Barium Chloride Catalysed Synthesis Of Acridine/Tetrahydro Acridine Derivatives Under Microwave Heating

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Abstract

Single step syntheses of acridine derivatives have been reported under microwave heating at room temperature. The oxidative cyclization of diphenyl amine and aromatic ketone/ aromatic acid under solvent free condition leads to formation of 9-aryl-acridine using barium chloride as a catalyst. The title compounds were characterised by IR, ^{1}H-NMR and Mass spectrometry.

Keywords: Barium chloride, microwave method, acridines.

Introduction

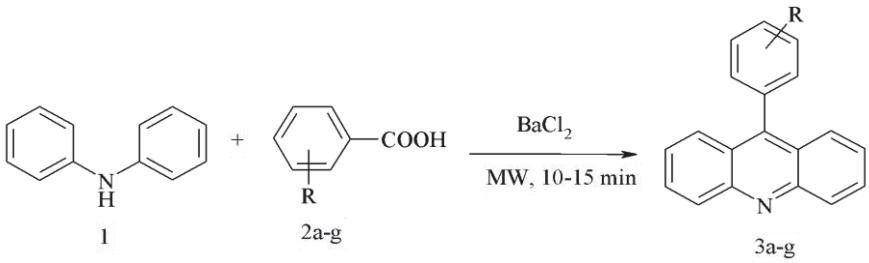
Barium chloride is an ionic water-soluble salt mostly used inexpensive, commercially available catalysts that can be easily separated and reused[1]. The use of barium dichloride as a Lewis acid catalyst in the synthesis of substituted coumarins via Pechmanncyclocondensation proved the catalytic efficiency under thermal and solvent-free conditions[2]. The extensiveinvestigation was done by exploring one pot Biginelli reaction using barium chloride under different solvents. The high yield, mild and solvent-free reaction conditions explains the synthetic utility in accord with green chemistry criteria[3].

Microwave technique for one-pot cyclocondensationprovides 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 nucleophilic character at atmospheric pressure in open vessel[4]. High density microwave irradiation has matured into a reliable and useful methodology for accelerating time consuming reactions[5]. Acridine is widely exploited pharmacophore in synthetic chemistry having practical application in the medicinal sciences. From the extensive literature survey it has been found that acridine and their derivatives exhibit anti-inflammatory, anti-tumour, antimalarial and anticancer activities[6-8]. The use of acridine nucleus as a vector leads to numerous clinical trials for DNA-targeting drugs studies is well known application andstudies on acridine derivatives have been published recently, focusing on their therapeutics properties against cancer, parasites and bacteria[9-11].

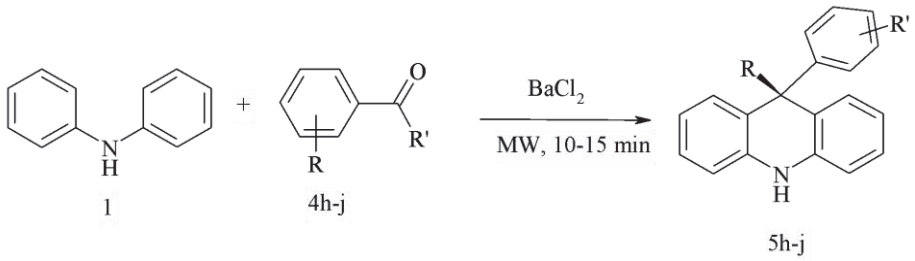
Keeping in view of biological significance, Here-in we report an efficient MW synthesis of 9-aryl-acridines and 9-alkyl/aryl-9-aryl-tetra hydro-acridines using $BaCl_2$ as a catalyst under microwave condition.

Material And Method

All MW irradiation experiments were carried out in synthetic microwave oven with continuous irradiation of power 120W. Purity of title compounds checked by TLC till single spot is observed. Melting points were determined on a digital melting point apparatus (Veego, VMP-D) and are uncorrected. All chemicals used were of AR grade.The IR spectra were recorded on Agilent Cary 630 FTIR spectrophotometer using KBr disc. ^{1}H-NMR spectra were obtained on a Bruker-Avance-600 MHz spectrophotometer in $CDCl_3$ using tetramethyl silane as internal standard. Mass spectral measurements were carried out by EI method on a Jeol, JMC-300 spectrometer at 70 eV.



Scheme 1: *9-Substituted-aryl-acridines*, **3a-g**



Scheme 2: *9-alkyl/aryl-9-aryl-tetra hydro-acridines*, **3h-j**

Result And Discussion

***Synthesis of 9-phenyl-acridines,* 3a**

9-phenyl-acridine **(3a)**was prepared by irradiating the mixture ofdiphenyl amine and benzoic acid using $BaCl_2$ 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-acridine **(3b-g)** were prepared by irradiating the mixture ofdiphenyl amine (**1**) and various aromatic acid (**2b-g**) using $BaCl_2$ as a catalyst under microwave condition.

***Synthesis of 9-methyl-9-aryl-tetra hydro-acridines,* 5h**

9-methyl-9-aryl-tetra hydro-acridines **(5h)** was prepared by irradiating the mixture ofdiphenyl amine and Acetophenone using $BaCl_2$ 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-methyl-9-aryl-tetra hydro-acridines **(5h)**.

Similarly 9-substituted aryl-9-aryl-tetra hydro-acridine **(5i, 5j)** were prepared by irradiating the mixture of diphenyl amine (**1**) and substituted ketone (**4i, 4j**) using $BaCl_2$ as a catalyst under microwave condition.

Table 1: Analytical data compounds, **3a-g, 5h-j**

Entry 2a-g, 4h-j	Product 3a-g, 5h-j	Yield (%)	m.p. (°C)
Benzoic acid	9-phenyl acridine	82 %	115°C
p-chloro benzoic acid	9-(4-chloro-phenyl) acridine	84.30 %	108°C
p-methoxy benzoic acid	9-(4-methoxy-phenyl) acridine	70 %	124°C
p-amino benzoic acid	9-(4-amino-phenyl) acridine	79.93 %	117°C
o-amino benzoic acid	9-(2-amino-phenyl) acridine	68 %	126°C
Pthallic acid	o-acridinyl benzoic acid	80 %	130°C
Cinnamic acid	9-styryl acridine	82.45 %	110°C
Acetophenone	9-methyl-9-phenyl-tetrahydro acridine	90 %	121°C
Benzophenone	9, 9-diphenyl-tetrahydro acridine	78 %	114°C
p-bromo Acetophenone	9-(4-bromo-phenyl)-9-phenyl-tetrahydro acridine	80 %	108°C

Conclusion

The diphenyl amine on cyclo-condensation with aromatic aldehydes/ Ketones under microwave condition using $BaCl_2$ as a catalyst resulted the title compounds 9-aryl-acridines**3a-g/** 9-alkyl/aryl-9-aryl-tetra hydro-acridines **5h-j**. The spectral analysis fully supported the formation of the structures of the compounds **3a-g** and **5h-j**. The IR spectrum of compoundsshowed characteristic peak at 1506-1530 $cm^{-1}$for aromatic carbon double bond group[12]. In^{1}H-NMR spectrum signal at 6.8-7.2 ppm for aromatic ring and at 7.6-8.0 ppm for acridinyl ring[13] were observed. In mass spectrum base peak observed at m/z 178.22.

On observing the results, it is concluded that title compounds9-aryl-acridines **3a-g** and 9-alkyl/aryl-9-aryl-tetra hydro-acridines **5h-j** have been prepared by using reusable $BaCl_2$ catalyst employing microwave heating method provides clean, inexpensiveprotocoland study will be of great importance to those involved in drug discovery.

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