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SYNTHESIS OF BENZO[*a*] ACRIDONES USING A MICROWAVE REACTOR

Nadaraj Vetrivel[1], Thamarai Selvi Senniappan,[2*] and Abirami Maharajan[3]
[1]Department of Chemistry, Tamilnadu College of Engineering, Karumathampatti, Coimbatore-641659, India.
[2]Department of Chemistry, L.R.G. Govt. Arts College for Women, Tirupur-641 604, India.
[3]Department of Chemistry, Sri Ramakrishna Engineering College, Vattamalaipalayam, Coimbatore-641022, India.
*E-mail: thamaraimohan@yahoo.co.in

ABSTRACT
In the present communication a simple and efficient synthesis of some acridone derivatives are described by the reaction of 2-methylquinolin-4(*2H)*-one and *o*-chlorobenzaldehyde under microwave irradiation. High yield, less by products, short reaction time (9-12 min), mild conditions and easy work-up are the advantages of this methodology.
Keywords: microwave, aldehyde, acridone, quinoline

INTRODUCTION

Heterocyclic compounds constitute the largest family of organic compounds, regardless of structure and functionality. Heterocyclic compounds are of particular interest in medicinal chemistry and this has catalyzed the discovery and development of many new heterocyclic compounds. 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-damagingability[3], antileishmanial[4] and antimicrobial activities[5]. Most of the acridine derivatives are also used in the pigments and dyes[6,7].

Microwave-assisted reactions have attracted much interest because of the simplicity in operation, greater selectivity and rapid synthesis of a variety of organiccompounds[8-10]. The notable features of the microwave approach are enhanced reaction rates, formation of pure products in high yield and the ease of manipulation. In recent years, solvent-free microwave assisted reactions have gained greater popularity as they provide an opportunity to work with open vessels. This avoids the risk of the development of high pressure and provides a possibility of scaling up the reaction and helps the induction of the reaction under dry conditions. Thus, microwave irradiation has become a powerful tool for the rapid synthesis of a variety of bioactive molecules under solvent-free conditions. In continuation of our interest in the synthesis of nitrogen heterocyclic compounds[11-16], we herein report a rapid and efficient synthesis of acridones involving the two component condensation of 2-methylquinolin-4-(2*H*)-ones, *o*-chlorobenzaldehyde under microwave irradiation under solvent-free conditions.

EXPERIMENTAL

Melting points (mp) were determined using Boetieus micro heating table and are uncorrected. The purity of the products was checked by TLC on pre-coated sheets of silica gel IR (KBr, cm^{-1}) spectra were obtained on Shimadzu–8201 spectrometer. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker AMX-400 MHz spectrometer using TMS as an internal reference (Chemical shifts in δ, ppm). Elemental analyses were performed on Perkin Elmer CHN-analyzer. Mass spectra were recorded on Shimadzu GCMS-QP5050A (70 eV) mass spectrometer. The microwave system used for this experiment is Ragas Electro Magnetic System [RG3IL], complete with glass door, 700 Watt delivered power, exhaust system,

triple safety interlocks, magnetic stirrer, automatic temperature control. All reactions are carried out at 5th level [120°C] in a 100 mL beaker.

General procedure for preparation of Benz[*a*]acridin-12(7*H*)-ones (3a-g)

A mixture of 2-methylquinolin-4(*2H)*-ones, (**1a-g**, 5.0 mmol),*o*-chlorobenzaldehye (6.0 mmol) and small amount of Triethylamine was placed in a 100 mL beaker. The mixture was irradiated at 5th level for appropriate time(Scheme-1).The completion of reaction was monitored through TLC and reaction medium was cooled, the yellow precipitate formed was poured into ice, filtered and dried.

Benzo[*a*]acridin-12(7*H*)-one 3a

Time-10min, Yield-90%; mp.>300°C; IR (KBr, cm^{-1}): 1630 (>C=O), 3200-3000 (NH); ^1H NMR (DMSO-d_6) δ: 7.41-8.22(m, 8H, Ar-H), 8.53 (d, 1H, C_{11}-H), 10.30 (d,1H, C_1-H), 12.33 (s,1H, NH); Ms (m/z): 245; Anal. Calc. ($C_{17}H_{11}NO$): C, 83.27, H, 4.53, N, 5.71; Found: C,83.22, H, 4.50, N, 5.66.

10-Methylbenzo[*a*]acridin-12(7*H*)-one 3b

Time-9 min, Yield-91%; mp.>300 °C; IR (KBr, cm^{-1}): 1640 (>C=O), 3200-3100 (NH); ^1H NMR (DMSO-d_6) δ: 2.51 (s, 3H, CH_3), 7.35-8.05 (m, 7H, Ar-H), 8.75 (s, 1H, C_{11}-H), 10.28 (s,1H, C_1-H), 12.31 (s,1H, NH);Ms (m/z): 259; Anal. Calc. ($C_{18}H_{13}NO$): C, 83.40, H, 5.06, N, 5.41; Found: C, 83.38, H, 5.06, N, 5.40.

8-Methylbenzo[*a*]acridin-12(7*H*)-one 3c

Time-10min, Yield-91%; mp.>300 °C; IR (KBr,cm^{-1}): 1640 (>C=O), 3300-3100 (NH); ^1H NMR (DMSO-d_6) 2.52 (s, 3H, CH_3), 7.33-8.20 (m, 7H, Ar-H), 8.58 (d, 1H, C_{11}-H), 10.26 (s,1H, C_1-H), 12.20 (s,1H, NH); Ms (m/z): 259; Anal. Calc. ($C_{18}H_{13}NO$): C, 83.40, H, 5.06, N, 5.41;Found: C, 83.41, H, 5.05, N, 5.41.

10-Methoxylbenzo[*a*]acridin-12(7*H*)-one 3d

Time-11 min, Yield-89%; mp.>300 °C; IR (KBr, cm^{-1}): 1635 (>C=O), 3300-3000 (NH); ^1H NMR (DMSO-d_6) δ: 3.93 (s, 3H, OCH_3), 7.22-8.00 (m, 7H, Ar-H), 8.66 (s, 1H, C_{11}-H), 10.22 (s,1H, C_1-H), 12.30 (s,1H, NH); Ms (m/z): 275; Anal. Calc. ($C_{18}H_{13}NO_2$): C, 78.55, H, 4.77, N, 5.09; Found: C, 78.50, H, 4.72, N, 5.06.

8-Methoxylbenzo[*a*]acridin-12(7*H*)-one 3e

Time-10min, Yield-85%; mp.>300 °C; IR (KBr, cm^{-1}): 1640 (>C=O), 3200-3000 (NH); ^1H NMR (DMSO-d_6) δ: 3.90 (s, 3H, OCH_3), 7.40-8.22 (m, 7H, Ar-H), 8.40 (d, 1H, C_{11}-H), 10.33 (s,1H, C_1-H), 12.33 (s,1H, NH); Ms (m/z): 275; Anal. Calc. ($C_{18}H_{13}NO2$): C, 78.55, H, 4.77, N, 5.09; Found: C, 78.52, H, 4.72, N, 5.05.

10-Chlorobenzo[*a*]acridin-12(7*H*)-one 3f

Time-12 min, Yield-81%; mp.>300 °C; IR (KBr, cm^{-1}): 1630 (>C=O), 3200-3150 (NH); ^1H NMR (DMSO-d_6) δ: 7.41-8.38 (m, 8H, Ar-H), 10.30 (d, 1H, C_1-H), 12.22 (s,1H, NH); Ms (m/z): 279; Anal. Calc. ($C_{17}H_{10}NOCl$): C, 73.12, H, 3.61, N, 5.02; Found: C, 73.10, H, 3.60, N, 5.02.

10-Bromobenzo[*a*]acridin-12(7*H*)-one 3g

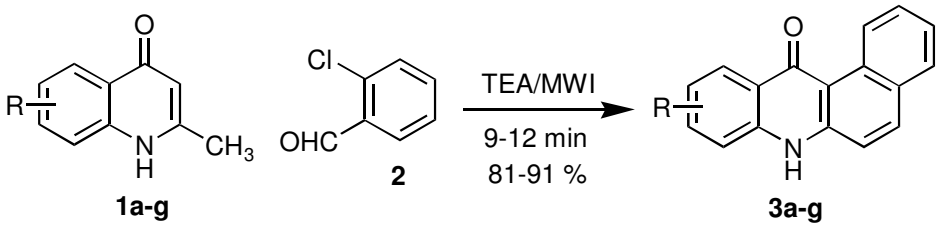
Time-12 min, Yield-81%; mp.>300 °C; IR (KBr, cm^{-1}): 1640 (>C=O), 3200-3000 (NH); ^1H NMR (DMSO-d_6) δ: 7.33-8.40 (m, 8H, Ar-H), 10.28 (d, 1H, C_1-H), 12.20 (s,1H, NH); Ms (m/z): 323; Anal. Calc. ($C_{17}H_{10}NOBr$): C, 63.16, H, 3.12, N, 4.33; Found: C, 63.11, H, 3.09, N, 4.30.

RESULTS AND DISCUSSION

To develop one-pot synthesis route for the titled products, we first focused on optimization of the reaction conditions using readily available materials. The reaction of 2-methylquinolin-4-(2*H*)-ones (**1a**) was

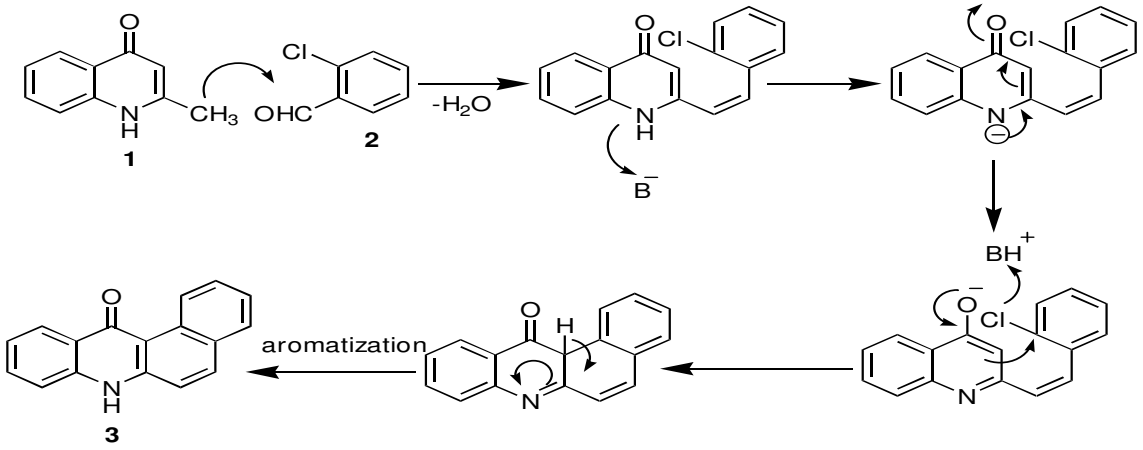
carried out using a mixture of *o*-chlorobenzaldehyde (**2**) and triethylaminewithout solvent at microwave conditions. It was noticed that, condensation take place between aldehyde and methyl group (in **1a**) to form olefin and followed by cyclisation result into desired product, benzo[a]acridone (**3a,** Scheme-1). All the reactions were carried out at 5th level. The cyclization confirmed by ^{1}H-NMR spectrum, it indicates the absence of olefinic proton peaks. The structure of compounds **3**(**a-g**) were deduced from their ^{1}H NMR, IR spectral data and their molecular weight were confirmed by mass spectrometry. The mass spectra of these compounds showed the expected molecular ion signals and the selected spectroscopic data have been given in general procedure section.

According to a plausible mechanism which is outline in Scheme-2, the formation of **3**is expected to proceed via initial condensation of 2-methylquinolin-4(*2H)-o*ne**1**with aldehyde to afford olefin **4**, which further undergoes *in situ* cyclization to yield target product **3**.



R= H, 8-CH_3, 10-CH_3, 8-OCH_3, 10-OCH_3,Cl, Br

Scheme-1: Synthesis of benzo[*a*]acridin-12(7*H*)-ones



Scheme-2

CONCLUSION

In conclusion, we have developed efficient and simple procedure for the synthesis of benzo[*a*]acridin-12(7*H*)-one derivatives via condensation of aromatic aldehyde and 2-methylquinolin-4(*2H)*-one(**1**) which offers significant preparative advantages over the existing methods.

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