COMPARATIVE STUDY OF SYNTHESIS OF 9-ARYL-ACRIDINES USING IODINE AS CATALYST

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ABSTRACT

A series of 9-substituted aryl-acridines have been synthesized byinteraction of diphenyl amine and various aromatic acids/ aldehydes using iodine as a recyclable catalyst under microwave condition and evaluated for antimicrobial activity.The formation of title compounds were confirmed by TLC till to get single spot on silica plate and characterised by IR, ^{1}H-NMR and Mass spectrometry.All the compounds were screened for their antimicrobial activity against selected microorganismsE. coliand S. aureus.

***Keywords**: Microwave heating method, iodine, acridines.*

Introduction

Microwave technique for one-pot cyclocondensations provides a number of advantages in synthesis of a series of novel five and six member ring containing nitrogen and in cyclization 1,3 dicarbonyl compounds with compound of nucleophillic character at atmospheric pressure in open vessel(Lindstrom et al., 2001). High density microwave irradiation has matured into a reliable and useful methodology for accelerating time consuming reactions (Gronnowet al., 2005). Numerous advantages of iodine as a catalyst have proved its effectiveness in synthetic chemistry under different methodology such as classical heating, microwave heating, ultrasonic induced or simple mechanochemical stirring method (Samajdaret al., 2001). The transformation of functional group from one to other using iodine as a catalyst has attracted attention of chemists since economical, efficient and ecofriendly alternative to transition metal Ni, Pd, etc in organic synthesis (Renet al., 2013). The protection and deprotection of aldehyde and ketone via acetals, ketals can also be performed successfully with molecular iodine as a catalyst in acetone(Banik, 2014).

Acridineiswidely exploited moiety in synthetic chemistry having practical application in the pharmaceutical sciences. From the extensive literature survey it has been found that acridines exhibit anti-tumour(Srivastavaet al., 2004), anti-inflammatory(Elslageret al., 1969), antimalarial and anticancer activities(Mayeret al., 1963). The acridine nucleus utilised as a vector leads to numerous clinical trials for DNA-targeting drugs studies is well known application. Research studies on acridine derivatives have been published recently, focusing on their therapeutics properties against cancer (Antonini, 2004), parasites (Denny, 2004) and bacteria (Kelland, 2005).

Keeping in view of biological significance, here-in we report a9-substituted aryl-acridines have been synthesized using iodine as a recyclable catalyst under microwave condition and evaluated for antimicrobial activity againstselected microorganisms.

Materials and Methods

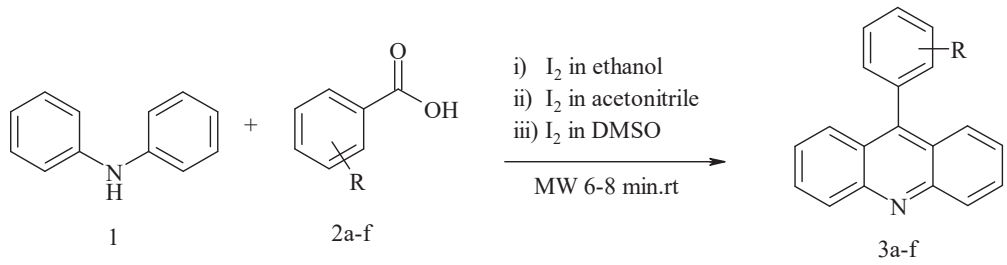
Melting points were determined on a Thiels apparatus and are uncorrected. All chemicals used were of AR gradeand purchased from Sigma Aldrich.Purity of title compounds checked by TLC till single spot is observed employing petroleum ether and ethyl acetate (2:3) as eluent.The IR spectra (4000-400 cm^{-1}) were recorded on Agilent Cary 630 FTIR spectrophotometer using KBr disc. The ^{1}H-NMR spectra were obtained on a Bruker,Avance-600 MHz spectrophotometer in $CDCl_3$as a solvent using tetramethylsilane (TMS) as an internal standard.Mass spectral measurements were carried out by EI method onJeol, JMC-300 spectrometer at 70 eV.Antimicrobial screening of titlecompoundswas performed against *E. coli*and *S. aureus*using agar well diffusion

method and compared with the standard drug streptomycin.

Synthesis of 9-phenyl-acridines, 3a

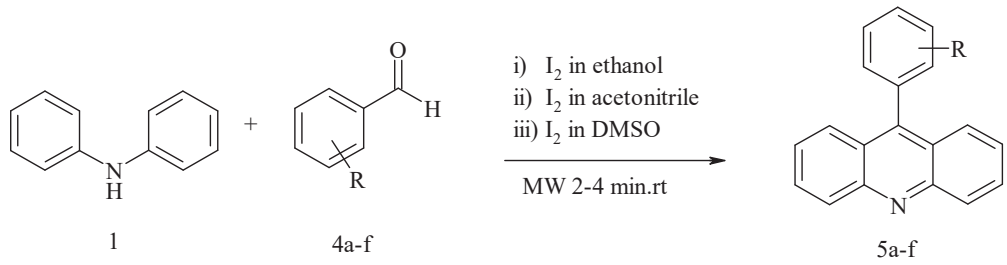
The 9-phenyl-acridine**(3a)**was prepared by irradiating the mixture ofdiphenyl amine and benzoic acid**(2a)**/ benzaldehyde **(4a)** usingiodine as a catalyst under microwave condition for 10-15 min., progress of reactions monitored by TLC, crude solid was recrystallized form absolute alcohol in cold condition and identified as 9-phenyl-acridine**(3a)**.

Similarly 9-aryl-acridines **(3b-f)** were prepared by irradiating the mixture ofdiphenyl amine **(1)** and various aromatic acid (**2b-f**)/ aldehydes **(4a-f)** using iodine as a catalyst under microwave condition.



1 2a-f 3a-f

Scheme 1. Iodine-catalyzed condensation of diphenyl amine (**1**) and benzoic acid (**2a**)



1 4a-f 5a-f

Scheme 2.Iodine-catalyzed condensation of diphenyl amine (**1**) and benzaldehyde (**4a**)

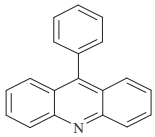
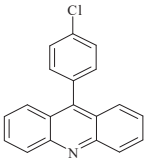
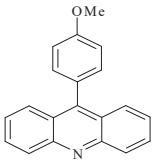
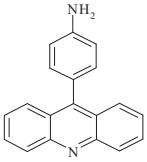
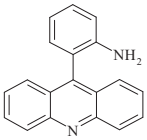
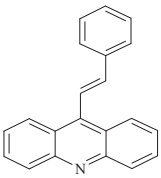
Table 1: Iodine-catalyzed condensation of diphenyl amine (**1**) and benzoic acid (**2a**)

Entry	Solvent	Temp. (°C)	I_2(Mol%)	Time (min.)	Yield 3a (%)
1	EtOH	rt	20	6-8	68
2	acetonitrile	rt	20	4-5	72
3	DMSO	rt	20	1-2	78

Table 2: Iodine-catalyzed condensation of diphenyl amine (**1**) and benzaldehyde (**4a**)

Entry	Solvent	Temp. (°C)	I_2 (Mol%)	Time (min.)	Yield 5a (%)
1	EtOH	rt	20	4-6	66
2	acetonitrile	rt	20	3-4	80
3	DMSO	rt	20	1-2	81

Table 3 Scheme2:Synthesis of 9-aryl-acridines5a-f obtained in good to excellent yield.

Entry 2a-f	Product 5a-f	Yield (%)	m.p. (^{o}C)
Benzaldehyde		82 %	115^{o}C
4-chloro-benzaldehyde		84.30 %	108^{o}C
4-methoxy-benzaldehyde		70 %	124^{o}C
4-amino-benzaldehyde		79.93 %	117^{o}C
2-amino-benzaldehyde		68 %	126^{o}C
Cinnmaldehyde		82.45 %	110^{o}C

Result and Discussion

The target compounds have been synthesized bycyclo-condensation reaction of diphenyl amine and various substituted aromatic acid/ aldehydes using iodine as a catalyst at room temperature under microwave condition.The title compounds9-aryl-acridines**3a-f** and spectral analysis fully supported the formation of the structures of the compounds. The IR spectrum of compoundsshowed characteristic bands in the range of 1506-1530 cm^{-1}for aromatic carbon double bond group(Dudleyand Williams2004). In^{1}H-NMR spectrum signalat δ 6.8-7.2 ppm and 7.6-8.0 ppm found to be in accordance with substitution pattern on aromatic ring and acridinyl ring respectively(Silverstein, Bassler and Morril1981).In mass spectrum base peak observed at m/z 178.22.

The titled compounds were screened for their *in vitro* antimicrobial activity against *S. aureus* MTCC 96, and *E. coli* MTCC 443 using Kirby Bauer method(Greenwood, Slack, and Peutherer, 1992).Inhibition zonein mm was measured for all the synthesized compounds and compared with that of standard drugs such as streptomycin.Out of all these compounds **3f** and **3c** found to be more active against *E. coli* and *S. aureus* respectively.

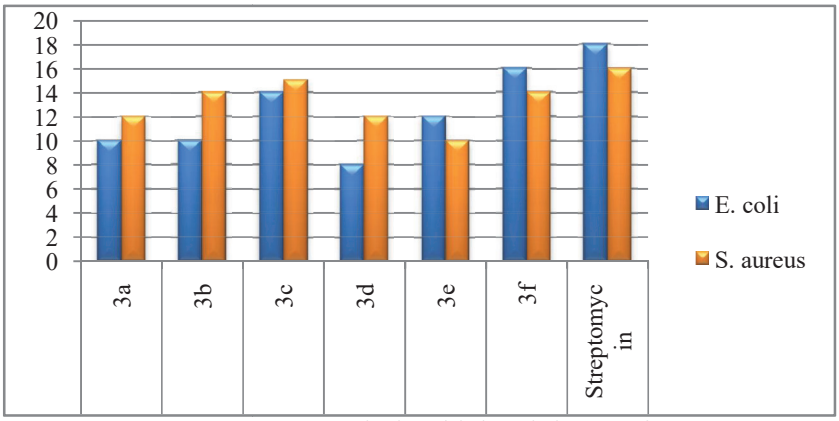


Figure 1 Antimicrobial activity, 3a-f

Conclusion

In conclusion, we have been synthesized the title compounds9-aryl-acridines derivatives **3a-f** by using reusable molecular iodine catalyst employing microwave heating method provides clean, inexpensiveprotocol and study will be of great importance to those involved in drug discovery.All 9-aryl-acridines **3a-f** exert good enough activity against *E. coli* and *S. aureus*. Out of all these compounds **3f** and **3c** found to be more active against *E. coli* and *S. aureus* respectively.

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