Res Chem Intermed
DOI 10.1007/s11164-014-1677-7

Montmorillonite-KSF-catalyzed synthesis of 4-heteroarylidene-*N*-arylhomophthalimides by Knoevenagel condensation

Varadhan Krishnakumar · Fazlur-Rahman Nawaz Khan · Badal Kumar Mandal · Euh-Duck Jeong · Jong Sung Jin

Received: 15 November 2013 / Accepted: 16 April 2014

Abstract A simple, efficient and rapid method for clay-catalyzed Knoevenagel condensation of heterocyclic aldehydes with active methylene compound under reflux condition is reported. This protocol offers high yield, shorter time and simple work procedure. The protocol does not require column chromatography for purification, and the process is environmentally benign.

Keywords Montmorillonite KSF · 4-Heteroarylidene-*N*-arylhomophthalimides · Knoevenagel condensation

Introduction

In recent decades, organic reactions have been performed using the concept of green chemistry [1, 2]. Use of heterogeneous catalysts offers researchers an important

Electronic supplementary material The online version of this article (doi:10.1007/s11164-014-1677-7) contains supplementary material, which is available to authorized users.

V. Krishnakumar · F.-R. N. Khan (✉)
Organic and Medicinal Chemistry Research Laboratory, Organic Chemistry Division, School of Advanced Sciences, VIT-University, Vellore 632 014, Tamil Nadu, India
e-mail: nawaz_f@yahoo.co.in

V. Krishnakumar · B. K. Mandal (✉)
Trace Elements Speciation Research Laboratory, Environmental and Analytical Chemistry Division, School of Advanced Sciences, VIT-University, Vellore 632 014, Tamil Nadu, India
e-mail: mbadal@hotmail.com

F.-R. N. Khan · E.-D. Jeong (✉) · J. S. Jin (✉)
Korea Basic Science Institute, Busan Center, Busan 618 230, South Korea
e-mail: edjeong@kbsi.re.kr

J. S. Jin
e-mail: jsjin@kbsi.re.kr

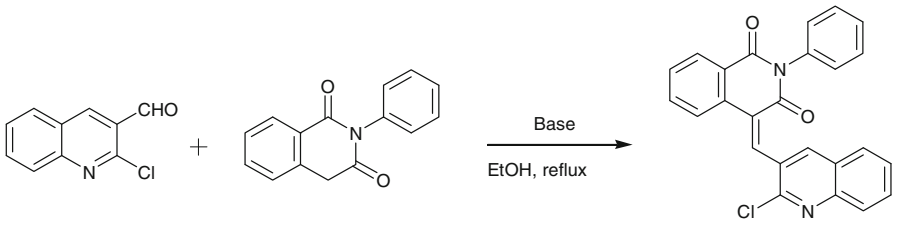
Published online: 05 June 2014

vehicle to achieve target molecules in a greener way [3–6]. Although these reactions can be carried out with traditional catalysts such as Lewis and Brønsted acids, bases and metal salts, such reagents are corrosive and dangerous to the environment, as well as not being recoverable from the reaction mixture. Montmorillonite clay catalysis has provided promising solutions for a wide range of organic transformations [7–9], with such processes proceeding with high selectivity, straightforward reactions, shorter reaction time, and high product yield and purity. These catalysts are also inexpensive, readily available and easily recovered and recycled. Quinolines and isoquinolinones are common moieties in biologically active compounds, having significant pharmaceutical [10], synthetic and material applications [11], including medicinal properties such as anti-microbial [12], anti-inflammatory [13], anti-oxidant [14] and anti-cancer activities [15, 16]; they are also used as dyes and pigments [17], and in sensors and organic light-emitting diodes (OLEDs) [18, 19] and positron emission tomography (PET) scan imaging probes [20]. Isoquinolinone, a structural unit of several naturally occurring alkaloids [21, 22], has attracted the attention of both synthetic and natural product chemists due to diverse biological activities [23, 24]. Isoquinolinones form key intermediates in synthesis of various alkaloids such as indenoisoquinolines [25] and protoberberines [26]. Quinolines are functionalized intermediates in preparation of many pharmaceutically active compounds [27, 28], such as camptothecin [29, 30] and luotonins [31]. Introduction of an additional heterocyclic moiety into the molecule may significantly increase the biological action of these compounds [32]. C–C bond-forming reactions are of great interest in many organic transformations [33–50] involved in total synthesis and synthesis of many natural products and functionalized intermediates [35–37]. Herein, we report a facile synthesis of 4-[(2-chloroquinolin-3-yl)methylene]-*N*-arylhomophthalimide from *N*-arylhomophthalimide in excellent yield. The 2-chloro-3-formylquinolines (**1**) and corresponding *N*-arylhomophthalimides (**2**) required for our study were obtained from our earlier reports [38, 39].

Results and discussion

In the preliminary investigation, the 2-chloro-3-formylquinoline **1a** was treated with *N*-arylhomophthalimide **2a** in the presence of piperidine as base with ethanol (EtOH) as solvent under reflux condition to give the Knoevenagel product **3a** in 55 % yield (Scheme 1).

We further examined different bases and solvents to optimize the reaction conditions for condensation. The observed results are listed in Table 1. In the comparison of other bases, triethylamine (TEA) gave good yield of product (Table 1, entry 6). Generally, the reaction was incomplete in the presence of inorganic bases such as K_2CO_3 and *t*-BuOK. Piperidine and the strong base NaH gave moderate yield of the desired product. The reaction required more time in the absence of catalyst with lower product yield (Table 1, entry 1), and the reaction was generally incomplete even after 12 h.



1a 2a 3a

Scheme 1 Synthesis of 4-[(2-chloroquinolin-3-yl)methylene]-*N*-arylhomophthalimide (**3a**)

Table 1 Optimization of the catalyst

S. no.	Catalyst	Time (h)	Yield (%)[a]
1	None	12	35
2	K_2CO_3	4	45
3	*t*-BuOK	4	56
4	NaH	1	60
5	Piperidine	4	55
6	TEA	2	80
7	Basic alumina	4	68
8	KF/alumina	3	75
9	Mont. KSF	1	92
10	Zeolite	1	80

Reaction carried out with 1 equiv. of **1a** and **2b**. Catalyst loading (entries 2–6, 1 eq.; entries 6–9, 100 mg) in 10 mL EtOH under reflux condition

[a] Isolated yield

Table 2 Effect of solvent

Entry	1	2	3	4	5
Solvent	MeOH	EtOH	$CHCl_3$	CH_2Cl_2	CH_3CN
Yield (%)	55	92	58	52	62

Reaction carried out with 1 mmol **1a** with **2b**, 100 mg of mont. KSF catalyst, under reflux condition

Based on this evidence, we extended the scope of the work to use a reusable heterogeneous catalyst for our reaction. Initially, we tried basic alumina as a catalyst, which gave a moderate yield of 68 %. Furthermore, we investigated various heterogeneous catalysts, and montmorillonite KSF offered the best yield and high purity of the product (92 %) (Table 1, entry 8). In addition, we optimized the effect of solvent on the reaction. EtOH used as solvent for the reaction gave the maximum product yield (Table 2, entry 2). MeOH, $CHCl_3$, CH_2Cl_2 and CH_3CN gave moderate yield (Table 2, entries 1, 3–5).

It is noteworthy that mont. KSF was found to be more efficient and took less time to complete the reaction. Based on the above facts, we selected mont. KSF as an efficient base for our reaction (Table 3). The products **3a**–**n** were isolated from the reaction mass by simple filtration with minimum amount of EtOH washing without need for column chromatography. The additional advantage of this method is the shorter reaction time (50–120 min). The reaction proceeds well in the presence of inexpensive clay with high yield and without the need for special equipment such as microwave [51], ultrasonication [52], microreactor [53] or ball-mill method [54–56].

In the ^{1}H nuclear magnetic resonance (NMR) spectra, the peak at δ 4.24 appeared as a singlet of two protons at C_4-position of **2a**, and δ 10.57 appeared as a singlet of one proton due to the aldehyde group of compound **1a**. Both disappeared and a new peak appeared at δ 8.21 as singlet of alkenic proton for product **3a**. There is no coupling partner for the alkenic proton present in the product **3a**, because the neighbouring carbon does not have a proton, and it appeared as a singlet. The *trans* orientation of the proton resulted in the maximum value at 8.21 ppm in the ^{1}H NMR spectrum. Generally, alkenic protons appear in the 6–7 ppm region. Due to the bulkier nature of the 2-chloro-3-formylquinoline, the δ value of the alkenic proton shifted downfield to 8.21 ppm and was obtained as *E*-isomer, as further supported by the literature report [56]. Condensation of Knoevenagel product was also supported by the ^{13}C NMR spectra, in which the δ 36.98 of C_4-carbon peak disappeared and a new peak appeared for alkenic carbon at δ 139.05. The liquid chromatography–mass spectroscopy (LC–MS) spectra of synthesized compounds **3a** and **3g** showed molecular-ion peaks at *m/e* of 410.00 and 446.60. All these data were found to be in good agreement with the assigned structure.

Importantly, purification of the product and recovery of the catalyst were very easy. After completion of the reaction, the reaction mixture was cooled to room temperature, then the formed precipitate was filtered and washed with small amount of EtOH. The collected material was dissolved in EtOAc, and the catalyst was separated by simple filtration. The filtrate was evaporated under reduced pressure, and the obtained material was pure enough for further analysis. The collected catalyst was dried in a hot-air oven for 1 h, then used for further cycles.

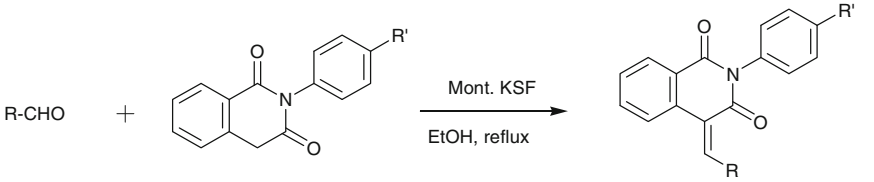
The reusability of the catalyst was checked, resulting in 92, 89 and 88 % in subsequent cycles. These recoveries indicate that no significant loss of catalytic activity was observed.

Experimental

Materials and methods

Melting points were measured with open capillary tubes and were corrected with benzoic acid as reference. The progress of the reaction was monitored by thin-layer chromatography (TLC) plates. Infrared (IR) spectra (KBr, υ cm^{-1}) were recorded on a JASCO FT-IR 4100 spectrometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker 400-MHz spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as internal reference. LC–MS analyses were performed

Table 3 Knoevenagel condensation of *N*-arylhomophthalimide with 2-chloro-3-formylquinoline



1a-h 2a-b 3a-n

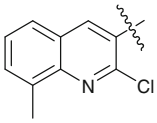
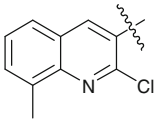
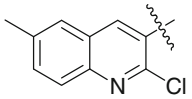
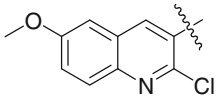
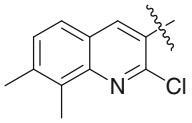
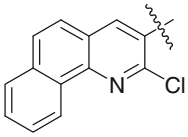
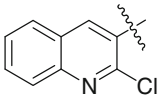
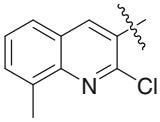
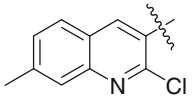
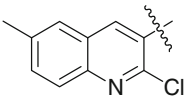
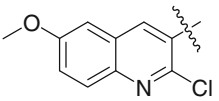
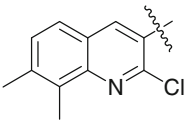
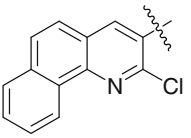
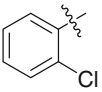
Compound	R		R′	Time (min)	Yield (%)[a]
3a		**1a**	H	60	92
3b		**1b**	H	70	94
3c		**1d**	H	90	89
3d		**1e**	H	45	94
3e		**1f**	H	80	87
3f		**1g**	H	45	90
3g		**1a**	Cl	60	86
3h		**1b**	Cl	100	85
3i		**1c**	Cl	90	83

Table 3 continued

Compound	R		R′	Time (min)	Yield (%)[a]
3j		**1d**	Cl	35	79
3k		**1e**	Cl	50	91
3l		**1f**	Cl	120	85
3m		**1g**	Cl	50	90
3n		**1h**	H	35	82

Reaction carried out with 1 equiv. of **1** and **2**, 100 mg mont. KSF, 10 mL EtOH under reflux condition

[a] Isolated (recrystallized from hot EtOH)

with an Agilent-1100 series ion trap. Chemicals purchased from Sigma-Aldrich (India), Sd-Fine (India) were used without further purification.

*General procedure for synthesis of 2-chloro-3-formylquinolines **1a–g***

To a solution of acetanilide (5 mmol) in dry dimethylformamide (DMF) (20 mmol) at 0–5 °C with stirring, $POCl_3$ (35 mmol) was added dropwise, and the mixture was stirred at 80–90 °C for time ranging between 8 and 16 h. The mixture was poured into crushed ice and stirred for 5 min, and the resulting solid was filtered and washed well with water and dried. The compounds were subjected to silica gel column chromatography.

*General procedure for synthesis of N-arylhomophthalimides **2a, b***

A mixture of homophthalic acid (10 mmol) and anilines (10 mmol) in dry toluene and 5 mol% nano-ZnO were amended to the suspension. The reaction mixture was heated under reflux condition. The progress of the reaction was monitored by thin-layer chromatography. After completion of the reaction, the catalyst was separated by filtration. The solvent was removed under vacuum, then the crude sample was purified by silica gel column chromatography using ethyl acetate and *n*-hexane mixture as eluant.

General procedure for synthesis of (E)-4-((2-chloroquinolin-3-yl)methylene)-2-phenylisoquinoline-1,3(2H,4H)-diones ***3a–n***

A mixture of 2-chloro-3-formylquinoline **1a–g** (1 mmol) was treated with *N*-arylhomophthalimide **2a**, **b** (1 mmol) in ethanol, and 100 mg mont. KSF was added to the suspension. Completion of the reaction was monitored by TLC, after which the reaction mixture was filtered and recrystallized using hot ethanol. The pure compound was analyzed by various spectral and analytical methods.

*4-((2-Chloroquinolin-3-yl)methylene)-2-phenylisoquinoline-1,3(2H,4H)-dione (**3a**)* Yellow solid; m.p. 152–154 °C; IR (KBr) 1,710 (C_3-CO), 1,674 (C_1-CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.31–8.33 (d, $J = 7.2$ Hz, 2H), 8.22 (s, 1H), 8.08–8.11 (d, $J = 8.4$ Hz, 1H), 7.80–7.84 (t, $J = 7.6$ Hz, 1H), 7.72–7.74 (d, $J = 8.0$ Hz, 1H), 7.53–7.57 (m, 2H), 7.45–7.50 (m, 2H), 7.38–7.40 (d, $J = 8.0$ Hz, 1H), 7.26–7.31 (m, 4H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.10 (C_3-CO), 164.04 (C_1-CO), 149.17, 147.76, 138.78, 137.96, 135.21, 133.15, 131.66, 131.50, 129.96, 129.69, 129.42, 128.88, 128.61, 128.48, 128.34, 127.85, 127.82, 126.74, 126.65, 126.17, 30.96, ppm; LC–MS *m/e* calcd. for $C_{25}H_{15}ClN_2O_2$ 410.08, found 410.00.

*4-((2-Chloro-8-methylquinolin-3-yl)methylene)-2-phenylisoquinoline-1,3(2H,4H)-dione (**3b**)* Yellow solid; m.p. 231–233 °C; IR (KBr) 1,707 (C_3-CO), 1,660 (C_1-CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.33–8.36 (d, $J = 6.8$ Hz, 1H), 8.08 (s, 1H), 7.98–8.00 (d, $J = 8.0$ Hz, 1H), 7.77–7.81 (t, $J = 6.0$ Hz, 1H), 7.60–7.65 (m, 2H), 7.55–7.56 (d, $J = 6.8$ Hz, 1H), 7.38–7.48 (m, 4H), 7.19–7.21 (m, 2H), 2.74 (s, 3H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.10 (C_3-CO), 163.57 (C_1-CO), 149.50, 147.77, 147.77, 144.32, 139.53, 137.59, 134.70, 134.64, 134.46, 134.46, 134.38, 133.17, 129.86, 129.40, 129.22, 129.06, 128.37, 128.29, 128.16, 127.87, 125.84, 123.32, 21.06, ppm; LC–MS *m/e* calcd. for $C_{26}H_{17}ClN_2O_2$ 424.09, found 425.00.

*4-((2-Chloro-6-methylquinolin-3-yl)methylene)-2-phenylisoquinoline-1,3(2H,4H)-dione (**3c**)* Pale-yellow solid; m.p. 240–242 °C; IR (KBr) 1,715 (C_3-CO), 1,673 (C_1-CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.31–8.32 (d, $J = 5.2$ Hz, 2H), 8.11 (s, 1H), 7.97–7.99 (d, $J = 8.4$ Hz, 1H), 7.62–7.65 (d, $J = 6.8$ Hz, 1H), 7.46–7.57 (m, 4H), 7.44 (s, 1H), 7.38–7.40 (d, $J = 8.8$ Hz, 1H), 7.28–7.31 (m, 3H), 2.74 (s, 3H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.93 (C_3-CO), 163.87 (C_1-CO), 148.11, 146.43, 139.36, 138.04, 137.23, 134.79, 133.99, 133.64, 133.26, 131.54, 129.94, 129.66, 129.61, 128.63, 128.29, 127.96, 126.81, 126.67, 126.60, 125.95, 21.59, ppm; LC–MS *m/e* calcd. for $C_{26}H_{17}ClN_2O_2$ 424.09, found 425.00.

*4-((2-Chloro-6-methoxyquinolin-3-yl)methylene)-2-phenylisoquinoline-1,3(2H,4H)-dione (**3d**)* Yellow solid; m.p. 234–236 °C; IR (KBr) 1,714 (C_3-CO), 1,672 (C_1-CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.30–8.33 (d, $J = 7.2$ Hz, 2H), 8.08 (s, 1H), 7.97–7.99 (d $J = 9.2$ Hz, 1H), 7.53–7.57 (m, 2H), 7.43–7.50 (m, 3H), 7.37–7.40 (d, $J = 7.2$ Hz, 1H), 7.28–7.33 (m, 3H), 6.96 (d, $J = 2.8$ Hz, 1H), 3.90

(s, 3H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.08 (C_3-CO), 164.03 (C_1-CO), 158.69, 146.38, 143.88, 139.14, 136.49, 135.25, 133.13, 131.61, 129.99, 129.90, 129.59, 129.38, 129.09, 128.84, 128.49, 128.23, 127.85, 126.79, 126.17, 124.36, 105.18, 55.71, ppm; LC–MS *m/e* calcd. for $C_{26}H_{17}ClN_2O_3$ 440.09, found 441.00.

*4-((2-Chloro-7,8-dimethylquinolin-3-yl)methylene)-2-phenylisoquinoline-1,3(2H,4H)-dione (**3e**)* Pale-orange solid; m.p. 194–196 °C; IR (KBr) 1,708 (C_3-CO), 1,668 (C_1-CO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29–8.32 (d, $J = 4.8$ Hz, 2H), 8.12 (s, 1H), 7.52–7.56 (t, $J = 7.2$ Hz, 2H), 7.44–7.49 (m, 3H), 7.38–7.42 (t, $J = 7.6$ Hz, 1H), 7.25–7.30 (m, 4H), 2.75 (s, 3H), 2.53 (s, 3H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.16 (C_3-CO), 164.07 (C_1-CO), 147.97, 146.99, 140.01, 139.47, 138.05, 134.30, 133.01, 131.76, 130.56, 129.83, 129.46, 129.35, 128.78, 128.51, 127.82, 127.29, 126.71, 126.15, 125.04, 124.72, 20.87, 13.34, ppm; LC–MS *m/e* calcd. for $C_{27}H_{19}ClN_2O_2$ 438.11, found 439.00.

*4-((2-Chlorobenzo[h]quinolin-3-yl)methylene)-2-phenylisoquinoline-1,3(2H,4H)-dione (**3f**)* Yellow solid; m.p. >300 °C (charring); IR (KBr) 1,710 (C_3-CO), 1,657 (C_1-CO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16–9.18 (d, $J = 2.4$ Hz, 1H), 8.57 (s, 1H), 8.34–8.36 (d, $J = 6.4$ Hz, 1H), 8.12 (s, 1H), 8.00–8.02 (d, $J = 8.0$ Hz, 1H), 7.87–7.89 (m, 1H), 7.77–7.86 (m, 2H), 7.69–7.72 (m, 2H), 7.60–7.66 (m, 2H), 7.44–7.48 (m, 2H), 7.36–7.40 (m, 1H), 7.20–7.22 (d, $J = 5.2$ Hz, 2H), ppm; LC–MS *m/e* calcd. for $C_{29}H_{17}ClN_2O_2$ 460.09, found 461.00.

*2-(4-Chlorophenyl)-4-((2-chloroquinolin-3-yl)methylene)-isoquinoline-1,3(2H,4H)-dione (**3g**)* Yellow solid; m.p. 258–260 °C; IR (KBr) 1,710 (C_3-CO), 1,666 (C_1-CO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30–8.32 (t, $J = 3.2$ Hz, 2H), 8.21 (s, 1H), 8.09–8.11 (d, $J = 8.4$ Hz, 1H), 7.82–7.84 (t, $J = 5.6$ Hz, 1H), 7.72–7.74 (d, $J = 8.0$ Hz, 1H), 7.60–7.62 (t, $J = 6.0$ Hz, 1H), 7.50–7.53 (m, 2H), 7.45–7.47 (m, 1H), 7.38–7.40 (d, $J = 7.6$ Hz, 1H), 7.30–7.32 (d, $J = 4.4$ Hz, 1H), 7.23–7.25 (m, 2H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.92 (C_3-CO), 163.85 (C_1-CO), 149.07, 147.79, 139.05, 134.81, 133.61, 133.28, 131.69, 131.46, 129.97, 129.93, 129.74, 129.62, 128.78, 128.14, 127.83, 126.76, 126.60, 125.96, ppm; LC–MS *m/e* calcd. for $C_{25}H_{14}Cl_2N_2O_2$ 444.04, found 446.60.

*4-((2-Chloro-8-methylquinolin-3-yl)methylene)-2-(4-chlorophenyl)-isoquinoline-1,3(2H,4H)-dione (**3h**)* Yellow solid; m.p. 240–242 °C; IR (KBr) 1,718 (C_3-CO), 1,676 (C_1-CO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29–8.32 (t, $J = 6.8$ Hz, 2H), 8.15 (s, 1H), 7.64–7.66 (d, $J = 6.8$ Hz, 1H), 7.38–7.56 (m, 7H), 7.29–7.31 (d, $J = 6.0$ Hz, 1H), 7.22–7.25 (m, 2H), 2.81 (s, 3H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.96 (C_3-CO), 163.88 (C_1-CO), 149.94, 147.03, 139.45, 138.14, 136.96, 134.76, 133.68, 133.25, 131.74, 131.58, 129.95, 129.64, 129.60, 128.39, 127.90, 127.54, 126.77, 126.66, 125.92, 125.70, 17.73, ppm; LC–MS *m/e* calcd. for $C_{26}H_{16}Cl_2N_2O_2$ 458.05, found 459.00.

*4-((2-Chloro-6-methylquinolin-3-yl)methylene)-2-(4-chlorophenyl)-isoquinoline-1,3(2H,4H)-dione (**3i**)* Yellow solid; m.p. 270–272 °C; IR (KBr) 1,710 (C_3-CO), 1,668 (C_1-CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.30–8.31 (t, $J = 4.0$ Hz, 2H), 8.10 (s, 1H), 7.97–7.99 (d, $J = 8.4$ Hz, 1H), 7.63–7.65 (d, $J = 6.8$ Hz, 1H), 7.50–7.52 (d, $J = 6.8$ Hz, 2H), 7.44–7.47 (m, 2H), 7.38–7.40 (d, $J = 7.6$ Hz, 1H), 7.27–7.30 (m, 1H), 7.23–7.25 (m, 2H), 2.53 (s, 3H), ppm; LC–MS *m/e* calcd. for $C_{26}H_{16}Cl_2N_2O_2$ 458.05, found 460.80.

*4-((2-Chloro-7-methylquinolin-3-yl)methylene)-2-(4-chlorophenyl)-isoquinoline-1,3(2H,4H)-dione (**3j**)* Yellowish-orange solid; m.p. >300 °C; IR (KBr) 1,699 (C_3-CO), 1,657 (C_1-CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.32–8.35 (d, $J = 6.4$ Hz, 1H), 8.08 (s, 1H), 7.97–7.99 (d, $J = 8.0$ Hz, 1H), 7.77–7.81 (t, $J = 8.4$ Hz, 2H), 7.70–7.72 (d, $J = 8.0$ Hz, 1H), 7.60–7.64 (t, $J = 7.6$ Hz, 1H), 7.41–7.43 (d, $J = 4.8$ Hz, 2H), 7.36–7.38 (d, $J = 8.0$ Hz, 1H), 7.14–7.16 (d, $J = 4.8$ Hz, 2H), 2.55 (s, 3H), ppm; LC–MS *m/e* calcd. for $C_{26}H_{16}Cl_2N_2O_2$ 458.05, found 459.80.

*4-((2-Chloro-6-methoxyquinolin-3-yl)methylene)-2-(4-chlorophenyl)-isoquinoline-1,3(2H,4H)-dione (**3k**)* Yellow solid; m.p. 242–244 °C; IR (KBr) 1,715 (C_3-CO), 1,671 (C_1-CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29–8.32 (d, $J = 4.0$ Hz, 2H), 8.07 (s, 1H), 7.96–7.99 (d $J = 9.2$ Hz, 1H), 7.50–7.52 (m, 2H), 7.43–7.46 (m, 2H), 7.37–7.39 (d, $J = 7.2$ Hz, 1H), 7.29–7.33 (t, $J = 5.6$ Hz, 1H), 7.23–7.25 (m, 2H), 6.95–6.96 (d, $J = 2.8$ Hz, 1H), 3.90 (s, 3H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.93 (C_3-CO), 163.87 (C_1-CO), 158.73, 146.28, 143.91, 139.44, 136.46, 134.81, 133.66, 133.29, 131.58, 130.01, 129.95, 129.67, 129.62, 128.95, 128.05, 127.82, 126.83, 125.95, 124.41, 105.19,55.71, ppm; LC–MS *m/e* calcd. for $C_{26}H_{16}Cl_2N_2O_3$ 474.05, found 475.00.

*4-((2-Chloro-7,8-dimethylquinolin-3-yl)methylene)-2-(4-chlorophenyl)-isoquinoline-1,3(2H,4H)-dione (**3l**)* Greenish-yellow solid; m.p. 198–200 °C; IR (KBr) 1,712 (C_3-CO), 1,674 (C_1-CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29–8.33 (d, $J = 8.4$ Hz, 2H), 8.11 (s, 1H), 7.49–7.52 (d, $J = 8.8$ Hz, 2H), 7.39–7.47 (m, 4H), 7.29 (d, $J = 1.2$ Hz, 1H), 7.22–7.27 (m, 2H), 2.75 (s, 3H), 2.54 (s, 3H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.01 (C_3-CO), 163.91 (C_1-CO), 147.87, 147.01, 140.09, 139.78, 138.03, 134.74, 134.32, 133.71, 133.17, 131.71, 130.59, 129.95, 129.85, 129.58, 129.52, 127.60, 127.15, 126.74, 125.91, 125.00, 124.71, 20.86, 13.33, ppm; LC–MS *m/e* calcd. for $C_{27}H_{18}Cl_2N_2O_2$ 472.07, found 473.00.

*4-((2-Chlorobenzo[h]quinolin-3-yl)methylene)-2-(4-chlorophenyl)-isoquinoline-1,3(2H,4H)-dione (**3m**)* Yellow solid; m.p. >300 °C (charring); IR (KBr) 1,712 (C_3-CO), 1,676 (C_1-CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.16–9.19 (d, $J = 2.8$ Hz, 1H), 8.55 (s, 1H), 8.34–8.36 (d, $J = 6.4$ Hz, 1H), 8.14 (s, 1H), 8.01–8.03 (d, $J = 8.0$ Hz, 1H), 7.87–7.90 (m, 1H), 7.79–7.83 (m, 2H), 7.70–7.73 (m, 2H), 7.61–7.67 (m, 2H), 7.41–7.43 (d, $J = 4.4$ Hz, 2H), 7.14–7.16 (d, $J = 4.4$ Hz, 2H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.02 (C_3-CO), 163.06

(C_1-CO), 149.19, 147.82, 142.27, 140.16, 139.90, 139.09, 138.97, 134.76, 134.43, 134.40, 133.46, 130.00, 129.67, 129.61, 129.55, 128.07, 127.42, 127.07, 126.66, 124.93, 124.90, 124.66, 124.35, 123.33, ppm; LC–MS *m/e* calcd. for $C_{29}H_{16}Cl_2N_2O_2$ 494.05, found 494.80.

*4-(2-Chlorobenzylidene)-2-phenylisoquinoline-1,3(2H,4H)-dione (**3n**)* Greenish-yellow solid; m.p. 190–192 °C; IR (KBr) 1,721 (C_3-CO), 1,674 (C_1-CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51–7.55 (m, 3H), 7.42–7.48 (m, 2H), 7.30–7.39 (m, 4H), 7.27–7.29 (m, 3H), 7.23–7.24 (d, $J = 0.8$ Hz, 2H), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.30 (C_3-CO), 164.17 (C_1-CO), 141.54, 135.41, 134.79, 134.79, 133.75, 132.87, 132.00, 130.57, 130.33, 129.57, 129.37, 129.31, 129.22, 128.71, 128.52, 127.17, 126.98, 125.92, ppm; LC–MS *m/e* calcd. for $C_{22}H_{14}ClNO_2$ 359.07, found 360.00.

Conclusions

An efficient method for montmorillonite-KSF-catalyzed synthesis of 4-[(2-chloroquinolin-3-yl)methylene]-*N*-arylhomophthalimide is reported. The catalyst is reusable and inexpensive and offers easy workup and column-free synthesis in shorter reaction time with high product yield.

Acknowledgments V.K. is grateful to VIT University for their financial assistance as research associateship. We also acknowledge SIF-VIT and STIC-CUSAT, Cochin for providing NMR facilities.

References

1. P.T. Anastas, M.M. Kirchhoff, Acc. Chem. Res. **35**, 686–694 (2002)
2. J.C. Warner, A.S. Cannon, K.M. Dye, Environ. Impact Assess. Rev. **24**, 775–799 (2004)
3. N. Narender, Catal. Sci. Technol. **2**, 471–487 (2012)
4. P. Manivel, K. Prabakaran, F. Nawaz Khan, J. Jin, Res. Chem. Intermed. **38**, 347–357 (2012)
5. A. Khazaei, A.R. Moosavi-Zare, Z. Mohammadi, A. Zare, V. Khakyzadeh, G. Darvishi, RSC Adv. **3**, 1323–1326 (2013)
6. X. Zhou, Y. Lu, L.-L. Zhai, Y. Zhao, Q. Liu, W.-Y. Sun, RSC Adv. **3**, 21691–21696 (2013)
7. P.P. Sarmah, D.K. Dutta, Green Chem. **14**, 1086–1093 (2012)
8. N. Kapuriya, R. Kakadiya, M.M. Savant, A.M. Pansuriya, C.V. Bhuva, A.S. Patel, P.V. Pipaliya, V.B. Audichya, S. Gangadharaiah, S.M. Anandalwar, Indian J. Chem. B **2012**, 51 (1032)
9. G. Nagendrappa, Appl. Clay Sci. **53**, 106–138 (2011)
10. D.B. Khadka, W.-J. Cho, Bioorg. Med. Chem. **19**, 724–734 (2011)
11. A. Danel, E. Gondek, I. Kityk, Opt. Mater. **32**, 267–273 (2009)
12. F. O'Donnell, T.J.P. Smyth, V.N. Ramachandran, W.F. Smyth, Int. J. Antimicrob. Agents **35**, 30–38 (2010)
13. A.A. Bekhit, O.A. El-Sayed, E. Aboulmagd, J.Y. Park, Eur. J. Med. Chem. **39**, 249–255 (2004)
14. C. Praveen, P. DheenKumar, D. Muralidharan, P.T. Perumal, Bioorg. Med. Chem. Lett. **20**, 7292–7296 (2010)
15. A.R. Ellanki, A. Islam, V.S. Rama, R.P. Pulipati, D. Rambabu, G. Rama Krishna, C. Malla Reddy, K. Mukkanti, G.R. Vanaja, A.M. Kalle, K. Shiva Kumar, M. Pal, Bioorg. Med. Chem. Lett. **22**, 3455–3459 (2012)
16. F. O'Donnell, T. Smyth, V. Ramachandran, W. Smyth, Int. J. Antimicrob. Agents **35**, 30–38 (2010)
17. D.G. Krotko, K.V. Fedotov, A.I. Tolmachev, Dyes Pigm. **65**, 183–189 (2005)

18. E. Gondek, A. Danel, J. NizioŁ, P. Armatys, I.V. Kityk, P. Szlachcic, M. Karelus, T. Uchacz, J. Chwast, G. Lakshminarayana, J. Lumin. **130**, 2093–2099 (2010)
19. H. Tsujimoto, S. Yagi, H. Asuka, Y. Inui, S. Ikawa, T. Maeda, H. Nakazumi, Y. Sakurai, J. Organomet. Chem. **695**, 1972–1978 (2010)
20. M. Gao, M. Wang, K.D. Miller, G.D. Hutchins, Q.-H. Zheng, Bioorg. Med. Chem. **18**, 2099–2106 (2010)
21. R.P. Korivi, C.H. Cheng, Chemistry **16**, 282–287 (2010)
22. X. Zhang, W. Ye, S. Zhao, C.T. Che, Phytochemistry **65**, 929–932 (2004)
23. T. Eltze, R. Boer, T. Wagner, S. Weinbrenner, M.C. McDonald, C. Thiemermann, A. Burkle, T. Klein, Mol. Pharmacol. **74**, 1587–1598 (2008)
24. A. Mukherjee, S. Dutta, M. Shanmugavel, D.M. Mondhe, P.R. Sharma, S.K. Singh, A.K. Saxena, U. Sanyal, J. Exp. Clin. Cancer Res. **29**, 175 (2010)
25. G. Ahn, N. Schifano-Faux, J.-F. Goossens, B. Baldeyrou, A. Couture, P. Grandclaudon, A. Lansiaux, A. Ryckebusch, Bioorg. Med. Chem. Lett. **21**, 2259–2263 (2011)
26. P.S. Cutter, R.B. Miller, N.E. Schore, Tetrahedron **58**, 1471–1478 (2002)
27. K. Karthik Kumar, S. Prabu Seenivasan, V. Kumar, T. Mohan Das, Carbohydr. Res. **346**, 2084–2090 (2011)
28. W. Zhong, W. Ma, Y. Liu, Tetrahedron **67**, 3509–3518 (2011)
29. T. Hara, T. Ishii, M. Fujishiro, M. Masuda, T. Ito, J. Nakajima, T. Inoue, T. Matsuse, Cancer Lett. **203**, 199–207 (2004)
30. S. Yu, Q-.Q. Huang, Y. Luo, W. Lu, J. Org. Chem. **77**, 713–717 (2011)
31. T. Harayama, A. Hori, G. Serban, Y. Morikami, T. Matsumoto, H. Abe, Y. Takeuchi, Tetrahedron **60**, 10645–10649 (2004)
32. M. Gund, F.-R.N. Khan, A. Khanna, V. Krishnakumar, Eur. J. Pharm. Sci. **49**, 227–232 (2013)
33. K. Prabakaran, F. Nawaz Khan, J.S. Jin, Tetrahedron Lett. **52**, 2566–2570 (2011)
34. K.S. Kumar, S. Kiran Kumar, B. Yogi Sreenivas, D.R. Gorja, R. Kapavarapu, D. Rambabu, G. Rama Krishna, C.M. Reddy, M.V. Basaveswara Rao, K.V.L. Parsa, M. Pal, Bioorg. Med. Chem. **20**, 2199–2207 (2012)
35. V. Krishnakumar, F.-R. Khan, B. Mandal, S. Mitta, R. Dhasamandha, V. Govindan, Res. Chem. Intermed. **38**, 1819–1826 (2012)
36. M.V. Kirthana, F. Nawaz Khan, P. Sivakumar, M. Doble, P. Manivel, K. Prabakaran, V. Krishnakumar, Med. Chem. Res. **22**, 4810–4817 (2013)
37. S.S. Tajudeen, F.N. Khan, Synth. Commun. **37**, 3649–3656 (2007)
38. V. Krishnakumar, K.M. Kumar, B.K. Mandal, F.R.N. Khan, Res. Chem. Intermed. **27**, 1–12 (2012)
39. R. Subashini, S. Mohana Roopan, F. Nawaz Khan, J. Chil. Chem. Soc. **55**, 317–319 (2010)
40. K. Prabakaran, P. Manivel, F. Nawaz Khan, Tetrahedron Lett. **51**(33), 4340–4343 (2010)
41. S.M. Roopan, F.R.N. Khan, B.K. Mandal, Tetrahedron Lett. **51**(17), 2309–2311 (2009)
42. S.M. Roopan, F.R.N. Khan, Med. Chem. Res. **20**(6), 732–737 (2011)
43. S.M. Roopan, B.R. Reddy, A.S. Kumar, F.N. Khan, Indian J. Heterocycl. Chem. **19**(1), 81–82 (2009)
44. Y. Isogai, F. Nawaz Khan, N. Asao, Tetrahedron **65**(46), 9575–9582 (2009)
45. F.N. Khan, R. Jayakumar, C.N. Pillai, Tetrahedron Lett. **43**(38), 6807–6809 (2002)
46. F.N. Khan, P. Manivel, K. Prabakaran, V.R. Hathwar, S.W. Ng, Acta Cryst. E **66**(2), o488 (2010)
47. S.M. Roopan, F.R.N. Khan, Chem. Pap. **64**(6), 812–817 (2010)
48. F.N. Khan, S. Mohana Roopan, V. Hathwar, S.W. Ng, Acta Cryst. E **66**(1), o201 (2009)
49. R. Subashini, F.N. Khan, S. Mittal, V.R. Hathwar, S.W. Ng, Acta Cryst. **E65**, o2986 (2009)
50. R. Subashini, F.R.N. Khan, Monatsh. Chem. **143**, 485–489 (2012)
51. J.S. Biradar, B.S. Sasidhar, Eur. J. Med. Chem. **46**, 6112–6118 (2011)
52. J.-T. Li, T.-S. Li, L.-J. Li, X. Cheng, Ultrason. Sonochem. **6**, 199–201 (1999)
53. X. Zhang, E.S. Man Lai, R. Martin-Aranda, K.L. Yeung, Appl. Catal. A **261**, 109–118 (2004)
54. G. Kaupp, M. Reza, J. Naimi-Jamal, Tetrahedron **59**, 3753–3760 (2003)
55. S. Mashkouri, M. Reza Naimi-Jamal, Molecules **14**, 474–479 (2009)
56. N. Jegham, N. Tka, Y. Kacem, B.B. Hassine, Synth. Commun. **42**, 3328–3336 (2012)