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# Ionic Liquid-Promoted Green Protocol for the Synthesis of Novel Naphthalimide-Based Acridine-1,8-dione Derivatives via a Multicomponent Approach

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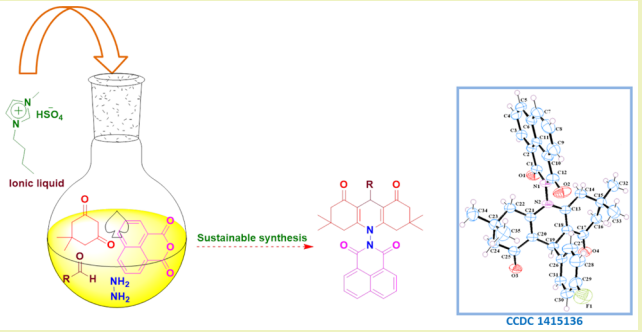
Supporting Information

**ABSTRACT:** An efficient, one-pot multicomponent synthesis of novel naphthalimide-based acridine-1,8-dione derivatives was achieved by condensation of dimedone, aromatic aldehydes, hydrazine hydrate, and 1,8-naphthanoic anhydride in the presence of a [bmim]$HSO_4$ ionic liquid, which acts as a green solvent medium. Mild conditions with excellent conversions and a simple isolation procedure are noteworthy advantages of this method. The recovery and recyclability of the ionic liquid make this protocol environmentally desirable.




**KEYWORDS:** *Ionic liquid, Multicomponent reaction, Naphthalimide-based acridine-1,8-dione derivatives, [bmim]$HSO_4$, Environmentally friendly protocol*



## INTRODUCTION

As there is lot of focus on diversity, speed, and efficiency, particularly in the drug discovery process, multicomponent reactions (MCRs) have become very powerful tools in organic and medicinal chemistry.[1,2] A MCR in which three or more reactants are combined in a single chemical operation is one of the perfect solutions for sustainable manufacture.[3−5] Isoquinolindione (naphthalimide) derivatives have been assessed as anticancer agents,[6−10] and particular analogues, such as amonafide and mitonafide, have exhibited notable anticancer activity both preclinically and in clinical trials.[11−14] On the other hand, acridines make up a known significant class of organic molecules, which have attracted attention from many medicinal and pharmaceutical chemists, because of their anticancer activity.[15−17] Here, we planned to develop a molecular system consisting of naphthalimide and acridine moieties that may be having important biological applications.

Ionic liquids (ILs)[18−20] have attracted considerable interest in the context of sustainable green synthesis during recent years, because they can also act as efficient media for organic syntheses. ILs possess various attractive physicochemical properties such as nonvolatility, low vapor pressure, nonexplosiveness, recyclability, easy operation, and thermal stability over a wide range of temperatures. ILs can be considered as alternative green solvents because of their unique ionic character and structural organization. There are several reports about the applications of ionic liquids in organic reactions such as Beckmann rearrangement,[21] Biginelli reaction,[22] Diels−Alder reaction,[23] Friedel−Crafts reaction,[24] Pechmann condensation,[25] Heck reaction,[26] and other reactions.[27−29]

In continuation of our efforts toward the development of novel heterocyclic compounds using ionic liquids,[30−32] herein we report a facile synthesis of naphthalimide-based acridine-1,8-dione derivatives. To the best of our knowledge, this is the first report of the synthesis of naphthalimide-based acridine-1,8-dione derivatives via multicomponent reaction of dimedone, aromatic aldehydes, hydrazine hydrate, and 1,8-naphthanoic anhydride in the presence of [bmim]$HSO_4$ (1-butyl-3-methylimidazolium hydrogen sulfate).

## RESULTS AND DISCUSSION

An environmentally benign protocol was used for the synthesis of naphthalimide-based acridine-1,8-dione derivatives via a multicomponent process from the reaction of dimedone (**1**, 2 mmol), aromatic aldehydes (**2a−j**, 1 mmol), hydrazine hydrate (**3**, 1 mmol), and 1,8-naphthanoic anhydride (**4**, 1 mmol) in [bmim]$HSO_4$, which act as an eco-friendly green medium.

To avoid the drawbacks such as the toxicity and volatility of various organic solvents, the ionic liquid was employed in the multicomponent reaction as a green solvent medium. First, a trial reaction was conducted using a multicomponent approach with dimedone (**1**), 4-fluorobenzaldehyde (**2a**), hydrazine

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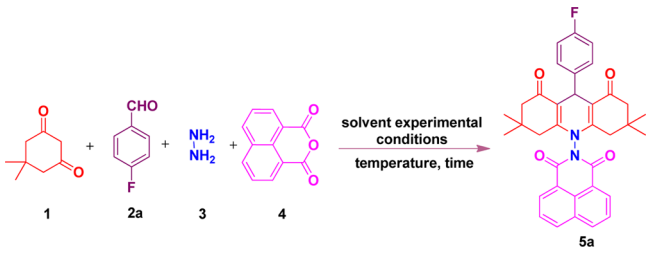
hydrate (**3**), and 1,8-naphthanoic anhydride (**4**) as a simple model reaction to investigate the probability of the approach and to optimize the reaction conditions. However, the effects of reaction temperature and solvents were assessed from this model reaction, and the results are summarized in Table 1.

**Table 1. Optimization of Reaction Conditions for the Synthesis of 5a**




| entry[a] | solvent | temp (°C) | time | yield[b] (%) |
|---|---|---|---|---|
| 1 | neat | 60 | 24 h | NR |
| 2 | methanol | 60 | 12 h | 11 |
| 3 | ethanol | 60 | 12 h | 14 |
| 4 | acetonitrile | 60 | 11 h | 20 |
| 5 | acetone | 60 | 16 h | 16 |
| 6 | acetic acid | 60 | 20 h | 38 |
| 7 | [bmim]Br | 60 | 2 h | 52 |
| 8 | [bmim]$PF_6$ | 60 | 1.5 h | 48 |
| 9 | [bmim]$BF_4$ | 60 | 2 h | 56 |
| **10** | **[bmim]$HSO_4$** | **60** | **35 min** | **93** |
| 11 | [bmim]$HSO_4$ | rt | 1 h | 54 |
| 12 | [bmim]$HSO_4$ | 40 | 1 h | 75 |
| 13 | [bmim]$HSO_4$ | 80 | 35 min | 94 |

[a]Reaction conditions: dimedone (2 mmol), 4-fluorobenzaldehyde (1 mmol), hydrazine hydrate (1 mmol), 1,8-naphthoic anhydride (1 mmol), and solvent (1 mL). [b]Yields of the isolated products.

During the optimization of reaction conditions, it was observed that the absence of solvent did not give the required products even after 24 h under neat conditions. When solvents such as methanol, ethanol, acetonitrile, acetone, and acetic acid were used, their effect was only moderate (Table 1, entries 2–6), but when typical ionic liquids such as [bmim]Br, [bmim]$PF_6$, [bmim]$BF_4$, and [bmim]$HSO_4$ were used, shorter reaction times and higher yields compared to those of conventional solvents were observed. Ionic liquid [bmim]$HSO_4$ proved to be considerably superior to the analogous bromide, hexafluorophosphate, and tertafluoroborate ionic liquids for this reaction (Table 1, entries 7–9). The yield of product **5a** was improved, and the reaction time was reduced as the temperature was enhanced from room temperature to 60 °C. No further improvement in the product yield was observed, when the temperature was increased to 80 °C (Table 1, entries 10–13). Therefore, 60 °C was chosen as the optimal reaction temperature for all these reactions.

To specify the scope of the reaction, we have investigated the progress of the reaction under different conditions for dimedone (**1**), aromatic aldehydes (**2a–j**), hydrazine hydrate (**3**), and 1,8-naphthanoic anhydride (**4**). The naphthalimide-based acridine-1,8-dione derivatives (**5a–j**) were obtained in decent yields at 60 °C in [bmim]$HSO_4$. The results are summarized in Table 2. The protocol was effective with aromatic aldehydes having either electron-donating (-OMe) or electron-withdrawing (-F, -Cl, or -Br) groups to produce the corresponding 10-[1.3-dioxo-1*H*-benzo[*de*]isoquinoline-2(3*H*)-yl]-9-aryl-hexahydroacridine-1,8-dione derivatives in good yields. The electron effects did not have any significant impact on the reaction rate. We herein propose a mechanism in Scheme 1 for the formation of naphthalimide-based acridine-1,8-dione derivatives in the presence of ionic liquid [bmim]-$HSO_4$, which acts as a promoter. As the first step, a hydrogen bond between the hydrogen atom of [bmim]$HSO_4$ and the carbonyl group of aldehyde **2** produces a complex which upon condensation with dimedone **1** forms a chalcone-type intermediate (**A**). The formation of intermediate **B** takes place by a condensation between 1,8-naphthanoic anhydride **4** and hydrazine hydrate **3**. Dimedone **1** reacts with intermediate **B** forming another intermediate (**C**). Subsequently, a Michael-type addition occurs between intermediates **A** and **C**, producing intermediate **D**. Intermediate **D** undergoes intermolecular cyclization to afford the final product **5**. The reaction mixture was poured into ice-cold water; the obtained solid product was isolated by filtration, and the filtrate containing ionic liquid [bmim]$HSO_4$ was extracted with ethyl acetate to remove the nonionic organic impurities. The ionic liquid was recovered from water under reduced pressure, dried at 60–70 °C, and reused for subsequent reactions for four additional cycles. A slight decrease in its activity in terms of product yields (Figure 1) was observed when the ionic liquid was used beyond four cycles.

The structures of the synthesized compounds were well-characterized by infrared (IR), $^1$H nuclear magnetic resonance (NMR), and $^{13}$C NMR spectroscopy, mass spectrometry, and elemental analysis. Further, the structure of compound **5a** was confirmed by the single-crystal X-ray diffraction method (Figure 2, CCDC-1415136). Compound **5a** crystallizes in centrosymmetric monoclinic space group $P21/c$ with one molecule in the asymmetric unit. Crystal structure analysis reveals that the molecules form a closely packed structure with C–H···F and C–H···O hydrogen bonds. Two inversion-related molecules combine via C–H···F hydrogen bonds and form a discrete dimer. These dimers are interconnected by C–H···O hydrogen bonds. The overall structure is a closely packed structure. Table 3 gives the pertinent crystallographic data, and Table 4 gives hydrogen bond parameters.

## EXPERIMENTAL SECTION

**General Information.** All reagents were procured from commercial sources and used without further purification. A Bruker WM-4 (X) spectrophotometer (577 model) was used for recording IR spectra (KBr). $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker WM-400 spectrophotometer at 400 and 100 MHz, respectively, in DMSO-$d_6$ with TMS as an internal standard. The chemical shifts are reported in parts per million ($\delta$). Elemental analysis was performed on a Carlo Erba EA 1108 automatic elemental analyzer. Mass spectra (ESI) were conducted on a jeo1 JMSD-300 spectrometer. Compound **5a** was crystallized from acetic acid to yield prismatic crystals.

**Single-Crystal X-ray Diffraction.** The single-crystal X-ray diffraction data of the crystals **5a** were collected on a Bruker Kappa APEX-II CCD DUO diffractometer at 293(2) K using graphite-monochromated Mo K$\alpha$ radiation ($\lambda$ = 0.71073 Å). No absorption correction was applied. The lattice parameters were determined from least-squares analysis, and reflection data were integrated using SHELXTL.[33] The crystal structures were determined by direct methods using SHELXS-97 and refined by full-matrix least-squares refinement on $F^2$ with anisotropic displacement parameters for non-H atoms using SHELXL-97.[34] All the aromatic and aliphatic C–H hydrogens were generated by the riding model in idealized geometries.


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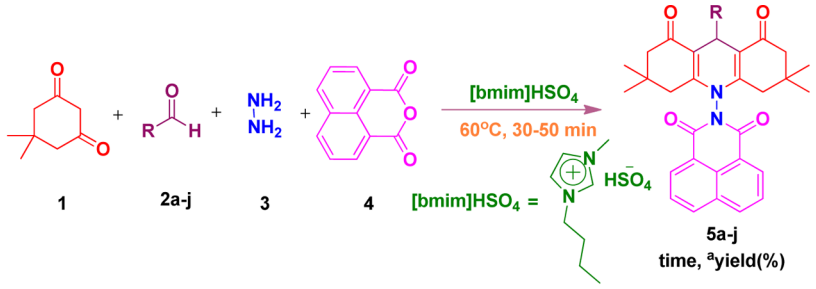
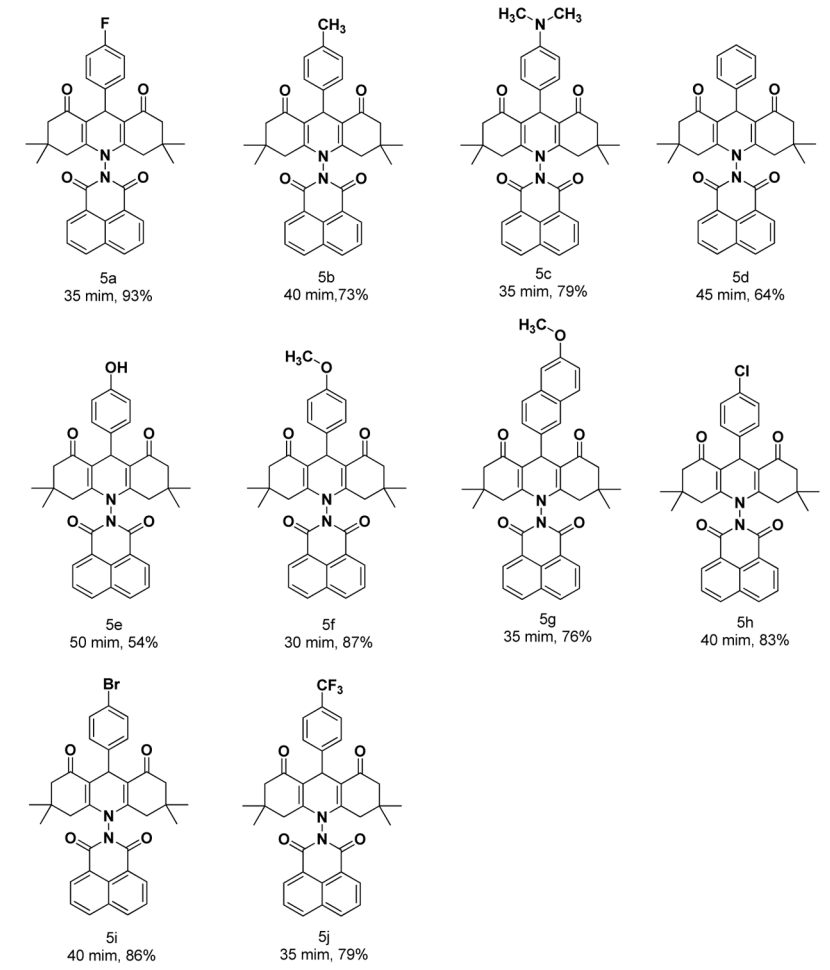
**Table 2. Synthesis of Naphthalimide-Based Acridine-1,8-dione Derivatives (5a–j)**[b]




[a]Yields of the isolated products. [b]Reaction conditions: dimedone (2 mmol), 4-fluorobenzaldehyde (1 mmol), hydrazine hydrate (1 mmol), 1,8-naphthoic anhydride (1 mmol), and [bmim]$HSO_4$ (1 mL).

Mercury 2.3 (Build RC4), ORTEP-3, and X-Seed[35−37] were used to prepare material for publication.

*General Procedure for the Synthesis of [1,3-Dioxo-1H-benzo-[de]isoquinolin-2(3H)-yl]-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione Derivatives (**5a–j**).* A mixture of aromatic aldehydes (1 mmol), 1,8-naphthoic anhydride (1 mmol), hydrazine hydrate (1 mmol), and dimedone (2 mmol) in [bmim]-$HSO_4$ (1 mL) was heated to 60 °C. The progress of the reaction was monitored by TLC [eluent, ethyl acetate/*n*-hexane (2:8)]; after completion of the reaction, the reaction mixture was allowed to cool to room temperature, and 10 mL of water was added to the mixture. The resultant precipitate was filtered and purified by column chromatography using silica gel [ethyl acetate/*n*-hexane (1:9)] to afford the pure compounds (**5a–j**).

*10-[1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-9-(4-fluorophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-(2H,5H)-dione (**5a**).* Pale yellow solid: mp 270−272 °C; IR (KBr) $\nu_{max}$ 2966, 1702, 1677, 1665, 1647 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 0.71 (s, 6H, $CH_3$), 0.87 (s, 6H, $CH_3$), 1.97−2.33 (m, 8H, $CH_2$), 4.95 (s, 1H), 7.07 (t, $J$ = 8.8 Hz, 2H, ArH), 7.57−7.61 (m, 2H, ArH), 7.99−8.04 (m, 2H, ArH), 8.66−8.76 (m, 4H, ArH); $^{13}C$ NMR (100 MHz, DMSO-$d_6$) $\delta$ 24.05, 26.96, 28.68, 32.17, 50.17, 111.88, 118.16, 123.08, 126.27, 127.94, 129.47, 130.58, 139.27, 141.69, 146.47, 148.41, 148.77, 165.76, 194.68; ESI-MS $m/z$ 563 (M + 1). Anal. Calcd for $C_{35}H_{31}FN_2O_4$: C, 74.72; H, 5.55; N, 4.98. Found: C, 74.52; H, 5.44; N, 4.82.

*10-[1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-3,3,6,6-tetramethyl-9-(p-tolyl)-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (**5b**).* White solid: mp 261−262 °C; IR (KBr) $\nu_{max}$ 2969, 1701, 1675, 1661, 1649 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 0.95 (s, 6H, $CH_3$), 1.01 (s, 6H, $CH_3$), 2.00−2.17 (m, 8H, $CH_2$), 2.38 (s, 3H, $CH_3$), 4.95 (s, 1H), 7.07 (t, $J$ = 8.8 Hz, 2H, ArH), 7.57−7.61 (m, 2H, ArH), 7.99−8.04 (m, 2H, ArH), 8.66−8.75 (m, 4H, ArH); $^{13}C$ NMR (100 MHz, DMSO-$d_6$) $\delta$ 24.04, 26.97, 28.63, 32.13, 37.19, 50.13, 112.01,



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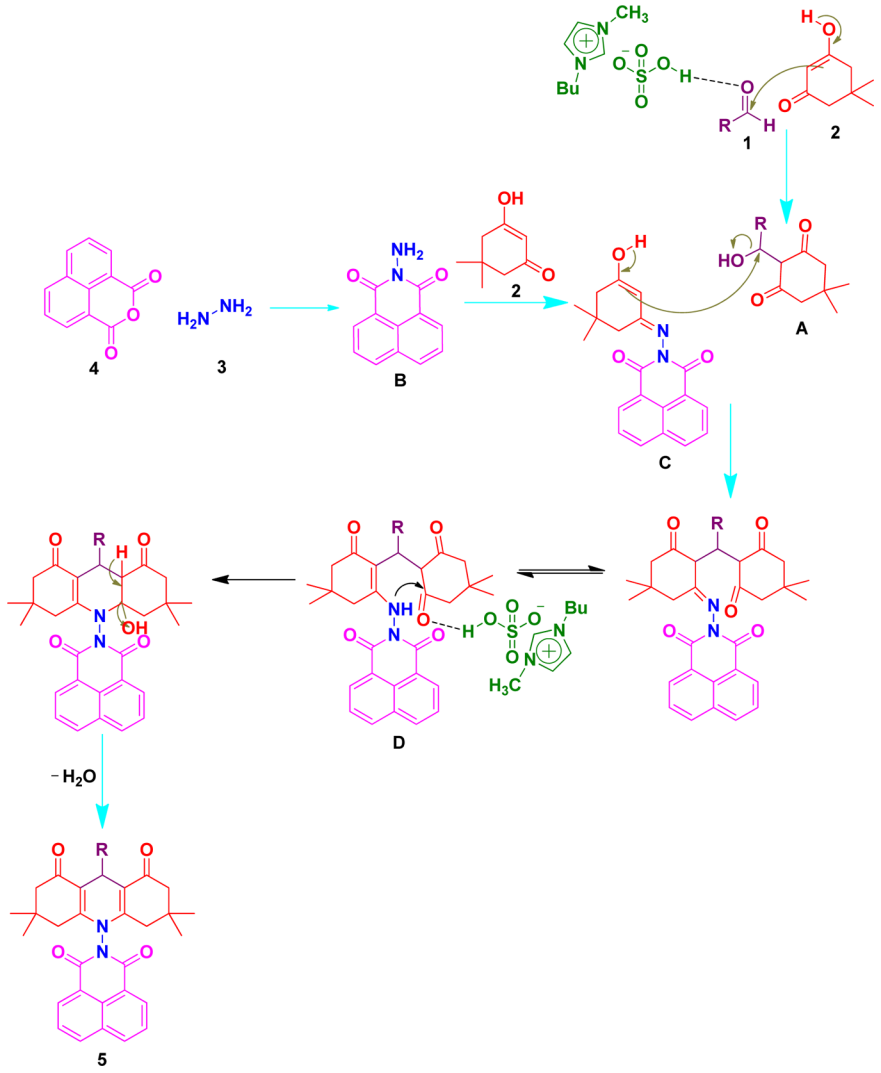
**Scheme 1. Proposed Mechanism for the Formation of Naphthalimide-Based Acridine-1,8-dione Derivatives (5a–j)**



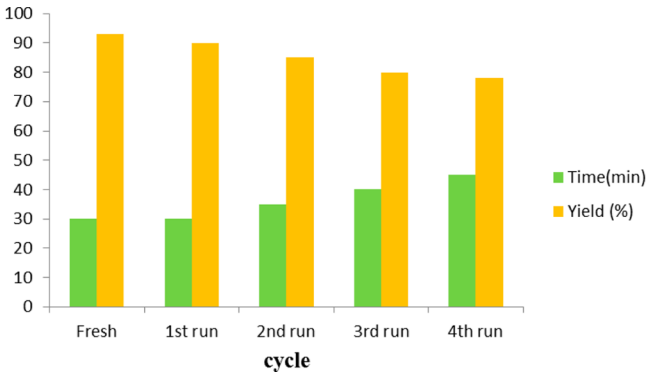




**Figure 1.** Recycling of the [bmim]$HSO_4$ ionic liquid used for the synthesis of compound **5a**.

118.15, 123.04, 126.26, 127.94, 129.46, 131.18, 139.12, 141.53, 146.47, 148.69, 165.79, 194.55; ESI-MS *m/z* 559 (M + 1). Anal. Calcd for $C_{36}H_{34}N_2O_4$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.22; H, 6.14; N, 5.33.

*9-[4-(Dimethylamino)phenyl]-10-[1,3-dioxo-1H-benzo[de]-isoquinolin-2(3H)-yl]-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione* (***5c***). Pale red solid: mp 264–266 °C; IR (KBr) $\nu_{max}$ 2968, 1702, 1678, 1661, 1648 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 0.71 (s, 6H, $CH_3$), 0.87 (s, 6H, $CH_3$), 1.97–2.33 (m, 8H, $CH_2$), 3.19 [s, 6H, -N($CH_3$)$_2$], 5.03 (s, 1H), 7.06 (t, *J* = 8.8 Hz, 2H, ArH), 7.57–7.61 (m, 2H, ArH), 7.99–8.04 (m, 2H, ArH), 8.66–8.75 (m, 4H, ArH); $^{13}C$ NMR (100 MHz, DMSO-$d_6$) $\delta$ 24.08, 26.65, 28.66, 32.21, 44.31, 50.16, 111.11, 118.21, 123.05, 126.23, 127.91, 129.47, 131.15, 139.14, 141.54, 146.43, 148.59, 148.75, 165.81, 195.05; ESI-MS *m/z* 588 (M + 1). Anal. Calcd for $C_{37}H_{37}N_3O_4$: C, 75.65; H, 6.35; N, 7.15. Found: C, 75.96; H, 6.24; N, 7.36.

*10-[1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-3,3,6,6-tetramethyl-9-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione* (***5d***). Yellow solid: mp 271–273 °C; IR (KBr) $\nu_{max}$ 2959, 1701, 1676, 1663, 1647 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 0.98 (s, 6H, $CH_3$), 1.05 (s, 6H, $CH_3$), 1.97–2.33 (m, 8H, $CH_2$), 5.01 (s, 1H), 7.45 (t, *J* = 8.8 Hz, 2H, ArH), 7.92 (t, *J* = 7.2 Hz, 2H, ArH), 8.03–8.07 (m, 3H, ArH), 8.73–8.77 (m, 4H, ArH); $^{13}C$ NMR (100 MHz, DMSO-$d_6$) $\delta$ 24.07, 26.93, 28.61, 32.15, 50.10, 111.97, 118.13, 123.05, 126.28, 127.91, 129.43, 130.99, 139.13, 141.55, 146.46, 148.71, 165.82, 194.63; ESI-MS *m/z* 545 (M + 1). Anal. Calcd for $C_{35}H_{32}N_2O_4$: C, 77.18; H, 5.92; N, 5.14. Found: C, 77.32; H, 5.88; N, 5.31.

*10-[1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-9-(4-hydroxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-(2H,5H)-dione* (***5e***). White solid: mp 257–259 °C; IR (KBr) $\nu_{max}$ 3302, 2964, 1700, 1678, 1661, 1648 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-$d_6$) $\delta$ 0.71 (s, 6H, $CH_3$), 0.87 (s, 6H, $CH_3$), 1.98–2.33 (m, 8H, $CH_2$), 4.03 (s, 1H, -OH), 4.96 (s, 1H), 7.07 (t, *J* = 8.8 Hz, 2H, ArH), 7.57–7.61 (m, 2H, ArH), 7.99–8.04 (m, 2H, ArH), 8.66–8.76 (m, 4H, ArH); $^{13}C$ NMR (100 MHz, DMSO-$d_6$) $\delta$ 24.05, 26.96, 28.68, 32.17, 50.30, 112.95, 118.84, 126.78, 126.98, 127.58, 128.99, 129.16,



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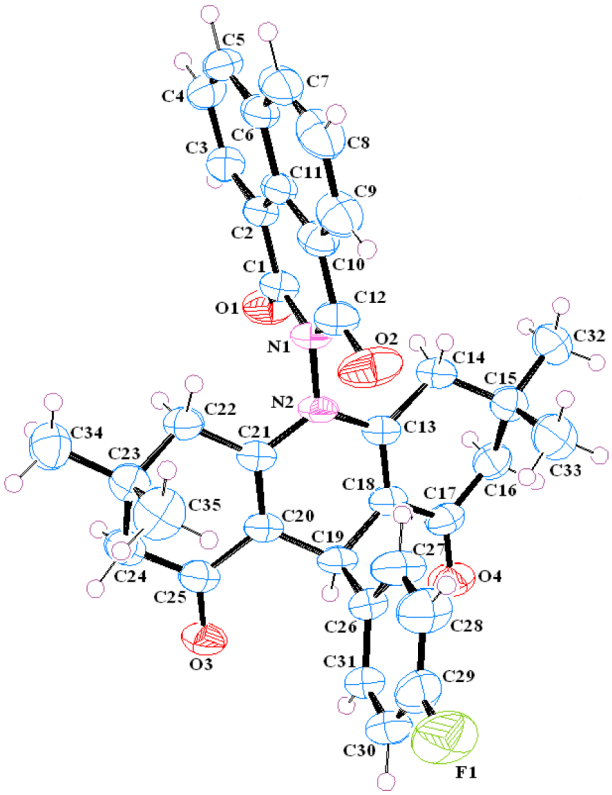


**Figure 2.** ORTEP representation of compound **5a**. The thermal ellipsoids are drawn at the 50% probability level.

**Table 3. Salient Crystallographic Data and Structure Refinement Parameters of Compound 5a**

| | |
|---|---|
| empirical formula | $C_{35}H_{31}FN_2O_4$ |
| formula weight | 562.62 |
| crystal system | monoclinic |
| space group | $P2_1/n$ |
| $T$ (K) | 293(2) |
| $a$ (Å) | 12.4943(12) |
| $b$ (Å) | 17.1761(16) |
| $c$ (Å) | 13.3901(13) |
| $\alpha$ (deg) | 90 |
| $\beta$ (deg) | 99.264(2) |
| $\gamma$ (deg) | 90 |
| $Z$ | 4 |
| $V$ (Å$^3$) | 2836.1(5) |
| $D_{calc}$ (g/cm$^3$) | 1.318 |
| $F(000)$ | 1184 |
| $\mu$ (mm$^{-1}$) | 0.091 |
| $\theta$ (deg) | 2.37−27.7 |
| index ranges | $-16 \le h \le 16$ |
| | $-22 \le k \le 21$ |
| | $-17 \le l \le 17$ |
| total no. of reflections | 32325 |
| no. of independent reflections | 6777 |
| no. of observed reflections | 5278 |
| no. of parameters | 383 |
| $R_1$ $[I > 2\sigma(I)]$ | 0.0508 |
| $wR_2$ (all data) | 0.1408 |
| GOF | 1.046 |
| CCDC | 1415136 |

**Table 4. Geometrical Parameters of Hydrogen Bonds in Compound 5a**

| D−H···A | D···A (Å) | H···A (Å) | D−H···A (deg) | symmetry code |
|---|---|---|---|---|
| C(7)−H(7)···O(1) | 3.138(2) | 2.43 | 122 | $-^1/_2 + x, ^1/_2 - y, -^1/_2 + z$ |
| C(30)−H(30)···F(1) | 3.423(2) | 2.37 | 163 | $1 - x, -y, 1 - z$ |

129.48, 139.79, 140.51, 149.65, 164.10, 194.51; ESI-MS $m/z$ 561 (M + 1). Anal. Calcd for $C_{35}H_{32}N_2O_5$: C, 74.98; H, 5.75; N, 5.00. Found: C, 74.84; H, 5.72; N, 5.29.

*10-[1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-9-(4-methoxyphenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-(2H,5H)-dione* (***5f***). Pale yellow solid: mp 268−270 °C; IR (KBr) $\nu_{max}$ 2963, 1701, 1678, 1660, 1645 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 0.71 (s, 6H, $CH_3$), 0.87 (s, 6H, $CH_3$), 1.98−2.33 (m, 8H, $CH_2$), 3.47 (s, 3H, -$OCH_3$), 4.96 (s, 1H), 7.06 (t, $J$ = 8.8 Hz, 2H, ArH), 7.57−7.61 (m, 2H, ArH), 7.99−8.04 (m, 2H, ArH), 8.66−8.76 (m, 4H, ArH); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 24.05, 26.96, 28.68, 32.17, 50.17, 54.95, 112.08, 117.74, 125.62, 127.18, 128.23, 128.53, 129.25, 129.42, 131.90, 136.06, 148.53, 150.60, 164.99, 194.35; ESI-MS $m/z$ 575 (M + 1). Anal. Calcd for $C_{36}H_{34}N_2O_5$: C, 75.24; H, 5.96; N, 4.87. Found: C, 75.18; H, 5.94; N, 4.62.

*10-[1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-9-(6-methoxynaphthalen-2-yl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione* (***5g***). White solid: mp 284−286 °C; IR (KBr) $\nu_{max}$ 2969, 1704, 1678, 1665, 1642 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 0.98 (s, 6H, $CH_3$), 1.05 (s, 6H, $CH_3$), 2.09−2.25 (m, 8H, $CH_2$), 3.71 (s, 3H, -$OCH_3$), 5.10 (s, 1H), 7.28 (d, $J$ = 8.0 Hz, 1H, ArH), 7.47 (s, 1H, ArH), 7.91−8.03 (m, 4H, ArH), 8.22 (d, $J$ = 8.0 Hz, 1H, ArH), 8.33 (s, 1H, ArH), 8.52−8.67 (m, 4H, ArH); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 25.11, 28.86, 30.37, 34.83, 50.01, 54.91, 109.13, 116.26, 117.77, 119.16, 120.62, 122.45, 122.69, 126.12, 127.59, 128.35, 128.83, 129.45, 139.35, 141.24, 147.54, 148.79, 165.09, 195.76; ESI-MS $m/z$ 625 (M + 1). Anal. Calcd for $C_{40}H_{36}N_2O_5$: C, 76.90; H, 5.81; N, 4.48. Found: C, 76.76; H, 5.76; N, 4.57.

*9-(4-Chlorophenyl)-10-[1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-(2H,5H)-dione* (***5h***). Pale yellow solid: mp 251−253 °C; IR (KBr) $\nu_{max}$ 2967, 1702, 1677, 1661, 1645 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 0.71 (s, 6H, $CH_3$), 0.86 (s, 6H, $CH_3$), 1.97−2.32 (m, 8H, $CH_2$), 5.01 (s, 1H), 7.06 (t, $J$ = 8.8 Hz, 2H, ArH), 7.57−7.60 (m, 2H, ArH), 7.99−8.04 (m, 2H, ArH), 8.67−8.77 (m, 4H, ArH); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 24.09, 26.91, 28.59, 32.19, 50.09, 111.93, 118.17, 123.07, 126.30, 127.96, 129.45, 131.05, 139.15, 141.51, 146.47, 148.78, 165.81, 194.59; ESI-MS $m/z$ 579 (M + 1). Anal. Calcd for $C_{35}H_{31}ClN_2O_4$: C, 72.59; H, 5.40; N, 4.84. Found: C, 72.36; H, 5.48; N, 4.91.

*9-(4-Bromophenyl)-10-[1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-(2H,5H)-dione* (***5i***). Yellow solid: mp 274−276 °C; IR (KBr) $\nu_{max}$ 2968, 1701, 1675, 1660, 1641 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 1.08 (s, 6H, $CH_3$), 1.11 (s, 6H, $CH_3$), 2.09−2.29 (m, 8H, $CH_2$), 5.03 (s, 1H), 7.16 (t, $J$ = 8.8 Hz, 2H, ArH), 7.50−7.55 (m, 2H, ArH), 7.99−8.04 (m, 2H, ArH), 8.65−8.69 (m, 4H, ArH); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 24.11, 26.89, 28.55, 32.18, 50.11, 111.91, 118.16, 123.05, 126.33, 127.94, 129.47, 131.07, 139.14, 141.49, 146.46, 148.78, 165.83, 194.60; ESI-MS $m/z$ 624 (M + 2). Anal. Calcd for $C_{35}H_{31}BrN_2O_4$: C, 67.42; H, 5.01; N, 4.49. Found: C, 67.68; H, 5.15; N, 4.63.

*10-[1,3-Dioxo-1H-benzo[de]isoquinolin-2(3H)-yl]-3,3,6,6-tetramethyl-9-[4-(trifluoromethyl)phenyl]-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione* (***5j***). Pale yellow solid: mp 304−306 °C; IR (KBr) $\nu_{max}$ 2977, 1703, 1677, 1660, 1646 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 0.71 (s, 6H, $CH_3$), 0.87 (s, 6H, $CH_3$), 1.97−2.33 (m, 8H, $CH_2$), 4.95 (s, 1H), 7.07 (t, $J$ = 8.8 Hz, 2H, ArH), 7.57−7.61 (m, 2H, ArH), 7.99−8.04 (m, 2H, ArH), 8.66−8.76 (m, 4H, ArH); $^{13}$C NMR (100 MHz, DMSO-$d_6$) $\delta$ 24.10, 26.89, 28.60, 32.20, 50.08, 111.89, 118.12, 123.10, 126.28, 128.01, 129.42, 131.06, 139.14, 141.55, 146.50, 148.80, 165.79, 194.61; ESI-MS $m/z$ 613 (M + 1). Anal. Calcd for $C_{36}H_{31}F_3N_2O_4$: C, 70.58; H, 5.10; N, 4.57. Found: C, 70.28; H, 5.01; N, 4.81.



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## CONCLUSION

In conclusion, we have demonstrated a very concise, efficient, environmentally benign, atom economical, and facile protocol for the synthesis of a novel naphthalimide-based acridine-1,8-dione derivative in the presence of [bmim]$HSO_4$ via a multicomponent reaction. This new chemistry would provide a simple, compatible, and potentially powerful method for the modular construction of naphthalimide-based acridine-1,8-dione derivatives. The prominent advantages of this method are mild reaction conditions, high atom economy, shorter reaction times, and higher yields. Meanwhile, the reusability of ionic liquid [bmim]$HSO_4$ makes this an environmentally friendly protocol amenable for scale-up.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acssuschemeng.5b00900.

$^1$H NMR, $^{13}$C NMR, and mass spectra of the obtained compounds (PDF)

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### Notes

The authors declare no competing financial interest.

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