International Journal of ChemTech Research
CODEN (USA): IJCRGG, ISSN: 0974-4290, ISSN(Online):2455-9555
Vol.10 No.9, pp 1011-1017, 2017

Facile one pot Synthesis of Fluoroscent acridinediones employing nano copper ferrite as reusable catalyst

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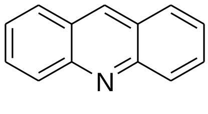
Abstract : Copper ferrite nanoparticle–catalyzed efficient one pot synthesis of acridinediones by multicomponent reaction of dimedone, aldehydes, ammonium acetate under solvent free conditions has been investigated. The present method has an advantage of short reaction time, easy to work up procedure and recyclability of catalyst. The obtained products were characterized and their 3D-fluorescence properties were studied.

Key words : Nano copper ferrite catalyst, dimedone, acridinediones, reusability, 3D-fluoroscence.

Introduction

Acridine is Nitrogen containing planner heterocyclic compound, in which the central -CH group of anthracene is replaced by nitrogen molecule.



Earlier, acridine's were reported as dyes latter in early 20thcentury their pharmacological properties were evaluated. Proflavin was used as a topical antimicrobial agent.[1]In 1940's acridine analogues viz., quinacrine, pyronaridine and acranil have been used as anti-malarial drugs.[2] During 1970's Acridine-based anticancer agents were designed. In 1976 *m*-amsacrine, a 9-anilinoacridine was introduced into clinical use. Accordingly,this acridine has been clinically utilized as a single agent or in combination with other antineoplastic drugs in the treatment of acute nonlymphocytic, lymphocytic,[3, 4] and acute myeloid[5, 6] leukemias.

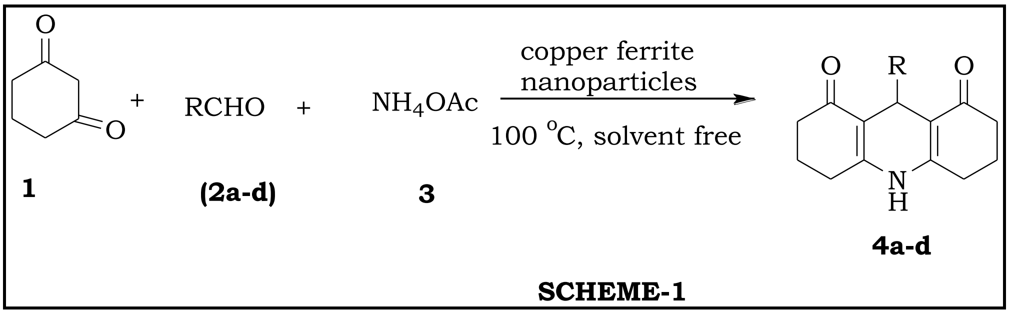
Acridines and their fused derivatives possess wide spectrum of biological activities, *viz* antimicrobial,[7] anti-tubercular,[8-10] antimalarial,[11] anti-cancer,[12] acetylcholinesterase inhibitor,[13,14]vasorelaxing[15] and anti-viral.[16] The antitumor and anti-infectious activities of acridines were due to their reversible binding with DNA.[17]Synthesis of Acridinediones &Study of their fluorescence properties is a continuing focal point of current research because these moieties are active pharmaceutical ingredients (API's) and also valuable reactive intermediates in both synthetic and medicinal chemistry.[18]

Literature survey reveals that various methodologieshave been reported for synthesis of acridinediones and substituted acridinediones. Many of these reported catalysts has so many disadvantages such as long reaction time, high catalyst loading, use of solvents and deactivation of catalyst on repeated use. Hence there is a need to develop an environmentally benign protocol for the synthesis of acridinediones.

Though there are many advantages of homogeneous metal catalysts, there are some difficulties in recovering the catalyst from the reaction mixture, which severely inhibit their use in industry. Heterogeneous catalyst effects in easy separation and recycling of nano catalyst. Recent reports showed that magnetic nano particles are efficient catalysts and they can be easily separated from the reaction mixture.[19, 20, 21]Ferrite nano material is one such reusable catalyst which shows profound catalytic activity in organic synthesis. Nano copper ferrite is a non-hygroscopic, inexpensive, non-toxic material, which has been utilized as a heterogeneous catalyst for various organic reactions. Recently, because of the unique properties of nano particles, synthetic chemists concentrated on nano-catalysts. Therefore, synthesis and characterization of catalysts with lower dimensions have become the most interesting topic of research. This method offers advantages such as short reaction time, recyclability of the catalyst and easy to work-up procedure.

Results and Discussion:

In this paper, we have reported the synthesis of acridinones (4a-d) (Scheme 1) and nano copperferrite particles by suitable synthetic pathway. The reaction of dimedone, aldehydes, ammonium acetate under solvent free conditions were carried. The structures of all the synthesized compounds have been characterized by ^{1}H NMRand the spectral data is given in the experimental section.



SCHEME-1

Scheme-1: Synthesis of 9 - aryl - 3, 3, 6, 6-tetramethylhexahydro acridine-1,8-diones employing reusable nano copper ferrite as catalyst.

Synthesis & Reusability of nano catalyst:

The catalyst was synthesized by citrate gel precursor method as earlier reported[22] and characterized using SEM & TEM. Copper (II) nitrate and iron (III) nitrate were taken in molar ratio of metal ion solutions were mixed. The finely powdered particles were calcinated at 600^{0}C. The powder was then characterized and compared with authenticate and found the nanoparticles formed & super imposed with reference particles[22, 23].

The catalyst was recovered by magnetization after completion of the reaction, washed with diethyl ether and the recovered catalyst was reused for four cycles. During washing with the solvent acetone, it was observed that there was no leaching of catalyst and was confirmed by performing the reaction with the filtrate. From our investigations, we observe that nano catalyst shows excellent to good reactivity with promising yields even after five cycles where yield of the product decreased slightly.

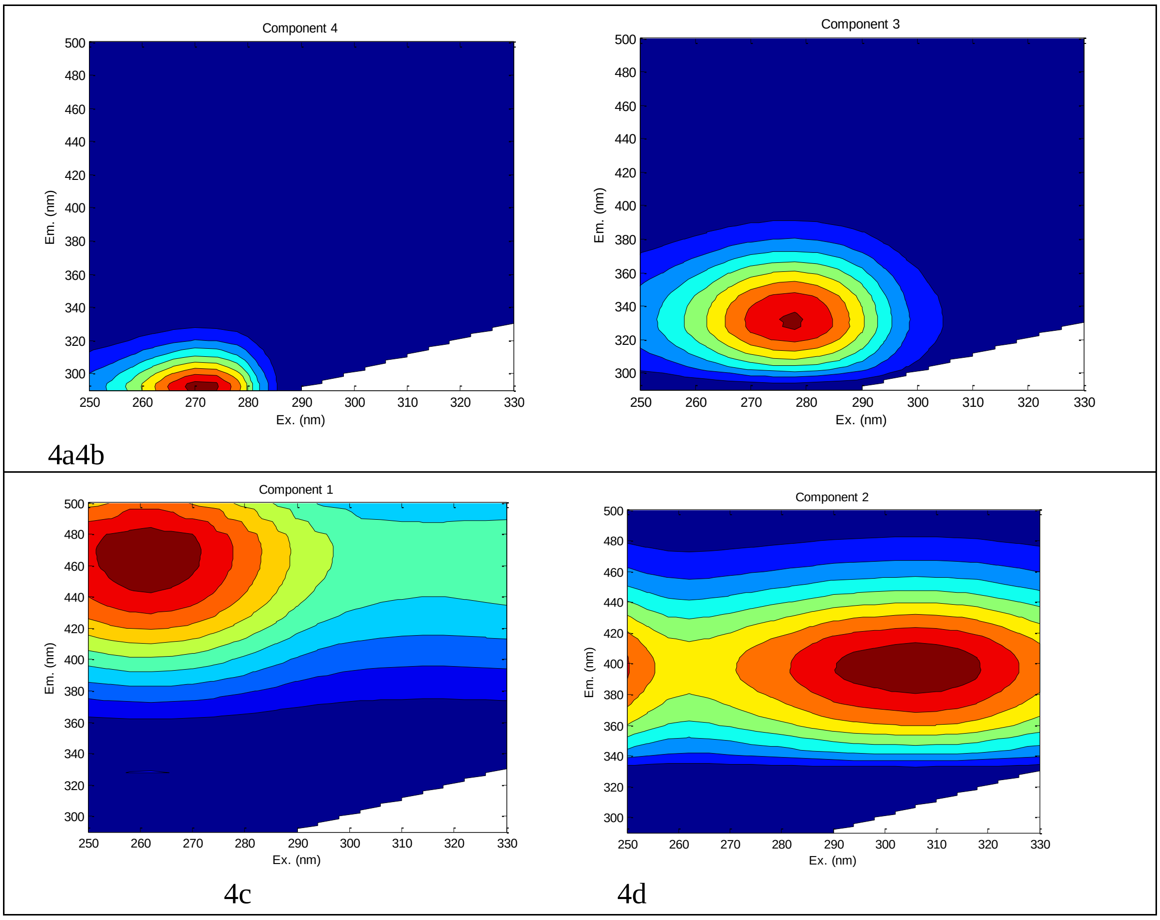
Fluorescence measurements:

Absorption spectra and excitation spectra of 9-substituted aryl-1,8-Dioxo-octahydroacridines (compounds 4a-4d) for diluted solution of acridine analogues were measured by a UV visible spectrophotometer (**OCEAN OPTICS INC**) Spectrophotometer. The fluorescence experiments were performed at fixed absorbance maxima and fluorescence emission spectra were obtained by using Fluoromax. The absorption maxima of **4a – 4d** were recorded in Acetone, and presented in **Fig-1**& the data of emission and the excitation maxima of the molecules were studied and presented in **Table-1.**4a-4d in acetone showed fluorescence emissions at 292 nm, 332 nm, 396 nm and 468 nm respectively. Whereas they showed 270 nm, 278 nm, 306 nm & 262 nm excitation respectively. From absorption and emission spectra's the stokes shifts observed as 22, 54, 90 and 206 nm. The detailed description with Stokes shifts were presented in table-1. This shows that the functional group on aldehyde enhances & exhibiting high emission values.

Hence, it is clearly evident that these molecules are suitable as NLO &biomarkers and further studies are under study regarding the NLO &biomarking.

Table-1

Compound	Solvent	Excitation (nm)	Emission (nm)	Stocks shift (nm)
4a	Acetone	270	292	22
4b	Acetone	278	332	54
4c	Acetone	306	396	90
4d	Acetone	262	468	206



4a4b

4c 4d

Figure 1: Excitation–emission matrices for 4a-4d in acetone. Fluorescence intensity in Raman units

Table 2: Setup parameters for creation of EEMs

Parameter	
Scan Mode	Emission
Data Mode	Fluorescence
Excitation Wavelength Range (nm)	300 - 500
Excitation Step Invertval (nm)	5
Emission Wavelength Range (nm)	320 - 700
Emission Interval (nm)	5
Speed (nm/min)	12,000

Delay (s)	0
Excitation Shutter Opening (nm)	5
Emissiom Shutter Opening (nm)	5
PMT Voltage (V)	700
Response	Auto
Replicates	1
Shutter Control	ON
Spectrum Correction	ON

Synthesis of nano particles:

The catalyst was synthesized by citrate gel precursor methodas earlier reported 22. Copper (II) nitrate and iron (III) nitrate were taken with 1:1 molar ratio of metal ion solutions were mixed.Citric acid was added in equimolar ratio to the above mixed metal ion solution. pH was adjusted to 7 by adding ammonia solution. The aqueous mixture was kept for stirring to form a highly viscous gel. The gel was then heated gradually up to 90◦C to evolve reddish brown gases and became dried gel which was finally treated at 350◦C for 1 h to observe whether the dry gel burnt out in self propagating manner to form loose powder. The finely powdered particles were calcinated at 600◦C. The powder was then characterized and compared with authenticate and found the nanoparticles formed & super imposed with reference particles[22, 23].

After the synthesis and characterization of nano particles done, herein we report for the first time on use of nano copper ferrite as heterogeneous support for the synthesis of 9-arylsubstituted-3, 3, 6, 6-tetramethylhexahydroacridine-1, 8-dione and their derivatives. The synthetic scheme is presented in **Scheme-1.** This method offers advantages such as short reaction time, recyclability of the catalyst and easy to work-up procedure.

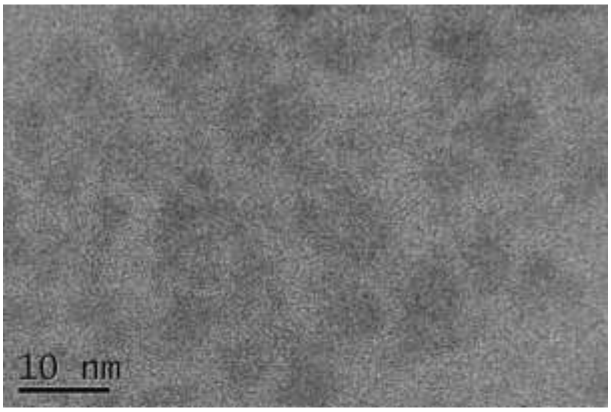


Figure 2. TEM image of $CuFe_2O_4$.

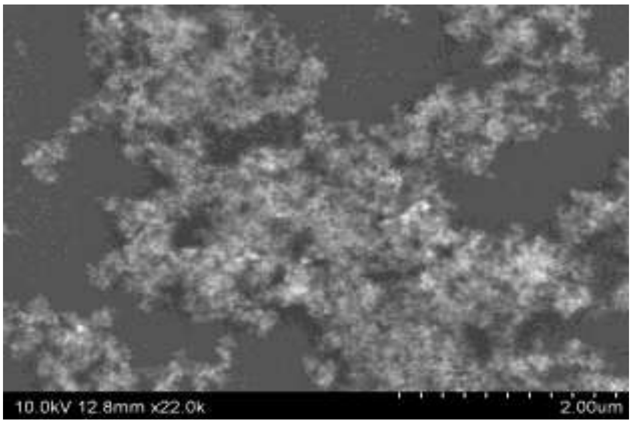
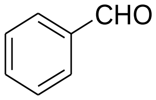


Figure 3. SEM image $CuFe_2O_4$.

Synthesis of acridinones(4a-d) using copper ferrite nanoparticles as catalyst:

A mixture of dimidone**(1)** (2 eq), substituted aromatic aldehydes**(2a-d)** (1 eq), ammonium acetate **(3)**and freshly prepared nano copper ferrite catalyst (10mg) were stirred at 100^{0}C in oil bath under solvent free conditions for 30 minutes **(Scheme-1).** After completion of the reaction, the contents were cooled to room temperature and a solid product was obtained. The product was dissolved in ethanol and the catalyst was recovered by magnetization. The crude product was further purified by crystallization. 9-substituted aryl-1,8-Dioxo-octahydroacridines**(4a-d)** were synthesized. All the synthesized products were characterized by 1H-NMRdata and their melting points were compared with authentic samples[24]. The reaction time and percentage of yields were presented in **(table-3).** The spectral data of the synthesized compounds **(4a-d)** are given below.

Table-3. Reaction time, percentage of yields of acridines (4a-d)

Entry	**R=Aldehyde**	Product	Time (min)	Yield[a] (%)
1	HCHO	**4a**	6	88
2		**4b**	8	93
3	4-Chloro benzaldehyde	**4c**	6	92
4	4-nitro benzaldehyde	**4d**	7	91

Reaction condition: Catalyst (10 mg), temperature 100^{0}C,[a]Isolated yields.

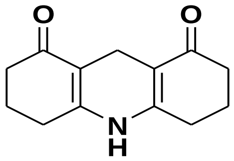
Conclussion:

9-substituted aryl-1,8-Dioxo-octahydroacridines4a-d has been reported. The fluorescence properties of all the synthesized compounds were studied in acetone. The results obtained were interesting that the compounds shows fluorescent in acetone with high stocks shifts. The above studies confirme that acridinonens are potential organic molecules for forther studies to explore as potential bioimaging and molecules for NLO properties.

Acknowledgments:

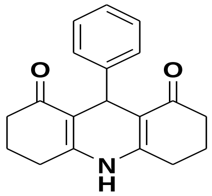
The authors are thankful to UGC-Grants, Govt. of INDIA, for providing funds to carry the work, Prof Y L N Murthy, Department of Organic Chemistry, Andhra University, Visakhapatnam, for providing laboratory facility & Prof N S Sharma,Department of PNCO, Andhra University, Visakhapatnam, for providing fluorescence spectral data.

Spectroscopic data of synthesized Acridinone derivatives:*3,4,6,7-tetrahydroacridine-1,8-dione (4a)*



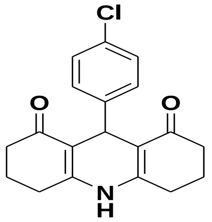
m.p 252-257^{0}C, ^{1}HNMR (400MHz, DMSO, δ, ppm): 1.8-2.50 (m, 8H, 4CH_2), 2.8 (s, 2H, CH_2), 8.8 (s, 1H, NH);

9-Phenyl3,4,6,7,9,10-hexahydro-acridine -1,8-diones (4b)



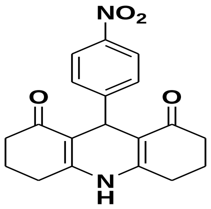
m.p-278-281^{0}C, ^{1}HNMR (400MHz, DMSO, δ, ppm): 1.9-2.5 (m, 8H, 4CH$_2$), 4.8 (s, 1H,CH), 7.3-6.7 (m, 5H, Ar-H), 9.2 (s, 1H, NH);

9-(4-Chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-acridine -1,8-diones (4c)



m.p -291-294^{0}C, ^{1}HNMR (400MHz, DMSO, δ, ppm): 1.79-2.54 (m, 8H, 4CH$_2$), 4.6 (s, 1H,CH), 7.4-7.12 (m, 4H, Ar-H), 9.8 (s, 1H, NH);

9-(4-Nitrophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-acridine -1,8-diones (4d)



m.p-269-272^{0}C, ^{1}HNMR (400MHz, DMSO, δ, ppm): 1.55-2.7 (m, 8H, 4CH$_2$), 3.51 (s, 3H, OCH$_3$), 4.73 (s, 1H,CH), 6.9-7.15 (m, 4H, Ar-H), 9.13 (s, 1H, NH);

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