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Novel Brønsted Acidic Ionic Liquid ([CMIM][CF_3COO]) Prompted Multicomponent Hantzsch Reaction for the Eco-Friendly Synthesis of Acridinediones: An Efficient and Recyclable Catalyst

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Abstracts A novel, highly efficient and recyclable Brønsted acidic ionic liquid ([CMIM][CF_3COO]) has been successfully implemented for the synthesis of acridinediones in aqueous media. Recyclability of novel catalyst, high yields, use of environmentally benign aqueous media as solvent, simple product isolation, high atom economy and sidestep to column chromatography are the noteworthy features of this protocol. This protocol is competent for producing wide library of acridinediones in good to excellent yields. Furthermore, molecular structure and relative stereochemistry of **4c** and **4s** derivatives were confirmed by single-crystal X-ray diffraction.

Keywords Acridinediones · Brønsted ionic liquid · Enamine · Multicomponent reaction

1 Introduction

MCR's endowed with notable properties as simpler methods and operations as compared to the conventional multistep methods of heterocycles synthesis have gained enormous interest in diversity oriented synthesis of skeletons found in natural products, drug like molecules [1–3]. MCRs tactics are proclaimed to be economic, cost- and time-effective attributing its properties such as reduction in steps thereby saving synthetic time, efficient inexpensive purification process, synthetic convergence as well as selectivity and synthetic efficiency over traditional chemical reactions thereby attracted contemporary organic chemistry [4, 5].

Acridine 1,8-diones are an important class of heterocycles containing a 1;4-DHP parent nucleus, are induced with high efficiencies with several applications such as photoinitiators, laser activity, fluorescence [6–9], laser dyes [10–12], electrochemical and photo-physical properties [13]. The 1,4-DHP derivatives contribute as a very significant compound due of their abundant pharmacological properties [14]. In particulars dihydropyridine drugs such as nifedipine, nicardipine, amlodipine and other are effective cardiovascular agents for the treatment of hypertension [15–17] (Fig. 1). 1,4-DHP have also been known for their calcium channel activity, moreover this heterocyclic ring constitutes variety of bioactive compounds such as vasodilator, bronchodilator, antiatheroscntific, antidiabetic, antitumor, and anti-inflammatory agents [18]. Further studies have discovered that these compounds exhibit diverse medical function such as neuroprotectus, platelet antiaggregaters and chemosensitizers [19].

The general synthesis of 1,4-DHP by Hantzsch method involves one pot cyclocondensation of aldehydes with dicarbonyls and ammonium acetate refluxing in ethanol [20]. There are several methods reported for the synthesis of 1,4-dihydropyridines from dimedone, aldehyde through different nitrogen sources like urea [21], methyl amine [22], different aniline or ammonium acetate [23] via traditional heating in organic solvent and in presence of triethyl benzyl ammonium chloride (TEBAC) [24], p-dodecyl benzene sulphonic acid (DBSA) [25], L-proline [26], amberlyst-15

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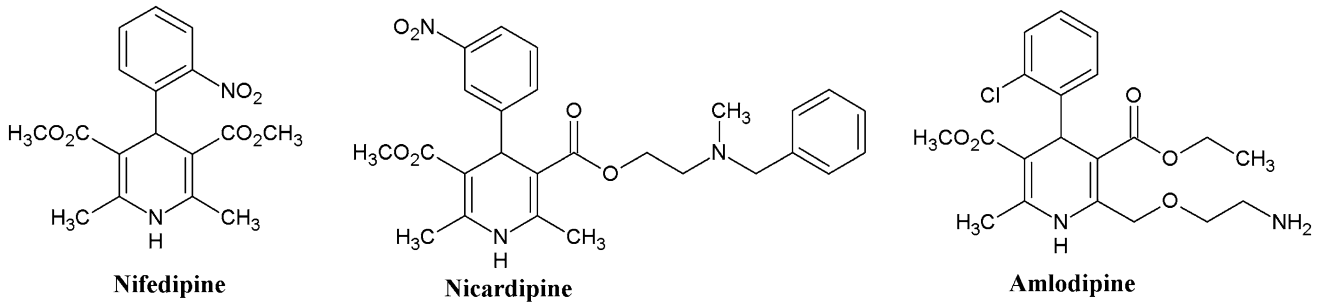


Fig. 1 Representative antihypertensive compounds

[27], under microwave [28], TMSCl-NaI [29], metal triflates [30], I_2 [31],$CeCl_3{\cdot}7H_2O$ [32], SiO_2-Pr-SO_3H [33], CAN [34], Fe_3O_4 Nanoparticles [35] and MCM-41-SO_3H [36].

However, most of the methods are blemished by aspects such as unsatisfactory yield, prolonged duration, inconvenient availability of reagent, toxic solvents and expensive catalysts, Hence the development of an efficient synthesis of Hantzsch 1,4-dihydropyridines seemed to be of prime importance. Recently avail of ionic liquids as catalyst or solvents in multicomponent reactions has been gaining elevated interest in green synthesis [37–39]. Initially ionic liquids have been introduced as alternative green reaction media attributed to their unique physico-chemical properties, such as negligible vapor pressure, non-volatility, non-inflammability, thermal and chemical stability and controlled miscibility in organic solvents which proves their importance in controlling reactions as catalysts [40–42].

Amongst them, Brønsted acidic ionic liquids displayed potential catalytic characteristics over conventional homogeneous/heterogeneous acidic catalysts in chemical procedures as they are flexible, recyclable and reusable, non-corrosive and possess ability to be used as dual solvents and catalysts [43–46]. In continuation of our investigation on the development of eco-friendly methodologies and applications of ionic liquids as catalysts in multicomponent reactions [47], herein, we demonstrate an expedient and highly efficient protocol for one pot multicomponent synthesis of acridinediones derivatives from various aryl aldehydes, dimedone and ammonium acetate using novel Brønsted acidic ionic liquid [CMIM][CF_3COO] as an effective, recyclable and reusable catalyst (Scheme 1). To the best of our knowledge, our catalyst [CMIM][CF_3COO] is novel and used for first time.

2 Experimental

2.1 General

The chemicals were purchased from Thomas Baker, Sigma-Aldrich and used as received without further purification. All the melting point check on Labstar melting apparatus was uncorrected. The IR spectra was run on a Perkin-Elmer, FTIR-1600 spectrophotometer and expressed in cm^{-1} (KBr). ^1H and ^{13}C NMR spectra were recorded on Bruker Avance (300 MHz) spectrometer in $CDCl_3$, D_2O or DMSO-d_6 using TMS as the internal standard. The LC-MS spectrums were recorded by Shimadzu LC-MS-2010 equipped with electron spray ionization interface.

2.2 X-Ray Structure Analysis

X-ray diffraction data of compounds **4c** and **4s** were collected at T = 298 and 293 K on a Bruker APEXII CCD and CrysAlis PRO Oxford diffractometer with graphite monochromated Mo Kα (λ = 0.71073 Å) radiation. Table 4 shows the unit cell parameters and other crystallographic details. The determination of cell refinement and data reduction were performed with program SAINT and CrysAlis PRO [51]. The structure was solved using the direct methods of program SHELXS97 and refined anisotropically by full-matix least-square on F^2 was carried out with the program SHELXL97 [52].

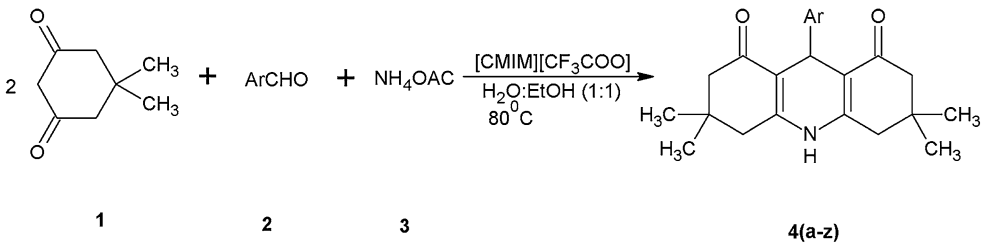
2.3 Synthesis of Ionic Liquid

The Brønsted acidic ionic liquid such as 3-(carboxymethyl)-1-methyl-1H-imidazol-3-ium trifluoroacetate [CMIM][CF_3COO] was synthesized as shown in Scheme 2.

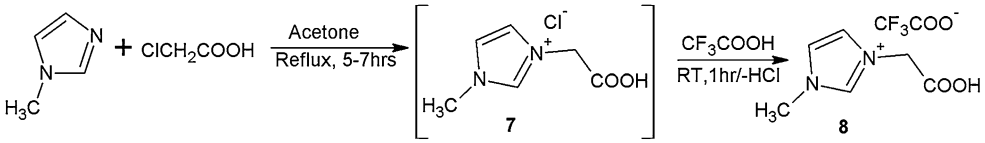
2.3.1 Preparation of [CMIM][CF_3COO]

A mixture of 1-methyl imidazole (10 mmol), chloroacetic acid (10 mmol) and dry acetone (40 ml) were charged into 250 ml round bottom flask at RT. The reaction was performed 5–7 h under reflux condition. After completion of reaction (checked by TLC), the reaction mixture was cooled and then a stoichiometric amount of trifluoroacetic acid (99 %) was slowly added at 5–10 °C under stirring over 30 min. Then the reaction was stirred an additional period of 1 h at RT. The white solid was observed, filter and washed

Scheme 1 Synthesis of 1,8-dioxoacridinediones



Scheme 2 Synthesis of ionic liquid [CMIM][CF_3COO]



3–4 times with acetone (10 ml) to remove non-ionic residue. Finally, it was dried under vacuum at 50 °C for 2 h to give [CMIM][CF_3COO] as a white solid in 97 % yield and further it used as a catalyst after checking pH (pH 1.7).

[Compound **8**: 3-(Carboxymethyl)-1-methyl-1H-imidazol-3-ium trifluoroacetate]

2.4 General Procedure for the Synthesis of Acridinediones (**4a**–**4z**)

In a 50 ml round bottom flask, a mixture of dimedone **1** (2 mmol), aldehyde **2** (1 mmol), ammonium acetate **3** (1.5 mmol) and [CMIM][CF_3COO] (30 mol%) in aqueous ethanol (1:1, 7 ml) was stirred at 80 °C for 1–1.5 h. The progress of reaction was monitored by TLC. After completion of reaction, the mixture was gradually cool to RT and poured on ice water under stirring, solid was precipitate out. Then, filter the product and recrystallized in ethanol. The catalyst [CMIM][CF_3COO], being aqueous ethanol soluble, was recovered from the filtrate.

2.5 Spectral Data for IL_s and Some Representative Acridinediones Derivatives

*2.5.1 3-(Carboxymethyl)-1-methyl-1H-imidazol-3-ium trifluoroacetate [CMIM][CF_3COO] (**8**)*

White solid; mp 190–195 °C;

Fresh ^{1}H NMR (300 MHz, DMSO-d_6): δ 13.67 (brs, 1H, OH), 9.20 (s, 1H, Ar–H), 7.74-7.76(m, 2H, Ar–H), 5.18 (s, 2H, CH_2), 3.91 (s, 3H, CH_3);

^{1}H NMR (300 MHz, D_2O): δ 9.0 (s, 1H, Ar–H), 7.64–7.65 (d, 2H, Ar–H), 5.12 (s, 2H, CH_2), 3.89 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 168.2, 159.5, 159.0, 158.5, 158.0, 137.9, 123.9, 123.2, 120.9, 117.1, 113.3, 109.5, 49.9, 35.9;

ESI–MS (+ve ion) (m/z): 141(M^+); ESI–MS (−ve ion) (m/z): 112.9(M^+);

After 4th run ^{1}H NMR (300 MHz, D_2O): δ 8.88 (s, 1H, Ar–H), 7.49-7.62 (m, 2H, Ar–H), 5.08 (s, 2H, CH_2), 3.84 (s, 3H, CH_3);

Anal. Calcd.for $C_8H_9F_3N_2O_4$ (254.162): C, 37.80; H, 3.57; N, 11.02. Found: C, 37.73; H, 3.63; N, 11.09.

*2.5.2 3,3,6,6-Tetramethyl-9-(4-chlorophenyl)-3,4,6,7,9,10-hexahydroacridine-1,8-dione (**4c**)*

Yellow solid; mp >300 °C; IR (KBr): 3432, 3279, 3174, 3057, 2955, 1649, 1609, 1489, 1398, 1366 cm^{-1}; ^{1}H NMR(300 MHz, DMSO-d_6): δ 8.18 (s, 1H, NH), 7.28–7.26(d, 2H, $J = 5.7$ Hz, Ar–H),7.17–7.14 (d, 2H, $J = 8$ Hz, Ar–H), 5.04 (s, 1H, CH), 2.29–2.11 (m, 8H, CH_2), 1.08 (s, 6H, CH_3), 0.96 (s, 6H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 195.9, 153.8, 149.9, 145.1, 131.6, 129.4, 128.0, 112.5, 50.8, 40.6, 40.4, 33.2, 32.5, 29.6, 27.0; ESI–MS (m/z): 384.3 $(M+H)^+$;

Anal. Calcd. for $C_{23}H_{26}ClNO_2$ (383.911): C, 71.96; H, 6.83; N, 3.65. Found: C, 71.87; H, 6.75; N, 3.73.

*2.5.3 3,3,6,6-Tetramethyl-9-(4-hydroxy,3-methoxyphenyl)-3,4,6,7,9,10-hexahydroacridine-1,8-dione (**4m**)*

Yellow solid; mp 295–298 °C; IR (KBr): 3409, 3274, 3168, 3049, 1623, 1511, 1370 cm^{-1};

^{1}H NMR (300 MHz, DMSO-d_6): δ 9.69(s, 1H, OH), 8,71 (brs, 1H, NH), 7.69 (s, 1H, Ar–H), 7.44

(s, 2H, Ar–H), 5.69(s, 1H, CH), 4.61 (s, 3H, OCH_3), 3.25–2.88 (m, 8H, CH_2), 1.89 (s, 6H, CH_3), 1,77 (s, 6H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 195.4, 149.0, 138.9, 114.6, 112.8, 55.7, 50.8, 32.6, 32.4, 29.6, 26.9;

Anal. Calcd. for $C_{24}H_{29}NO_4$ (395.491): C, 72.89; H, 7.39; N, 3.54. Found: C, 72.81; H, 7.33; N, 3.63.

*2.5.4 3,3,6,6-Tetramethyl-9-(3,4-dimethoxyphenyl)-3,4,6,7,9,10-hexahydroacridine-1,8-dione (**4n**)*

Yellow solid; mp 286–290 °C; IR (KBr): 3273, 3200, 3071, 2954, 1642, 1610 cm^{-1};

^1H NMR(300 MHz, $CDCl_3$): δ 7.69 (s, 1H, NH), 6.92-6.91 (d, 1H, $J = 1.8$ Hz, Ar–H), 6.84–6.81 (m, 1H, Ar–H), 6.68–6.65 (d, 1H, $J = 8.4$ Hz, Ar–H), 5.04 (s, 1H, CH), 3.80 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 2.31–2.12 (m, 8H, CH_2), 1.05 (s, 6H, CH_3), 0.96 (s, 6H, CH_3);

^{13}C NMR (75 MHz, $CDCl_3$): δ 195.8, 148.7, 148.4, 147.1, 139.4, 119.8, 113.2, 111.8, 110, 55.7, 55.6, 50.8, 40.7, 32.9, 32.5, 29.5, 26.9; ESI–MS (m/z): 432.15 $(M+Na)^+$;

Anal. Calcd. for $C_{25}H_{31}NO_4$ (409.571): C, 73.32; H, 7.63; N, 3.42. Found: C, 73.41; H, 7.72; N, 3.47.

*2.5.5 3,3,6,6-Tetramethyl-9-(3-trifluoromethylphenyl)-3,4,6,7,9,10-hexahydroacridine-1,8-dione (**4o**)*

Yellow solid; mp >300 °C; IR (KBr): 3270, 3186, 3068, 2963, 1644, 1616 cm^{-1};

^1H NMR(300 MHz, DMSO-d_6): δ 8.92 (brs,1H,NH), 7.51–7.40 (m, 2H, Ar–H), 7.21–7.20 (d, 2H, $J = 4.8$ Hz, Ar–H), 4.92(s, 1H, CH), 2.49–1.95 (m, 8H, CH_2), 0.98 (s, 6H, CH_3), 0.82 (s, 6H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 195.2, 149.6, 148.1, 131.8, 128.1, 112.0, 50.6, 40.4, 40.3, 40.2, 39.9, 39.6, 39.3, 33.7, 32.4, 29.5, 26.7; ESI–MS (m/z): 418 (M^+);

Anal. Calcd. for $C_{24}H_{26}F_3NO_2$ (417.463): C, 69.05; H, 6.28; N, 3.36. Found: C, 68.95; H, 6.19; N, 3.34.

*2.5.6 3,3,6,6-Tetramethyl-9-(3-fluorophenyl)-3,4,6,7,9,10-hexahydroacridine-1,8-dione (**4p**)*

Yellow solid; mp >300 °C; IR (KBr): 3217, 3070, 2954, 1627 cm^{-1};

^1H NMR (300 MHz, DMSO-d_6): δ 9.19 (brs, 1H, NH), 7.64–7.48 (m, 3H, Ar–H), 7.26–7.24 (d, 1H, $J = 6.6$ Hz, Ar–H), 5.53 (s, 1H, CH), 2.91–2.59 (m, 8H, CH_2), 1.57 (s, 6H, CH_3), 1.44 (s, 6H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 190.5, 159.3, 144.7, 144.6, 144.4, 124.2, 124.1, 118.9, 110.0, 109.0, 107.0, 45.0, 53.0, 34.0, 28.0, 27.0, 23.0, 22.0; ESI–MS (m/z): 368 $(M+H)^+$;

Anal. Calcd. for $C_{23}H_{26}FNO_2$ (367.456): C, 75.18; H, 7.13; N, 3.81. Found: C, 75.25; H, 7.19; N, 3.87.

*2.5.7 3,3,6,6-Tetramethyl-9-(3-pyridine)-3,4,6,7,9,10-hexahydroacridine-1,8-dione (**4r**)*

Light yellow solid; mp 298–300 °C; IR (KBr): 3432, 3270, 3172, 2957, 1634 cm^{-1};

^1H NMR (300 MHz, $CDCl_3$): δ 11.89 (s, 1H, NH), 8.42-8.37 (m, 2H, Ar–H), 7.39–7.37 (d, 1H, $J = 8.1$ Hz, Ar–H), 7.26–7.18 (m, 1H, Ar–H), 5.53 (s.1H, CH), 2.50–2.19 (m, 8H, CH_2), 1.23 (s, 6H, CH_3), 1.11 (s, 6H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 190.8, 189.4, 148.6, 147.0, 134.4, 133.7, 122.9, 114.6, 46.9, 31.3, 31.0, 29.6, 27.3; ESI–MS (m/z): 351.15 $(M+H)^+$;

Anal. Calcd. for $C_{22}H_{26}N_2O_2$ (350.454): C, 75.40; H, 7.48; N, 7.99. Found: C, 75.31; H, 7.44; N, 8.05.

*2.5.8 3,3,6,6-Tetramethyl-9-(2-hydroxyphenyl)-3,4,6,7,9,10-hexahydroacridine-1,8-dione (**4s**)*

Yellow solid; mp >300 °C; IR (KBr): 3405, 3265, 3083, 2943, 1649 cm^{-1};

^1H NMR(300 MHz, DMSO-d_6): δ 9.64 (brs, 1H, OH), 9.48 (s, 1H, NH), 6.96–6.89 (m, 2H, Ar–H), 6.70–6.66 (m, 2H, Ar–H), 4.85 (s, 1H, CH), 2.52-2.03 (m, 8H, CH_2), 1.02 (s, 6H, CH_3), 0.90 (s, 6H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6): δ 196.4, 153.6, 151.6, 134.4, 128.6, 127.4, 120.1, 117.7, 111.7, 50.3, 32.5, 29.3, 27.0, 26.9; ESI–MS (m/z): 366.3 $(M+H)^+$;

Anal. Calcd. for $C_{23}H_{27}NO_3$ (365.465): C, 75.59; H, 7.45; N, 3.83. Found: C, 75.54; H, 7.42; N, 3.87.

Table 1 Optimization solvent and reaction conditions for the synthesis of acridinediones

Entry	Solvent	Temp. (°C)	Time (min)	Yield (%)[a]
1	Water	RT	360	–[b]
2	Ethanol	RT	240	–[b]
3	Methanol	RT	240	–[b]
4	Water	80	300	–[b]
5	Ethanol	78	150	75
6	Methanol	64	180	67
7	Water+ethanol (2:1)	80	130	63
8	Water+ethanol (1:1)	80	85	86
9	Acetone	60	180	20
10	Isopropyl alcohol	80	120	70
11	Glycerol	80	110	75
12	Acetonitrile	80	135	45
13	Dimethyl formamide	80	300	25
14	Dimethyl sulfoxide	80	240	37
15	[CMIM][CF_3COO]	80	120	Trace
16	–	80	180	–[b]

Reaction condition: dimedone (2 mmol), 4-OH benzaldehyde (1 mmol), ammonium acetate (1.5 mmol), [CMIM][CF_3COO] (30 mol%)

[a] Isolated yield

[b] No reaction

Table 2 Screening of catalyst concentration

Entry	Catalyst (mol%)	Time (min)	Yield (%)[a]
1	–	350	–[b]
2	5	300	Trace
3	10	170	35
4	20	110	63
5	30	85	86
6	40	85	85

Reaction condition: dimedone (2 mmol), 4-OH benzaldehyde (1 mmol), ammonium acetate (1.5 mmol) in 7 ml aqueous ethanol (1:1) at 80 °C

[a] Isolated yield

[b] No reaction

3 Results and Discussion

At this instance, we outlined an eco-friendly protocol for the multicomponent synthesis of acridinediones scaffolds using novel ionic liquid [CMIM][CF_3COO] as a green and recyclable catalyst in aqueous ethanol (1:1) at 80 °C (Scheme 1).

Initially, the ionic liquid 3-(carboxymethyl)-1-methyl-1H-imidazol-3-ium trifluoroacetate was synthesized (Scheme 2) and identified by ^{1}H NMR, ^{13}C NMR, mass and elemental analyses. After characterization of ionic liquid, to evaluate the efficiency and applicability of our new catalyst to synthesis of acridinediones, we choose dimedone (2 mmol), 4-OH benzaldehyde (1 mmol), ammonium acetate (1.5 mmol) as a substrates and 30 mol% of [CMIM][CF_3COO] as catalyst proportion for model reaction. Successively, we focused our initial investigation on the effect of various solvents and their mixtures on model reaction at different temperatures (Table 1). It was observed that, the reaction doesn't marches successfully in sole solvents like water, EtOH and MeOH even after prolonged stirring at room temperature (Table 1, entries 2, 3). However, best result was observed using same proportional mixture (1:1) of water/ethanol at

Table 3 [CMIM][CF_3COO] catalyzed synthesis of acridinediones derivatives

Entry	Ar	Product	Time (min)	Yield[a] (%)	MP °C (observed)	MP °C (literature)[Ref.]
1	4-NO_2 C_6H_4	**4a**	70	90	>300	261–262 [24]
2	C_6H_5	**4b**	80	87	285–289	251–252 [24]
3	4-Cl C_6H_4	**4c**	65	89	>300	>300 [24]
4	4-OH C_6H_4	**4d**	85	86	271–274	284–286 [29]
5	4-CH_3 C_6H_4	**4e**	90	84	270–275	227–228 [29]
6	3-NO_2 C_6H_4	**4f**	67	88	>300	285–286 [29]
7	3-Cl C_6H_4	**4g**	72	87	283–285	281–282 [29]
8	4-OCH_3 C_6H_4	**4h**	90	84	275–277	266–267 [29]
9	2;3-$(OCH_3)_2C_6H_3$	**4i**	87	83	>300	324–326 [29]
10	3-OH,4-OCH_3 C_6H_3	**4j**	85	85	>300	324–326 [29]
11	2-OCH_3 C_6H_4	**4k**	80	83	>300	294–296 [29]
12	2-Cl C_6H_4	**4l**	78	84	263–264	221–223 [28]
13	4-OH, 3-OCH_3 C_6H_3	**4m**	85	83	294–296	295–298 [48]
14	3,4-$(OCH_3)_2$ C_6H_3	**4n**	85	85	288–291	286–290 [49]
15	3-F_3C C_6H_4	**4o**	70	87	>300	–
16	3-F C_6H_4	**4p**	70	89	>300	300 [50]
17	4-F C_6H_4	**4q**	65	90	>300	275–276 [24]
18	3-CHO C_5H_4N	**4r**	60	81	298-300	–
19	2-OH C_6H_4	**4s**	87	82	>300	–
20	4- $(CH_3)_2N$ C_6H_4	**4t**	85	83	269–271	256–257 [24]
21	4-Br C_6H_4	**4u**	78	87	>300	330–332 [32]
22	3-Br C_6H_4	**4v**	73	86	294–297	288–289 [24]
23	4-CN C_6H_4	**4w**	80	88	>300	328–330 [32]
24	3-OH C_6H_4	**4x**	75	83	>300	>302 [32]
25	2-NO_2 C_6H_4	**4y**	81	84	284–287	293–295 [28]
26	n-butanal	**4z**	180	–[b]	–	–

Reaction condition: dimedone (2 mmol), aldehyde (1 mmol), ammonium acetate (1.5 mmol) and [CMIM][CF_3COO] (30 mol%) in 7 ml aqueous ethanol (1:1) at 80 °C

[a] Isolated yields

[b] No reaction

80 °C, which afforded 86 % yield of targeted molecules within 85 min (Table 1, entry 8).

Next, the same model reaction was carried out at 80 °C in excess of [CMIM][CF_3COO], only trace amount of product was formed, furthermore at solvent free condition the reaction didn't progressed even after prolonged stirring (Table 1, entries 15,16).

The results revealed that the reaction temperatures and choice of solvents significantly influence on the product yield and time of reaction completion.

Consequently, to optimize the concentration of catalyst for the synthesis of targeted molecule, we carried a reaction of dimedone, 4-OH benzaldehyde and ammonium acetate with different amount of [CMIM][CF_3COO] in aqueous ethanol (1:1) medium at 80 °C (Table 2, entries 1–5). The result signifies that with increase in the concentration of catalyst from 0 to 30 mol%, the yield of product **4a** increased up to 86 %. However, further increasing the concentration of catalyst from 30 to 40 mol%, there was no considerable change in the yield of product observed

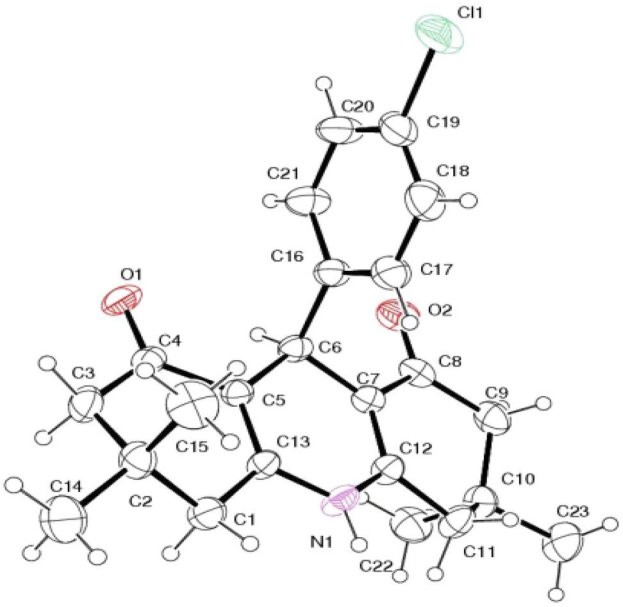


Fig. 2 X-ray crystal structure of **4c** with atom-labeling scheme

Table 4 Crystal data and structure refinement for **4c** and **4s**

Identification code	**4c**	**4s**
Empirical formula	C_{23} $H_{26}ClNO_2$	C_{23} $H_{27}NO_3$
Formula weight	383.90	365.46
Temperature	298(2) K	293(2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal system, space group	Orthorhombic, Pna2(1)	Orthorhombic, Pna2(1)
Unit cell dimensions	a = 14.1368(4) Å α = 90^0.	a = 13.669(5) Å α = 90°
	b = 14.1212(4) Å β = 90^0.	b = 14.753(5) Å β = 90°
	c = 10.7332(3) Å γ = 90^0.	c = 10.043(5) Å γ = 90°
Volume	2142.65(10) A^3	2025.3(14) A^3
Z, calculated density	4, 1.190 mg/m^3	4, 1.199 mg/m^3
Absorption coefficient	0.195 mm^{-1}	0.079 mm^{-1}
F(000)	816	784
Crystal size	0.22 × 0.16 × 0.10 mm	0.3 × 0.2 × 0.1 mm
Theta range for data collection	2.04° to 24.99°	3.61° to 26.00°
Limiting indices	$-16 \le h \le 16$, $-16 \le k \le 16$, $-11 \le l \le 12$	$-16 \le h \le 16$, $-18 \le k \le 18$, $-12 \le l \le 12$
Reflections collected/unique	24469/3,642 [R(int) = 0.0,208]	28,953/3,959 [R(int) = 0.0402]
Completeness to theta	= 24.99 99.8 %	= 26.00 99.7 %
Absorption correction Multi-scan	0.9808 and 0.9584	1.00000 and 0.86047
Max. and min. transmission		
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	3,642/1/248	3,959/1/253
Goodness-of-fit on F^2	1.033	1.332
Final R indices [I > 2sigma(I)]	R1 = 0.0314, wR2 = 0.0834	R1 = 0.1017, wR2 = 0.2985
R indices (all data)	R1 = 0.0355, wR2 = 0.0877	R1 = 0.1226, wR2 = 0.3321
Absolute structure parameter	0.01(7)	−1(3)
Largest diff. peak and hole	0.209 and −0.274 e.A^{-3}	0.799 and −0.331 e.A^{-3}
CCDC number	CCDC 965866	CCDC 965867

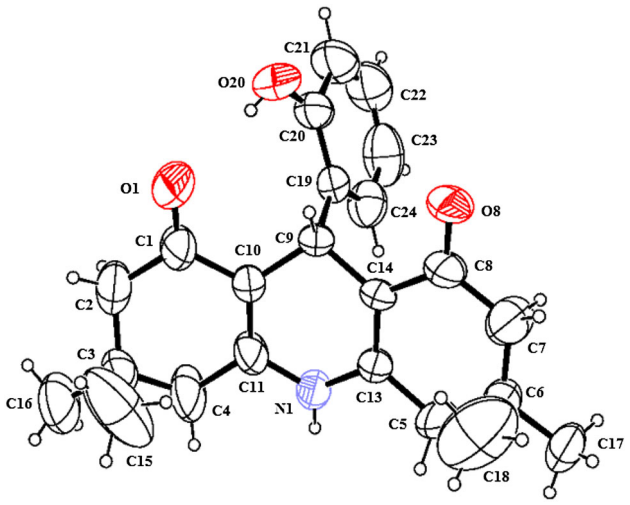


Fig. 3 X-ray crystal structure of **4s** with atom-labeling scheme

Table 5 Geometry of intra- and inter molecular hydrogen bonds for **4c** and **4s**

Compound	D–H…A	D–H (Å)	H…A (Å)	D…A (Å)	[D–H…A (°)]
4c	N1–H1…O1	0.86	1.86	2.718	178.00
4s	O20–H20…O1	0.728	1.946	2.661	167.60
	C9–H9…O20	0.98	2.502	2.898	103.95
	N1–H12…O8^{i}	0.86	2.195	2.809	128.23

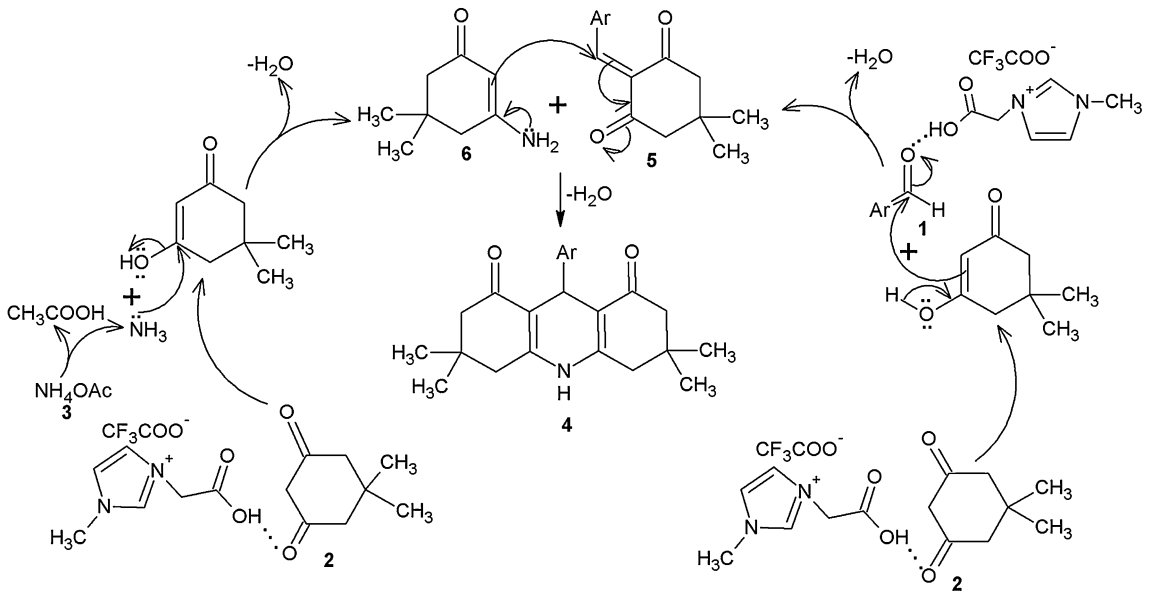
Symmetry code: (i) x − 1/2, −y + 1/2, +z

(Table 2, entry 6). Using these optimized conditions of 30 mol% of [CMIM][CF_3COO] and aqueous ethanol (1:1) to check the generality and versatility of the protocol we reacted several substituted aryl aldehydes, dimedone and ammonium acetate which afforded good to excellent yields (Table 3, entries 1–25).

In general, we found that the reactions of aromatic aldehydes containing electron withdrawing group at different positions (Table 3, entries 1,3,6,7,12,15–17,21–23,25) prove to be predominant attributed to high yield of products than the reactions of aldehydes containing electron donating group (Table 3, entries 4,5,8–11,13,14,19,20,24). Along with this our protocol has also been found to be in good agreement with heteroaromatic aldehyde affording resultant product in good yield (Table 3, entry 18). Further, we examined aliphatic aldehyde such as n-butanal instead of aromatic or heteroaromatic aldehydes, however there was no product formed after prolonged stirring (Table 3, entry 26).

All the products were crystalline and fully characterized on the basis of their melting points and spectral data (IR, ^{1}H-NMR, ^{13}C-NMR and LC–MS) with those of authentic sample [24, 28, 29, 32, 48–50]. The molecular structure of compound 3,3,6,6-tetramethyl-9-(4-chlorophenyl)-3,4,6,7,9,10-hexahydroacridine-1,8-dione **4c** and 3,3,6,6-tetramethyl-9-(2-hydroxyphenyl)-3,4,6,7,9,10-hexahydroacridine-1,8-dione **4s** were also confirmed by single crystal X- ray analysis (Table 4; Figs. 2, 3).

In X-ray single crystal analysis the geometry of **4c** and **4s** are orthorhombic. The central rings of acridinediones in **4c** and **4s** are in boat conformation whiles other two cyclohexanone rings of dimedone in half chair conformations. The geometry of inter and intra-molecular hydrogen



Scheme 3 Pausible mechanism for the formation of 1,8-dioxoacridinediones

bonds for **4c** and **4s** as shown in Table 5, Moreover the intermolecular packing arrangement of molecules along b axis for **4s** as shown in Fig. 4.

A plausible mechanism for the formation of acridinediones **4** is outlined in Scheme 3. The reaction is initiated by the Knoevenagel condensation of aryl aldehyde **1** with a molecule of dimedone **2** to form Knoevenagel product **5**, and simultaneously condensation of another molecule of dimedone **2** with ammonium acetate **3** to provide enamine **6**. Finally, the subsequent Michael addition between **6** and **5** followed by intramolecular cyclization and dehydration affords the product **4**.

The reusability and recyclability are the key aspects in viewpoint point of green chemistry, thus checked it for our novel catalyst [CMIM][CF_3COO]. The recyclability of the catalyst was checked on the model reaction using 30 mol% of [CMIM][CF_3COO] in aqueous ethanol media. After each run, the filtrate was collected of filtered product and the containing ionic liquid was extracted with diethyl ether (2 × 15 ml) to remove organic impurities. Then the water was evaporated and catalyst was further dried at 50 °C under reduced pressure. The catalyst was recovered in excellent yields (96 %) and reused in the subsequent reaction for four consecutive times, giving an average of 84 % yield of isolated product (Fig. 5). From these results, it was noticed that the [CMIM][CF_3COO]proved as highly efficient and recyclable catalyst with negligible loss in its catalytic activity. The recovered catalyst after four

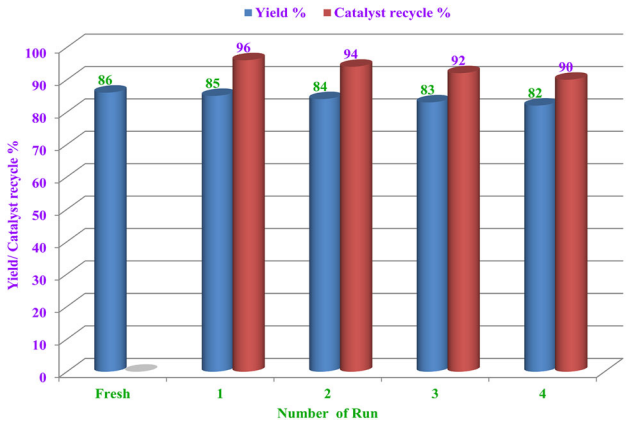


Fig. 5 Reusable and recyclability of catalyst for synthesis of **4d**

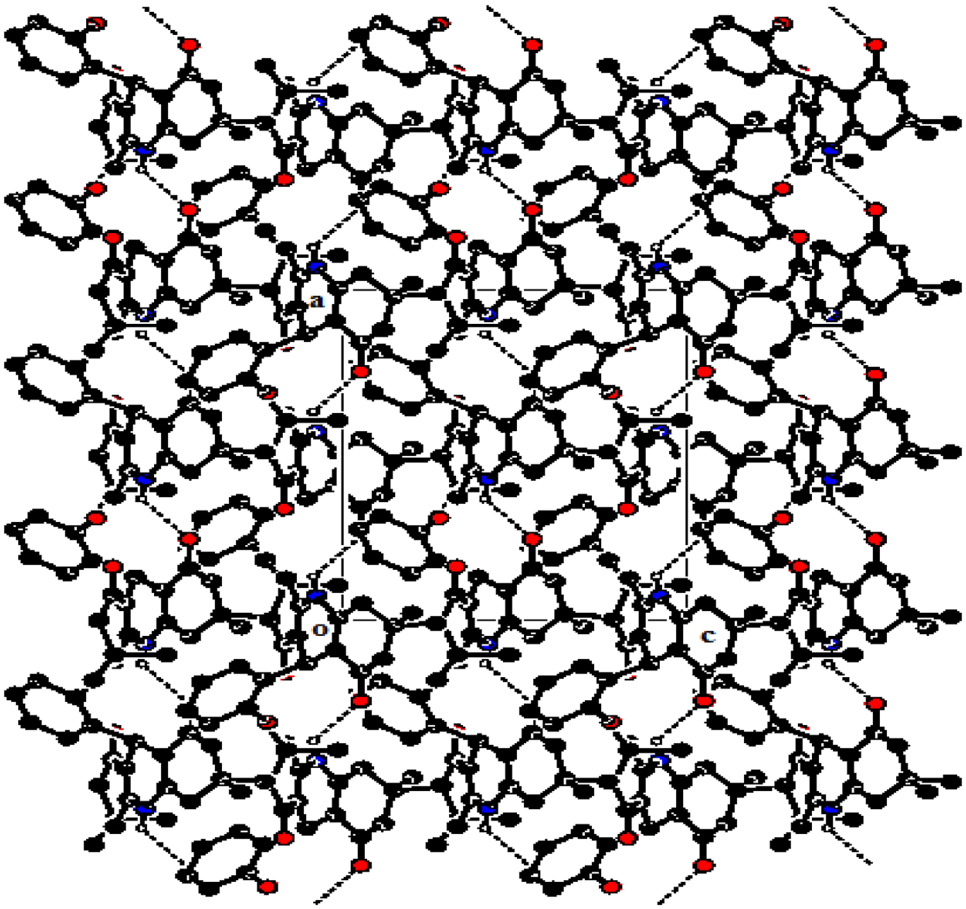


Fig. 4 The packing arrangement of molecules viewed along the b axis. The *dashed lines* show intermolecular N–H…O hydrogen bonds. Only H atoms involved in hydrogen bonds are shown

Table 6 Comparison of the results of [CMIM][CF_3COO] with literature reported catalysts

Entry	Catalyst	Conditions	Reaction time (h/min)	Yield (%)	Reference
1.	L-proline	H_2O/reflux	130–200 min	78–92	[26]
2.	_	H_2O/100 °C/microwave	3–5 min	88–95	[28]
3.	$CeCl_3.7H_2O$	[Bmim][BF_4]/55 °C	3 h	85–95	[32]
4.	CAN	PEG 400/50 °C	3.5–4 h	94–98	[34]
5.	Nano-Fe_3O_4	Solvent free/120 °C	10–50 min	75–90	[35]
6.	MCM-41-SO_3H	Solvent free/110 °C	10–110 min	61–98	[36]
7.	[CMIM][CF_3COO]	H_2O:EtOH (1:1)/80 °C	60–90 min	81–90	[This work]

consecutive runs had no observable change in the structure referring to the ^{1}H-NMR spectrum in comparison with fresh catalyst ^{1}H NMR (**8**). These results imply that the catalyst was highly stable and appropriately capable for its reuse under these reaction's conditions.

The applicability of the protocol for the synthesis of acridinediones has been compared with some of the previously reported catalysts in Table 6. The results have been compared with respect to the reaction times and yields. As demonstrated in Table 6, [CMIM][CF_3COO] is an uniformly or more proficient catalyst for this multicomponent reaction in terms of yield and reaction time.

4 Conclusions

In conclusion, we have developed a superficial and expedient method for the one pot synthesis of acridinediones derivatives using novel [CMIM][CF_3COO] as an eco-friendly and efficient catalyst. The advantage of this protocol in which recyclable and reusable Brønsted acidic ionic liquid is employed as an effective catalyst, high catalytic efficiency, shorter reaction time, high yield and atom economy, a convenient work up and environmental benignancy.

5 Supplementary Information

Crystallographic data for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as Supplementary Publication No. CCDC 965866, 965867. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (www.ccdc.cam.ac.uk/data_request/cif or e-mail: deposit@ccdc.cam.ac.Uk).

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