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Green Synthesis of 9-Acridone Derivatives

V Nadaraj[1], M Abirami[2] and S Thamarai Selvi[3*]

[1]Department of Chemistry, Tamilnadu College of Engineering, Karumathampatti, Coimbatore, India
[2]Department of Chemistry, Sri Ramakrishna Engineering College, Vattamalaipalayam, Coimbatore, India
[3]Department of Chemistry, L.R.G. Govt. Arts College for Women, Tirupur, India

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ABSTRACT

A highly efficient method for the synthesis of 9-acridone derivatives by using a cyclic condensation of aromatic amines with o-chlorobenzoic acid over Lewis acid catalysts in microwave reactor is described.

Keyword: Microwave; Condensation; Acridone

INTRODUCTION

Acridone derivatives exist in numerous natural products and pharmaceutical agents that show broad biological activities [1-4]. Derivatives and salts of acridines are characteristically crystalline, stable, attractively coloured, and often strongly fluorescent and rewardingly display a range of anti-microbial properties, which have influenced a secured position in the field of chemotherapy [5-8]. Various new synthesis methods [9-12] for the acridone derivatives have been reported and Concentrated H_2SO_4, PPA, $POCl_3$, P_2O_5 were widely employed as catalyst for the cyclisation of N-phenylanthranilic acids to give acridones.

Recently [13], we also reported a synthesis of such compounds through a PTSA catalyzed cyclisation of N-phenylanthranilic acids under microwave irradiation. A microwave (MW, frequency 2.45 GHz) heating technique should be a promising candidate, replacing conventional heating because microwave-assisted organic syntheses can lead to large reductions in reaction time, clean and to enhancement in conversion and selectivity compared to conventional heating [14-17]. The concept of green chemistry [18] encouraged us to develop a new synthetic route using an even safer and non-waste-producing alternative catalyst. Solid acid catalysts are not only environmentally friendly but also have many economic advantages [19, 20]. Though a number of thermal synthetic methods of acridines are available in the literature, microwave induced synthesis of acridines are very few. Herein we wish to report a simple, clean and efficient method for the synthesis of 9-acridone derivatives by the reaction of aromatic amine compounds and *o*-chlorobenzoic acid catalyzed by a Lewis acid $ZnCl_2$ in microwave reactor.

EXPERIMENTAL SECTION

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^{o}C] in a 100 mL beaker.

General procedure for preparation of 9-acridones (3a-e)

A mixture of *o*-Chlorobenzoic acid (0.780 g, 0.005 mole), substituted anilines (0.005 mole) and the catalyst zinc chloride were taken in a 100 mL beaker, mixed well and the reaction mixture was irradiated in an microwave oven at the power of output 160W for specified times (**Table 1**). The reaction was monitored for every 30 seconds by the tic. After completion of the reaction, the reaction mixture was poured into boiling water. The precipitate formed was filtered and boiled for five minutes with a solution of sodium carbonate. Again precipitate was filtered, washed well with water and purified by silical gel column chromatography [Petroleum ether: ethyl acetate; [70:30] as an elutent].

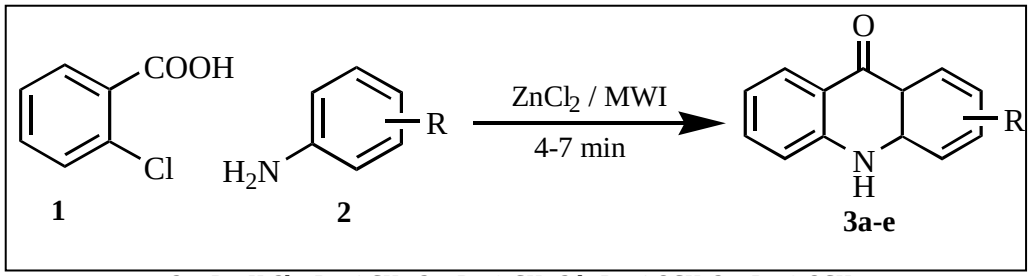
9-Acridone 3a: Time-4 min, Yield-95%; mp.>300°C; IR (KBr, cm^{-1}): 1635 (>C=O), 3744-3280 (NH), 1598, 1526, 1470; ^{1}H NMR (DMSO-d_6) δ: 7.25-7.29 (t, 2H, C_2-H and C_7-H), 7.55-7.57 (d, 2H, C_4-H and C_5-H), 7.72-7.76 (t, 2H, C_3 -H and C_6-H), 8.23-8.25 (d, 2H, C_1-H and C_8-H), 11.72 (s, 1H, NH); Ms (m/z): 195 ($M^{+\cdot}$,53%),167 ($M^{+\cdot}$-CO, 20%), 139, 111, 97, 85, 71, 57 (100%); Anal. Calc. ($C_{13}H_9NO$): C, 80.00, H, 4.65, N, 7.18; Found: C, 79.22, H, 4.55, N, 7.16.

4-Methyl-9-acridone 3b: Time-6 min, Yield-91%; mp.>300 °C; IR (KBr, cm^{-1}): 1633 (>C=O), 3700-3300 (NH), 1464, 1322; ^{1}H NMR (DMSO-d_6) δ: 2.46 (s, 3H, C_2-CH_3), 7.25-8.38 (m, 7H, Ar-H), 10.95 (s, 1H, NH); Ms (m/z): 209; Anal. Calc. ($C_{14}H_{11}NO$): C, 80.38, H, 5.31, N, 6.70; Found: C, 80.33, H, 5.26, N, 6.60.

2-Methyl-9-acridone 3c: Time-5.3 min, Yield-93%; mp.>300 °C; IR (KBr, cm^{-1}): 1633 (>C=O), 3700-3270 (NH); ^{1}H NMR (DMSO-d_6) δ: 2.48 (s, 3H, C_4-CH_3), 7.24-8.35 (m, 7H, Ar-H), 10.65 (s, 1H, NH); Ms (m/z): 209; Anal. Calc. ($C_{14}H_{11}NO$): C, 80.38, H, 5.31, N, 6.70; Found: C, 80.31, H, 5.28, N, 6.62.

4-Methoxy-9-acridone 3d: Time-7 min, Yield-93%; mp.>300 °C; IR (KBr, cm^{-1}): 1634(>C=O), 3720-3300 (NH); ^{1}H NMR (DMSO-d_6) δ: 3.86 (s, 3H, C_2-OCH_3), 7.28-8.40 (m, 7H, Ar-H), 11.70 (s, 1H, NH); Ms (m/z): 225; Anal. Calc. ($C_{14}H_{11}NO_2$): C, 74.67, H, 4.93, N, 6.22; Found: C, 74.65, H, 4.87, N, 6.16.

2-Methoxy-9-acridone 3e: Time-6.3 min, Yield-95%; mp.>300 °C; IR (KBr, cm^{-1}): 16350 (>C=O), 3700-3720 (NH); ^{1}H NMR (DMSO-d_6) δ: 3.90 (s, 3H, C_4-OCH_3), 7.27-8.39 (m, 7H, Ar-H), 11.65 (s, 1H, NH); Ms (m/z): 275; Anal. Calc($C_{14}H_{11}NO_2$): C, 74.67, H, 4.93, N, 6.22; Found: C, 74.62, H, 4.90, N, 6.19.



3a : R = H**, 3b :** R = 4-CH_3 **, 3c :** R = 2-CH_3, **3d :** R = 4-OCH_3, **3e :** R = 2-OCH_3

Scheme 1: Synthesis of 9-acridones

Table 1: Physical data of 9-acridones

Compounds	Reaction Time (min)	Yield (%)
3a	4	95
3b	6	91
3c	5.3	93
3d	7	93
3e	6.3	95

RESULTS AND DISCUSSION

To develop one-pot synthesis route for the titled compounds, by the reaction of *o*-chlorobenzoic acid (0.005 mol), anilines (0.005 mol) and $ZnCl_2$ (1g) were taken in a beaker and irradiated in the microwave reactor at a power of output of 160 W for 4 min.

After irradiation, boiling water was added; the solid obtained was boiled with sodium carbonate solution, filtered, dried and recrystallized from a mixture of aniline and acetic acid. It was noticed that, condensation take place between chlorine (1) and amine group (2) with liberation of HCl and followed by cyclisation result into desired product 9-acridone (3a, Scheme 1). All the reactions were carried out at the minimum power of 160 W. The cyclization confirmed by ^{1}H-NMR spectrum, it indicates the absence of acidic proton peaks.

Thus, IR spectrum of the solid showed characteristic absorption band at 1635 cm^{-1} and in the range 3744-3280 cm^{-1} for >C=O and -NH groups respectively. The ^{1}H-NMR spectrum registered two triplet at δ 7.25-7.29 for C_2& C_7 protons and δ 7.72-7.76 for C_3 & C_6 protons and two doublet at δ 7.55 -7.57 for C_4 & C_5 protons and δ 8.23-8.25 for C_1& C_8-protons. The spectrum also showed a singlet at δ 11.72 for >NH proton. The mass spectrum showed a molecular ion peak at m/z 195 ($M^{+\cdot}$, 53%) along with other fragment ion peaks at m/z 167 ($M^{+\cdot}$–CO, 20%), 139, 111, 97, 85, 71, 57 (100%). The structure of compounds 3(a-e) were deduced from their ^{1}H NMR, ^{13}C NMR and IR spectral data and their molecular weight confirmed by mass spectrometry [13, 21]. The mass spectra of these compounds showed the expected molecular ion signals, selected spectroscopic data have been given in general procedure section.

CONCLUSIONS

In conclusion, we have developed clean, highly efficient and green procedure for the synthesis of 9-acridone derivatives via condensation of aromatic amines (2) and o-chlorobenzoic acid (1) which offers significant preparative advantages over the existing methods.

REFERENCES

[1] D Carole; D Michel; C Julien; D Florence; N Anna; J Séverine; D Gérard; T Pierre; G Pierre. *Bioorg. Medic. Chem.,* **2005,** 13,19, 5560-5568**.**
[2] I Sánchez; R Reches; D Henry; C Pierre; R Maria; D. Pujol. *Eur. J. Med. Chem.,* **2006**, 41, 3, 340-352.
[3] F Gay; B Traoré; J Zanoni; M Danis; A Fribourg-Blanc. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **1996,** 90, 5, 516-518.
[4] P Yang; Q Yang; X Qian; L Tong; X Li. *Journal of Photochemistry and Photobiology B: Biology*, **2006**, 84, 3, 221-226.
[5] A Albert. "Selective Toxicity", Chapman and Hall, London, **1985**, 379.
[6] B Reil; M Soll; K Masson; W Oettmeier. *Biochem. Soc. Trans.,* **1994**, 22, 625.
[7] H Taniyama. *J. Pharm. Soc.,* **1947**, 67, 4.
[8] H Graboyes; E L Anderson; S H Levinson; T M Resnick. *Synthesis of Acridines*, **1975**, 12, 1225.
[9] U Thull; B Testa. *Biochem. Pharmacol.,* **1994**, 47, 230.
[10] Y Mandi; K Regely; I Ocsovszky; J Barbe; J P Galy; J Moinar, *Anticancer Rec.,* **1994,** 14, 2633.
[11] C F H Allen;, G H W Mckee; *Organic Synthesis Coll Vol* 2, 15.
[12] M Ogata; H Matsumoto; H Kano. *Tetrahedron*, **1969**, 25, 5205.
[13] V Nadaraj; S Kalaivani; S Thamarai Selvi. *Indian J. Chem*., **2006**, 45B, 1958-1960.
[14] V Nadaraj; S Thamarai Selvi; S Mohan. *Euro. J. Chem*., **2009**, 44, 976-980.
[15] V Nadaraj; S Thamarai Selvi; S Mohan; T Daniel Thangadurai. *Med. Chem. Res.*, **2012**, 21, 2911.
[16] V Nadaraj; S Thamarai Selvi; *J. Chem. Pharm. Res.,* **2012**, 4, 2850.
[17] S Caddick. *Tetrahedron*, **1995**, 51, 10403.
[18] P Anastas; J C Warner. *Green Chemistry, Theory and Practice*, Oxford University Press, New York, **1998**.
[19] J H Clark. *Acc. Chem. Res.*, **2002**, 35, 791.
[20] MA Harmer; Q Sun. *Appl. Catal. A: Gen.*, **2001**, 221, 45.
[21] K Lehmstedt. *Chem Ber.*, **1932,** 65, 999.