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# Microwave-assisted expeditious and efficient synthesis of novel quinolin-4-yl methoxychromen-2-and-4-ones catalyzed by YbCl3 under solvent free one-pot three components domino reaction and their antimicrobial activity



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## Graphical Abstract

# Microwave-assisted expeditious and efficient synthesis of novel quinolin-4-yl methoxychromen-2- and -4-ones catalyzed by $YbCl_3$ under solvent free one-pot three components domino reaction and their antimicrobial activity

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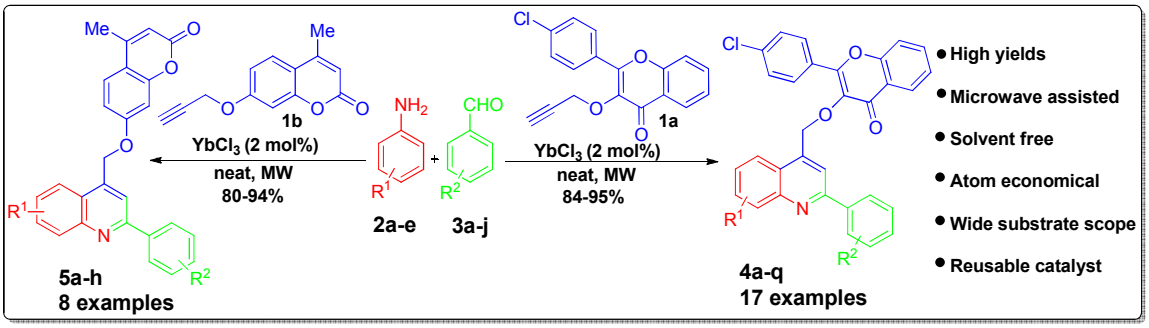


- A novel catalytic method for MW assisted multicomponent $A^3$ synthesis was developed.
- Novel Quinolin-4-yl methoxy-chromen-2 and-4-ones were synthesized.
- High yields,shorter reaction time, neat condition, reuse of $YbCl_3$are main features.
- This method is green and milder but more advanced than those earlier reported.

Journal Name

ARTICLE

# Microwave-assisted expeditious and efficient synthesis of novel quinolin-4-yl methoxychromen-2-and-4-ones catalyzed by $YbCl_3$ under solvent free one-pot three components domino reaction and their antimicrobial activity

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An efficient and highly eco-friendly synthesis of diverse and functionalized quinolin-4-yl methoxychromen-2- and -4-ones viaone-pot three-componentsdomino reaction of propargylated-flavone or -coumarin with aldehydes and anilines under solvent-free and microwavecondition is describedusing $YbCl_3$as catalyst. The reaction took 4 min to give the desired products in excellent yields (80–95%) at 100 $^0$C.This approach has advantagessuch as high yields, solvent-free mild reaction conditions, functional group tolerance, 95% atom-economyand recyclability of catalyst. Synthesized compounds were examined for their antimicrobial activity. Among the tested compounds, compounds **4n**, **5f**, **5g** and **5h** showed the excellent antimicrobial activity.

## 1.Introduction

Quinoline-containingmolecules are present in a number of natural products and have shown different uses such as luminescent materials,[1] tunable ligands[2] and drug agents like antimalarial, antibacterial, anticancer, antihypertensive, antitubercular and anti-inflammatory[3-7](Fig. 1).

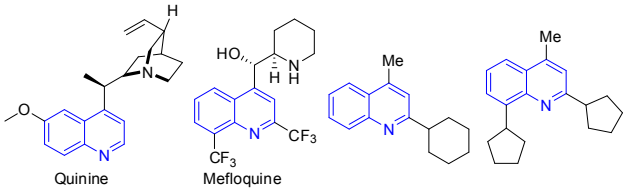


**Fig. 1**Some clinically used drugs bearing a Quinoline moiety.

Therefore, various methods have been reported over the past 130 yearsfor their synthesis thatincludesSkraup,[8] Doebner-Von Miller,[9] Pfitzinger,[10] Conrad-Limpach,[11] Combes[12] and Friedländer syntheses.[13]Recently, different catalysts such asCuCl,[14] CuBr,[15] $Cu(OTf)_2$,[16] $InCl_3$,[17] $FeCl_3$,[18] $Fe(OTf)_3$,[19] AgOTf,[20] $AuCl_3$/CuBr,[21] $NbCl_5$,[22] $Yb(pfb)_3$,[23] CuI/$La(OTf)_3$,[24] montmorillonite K-10[25] for A$^3$-coupling reaction of alkyne, aldehyde and amine have been explored. Mostly, these procedures are marred by one or other drawbacks such as conventional Lewis and Brønsted acids, long reaction time, harsher reaction conditions, low atom economy, and use of refractory substrates. Therefore, the development of expeditious, efficient and eco-friendly approaches for their preparation is of crucial importance.

In recent years, the chemistry of rare earth metals has been under broad examinations due to their extensive applications in organic chemistry.[26,27]Especially,the salts of inner- transition metals like chlorides and triflateshave been used as Lewis acid catalysts due to low water sensitivity, reusability and stoichiometric usecompared to commonly usedwater sensitiveLewis acid catalysts like $BF_3$, $AlCl_3$, $TiCl_4$,etc.[28]
Recently, microwave-assisted synthesis has been recognized for its capability to enhance chemical transformations and produce clean and high-yielding chemical reactions without further purification.[29]Similarly, multicomponent/tandem reactions (MCRs) are a powerful method for the synthesis of heterocyclic compounds and are found to be more efficient compared to conventional stepwise synthesis because of excellent atom economy, reduction of wastes, reaction time, cost and labour.[30]
In continuous pursuit of ourinterest for both the academic and the industrial researchers,[31] it is desirable to explore the scope of rare earth metals as Lewis acids under microwave-assistedorganic synthesis due to their unique and substantial advantages.Recently, we found $YbCl_3$an efficient catalyst in the synthesis of biologically active heterocycles.[31a] Therefore, keeping in mind the extraordinary pharmacological potential of various heterocyclic moieties such as quinoline, flavone and coumarin, herein we devise an efficient and eco-friendly green approach for the synthesis of bioactive novel Quinolin-4-yl methoxychromen-2- and -4-ones via employing one-pot three-component domino reaction of aldehydes, amines and propargylated-flavone or-coumarin using $YbCl_3$ (2 mol%) under solvent free microwave condition (Scheme 1).

## 2. Results and discussion

### 2.1. Chemistry

The starting materials 2-(4-chlorophenyl)-3-(prop-2-yn-1-yloxy)-4H-chromen-4-one (**1a**) and 4-methyl-7-(prop-2-yn-1-yloxy)-2H-chromen-2-one (**1b**) were synthesized by following the literature procedure.[31b]

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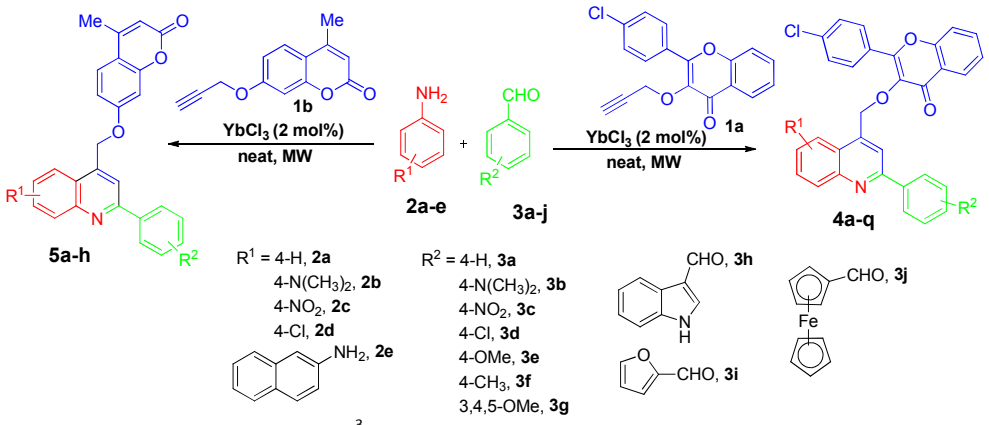
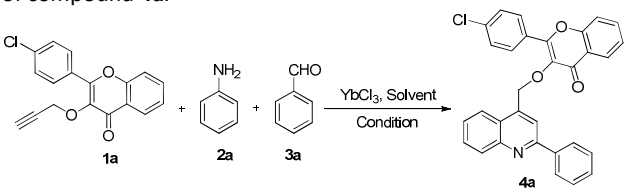



**Scheme 1.**Microwave-assisted A$^3$ synthesis of quinolin-4-yl methoxy-chromen-2 and -4-ones.

As shown in Table 1, in a prototypical reaction, 2-(4-chlorophenyl)-3-(prop-2-yn-1-yloxy)-4H-chromen-4-one**1a**, was treated with aniline **2a** and benzaldehyde**3a**at 100 $^0$C(oil bath) for 60 min which afforded the product **4a** in 81% yield (Table 1, entry 1). In spite of appreciable results, to find optimum protocol for the transformation, several other conditions for the reaction were explored.

**Table 1.**Optimization of reaction conditions for the formation of compound **4a**.[a]




| Entry | Solvent | Catalyst (mol%) | Condition | Temp. ($^0$C) | Time (min) | Yield[d] (%) |
|---|---|---|---|---|---|---|
| 1 | neat | 2 | CH[c] | 100 | 60 | 81 |
| 2 | neat | 2 | MW[b] | 100 | 10 | 95 |
| 3 | neat | 2 | MW[b] | 100 | 7 | 95 |
| **4** | **neat** | **2** | **MW[b]** | **100** | **4** | **95** |
| 5 | neat | 2 | MW[b] | 100 | 3 | 77 |
| 6 | neat | 2 | MW[b] | 120 | 4 | 89 |
| 7 | neat | 2 | MW[b] | 80 | 8 | 62 |
| 8 | neat | 3 | MW[b] | 100 | 4 | 95 |
| 9 | neat | 1 | MW[b] | 100 | 7 | 79 |
| 10 | neat | 2 | grinding | rt | 50 | 5 |
| 11 | ACN | 2 | MW[b] | 80 | 10 | 65 |
| 12 | THF | 2 | MW[b] | 65 | 10 | 59 |
| 13 | $CHCl_3$ | 2 | MW[b] | 60 | 10 | 71 |

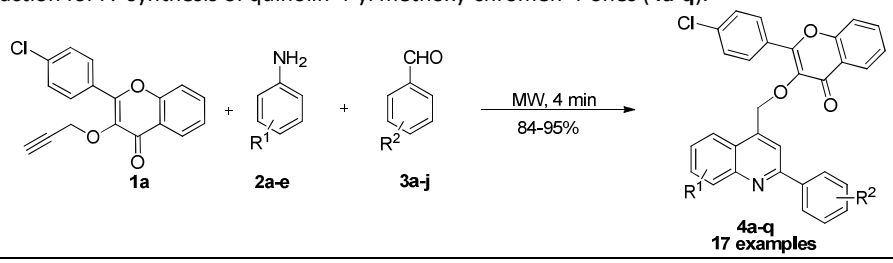
[a]General condition: 2-(4-chlorophenyl)-3-(prop-2-yn-1-yloxy)-4H-chromen-4-one**1a** (1.5 mmol), aniline **2a** (1 mmol), benzaldehyde**3a** (1 mmol); [b]AntonPaarMonowave 300 reactor. Irradiation Power: 850 W; Ramp time: 1 min. 70 $^0$C; holding temp: 100 $^0$C, [c]Conventional heating; [d]Isolated yield.

The efficiency of the reaction was studied in different heatingregime for example in microwave condition and to our delight;reaction proceeded smoothly increasing the yield of **4a** to 95%in just 10 min (Table 1, entry 2).To observe the effect of microwave condition, the reaction was irradiated for variable times (Table 1, entries 3-5) and temperature (Table 1, entries 6-7). It was observed that lowering down the irradiation time to 7 and 4 min remained equally effective(Table 1, entries 3, 4), but further reducing it to 3 min decreased the yield of **4a**to 77% (Table 1, entry 5). Similarly, increasing and decreasing the temperature of the reaction system did not bring the desired results (Table 1, entries 6, 7). Then, the effect and the amount of the $YbCl_3$ on the efficiency and yield of the product were briefly examined.It was notable that $YbCl_3$ played a vital role in the reaction system; in its absence reaction did not proceed under the same reaction conditions. However, increasing the catalyst loading of $YbCl_3$ to 3 mol% did not improve the product yield whereas decreasing the loading to 1 mol%lowered the yield significantly to 79% (Table 1, entries 8, 9).On the other hand, neat grinding of substrates and the catalyst for 50 min at ambient temperature resulted in scanty yield of the product **4a** (5%, Table 1, entry 10).

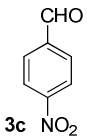
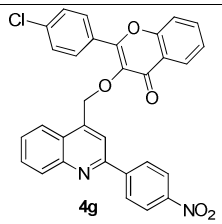
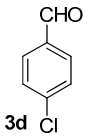
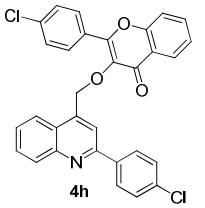
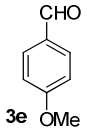
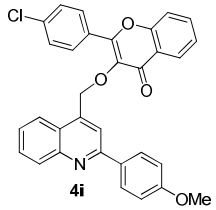
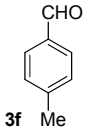
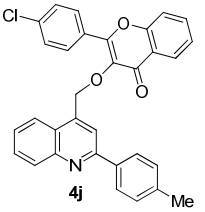
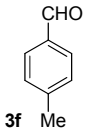
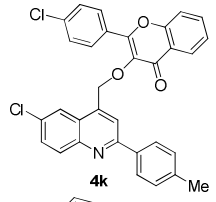
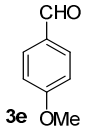
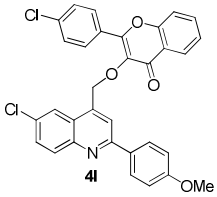
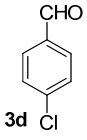
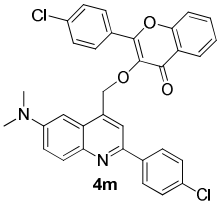
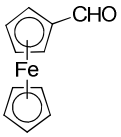
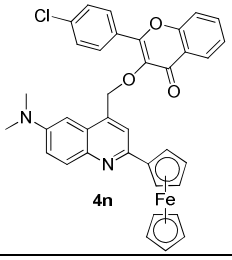
After that theeffect of the solvent on the reaction system was alsoinvestigated. $CHCl_3$ was found to be agood solvent affording the product **4a** in 71% yield (Table 1, entry 13) while acetonitrile and THF provided the moderate yields (Table 1, entries 11, 12). So, it led to conclude that microwave irradiation at 100 $^0$C for 4 minutes in neat condition was the optimal condition for the reaction to get best yield of the product**4a**. Recently, from the viewpoint ofgreenchemistry, solvent-free condition is highly demanded, so we carried out the reaction in neat condition.

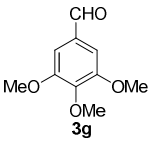
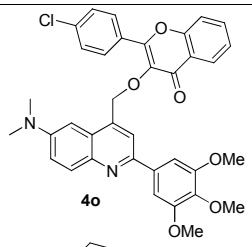
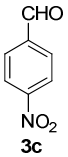
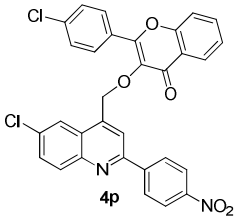
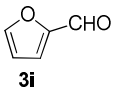
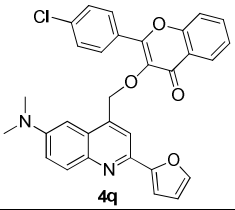
After getting optimization conditions, the substrate scope with respect to aldehyde and aryl amine was also examined (Table 2). Both electron-rich and electron-deficient anilines provided excellent yields. Electron-deficient aldehydes reacted with aniline and propargylated-flavone very efficiently in excellent yields but some electron-rich aromatic aldehydes need harsher condition (120 $^0$C MW). However, it should be mentioned that substituent effect on arylamine might affect the yields. This may be ascribed to the nature of nucleophilicity of amines, which is critical in the formation of imines from benzaldehydes and amines.

**Table 2.** Scope of reaction for $A^3$ synthesis of quinolin-4-yl methoxy-chromen-4-ones (**4a-q**).




| Entry | Propargylated flavone | Aniline | Aldehyde | Product | Temp (°C) | Yield[a] (%) |
|---|---|---|---|---|---|---|
| 1 | **1a** | **2a** | **3a** | **4a** | 100 | 95 |
| 2 | **1a** | **2b** | **3a** | **4b** | 100 | 94 |
| 3 | **1a** | **2c** | **3a** | **4c** | 100 | 91 |
| 4 | **1a** | **2d** | **3a** | **4d** | 100 | 89 |
| 5 | **1a** | **2e** | **3a** | **4e** | 100 | 86 |
| 6 | **1a** | **2a** | **3b** | **4f** | 120 | 84 |

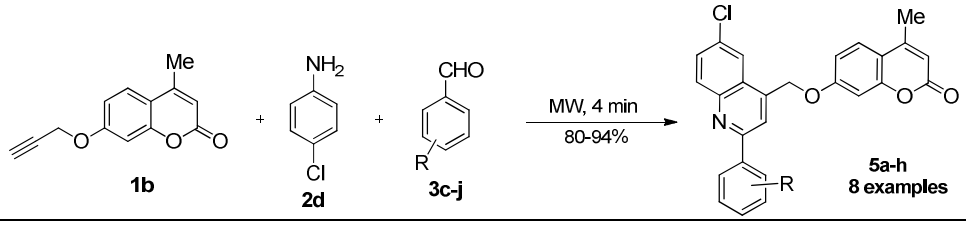
| | | | | | | |
|---|---|---|---|---|---|---|
| 7 | **1a** | **2a** |  **3c** |  **4g** | 100 | 90 |
| 8 | **1a** | **2a** |  **3d** |  **4h** | 100 | 88 |
| 9 | **1a** | **2a** |  **3e** |  **4i** | 120 | 86 |
| 10 | **1a** | **2a** |  **3f** |  **4j** | 120 | 90 |
| 11 | **1a** | **2d** |  **3f** |  **4k** | 120 | 89 |
| 12 | **1a** | **2d** |  **3e** |  **4l** | 120 | 85 |
| 13 | **1a** | **2b** |  **3d** |  **4m** | 100 | 90 |
| 14 | **1a** | **2b** |  **3j** |  **4n** | 100 | 85 |

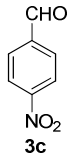
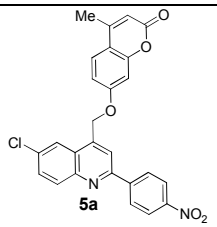
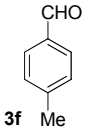
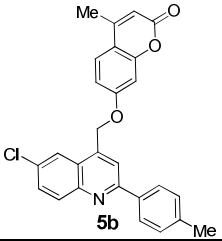
| | | | | | | |
|---|---|---|---|---|---|---|
| 15 | **1a** | **2b** |  **3g** |  **4o** | 120 | 86 |
| 16 | **1a** | **2d** |  **3c** |  **4p** | 100 | 92 |
| 17 | **1a** | **2b** |  **3i** |  **4q** | 100 | 87 |

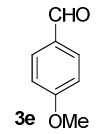
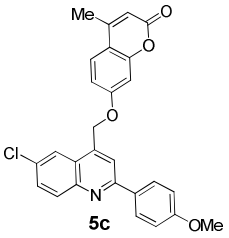
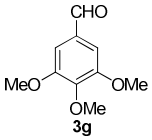
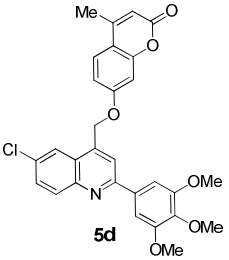
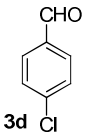
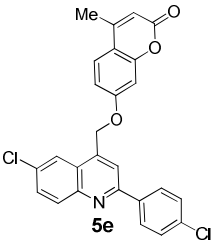
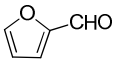
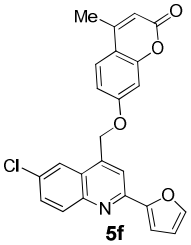
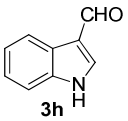
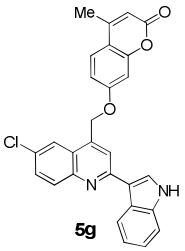
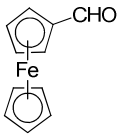
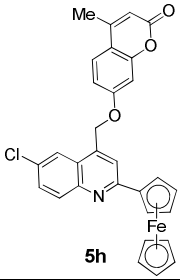
[a]Isolated yield.

Furthermore, the reaction was tested on other terminal alkyne 4-methyl-7-(prop-2-yn-1-yloxy)-2H-chromen-2-one (**1b**) also. After having obtained success with quinolin-4-yl methoxy-chromen-4-ones (**4a-q**), we extended the protocol for the formation of quinolin-4-yl methoxy-chromen-2-ones (**5a-h**)and delightfully on this scaffold also it worked equally well as shown in Table 3.The reaction tolerated variousaryl- or heteroaryl-aldehydes and generally similar reactivity trend was observed in both the series.

**Table 3.** Scope of reaction for A$^3$ synthesis of quinolin-4-yl methoxy-chromen-2-ones (**5a-h**).




| Entry | PropargylatedCoumarin | Aniline | Aldehyde | Product | Temp (°C) | Yield[a] (%) |
|---|---|---|---|---|---|---|
| 1 | **1b** | **2d** |  **3c** |  **5a** | 100 | 94 |
| 2 | **1b** | **2d** |  **3f** |  **5b** | 120 | 91 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 3 | **1b** | **2d** |  **3e** |  **5c** | 120 | 89 |
| 4 | **1b** | **2d** |  **3g** |  **5d** | 120 | 85 |
| 5 | **1b** | **2d** |  **3d** |  **5e** | 100 | 86 |
| 6 | **1b** | **2d** |  **3i** |  **5f** | 100 | 88 |
| 7 | **1b** | **2d** |  **3h** |  **5g** | 120 | 85 |
| 8 | **1b** | **2d** |  **3j** |  **5h** | 100 | 80 |

[a]Isolated yield.

The assigned structures of new products (**4a-q** and **5a-h**) were established from their spectroscopic data (IR, $^{1}$H, $^{13}$C NMR and HRMS). For example, IR spectrum of **4f** showed absorptions at 1703(>C=O), 1695(>C=C< flavone moeity) and 1630 (>C=N-) $cm^{-1}$. HR-MS of **4f** supported a molecular composition of $C_{33}H_{25}ClN_2O_3$, representing 22 degrees of unsaturation. In the $^{1}$H-NMR spectrum of **4f**, peak at $\delta_H$6.59 ppm (d, *J* = 10 Hz, 2H) appeared for 10'-H, dimethylamino group occurred at $\delta_H$2.96 ppm (s, 6H) and two methylene protons (-$CH_2$) resonating at $\delta_H$4.94 ppm (s, 2H). In $^{13}$C-NMR spectrum, δc 174.6ppm

confirms the presence of carbonyl group of flavone moiety. The characteristic peaks at δc 160.3 (C-4'), 155.2 (C-2), 155.0 (C-9), 154.2 (C-2'), 152.7 (C-13') and 76.5 (C-15) ppm confirm the formation of product **4f**. Likewise, in second series of the compounds (**5a-h**), characteristic peaks ofcoumarin moiety such as olefinic proton in the range of$\delta_H$ 6.15-6.65 ppm and ester carbonyl at δc 161.9-164.9 ppm are in full agreement withthe formation of the title compounds(Please see ESI).

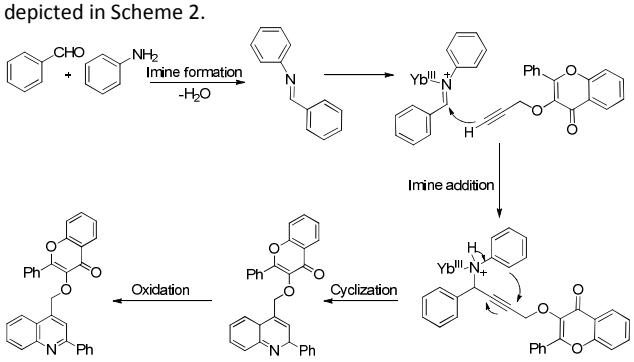
An important feature of catalyst is the recovery and reusability of the catalyst in the reaction which is shown in the recycling experiments of this catalysis on the reaction of benzaldehyde, aniline and 2-(4-chlorophenyl)-3-(prop-2-yn-1-yloxy)-4H-chromen-4-one (**1a**) (Table 4).After completion, the reaction mixture was dissolved in $CHCl_3$, the catalyst was filtered off and washed with $CHCl_3$ (3×10 mL) and recovered $YbCl_3$ showed goodcatalytic activity as the product **4a**obtained in 95, 90, 86 and 79% yield in at least four cycles insubsequent reactions respectively.

**Table 4.**Catalyst reuses.

| Entry | Run | Time (min) | Yield (%)[a] |
|---|---|---|---|
| 1 | 1st | 4 | 95 |
| 2 | 2nd | 4 | 90 |
| 3 | 3rd | 4 | 86 |
| 4 | 4th | 4 | 79 |

[a]Isolated yield.

On the basis of above results, the proposed mechanism for this one-pot synthesis of quinolin-4-yl methoxy-chromen-4-ones is depicted in Scheme 2.




**Scheme 2.**The plausible mechanism of one-pot synthesis of quinolin-4-yl methoxy-chromen-4-onescatalyzed by $YbCl_3$.

This one-pot three component reaction undergoes domino imine formation, subsequently imine addition and cyclization then finally oxidation. The high reactivity of $YbCl_3$ isascribed to the smaller radius of the $Yb^{3+}$ and the $H_2O$ in the reaction system do not deactivate or decompose the catalyst. On the basis of HSAB theory, the hard Lewis base site of nitrogen lone pair is coordinated by hard Lewis acid $Yb^{3+}$ and enhances the electrophilicity of the imine and then cyclization occurs followed by aromatization. $Yb^{3+}$ played an important role in both processes of imine addition and cyclization.

### 2.2. Biological Activity

The newly synthesized compounds were evaluated for their *in vitro* antibacterial activity against *S. aureus* and *B. subtilis* as examples of Gram-positive bacteria and *E. coli* and *S. flexneri* as examples of Gram-negative bacteria. They were also evaluated for their *in vitro* antifungal potential against *Candida albicans*fungal strain.

**Table 5.** Minimum inhibitory concentration (MIC, $mg/mL^{-1}$) of some newly synthesized compounds against bacterial and fungal strains

| Compound | Gram-positive | | Gram-negative | | Fungus |
|---|---|---|---|---|---|
| | *S.aureus* | *B. subtilis* | *E.coli* | *S.flexneri* | *C.albicans* |
| **4a** | >100 | >100 | >100 | 50 | 25 |
| **4b** | 12.5 | 12.5 | 50 | 12.5 | 12.5 |
| **4e** | 25 | >100 | 25 | 12.5 | 12.5 |
| **4f** | 12.5 | 12.5 | **0.78** | **3.12** | 25 |
| **4g** | 25 | 25 | 12.5 | 50 | **3.12** |
| **4m** | 25 | 50 | >100 | 12.5 | 50 |
| **4n** | **0.39** | **3.12** | **1.56** | **3.12** | **6.25** |
| **4o** | 25 | 6.25 | 12.5 | 6.25 | 25 |
| **4p** | 50 | 25 | 50 | 50 | >100 |
| **4q** | **1.56** | 6.25 | **1.56** | 12.5 | 25 |
| **5a** | >100 | 12.5 | >100 | 50 | **3.12** |
| **5d** | 6.25 | **3.12** | **3.12** | 12.5 | 25 |
| **5f** | **3.12** | 50 | **0.39** | **3.12** | 25 |
| **5g** | 6.25 | **3.12** | **0.39** | 6.25 | **0.39** |
| **5h** | **1.56** | **0.39** | **0.78** | **3.12** | 12.5 |
| Ampicillin | 0.78 | 0.39 | 1.56 | 0.78 | - |
| Cefadroxil | 1.56 | 3.12 | 0.78 | 1.56 | - |
| Fluconazole | - | - | - | - | 3.12 |

**2.2.1. Antibacterial activity.** As seen in the Table 5, compound **4n** (MIC: 0.39 mg/ml) and compounds **4q**, **5h** (MIC: 1.56 mg/ml) have shown better or equal antibacterial activity than positive controls against *S. aureus*. In case of *B. subtilis*, all compounds have shown lower activity than Ampicillin while compound **5h** (MIC: 0.39 mg/ml) has shown equal antibacterial activity against *B. subtilis*. Moreover, compounds **4n**, **5d**, **5g** (MIC: 3.12 mg/ml) were found equally potent as Cefadroxil against *B. subtilis*. Compounds **5f** and **5g** (MIC: 0.39 mg/ml) have shown better activity than positive controls against *E. coli* while compounds **4f**, **5h** (MIC: 0.78 mg/ml) and **4n**, **4q** (MIC: 1.56 mg/ml) have shown equal activity to the reference drugs. Compounds **4f**, **4n**, **5f**, **5h** have shown admirable antibacterial activity (MIC: 3.12 mg/ml) against *Shigella flexneri* compared to Ampicillin and Cefadroxil. Thus, the electron releasing group ($N(CH_3)_2$) and the compounds carrying heterocyclic moiety like furan, indoleorferrocene(**4n**, **4q** and **5h**)have shown excellent (MIC: 0.39 mg/ml) to good (MIC: 1.56 mg/ml) activity against *S. aureus*. Against *B. subtilis* also, either the electron donating group (OMe) or furan, indole and ferrocene carrying compounds (**4n**, **5d**, **5g**, **5h**) have shown equal (MIC: 0.39 and 3.12 mg/ml) antibacterial activity to the standard drugs. Against *E. coli*, compounds (**4f**, **4n,4q**, **5f,5g**, and **5h**) have shown excellent activity compared to Ampicillin and Cifadroxil depending on the electron releasing group ($N(CH_3)_2$) and hetrocyclic moiety(furan, indole or ferrocene) on the quinoline scaffold. Against *Shigella flexneri*, all compounds have shown low activity compared to the standard drugs without depending on functional groups on aromatic ring.

**2.2.2. Antifungal activity.** Compounds were subjected to MIC (minimum inhibitory concentration) determination by micro-dilution method [31] and the results are given in Table 5. Reference drugs Fluconazole was selected as positive control in antifungal activity assay. Compounds **5g** had shown excellent antifungal activity (MIC: 0.39 mg/ml) against *C. albicans*. Compounds **4g**, **5a** have shown similar antifungal activity (MIC: 3.12 mg/ml) as Fluconazole against *C. albicans* while others have shown lower activity. Thus, compounds carrying either electron withdrawing group ($-NO_2$) or indole and ferrocene (**4g**, **4n**, **5a** and **5g**) have shown excellent to moderate antifungal activity (MIC: 1.95 mg/ml) against *C. albicans* compared to standards drug.

## 3. Conclusion

In summary, we have reported a simple, fast and efficient three-component tandem reaction protocol for the synthesis of novel bioactive quinolin-4-yl methoxy-chromen-2- and -4-ones from aldehydes, amines, and propargylated-flavone or –coumarin using $YbCl_3$as catalyst under solvent-free and microwave condition. Products were obtained in excellent yields (80–95%) within 4 min. Mild reaction condition, improved yields, neat condition and reusability of catalyst without any appreciable loss of activity are the main advantages of our protocol. Compounds **4n** and **5h** exhibited the highest biological activity toward Gram-positive bacteria, while compounds **5f** and **5g** showed highest toward Gram-negative bacteria. On the other hand, compound **5g** displayed the highest activity against pathogenic fungi *C. albicans* using the MIC method. Further studies on the synthetic application of $YbCl_3$ as catalyst in organic transformations are currently underway in our group.

## 4. Experimental

All the required chemicals were purchased from Merck and Aldrich Chemical Company. Pre-coated aluminium sheets (silica gel 60 F254, Merck) were used for thin-layer chromatography (TLC) and spots were visualized under UV light.IR spectra were recorded with KBr on Thermo Nicolet FT-IR spectrophotometer.$^1$H NMR and $^{13}$C NMR spectra were recorded respectively on BrukerSpectrospin DPX 500 and Jeol Resonance ECX 400IIspectrometer using as solvent and trimethylsilane (TMS) as an internal standard. Spectra were processed using Bruker Topspin® 3.0.b.8. Splitting patterns are designated as follows; s = singlet, d = doublet, dd = doublets of doublet, m = multiplet. Chemical shift (δ) values are given in ppm. High-resolution mass spectra (HRMS) were obtained on a BrükermicrOTOF™-Q II mass spectrometer (ESIMS).

**4.1. Microwave Irradiation Experiment.** All microwave experiments were carried out in a dedicated Anton Paar Monowave-300 reactor, operating at a frequency of 2.455 GHz with continuous irradiation power of 0 to 850 W. The reactions were performed in a G-10 Borosilicate glass vial sealed with Teflon septum and placed in amicrowave cavity. Before microwave heating, oxygen was purgedinto the reaction vial. Initially, microwave of required power was used and temperature was being ramped from room temperature to a desired temperature. Once this temperature was attained, the process vial was held at this temperature for required time. The reactions were continuously stirred. Temperature was measured by an IR sensor. After the experiments a cooling jet cooled the reaction vessel to ambient temperature.

**4.2. General procedure for the synthesis of compounds (4a-q and 5a-h):**Aldehyde (1 mmol), arylamine (1 mmol), propargylated-flavone or -coumarin (1.2mmol) and $YbCl_3$ (6 mg, 2 mol %) were mixed well in a G-10 process vial capped with Teflon septum and oxygen was purged into it. After a pre-stirring for one minute, the vial was subjected to microwave irradiation with the initial ramp time of 1 minute at 70 $^0$C. The temperature was then raised to 100 $^0$C with the holding time of 4 min. The reaction was brought to room temperature, then crude product was dissolved in $CHCl_3$ (10 mL) and the catalyst was filtered off and washed with $CHCl_3$ (3×10 mL). The filtrate was washed with water (3×20 mL), dried over anhydrous $Na_2SO_4$ and concentrated under reduced pressure. The crude material was chromatographed on a silica gel column eluting with a mixture of ethyl acetate and hexane. (The purified products were identified by FTIR, NMR and HRMS spectra).

**4.3. Characterization data:**

**4.3.1. 2-(4-chlorophenyl)-3-((2-phenylquinolin-4-yl)methoxy)-4H-chromen-4-one (4a).** Yield: 95% as pale yellow liquid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.11 (d, *J* = 11 Hz, 1H), 7.89-7.87 (m, 3H), 7.71-7.68 (m, 1H), 7.65-7.60 (m, 2H), 7.53 (d, *J* = 9.5 Hz, 3H), 7.52-7.49 (m, 1H), 7.48-7.46 (m, 1H), 7.44-7.39 (m, 1H), 7.24-7.20 (m, 2H), 6.91-6.87 (m, 3H), 4.98 (s, 2H). $^{13}$C NMR (100MHz, $CDCl_3$, ppm): δ 175.4, 158.5, 156.2, 155.3, 140.6, 138.7, 137.2, 136.3, 134.7, 134.1, 133.7, 130.4, 130.2, 129.9, 129.7, 129.3, 129.1, 128.8, 128.5, 125.9, 125.3, 123.8, 120.3, 118.2, 115.5, 86.3, 76.6. FTIR (KBr, *v* = cm$^{-1}$): 3092, 3075, 2953, 2917, 1704, 1695, 1630, 1592, 1513, 1465, 1410, 1325, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{31}H_{20}ClNNaO_3$ $[M+Na]^+$: 512.1023, found: 512.1021.

**4.3.2. 2-(4-chlorophenyl)-3-((6-(dimethylamino)-2-phenylquinolin-4-yl)methoxy)-4H-chromen-4-one (4b)**. Yield: 94% as brownish semi-solid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.16 (dd, *J* = 2, 10 Hz, 1H), 8.06 (d, *J* = 11 Hz, 2H), 7.93 (dd, *J* = 1.5, 10 Hz, 2H), 7.73 (dd, *J* = 2, 10.5 Hz, 2H), 7.64-7.62 (m, 3H), 7.46 (d, *J* = 10 Hz, 1H), 7.39 (d, *J* = 11 Hz, 4H), 7.34-7.30 (m, 1H), 7.18 (s, 1H), 4.96 (s, 2H), 2.98 (s, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 174.2, 160.4, 155.1, 155.0, 154.3, 152.5, 143.1, 141.5, 138.4, 136.7, 133.5, 131.5, 130.0, 129.8, 129.7, 129.0, 128.5, 125.5, 125.2, 124.8, 123.7, 118.0, 111.1, 110.8, 110.5, 86.3, 76.5, 42.1. FTIR (KBr, *v* = cm$^{-1}$): 3090, 3072, 2949, 2915, 1705, 1692, 1625, 1594, 1515, 1460, 1412, 1303, 1244, 1176, 1029. HRMS (ESI+): m/z calcd. for $C_{33}H_{25}ClN_2NaO_3$ $[M+Na]^+$: 555.1445, found: 555.1432.

**4.3.3. 2-(4-chlorophenyl)-3-((6-nitro-2-phenylquinolin-4-yl)methoxy)-4H-chromen-4-one (4c)**. Yield: 91% as yellow semi-solid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.35 (d, *J* = 11 Hz, 2H), 8.15 (dd, *J* = 1.5, 10 Hz, 2H), 8.09-8.05 (m, 4H), 7.99 (d, *J* = 10 Hz, 1H), 7.78 (dd, *J* = 1.5, 10.5 Hz, 1H), 7.69-7.64 (m, 2H), 7.50-7.39 (m, 3H), 7.23-7.22 (m, 2H), 4.98 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 175.1, 160.5, 155.8, 155.5, 151.2, 146.2, 141.3, 140.2, 138.6, 136.8, 133.2, 133.6, 130.5, 130.2, 129.4, 129.0, 128.5, 125.6, 125.5, 125.1, 124.4, 123.9, 121.2, 118.3, 115.2, 86.3, 76.5. FTIR (KBr, *v* = cm$^{-1}$): 3095, 3077, 2953, 2915, 1702, 1685, 1628, 1598, 1517, 1490, 1455, 1410, 1360, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{31}H_{19}ClN_2NaO_5$ $[M+Na]^+$: 557.0874, found: 557.0871.

**4.3.4. 3-((6-chloro-2-phenylquinolin-4-yl)methoxy)-2-(4-chlorophenyl)-4H-chromen-4-one (4d)**. Yield: 89% as brownish semi-solid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.25 (dd, *J* = 2, 10 Hz, 1H), 8.11 (d, *J* = 10.5 Hz, 2H), 7.87 (d, *J* = 9 Hz, 2H), 7.70-7.41 (m, 6H), 7.28 (d, *J* = 3 Hz, 2H), 7.10 (dd, *J* = 3.5, 11 Hz, 2H), 6.95 (d, *J* = 11 Hz, 2H), 4.96 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 175.5, 161.4, 156.4, 155.3, 150.6, 138.7, 137.3, 136.2, 134.7, 134.1, 130.4, 130.2, 129.9, 129.2, 129.1, 128.8, 128.5, 128.4, 125.9, 125.4, 125.3, 123.7, 120.7, 118.1, 117.3, 86.5, 76.6. FTIR (KBr, *v* = cm$^{-1}$): 3092, 3075, 2953, 2917, 1701, 1695, 1629, 1592, 1513, 1465, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{31}H_{19}Cl_2NNaO_3$ $[M+Na]^+$: 546.0634, found: 546.0635.

**4.3.5. 2-(4-chlorophenyl)-3-((2-phenylbenzo[g]quinolin-4-yl)methoxy)-4H-chromen-4-one (4e)**. Yield: 86% as brownish semi-solid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.1-7.0 (m, 20 H), 4.83 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 175.7, 159.4, 156.5, 155.3, 153.9, 138.7, 137.3, 136.1, 134.8, 134.2, 133.7, 130.4, 130.2, 130.0, 129.7, 129.3, 129.1, 128.8, 128.5, 127.8, 126.5, 126.4, 125.8, 125.4, 123.4, 118.1, 109.5, 86.1, 76.8. FTIR (KBr, *v* = cm$^{-1}$): 3098, 3055, 2955, 2919, 1701, 1686, 1627, 1594, 1517, 1462, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{35}H_{22}ClNNaO_3$ $[M+Na]^+$: 562.1180, found: 562.1169.

**4.3.6. 2-(4-chlorophenyl)-3-((2-(4-(dimethylamino)phenyl)quinolin-4-yl)methoxy)-4H-chromen-4-one (4f)**. Yield: 84% as pale yellow semi-solid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.14 (dd, *J* = 2, 10 Hz, 1H), 8.04 (d, *J* = 11 Hz, 1H), 7.91 (dd, *J* = 1.5, 10 Hz, 1H), 7.72 (dd, *J* = 2, 10.5 Hz, 1H), 7.64-7.62 (m, 6H), 7.46 (d, *J* = 10 Hz, 1H), 7.39 (d, *J* = 11 Hz, 1H), 7.34-7.30 (m, 1H), 7.18-7.14 (m, 2H), 6.59 (d, *J* = 10 Hz, 2H), 4.94 (s, 2H), 2.96 (s, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 174.6, 160.3, 155.2, 155.0, 154.2, 152.7, 143.2, 141.7, 138.5, 136.7, 133.7, 133.4, 131.8, 130.1, 129.2, 129.0, 128.5, 125.5, 125.2, 124.8, 123.7, 118.0, 111.1, 110.8, 110.5, 86.0, 76.5, 39.9. FTIR (KBr, *v* = cm$^{-1}$): 3092, 3075, 2953, 2917, 1703, 1695, 1630, 1592, 1513, 1465, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{33}H_{25}ClN_2NaO_3$ $[M+Na]^+$: 555.1445, found: 555.1441.

**4.3.7. 2-(4-chlorophenyl)-3-((2-(4-nitrophenyl)quinolin-4-yl)methoxy)-4H-chromen-4-one (4g)**. Yield: 90% as yellow semi-solid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.34 (d, *J* = 11 Hz, 2H), 8.17 (dd, *J* = 1.5, 10 Hz, 2H), 8.08-8.03 (m, 4H), 7.98 (d, *J* = 10 Hz, 1H), 7.79 (dd, *J* = 1.5, 10.5 Hz, 1H), 7.67-7.65 (m, 2H), 7.52-7.35 (m, 3H), 7.25-7.21 (m, 2H), 4.96 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 174.8, 160.9, 155.5, 155.2, 151.1, 146.5, 141.9, 140.0, 138.6, 136.9, 133.9, 133.5, 130.5, 130.3, 129.3, 129.1, 128.7, 125.7, 125.4, 125.0, 124.3, 123.9, 121.1, 118.1, 115.3, 86.2, 76.5. FTIR (KBr, *v* = cm$^{-1}$): 3095, 3077, 2953, 2915, 1700, 1685, 1627, 1598, 1517, 1490, 1455, 1410, 1360, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{31}H_{19}ClN_2NaO_5$ $[M+Na]^+$: 557.0874, found: 557.0865.

**4.3.8. 2-(4-chlorophenyl)-3-((2-(4-chlorophenyl)quinolin-4-yl)methoxy)-4H-chromen-4-one (4h)**. Yield: 88% as brownish semi-solid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.16 (d, *J* = 10 Hz, 1H), 8.05 (d, *J* = 11 Hz, 1H), 7.94 (d, *J* = 9.5 Hz, 1H), 7.77-7.72 (m, 5H), 7.65-7.61 (m, 1H), 7.43-7.40 (m, 6H), 7.34 (t, *J* = 9.5 Hz, 1H), 7.21-7.17 (m, 1H), 4.96 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 174.7, 161.4, 155.4, 155.1, 152.8, 144.8, 141.8, 140.8, 138.6, 136.8, 134.6, 133.8, 133.4, 130.8, 130.2, 129.4, 129.3, 129.0, 128.6, 125.6, 125.3, 124.9, 123.8, 121.1, 118.0, 86.2, 76.5. FTIR (KBr, *v* = cm$^{-1}$): 3092, 3075, 2953, 2917, 1699, 1695, 1627, 1592, 1513, 1465, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{31}H_{19}Cl_2NNaO_3$ $[M+Na]^+$: 546.0634, found: 546.0634.

**4.3.9. 2-(4-chlorophenyl)-3-((2-(4-methoxyphenyl)quinolin-4-yl)methoxy)-4H-chromen-4-one (4i).** Yield: 86% as brownish semi-solid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.22 (dd, *J* = 1.5, 11.5 Hz, 1H), 8.09 (dd, *J* = 2.5, 8.5 Hz, 2H), 8.00 (dd, *J* = 1.5, 9.5 Hz, 1H), 7.82-7.79 (m, 5H), 7.71-7.67 (m, 1H), 7.52 (d, *J* = 10.5 Hz, 1H), 7.47-7.44 (m, 3H), 7.41-7.39 (m, 1H), 7.27- 7.23 (m, 1H), 6.98 (s, 1H), 4.98 (s, 1H), 3.85 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 174.9, 164.7, 155.6, 155.3, 153.0, 151.0, 145.9, 142.0, 138.7, 137.0, 133.9, 133.5, 132.1, 130.4, 130.0, 129.5, 129.1, 128.8, 125.9, 125.5, 125.1, 124.0, 120.4, 118.1, 114.4, 86.3, 76.5, 55.7. FTIR (KBr, *v* = cm$^{-1}$): 3089, 3067, 2950, 2916, 1702, 1695, 1629, 1592, 1513, 1425, 1410, 1246, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{32}H_{22}ClNNaO_4$ $[M+Na]^+$: 542.1129, found: 542.1118.

**4.3.10. 2-(4-chlorophenyl)-3-((2-(p-tolyl)quinolin-4-yl)methoxy)-4H-chromen-4-one (4*j*)**. Yield: 90% as brownish semi-solid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.23 (dd, *J* = 1.5, 10 Hz, 2H), 8.09 (d, *J* = 11 Hz, 1H), 8.00 (dd, *J* = 1.5, 10 Hz, 1H), 7.81 (dd, *J* = 1.5 Hz, 10 Hz, 2H), 7.74 (d, *J* = 10.5 Hz, 1H), 7.48-7.44 (m, 3H), 7.39 (t, *J* = 1.5 Hz, 1H), 7.29 (d, *J* = 10 Hz, 2H), 7.25-7.22 (m, 2H), 4.99 (s, 2H), 2.40 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 174.8, 158.5, 155.5, 155.2, 153.0, 148.1, 145.6, 143.4, 141.9, 138.7, 136.9, 134.2, 133.8, 133.5, 130.3, 129.9, 129.8, 129.4, 129.1, 128.7, 125.8, 125.4, 125.0, 123.9, 118.1, 86.3, 76.5, 21.9. FTIR (KBr, *v* = cm$^{-1}$): 3092, 3075, 2953, 2917, 1705, 1695, 1630, 1592, 1513, 1465, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{32}H_{22}ClNNaO_3$ $[M+Na]^+$: 526.1180, found: 526.1183.

**4.3.11. 3-((6-chloro-2-(p-tolyl)quinolin-4-yl)methoxy)-2-(4-chlorophenyl)-4H-chromen-4-one (4k)**. Yield: 89% as brownish semi-solid; $^1$H NMR (500 MHz, $CDCl_3$, ppm): δ 8.17 (m, 3H), 7.75 (d, *J* = 7.5 Hz, 2H), 7.69 (t, *J* = 7 Hz, 1H), 7.54-7.46 (m, 3H), 7.40 (t, *J* = 7.5 Hz, 1H), 7.31-7.28 (m, 2H), 7.09 (d, *J* = 8 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 4.98 (s, 2H), 2.42 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 175.2, 156.0, 155.4, 150.8, 149.0, 145.9, 141.5, 138.8, 137.2, 134.2, 134.0, 130.4, 130.0, 129.8, 129.4, 129.0, 128.8, 128.3, 125.9, 125.3, 125.2, 123.9, 120.8, 118.2, 117.4, 86.4, 76.6, 22.0. FTIR (KBr, *v* = cm$^{-1}$): 3096, 3075, 2959, 2915, 1698, 1695, 1630, 1592, 1513, 1465, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{32}H_{21}Cl_2NNaO_3$ $[M+Na]^+$: 560.0790, found: 560.0785.

**4.3.12. 3-((6-chloro-2-(4-methoxyphenyl)quinolin-4-yl)methoxy)-2-(4-chlorophenyl)-4H-chromen-4-one (4l)**. Yield: 85% as pale yellow semi-solid; $^1$H NMR (500 MHz, $CDCl_3$, ppm): δ 8.22-8.08 (m, 2H), 7.81-7.66 (m, 4H), 7.53-7.37 (m, 3H), 7.25 (s, 1H), 7.07 (d, *J* = 8 Hz, 1H), 6.97-6.93 (m, 5H), 4.96 (s, 2H), 3.85 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 175.1, 164.8, 155.9, 155.3, 150.8, 145.7, 141.7, 138.7, 137.1, 135.6, 134.0, 132.2, 130.3, 129.8, 129.3, 129.0, 128.8, 128.2, 125.8, 125.2, 123.8, 120.8, 118.1, 117.4, 114.4, 87.0, 76.6, 55.6. FTIR (KBr, *v* = cm$^{-1}$): 3092, 3075, 2953, 2917, 1701, 1695, 1628, 1592, 1513, 1465, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{32}H_{21}Cl_2NNaO_4$ $[M+Na]^+$: 576.0739, found: 576.0735.

**4.3.13. 2-(4-chlorophenyl)-3-((2-(4-chlorophenyl)-6-(dimethylamino) quinolin-4-yl)methoxy)-4H-chromen-4-one (4m).** Yield: 90% as brownish semi-solid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.21-8.09 (m, 2H), 7.69-7.67 (m, 4H), 7.52-7.37 (m, 3H), 7.05-6.94 (m, 3H), 6.62 (d, *J* = 10 Hz, 4H), 4.96 (s, 2H), 3.01 (s, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 175.1, 155.9, 155.1, 154.5, 151.2, 145.2, 141.5, 138.6, 137.0, 134.0, 132.3, 130.3, 129.2, 129.0, 128.7, 128.0, 125.6, 125.1, 124.7, 124.5, 123.7, 121.0, 118.1, 117.4, 111.0, 86.3, 76.6, 39.9. FTIR (KBr, *v* = cm$^{-1}$): 3092, 3075, 2953, 2917, 1701, 1695, 1629, 1592, 1513, 1465, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{33}H_{24}Cl_2N_2NaO_3$ $[M+Na]^+$: 589.1056, found: 589.1051.

**4.3.14. 3-((6-dimethylamino-2-(ferrocenyl)quinolin-4-yl)methoxy)-2-(4-chlorophenyl)-4H-chromen-4-one (4n)**. Yield: 85% as blackish semi-solid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.23 (dd, *J* = 1.5, 10 Hz, 1H), 8.10 (dd, *J* = 2.5, 9 Hz, 2H), 7.69-7.67 (m, 1H), 7.53 (d, *J* = 10.5 Hz, 1H), 7.48-7.45 (m, 2H), 7.42-7.38 (m, 1H), 7.28 (d, *J* = 3 Hz, 1H), 7.09 (dd, *J* = 3, 11 Hz, 2H), 6.96 (s, 1H), 4.96 (s, 2H), 4.79 (t, *J* = 2.5 Hz, 2H), 4.62 (t, *J* = 2.5 Hz, 2H), 4.25 (s, 5H), 3.01 (s, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 175.4, 156.2, 155.3, 150.8, 146.1, 142.3, 138.7, 137.2, 134.1, 130.4, 129.3, 128.9, 128.8, 128.3, 125.8, 125.3, 125.2, 123.8, 120.8, 118.1, 117.4, 87.2, 78.4, 76.9, 73.8, 70.0, 69.9, 42.5. FTIR (KBr, *v* = cm$^{-1}$): 3102, 3092, 3078, 2956, 2915, 1703, 1695, 1630, 1592, 1513, 1465, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{37}H_{29}ClFeN_2NaO_3$ $[M+Na]^+$: 663.1108, found: 663.1102.

**4.3.15. 2-(4-chlorophenyl)-3-((6-(dimethylamino)-2-(3,4,5-trimethoxyphenyl)quinolin-4-yl)methoxy)-4H-chromen-4-one (4o).** Yield: 86% as brownish semi-solid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.09 (dd, *J* = 3, 10 Hz, 2H), 7.68-7.65 (m, 4H), 7.51-7.37 (m, 3 H), 7.32-7.28 (m, 3H), 7.25 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 175.3, 156.2, 155.1, 151.0, 150.4, 147.1, 142.6, 140.0, 138.7, 137.3, 134.2, 132.4, 130.6, 130.4, 129.3, 128.8, 128.1, 125.7, 125.3, 125.1, 124.5, 123.5, 120.8, 118.1, 102.2, 86.5, 76.6, 61.0, 56.3, 42.2. FTIR (KBr, *v* = cm$^{-1}$): 3092, 3075, 2953, 2917,1699, 1695, 1627, 1592, 1513, 1465, 1410, 1346, 1247, 1174, 1030. HRMS (ESI+): m/z calcd. for $C_{36}H_{31}ClN_2NaO_6$ $[M+Na]^+$: 645.1762, found: 645.1756.

**4.3.16. 3-((6-chloro-2-(4-nitrophenyl)quinolin-4-yl)methoxy)-2-(4-chlorophenyl)-4H-chromen-4-one (4p)**. Yield: 92% as yellow liquid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.33 (dd, *J* = 2, 10.5 Hz, 2H), 8.21 (d, *J* = 10.5 Hz, 1H), 8.09-8.01 (m, 2H), 8.03-8.01 (m, 2H), 7.70-7.66 (m, 1H), 7.53 (d, *J* = 10.5 Hz, 1H), 7.45 (dd, *J* = 3, 11 Hz, 2H), 7.41-7.37 (m, 1H), 7.25-7.24 (m, 2H), 7.09-7.07 (m, 1H), 6.93 (d, *J* = 3H), 4.93 (s, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 175.5, 156.4, 155.4, 151.2, 150.6, 147.0, 142.6, 140.0, 138.7, 137.3, 134.2, 132.4, 130.6, 130.4, 129.3, 128.8, 128.4, 125.9, 125.4, 125.3, 124.4, 123.7, 120.7, 118.2, 117.4, 87.6, 76.7. FTIR (KBr, *v* = cm$^{-1}$): 3092, 3075, 2953, 2917, 1695, 1693, 1624, 1592, 1513, 1455, 1418, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{31}H_{18}Cl_2N_2NaO_5$ [M+Na]$^+$: 591.0484, found: 591.0475.

**4.3.17. 2-(4-chlorophenyl)-3-((6-(dimethylamino)-2-(furan-2-yl)quinolin-4-yl)methoxy)-4H-chromen-4-one (4q)**. Yield: 87% as black-brown liquid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.21 (d, *J* = 10 Hz, 1H), 8.09 (d, *J* = 10.5 Hz, 1H), 7.69-7.67 (m, 2H), 7.53 (d, *J* = 10.5 Hz, 1H), 7.45 (d, *J* = 10 Hz, 1H), 7.41-7.37 (m, 1H), 7.26-7.25 (m, 3H), 7.08-7.05 (m, 2H), 6.93 (dd, *J* = 1, 11 Hz, 2H), 6.58 (s, 1H), 4.94 (s, 2H), 3.01 (s, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 175.3, 160.9, 156.2, 155.3, 152.9, 150.8, 148.5, 143.2, 138.7, 137.2, 134.1, 132.1, 130.4, 129.2, 128.9, 128.8, 128.2, 125.8, 125.3, 125.2, 123.7, 121.8, 120.8, 118.1, 117.4, 112.8, 76.7, 41.8. FTIR (KBr, *v* = cm$^{-1}$): 3092, 3075, 2953, 2917, 1701, 1695, 1628, 1592, 1513, 1465, 1410, 1348, 1321, 1247, 1174, 1042. HRMS (ESI+): m/z calcd. for $C_{31}H_{23}ClN_2NaO_4$ [M+Na]$^+$: 545.1238, found: 545.1229.

**4.3.18. 7-((6-chloro-2-(4-nitrophenyl)quinolin-4-yl)methoxy)-4-methyl-2H-chromen-2-one (5a)**. Yield: 94% as brown liquid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.38 (d, *J* = 11 Hz, 3H), 8.07 (d, *J* = 10.5Hz, 3H), 7.52 (d, *J* = 11.5 Hz, 1H), 7.30 (d, *J* = 3 Hz, 1H), 7.12 (dd, *J* = 3, 11 Hz, 2H), 6.92 (d, *J* = 4 Hz, 1H), 6.16 (s, 1H), 4.75 (s, 2H), 2.40 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 163.4, 161.7, 160.5, 155.1, 153.0, 151.2, 150.5, 140.1, 136.1, 130.7, 128.8, 128.6, 125.8, 125.6, 124.4, 120.6, 117.3, 114.4, 113.0, 112.4, 102.2, 86.1, 72.4, 18.8. FTIR (KBr, *v* = cm$^{-1}$): 3105, 3078, 2958, 2917, 1720, 1628, 1599, 1513, 1475, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{26}H_{17}ClN_2NaO_5$ [M+Na]$^+$: 495.0718, found: 495.0712.

**4.3.19. 7-((6-chloro-2-(p-tolyl)quinolin-4-yl)methoxy)-4-methyl-2H-chromen-2-one (5b)**. Yield: 91% as brown liquid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 7.78 (d, *J* = 10 Hz, 2H), 7.53 (d, *J* = 7.53, *J* = 10.5 Hz, 1H), 7.34-7.30 (m, 4H), 7.12 (dd, *J* = 10, 18 Hz, 2H), 6.97-6.93 (m, 2H), 6.18 (s, 1H), 4.76 (s, 2H), 2.44 (s, 3H), 2.40 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 162.7, 161.6, 160.3, 154.7, 152.9, 150.4, 145.6, 135.8, 133.9, 129.8, 129.6, 128.6, 128.2, 125.5, 125.1, 120.5, 117.1, 114.1, 112.8, 112.0, 101.9, 86.6, 72.4, 21.7, 18.5. FTIR (KBr, *v* = cm$^{-1}$): 3105, 3078, 2958, 2917, 1725, 1627, 1513, 1465, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{27}H_{20}ClNNaO_3$ [M+Na]$^+$: 464.1023, found: 464.1019.

**4.3.20. 7-((6-chloro-2-(4-methoxyphenyl)quinolin-4-yl)methoxy)-4-methyl-2H-chromen-2-one (5c)**. Yield: 89% as light yellow liquid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 7.85 (d, *J* = 11 Hz,2H), 7.54 (d, *J* = 11.5 Hz, 1H), 7.32 (d, *J* = 3 Hz, 1H), 7.14 (dd, *J* = 3, 10.5 Hz, 2H), 7.01 (d, *J* = 11 Hz, 2H), 6.97-6.94 (m, 3H), 6.19 (s, 1H), 4.84 (s, 2H), 3.90 (s, 3H), 2.41 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 164.9, 161.9, 160.6, 155.1, 153.1, 150.6, 134.4, 132.3, 129.9, 128.8, 128.5, 125.8, 125.5, 123.5, 120.7, 117.3, 114.5, 114.4, 113.1, 112.4, 102.2, 86.8, 76.7, 55.7, 18.8. FTIR (KBr, *v* = cm$^{-1}$): 3105, 3078, 2958, 2917, 1723, 1629, 1592, 1513, 1465, 1410, 1245, 1173, 1024. HRMS (ESI+): m/z calcd. for $C_{27}H_{20}ClNNaO_4$ [M+Na]$^+$: 480.0973, found: 480.0965.

**4.3.21. 7-((6-chloro-2-(3,4,5-trimethoxyphenyl)quinolin-4-yl)methoxy)-4-methyl-2H-chromen-2-one (5d).** Yield: 85% as brown liquid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.02 (d, *J* = 10.5 Hz, 1H), 7.79 (d, *J* = 3 Hz, 1H), 7.63 (s, 3H), 7.60 (dd, *J* = 3, 11 Hz, 1H), 7.45-7.41 (m, 3H), 6.65 (s, 1H), 5.26 (s, 2H), 3.80 (s, 9H), 2.4 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 162.5, 161.5, 160.5, 155.0, 153.7, 152.9, 150.7, 143.6, 137.9, 131.7, 128.9, 128.2, 125.7, 125.2, 120.7, 117.3, 114.3, 112.9, 112.3, 106.8, 102.2, 86.3, 76.6, 61.0, 56.3, 18.7. FTIR (KBr, *v* = cm$^{-1}$): 3105, 3078, 2958, 2917, 1726, 1627, 1593, 1513, 1468, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{29}H_{24}ClNNaO_6$ [M+Na]$^+$: 540.1184, found: 540.1186.

**4.3.22. 7-((6-chloro-2-(4-chlorophenyl)quinolin-4-yl)methoxy)-4-methyl-2H-chromen-2-one (5e).** Yield: 86% as brown liquid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 8.33-8.32 (m, 3H), 8.01-7.99 (m, 4H), 7.62-7.59 (m, 1H), 7.46-7.43 (m, 3H), 6.66 (s, 1H), 5.26 (s, 2H), 2.42 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 162.5, 161.5, 160.5, 155.0, 152.8, 150.7, 141.1, 137.7, 134.7, 131.0, 129.5, 128.9, 128.3, 125.8, 125.3, 120.7, 117.3, 114.3, 112.9, 112.4, 102.2, 86.5, 76.6, 18.7. FTIR (KBr, *v* = cm$^{-1}$): 3102, 3078, 2958, 2917, 1722, 1629, 1595, 1513, 1465, 1410, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{26}H_{17}Cl_2NNaO_3$ [M+Na]$^+$: 484.0477, found: 484.0469.

**4.3.23. 7-((6-chloro-2-(furan-2-yl)quinolin-4-yl)methoxy)-4-methyl-2H-chromen-2-one (5f).** Yield: 88% as brown liquid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 7.75 (t, *J* = 1Hz, 1H), 7.58 (dd, *J* = 3, 9 Hz, 1H), 7.35 (d, *J* = 3 Hz, 2H), 7.31 (dd, *J* = 0.5, 3 Hz, 1H), 7.16 (dd, *J* = 3.5, 11 Hz, 2H), 7.01-6.97 (m, 2H), 6.66-6.65 (m, 1H), 6.21 (s, 1H), 4.85 (s, 2H), 2.44 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 162.9, 161.6, 160.5, 155.0, 153.0, 152.9, 150.7, 148.3, 136.1, 128.9, 128.4, 125.8, 125.3, 121.5, 120.7, 117.4, 114.3, 112.9, 112.8, 112.4, 102.2, 86.3, 76.6, 18.8. FTIR (KBr, *v* = cm$^{-1}$): 3107, 3075, 2953, 2915, 1725, 1630, 1595, 1513, 1465, 1410, 1247, 1174, 1024. HRMS (ESI+): m/z calcd. for $C_{24}H_{16}ClNNaO_4$ [M+Na]$^+$: 440.0660, found: 440.0664.

**4.3.24. 7-((6-chloro-2-(1H-indol-3-yl)quinolin-4-yl)methoxy)-4-methyl-2H-chromen-2-one (5g)**. Yield: 85% as brown liquid; $^1$H NMR (500 MHz, $CDCl_3$, ppm): δ 8.17 (br, s, 1H, $D_2O$ exchangeable), 7.75 (d, *J* = 8 Hz, 1H), 7.42-7.37 (m, 3H), 7.29 (t, *J* = 7 Hz, 1H), 7.22 (t, *J* = 7 Hz, 1H), 7.18-7.16 (m, 3H), 6.99 (m, 2H), 6.63 (s, 1H), 6.20 (s, 1H), 4.74 (s, 2H), 2.35 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 162.6, 160.6, 160.2, 155.7, 154.1, 152.5, 144.8, 136.3, 132.5, 131.0, 130.7, 128.4, 125.6, 124.3, 123.2, 121.4, 121.2, 120.9, 119.6, 114.0, 112.3, 111.5, 110.8, 110.2, 102, 86.4, 76.6, 18.5. FTIR (KBr, *v* = cm$^{-1}$): 3307, 3114, 3075, 2958, 2917, 1723, 1628, 1599, 1515, 1463, 1410, 1247, 1174, 1024. HRMS (ESI+): m/z calcd. for $C_{28}H_{19}ClN_2NaO_3$ [M+Na]$^+$: 489.0976, found: 489.0968.

**4.3.25. 7-((6-chloro-2-(ferrocenyl)quinolin-4-yl)methoxy)-4-methyl-2H-chromen-2-one (5h).** Yield: 80% as black liquid; $^1$H NMR (400 MHz, $CDCl_3$, ppm): δ 7.50 (d, *J* = 10.5 Hz, 1H), 7.29 (s, 1H), 7.10 (d, *J* = 3.5 Hz, 2H), 6.91 (d, *J* = 11 Hz, 3H), 6.15 (s, 1H), 4.78 (s, 2H), 4.73 (s, 2H), 4.61 (s, 2H), 2.38 (s, 3H). $^{13}$C NMR (100 MHz, $CDCl_3$, ppm): δ 161.9, 160.5, 155.0, 153.2, 150.8, 147.6, 133.5, 128.9, 128.4, 125.8, 125.3, 120.8, 117.4, 114.3, 113.0, 112.3, 102.2, 86.5, 79.1, 76.7, 73.7, 69.9, 69.9, 18.8. FTIR (KBr, *v* = cm$^{-1}$): 3102, 3077, 2952, 2915, 1720, 1629, 1594, 1515, 1465, 1412, 1247, 1174, 1029. HRMS (ESI+): m/z calcd. for $C_{30}H_{22}ClFeNNaO_3$ [M+Na]$^+$: 558.0529, found: 558.0518.

### 4.4. Biological activity

**4.4.1. Antibacterial assay.** Minimum inhibitory concentration (MIC) is the lowest concentration of an antimicrobial compound that inhibits the visible growth of a microorganism. MIC values of the compounds against bacterial isolates were determined on the basis of micro-well dilution method following National committee for clinical laboratory standards (NCCLS) recommendations.[32] In this method we made stock of chemically synthesized compounds at a

concentration of 10 mg/ml in DMSO, which was further converted to working solution of concentration 1 mg/ml. Using a micropipette, 100 µl of media into all wells of pre-sterilized micro titre plate was dispensed (experiment was done in triplicate). Two fold serial dilutions (100, 50, 25, 0.78125 mg/mL) were carried out from the well # 1 to the well # 10 and excess media (100 µl) was discarded from the last well (# 10). Liquid broth culture of test organism was grown to log phase in Luria Bertani broth (LB broth) for 24 h at 37 °C. The optical density of liquid culture was determined at 600 nm and diluted in such a way that each well received 107 cfu/ ml of bacterial culture. Appropriate positive and negative control was also included in the study. Positive control contained only microbial cells whereas negative control contained only standard drug solution (Ampicillin and Cefadroxil). All experimental procedures were performed under sterile condition using bio-safety hood and microtitre plates were incubated at 37 °C for 24 h.

**4.4.2. Antifungal assay.**MIC of standard antifungal drugs viz. Fluconazole and the synthesized compounds against fungal isolates were determined by the broth micro dilution method as described by the NCCLS, 1997.[32]Liquid broth culture of test organism was grown to a suitable phase in Yeast, Peptone, and D-Glucose (YPD) media for 48 h at 30 °C. The optical density of liquid culture was determined at 600 nm and diluted in such a way that each well received 104 cfu/ml of fungal suspension. The further procedure was similar to above mentioned antibacterial assay.

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## Supplementary Material

Characterization data $^{1}$H, and $^{13}$C NMRspectra associated with this article are available.

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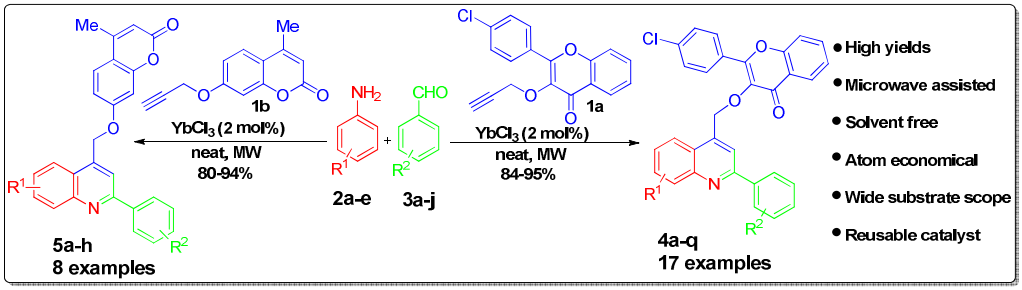


A novel catalytic MW assisted approach for multicomponent $A^3$ synthesis of Quinolin-4-yl methoxy-chromen-2 and -4-ones has been developed. Main features include high yields, short reaction time, avoids use of organic solventsand reuse of $YbCl_3$.