Received: 2 November 2018 | Revised: 21 March 2019 | Accepted: 25 March 2019

DOI: 10.1002/jccs.201800411

JOURNAL OF THE CHINESE CHEMICAL SOCIETY

COMMUNICATION

Eco-friendly, ultrasound-assisted, and facile synthesis of one-pot multicomponent reaction of acridine-1,8(2H,5H)-diones in an aqueous solvent

Pravin N. Chavan[1] | **Dattatraya N. Pansare**[2] | **Rohini N. Shelke**[2]

[1]Department of Chemistry, Doshi Vakil College, Goregaon, India

[2]Department of Chemistry, Deogiri College, Aurangabad, India

Correspondence
Dattatraya N. Pansare, Department of Chemistry, Deogiri College, Station Road, Aurangabad, 431005, Maharashtra, India.
Email: dattatraya.pansare7@gmail.com

Abstract

A one-pot, multistep synthesis of acridine-1,8(2H,5H)-diones (**4a–m**) was achieved by three-component reaction of dimedone (**1**) with an aromatic aldehyde (**2a–m**) and an ammonium acetate (**3**) using water as a green solvent without any catalyst and a simple, easily handled, and ultrasonic technique as well as conventional method.

KEYWORDS

ammonium acetate, aqueous solvent, aromatic aldehydes, dimedone, ultrasound irradiation

1 | INTRODUCTION

Acridines are heterocyclic natural products. Acridinedione derivatives have a wide range of biological active properties such as antimalarial and anticancer properties.[1–6] Furthermore, their derivatives are also used in laser dyes.[7–9] Use of acridine derivatives in the synthesis of proteins, peptides, and nucleic acid also reported to show antitumor and binding (DNA) activities.[10–13] Substituted acridines were synthesized from aromatic aldehydes, dimedone, and nitrogen-containing reagents such as urea,[14] ammonium acetate and basic alumina catalyst,[15] ammonium bicarbonate,[16] ammonium hydroxide,[17] hydroxyl amine,[18] various anilines,[19] and using different catalysts such as ceric ammonium nitrate,[20] SPNP,[21] ammonium chloride,[22] copper sulfate pentahydrate,[23] SiO_2-I,[24] CuO,[25] dodecyl benzenesulfonic acid (phase transfer catalyst)[26] in hazardous/nonhazardous solvents using microwave, reflux, and traditional heating methods.

Some of these methods have drawbacks for synthesis of substituted acridines such as complicated handling, multistep reaction, low yield, prolonged reaction time, expensive reagents, which necessitated the development of newest methodology for synthesis of substituted acridine.

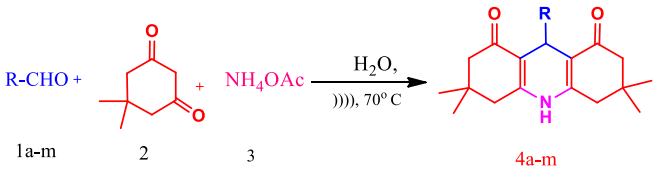
Nowadays, many time reactions are carried out using the ultrasonic irradiation method. The ultrasonic irradiation method has been acknowledged as an innocuous, environmentally friendly, and green technique, and its application today has been a boon in serving a new pathway for several chemical processes. [27–32]

Herein, we report an efficient, easy to handle, and convenient experimental procedure for the synthesis of 3,3,6,6-tetramethyl-9-R-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione in an aqueous solvent through a one-pot multicomponent reaction of aromatic aldehyde (**1a–m**), dimedone (**2**), ammonium acetate (**3**), without catalyst using ultrasonic irradiation as well as a conventional method.

2 | RESULTS AND DISCUSSION

We report here the eco-friendly synthesis of substituted acridinediones via one-pot Knoevenagel condensation, Michael addition, and cyclization of aromatic aldehydes (**1a–m**), dimedone (**2**), ammonium acetate in aqueous medium as a green solvent under controlled ultrasonic irradiation without the use of catalysts (Scheme 1).

First, we examined different solvents in reactions, we carried out a model reaction of 2,5-dimethoxy benzaldehyde



SCHEME 1 General reaction of 3,3,6,6-tetramethyl-9-substitited phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione

(**1a**), dimedone (**2**), ammonium acetate(**3**) in a solvent viz. ethanol acetonitrile, methanol, dichloromethane, and water at room temperature, reflux, and using an ultrasonic irradiation method at different temperatures. The results are summarized in Table 1. Yields of 88, 82, 70, and 79% of the products were obtained in ethanol, methanol, dichloromethane, and water solvents under reflux conditions (entries 1, 3–5). However, in the case of acetonitrile, a very low (30%) yield of the product (entry 2) was observed (Table 1).

Furthermore, we have compared the reaction methods for a conventional, eco-friendly procedure such as at room temperature, reflux (110°C), and under ultrasonic irradiation (with room temperature and 70°C temperature) conditions using a choosable reaction model. Ultrasonic bath temperatures were controlled by adding water in the sonication bath time to time (Table 1).

As we have observed, low yields (35, 33, 26, 32, and 23%) of the products were obtained using methanol, ethanol, acetonitrile, water, and dichloromethane solvents (entries 6–10) under ultrasonic irradiation at room temperature, so we increased the temperature of the sonication bath up to 70°C. As a result, we observed yields of products (81, 83, 80, and 91%) in methanol, ethanol, acetonitrile, and water solvents (entries 11–13 and 15) increased with time. However, in the case of dichloromethane, yield of the product (60%) (entry 14) is low as compared to other solvents (Table 1).

We have concentrated here in the case of acetonitrile, under reflux conditions, low (30%) yield of the product (entry 2) was observed, but high (80%) yield of the product (entry 12) was observed under ultrasonication because of the effect of ultrasonic irradiation. It was observed that all solvents are favorable for synthesis of acridinedione derivatives under ultrasonic irradiation at 70°C. However, we selected water solvent because water is a green solvent.

Finally, we have checked the reaction conditions at room temperature in water solvent without reflux and ultrasonic irradiation, (0%) yield of the product was observed (Table 1).

Under the optimized set of model reaction conditions (entry 15) in one-pot containing dimedone (**1**), aromatic aldehyde (**2a–m**), and ammonium acetate (**3**) without any catalyst in aqueous medium under ultrasonic irradiation at 70°C. The results are reported in Table 1. We report that all aromatic aldehydes containing acridinedione derivatives are given in Table 2. We have observed that the electron-withdrawing aldehydes give more time for reaction completion than

TABLE 1 To optimize the reaction conditions for synthesis of substituted acridinediones (**4a**)[a]

Entry	Solvent	Method	Temperature (°C)	Time (hr)	% yield
1	Ethanol	Reflux	110	03	88
2	Acetonitrile	Reflux	110	09	30
3	Methanol	Reflux	110	03	82
4	Dichloromethane	Reflux	110	04	70
5	Water	Reflux	110	04	60
6	Ethanol	US	R.T.	03	33
7	Acetonitrile	US	R.T.	03	26
8	Methanol	US	R.T.	03	35
9	Dichloromethane	US	R.T.	03	23
10	Water	US	R.T.	03	32
11	Ethanol	US	70°C	1.30	83
12	Acetonitrile	US	70°C	1.30	80
13	Methanol	US	70°C	1.30	81
14	Dichloromethane	US	70°C	1.30	76
15	Water	US	70°C	1.30	91
16	Water	—	R.T.	09	0

Abbreviations: R.T., room temperature; US: ultrasonication.

[a]*Reaction conditions*: The reaction was carried out by the addition of 2,5-dimethoxybenzaldehyde (1 mmol), dimedone (2 mmol), ammonium acetate (1 mmol), and each solvent 8 mL).

TABLE 2 Synthesis of 3,3,6,6-tetramethyl-9-R-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione derivatives via one-pot multicomponent reaction under ultrasonic irradiation at 70°C (**4a–m**)[a]

Entry	Ar	Product	Time (min)	Yield (%)
1.	2,5-$(CH_3O)_2C_6H_3$	**4a**	41	91
2.	3,4-$(OH)_2C_6H_3$	**4b**	39	89
3.	4-CNC_6H_4	**4c**	47	83
4.	3-OH-4-$CH_3OC_6H_3$	**4d**	43	88
5.	C_6H_5	**4e**	35	90
6.	3-BrC_6H_4	**4f**	52	87
7.	4- $CH_3OC_6H_4$	**4g**	36	91
8.	4-OHC_6H_4	**4h**	34	92
9.	4- ClC_6H_4	**4i**	40	95
10.	2,4-$(cl)_2C_6H_3$	**4j**	42	90
11.	4-$NO_2C_6H_4$	**4k**	54	82
12.	2-$NO_2C_6H_4$	**4l**	55	83
13.	4-FC_6H_4	**4m**	32	92

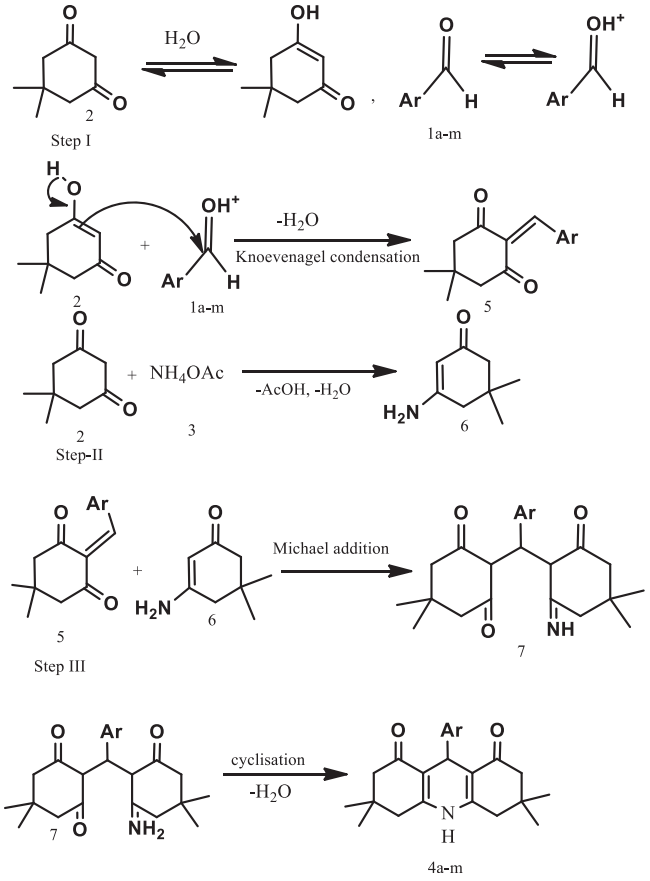
[a]*Reaction condition*: The reaction was carried out by the addition of aromatic aldehyde (1 mmole) dimedone (2 mmol), ammonium acetate (1 mmol), and aqueous solvent 08 mL.

electron-donating aldehyde. All electrons withdrawing and donating aromatic aldehydes worked well, leading to good to excellent yields of products due to the ultrasonic effect.

A possible mechanism to the synthesis of acridinedione derivatives (**4a–m**) is outlined in Scheme 2. These products were formed by a multistep reaction in one-pot as discussed below.

In step I, aromatic aldehyde (**1a–m**) was condensed with dimedone (**2**) by knoevenagel condensation to form intermediate (**5**) and simultaneously another molecule of dimedone (**2**) was condensed with ammonium acetate (**3**) to form enaminone (**6**). In step II, addition of intermediate (**5**) and enaminone (**6**) called Michael addition was carried out, and finally cyclization of Michael addition is shown in step III, forming substituted acridinediones (**4a–m**).

The reaction progress and completion was monitored by thin layer chromatography (TLC) using the hexane and ethyl acetate ratio of 8:2. After completion of the reaction, the reaction mixture was allowed to cool, filtered, washed, dried, and recrystallized by using AR grade ethanol to afford the pure product (Figure 1).



SCHEME 2 A possible mechanism of acridinedione derivatives

FIGURE 1 Ultrasonication (frequency of 50 Hz and power of 250 V AC, 5.5 L and temperature 70°C)

3 | EXPERIMENTAL

3.1 | Materials and methods

All the chemicals were purchased from Sigma-Aldrich. Reactant were purified before starting the reactions. The melting point was measured using *SRS optimelt* instruments and all the synthesized compounds were characterized using ^{1}H NMR and ^{13}C NMR. Both NMR spectra were obtained in $CDCl_3$ using TMS as an internal standard (Bruker) 400 and 100 MHz Frequency. ESI-MS analysis was obtained using an ESI-QTOF Analytical instrument, elemental analysis was performed using an

Elementar vario MICRO cube analyzer instrument, and the IR spectra were recorded on a Perkin-Elmer FT-IR Spectrometer.

3.2 | General procedure for synthesis of acridine-1,8 (2H,5H)-dione derivatives

In a 50 mL round bottom flask, a mixture of aromatic aldehyde (1 mmol), dimedone (2 mmol), ammonium acetate (1 mmol), and water (8 mL) was irradiated to ultrasonication (a frequency of 50 Hz and a power of 250 V AC, 5.5 L) at 70°C temperature for nearly about 2 hr. The round bottom flask was placed at the center of the ultrasonic bath using a stand and the surface of the reactants in round bottom flasks was placed slightly lower than the water level in the sonication bath. The reaction progress was assessed by a TLC plate using 20% n-hexane: ethyl acetate (8:2). After the completion of reaction, the reaction mixture was cooled at room temperature, filtered, and washed with 3 × 10 mL water. The solid products were dissolved in ethyl acetate (7 mL). The organic layer was dried over anhydrous NaS_2O_4, separated, and ethyl acetate was evaporated using a vacuum pressure pump. The solid products were then collected and purified by recrystallization using pure A.R. grade ethanol.

3.3 | Spectral data of the synthesized derivatives of 9-R-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione

3.3.1 | 9-(2,5-dimethoxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4a)

Light yellow crystals, m.p. 295–297°C. FTIR (KBr cm^{-1}): 3,290, 2,950, 1,640, and 1,604; ^1H NMR (400 MHz, $CDCl_3$) δ 11.94 (s, 1H, D_2O exchangeable NH), 7.56 (s, 1H,Ar), 6.88 (d, 1H,Ar), 6.78 (d, 1H,Ar), 4.81 (s, 1H, CH), 3.91 (s, 6H, $2CH_3$), 2.59 (s,4H, $2CH_2$), 2.10 (s, 4H $2CH_2$) 1.03 (s, 6H, $2CH_3$), and 0.99 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 194.1, 152.97, 152.12, 151.41, 115.52, 113.29, 112.95, 112.21, 56.7, 55.89, 52.32, 41.75, 36.15, 34.30, and 28.45 ppm; Mass (*m/z*): $[M + 1]^+$ 409.2. Element Analysis: Mol. Formula $C_{25}H_{31}NO_4$: C, 73.32, H, 7.63, N, 3.42; and O, 15.63%. Founded: C, 73.42; H, 7.69; and N, 3.41.

3.3.2 | 9-(3,4-dihydroxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4b)

White crystals, m.p 308–310°C. FTIR (KBr cm^{-1}): 3,387, 3,289, 2,944, 1,686, and 1,606; ^1H NMR (400 MHz, $CDCl_3$) δ 11.91 (s, 1H, D_2O exchangeable NH), 7.51 (s, 1H,Ar), 6.79 (d, 1H,Ar), 6.70 (d, 1H,Ar), 5.69 (s, 2H, 2OH), 4.82 (s, 1H, CH), 2.60 (s,4H, $2CH_2$), 2.11 (s, 4H $2CH_2$),1.04 (s, 6H, $2CH_3$), and 0.99 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 191.12, 151.44, 147.52, 146.21, 140.62, 127.85, 119.13, 117.95, 115.52, 113.29, 112.95, 112.21, 56.7, 55.89, 52.65, 43.15, 34.75, 33.89, and 28.68 ppm. Mass (*m/z*): $[M + 1]^+$ 381.19. Element Analysis: Mol. Formula $C_{23}H_{27}NO_4$: C, 72.42; H, 7.13; N, 3.67; and O, 16.78%. Founded: C, 72.49; H, 7.20; and N, 3.71.

3.3.3 | 4-(3,3,6,6-tetramethyl-1,8-dioxo-1,2,3,4,5,6,7,8,9,10-decahydroacridin-9-yl) benzonitrile (4c)

Dark Yellow crystals, m.p. 270–272°C. FTIR (KBr cm^{-1}): 3,291, 2,989, 2,286, 1,675, and 1,608; ^1H NMR (400 MHz, $CDCl_3$) δ 11.93 (s, 1H, D_2O exchangeable NH), 7.81 (d, 2H,Ar), 7.66 (d, 2H,Ar), 4.86 (s, 1H, CH), 2.61 (s,4H, $2CH_2$), 2.13 (s, 4H $2CH_2$),1.05 (s, 6H, $2CH_3$), and 1.00 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 195.11, 151.14, 150.52, 136.21, 130.52, 119.10, 112.85, 111.21, 52.7, 41.15, 33.65, 33.79, and 28.72 ppm. Mass (*m/z*): $[M + 1]^+$ 374.2. Element Analysis: Mol. Formula $C_{24}H_{26}N_2O_2$: C, 76.98; H, 7.00; N, 7.48; and O, 8.54%. Founded: C, 72.49; H, 7.20; and N, 3.71.

3.3.4 | 9-(3-hydroxy-4-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4d)

Yellow crystals, m.p. 300–304°C. FTIR (KBr cm^{-1}): 3,392, 3,278, 2,942, 1,682, and 1,601; ^1H NMR (400 MHz, $CDCl_3$) δ 11.89 (s, 1H, D_2O exchangeable NH), 7.03 (s, 1H,Ar), 6.89 (d, 1H,Ar), 6.71 (d, 1H,Ar), 5.73 (s, 1H, OH), 4.83 (s, 1H, CH), 2.62 (s,4H, $2CH_2$), 2.13 (s, 4H $2CH_2$), 1.12 (s, 6H, $2CH_3$), and 0.99 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 195.12, 151.84, 149.32, 148.32, 123.45, 115.13, 113.95, 112.95, 112.21, 57.01, 52.65, 42.15, 39.87, 35.15, 33.79, and 28.79 ppm. Mass (*m/z*): $[M + 1]^+$395.2. Element Analysis: Mol. Formula $C_{24}H_{29}NO_4$: C, 72.89; H, 7.39; N, 3.54; and O, 16.18%. Founded: C, 72.90; H, 7.38; and N, 3.55.

3.3.5 | 3,3,6,6-tetramethyl-9-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4e)

White crystals, m.p. 290–293°C. FTIR (KBr cm^{-1}): 3,299, 2,986, 1,646, and 1,610; ^1H NMR (400 MHz, $CDCl_3$) δ 11.88 (s, 1H, D_2O exchangeable NH), 7.30–7.68 (m, 5H,Ar), 4.80 (s, 1H, CH), 2.82 (s,4H,

$2CH_2$), 2.25 (s, 4H $2CH_2$),1.16 (s, 6H, $2CH_3$), and 0.98 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 194.12, 150.74, 143.32, 129.94, 129.24, 126.54, 112.65, 52.32, 42.35, 36.87, 33.65, and28.65 ppm. Mass (*m/z*): $[M + 1]^+$349.2. Element Analysis: Mol. Formula $C_{23}H_{27}NO_2$: C, 79.05; H, 7.79; N, 4.01; and O, 9.16%. Founded: C, 79.1; H, 7.75; and N, 4.06.

3.3.6 | 9-(3-bromophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4f)

White crystals, m.p. 288–291°C. FTIR (KBr cm^{-1}): 3,278, 2,961, 1,660, and 1,607; ^1H NMR (400 MHz, $CDCl_3$) δ 11.94 (s, 1H, D_2O exchangeable NH), 7.71 (d, 1H,Ar), 7.61 (s, 1H,Ar), 7.52–7.40 (m, 2H,Ar), 4.82 (s, 1H, CH), 2.63 (s,4H, $2CH_2$), 2.16 (s, 4H $2CH_2$),1.15 (s, 6H, $2CH_3$), and 0.99 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 195.01, 150.62, 145.12, 136.21, 130.52, 129.41, 127.52, 124.85, 112.16, 52.35, 40.95, 33.70, 33.59, and 28.78 ppm. Mass (*m/z*): $[M + 1]^+$ 427.1. Element Analysis: Mol. Formula $C_{23}H_{26}BrNO_2$: C, 64.49; H, 6.12; Br, 18.65; N, 3.27; and O, 7.47%. Founded: C, 64.50; H, 6.18; and N,3.32.

3.3.7 | 9-(4-methylphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4g)

Light Yellow crystals, m.p. 290–293°C. FTIR (KBr cm^{-1}): 3,301, 1,636, and 1,462; ^1H NMR (400 MHz, $CDCl_3$) δ 11.88 (s, 1H, D_2O exchangeable NH), 7.58–7.61 (d, 4H,Ar), 4.84 (s, 1H, CH), 2.59 (s,4H, $2CH_2$), 2.26 (s, 4H $2CH_2$), 1.11 (s, 6H, $2CH_3$), and 0.99 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 195.12, 151.96, 142.58, 136.32, 132.20, 112.09, 52.31, 41.51, 33.24, 33.15, and 128.69 ppm. Mass (*m/z*): $[M + 1]^+$363.2. Element Analysis: Mol. Formula $C_{24}H_{29}NO_2$: C, 79.30; H, 8.04;N, 3.85; and O, 8.80%. Founded: C, 79.36; H, 8.10; and N,3.84.

3.3.8 | 9-(4-hydroxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4h)

White crystals, m.p. 306–308°C. FTIR (KBr cm^{-1}): 3,290, 2,926, 1,635, and 1,437; ^1H NMR (400 MHz, $CDCl_3$) δ 11.88 (s, 1H, D_2O exchangeable NH),7.75 (d, 2H,Ar),6.92 (d, 2H,Ar), 5.62 (s, 1H, OH), 4.82 (d, 1H, CH), 2.60 (s,4H, $2CH_2$), 2.32 (s, 4H $2CH_2$),1.14 (s, 6H, $2CH_3$), and 0.99 (s, 6H, $2CH_3$);^{13}C NMR (100 MHz, $CDCl_3$): 194.98, 160.01, 151.48, 140.21, 132.54, 116.84, 113.04, 52.10, 41.15, 39.41, 35.41, 33.74, and 28.70.ppm. Mass (*m/z*): $[M + 1]^+$365.2. Element Analysis: Mol. Formula $C_{23}H_{27}NO_3$: C, 75.59; H, 7.45; N, 3.83; and O, 13.13%. Founded: C,75.60; H, 7.47; and N, 3.83.

3.3.9 | 9-(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4i)

White crystals, m.p. 245–249°C. FTIR (KBr cm^{-1}): 3,302, 2,951, 1,638, and 1,601;^1H NMR (400 MHz, $CDCl_3$) δ 11.88 (s, 1H, D_2O exchangeable NH),7.75 (d, 2H,Ar),7.26 (d, 2H,Ar), 4.81 (d, 1H, CH), 2.61 (s,4H, $2CH_2$), 2.31(s, 4H $2CH_2$),1.12 (s, 6H,$2CH_3$), and 0.99 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$):195.08, 151.00, 144.01, 132.14, 131.12, 129.57, 111.94, 52.11, 41.05, 36.41, 33.74, and 28.68.ppm. Mass (*m/z*): $[M + 1]^+$383.1. Element Analysis: Mol. Formula $C_{23}H_{26}ClNO_2$: C, 71.96; H, 6.83; Cl, 9.23; N, 3.65; and O, 8.33%. Founded: C,71.98; H, 6.86; and N, 3.70.

3.3.10 | 9-(2,4-dichlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4j)

White crystals, m.p. 278–281°C. FTIR (KBr cm^{-1}): 3,299, 2,949, 1,641, and 1,604; ^1H NMR (400 MHz, $CDCl_3$) δ 11.89 (s, 1H, D_2O exchangeable NH), 7.03 (s, 1H,Ar), 6.89 (d, 1H,Ar), 6.71 (d, 1H,Ar), 5.73 (s, 1H, OH), 4.83 (s, 1H, CH), 2.62 (s,4H, $2CH_2$), 2.13 (s, 4H $2CH_2$),1.09 (s, 6H, $2CH_3$), and 0.99 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 195.12, 151.84, 149.32, 148.32, 123.45, 115.13, 113.95,112.95, 112.21, 57.01, 52.65, 42.15, 39.87, 35.15, 33.79, and 28.79 ppm. Mass (*m/z*): $[M + 1]^+$ 395.2. Element Analysis: Mol. Formula $C_{23}H_{25}Cl_2NO_2$: C, 66.03; H, 6.02; Cl, 3.35; N, 3.35; and O, 7.65%. Founded: C, 66.10; H, 605; and N, 3.32.

3.3.11 | 9-(4-nitrophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4k)

Colorless crystals, m.p. 298–300°C. FTIR (KBr cm^{-1}): 3,292, 2,963, 1,681, and 1,609; ^1H NMR (400 MHz, DMSO: ^1H NMR 400 MHz, $CDCl_3$) δ 11.76 (s, 1H, D_2O exchangeable NH), 8.15 (d, 2H,Ar), 7.36 (d, 2H,Ar), 4.98 (s, 1H, CH), 2.51 (s,4H, $2CH_2$), 2.23 (s, 4H $2CH_2$), 1.15 (s, 6H, $2CH_3$), and 1.01 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 190.21, 181.60, 147.52, 146.12, 127.21, 123.52, 114.10, 111.21, 50.7, 33.65, 32.79,, 30.14, and 28.54 ppm. Mass (*m/z*): $[M + 1]^+$394.1. Element Analysis: Mol. Formula $C_{23}H_{26}N_2O_4$: C, 70.03; H,

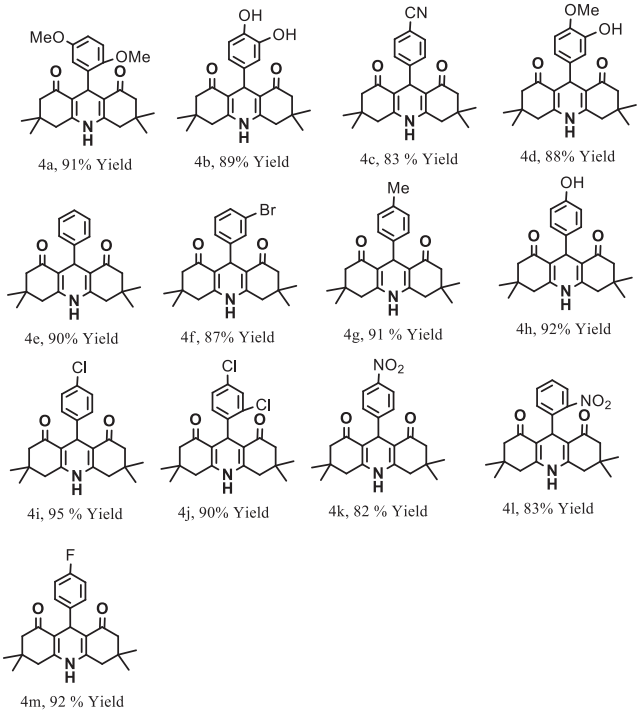
6.64; N, 7.10; and O, 16.22%. Founded: C, 70.10; H, 6.63; and N, 7.09.

3.3.12 | 9-(2-nitrophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4l)

White crystals, m.p. 289–292°C. FTIR (KBr cm^{-1}): 3,210, 2,968, 1,687, and 1,607; ^1H NMR (400 MHz, $CDCl_3$) δ 11.78 (s, 1H, D_2O exchangeable NH), 8.31 (d, 2H,Ar), 7.68 (d, 2H,Ar), 4.92 (s, 1H, CH), 2.66 (s,4H, $2CH_2$), 2.34 (s, 4H $2CH_2$), 1.13 (s, 6H, $2CH_3$), and 1.06 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 195.21, 153.14, 150.56, 136.11, 131.52, 120.10, 112.87, 111.22, 52.7, 41.15, 33.60, 33.75, and 28.74 ppm. Mass (*m/z*): $[M + 1]^+$ 394.1. Mol. Formula $C_{23}H_{26}N_2O_4$: C, 70.03; H, 6.64; N, 7.10; and O, 16.22%. Founded: C, 70.11; H, 6.61; and N, 7.12.

3.3.13 | 9-(4-flurophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (4m)

White Crystals, m.p. 275–277°C. FTIR (KBr cm^{-1}): 3,289, 2,964, 1,688, and 1,608; ^1H NMR (400 MHz, $CDCl_3$) δ 11.89 (s, 1H, D_2O exchangeable NH), 7.22 (d, 2H,Ar), 6.78 (d, 2H,Ar), 5.10 (s, 1H, CH), 2.55 (s,4H, $2CH_2$), 2.22 (s, 4H $2CH_2$), 1.30–1.03 (s, 6H, $2CH_3$), and 0.99 (s, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): 191.11, 187.54, 151.14, 150.52, 136.21, 130.52, 119.10, 112.85, 111.21, 52.7, 41.15, 33.65, 33.79, and 28.72 ppm. Mass (*m/z*): $[M + 1]^+$367.1. Element Analysis: Mol. Formula $C_{23}H_{26}FNO_2$: C, 75.18; H, 7.13; F, 5.17; N, 3.81; and O, 8.71%. Founded: C, 75.9; H, 7.20; and N, 3.73 (Scheme 3).



SCHEME 3 Synthesized of acridinedione derivatives (**4a–m**)

4 | CONCLUSIONS

We have developed an efficient, short reaction time, easily handled ultrasonic irradiation method for synthesis of acridinedione derivatives (**4a–m**) by one-pot multicomponent reaction of aromatic aldehyde (**1a–m**), dimedone (**2**), ammonium acetate (**3**) without catalysts using an aqueous solvent as a green solvent. Thus, hazardous pollution is minimized to achieve an environmentally friendly method.

ACKNOWLEDGMENTS

We are grateful to Department of Chemistry, DoshiVakil Arts, G.C.U.B. Science and Commerce College, Goregaon, Raigad for providing the necessary laboratory facility during our research.

ORCID

Dattatraya N. Pansare https://orcid.org/0000-0002-0419-3538

REFERENCES

[1] S. Girault, P. Grellier, A. Berecibar, L. Maes, E. Mouray, P. Lemiere, M. Debreu, E. Davioud-Charvet, C. Sergheraet, *J. Med. Chem.* **2000**, *43*, 2646.
[2] W. Cholody, B. Horowska, J. Paradziej-Lukowicz, S. Martelli, J. Konopa, *J. Med. Chem.* **1996**, *39*, 1028.
[3] T. Chen, R. Fico, E. S. Cancellakis, *J. Med. Chem.* **1978**, *21*, 868.
[4] W. Denny, G. J. Atwell, B. C. Baguley, L. P. G. Wakelin, *J. Med. Chem.* **1985**, *28*, 1568.
[5] G. Rewcastle, G. J. Atwell, D. Chambers, B. C. Baguley, W. A. Denny, *J. Med. Chem.* **1986**, *29*, 472.
[6] A. Lacassagne, N. P. Buu-Ho, R. Daudel, F. Zajdela, *Adv. Cancer Res.* **1956**, *4*, 315.
[7] P. Murugan, P. Shanmugasundaram, V. T. Ramakrishnan, B. Venkatachalapathy, N. Srividya, P. Ramamurthy, K. Gunasekaran, D. Velmurugan, *J. Chem. Soc., Perkin Trans.* **1998**, *2*, 999.
[8] K. J. Prabahar, V. T. Ramakrishnan, D. Sastikumar, D. Selladurai, V. Masilamani, *Indian J. Pure Appl. Phys.* **1991**, *29*, 382.
[9] A. Islam, P. Murugan, K. C. Hwang, C. H. Cheng, *Synth. Metals* **2003**, *139*, 347.
[10] A. Albert, *The Acridines*, Edward Arnold, London **1966**.
[11] E. Delfourne, C. Roubin, J. Bastide, *J. Org. Chem.* **2000**, *65*, 5476.
[12] J. Antonini, P. Polucci, A. Magnano, S. Martelli, *J. Med. Chem.* **2001**, *44*, 3329.

[13] M. G. Ferlin, C. Marzano, G. Chiarelotto, F. Baccichetti, F. Bordin, *Eur.J. Med. Chem.* **2000**, *35*, 827.
[14] A. A. Bakibaev, V. D. Fillimonov, E. S. Nevgodova, *Zh.Org. Khim.* **1991**, *27*, 1519.
[15] M. Suárez, A. Loupy, E. Salfrán, L. Moran, E. Rolando, *Heterocycles* **1999**, *51*, 21.
[16] S. J. Tu, Z. Lu, D. Shi, C. Yao, Y. Gao, C. Guo, *Synth. Commun.* **2002**, *32*, 2181.
[17] F. Darvish, S. Balalaei, F. Chadegani, P. Salehi, *Synth. Commun.* **2007**, *37*, 1059.
[18] S. Tu, F. Fang, S. Zhu, T. Li, X. Zhang, Q. Zhuang, *J. Heterocycl. Chem.* **2004**, *41*, 767.
[19] N. Martín, M. Quinteiro, C. Seoane, J. L. Soto, A. Mora, M. Suárez, E. Ochoa, A. Morales, J. R. Del Bosque, *J. Heterocycl. Chem.* **1995**, *32*, 235.
[20] M. Kidwai, D. Bhatnagar, *Chem. Pap.* **2010**, *64*(6), 825.
[21] A. Javid, A. Khojastehnezhad, M. Heravi, F. F. Bamoharram, *Synth. React. Inorg., Met.-Org., Nano-Met. Chem.* **2012**, *42* (1), 14.
[22] B. Saeed, C. Fatemeh, D. Fatemeh, B. Hamid Reza, *Chin. J. Chem.* **2009**, *27*, 1953.
[23] M. A. Pasha, R.-u.-R. Khan, K. B. Ramesh, *Can. Chem. Trans.* **2016**, *4*(1), 90.
[24] K. B. Ramesh, M. A. Pasha, *Bioorg. Med. Chem. Lett.* **2014**, *24*, 3907.
[25] P. Iniyavan, G. L. Balaji, S. Sarveswari, V. Vijayakumar, *Tetrahedron Lett.* **2015**, *56*, 5002. https://doi.org/10.1016/j.tetlet.2015.07.016.
[26] T. S. Jin, J. S. Zhang, T. T. Guo, A. Q. Wang, T. S. Li, *Synthesis* **2004**, *2004*, 2001.
[27] V. S. Dofe, A. P. Sarkate, Z. M. Shaikh, C. K. Jadhav, A. S. Nipte, C. H. Gill, *J. Heterocycl. Chem.* **2018**, *55*(3), 756.
[28] V. S. Dofe, A. P. Sarkate, Z. M. Shaikh, A. S. Nipte, C. H. Gill, *Het. Comm.* **2018**, *24*(1), 59.
[29] V. S. Dofe, A. P. Sarkate, Z. M. Shaikh, C. H. Gill, *J. Heterocycl. Chem.* **2017**, *54*, 3195.
[30] V. S. Dofe, A. P. Sarkate, D. K. Lokwani, D. B. Shinde, S. H. Kathwate, C. H. Gill, *J. Heterocycl. Chem.* **2678**, *54*, 2017.
[31] S. V. Tiwari, J. A. Seijas, M. P. Vazquez-Tato, A. P. Sarkate, D. K. Lokwani, A. P. G. Nikalje, *Molecules* **2016**, *21*(8), 1.
[32] R. N. Shelke, D. N. Pansare, C. D. Pawar, D. B. Shinde, S. N. Thore, U. D. Pawar, R. P. Pawar, S. R. Bembalkar, *World J. Pharm. Res.* **2016**, *5*, 2031.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Chavan PN, Pansare DN, Shelke RN. Eco-friendly, ultrasound-assisted, and facile synthesis of one-pot multicomponent reaction of acridine-1,8(2H,5H)-diones in an aqueous solvent. *J Chin Chem Soc*. 2019;1–7. https://doi.org/10.1002/jccs.201800411