ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 5, Issue, 10, pp.3076-3081, October, 2013

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL STUDIES OF 9-ARYL SUBSTITUTED ACRIDINEDIONE DERIVATIVES BY HANTZSH CONDENSATION

***Nalini, V. and Girija, R.**

Department of Chemistry, Queen Mary's College (A), Chennai - 600 004, Tamilnadu, India

ARTICLE INFO

Article History:
Received 24th July, 2013
Received in revised form
08th August, 2013
Accepted 10th September, 2013
Published online 23rd October, 2013

Key words:
Thermal method, Microwave irradiation,
Three component reaction, Acridinedione.

ABSTRACT

Nearly twenty four acridinedione derivatives are prepared by thermal method using P_2O_5 / ethanol catalyst. The same compounds are prepared by solvent free green approach involves the exposure of neat reactants to microwave irradiation of three component reaction of dimedone, aromatic aldehydes and amines in a stoichiometric ratio 2:1:1 for few minutes afforded the formation of stable acridinedione derivatives in an excellent yield (80-95%). The structure of all the products has been characterized by IR, ^1H, ^{13}C NMR and mass spectral studies. The percentage of yield and purity is compared and found to be excellent in greener method and this method is found to be environmental friendly.

INTRODUCTION

Microwave irradiation can be used as a facile and general method for the construction of a wide variety of acridine derivatives. Multi-component reactions (MCRs) are a promising and vital field of chemistry because the synthesis of complicated molecules can be achieved in a very fast, efficient and time saving manner without the isolation of any intermediate. These reactions offer a wide range of possibilities for the efficient construction of highly complex molecules in a single step. In recent years, the discovery of MCRs has become an increasingly active area of research yielding novel chemical scaffolds for drug discovery. Thus the development of new multicomponent reaction is a popular area of research in current organic chemistry [14]. In the past decade there have been tremendous development in three and four component reactions and great efforts continue to be made to develop new MCRs [4, 5, 12]. It is well documented that the acridinediones are of great importance both in organic synthesis and in biological chemistry [15, 21]. Synthetic methods for these compounds have been developed to a great extent, including conventional thermal reactions[13, 18], microwave irradiation reaction [22, 23] by using catalysts P_2O_5 and Amberolite[7]. Acridinedione derivatives have a wide spectrum of biological activities such as antibacterial, antimalarial, anticancer and mutagenic properties. Acridine systems have attracted considerable attention due to their potential pharmacological activity and there are many industrial applications for acridines[3, 19, 20]. A three-component Hantzsch-type condensation of different anilines with dimedone and benzaldehye leads to the formation of a unique acridine derivative with an unusual breaking of a C-N bond. The reaction was also carried out employing rapid microwave or conventional heating and sonication as alternative energy source[9]. Because of its biological activity and applications, our interest is to synthesize new acridinedione derivatives. The interaction between microorganism with plants and animals are natural and constant. Many chemicals kill or prevent the growth of microorganisms. Such chemicals have been called antimicrobial agents[16]. Concentration and contact time are critical factors that determine the effectiveness of an antimicrobial agent against a particular microorganism. Microorganisms vary in their sensitivity to particular antimicrobial agents. Many antimicrobial agents block active metabolism and prevent the organism generating the macro molecular constituents needed for reproduction. The important of heterocyclic chemistry in biological system as well as in chemotherapy is well established[6, 10, 11, 17]. Acridines the earliest known antibiotics[1, 2, 8] are toxic towards bacteria and particularly towards malarial parasites due to their ability to inhibit DNA and RNA synthesis. In continuation of our interest in the synthesis of biologically active acridinediones, it was considered worthwhile to evaluate antimicrobial activity of some new acridinediones.

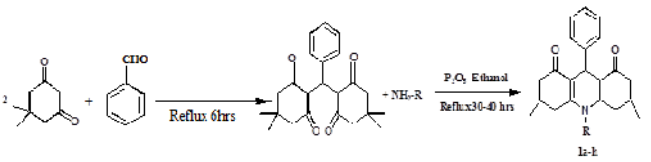
**Corresponding author: Nalini, V. Department of Chemistry, Queen Mary's College (A), Chennai - 600 004, Tamilnadu, India.*

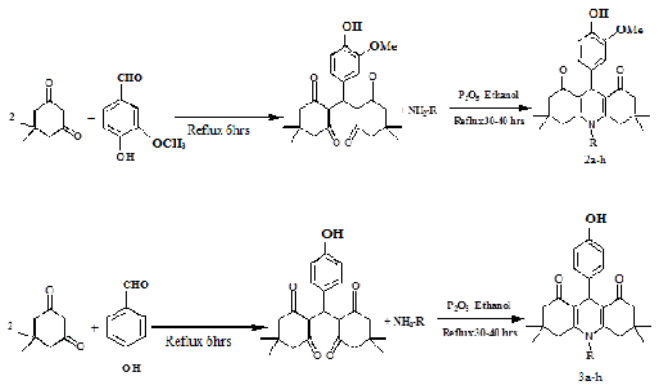
MATERIAL AND METHODS

All the melting points are uncorrected; IR spectra were recorded on FTIR – 8300 shimadzu spectrometer. ^1H NMR spectra were recorded on Jeol- FXQ (90 MHz), Jeol GSX (400 MHz) and DPX 200 (200 MHz). Mass spectra were recorded on Jeol- JMS- DX 303hf.

Synthesis of 9-Aryl substituted acridinedione derivatives 1a-3h Scheme 1

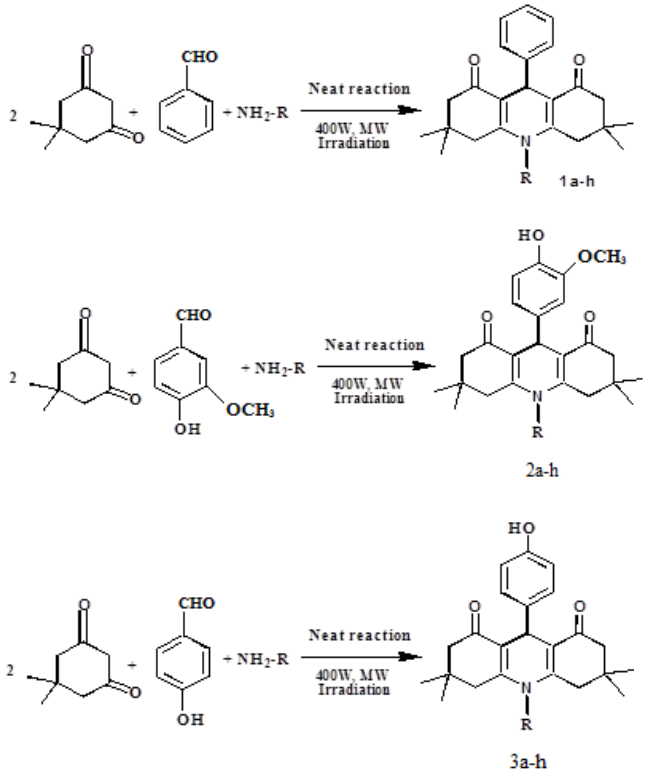
Thermal method





Two equivalents of dimedone with benzaldehyde were refluxed for 6 hours the tetra ketone compound is obtained. The structure of the tetra ketone is identified by ^{1}H NMR studies. This tetra ketone compound is refluxed with amine substituents for 30-40 hours in thermal condition in presence of P_2O_5 and excess ethanol. It gives the substituted acridinedione derivatives of yield 65-72%.

Neat reaction



Hantzsh condensation of dimedone, benzaldehyde and substituents (2:1:1) in a solvent free conditions (neat reaction) is treated on microwave irradiation for 10 minutes afforded the formation of the orange solid mass of acridinedione derivative of an excellent yield (85-92%). Various substituted acridinediones were prepared and reported below.

RESULTS AND DISCUSSION

Chemical and pharmaceutical industries are facing constraints regarding environmental aspects and saving energy. To overcome such problems in organic synthesis, the microwave (MW) irradiation as a source of energy is used. In this study we use an excellent synthetic method for new decahydroacridine-1,8-dione derivatives 1a-3h through three component condensation reactions by microwave technique. The employed amines exhibit an excellent substrate for synthesis of acridinediones under our reaction conditions.

Table 1. Amine Substituents (R) used for the synthesis of acridinedione derivatives

Compounds	R
1a, 2a, 3a	$NHCOCH_2NH_2$
1b, 2b, 3b	$NHCOCH(CH_3)NH_2$
1c, 2c, 3c	$NHCOC\ H(CH_2C_6H_5)NH_2$
1d, 2d, 3d	$NHCOCH(NH_2)(CH_2)_3NHC(NH_2)_2$
1e, 2e, 3e	$NHCOCH(NH_2)CH_2(OH)$
1f, 2f, 3f	$NHCOCH(NH_2)CH_2CH(CH_3)_2$
1g, 2g, 3g	$NHCOCH(NH_2)CH_2CH_2CH_3$
1h, 2h, 3h	$NH(CO(NH_2)CH_2S)_2$

Characterization

2, 2'-(benzylidene) bisdimedone

^{1}H NMR: δ 1.98, 2.56 (Gem dimethyl, 2d), 2.35 (1, 3, 7, 8, CH_2,m), 6.9 – 7.8 (Ar-H, m), ^{13} C-NMR: δ 28.5, 31.0, 33.6, 40.39(aliphatic carbons), 112.2, 155.8 (olefinic carbons), 114.1, 122.5, 129.7, 131.6, 136.8 (aryl carbons), 196.7 (ketocarbonyl)

10-Glycine-9-Phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (1a)

Hantzsh condensation of two equivalents of dimedone (3.08g, 0.022m) with glycine hydrazide (1g, 0.011m), benzaldehyde (1.166g, 0.011m) in solvent free condition, is treated on microwave irradiation for 3 minutes. The formation of pale yellow solid confirm acridinedione derivative (1a), in an excellent yield. ^{1}H NMR = δ 0.98-1.17 (gem dimethyl), 2.14-2.25 (d, 4H, C2&C4), 2.46 (m, -CH), 4.74 (s, CH-NH_2), 7.08-7.29 (m, Ar-H).^{13}C NMR= δ27.35, 28.10, 29.31, 31.85, 32.24, 35.09, 40.89, 50.75 (aliphatic carbons), 115.68 (olefinic carbon), 126.41, 128.08, 128.40, 128.47, 128.95, 129.63, 130.12, 144.09 (aryl carbons), 162.33 (amide carbon), 196.52 (ketocarbonyl). IR: 1540, 1655, 1723, 3327 cm^{-1}. Mass: m/z= 422, 421.

10-Alanine-9-Phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (1b)

The microwave irradiation of two equivalents of dimedone (2.71g, 0.019m) with alanine hydrazide (1g, 0.009m), benzaldehyde (1.06g, 0.009m) in solvent free condition, is treated for 4 minutes. The formation of pale orange solid confirm acridinedione derivative **(1b),** in an excellent yield. ^{1}H NMR = δ 0.98-1.168 (gem dimethyl), 2.14-2.25 (d, 4H, C2&C4), 2.46 (m, -CH), 4.74 (s, CH-NH_2), 7.09-7.53 (m, Ar-H). ^{13}C NMR = δ 27.37, 28.15, 29.33, 31.86, 32.93, 40.93, 50.77 (aliphatic carbons), 115.70 (olefinic carbon), 126.42, 128.09, 128.41, 128.49, 128.94, 129.06, 129.52, 129.81, 130.16, 133.57, 144.10 (aryl carbons), 162.33 (amide carbon), 196.53 (keto carbonyl). IR: 1540, 1655, 1723, 3327 cm^{-1}. Mass: m/z= 436, 435.

9-Phenyl-10-phenylalanine-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (1c)

Hantzsh condensation of two equivalents of dimedone (1.4g, 0.05m) with phenyl alaninehydrazide (1g, 0.005m), benzaldehyde (0.53g, 0.005m) in solvent free condition, is treated on microwave irradiation for 3 minutes. The formation of yellowish orange solid confirm acridinedione derivative **(1c),** in an excellent yield.^{1}H NMR = δ 0.98-1.168 (gem dimethyl), 2.14-2.27 (d, 4H, C2&C4), 2.48 (m, -CH), 4.76 (s, CH-NH_2), 7.09-7.60 (m, Ar-H).^{13}C NMR = δ 27.38, 28.20, 29.35, 31.85, 32.95, 40.95, 52.70 (aliphatic carbons), 115.75 (olefinic carbon), 126.42, 128.09, 128.41, 128.94, 129.06, 129.52, 130.16, 133.57, 144.21 (aryl carbons), 162.33 (amide carbon), 196.57 (keto carbonyl). IR: 1540, 1655, 1723, 3327 cm^{-1}. Mass: m/z= 512, 511.

Table 2. Comparison of Thermal and Microwave method (Yield and reaction time of acridinedione derivatives)

Compound	R	Thermal method (Hrs.)	Yield %	Micro wave method (min)	Yield %	Melting point ^{0}C
1a	$NHCOCH_2NH_2$	31	65-67	3	92	153-155
1b	$NHCOCH(CH_3)NH_2$	35	70	4	80	168-170
1c	$NHCOCH(CH_2C_6H_5)NH_2$	30	72	3	89	162-165
1d	$NHCOCH(NH_2)(CH_2)_3NHC(NH_2)_2$	32	65-68	5	92	160-162
1e	$NHCOCH(NH_2)CH_2(OH)$	39	58	6	90	158-160
1f	$NHCOCH(NH_2)CH_2CH(CH_3)_2$	40	62	5	85	148-150
1g	$NHCOCH(NH_2)CH_2CH_2CH_3$	36	60	4	92	148-150
1h	$NH(CO(NH_2)CH_2S)_2$	38	68	6	90	195-197
2a	$NHCOCH_2NH_2$	35	65	3	91	208-210
2b	$NHCOCH(CH_3)NH_2$	34	56	4	92	180-182
2c	$NHCOC\ H(CH_2C_6H_5)NH_2$	37	62	3	89	175-177
2d	$NHCOCH(NH_2)(CH_2)_3NHC(NH_2)_2$	31	60	5	88	184-186
2e	$NHCOCH(NH_2)CH_2(OH)$	30	70	6	92	198-200
2f	$NHCOCH(NH_2)CH_2CH(CH_3)_2$	39	65	5	90	213-215
2g	$NHCOCH(NH_2)CH_2CH_2CH_3$	35	69	4	91	167-169
2h	$NH(CO(NH_2)CH_2S)_2$	32	68	6	92	192-195
3a	$NHCOCH_2NH_2$	34	62	3	87	215-217
3b	$NHCOCH(CH_3)NH_2$	36	64	4	76	212-215
3c	$NHCOC\ H(CH_2C_6H_5)NH_2$	40	65	3	89	188-190
3d	$NHCOCH(NH_2)(CH_2)_3NHC(NH_2)_2$	32	68	5	85	205-207
3e	$NHCOCH(NH_2)CH_2(OH)$	33	66	6	89	210-212
3f	$NHCOCH(NH_2)CH_2CH(CH_3)_2$	34	70	5	90	204-206
3g	$NHCOCH(NH_2)CH_2CH_2CH_3$	31	69	4	91	209-211
3h	$NH(CO(NH_2)CH_2S)_2$	35	67	6	87	185-187

10-Arginine-9-Phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (1d)

The microwave irradiation of two equivalents of dimedone (1.4g, 0.010m) with arginine hydrazide (1g, 0.005m), benzaldehyde (0.53g, 0.005m) in solvent free condition, is treated for 5 minutes. The formation of pale orange solid confirm acridinedione derivative **(1d),** in an excellent yield.^{1}H NMR = δ 0.98-1.165 (gem dimethyl), 2.14-2.26 (d, 4H, C2&C4), 2.52 (m, -CH), 3.00 (d, CH_2), 4.74 (s, CH-NH2), 7.08-7.59 (m, Ar-H).^{13}C NMR = δ 27.34, 28.01, 29.31, 31.85, 32.24, 35.08, 40.88, 50.74, 53.56 (aliphatic carbons), 115.68 (olefinic carbon), 126.41, 128.08, 128.40, 128.46, 128.91, 129.04, 129.60, 129.80, 130.13, 133.51, 144.09 (aryl carbons), 162.34, 170.16 (amide carbons), 196.54 (keto carbonyl). IR: 1540, 1655, 1723, 3327 cm^{-1}. Mass: m/z= 522, 521.

9-Phenyl-10-serine-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (1e)

Hantzsh condensation of two equivalents of dimedone (2.24g, 0.016m) with serine hydrazide (1g, 0.008m), benzaldehyde (0.84g, 0.008m) in solvent free condition, is treated on microwave irradiation for 6 minutes. The formation of brownish yellow solid confirm acridinedione derivative (1e), in an excellent yield.^{1}H NMR = δ 0.98-1.15 (gem dimethyl), 2.14-2.25 (d, 4H, C2&C4), 2.46 (m, -CH), 4.74 (s, CH-NH_2), 7.0-7.29 (m, Ar-H).^{13}C NMR = δ 27.34, 28.11, 28.29, 29.30, 31.85, 32.23, 35.04, 35.08, 40.88, 50.75 (aliphatic carbons), 115.68 (olefinic carbon), 126.41, 128.08, 128.40, 128.45, 128.88, 129.50, 144.09 (aryl carbons), 162.34 (amide carbon), 196.52 (keto carbonyl). IR: 1540, 1655, 1723, 3327 cm^{-1}. Mass: m/z= 452, 451.

10-leucine-9-Phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (1f)

The microwave irradiation of two equivalents of dimedone (1.9g, 0.013m) with leucine hydrazide (1g, 0.0068m), benzaldehyde (0.72g, 0.0068m) in solvent free condition, is treated for 5 minutes. The formation of orange solid confirm acridinedione derivative (1f), in an excellent yield.^{1}H NMR = δ 0.98-1.16 (gem dimethyl), 2.14-2.25 (d, 4H, C2&C4), 2.46 (m, -CH), 2.97 (d, CH_2), 4.74 (s, CH-NH2), 7.08-7.53 (m, Ar-H).^{13}C NMR = δ 27.35, 28.11, 29.31, 31.85, 32.24, 35.09, 40.88, 50.75 (aliphatic carbons), 115.68 (olefinic carbon), 126.41 128.08, 128.40, 128.89, 129.55, 130.10, 144.09 (aryl carbons), 160.33 (amide carbon), 196.52(keto carbonyl). IR: 1540, 1655, 1723, 3327 cm^{-1}. Mass: m/z= 478, 477.

9-Phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-10-valine acridinedione: (1g)

Hantzsh condensation of two equivalents of dimedone (2.12g, 0.014m) with valinehydrazide (1g, 0.007m), benzaldehyde (0.80g, 0.007m) in solvent free condition, is treated on microwave irradiation for 4 minutes. The formation of yellowish brown solid confirm acridinedione derivative (1g), in an excellent yield.^{1}H NMR = δ 0.98-1.16 (gem dimethyl), 2.14-2.25 (d, 4H, C2&C4), 2.47 (m, -CH), 4.74 (s, CH-NH_2), 7.08-7.20 (m, Ar-H).^{13}C NMR = δ 27.32, 28.28, 29.36, 31.34, 32.25, 40.89, 50.77, 54.18, 55.93, 57.35 (aliphatic carbons), 115.85 (olefinic carbon), 120.05, 136.48, 144.06, 145.88 (aryl carbons), 162.24 (amide carbon), 196.78 (keto carbonyl). IR: 1540, 1655, 1723, 3327 cm^{-1}. Mass: m/z= 452, 451.

10-Cystine-9-Phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (1h)

The microwave irradiation of two equivalents of dimedone (1.0g, 0.008m) with cystinehydrazide (1g, 0.004m), benzaldehyde (0.42g, 0.004m) in solvent free condition, is treated for 6 minutes. The formation of dark red solid confirm acridinedione derivative (1h), in an excellent yield.^{1}H NMR = δ 1.0-1.10 (gem dimethyl), 2.16-2.3 (d, 4H, C2&C4), 2.53 (m, -CH), 3.89 (d, CH_2), 4.65(s, CH-NH_2), 6.57-7.28 (m, Ar-H).^{13}C NMR = δ 27.28, 29.34, 31.30, 32.22, 37.89, 40.08, 40.30, 40.50, 40.86, 50.78, 55.91 (aliphatic carbons), 115.80 (olefinic carbon), 120.07, 136.41, 144.07, 145.98 (aryl carbons), 162.15 (amide carbon), 196.69 (keto carbon). IR: 1540, 1655, 1723, 3327 cm^{-1}. Mass: m/z= 570, 569.

10-Glycine-(3-methoxy-4-hydroxy)-9-Phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (2a)

Hantzsh condensation of two equivalents of dimedone (3.08g, 0.022m) with glycine hydrazide (1g, 0.011m), 4-hydroxy-3-methoxy benzaldehyde (1.67g, 0.011m) in solvent free condition, is treated on microwave irradiation for 3 minutes. The formation of yellow solid confirm acridinedione derivative (2a), in an excellent yield.^{1}H NMR = δ 0.98-1.10 (gem dimethyl), 2.14-2.25 (d, 4H, C2&C4), 2.46 (m, -CH), 3.12 (-OCH_3), 4.74 (s, CH-NH_2), 7.08-7.29 (m, Ar-H).^{13}C NMR

= δ 27.35, 29.31, 31.85, 32.24, 40.89, 50.76 (aliphatic carbons), 115.69 (olefinic carbon), 126.40, 128.08, 128.40, 144.11 (aryl carbons), 162.29 (amide carbon), 196.47 (keto carbon). IR: 1520, 1665, 1703, 3307 cm^{-1}. Mass: m/z=468, 467.

10-Alanine-(4-hydroxy-3-methoxy)-9-Phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (2b)

The microwave irradiation of two equivalents of dimedone (2.71g, 0.019m) with alanine hydrazide (1g, 0.009m), 4-hydroxy-3-methoxy benzaldehyde (1.47g, 0.009m) in solvent free condition, is treated for 3 minutes. The formation of orange solid confirm acridinedione derivative (2b), in an excellent yield.^{1}H NMR = δ 1.0-1.10 (gem dimethyl), 2.16-2.27 (d, 4H, C2&C4), 2.45 (m, -CH), 3.89 (s, OCH_3), 4.65 (s, CH-NH_2), 6.58-7.26 (m, Ar-H).^{13}C NMR = δ 27.30, 28.27, 28.34, 29.34, 30.97, 31.33, 32.24, 40.88, 50.78, 54.15, 55.91, 57.35 (aliphatic carbons), 115.83 (olefinic carbon), 120.04, 136.47, 144.02, 145.90 (aryl carbon), 162.18 (amide carbon), 196.76 (keto carbonyl). IR: 1520, 1665, 1703, 3307 cm^{-1}. Mass: m/z= 482, 481.

(4-hydroxy-3-methoxy)-9-Phenyl-10-phenylalanine-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (2c)

Hantzsh condensation of two equivalents of dimedone (1.4g, 0.010m) with phenyl alaninehydrazide (1g, 0.005m), 4-hydroxy-3-methoxy benzaldehyde (0.76g, 0.005m) in solvent free condition, is treated on microwave irradiation for 4 minutes. The formation of yellow solid confirm acridinedione derivative **(2c),** in an excellent yield.^{1}H NMR = δ 0.98-1.168 (gem dimethyl), 2.14-2.25 (d, 4H, C2&C4), 2.46 (m, -CH), 3.08 (s, OCH_3), 4.74 (s, CH-NH_2), 7.09-7.53 (m, Ar-H).^{13}C NMR = δ 27.37, 28.15, 29.33, 31.86, 32.93, 40.93, 50.77 (aliphatic carbons), 115.70 (olefinic carbon), 126.42, 128.09, 128.41, 128.49, 128.94, 129.06, 129.52, 129.81, 130.16, 133.57, 144.10 (aryl carbons), 162.33 (amide carbon), 196.53 (keto carbonyl). IR: 1520, 1665, 1703, 3307 cm^{-1}. Mass: m/z= 558, 557.

10-Arginine-(4-hydroxy-3-methoxy)-9-Phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (2d)

The microwave irradiation of two equivalents of dimedone (1.4g, 0.010m) with arginine hydrazide (1g, 0.005m), 4-hydroxy-3-methoxy benzaldehyde (0.76g, 0.005m) in solvent free condition, is treated for 3 minutes. The formation of reddish orange solid confirm acridinedione derivative (2d), in an excellent yield.^{1}H NMR = δ 1.0-1.10 (gem dimethyl), 2.17-2.21 (d, 4H, C2&C4), 2.46 (m, -CH), 3.88 (s, OCH_3), 4.65 (s, CH-NH_2), 6.5-7.30 (m Ar-H).^{13}C NMR = δ 27.28, 29.34, 30.97, 31.26, 32.19, 40.88, 50.80, 55.95 (aliphatic carbons), 115.79 (olefinic carbon), 120.13, 136.34, 144.15, 146.09 (aryl carbons), 162.16 (amide carbon), 196.65(keto carbon). IR: 1520, 1665, 1703, 3307 cm^{-1}. Mass: m/z= 568, 567.

(4-hydroxy-3-methoxy)-9-Phenyl-10-serine-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (2e)

The microwave irradiation of two equivalents of dimedone (2.24g, 0.016m) with serine hydrazide (1g, 0.008m), 4-hydroxy-3-methoxy benzaldehyde (1.21g, 0.008m) in solvent free condition, is treated for 5 minutes. The formation of pale red solid confirm acridinedione derivative **(2e),** in an excellent yield.^{1}H NMR = δ 1.0-1.10 (gem dimethyl), 2.20-2.26 (d, 4H, C2&C4), 2.46 (m, -CH), 3.87 (s, OCH_3), 4.66 (s, CH-NH_2), 6.58-6.98 (m, Ar-H). ^{13}C NMR = δ 27.34, 29.39, 31.31, 32.21, 40.94, 50.84, 56.01 (aliphatic carbons), 115.82 (olefinic carbon), 120.14, 136.39, 144.11, 146.01 (aryl carbons), 162.22 (amide carbon), 196.74 (keto carbon). IR: 1520, 1665, 1703, 3307 cm^{-1}. Mass: m/z= 498, 497.

(4-hydroxy-3-methoxy)-10-leucine-9-Phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (2f)

Hantzsh condensation of two equivalents of dimedone (1.4g, 0.01m) with leucine hydrazide (1g, 0.005m), 4-hydroxy-3-methoxy benzaldehyde (1.03g, 0.005m) in solvent free condition, is treated on microwave irradiation for 6 minutes. The formation of yellow solid confirm acridinedione derivative (2f), in an excellent yield.^{1}H NMR = δ 1.0-1.10 (gem dimethyl), 2.15-2.26 (d, 4H, C2&C4), 2.46 (m, CH), 3.88 (s, OCH3), 4.65 (s, CH-NH2), 6.57-7.29(m, Ar-H).^{13}C NMR = δ 27.27, 29.33, 31.28, 32.21, 39.65, 39.86, 40.07, 40.28, 40.49, 40.85, 50.77, 55.90 (aliphatic carbons), 115.79 (olefinic carbon), 120.08, 136.38, 144.09, 146.02 (aryl carbons), 162.17 (amide carbon), 196.71 (keto carbonyl). IR: 1520, 1665, 1703, 3307 cm^{-1}. Mass: m/z= 524, 523.

(4-hydroxy-3-methoxy)-9-Phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-10-valine acridinedione: (2g)

Hantzsh condensation of two equivalents of dimedone (2.12g, 0.015m) with valinehydrazide (1g, 0.0076m), 4-hydroxy-3-methoxy benzaldehyde (1.15g, 0.0076m) in solvent free condition, is treated on microwave irradiation for 4 minutes. The formation of reddish yellow solid confirm acridinedione derivative (2g), in an excellent yield.^{1}H NMR = δ 1.0-1.10 (gem dimethyl), 2.16-2.26 (d, 4H, C2&C4), 2.45 (m, -CH), 3.89 (s, OCH_3), 4.66 (s, CH-NH_2), 6.56- 7.26 (m, Ar-H).^{13}C NMR = δ 27.31, 28.27, 29.35, 31.33, 32.24, 40.88, 50.79, 54.16, 55.92, 57.34 (aliphatic carbons), 115.83 (olefinic carbon), 120.03, 136.49, 144.01, 145.87 (aryl carbons), 162.14 (amide carbon), 196.70 (keto carbonyl). Mass: m/z= 510, 509.

10-Cystine-(4-hydroxy-3-methoxy)-9-phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: **(2h)**

The microwave irradiation of two equivalents of dimedone (1.0g, 0.008m) with cystinehydrazide (1g, 0.004m), 4-hydroxy-3-methoxy benzaldehyde (0.60g, 0.004m) in solvent free condition, is treated for 6 minutes. The formation of pale orange solid confirm acridinedione derivative (2h), in an excellent yield.^{1}H NMR = δ 1.0-1.10 (gem dimethyl), 2.16-2.22 (d, 4H, C2&C4), 2.45 (m, -CH), 3.96 (s, OCH_3), 4.65 (s, CH-NH_2), 6.56-7.26 (m, Ar-H).^{13}C NMR = δ 27.31, 28.28, 28.40, 29.35, 30.97, 31.34, 32.24, 40.89, 50.79, 54.15, 55.93, 56.16, 57.35 (aliphatic carbons), 115.83 (olefinic carbons), 120.04, 136.47, 144.02, 145.90 (aryl carbons), 162.19 (amide carbon), 196.77 (keto carbonyl). IR: 1520, 1665, 1703, 3307 cm^{-1}. Mass: m/z= 616, 615.

9-Phenyl-10-(Glycine)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (3a)

Hantzsh condensation of two equivalents of dimedone (3.08g, 0.022m) with glycine hydrazide (1g, 0.011m), 4-hydroxy benzaldehyde (1.34g, 0.011m) in solvent free condition, is treated on microwave irradiation for 3 minutes. The formation of yellow solid confirm acridinedione derivative (3a), in an excellent yield.^{1}H NMR = δ 0.98-1.19 (gem dimethyl), 2.14-2.26 (d, 4H, C2&C4), 2.47 (m, CH), 4.75 (s, CH-NH_2), 7.08-7.28 (m, Ar-H), 8.02 (-OH).^{13}C NMR = δ 27.36, 28.19, 29.36, 31.88, 32.22, 34.09, 40.89, 50.65 (aliphatic carbons), 115.68 (olefinic carbon), 126.41, 128.08, 128.40, 128.47, 128.95, 129.63, 130.12, 144.09 (aryl carbons), 162.53 (amide carbon), 196.54 (keto carbonyl). IR: 1510, 1660, 1733, 3302 cm^{-1}. Mass: m/z= 438, 437.

10-Alanine-9-phenyl-10-(Glycine)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: **(3b)**

The microwave irradiation of two equivalents of dimedone (2.71g, 0.019m) with alanine hydrazide (1g, 0.009m), 4-hydroxy benzaldehyde (1.09g, 0.009m) in solvent free condition, is treated for 4 minutes. The formation of pale orange solid confirm acridinedione

derivative (3b), in an excellent yield.^{1}H NMR = δ 0.98-1.168 (gem dimethyl), 2.14-2.27 (d, 4H, C2&C4), 2.46 (m, CH), 4.74 (s, CH-NH_2), 7.09-7.53 (m, Ar-H), 8.10 (-OH).^{13}C NMR = δ 27.37, 28.15, 29.33, 31.86, 32.93, 40.93, 50.77 (aliphatic carbons), 115.70 (olefinic carbon), 126.42, 128.09, 128.41, 128.59, 128.94, 129.06, 129.42, 129.81, 130.16, 133.57, 144.10 (aryl carbons), 162.43 (amide carbon), 196.52 (keto carbonyl). IR: 1510, 1660, 1733, 3302 cm^{-1}. Mass: m/z= 452, 451.

9-Phenyl-10-phenylalanine-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (3c)

Hantzsh condensation of two equivalents of dimedone (1.4g, 0.010m) with phenyl alaninehydrazide (1g, 0.005m), 4-hydroxy benzaldehyde (0.61g, 0.005m) in solvent free condition, is treated on microwave irradiation for 3 minutes. The formation of yellowish red solid confirm acridinedione derivative (3c), in an excellent yield.^{1}H NMR = δ 0.98-1.168 (gem dimethyl), 2.14-2.28 (d, 4H, C2&C4), 2.48 (m, CH), 4.78 (s, CH-NH_2), 7.09-7.50 (m, Ar-H), 8.10 (-OH).^{13}C NMR = δ 27.38, 28.25, 29.34, 31.76, 32.83, 40.98, 50.67 (aliphatic carbons), 115.70 (olefinic carbon), 126.45, 128.19, 128.46, 128.49, 128.94, 129.06, 129.55, 129.81, 130.16, 133.57, 144.10 (aryl carbons), 162.53 (amide carbon), 196.52 (keto carbonyl). IR: 1510, 1660, 1733, 3302 cm^{-1}. Mass: m/z= 528, 527.

10-Arginine-4-hydroxyphenyl-9-phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (3d)

The microwave irradiation of two equivalents of dimedone (1.4g, 0.010m) with argininehydrazide (1g, 0.005m), 4-hydroxy benzaldehyde (0.61g, 0.005m) in solvent free condition, is treated for 5 minutes. The formation of reddish orange solid confirm acridinedione derivative (3d), in an excellent yield.^{1}H NMR= δ 0.98-1.165 (gem dimethyl), 2.14-2.25 (d, 4H, C2&C4), 2.53 (m, CH), 3.08 (d, CH_2), 4.75 (s, CH-NH_2), 7.07-7.59 (m, Ar-H), 8.09 (OH).^{13}C NMR = δ 27.34, 28.01, 29.31, 31.85, 32.24, 35.08, 40.88, 50.74, 53.56 (aliphatic carbons), 115.68 (olefinic carbon), 126.41, 128.08, 128.40, 128.46, 128.91, 129.04, 129.60, 129.80, 130.13, 133.51, 144.09 (aryl carbons), 162.44, 170.26 (amide carbons), 196.51 (keto carbonyl). IR: 1510, 1660, 1733, 3302 cm^{-1}. Mass: m/z= 538, 537.

4-Hydroxyphenyl-9-phenyl-10-serine-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (3e)

Hantzsh condensation of two equivalents of dimedone (2.24g, 0.016m) with serine hydrazide (1g, 0.008m), 4-hydroxy benzaldehyde (0.97g, 0.008m) in solvent free condition, is treated on microwave irradiation for 6 minutes. The formation of yellow solid confirm acridinedione derivative (3e), in an excellent yield.^{1}H NMR= δ 0.98-1.15 (gem dimethyl), 2.14-2.29 (d, 4H, C2&C4), 2.45 (m, CH), 4.74 (s, CH-NH_2), 7.0-7.30 (m, Ar-H), 8.13 (-OH).^{13}C NMR= δ 27.34, 28.11, 28.29, 29.30, 31.85, 32.23, 35.04, 35.08, 40.88, 50.75 (aliphatic carbons), 115.68 (olefinic carbon), 126.41, 128.08, 128.40, 128.45, 128.88, 129.50, 130.04, 144.09 (aryl carbons), 162.34 (amide carbon), 196.52 (keto carbonyl). IR: 1510, 1660, 1733, 3302 cm^{-1}. Mass: m/z= 468, 467.

4-Hydroxyphenyl-9-phenyl-10-leucine-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (3f)

The microwave irradiation of two equivalents of dimedone (1.90g, 0.013m) with leucine hydrazide (1g, 0.0068m), 4-hydroxy benzaldehyde (0.73g, 0.0068m) in solvent free condition, is treated for 5 minutes. The formation of orange solid confirm acridinedione derivative (3f), in an excellent yield.^{1}H NMR = δ 0.98-1.16 (gem dimethyl), 2.14-2.25 (d, 4H, C2&C4), 2.46 (m, CH), 2.97 (d, CH_2), 4.74 (s, CH-NH_2), 7.08-7.53 (m, Ar-H), 8.00 (-OH).^{13}C NMR = δ 27.35, 28.11, 29.31, 31.85, 32.24, 35.09, 40.88, 50.75 (aliphatic carbons), 115.68 (olefinic carbon), 126.41, 128.08, 128.40, 128.89, 129.55, 130.10, 144.09 (aryl carbons), 160.33 (amide carbon), 196.52(keto carbonyl). IR: 1510, 1660, 1733, 3302 cm^{-1}. Mass: m/z= 494, 493.

4-Hydroxyphenyl-9-phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-10-valineacridinedione: (3g)

Hantzsh condensation of two equivalents of dimedone (2.12g, 0.015m) with valinehydrazide (1g, 0.0076m), 4-hydroxy benzaldehyde (0.92g, 0.0076m) in solvent free condition, is treated on microwave irradiation for 4 minutes. The formation of red solid confirm acridinedione derivative (3g), in an excellent yield.^{1}H NMR = δ 0.98-1.16 (gem dimethyl), 2.14-2.25 (d, 4H, C2&C4), 2.47 (m, CH), 4.74 (s, CH-NH_2), 7.08-7.20 (m, Ar-H), 8.11 (-OH).^{13}C NMR =

Table 3. Antimicrobial activity of the synthesized 9-Aryl Acridinedione compounds

Compound	Conc. (µ.g/well) In DMF	Zone of inhibition in mm*					
		Antibacterial activity				Antifungal activity	
		P. aeruginosa	*E. coli*	*S.pyogenes*	*S. aureus*	*C.albicans*	*A.flavus*
1a	600	10	8	17	8	8	10
1b	600	10	10	17	8	7	11
1c	600	12	8	9	12	6	9
1d	600	8	10	12	11	8	10
1e	600	10	11	11	8	8	8
1f	600	9	7	12	11	7	8
1g	600	8	8	8	12	7	9
1h	600	10	9	12	6	6	11
2a	600	8	10	11	8	9	9
2b	600	10	8	10	9	8	10
2c	600	9	10	9	7	7	8
2d	600	11	9	9	10	9	7
2e	600	12	8	8	11	8	9
2f	600	9	10	10	9	7	11
2g	600	8	11	7	12	9	9
2h	600	10	9	11	8	7	8
3a	600	9	12	12	7	9	7
3b	600	12	10	10	6	8	10
3c	600	11	9	9	10	9	9
3d	600	10	11	7	9	8	10
3e	600	9	10	11	8	6	9
3f	600	8	11	10	7	9	8
3g	600	10	9	9	6	8	11
3h	600	12	9	10	10	7	9
Gentamycin	600	18	17	17	17	-	-
Ketaconozole	600	-	-	-	-	17	19

*Diameter of well (bore size) – 6mm

δ 27.32, 28.28, 29.36, 31.34, 32.25, 40.89, 50.77, 54.18, 55.93, 57.35 (aliphatic carbons), 115.85 (olefinic carbon), 120.05, 124.56, 128.41, 136.48, 144.06, 145.88 (aryl carbons), 162.24 (amide carbon), 196.78 (keto carbonyl).IR: 1514, 1666, 1735, 3305 cm^{-1}. Mass: m/z= 480, 479.

10-Cystine-4-hydroxyphenyl-9-phenyl-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydro-1,8-(2H,5H)-acridinedione: (3h)

The microwave irradiation of two equivalents of dimedone (1.0g, 0.008m) with cystinehydrazide (1g, 0.004m), 4-hydroxy benzaldehyde (0.48g, 0.004m) in solvent free condition, is treated for 6 minutes. The formation of reddish orange solid confirm acridinedione derivative (3h), in an excellent yield.^{1}H NMR = δ 1.0-1.10 (gem dimethyl), 2.16-2.3 (d, 4H, C2&C4), 2.53 (m, CH), 3.89 (d, CH_2), 4.65(s, CH-NH_2), 6.57-7.28 (m, Ar-H), 8.14 (-OH).^{13}C NMR = δ 27.28, 29.34, 31.30, 32.22, 37.89, 40.08, 40.30, 40.50, 40.86, 50.78, 55.91 (aliphatic carbons), 115.80 (olefinic carbon), 120.07, 122.08, 124.97, 128.89, 136.41, 144.07, 145.98 (aryl carbons), 162.15 (amide carbon), 196.69 (keto carbon).IR: 1513, 1662, 1733, 3305 cm^{-1}. Mass: m/z= 586, 585.

Biological studies of 9 -Aryl acridinedione derivatives

Antibacterial activity testing is done by well diffusion method. The nutrient agar medium is used, and the solvent is Chloroform of concentration ranging from 50 and 100µL. The acridinedione derivatives were screened *in vitro* for their potency against bacterial strains such as *S. aureus*, *E. coli*, *P. aeruginosa*, and *S. pyogenes*and fungal strains such as *C. albicans*and *A. flavus*. The *in vitro* activities of the test compounds were studied using agar plates containing Sabourauds dextrose broth for fungi and in Nutrient broth (Himedia, Mumbai) for bacteria. Three fixed concentrations of the test compounds were tested against each microbial species. The antibacterial and antifungal potencies of the test compounds were compared with gentamycin (bacteria) and ketaconozole (fungi). The relative antimicrobial potencies of test compounds are expressed as the area of zone of inhibition and summarized in Table 3. A clear distinction between the in vitro antibacterial and antifungal activity profiles of the acridinedione derivatives (1a-3h) is that all the derivatives display very good antibacterial and antifungal activity.

Acknowledgement

The authors are thankful to UGC for financial support in the form of minor research project (No. F. MRP-3788/11 (SERO-UGC)).

REFERENCES

1. Acheson. R. M, *Acridines;* Interscience Publishers, Inc.: New York, (1956).
2. Adcock, B. *Acridines: In Heterocyclic compounds, Weissberger Series*, 9, (1973).
3. Albert A, the Acridines, Second ed., Edward Arnold Ltd, London, (1996).
4. Bagley M. C, Cala JW & Bower. *J.ChemCommun*, 1682, (2002).
5. Bertozzi. F, Gustafsson M & Olsson R, *Org. Lett*, 4, 3147, (2002).
6. Caramella. P., Grunanger. P, *In, 3-Dipolar Cycloaddition Chemistry:* Padwa, A, Ed., John Wiley & Sons: New York, 1, 337, (1984).
7. Das B, Thirupathi P, Mahender I, Saidi Reddy V & KoteshwarRao, *J. Mol. Cat*, 247,233, (2006).
8. Denny. W. R., *The chemistry of Anti tumour agents;* Wilman, D.E.V, Ed.; Blackie & Sons, Ltd: Glasgow and London, (1990).
9. Gisela. C.M. Graciela.Y.V. Sylvia. E.A. *MonatschChem*, 140, 1529-1532, (2009).
10. Huisgen. R, *Angew. Chem. Int. Ed. Engl.*, 6, 16, (1967).
11. Huisgen. R, *In 1, 3-Dipolar Cycloaddition Chemistry:* Padwa, A, Ed., Wiley Interscience: New York, (1984).
12. Huma H Z S, Halder R, Kalra S, Das J &IQbal J, *Tetrahedron Lett*,43,6485, (2002).
13. Martin N, Quinterio M, Seoane C, Mora L, Suaroz M, Ockoa E & Morales A. *J. Heterocy. Chem*, 51, 235, (1993).
14. Menendez JC, *Synthesis*, 2624, (2006).
15. Murugan .P, Shanmugasundaram P, Rama Krishnan V. T, Venkatachalapathy. B, Srividya N, Ramamurthy P, Gunasekaran K &Velmurugan D, *J. Chem. Soc., Perkin Trans.*, 2,999, (1998).
16. Nalini V. and Girija R.*, *Res. J. Chem. Environ.*17, 4, (2013).
17. Padwa. A, *Angew. Chem. Int. Ed. Engl.*, 15, 123, (1976).
18. Rajanarendran. E, Nagi Reddy. M &FirozPbshashaik, *Indian Journal of chemistry Vol.* February, 50(B),245- 252, (2011).
19. Ramamurthy S. P. N, Shanmugasundram. P and Ramakrishnan V.T., *J. Org. Chem.*, 61,5083, (1996).
20. Ramamurthy S. P. N, Shanmugasundram. P and Ramakrishnan V.T., *Acta.Spectrochemic*, 54, 245, (1998).
21. Thull V. &Testa B, *BiochemPharma Col*, 47, 2307, (1994).
22. Tu. S, Miao C, Gao Y, Fang F, Zhuang Q, Feng Y & Shi D, *SynLett*, 255,(2004).
23. HVA GP, Zhang XJ, Shi F, Tu SJ, XUJN, Wang Q, Zhu X.T, Zhang JP & J1 SJ, *Chinese J Chem*, 23,1641,(2005).

****