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ORIGINAL PAPER

An efficient solvent-free synthesis of 3-acetyl-4-arylquinoline-based enaminones and its derivatives using DMFDMA reagent

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Abstract

A series of 3-substituted-4-arylquinoline derivatives were synthesized using 3-acetyl-4-arylquinoline. The acetyl function of 3-acetyl-4-arylquinoline was successfully converted into its corresponding enaminone using DMFDMA as a reagent which in turn successfully converted into pyrazole, isoxazole, pyrimidine, phenyl aminoprop-2-en-1-one, pyridin-2-yl-amino-prop-2-en-1-one, 2-methylpyridine-3-carboxylate by treating with reagents such as hydrazine, hydroxylamine, guanidine hydrochloride, aniline, 2-amino pyridine, ethyl acetoacetate, respectively, under solvent-free microwave irradiation as well as under the conventional thermal heating processes. All the synthesized compounds were found to be obtained in better yields under the microwave irradiation over the conventional process.

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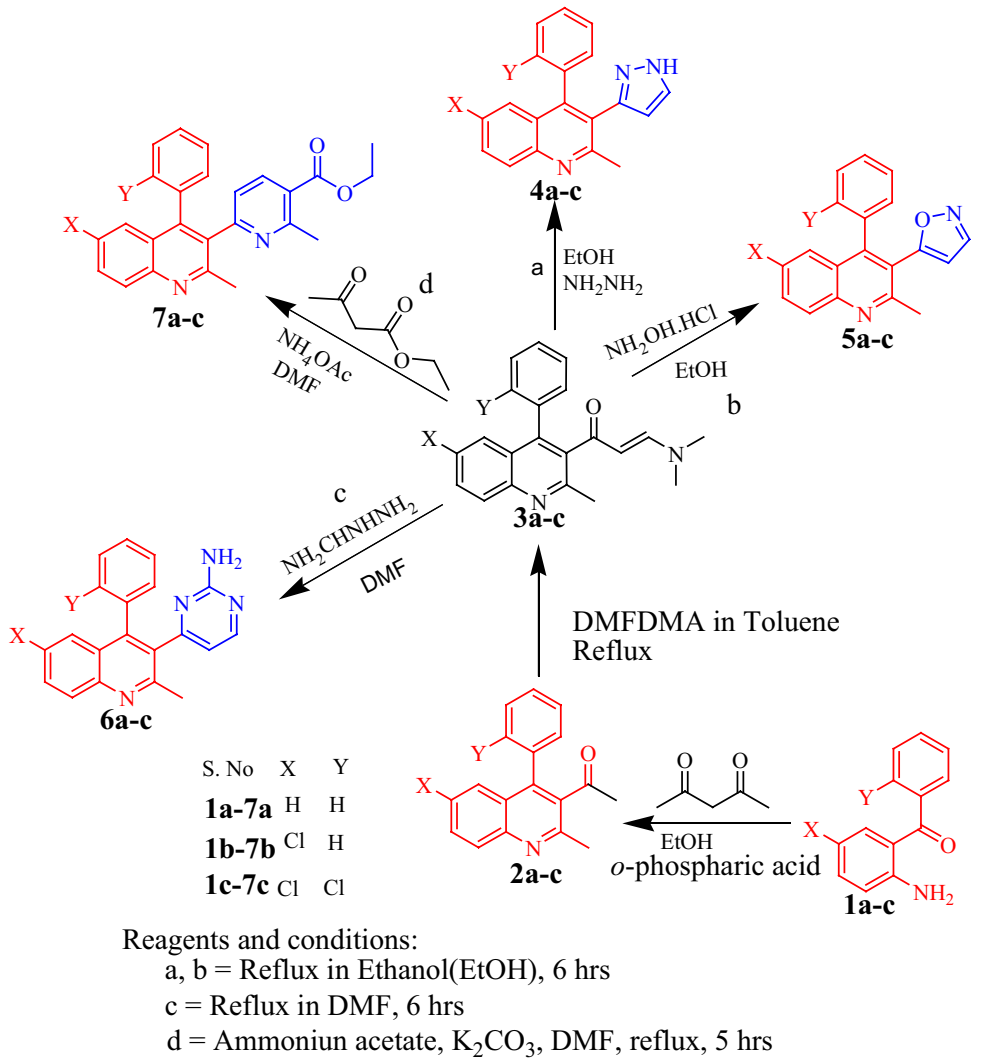
Graphical abstract



Reagents and conditions:
a, b = Reflux in Ethanol(EtOH), 6 hrs
c = Reflux in DMF, 6 hrs
d = Ammoniun acetate, K_2CO_3, DMF, reflux, 5 hrs

Keywords DMFDMA · Enaminones · Microwave irradiation · Solvent-free conditions

Introduction

DMFDMA is one of the important synthetic reagents in organic synthesis due to its higher reactivity (Abu-Shanab et al. 2009). Literature references (Abu-Shanab et al. 2009; Elassar and El-Khair 2003; Mabkhot et al. 2011) emphasized several methods in which formamide acetal had been reported. Enaminones are obtained by treating the compounds with keto functions and DMFDMA have proved to be very useful intermediate (Abu-Shanab et al. 2009; Kumar et al. 2012, Borah et al. 2015; Abu-Shanab et al. 2009, 2003, Y. Liu et al. 2013) as well as useful building blocks in the organic synthesis with enriched structural diversity (Wan et al. 2016a) and displayed numerous applications in synthetic chemistry by the construction of various organic compounds (Wan et al. 2016b , 2015a) especially in the synthesis of wide variety of biologically active heterocycles (Wan et al. 2014, 2015b , Abu-Shanab et al. 2009, 2003), enaminones with electron-deficient amines, exhibiting the extensive applications in organic syntheses (Wan et al. 2016c).

On the other hand, the quinolines are often used to design and synthesize the compounds with various pharmacological properties such as antimicrobial (Rao et al. 2017), antiprotozoal (Fakhfakh et al. 2003), anti-inflammatory (Bekhit et al. 2004) anticancer (Kalita et al. 2015) and anti-tubercular activity (Rao et al. 2017; Vangapandu et al. 2004; Nayyar et al. 2006; Venkatesham et al. 2013). The synthesis of

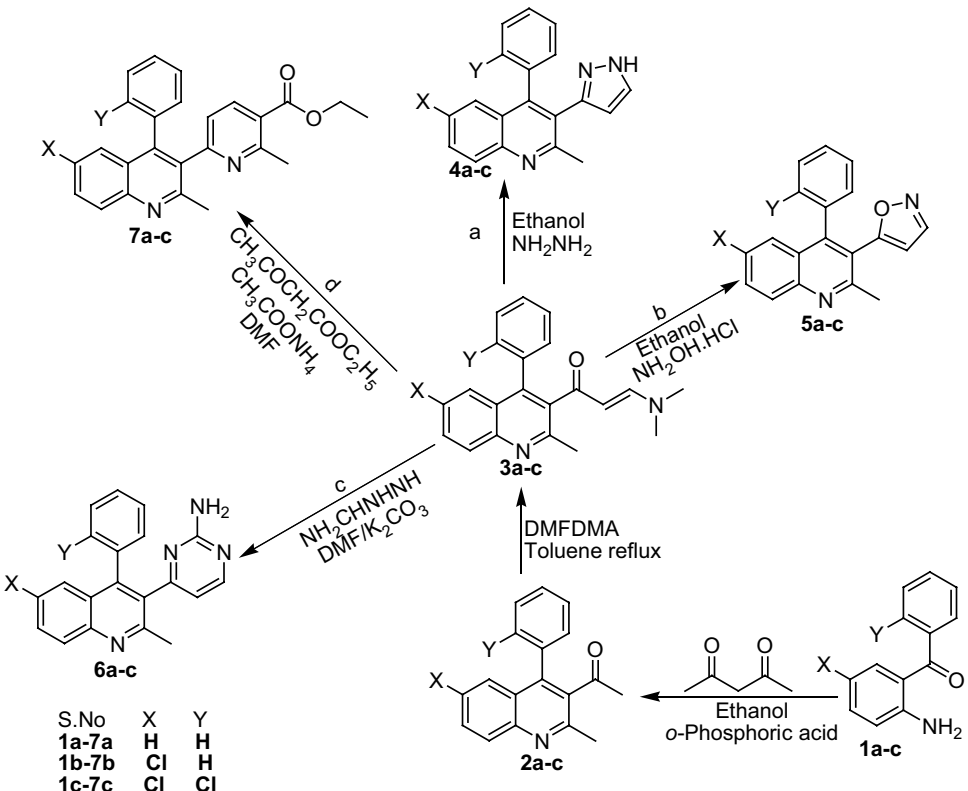
enaminone and its derivatives from simple ketones using DMFDMA are available in the literature (Kumar et al. 2012; Mabkhot et al. 2011; Djung et al. 2011, El-Kateb et al. 2012; Pleier et al. 2001; Rosa et al. 2008; Arioli et al. 2011; Ldehna et al. 2015; Prasanna et al. 2014; Cao et al. 2015).

This prompted us to attempt the present work in which we have used the 3-acetyl-2-methyl-4-arylquinoline to synthesize corresponding enaminone which in turn is used as a synthon to obtain corresponding pyrazole, isoxazole, pyrimidine, phenylamino-prop-2-en-1-one, (pyridin-2-yl-amino) prop-2-en-1-one and 2-methylpyridine-3-carboxylates using hydrazine, hydroxylamine, guanidine hydrochloride, aniline, 2-amino pyridine, ethylacetoacetate, respectively, by adopting conventional procedure in the presence of solvents and also via solvent-free microwave-assisted reactions. In general, improvement in yields and reduction in reaction time were observed when the reactions were carried out under microwave irradiation compared with conventional method.

Results and discussion

Chemistry

In the present work, a series of 3-acetyl-4-arylquinoline-based enaminones were synthesized by the conventional and microwave-assisted synthesis methodology. In the first step, different benzophenone derivatives (**1a–c**) were converted into 3-acetyl-4-aryl quinolines (Sarveswari and Vijayakumar 2012) (**2a–c**) by treating them with acetyl acetone (Scheme 1) in ethanol in the presence of *ortho*-phosphoric acid (catalyst). The obtained products (**2a–c**) were further treated with DMFDMA reagent to form corresponding enaminone compounds (**3a–c**) under the conventional method, in which different solvents such as dimethylformamide, xylene, toluene, acetonitrile and dioxane were examined for the effective conversion of **2a–c** to **3a–c** (Scheme 1). Out of which, in toluene the yield was observed to be better and hence, toluene was considered as a suitable solvent for this reaction (Table 1). The same conversion was also attempted under the microwave irradiation with 240 W power level. These results are compared with the conventional synthetic procedure in Table 2 which revealed that the conversion of **2a–c** to **3a–c** effected efficiently under



Scheme 1 Synthesis of 3-acetyl-4-phenylquinoline derivatives

Table 1 Optimization for the synthesis of 3-acetyl-4-phenylquinoline-based enaminones

S. no.	Solvents	*T* (°C)	Time (h)	Yield (%)
1	DMF	90	14	20
2	DMF	100	12	28
3	DMF	> 110	8	47
4	Xylene	120	6	78
5	Toluene	110	6	85
6	Acetonitrile	90	48	15
7	Dioxane	100	36	10

Table 2 Scope of the synthesis of 3-acetyl-4-phenyl quinolines with DMFDMA

Products	Reactants	Reagent	Conventional method[a] (in toluene)	Microwave method[b] (240 W) (no solvent)
			Yield (%)	Yield (%)
3a	**2a**	DMFDMA	84	89
3b	**2b**	DMFDMA	85	91
3c	**2c**	DMFDMA	86	97

[a]Reaction time: 10 h; [b] reaction time: 8 min

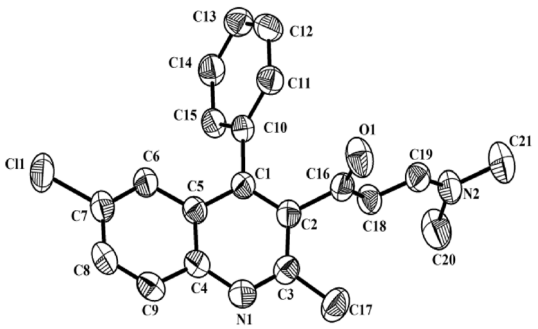


Fig. 1 ORTEP of the compound **3b**

microwave irradiation method with better yield with less reaction duration. All the newly formed enaminones **3a–c** were characterized using ^{1}H-NMR, ^{13}C-NMR, DEPT-135, ^{1}H, ^{1}H-COSY, HSQC, HRMS (ESI) and the detailed data are included in the experimental part.

The compound **3b** was grown as single crystal in ethyl acetate and toluene (1:1) mixture and subjected to single-crystal X-ray diffraction studies and the ORTEP of **3b** is given as Fig. 1 (CCDC no: 1518424). The above enaminones (**3a–c**) afford various 4-phenylquinoline derivatives such as **4a–c**, **5a–c**, **6a–c** and **7a–c** (Scheme 1) when treated with reagents such as hydrazine, hydroxylamine hydrochloride, guanidine hydrochloride, ethylacetoacetate, respectively, whereas the corresponding substituted products such as **8a–c** and **9a–c** (Scheme 2) were found when the enaminones were treated with aniline and 2-amino pyridine. The attempts to convert **8a–c**, **9a–c** into their corresponding pyrazole, isoxazole, pyrimidine, 2-methylpyridine-3-carboxylate failed, whereas the conversion of **3a–c** into **4a–c**, **5a–c**, **6a–c**, **7a–c**, **8a–c** and **9a–c** was successful under the microwave irradiation, which in turn was also compared with conventional method (Table 3). All these newly synthesized compounds were characterized using ^{1}H-NMR, ^{13}C-NMR, ^{1}H, ^{1}H-COSY, HSQC, DEPT-135 and HRMS (ESI) spectral data and included in the experimental section.

Experimental

Materials and methods

Melting points (mp) reported in this work were recorded in Elchem microprocessor-based DT apparatus in open capillary tubes and are uncorrected. ^{1}H NMR and ^{13}C NMR are recorded either in Bruker 400 or 500 MHz NMR spectrometer with TMS as an internal reference. The chemical shift values are reported in parts per million (δ, ppm) from internal standard TMS. High-resolution mass spectra were recorded using Bruker *MaXis* HRMS (ESI-Q-TOF-MS)

Scheme 2 Synthesis of substituted 4-phenylquinoline derivatives

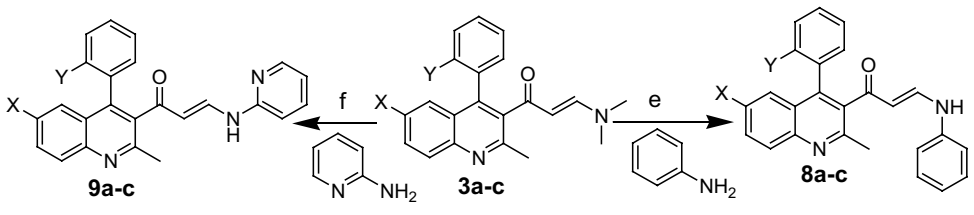
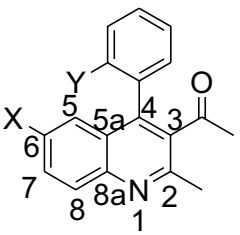


Table 3 Scope of the reaction under conventional and microwave-assisted methods

Products	Conventional method				Microwave-assisted method (240 W)		
	Solvents	Temp (°C)	Time (h)	Yield (%)	Solvent	Time (mins)	Yield (%)
4a	EtOH	80	7	55	No	4	91
4b	EtOH	80	7	54	No	4	92
4c	EtOH	80	7	51	No	4	90
5a	EtOH	80	7	45	No	4	87
5b	EtOH	80	7	48	No	4	88
5c	EtOH	80	7	46	No	4	89
6a	DMF	130	12	29	No	6	88
6b	DMF	130	12	27	No	6	89
6c	DMF	130	12	28	No	6	91
7a	AcOH	118	12	39	No	8	92
7b	AcOH	118	12	37	No	8	93
7c	AcOH	118	12	38	No	8	94
8a	DMF	130	24	28	No	8	89
8b	DMF	130	24	27	No	8	90
8c	DMF	130	24	21	No	8	91
9a	DMF	130	24	29	No	6	80
9b	DMF	130	24	24	No	6	91
9c	DMF	130	24	25	No	6	81

instrument. Microwave oven used is synthetic microwave: CATA R with maximum power of 700 W. All reagents were purchased from Aldrich and used as received. Solvents were removed under vacuum. Organic extracts were dried with anhydrous Na_2SO_4. Silica gel $60F_{254}$ aluminium sheets were used in analytical thin-layer chromatography. Visualization of spots on TLC plates was affected by UV illumination, exposure to iodine vapour and heating the plates dipped in $KMnO_4$ stain. In column chromatography, the silica gel with 230–400 mesh size was used for the purification.

General procedure for the synthesis of compounds (2a–c) 0.1 g (0.5 mmol, 1 eq) of 2-amino benzophenone **1a** was treated with 0.2 mL (0.5 mmol, 1 eq) of acetyl acetone in the presence of 0.04 mL (0.7 mmol, 1.5 eq) of *ortho*-phosphoric acid as catalyst in 5 mL of ethanol and refluxed for 12 h. After the completion of the reaction, the crude was poured into ice-cold water and the formed precipitate was filtered and dried to afford the product **2a**. The obtained product was used without further purification and the procedure was repeated with **1b–c** to get **2b–c**.



1-(2-Methyl-4-phenylquinolin-3-yl)ethanone (**2a**) Yellow solid, yield 90%, m.p.: 112–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.07 (d, J = 8.10 Hz, 1H, H-8), 7.69 (dt, J = 2.30 Hz, 8.10 Hz, 1H, H-7), 7.61 (d, J = 7.40 Hz, 1H, H-6), 7.50 (dd, J = 2.30 Hz, 4.80 Hz, 3H, H-5, 12 & 13), 7.41 (d, J = 7.40 Hz, 1H, H-9), 7.35 (dd, J = 2.30 Hz, 4.80 Hz, 2H, H-10 & 11), 2.70 (s, 3H, CH_3, H-16), 1.99 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 205.30 (C-15), 153.98 (C-2), 145.94 (C-3), 143.14 (C-4), 135.51 (C-17), 134.50 (C-8a), 132.51 (C-8), 131.02 (C-7), 130.55 (C-6), 129.95 (C-5a), 129.25 (C-5), 128.97 (C-9 & 13), 125.90 (C-10 & 12), 124.94 (C-11), 31.85 (C-16), 23.84 (C-14).

1-(6-Chloro-2-methyl-4-phenylquinolin-3-yl)ethanone (**2b**) Yellow solid, yield 93%, m.p.: 152–153 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.01 (d, J = 8.80 Hz, 1H, H-8), 7.65 (dd, J = 2.40 Hz, 8.80 Hz, 1H, H-7), 7.57 (d, J = 2.40 Hz, 1H, H-5), 7.53 (t, J = 3.30 Hz, 3H, H-9, 10 & 11), 7.33 (dd, J = 3.30 Hz, 6.60 Hz, 2H, H-12 & 13), 2.68 (s, 3H, CH_3, H-16), 2.00 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 205.25 (C-15), 153.98 (C-2), 145.94 (C-3), 143.15 (C-4), 135.53 (C-17), 134.51 (C-8a), 132.52 (C-8), 131.01 (C-7), 130.54 (C-6), 129.25 (C-5a), 129.09 (C-5), 128.95 (C-9 & 13), 128.32 (C-10), 125.91 (C-11), 124.94 (C-12), 31.83 (C-16), 23.80 (C-14).

1-(6-Chloro-4-(2-chlorophenyl)-2-methylquinolin-3-yl) ethanone (**2c**). Yellow solid, yield 93%, m.p.: 137–138 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.02 (d, J = 8.80 Hz, 1H, H-8), 7.65 (dd, J = 8.80 Hz, 2.40 Hz, 1H, H-7), 7.58 (d, J = 8.00 Hz, 1H, H-5), 7.49 (dt, J = 8.00 Hz, 1H, H-10),

7.42 (t, J = 7.40 Hz, 1H, H-11), 7.28 (d, J = 2.40 Hz, 1H, H-12), 7.24 (dd, J = 7.40 Hz, 1.40 Hz, 1H, H-13), 2.71 (s, 3H, CH_3, H-16), 2.16 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 204.41 (C-15), 154.08 (C-2), 145.56 (C-3), 135.71 (C-17), 133.40 (C-8a), 133.36 (C-8), 132.84 (C-8), 132.04 (C-7), 131.23 (C-6), 130.88 (C-5a), 130.60 (C-5), 130.07 (C-9), 127.43 (C-10), 125.45 (C-11 & 12), 124.60 (C-13), 31.29 (C-16), 23.80 (C-14).

General procedure for the synthesis of compounds (3a–c)

Conventional method

A mixture of 0.1 g (0.5 mmol, 1 eq) of compound **2a** and 0.1 mL (0.5 mmol, 1 eq) of DMFDMA in toluene (5 mL) was refluxed for 10 h to afford the product **3a**. The reaction mixture was then evaporated under reduced pressure to afford the solid, washed with hexane and then dried. The similar procedure was repeated with **2b–c** to get **3b–c**. The obtained product was used for further analysis without any purification process.

Microwave-assisted synthesis

A mixture of 0.1 g (0.5 mmol, 1 eq) of compound **2a** and 0.1 mL (0.5 mmol, 1 eq) of DMFDMA was mixed together in a tightly closed tube, and then subjected to microwave irradiation (240 W) for 8 min (The completion of the reaction was monitored by TLC). The obtained solid formed was collected and purified by recrystallization using ethanol to afford product **3a**. Similar procedure was repeated with **2b–c** to get **3b–c**.

(E)-3-(Dimethylamino)-1-(2-methyl-4-phenylquinolin-3-yl)prop-2-en-1-one (**3a**) Yellow solid, yield 89%, m.p.: 143–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.00 (d, J = 8.80 Hz, 1H, H-8), 7.61 (dd, J = 2.40 Hz, 8.80 Hz, 1H, H-7), 7.52 (d, J = 2.40 Hz, 2H, H-6&5), 7.44–7.41 (m, 4H, H-9 to 12), 7.36–7.33 (m, 2H, H-13&17), 4.90 (s, 1H, H-16), 2.94 (s, 3H, CH_3, H-19), 2.74 (s, 3H, CH_3, H-18), 2.63 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 192.74 (C-15), 162.53 (C-2), 156.28 (C-8a), 155.80 (C-5a), 154.77 (C-4), 147.22 (C-20), 145.60 (C-3), 130.31 (C-8), 130.18 (C-7), 129.95 (C-6), 129.35 (C-5), 128.61 (C-9), 128.30 (C-13), 128.00 (C-10), 126.46 (C-17), 126.33 (C-11), 125.61 (C-12), 99.13 (C-16), 44.88 (C-19), 37.01 (C-18), 23.82 (C-14). HRMS-ESI (m/z) calcd for $C_{21}H_{20}N_2O$ $[M + H]^+$ = 317.1654, found = 317.1657.

(E)-1-(6-Chloro-2-methyl-4-phenylquinolin-3-yl)-3-(dimethylamino)prop-2-en-1-one (**3b**). Pale yellow solid, yield 91%, m.p.: 191–192 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.03 (d, J = 8.80 Hz, 1H, H-8), 7.60 (dd, J = 1.65 Hz, 8.80 Hz, 1H, H-7), 7.52 (d, J = 1.65 Hz, 1H, H-5), 7.43–7.34 (m, 5H, H-9 to H-13), 7.27 (s, 1H, H-17), 4.90 (s, 1H, H-16), 2.94 (s, 3H, CH_3, H-19), 2.74 (s, 3H, CH_3, H-18), 2.63 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 192.17 (C-15), 166.28 (C-2), 145.63 (C-3), 143.21 (C-4), 135.50 (C-20), 131.82 (C-8a), 130.34 (C-5a), 130.18 (C-8), 129.95 (C-7), 128.30 (C-5), 126.46 (C-6), 125.10 (C-9 to C-13), 100.49 (C-17), 60.38 (C-16), 44.92 (C-19), 37.03 (C-18), 23.83 (C-14). HRMS-ESI (m/z) calcd for $C_{21}H_{19}ClN_2O$ $[M+H]^+$ = 351.1264, found = 351.1264.

(E)-1-(6-Chloro-4-(2-chlorophenyl)-2-methylquinolin-3-yl)-3-(dimethylamino)prop-2-en-1-one (**3c**) Yellow solid, yield 97%, m.p.: 187–188 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.01 (d, J = 8.60 Hz, 1H, H-8), 7.61 (d, J = 8.60 Hz, 1H, H-7), 7.46 (d, J = 6.80 Hz, 1H, H-10), 7.39–7.36 (m, 1H, H-11), 7.27–7.25 (m, 2H, H-5 & 12), 7.17–7.16 (m, 1H, H-13), 6.89 (s, 1H, H-17), 5.08 (d, J = 12.80 Hz, 1H, H-16), 2.91 (s, 3H, CH_3, H-19), 2.75 (s, 3H, CH_3, H-18), 2.69 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 192.45 (C-15), 157.17 (C-2), 156.56 (C-8a), 153.09 (C-5a), 145.29 (C-4), 140.67 (C-20), 134.15 (C-8), 132.49 (C-9), 132.17 (C-17), 131.23 (C-7), 130.48 (C-10), 130.36 (C-11), 130.08 (C-2), 129.22 (C-3), 127.30 (C-6), 125.79 (C-13), 124.72 (C-5), 100.72 (C-16), 44.08 (C-19), 37.04 (C-18), 23.70 (C-14). HRMS-ESI (m/z) calcd for $C_{21}H_{18}Cl_2N_2O$ $[M+H]^+$ = 385.0874, found = 385.0875.

General procedure for the synthesis of compounds (4a–c)

Conventional method

A mixture of 0.1 g (0.3 mmol, 1 eq) of compound **3a**, 0.05 mL (0.3 mmol, 1 eq) of hydrazine hydrate and acetic acid (1–2 drops) as catalyst in ethanol (10 mL) was refluxed at 80 °C for 7 h. The mixture was then extracted with ethyl acetate, dried over sodium sulphate and concentrated under reduced pressure to afford the crude product **4a**. The obtained crude product was purified by column chromatography using ethyl acetate/hexane (4:6) eluent. To check the reproducibility of the reaction and to get **4b–c**, the procedure was repeated with **3b–c**.

Microwave-assisted synthesis

A mixture of 0.1 g (0.3 mmol, 1 eq) of compound **3a** and 0.05 mL (0.3 mmol, 1 eq) of hydrazine hydrate was mixed together in a tightly closed tube, and subjected to microwave irradiation for about 4 min (the completion of the reaction was monitored by TLC). The obtained crude product was purified by column chromatography using ethyl acetate/hexane (4:6) eluent. To check the reproducibility of the reaction and to get **4b–c**, the procedure was repeated with **3b–c**.

2-Methyl-4-phenyl-3-(1H-pyrazol-3-yl)quinolone (**4a**). Light yellow solid, yield 91%, m.p.: 214–216 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.00 (d, J = 10.20 Hz, 1H, H-8), 7.61 (dd, J = 2.00 Hz, 10.20 Hz, 1H, H-7), 7.44 (dd, J = 2.00 Hz, 10.20 Hz, 2H, H-6 & 5), 7.32 (t, J = 2.60 Hz, 4H, H-9 to 12), 7.13 (dd, J = 2.60 Hz, 6.00 Hz, 2H, H-13 & 17), 6.01 (d, J = 2.00 Hz, 1H, H-15), 2.95 (s, 3H, CH_3, H-14), 1.25 (s, 1H, –NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 158.82 (C-2), 147.69 (C-8a), 145.78 (C-5a), 135.93 (C-4), 131.84 (C-3), 130.54 (C-8), 130.51 (C-16), 130.34 (C-20), 129.63 (C-7), 128.07 (C-17), 127.94 (C-10, 11 & 12), 126.75 (C-6 & 5), 125.36 (C-10 & C-13), 107.33 (C-15), 24.91 (C-14). HRMS-ESI (*m/z*) calcd for $C_{19}H_{15}N_3$ $[M+H]^+$ = 286.0944, found = 286.0915.

6-Chloro-2-methyl-4-phenyl-3-(1H-pyrazol-3-yl)quinolone (**4b**) Yellow solid, yield 92%, m.p.: 217–218 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.02 (d, J = 8.90 Hz, 1H, H-8), 7.62 (dd, J = 2.30 Hz, 8.90 Hz, 1H, H-7), 7.46 (d, J = 2.30 Hz, 1H, H-9), 7.43 (s, 1H, H-5), 7.33 (t, J = 2.90 Hz, 3H, H-10 to 12), 7.14 (dd, J = 2.90 Hz, 6.20 Hz, 2H, H-13 & 16), 6.02 (s, 1H, H-15), 2.61 (s, 3H, CH_3, H-14), 1.25 (s, 1H, –NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 158.86 (C-2), 147.68 (C-8a), 145.82 (C-5a), 135.96 (C-4), 135.80 (C-3), 131.85 (C-20) 131.84 (C-17), 130.53 (C-8), 130.30 (C-16), 129.66 (C-7), 128.11 (C-9 & 13), 127.97 (C-10, 11 & 12), 126.80 (C-6), 126.79 (C-5), 125.38 (C-15), 24.96 (C-14). HRMS- ESI (*m/z*) calcd for $C_{19}H_{14}ClN_3$ $[M+H]^+$ = 320.0955, found = 320.0951.

6-Chloro-4-(2-chlorophenyl)-2-methyl-3-(1H-pyrazol-3-yl)quinolone (**4c**). Yellow solid, yield 90%, m.p.: 219–220 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ ppm 8.08 (d, J = 9.00 Hz, 1H, H-8), 7.66 (dd, J = 1.25 Hz, 9.00 Hz, 1H, H-7), 7.46 (d, J = 6.85 Hz, 2H, H-5 & 13), 7.32 (t, J = 6.85 Hz, 1H, H-10), 7.24 (t, J = 1.25 Hz, 2H, H-11& 12), 7.09 (d, J = 9.00 Hz, 1H, H-16), 6.15 (s, 1H, H-15), 2.66 (s, 3H, CH_3, H-14), 1.27 (s, 1H, –NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 159.00 (C-2), 145.47 (C-8a), 145.27 (C-5a), 135.14 (C-4), 133.32 (C-17), 132.32 (C-9), 132.20 (C-3), 131.22 (C-16), 130.80 (C-3), 130.35 (C-8), 129.74 (C-7), 129.42 (C-6), 126.64 (C-5), 126.31 (C-10 & 11), 124.74 (C-12 & 13), 106.64 (C-15), 24.72 (C-14). HRMS-ESI (m/z) calcd for $C_{19}H_{13}Cl_2N_3$ $[M+H]^+$ = 354.0565, found = 354.0554.

General procedure for the synthesis of compounds (5a–c)

Conventional method

A mixture of 0.1 g (0.3 mmol, 1 eq) of compound **3a** in ethanol (10 mL) and 0.02 g (0.3 mmol, 1 eq) of hydroxyl amine hydrochloride was refluxed at 80 °C for 7 h. After the completion of the reaction, the reaction mixture was poured into ice water; the obtained crude was filtered and dried to afford the product **5a**. The obtained product was purified by column chromatography using ethyl acetate/hexane (4:6) eluent. Similar procedure was adopted with **3b–c** to get **5b–c**.

Microwave-assisted synthesis

A mixture of 0.1 g (0.3 mmol, 1 eq) of compound **3a** and 0.02 g (0.3 mmol, 1 eq) of hydroxylamine hydrochloride was mixed together in a tightly closed tube, and subjected to microwave irradiation (240 W) for 4 min (the completion of the reaction was monitored by TLC). The obtained product was purified by column chromatography using ethyl acetate/hexane (4:6) eluent. Similar procedure was adopted with **3b–c** to get **5b–c**.

3-(Isoxazol-3-yl)-2-methyl-4-phenylquinoline (**5a**) Yellow solid, yield 87%, m.p.: 159–161 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.05 (d, J = 9.00 Hz, 1H, H-16), 7.69 (dd, J = 2.25 Hz, 9.00 Hz, 1H, H-8), 7.51 (d, J = 2.25 Hz, 1H, H-7), 7.40 (dd, J = 2.10 Hz, 5.60 Hz, 1H, H-6), 7.26-7.18 (m, 3H, H-5, 9 & 10), 7.17 (dd, J = 2.10 Hz, 5.60 Hz, 3H, H-11 to 13), 5.85 (d, J = 2.10 Hz, 1H, H-15), 2.64 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 158.86 (C-2), 147.68 (C-8a), 145.82 (C-5a), 135.96 (C-4), 135.80 (C-3), 131.85 (C-20) 131.84 (C-17), 130.53 (C-8), 130.30 (C-16), 129.66 (C-7), 128.11 (C-9 & 13), 127.97 (C-10, 11 & 12), 126.80 (C-6), 126.79 (C-5), 125.38 (C-15), 24.96 (C-14). HRMS- ESI (*m/z*) calcd for $C_{19}H_{14}N_2O$ $[M+H]^+$ = 287.1184, found = 287.1185.

6-Chloro-3-(isoxazol-3-yl)-2-methyl-4-phenylquinoline (**5b**) Yellow solid, yield 88%, m.p: 156–157 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.11 (d, J = 1.20 Hz, 1H, H-16), 8.05 (d, J = 9.10 Hz, 1H, H-8), 7.69 (dd, J = 2.10 Hz, 9.10 Hz, 1H, H-7), 7.51 (d, J = 2.10 Hz, 1H, H-10), 7.40 (t, J = 2.60 Hz, 3H, H-10 to 12), 7.17 (d, J = 2.60 Hz, 2H, H 13 & 16), 5.45 (d, J = 1.20 Hz, 1H, H-15), 2.64 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 166.93 (C-17), 157.72 (C-2), 149.99 (C-16), 148.85 (C-8a), 146.56 (C-4), 135.10 (C-20), 132.45 (C-3), 131.83 (C-8), 130.67 (C-7), 129.34 (C-10, 11 & 12), 128.64 (C-9 & 15), 126.27 (C-6), 125.62 (C-5), 121.55 (C-5a), 104.82 (C-15), 24.55 (C-14). HRMS- ESI (*m/z*) calcd for $C_{19}H_{13}ClN_2O$ $[M+H]^+$ = 321.0795, found = 321.0789.

6-Chloro-4-(2-chlorophenyl)-3-(isoxazol-3-yl)-2-methylquinoline (**5c**) Pale yellow solid, yield 89%, m.p.: 151–152 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.11 (d, J = 9.10 Hz, 1H, H-16), 8.05 (d, J = 9.10 Hz, 1H, H-8), 7.69 dd (J = 2.20 Hz, 9.10 Hz, 1H, H-7), 7.51 (d, J = 2.20 Hz, 1H, H-10), 7.40 (t, J = 2.00 Hz, 2H, H-11 & 12), 7.17 (d, J = 2.20 Hz, 2H, H-13 & 15), 5.85 (d, J = 2.20 Hz, 1H, H-15), 2.67 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 166.33 (C-17), 157.80 (C-2), 150.02 (C-16), 146.42 (C-4), 145.98 (C-20), 134.23 (C-3),

133.27 (C-8a), 132.82 (C-5a), 131.75 (C-8), 130.87 (C-7), 130.70 (C-9), 130.35 (C-10), 129.63 (C-6), 127.01 (C-11), 125.83 (C-12), 125.02 (C-13), 121.98 (C-5), 104.36 (C-15), 29.69 (C-14). HRMS-ESI (*m/z*) calcd for $C_{19}H_{12}Cl_2N_2O$ $[M+H]^+$ = 355.0405, found = 355.0399.

General procedure for the synthesis of compounds (6a–c)

Conventional method

A mixture of 0.1 g (0.3 mmol, 1 eq) of compound **3a**, 0.04 g (0.6 mmol, 2 eq) of guanidine hydrochloride and 0.12 g (0.9 mmol, 3 eq) of potassium carbonate in DMF (5 mL) was refluxed at 130 °C for 12 h. After completion of the reaction, reaction mixture was cooled to room temperature, poured onto ice-cold water and the formed precipitate was filtered and dried with sodium sulphate to afford the product **6a**. The obtained crude product was purified by column chromatography using ethyl acetate/hexane (4:6) eluent. To check the reproducibility the compounds **6b–c** were derived from **3b–c** by adopting similar procedure.

Microwave-assisted synthesis

A mixture of 0.1 g (0.3 mmol, 1 eq) of compound **3a**, guanidine hydrochloride (0.6 mmol, 2 eq) and 0.12 g (0.9 mmol, 3 eq) of potassium carbonate in a tightly closed tube was subjected to microwave irradiation for about 6 min (the completion of the reaction was monitored by TLC). The obtained crude product was purified by column chromatography using ethyl acetate/hexane (4:6) eluent. To check the reproducibility the compounds **6b–c** were derived from **3b–c** by adopting similar procedure.

4-(2-Methyl-4-phenylquinolin-3-yl)pyrimidin-2-amine (**6a**). Colourless solid, yield 88%, m.p.: 251–252 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.08 (d, J = 5.20 Hz, 2H, H-16), 7.71 (t, J = 7.30 Hz, 1H, H-8), 7.54 (d, J = 7.30 Hz, 1H, H-7), 7.42 (d, J = 7.30 Hz, 1H, H-6), 7.32 (t, J = 4.00 Hz, 3H, H-10 to 12), 7.19 (t, J = 4.00 Hz, 2H, H-9 & 5), 6.29 (d, J = 5.20 Hz, 1H, H-15), 5.11 (s, 2H, –NH), 2.62 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 167.11 (C-2), 158.21 (C-18), 156.12 (C-17), 147.28 (C-8a), 146.46 (C-19), 135.80 (C-16), 131.01 (C-3), 130.70 (C-8), 130.46 (C-7), 129.95 (C-6), 129.84 (C-5), 129.80 (C-9), 128.77 (C-10), 128.24 (C-11), 127.92 (C-12), 126.57 (C-13), 125.77 (C-4), 125.34 (C-5a), 113.11 (C-15), 24.64 (C-14). HRMS-ESI (*m/z*) calcd for $C_{20}H_{16}N_4O$ $[M+H]^+$ = 313.1453, found = 313.1454.

4-(6-Chloro-2-methyl-4-phenylquinolin-3-yl)pyrimidin-2-amine (**6b**) Colourless solid, yield 89%, m.p.: 246–247 °C: ^{1}H NMR (500 MHz, $CDCl_3$): δ ppm 8.09 (d, J = 4.00 Hz, 1H, H-16), 8.04 (d, J = 7.20 Hz, 1H, H-8), 7.64 (dd, J = 2.00 Hz, 7.20 Hz, 1H, H-7), 7.49 (d, J = 1.80 Hz, 1H, H-9), 7.34 (dd, J = 1.80 Hz, 3.80 Hz, 3H, H-10 to 12), 7.17 (dd, J = 2.00 Hz, 3.80 Hz, 2H, H-5 & 13), 6.27 (d, J = 4.00 Hz, 1H, H-15), 5.10 (s, 2H, –NH), 2.60 (s, 3H, CH_3, H-14); ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 166.68 (C-2), 162.55 (C-18), 158.17 (C-16), 156.60 (C-17), 145.94 (C-19), 145.73 (C-8a), 135.12 (C-14), 132.08 (C-8), 131.80 (C-3), 130.69 (C-7), 130.44 (C-9, 10 & 11), 129.84 (C-12), 128.21 (C-13 & 5), 126.60 (C-6), 125.32 (C-5a), 113.12 (C-15), 24.52 (C-14). HRMS-ESI (*m/z*) calcd for $C_{20}H_{15}ClN_4$ [M+] = 346.0985, found = 346.0983.

4-(6-Chloro-4-(2-chlorophenyl)-2-methylquinolin-3-yl) pyrimidin-2-amine (**6c**) Dark brown solid, yield 91%, m.p.: 221–223 °C; ^{1}HNMR (400 MHz, $CDCl_3$): δ ppm 8.12 (d, J = 5.00 Hz, 1H, H-16), 8.05 (d, J = 9.10 Hz, 1H, H-8), 7.65 (dd, J = 2.00 Hz, 9.10 Hz, 1H, H-7), 7.43 (dd, J = 1.20 Hz, 7.90 Hz, 1H, H-10), 7.31 (dt, J = 1.20 Hz, 7.90 Hz, 1H, H-11), 7.23 (dd, J = 2.00 Hz, 9.10 Hz, 2H, H-5 & 12), 7.10 (dd, J = 1.20 Hz, 7.90 Hz, 1H, H-13), 6.47 (d, J = 5.00 Hz, 1H, H-15), 5.22 (s, 2H, –NH), 2.63 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 166.64 (C-18), 162.57 (C-2), 158.13 (C-16), 156.59 (C-17), 144.78 (C-8a), 144.78 (C-19), 135.07 (C-4), 132.01 (C-8), 131.78 (C-3), 130.72 (C-7), 130.39 (C-10, 11 & 12), 129.30 (C-5 & 13), 128.22 (C-6), 129.32 (C-5a), 125.30 (C-9), 111.85 (C-15), 24.49 (C-14). HRMS-ESI (m/z) calcd for $C_{20}H_{14}Cl_2N_4$ $[M+H]^+$ = 381.0674, found = 381.0675.

General procedure for the synthesis of compounds (7a–c)

Conventional method

A mixture of 0.1 g (0.3 mmol, 1 eq) of compound **3a** in acetic acid (5 mL), 0.08 mL (0.6 mmol, 2 eq) of ethyl acetoacetate and 0.04 g (0.6 mmol, 2 eq) of ammonium acetate was added. The reaction mixture was heated under reflux for 12 h. After the completion of the reaction, mixture was cooled, poured onto ice water, the residue obtained was filtered and washed with pet ether to afford the product **7a**. The obtained product was further purified by column chromatography using ethyl acetate/hexane (4:6) eluent. To check the reproducibility the same reaction procedure was adopted with **3b–c** which afforded **7b–c**.

Microwave-assisted synthesis

To a solution of 0.1 g (0.3 mmol, 1 eq) of compound **3a** and acetic acid (5 mL) taken in a tightly closed tube, a mixture of 0.08 mL (0.6 mmol, 2 eq) of ethylacetoacetate and 0.04 g (0.6 mmol, 2 eq) of ammonium acetate was added and then subjected to microwave irradiation (240 W) for 8 min (the completion of the reaction was monitored by TLC). The

obtained product was further purified by column chromatography using ethyl acetate/hexane (4:6) eluent. To check the reproducibility the same reaction procedure was adopted with **3b–c** which afforded **7b–c**.

Ethyl-2-methyl-6-(2-methyl-4-phenylquinolin-3-yl) pyridine-3-carboxylate (**7a**) Colourless solid, yield 92%, m.p.: 140–141 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.01 (d, J = 8.80 Hz, 1H, H-8), 7.65 (d, J = 8.80 Hz, 1H, H-7), 7.57 (s, 2H, H-15 & 16), 7.54–7.53 (m, 4H, H-9, 10, 12 & 13), 7.35–7.33 (m, 3H, H-5, 6 & 11), 4.39 (q, J = 7.20 Hz, 2H, CH_2, H-21), 2.68 (s, 3H, CH_3, H-14), 2.00 (s, 3H, CH_3, H-23), 1.41 (t, J = 7.20 Hz, 3H, CH_3, H-22); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 205.33 (C-20), 165.99 (C-2), 162.24 (C-18), 153.98 (C-17), 145.93 (C-19), 143.14 (C-8a), 140.93 (C-16), 135.51 (C-4), 134.59 (C-24), 132.50 (C-3), 131.03 (C-8), 130.54 (C-7, 9 & 13), 129.96 (C-5), 129.25 (C-15), 128.96 (C-6), 125.89 (C-5a), 124.96 (C-10, 11 & 12), 61.43 (C-21), 31.85 (C-23), 24.98, (C-14), 14.29 (C-22). HRMS- ESI (m/z) calcd for $C_{25}H_{22}N_2O_2$ $[M+H]^+$ = 383.1760, found = 383.1733.

Ethyl-6-(6-chloro-2-methyl-4-phenylquinolin-3-yl)-2-methylpyridine-3-carboxylate (**7b**) Yellow solid, yield 93%, m.p.: 149–151 °C: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.02 (d, J = 8.60 Hz, 1H, H-8), 7.65 (dd, J = 2.20 Hz, 8.60 Hz, 2H, H-7 & 13), 7.58 (d, J = 8.60 Hz, 1H, H-9), 7.49 (dt, J = 1.80 Hz, 7.40 Hz, 2H, H-10 & 11), 7.42 (dt, J = 1.80 Hz, 7.40 Hz, 2H, H-12 & 15), 7.23 (dd, J = 1.80 Hz, 7.40 Hz, 2H, C-16 & 15), 4.39 (q, J = 7.00 Hz, 2H, CH_2, H-21), 2.70 (s, 3H, CH_3, H-14), 2.15 (s, 3H, CH_3, H-23), 1.41 (t, J = 7.00 Hz, 3H, CH_3, H-22); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 205.25 (C-20), 153.98 (C-2), 145.95 (C-18), 143.13 (C-17), 140.90 (C-19), 135.53 (C-8a), 132.51 (C-16), 132.50 (C-3), 131.01 (C-4), 130.56 (C-24), 129.95 (C-8), 129.24 (C-7), 128.95 (C-6), 128.14 (C-5, 9 & 13), 125.91 (C-10, 11, 12 & 16), 124.94 (C-15), 61.41 (C-21), 31.83 (C-23), 29.70 (C-14), 23.83 (C-22). HRMS- ESI (m/z) calcd for $C_{25}H_{21}ClN_2O_2$ $[M+H]^+$ = 417.1370, found = 417.1365.

Ethyl-6-(6-chloro-4-(2-chlorophenyl)-2-methylquinolin-3-yl)-2-methylpyridine-3-carboxylate (**7c**) Light yellow solid, yield 94%, m.p.: 143-145 °C: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 8.02 (d, J = 8.90 Hz, 1H, H-8), 7.65 (dd, J = 1.30 Hz, 8.90 Hz, 2H, H-7 & 13), 7.58 (d, J = 7.90 Hz, 1H, H-10), 7.49 (dt, J = 1.00 Hz, 7.90 Hz, 1H, H-11), 7.42 (dt, J = 1.00 Hz, 7.90 Hz, 2H, H-12 & 13), 7.23 (dd, J = 1.30 Hz, 8.90 Hz, 2H, H-16 & 15), 4.40 (q, J = 6.80 Hz, 2H, CH_2, H-21), 2.70 (s, 3H, CH_3, H-14), 2.15 (s, 3H, CH_3, H-23), 1.42 (t, J = 7.20 Hz, 3H, CH_3, H-22); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 204.48 (C-20), 166.39 (C-2), 162.24 (C-18), 154.08 (C-17), 145.65 (C-19), 143.37 (C-8a), 140.94 (C-16), 138.59 (C-24), 135.69 (C-4), 132.80 (C-3), 131.67 (C-8), 131.20 (C-3), 130.88 (C-7), 130.72 (C-9), 130.64 (C-13), 129.84 (C-5), 128.12 (C-15), 127.43 (C-5a), 126.99 (C-10), 126.24 (C-11 & 12), 121.63 (C-16), 61.38 (C-21), 31.31 (C-23), 24.98 (C-14), 14.14 (C-22). HRMS-ESI (m/z) calcd for $C_{25}H_{20}Cl_2N_2O_2$ $[M+H]^+$ = 451.0980, found = 451.0956.

General procedure for the synthesis of compounds (8a–c)

Conventional method

A mixture of 0.1 g (0.3 mmol, 1 eq) of compound **3a** and 0.03 mL (0.3 mmol, 1 eq) of aniline in DMF (5 mL) was refluxed at 130 °C for 24 h. The reaction progress was monitored by TLC. After the completion of the reaction the solvent was removed under reduced pressure to afford the product **8a**. The obtained product was purified by column chromatography with pet ether–ethyl acetate (4:1 v/v) as an eluent. By adopting the same procedure with **3b–c** the compounds **8b–c** were obtained.

Microwave-assisted synthesis

A mixture of 0.1 g (0.3 mmol, 1 eq) of compound **3a** and 0.03 mL (0.3 mmol, 1 eq) of aniline was taken in a tightly closed tube, and subjected to microwave irradiation for 8 min (the completion of the reaction was monitored by TLC). The obtained product was purified by column chromatography with pet ether–ethyl acetate (4:1 v/v) as an eluent. By adopting the same procedure with **3b–c** the compounds **8b–c** were obtained.

(E)-1-(2-Methyl-4-phenylquinolin-3-yl)-3-(phenylamino) prop-2-en-1-one (**8a**). Brown solid, yield 89%, m.p.: 159–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 11.72 (d, J = 12.40 Hz, 1H, –NH), 8.01 (d, J = 8.80 Hz, 1H, H-8), 7.62 (dd, J = 2.40 Hz, 8.80 Hz, 1H, H-7), 7.55 (d, J = 2.40 Hz, 1H, H-6), 7.44 (d, J = 6.80 Hz, 3H, H-5, 9 & 13), 7.35 (d, J = 7.60 Hz, 3H, H-18 to 20), 7.31 (d, J = 8.00 Hz, 2H, H-21 & 22), 7.16 (dd, J = 7.60 Hz, 12.40 Hz, 1H, H-17), 7.08 (t, J = 7.60 Hz, 1H, H-11), 7.03 (d, J = 8.00 Hz, 2H, H-10 & 12), 5.06 (d, J = 7.60 Hz, 1H, H-16), 2.76 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 194.89 (C-15), 155.79 (C-2), 145.74 (C-8a), 144.16 (C-17), 144.39 (C-23), 139.77 (C-4), 135.41 (C-24), 130.48 (C-8), 130.37 (C-7), 129.89 (C-6), 129.74 (C-5), 128.49 (C-3), 128.39, (C-9 & 13), 126.42 (C-5a), 125.19 (C-10, 11 & 12), 124.08 (C-19, 20 & 21), 116.43 (C-18 & 22), 99.53 (C-16), 24.00 (C-14). HRMS-ESI (m/z) calcd for $C_{25}H_{20}N_2O$ $[M+H]^+$ = 365.1654, found = 365.1654.

(E)-1-(6-Chloro-2-methyl-4-phenylquinolin-3-yl)-3-(phenylamino)prop-2-en-1-one (**8b**). Brown solid, yield 90%, m.p.: 163–165 °C: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 11.71 (d, J = 12.40 Hz, 1H, –NH), 8.01 (d, J = 9.00 Hz, 1H, H-8), 7.62 (dd, J = 2.10 Hz, 9.00 Hz, 1H, H-7), 7.54 (d,

J = 2.10 Hz, 1H, H-13), 7.44 (t, J = 6.80 Hz, 3H, H-9 to 11), 7.35 (dd, J = 2.00 Hz, 7.40 Hz, 2H, H-18 to 20), 7.31 (d, J = 7.80 Hz, 2H, H-21 & 22), 7.16 (dd, J = 7.40, 12.40 Hz, 1H, H-17), 7.09 (d, J = 7.80 Hz, 1H, H-12), 7.02 (d, J = 8.00 Hz, 2H, H-13 & 5), 5.06 (d, J = 7.40 Hz, 1H, H-16), 2.78 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz,$CDCl_3$): δ ppm 194.89 (C-15), 155.75 (C-2), 144.75 (C-8a), 144.15 (C-17), 143.41 (C-23), 139.90 (C-4), 135.43 (C-24), 130.46 (C-8), 130.40 (C-7), 129.90 (C-6), 129.74 (C-5), 128.49 (C-3), 128.38 (C-9 & 13), 126.44 (C-5a), 125.18 (C-10, 11 & 12), 124.08 (C-19, 20 & 21), 116.45 (C-18 & 22), 99.55 (C-16), 23.98 (C-14). HRMS-ESI (m/z) calcd for $C_{25}H_{19}ClN_2O$ $[M+H]^+$ = 399.1264, found = 399.1263.

(E)-1-(6-Chloro-4-(2-chlorophenyl)-2-methylquinolin-3-yl)-3-(phenylamino)prop-2-en-1-one (**8c**) Yellow solid, yield 91%, m.p.: 161–162 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 11.74 (d, J = 12.00 Hz, 1H, –NH), 8.03 (d, J = 9.50 Hz, 1H, H-8), 7.64 (dd, J = 2.60 Hz, 9.50 Hz, 1H, H-7), 7.52 (dd, J = 1.40 Hz, 8.00 Hz, 1H, H-13), 7.41 (dt, J = 1.60 Hz, 7.60 Hz, 1H, H-11), 7.36–7.33 (m, 3H, H-10, 12 & 14), 7.29 (d, J = 1.40 Hz, 2H, 18 & 19), 7.26 (d, J = 2.60 Hz, 1H, H-22), 7.24–7.21 (m, 1H, H-21 & 22), 7.10 (t, J = 7.60 Hz, 1H, H-17), 7.04 (d, J = 12.00 Hz, 1H, H-11), 5.29 (d, J = 4.00 Hz, 1H, H-16), 2.76 (s, 3H, CH_3, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 194.05 (C-15), 155.99 (C-2), 145.46 (C-8a), 144.57 (C-17), 140.76 (C-23), 139.69 (C-4), 135.52 (C-24), 134.32 (C-9), 133.53 (C-13), 130.63 (C-8), 130.50 (C-7), 130.16 (C-6), 129.75 (C-5), 129.54 (C-3), 127.00 (C-5a), 125.87 (C-10, 11 & 12), 124.73 (C-19, 20 & 21), 116.46 (C-18 & 22), 98.12 (C-16), 23.96 (C-14). HRMS-ESI (m/z) calcd for $C_{25}H_{18}Cl_2N_2O$ $[M+H]^+$ = 433.0874, found = 433.0877.

General procedure for the synthesis of compounds (9a–c)

Conventional method

A mixture of 0.1 g (0.3 mmol, 1 eq) of compound **3a**, 0.028 g (0.3 mmol, 1 eq) of 2-aminopyridine, acetic acid (1 or 2 drops) as catalyst and a pinch of PTSA in DMF (10 mL) was refluxed at 130 °C for 24 h. After the completion of the reaction, the mixture was cooled and then extracted with ethyl acetate, dried over sodium sulphate to afford the product **9a**. The obtained crude product was purified by column chromatography using ethyl acetate/hexane (4:6) eluent. To check the reproducibility of the reaction **3b–c** was subjected to the same reaction which afforded **9b–c**.

Microwave-assisted synthesis

A mixture of 0.1 g (0.3 mmol, 1 eq) of compound **3a**, 0.028 g (0.3 mmol, 1 eq) of 2-aminopyridine, acetic acid (1 or 2 drops) as catalyst and a pinch of PTSA was taken in a tightly closed tube, and subjected to microwave irradiation for 6 min (the completion of the reaction was monitored by TLC). The obtained crude product was purified by column chromatography using ethyl acetate/hexane (4:6) eluent. To check the reproducibility of the reaction, **3b–c** was subjected to the same reaction which afforded **9b–c**.

(E)-1-(2-Methyl-4-phenylquinolin-3-yl)-3-(pyridin-2-ylamino)prop-2-en-1-one (**9a**). Pale yellow solid, yield 80%, m.p.: 151–152 °C: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 11.72 (d, J = 12.30 Hz, 1H), 8.01 (d, J = 8.80 Hz, 1H, H-19), 7.63 (dd, J = 2.40 Hz, 8.80 Hz, 1H, H-8), 7.55 (d, J = 2.40 Hz, 1H, H-17), 7.45 (d, J = 6.80 Hz, 3H, H-10 to 12), 7.35 (d, J = 7.60 Hz, 2H, H-13 & 5), 7.32 (d, J = 8.00 Hz, 2H, H-7), 7.17 (dd, J = 7.60 Hz, 12.40 Hz, 1H, H-16), 7.08 (t, J = 7.60 Hz, 1H, H-20), 7.03 (d, J = 8.00 Hz, 2H, H-21 & 22), 5.07 (d, J = 7.60 Hz, 1H, H-22), 2.76 (s, 3H, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 194.89 (C-15), 155.75 (C-2), 151.34 (C-23), 148.50 (C-19), 145.74 (C-8a), 144.16 (C-24), 144.39 (C-17), 139.77 (C-24), 135.41 (C-4), 135.25 (C-3), 131.98 (C-8), 130.40 (C-7), 129.89 (C-6), 129.74 (C-5, 9 & 13), 128.49 (C-10, 11 & 12), 126.42 (C-22), 125.19 (C-20 & 22), 124.08 (C-21), 116.43 (C-16), 24.00 (C-14). HRMS-ESI (m/z) calcd for $C_{24}H_{19}N_3O$ $[M+H]^+$ = 366.1606, found = 366.1604.

(E)-1-(6-Chloro-2-methyl-4-phenylquinolin-3-yl)-3-(pyridin-2-ylamino)prop-2-en-1-one (**9b**) Yellow solid, yield 91%, m.p.:169–170 °C: ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 11.72 (d, J = 11.90 Hz, 1H), 8.26 (dd, J = 1.80 Hz, 4.90 Hz, 1H, H-19), 8.02 (d, J = 8.80 Hz, 1H, H-8), 7.90 (dd, J = 7.90 Hz, 11.90 Hz, 1H, H-17), 7.64–7.59 (m, 2H, H-7 & 16), 7.54 (d, J = 1.80 Hz, 1H, H-10), 7.46 (d, J = 4.90 Hz, 3H, H-10 to 12), 7.34 (dd, J = 1.80 Hz, 7.60 Hz, 1H, H-13), 6.97–6.94 (m, 1H, H-20), 6.81 (d, J = 7.90 Hz, 1H, H-21), 5.19 (d, J = 7.90 Hz, 1H, H-22), 2.75 (s, 3H, H-14); ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 196.15 (C-15), 155.52 (C-2), 151.33 (C-23), 148.51 (C-19), 145.80 (C-8a), 143.52 (C-24), 142.30 (C-17), 138.42 (C-21), 135.38 (C-4), 135.07 (C-3), 132.06 (C-8), 130.57 (C-7), 130.40 (C-5, 10 & 13), 129.87 (C-11 & 12), 128.45 (C-5a), 126.40 (C-6), 125.18 (C-9), 118.90 (C-20), 111.84 (C-22), 100.96 (C-16), 23.97 (C-14). HRMS-ESI (m/z) calcd for $C_{24}H_{18}ClN_3O$ $[M+H]^+$ = 400.1217, found = 400.1213.

(E)-1-(6-Chloro-4-(2-chlorophenyl)-2-methylquinolin-3-yl)-3-(pyridin-2-ylamino)prop-2-en-1-one (**9c**) Brown solid, yield 81%, m.p.: 158–159 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 11.72 (d, J = 11.70 Hz, 1H, –NH), 8.14 (d, J = 5.00 Hz, 1H, H-19), 8.02 (d, J = 8.10 Hz, 1H, H-8), 7.96 (dd, J = 7.80, 11.70 Hz, 1H, H-17), 7.61 (dd, J = 8.10, 14.60 Hz, 2H, H-7 & 16), 7.51 (d, J = 7.60 Hz, 1H, H-10), 7.39 (t, J = 7.60 Hz, 1H, H-11), 7.33 (t, J = 7.30 Hz, 1H, H-21), 7.15 (dd, J = 7.30, 19.00 Hz, 2H, H-13 & 5), 6.95 (t, J = 5.00 Hz, 1H, H-20), 6.80 (d, J = 8.00 Hz, 1H,

H-21), 5.39 (d, J = 8.00 Hz, 1H, H-22), 2.77 (s, 3H, CH_3, H-14). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 196.15 (C-15), 155.53 (C-2), 151.34 (C-23), 148.50 (C-19), 145.79 (C-8a), 143.51 (C-24), 142.30 (C-17), 138.42 (C-21), 135.38 (C-4), 135.07 (C-3), 132.06 (C-8), 130.57 (C-7), 130.40 (C-5, 10 & 13), 129.87 (C-11 & 12), 128.45 (C-5a), 126.40 (C-6), 125.18 (C-9), 118.92 (C-20), 111.84 (C-22), 100.96 (C-16), 23.98 (C-14). HRMS-ESI (m/z) calcd for $C_{24}H_{17}Cl_2N_3O$ [M+] = 433.0749, found = 433.0746.

Conclusion

The 3-acetyl-4-arylquinoline-based enaminones were successfully synthesized by exploring the synthetic potential of DMFDMA under microwave-assisted solvent-free conditions (along with that the conventional procedure was also carried out and compared) which in turn were converted into a series of heterocycles. All the reactions were found to afford better yield in shorter duration under the microwave-assisted reaction. Hence, in our opinion, this synthetic protocol is a valuable investigation which could make a significant impact on the synthesis of quinoline-based heterocycles.

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