh, India. The antibiotic Tetracycline (25µg/mL) was used as reference antibacterial substance for comparison. Dimethyl sulphoxide (1%, DMSO) was used a control.

The culture strains of bacteria were maintained on nutrient agar slant at 37±0.5°C for 24 h. The antibacterial activity was evaluated using nutrient agar plate seeded with 0.1 mL of respective bacterial culture strain suspension prepared in sterile saline (0.85%) of $10^5$ CFU/mL dilutions. The wells of 6 mm diameter were filled with 0.1 mL of compound solution at fixed

concentration 25µg/mL separately for each bacterial strain. All the plates were incubated at 37±0.5 °C for 24 h. Zone of inhibition of compounds in mm were noted.

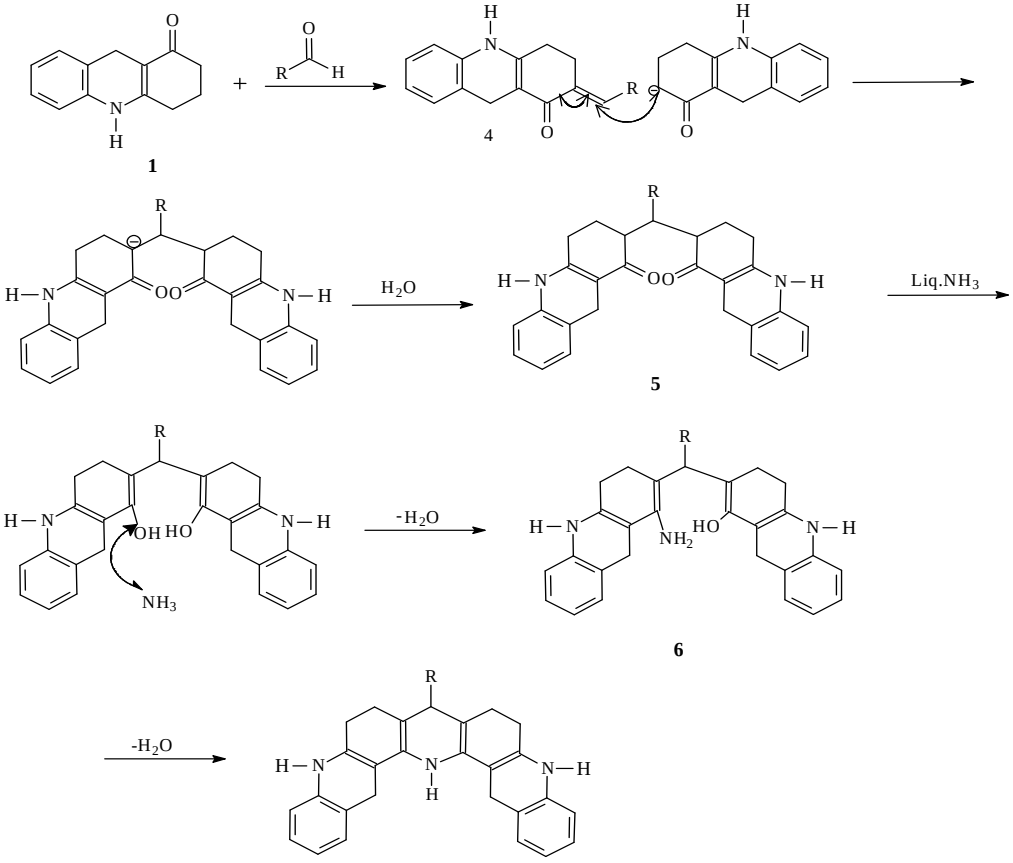
## RESULTS AND DISCUSSION

As part of our research programme, and in continuation of our work on the development of environmentally friendly methodologies using polyethylene glycol (PEG-400) as a reaction solvent for the preparation of biologically active compounds[12-15], herein we report an efficient synthesis of some novel acridine derivative by the one-pot condensation of 3, 4, 9, 10-tetrahydroacridine-1(2H)-one, substituted aldehyde and liquior ammonia in alkaline polyethylene glycol (PEG-400) as green reaction solvent.




**1** **2** **3**

Scheme-1:Synthesis of acridine derivatives.




**5** **6**

**Scheme 2: Mechanism of acridine derivatives**

**Table-1: Physical data of acridine derivatives 3(a-h)**

| Entry | Product | R | Yield (%) | M.P. (°C) |
|---|---|---|---|---|
| 1 | 3a | 4-Hydroxy phenyl | 85 | 210 |
| 2 | 3b | 4-Chloro phenyl | 88 | 180 |
| 3 | 3c | 4-Methoxy phenyl | 85 | 170 |
| 4 | 3d | 4-Nitro phenyl | 85 | 220 |
| 5 | 3e | 4-Fluro phenyl | 88 | 212 |
| 6 | 3f | 4-N$(CH_3)_2$-phenyl | 80 | 162 |
| 7 | 3g | 2-Hydroxy phenyl | 85 | 180 |
| 8 | 3h | 2-Hydroxy-3,5-dibromo phenyl | 82 | 175 |

The formation of product is achieved by the above mechanism (Scheme-2) in which first molecule of 3, 4, 9, 10-tetrahydroacridine-1(2H)-one 1 was condensed with aldehyde to form 4. later the second molecule 3, 4, 9, 10-tetrahydroacridine-1(2H)-one of active methylene group reacted with 4 by conjugate addition reaction to give intermediate 5.then intermediate 5 was attacked by ammonia on hydroxyl group to give intermediate 6.finally the intermediate 6 was cyclised by the nucleophilic attack of NH2 on another hydroxyl gave the product 3. Structure of the compounds was confirmed by the spectral analysis.

The results of the antibacterial data are given in Table-2. The antimicrobial data revealed that most of the compounds showed interesting biological activity. In comparison with standard tetracycline, compounds **3a** and **3b** showed very good activity against *B. subtillis*. Compounds **3b**, **3g** and **3h** were displayed good activity against *P. vulgaris*, while compounds **3e** showed excellent activity. Compounds **3a**, **3b** and **3c** were displayed good activity against *S. aureus*. All the compounds were found to be effective against *E. coli*. Compounds **3a**, **3e**, **3g**, and **3h** were showed very good activity against *E. coli*. Only the compound **3b** showed similar level of activity against *E. coli*.

**Table-2 Antibacterial activity of synthesized compounds 3(a-h)**

| Product | BS | PV | SA | EC |
|---|---|---|---|---|
| **3a** | 16 | 13 | 18 | 19 |
| **3b** | 15 | 14 | 17 | 18 |
| **3c** | 15 | 14 | 15 | 14 |
| **3d** | 14 | 12 | 15 | 14 |
| **3e** | 17 | 16 | 15 | 17 |
| **3f** | 14 | 11 | 13 | 14 |
| **3g** | 12 | 15 | 15 | 17 |
| **3h** | 16 | 13 | 14 | 13 |
| Tetracycline | 20 | 18 | 22 | 18 |

*Zone of inhibitions are expressed in mm*

BS=*Bacillus subtilis*, PV-*Proteus vulgaris*, Sa- *Staphylococcus aureus*, EC=*Escherichia coli*

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