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LETTER

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An environmentally benign, simple and proficient synthesis of quinoline derivatives catalyzed by $FeCl_3.6H_2O$ as a green and readily available catalyst

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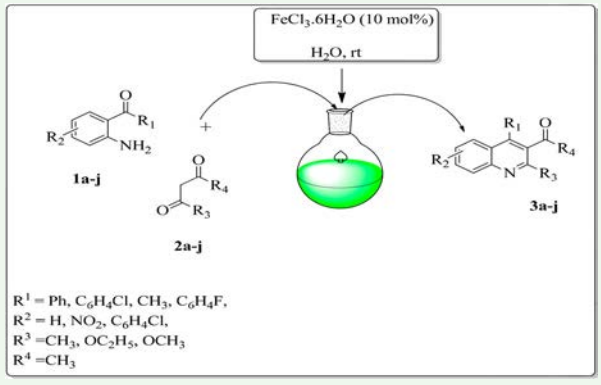
ABSTRACT

We report here a facile, one-pot, environmentally friendly, and efficient protocol for the synthesis of quinoline derivatives from the condensation of 2-aminoarylketones and active methylene compounds catalyzed by inexpensive, nontoxic and environmentally benign $FeCl_3.6H_2O$ catalyst. The results obtained by using $FeCl_3.6H_2O$ catalyst were also compared with those described in the literature. This methodology offers several advantages such as shorter reaction time, milder conditions, easy workup, and better yields. The non-extractive workup/purification, economic and environmentally benign catalyst make this operationally straightforward procedure affordable for a large scale.



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An environmentally benign $FeCl_3.6H_2O$ catalyst; substituted 2-arylketones; active methylene diketones; green synthesis

1. Introduction

Quinoline is the most privileged scaffold found in many natural products, drugs, and pharmaceutical substances (*1*). It is an important chemical moiety frequently used for the design and synthesis of large spectra of derivatives. In recent times, the quinoline nucleus has attracted many chemists as well as biologists as it is one of the key building elements for the construction of many pharmacologically active substances and drugs (*2*). Their derivatives have been found to possess a broad range of biological activities such as antifungal (*3*), anticancer (*4*), antihypertensive (*5*), anti-tuberculosis (*6*), antimalarial (*7*), antiprotozoal (*8*), antibiotic (*9, 10*), antineoplastic (*11*), and anti-inflammatory (*12*). Functionalized quinoline motifs are also used as asymmetric catalysts (*13*), ligands for Transition metal complexes (*14*), and dyestuff (*15*). A list of some pharmacologically active quinoline derivatives are shown in Figure 1.

As a consequence of the tremendous medicinal and industrial application of quinoline derivatives, chemists have discovered a plethora of methods to elaborate the structure of quinoline scaffolds includes Skraup (*16*), Conrad-Limpach-Knorr (*17*), Pfitzinger (*18*), Friedlander (*19*), and Friedlander condensation (*20–22*). Various new methods have also been developed which employed metallic or organometallic reagents such as CuCN, LiCl (*23*). Ruthenium (III) chloride $RuCl_3.nH_2O$/ $3PPh_3$ (*24*), Ytterbium (III) triflate $Yb(OTf)_3$ (*25*), Tungsten vinylidene complex $W(CO)_5(THF)$ (*26*), Boron trifluoride etherate $BF_3.OEt_2$ (*27, 28*), Benzotriazoleiminium salts (*29*), etc. for the synthesis of quinoline derivatives. Regardless of the many merits reported by these methods, they are also plagued by limitations like poor yields, difficult work-up, and effluent pollution.

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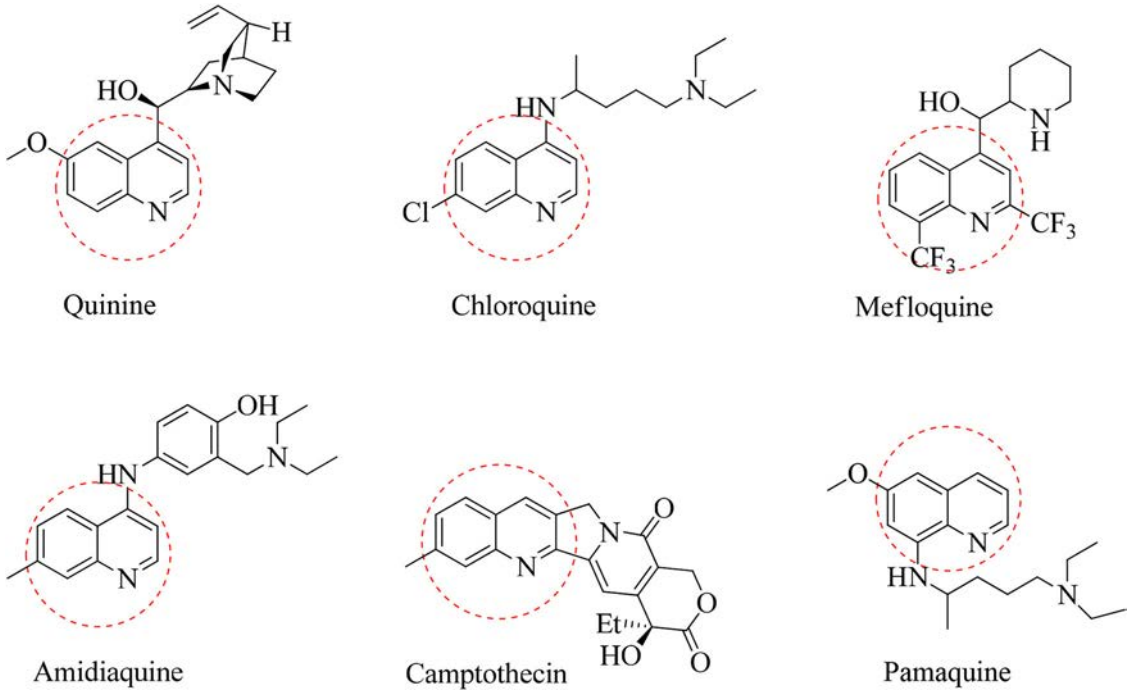


Figure 1. A few pharmacologically active quinoline derivatives (color dashed ovals represents the quinoline ring present in various active drugs).

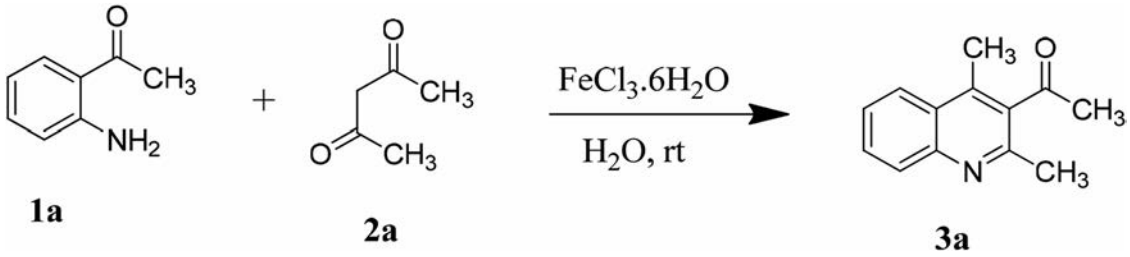
Nowadays, sustainable chemistry is receiving much attention due to resource challenge, the climate and the environmental challenge. Therefore, it is aimed to develop simple and facile methods to carry organic synthesis under mild conditions (*30*).

In our previous works, we have reported the synthesis of quinoline derivatives by using ionic liquids (*31*) and microwave method (*32*). So extension with this report and to maintain greener protocol, in the current work, quinoline derivatives were synthesized by using $FeCl_3.6H_2O$ as a catalyst in the presence of water as a solvent. As water being the most environmentally benign, cleanest, cheapest, nonflammable, and naturally occurring solvent, significant rate enhancement was observed in many reactions utilizing water. This could be due to hydrophobic interactions that induce a favorable aggregation of polar components in water (*33*). Moreover, transition metal-catalyzed organic syntheses are now serving as one of the most powerful tools to synthesize a large number of organic compounds (*34*). Among the transition metals catalyst, chemists pay more attention towards iron catalyzed synthesis (*35*, *36*) because of unusual properties of iron, including its easy availability, low price, and environmentally friendly character. It has been reported as an efficient catalyst in various organic reactions such as iron-catalyzed carbon-heteroatom and heteroatom-heteroatom bond forming reactions (*37*), Fe-catalyzed C–C bond forming reactions (*38*), the synthesis of functionalized pyrroles (*39*), and synthesis of 2-pyrrolines catalyzed by $FeCl_3$ (*40*). Besides this, iron in the form of various salts such as $FeCl_3.6H_2O$ has been employed as a Lewis acid in a number of organic syntheses such as Beckmann rearrangements (*41*), Biginelli condensations (*42*), and Hantzsch 1,4-dihydropyridines (*43*).

In this regard, we report herein the condensation of substituted 2-aminoarylketones with various substituted active methylene diketones catalyzed by inexpensive, eco-friendly and easily available catalyst $FeCl_3.6H_2O$ in water as a solvent. To the best of our knowledge there is no report on the synthesis of quinoline derivatives catalyzed by $FeCl_3.6H_2O$ catalyst in the presence of water as a solvent.

2. Results and discussions

In continuation to our ongoing research program on the synthesis of heterocyclic compounds (*44*, *45*), we decided to synthesize 1-(2,4-dimethylquinolin-3-yl)ethanone from the condensation of 2-aminoacetophenone **1** (10 mmol) with acetylacetone **2** (12 mmol) in the presence of $FeCl_3.6H_2O$ (10 mol%) as a catalyst and water as a solvent (Scheme 1). To optimize the reaction conditions, the below reaction Scheme 1, was used as a model reaction and the results are presented in Table 1. Interestingly, when $FeCl_3.6H_2O$ was used as a catalyst (Table 1, entry 5), the highest yield of the product (97% yield) was obtained. The yield of the product could not be improved by increasing the amount of catalyst (Table 1, entry 7,8).



Scheme 1. Synthesis of 1-(2,4-dimethylquinolin-3-yl)ethanone.

Table 1. Optimization of reaction conditions using different catalytic amounts[a].

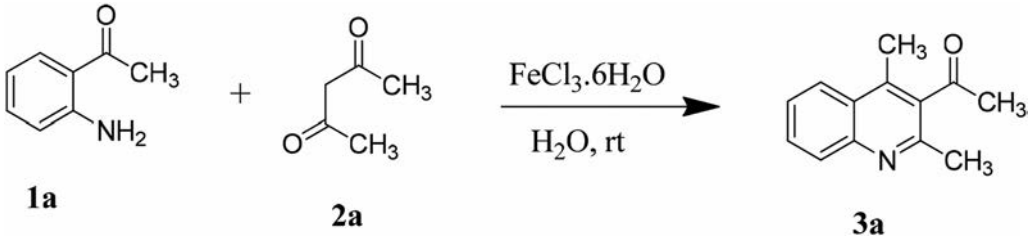
Entry	Catalyst (mol %)	Time (min)	Yield[b] (%)
1.	$ZnCl_2$(10)	30	80
2.	$CoCl_2$-$6H_2O$ (10)	30	60
3.	*p*-TSA (10)	45	80
4.	$InCl_3$	30	84
5.	$FeCl_3.6H_2O$ (10)	30	97
6.	–	720	0
7.	$FeCl_3.6H_2O$ (15)	30	95
8.	$FeCl_3.6H_2O$ (20)	30	90
9.	$FeCl_3.6H_2O$ (5)	30	75
10.	$FeCl_3.6H_2O$ (2)	30	50

[a]Reaction condition: **1** (1.0 mmol), **2** (2.0 mmol), water as a solvent, 30 min, at room temperature.
[b]Yields of the isolated products.
p-TSA (*p*-Toluenesulfonic acid)

However, the product yield dropped by decreasing the amount of catalyst (Table 1, entry 9,10). In the absence of the catalyst the model reaction failed to give the desired product (Table 1, entry 6).

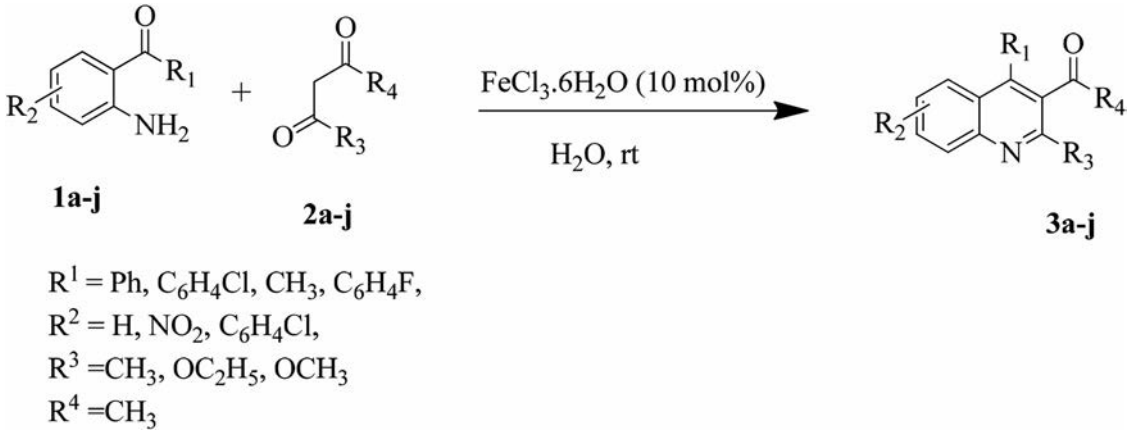
We then continued to optimize the model reaction (Scheme 1) by detecting the efficiency of the catalyst $FeCl_3.6H_2O$ and water as a solvent with other reaction conditions. Initially the reaction was carried out in the absence of solvent and catalyst. However, after 28 h at room temperature (rt), no product had been formed (Table 2, entry 1). When the same model reaction was conducted with different catalysts and solvents such as MgO/Ethanol, $MgSO_4$/Ethanol, *P*-toluenesulfonic acid/Tetrahydrofuran, *P*-toluenesulfonic acid/Toluene, Pyridinium *p*-toluene sulfonate/Ethanol, and Pyridinium *p*-toluene sulfonate/Glycerol (Table 2, entries 2, 3, 4, 5, 6, and 7), the completion of reaction took a longer time. The reaction was also carried out in Triethanolamine/Pyridinium acetate and PEG-600/Pyridinium acetate (Table 2, entries 8 and 9), again only trace amount of the desired product (3a) was obtained. We also examined the model reaction with the reported method

Table 2. Optimization of reaction conditions using various solvents and different catalyst for the synthesis of 1-(2,4-dimethylquinolin-3-yl)ethanone.



Entry	Catalyst (mol %)	Solvent (rt)	Time (h)	Yield[a](%)
1	–	–	28	0
2	MgO (10)	Ethanol	20	10
3	$MgSO_4$ (10)	Ethanol	20	15
4	*P*-toluenesulfonic acid (20)	Tetrahydrofuran	24	Trace
5	*P*-toluenesulfonic acid (20)	Toluene	18	40
6	Pyridinium *p*-toluene sulfonate (20)	Ethanol	12	0
7	Pyridinium *p*-toluene sulfonate (20)	Glycerol	10	0
8	Pyridinium acetate (20)	Triethanolamine	4	60
9	Pyridinium acetate (20)	PEG-600	4	65
10	Amberlyst-15 (5)	Ethanol (Reflux)	3	59–92(*46*)
11	Cellulose sulfuric acid (5)	Solvent free (100^{0}C)	50 (min)	21–60(*47*)
12	$HClO_4$-SiO_2 (5)	CH_3CN (60°C)	2	37–90(*48*)
13	$FeCl_3.6H_2O$ (10)	Water	30 (min)	97

[a]Yields of the isolated products.
Reaction condition: 2-aminoacetophenone **1** (1.0 mL, 10 mmol), acetylacetone **2** (1.3 mL, 12 mmol).



Scheme 2. Synthesis of 1-(2-methylquinolin-3-yl)ethanone derivatives from substituted 2-aminoacetophenone and active methylene compounds catalyzed by $FeCl_3.6H_2O$ in water solvent.

procedures which resulted in lower yields of the product 3a (Table 2, entries 10,11, and 12). Therefore, the best results were obtained from $FeCl_3.6H_2O$ (10 mol%) in water as a solvent at room temperature (Table 2 entry 13).

To explore the generality of this new protocol, we extended our study using $FeCl_3.6H_2O$ as a catalyst and water as a solvent for the condensation of various 2-aminoacetophenone (**1a-j**) with substituted active methylene compounds (**2a-j**) under optimized conditions. A series of 2-aminoacetophenone bearing either electron-donating or electron-withdrawing groups reacted successfully to afford a wide range of substituted quinoline derivatives in good to excellent yield. We explored further the electronic effect of various substituents present on the 2-aminoacetophenone. We noticed that various 2-aminoacetophenone having both electron-donating and electron-withdrawing substituents are equally facile for the reaction, and gave the corresponding quinoline derivatives in very good yields. We have observed that most of the 2-aminoacetophenone bearing electron-donating reacted in shorter reaction time and gave the corresponding quinoline derivatives in better yields than 2-aminoacetophenone bearing electron-withdrawing substituents. (Scheme 2) and the results were summarized in Table 3.

The efficiency of the catalyst $FeCl_3.6H_2O$ was also determined by comparing with other methods reported earlier in the literature. The results summarized in Table 4, proved the advantages of our method in terms of reaction time and yield of the products as compared with those reported methods.

To examine the reusability of the catalyst $FeCl_3.6H_2O$, the filtrate of the model reaction (Scheme 1) was treated with the same reactants under similar reaction conditions. The catalyst was reused as such for successive experiments up to five cycles. It was observed that the efficiency of the catalyst has not changed significantly and there was slightly decrease in the yield of the product which confirmed the recyclability and reusability of the $FeCl_3.6H_2O$ catalyst. The results of the screening and reusability were summarized in the Table 5.

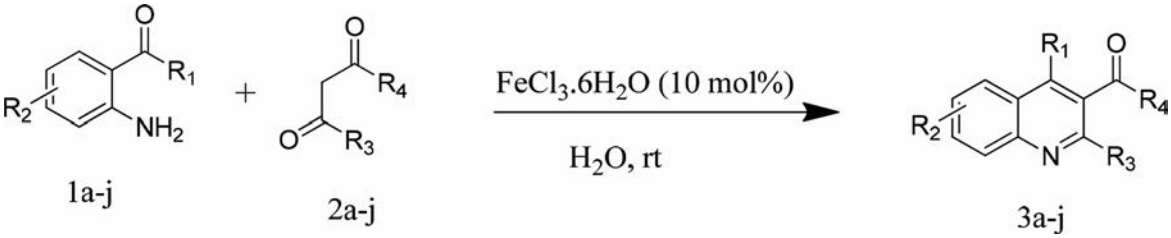
3. Conclusion

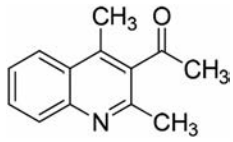
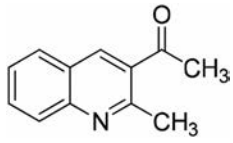
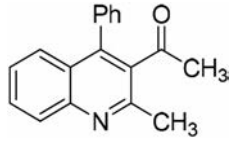
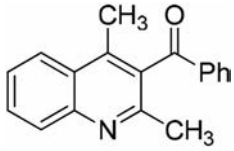
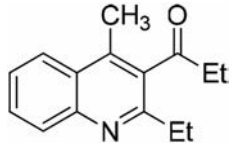
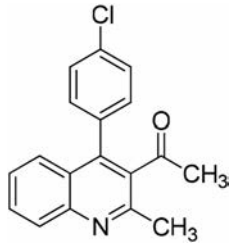
In conclusion, we have developed an expedient, efficient, facile, clean and environmentally benign methodology for the synthesis of quinoline derivatives by using an inexpensive, easily available $FeCl_3.6H_2O$ as a catalyst. The advantages of this environmentally benign and safe protocol include a simple reaction setup, very mild reaction conditions, high product yields, short reaction times, and the possibility of reusing the catalyst.

4. Experimental

All the commercially available chemicals and reagents were used without further purification. Column chromatography was carried out on silica gel (200-400 mesh). Melting points were determined using a Buchi melting point B-545 apparatus and are uncorrected. TLC checking was done on glass plates coated with Silica Gel-G and spotting was done by using iodine as well as a UV lamp. IR (KBr) spectra were recorded on PerkineElmer FTIR spectrophotometer. ^{1}H-NMR spectra were recorded on a Gemini-200 and AV-400 instruments operating at 200 and 400 MHZ respectively. The elemental analysis (C, H, N) of the compounds were performed using Flash EA 1112 elemental analyzer.

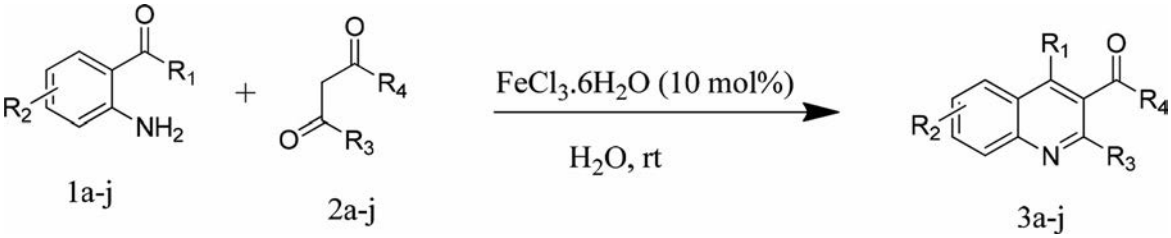
Table 3. Synthesis of quinoline derivatives catalyzed by $FeCl_3.6H_2O$ (10 mol%) in water.

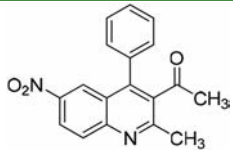
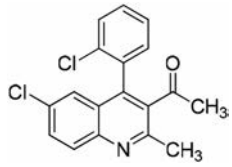
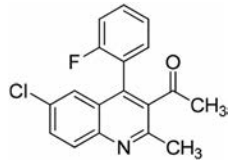


Entry	Product name	Structure	Time (min)	Yield[a] (%)	Melting point (°C) Found	Reported
3a	1-(2,4-dimethylquinolin-3-yl) Ethanone		30	97	131–132	–
3b	1-(2-methylquinolin-3-yl) Ethanone		45	95	oil	–
3c	1-(2-methyl-4-phenylquinolin-3-yl)ethanone		30	97	109–111	113(*31*)
3d	(2,4-dimethylquinolin-3-yl)(phenyl)methanone		30	95	oil	–
3e	1-(2-ethyl-4-methylquinolin-3-yl)propan-1-one		42	97	oil	–
3f	ethyl 2,4-dimethylquinoline-3-carboxylate		40	95	111–112	–
3g	1-(4-(4-chlorophenyl)-2-methylquinolin-3-yl)ethanone		40	95	151–153	151(*31*)

(*Continued*)

Table 3. Continued.



Entry	Product name	Structure	Time (min)	Yield[a] (%)	Melting point (°C) Found	Reported
3h	1-(2-methyl-6-nitro-4-phenylquinolin-3-yl)ethanone		45	95	166–167	–
3i	1-(6-chloro-4-(2-chlorophenyl)-2-methylquinolin-3-yl)ethanone		35	96	101–102	
3j	1-(6-chloro-4-(2-fluorophenyl)-2-methylquinolin-3-yl)ethanone		30	96	77–79	–

[a]Yields of the isolated products.
Reaction condition: Condensation of substituted 2-aminoacetophenone **1a-j** (1.0 mL, 10 mmol), substituted acetylacetone **2a-j** (1.3 mL, 12 mmol catalyzed by $FeCl_3.6H_2O$ (10 mol%) in water.

Table 4. Comparison of efficiency of various catalyst for the synthesis of quinoline derivatives.

Entry	Catalyst	Time (min)	Yield[a] (%)
1	KSF clay	360	75(*49*)
2	ZrO_2	210	92(*50*)
3	$SbCl_3$	300	82(*51*)
4	ZnO NPs	180	75(*52*)
5	CuO NPs	300	88(*53*)
6	$FeCl_3.6H_2O$	30	97

[a]Yields of the isolated products.

Table 5. Screening of the reusability of the catalyst $FeCl_3.6H_2O$[a].

Run no.	Yield[b] (%)	Time (min)
1	97	30
2	95	40
3	95	50
4	92	60
5	90	85

[a]Reaction condition: 2-aminoacetophenone **1** (1.0 mL, 10 mmol), acetylacetone **2** (1.3 mL, 12 mmol). $FeCl_3.6H_2O$ (10 mol%), water, room temperature.
[b]Yields of the isolated products.

4.1. General procedure for the synthesis of quinoline derivatives (3a-j)

A mixture of **1** (10 mmol), **2** (12 mmol) and $FeCl_3.6H_2O$ (10 mol%), in water was stirred in a round-bottomed flask for a period of 0.5 h. After the completion of the reaction (as shown by TLC analysis), the precipitate in water was collected by filtration, washed with water and dried to get 1-(2,4-dimethylquinolin-3-yl)ethanone. It was recrystallized and characterized with IR, ^{1}H NMR and ^{13}C NMR spectroscopy.

4.2. 1-(2,4-dimethylquinolin-3-yl)ethanone (3a)

Yield: 95%, mp:132°C; IR (KBr pellets, cm-1) υ: 1037.62, 1456.81, 1560.38, 1632.90, 3027.51, 3259.16; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.93 (d, 1H, $J = 8.5$ Hz); 7.85 (dd, 1H); 7.63-7.59 (m, 1H); 7.46-7.42 (m, 1H); 2.53 (s, 3H); 2.48 (s, 3H); 2.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.4, 152.3, 146.4, 138.2, 135.4, 129.3, 129.2, 126.1, 125.7, 123.4,

32.4, 23.3, 15.1. LCMS: m/z 199.1 [M^+]; anal. calc. for $C_{13}H_{13}NO$: C, 78.35; H, 6.57; N, 7.02; found: C, 78.36; H, 6.58; N. 7.03.

4.3. 1-(2-methylquinolin-3-yl)ethanone (3b)

Yield: 97%, Light yellow oil.^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (s, 1H); 8.04 (d, J = 8.5 Hz, 1H); 7.85 (d, J = 8.1 Hz, 1H); 7.78-7.76 (m, 1H); 7.57-7.53 (m, 1H); 2.91 (s, 3H), 2.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.9, 157.6, 148.2, 138.2, 131.7, 131.1, 128.5, 128.3, 126.7, 125.6, 29.2, 25.6. LCMS: m/z 185.08 [M^+]; anal. calc. for $C_{12}H_9NO$: C, 77.80; H, 5.98; N, 7.53; found: C, 77.81; H, 5.99; N. 7.56.

4.4. 1-(2-methyl-4-phenylquinolin-3-yl)ethanone (3c)

Yield: 97%, Yellow color solid, mp:111°C; IR (KBr pellets, cm-1) υ: 1081.72, 1482.30, 1572.16, 1624.80, 3047.13, 3254.10; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.07 (d, 1H, J = 8.3 Hz); 7.75-7.72 (m, 1H); 7.60 (d, 1H, J = 8.3 Hz); 7.50-7.48 (m, 3H); 7.45-7.43 (m, 1H), 7.35-7.34 (m, 2H); 2.70 (s, 3H); 1.97 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 205.6, 153.4, 147.7, 144, 135.2, 134.9, 130.1, 130.0, 128.8, 128.7, 128.6, 126.6, 126.3, 125.0, 31.8, 23.7. LCMS: m/z 261.12 [M^+]; anal. calc. for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36; found: C, 82.76; H, 5.81; N. 5.38.

4.5. (2,4-dimethylquinolin-3-yl)(phenyl)methanone (3d)

Yield: 95%, Light yellow oil.^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.10-8.06 (m, 1H); 8.04-8.01 (m, 1H); 7.87-7.82 (m, 2H); 7.77-7.71 (m, 1H); 7.67-7.54 (m, 2H); 7.52-7.44 (m, 2H); 2.55 (s, 3H), 2.48 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 198.9, 154.1, 147.1, 140.7, 136.5, 134.1, 132.1, 129.8, 129.5, 129.4, 129.2, 126.6, 126.2, 123.5, 24.2, 17.9. LCMS: m/z 261.12 [M^+]; anal. calc. for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36; found: C, 82.75; H, 5.81; N. 5.38.

4.6. 1-(2-ethyl-4-methylquinolin-3-yl)propan-1-one (3e)

Yield: 97%, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04-8.02 (m, 1H); 7.94-7.91 (m, 1H); 7.68-7.65 (m, 1H); 7.51-7.48 (m, 1H); 2.79-2.77 (m, 4H); 2.48 (s, 3H); 1.32 (t, 3H, J = 7.3 Hz); 1.22 (t, 3H, J = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.3, 157.3, 147.2, 138.8, 135.5, 134.4, 131.6, 129.3, 129.5, 126.3, 125.4, 123.8, 117.2, 115.3, 38.6, 30.1, 15.4, 13.8, 7.7. LCMS: m/z 227.13 [M^+]; anal. calc. for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N, 6.16; found: C, 79.29; H, 7.56; N. 6.18.

4.7. Ethyl 2,4-dimethylquinoline-3-carboxylate (3f)

Yield: 95%, Light yellow solid, mp:112°C; IR (KBr pellets, cm-1) υ: 1076.82, 1476.29, 1567.88, 1724.20, 2934.68; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.98 (d, 1H, J = 8.3 Hz); 7.93 (d, 1H); 7.67 (t, 1H); 7.53 (t, 1H), 4.45 (q, 2H); 2.72 (s, 3H); 2.63 (s, 3H); 1.45 (t, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 189.71, 159.85, 149.5, 138.21, 132.58, 131.71, 130.2, 129.56, 129.4, 127.61, 127.26, 126.21, 114.2, 44.36, 31.45, 26.48. LCMS: m/z 229.11 [M^+]; anal. calc. for $C_{14}H_{15}NO_2$: C, 73.30; H, 6.55; N, 6.09; found: C, 73.34; H, 6.59; N. 6.11.

4.8. 1-(4-(4-chlorophenyl)-2-methylquinolin-3-yl)ethanone (3g)

Yield: 95, mp: 151°C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.08 (d, 1H, J = 8.4 Hz); 7.76-7.71 (m, 1H); 7.57-7.56 (m, 1H,); 7.52-7.46 (m, 3H); 7.32-7.30 (m, 2H); 2.73 (s, 3H); 2.06 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 204.7, 153.7, 147.6, 142.8, 135.7, 134.4, 133.6, 131.3, 130.6, 129.9, 128.6, 126.4, 125.5, 124.1, 32.6, 23.3. LCMS: m/z 295.10 [M^+]; anal. calc. for $C_{18}H_{14}ClNO$: C, 73.10; H, 4.77; N, 4.74; found: C, 73.12; H, 4.79; N. 4.76.

4.9. 1-(2-methyl-6-nitro-4-phenylquinolin-3-yl)ethanone (3h)

Yield: 97, mp:167°C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.59 (d, 1H, J = 8.4 Hz); 8.51-8.48 (m, 1H); 8.22 (d, 1H, J = 9.3); 7.61-7.58 (m, 3H); 7.40-7.38 (m, 2H); 2.73 (s, 3H); 2.03 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 204.7, 157.7, 149.6, 145.8, 145.7, 136.4, 133.6, 132.3, 131.6, 130.9, 129.8, 129.6, 129.4, 129.2, 128.6, 124.4, 123.5, 123.1, 116.6, 31.6, 24.3. LCMS: m/z 306.10 [M^+]; anal. calc. for $C_{18}H_{14}N_2O_3$: C, 70.58; H, 4.61; N, 9.15; found: C, 70.61; H, 4.63; N. 9.17.

4.10. 1-(6-chloro-4-(2-chlorophenyl)2-methylquinolin3-yl)ethanone (3i)

Yield: 96%, mp:102°C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.04 (d, 1H, J = 9 Hz); 7.67 (dd, 1H); 7.61-7.58 (m, 1H); 7.52-7.48 (m, 1H); 7.44-7.41 (m, 1H); 7.28 (d, 1H); 7.25-7.23 (m, 1H); 2.72 (s, 3H); 2.17 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 204.2, 154, 145.3, 140.2, 135.3, 133.1, 133, 132.5, 131.8, 131, 130.6, 130.4, 130, 127.2, 125.1, 124.3, 31.1, 23.7. LCMS: m/z 329.04 [M^+]; anal. calc. for $C_{18}H_{13}Cl_2NO$: C, 65.46; H, 3.96; N, 4.23; found: C, 65.47; H, 3.97; N. 4.24.

4.11. 1-(6-chloro-4-(2-fluorophenyl)2-methylquinolin3-yl)ethanone (3j)

Yield: 96%, mp:77°C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.02 (d, 1H, $J = 9.1$ Hz); 7.68 (dd, 1H); 7.59-7.52 (m, 1H); 7.40-7.38 (m, 1H); 7.35-7.22 (m, 3H); 2.70 (s, 3H); 2.16 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ-112.3. ^{13}C-NMR (100 MHz, $CDCl_3$): δ 204.44, 160.2, 158.2, 153.8, 145.5, 137.4, 136.2, 132.7, 132.2, 132, 131.6, 131.54, 131.1, 130.4, 125.6, 124.7, 124.5, 124.3, 122, 121.8, 116.2, 116, 31.2, 23.6. LCMS: m/z 313.07 [M^+]; anal. calc. for $C_{18}H_{13}ClFNO$: C, 68.90; H, 4.17; N, 4.45; found: C, 68.91; H, 4.18; N. 4.46.

Availability of data and materials

The authors confirm that the data supporting the findings of this research are available within the article and its supporting supplementary materials.

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