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Prashant S. Mandal, A. Vijay Kumar

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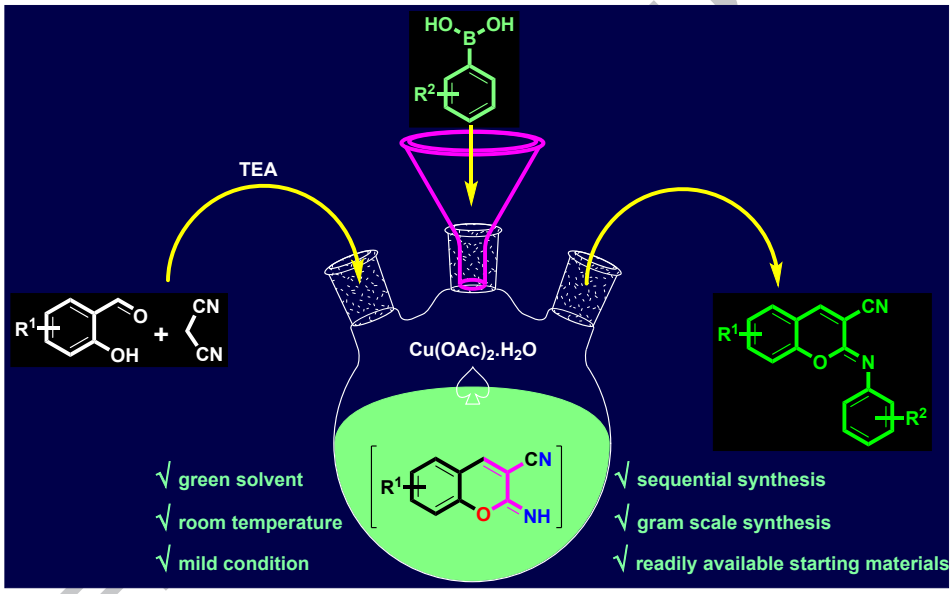
Prashant S. Mandal and A. Vijay Kumar*
Department of Chemistry, Institute of Chemical Technology, Matunga, Mumbai, Maharashtra, India – 400019



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ABSTRACT

An efficient approach for the synthesis of biologically interesting *N*-aryl-2-iminocoumarins by a copper-catalyzed one-pot procedure has been developed by the reaction of 2-hydroxybenzaldehydes, malononitrile and arylboronic acids using triethylamine as a base in a bio-mass-derived green solvent 2-MethylTHF at room temperature. This protocol allows access to several *N*-aryl-2-iminocoumarins in high yields in a relatively short period of time under mild reaction conditions. The procedure operates by a simple telescoped process wherein 2-imino-2*H*-chromene-3-carbonitriles are formed *in situ* by the reaction of 2-hydroxybenzaldehyde, malononitrile, and TEA. Further a subsequent one-pot reaction of imine with the arylboronic afforded the target compounds. To understand the reaction mechanism, MALDI-ESI studies were performed, which showed the *in situ* generated iminocoumarins to be in ligation cooper to form a copper-iminocoumarin complex thus facilitating the smooth formation of *N*-aryl-2-iminocoumarins in the reaction. Overall, this protocol is practically valuable, useful in organic synthesis, shows good functional group tolerance and provides access to a diverse array of *N*-aryl-2-iminocoumarins derivatives.

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1. **Introduction**

The *N*-arylation of imines is an active region of research in organic synthesis. Transition metal catalyzed C-N bond formation reactions are an important transformations that enables the synthesis of valuable aryl imine products.[1] Currently only two processes are generally available for the C-N bond formation *i.e.* Ullmann[2] and Chan-Lam-Evan [3] coupling reaction; both of these methods are quite general and are commonly used for synthesis of relevant nitrogen based compounds.[4] Chan-Lam-Evan is a robust copper-catalyzed reaction which involves the cross-coupling of aryl boronic acids with heteroatom nucleophiles such as amines, anilines, amides, imines, ureas, sulfoximines, carbamates, carboxylic acids, phenols and thiols.[5,6]

Coumarins and their derivatives are an important class of oxygen based heteroaromatic structural units that are found in several biologically active molecules and natural products. They are well-known for diverse applications[7-9] in perfumery [10] and as dyes in laser technology.[11] These compounds are known to show biological properties relevant for human health such as antibacterial,[12] antifungal,[13] anti-HIV, [14] and anti-tumor[15] activities. Analogous to coumarins, iminocoumarins are a class of coumarins that are of profound value due to their interesting applications. A recently discovered fused core iminocoumarin natural products *i.e.* Hyrtimomine A and B (Figure 1), which have been isolated from an Okinawan marine sponge *Hyrtios sp*[16] and several other fused core iminocoumarin natural products are found to show diverse biological properties such as antimalarial and anticancer,[17,18] antiproliferative activity,[19] antimicrobial,[20,21] anti-inflammatory,[22-24] mitogen-activated protein kinase inhibition (MK-2),[25] dynamins I and II GT Pase,[26] HIV-1 integrase inhibition,[27] and cell imaging.[28-31] Additionally, they are also useful as fluorescent dyes,[32] and sensors for thiols [33] and H_2S.[34]

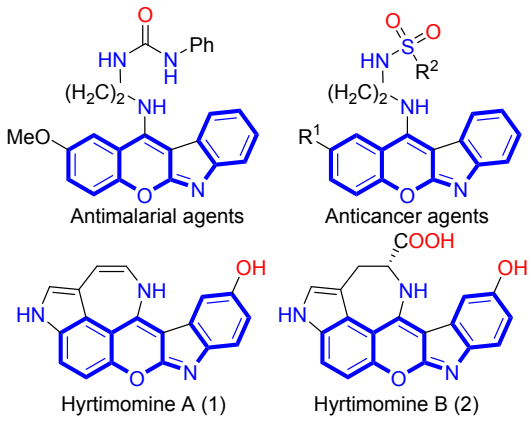

Figure 1 Representative molecules having the *N*-Phenyl iminocoumarin core structure

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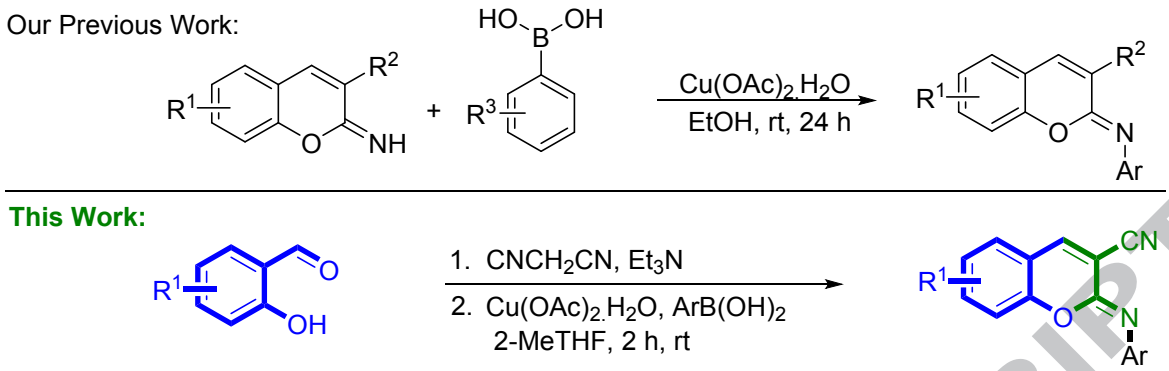
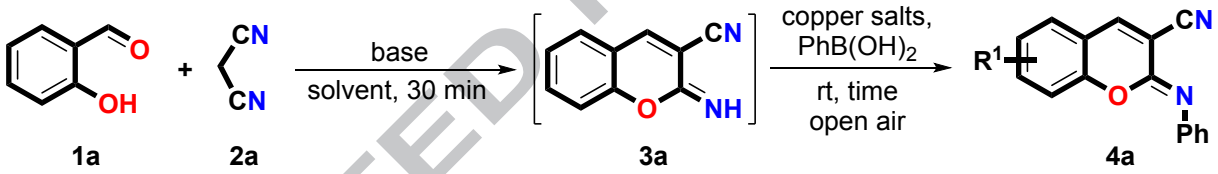


Figure 2. Copper-catalyzed cascade reactions

Despite their importance, these derivatives are less explored in Chan-Lam-Evans protocol. Our group was the first to report the Chan-Lam-Evans reaction of iminocoumarin derivatives[35] in which we developed a simple and mild protocol for the reaction of iminocoumarins with aryl boronic acids *via* a copper-catalyzed reaction. In this present work we showcase a one-pot procedure wherein one can easily synthesize *N*-aryl iminocoumarins using a copper-catalyst through a cascade/tandem reaction of 2-hydroxybenzaldehyde, malononitrile, and arylboronic acids TEA as base in greener solvent 2-MeTHF[36] (Figure 2).

All these precursors are readily available starting materials which are commercially accessible. Therefore, taking in to account of these advantages with a purpose to develop and improve alternate methodologies for *N*-aryliminocoumarins synthesis in a one-pot approach avoiding cumbersome steps of intermediate syntheses, purification steps and that too from readily available precursors. Thus in this context, we present herein a simple one-pot Knoevenagel-Chan-Evans-Lam coupling reaction for synthesis of *N*-aryl-2-iminocoumarins in bio-mass-derived green solvent 2-methylTHF operable at room temperature.

Table 1. Optimization reaction condition



1a **2a** **3a** **4a**

Sr. No.	copper Salts	solvent	base	time	yield[b]
1.	$CuBr_2$	2-MeTHF	TEA	12 h	36
2.	$CuCl_2.2H_2O$	2-MeTHF	TEA	12 h	65
3.	$CuSO_4.5H_2O$	2-MeTHF	TEA	6 h	69
4.	$Cu(OAc)_2$	2-MeTHF	TEA	3 h	72
5.	$Cu(OAc)_2.H_2O$	2-MeTHF	TEA	2 h	92
6.	$Cu(OAc)_2.H_2O$	2-MeTHF	TEA	2 h	89[c]
7.	$Cu(OAc)_2.H_2O$	2-MeTHF	TEA	2 h	90[d]
8.	$Cu(OAc)_2.H_2O$	2-MeTHF	TEA	2 h	62[e]
9.	$Cu(OAc)_2.H_2O$	THF	TEA	3 h	88
10.	$Cu(OAc)_2.H_2O$	THF	NaOH	4 h	75
11.	$Cu(OAc)_2.H_2O$	THF	KOH	4 h	63
12.	$Cu(OAc)_2.H_2O$	MeCN	DABCO	24 h	78
13.	$Cu(OAc)_2.H_2O$	DCE	DABCO	24 h	73
14.	$Cu(OAc)_2.H_2O$	DMF	DABCO	24 h	60
15.	$Cu(OAc)_2.H_2O$	2-MeTHF	-	24 h	0

[a]Reaction condition: **1a** (0.81 mmol), **2a** (0.81 mmol), base (0.081 mmol), $PhB(OH)_2$ (1.22 mmol), Copper salt (10 mol%) rt. [b]isolated yield, [c]$Cu(OAc)_2.H_2O$ (20 mol %). [d]$Cu(OAc)_2.H_2O$ (30 mol %), [e]$Cu(OAc)_2.H_2O$ (5 mol%).

2. Result and Discussion

Initially, the iminocoumarin intermediates **3a** necessary for *N*-aryliminocoumarin synthesis were prepared by the Knoevenagel condensation reaction of 2-hydroxybenzaldehyde (**1a**) malononitrile in presence of TEA (**2a**) in 2-MeTHF solvent at room temperature (Table 1). The formed intermediate iminocoumarin was further subjected to react with phenylboronic

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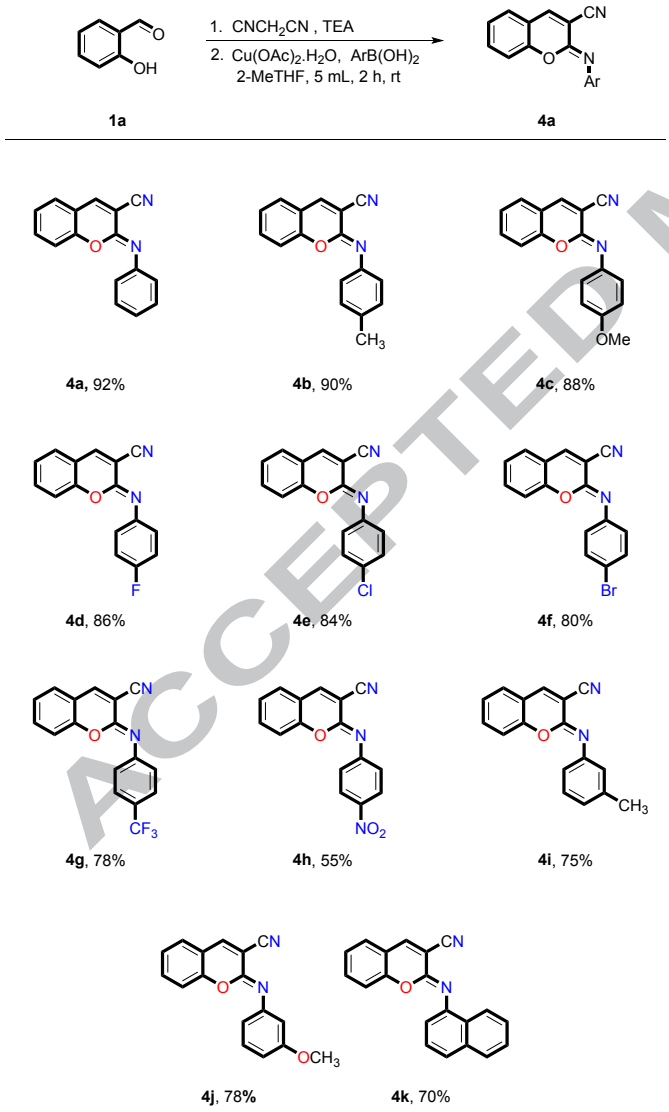
acid in presence $CuBr_2$ which successfully afforded the target compound only in lower yield 36% (entry 1).

After screening the different copper salts such as $CuCl_2.2H_2O$ the yield was increased up to 65% (entry 2), while using of $CuSO_4.5H_2O$ and $Cu(OAc)_2$ reaction work and give the corresponding product in 69 to 72% yields (entry 3 & 4). The use of $Cu(OAc).H_2O$ drastically increased the yield up to 92% (entry 5). Screening of commonly used bases and solvents such as, NaOH, KOH, DABCO THF, acetonitrile, DCE, DMF, and 2-MeTHF, suggested that TEA and 2-MeTHF is the most effective combination for this reaction. Notably, this method is insensitive to air and moisture, providing an operationally simple approach for the synthesis of *N*-aryliminocoumarin heterocycles.

Having established the optimum reaction conditions *i.e.* TEA/$Cu(OAc)_2.H_2O$/2-MeTHF, we sought to examine the substrate scope and the generality of this synthetic approach. (Table 2). All the substrates reacted smoothly and converted to the corresponding *N*-aryliminocoumarin in moderate to excellent yield.

Table 2. Substrate scope with different arylboronic acid derivatives[a,b]

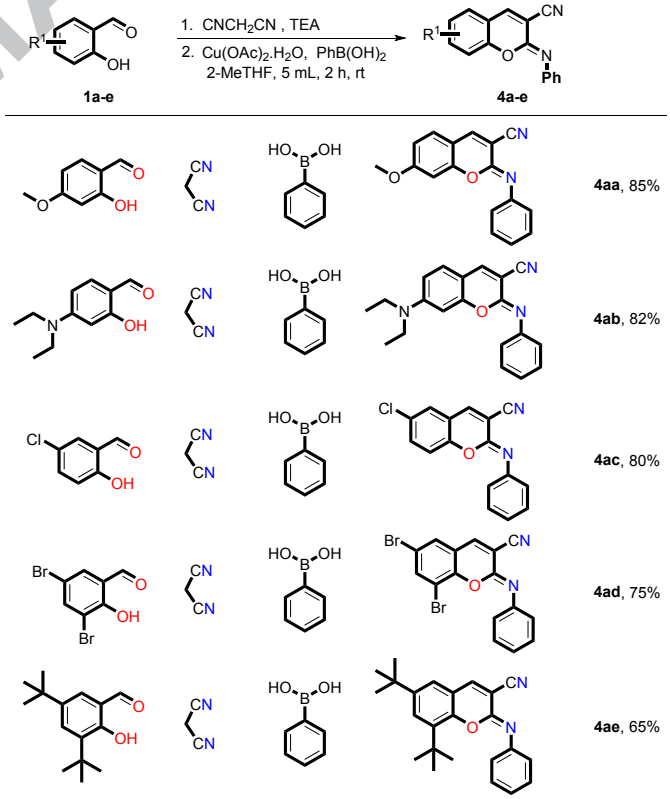


[a]Reaction condition: **1a** (0.81 mmol), $CNCH_2CN$ (0.81 mmol), TEA (0.081 mmol), $ArB(OH)_2$ (1.22 mmol), $Cu(OAc)_2.H_2O$ (10 mol %) rt. [b]isolated yield.

The scope of *N*-arylation reaction was examined with various aromatic boronic acids, the phenyl group gave excellent yield **4a**, 92%, where 4-Me and 4-OMe also formed the respective products in high yields **4b**, **4c** 90 and 88%. The halo derivatives also worked well to form the corresponding product with excellent yield such as fluoro, (**4d**, 86%), chloro (**4e**, 84%) and bromo (**4f**, 80%). The electron withdrawing group such as 4-CF_3 (**4g**, 78%), and for 4-NO_2 (**4h**, 55%) also worked well to form the desired product in moderate yield. The *meta* substituted derivatives 3-Me and 3-OMe also reacted smoothly to form the products in good to moderate yield (**4i**, 75% and **4j**, 78%) respectively. The sterically hindered naphthalene derivative also formed the desired product in good yield (**4k**, 70%).

Next, the reactivity of different salicylaldehydes (**1a-e**) and malononitrile with phenylboronic acid was investigated, and the results are summarized in Table 3. It was observed that aldehyde containing electron-donating groups and electron-withdrawing groups reacted well and successfully formed the corresponding product in excellent yield. The reaction with substituted aldehyde showed excellent result such as 4-OMe group gives (**4aa**, 85%) yield and the *N*, *N*-diethyl group (**4ab**, 82%) yield. Both these reactions worked and formed the products in excellent yield. The electron-withdrawing group such as -Cl and -Br successfully afforded products in high yield (**4ac**, 80%) and (**4ad**, 75%) respectively. The sterically hindered group *i.e. tert*-Butyl groups also afforded the desired product (**4ae**, 65%) in good yield.

Table 3 Scope of 2-hydroxybenzaldehyde derivatives with phenylboronic acid[a,b]



[a]Reaction condition: **1a** (0.81 mmol), $CNCH_2CN$ (0.81 mmol), TEA (0.081 mmol), $PhB(OH)_2$ (1.22 mmol), $Cu(OAc)_2.H_2O$ (10 mol %) rt. [b]isolated yield.

To test the efficacy of our protocol we performed some control experiments (Scheme 1), wherein a copper-free synthesis of 2-(phenylimino)-2*H*-chromene-3-carbonitrile was tried wherein the 2-imino-2*H*-chromene-3-carbonitrile **2a** was reacted with differently substituted aniline derivatives with NH_4OAc as a base in presence of glacial acetic acid as solvent under reflux conditions, which formed the expected product in lower yield (**4aa** 55%). Similarly we tried the reaction of **2a** with 4-OMe and

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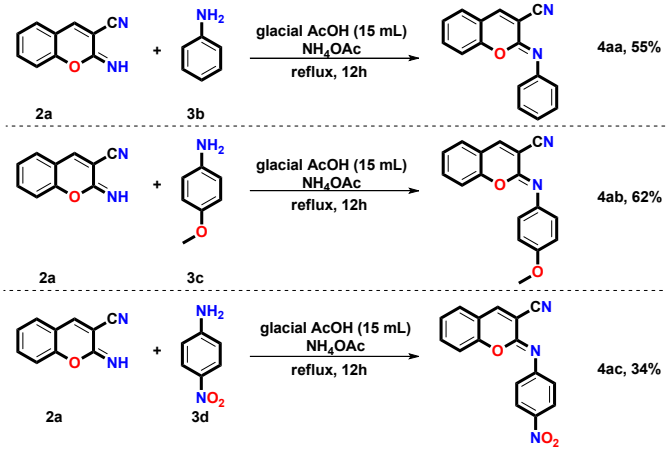
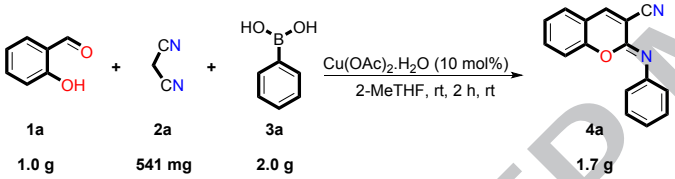
4-NO_2 aniline derivatives, reaction worked but afforded only lesser yields *i.e.* (**4ab** 62% and **4ac** 34%) respectively. It was observed that, the reaction work in presence of glacial acetic acid and NH_4OAc does not form the expected product in significantly good yields as compared to the Chan-Evans-Lam coupling reaction. These experiments endorse our one-pot sequential copper catalyzed protocol to be a superior methodology when compared to the existing methods to achieve the target compounds in excellent yields under mild reaction conditions.



Scheme 1: Control Experiments



Scheme 2 Gram Scale (*Z*)-2-(phenylimino)-2*H*-chromene-3-carbonitrile

To demonstrate the methods practicality, we checked a gram-scale (*Z*)-2-(phenylimino)-2*H*-chromene-3-carbonitrile synthesis in which reaction was carried out by employing 2-hydroxybenzaldehyde **1a** (8.19 mmol, 1.0 g), malononitrile **2a** (8.19 mmol, 541 mg) and phenylboronic acid **3a** (12.23 mmol, 1.49 g) under the standard reaction conditions (Scheme 1). This transformation proceeded smoothly to afford 1.7 g (84%) of the product **3a**. Thus, this result vouches for the scalability of the developed protocol.

Based on the previous reports of Chan-Lam-Evan coupling reaction and substrate study, we propose a plausible mechanistic pathway for *N*-aryliminocoumarin under copper-catalyzed reaction condition. Initially, Knoevenagel condensation reaction of 2-hydroxybenzaldehyde and malononitrile in presence of base takes place to form the iminocoumarin intermediate, which reacts with copper to form a copper acetate-iminocoumarin complex (see the supporting information) (Scheme 2). The evidence for the formation of this complex was proved by subjecting the reaction mixtures to MALDI analysis before the addition of aryl boronic acid. The MALDI-ESI spectra showed mass ions consistent with several proposed reaction-relevant complexes (Figure 3). The imino-ligand Cu-monomeric-complex, **5a** (Figure 3), were identified in comparatively high abundance. Monomeric and dimeric copper-complexes were clearly observed (see SI). Possibly Cu monomeric complex can be either with imino *N* and *O* bond or imino *N*-bond and CN functional groups, preferably a imino *N*-bond and CN mode due to the favoured chelation possibility. A tetragonal-complex of Cu-iminochromene with two iminocoumarin ligands similarly to the monomeric complexes **5aa** either *via* an imino *N* and nitrile CN functional group or imino *N* and *O*-bond are also possible. Peaks corresponding to acetate bridged Cu-dimeric-complex was also observed in the MALDI-ESI spectra. This evidence indicated the formation of various pre iminochromene – copper complexes during the reaction. We hypothesize that this association of the substrate with copper metal enables a more facile reaction.

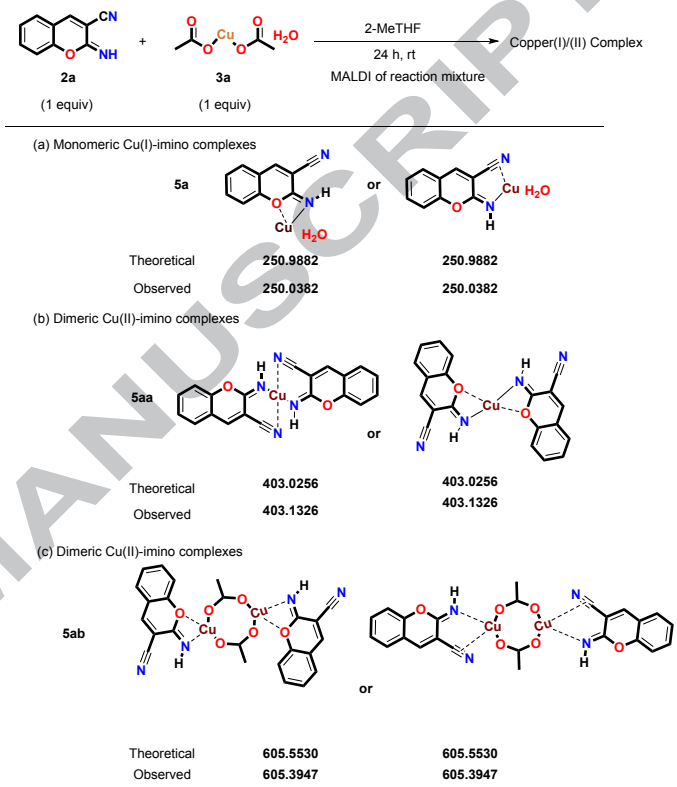


Figure 3. Proposed structure of mass fragment ions detected by MALDI-ESI analysis of 2-imino-2H-chromene-3-carbonitrile and $Cu(OAc)_2.H_2O$ reaction mixture

3. Conclusion

In conclusion, we report on the development of an efficient copper-catalyzed one-pot tandem protocol for the synthesis of *N*-arylated iminochromenes under Chan-Evans Lam reaction conditions in 2-MeTHF green solvent. To the best of our knowledge, this is the first strategy for preparing the *N*-arylated iminochromenes by a sequential synthetic method which is operationally simple and requires no isolation of the iminocoumarin intermediates. The broad substrate scope and good to excellent product yields suggest that this methodology would be synthetically useful. Further, the environmental and economic advantages derived from the use of such a benign solvent are clear in terms of safety, cost and innocuousness.

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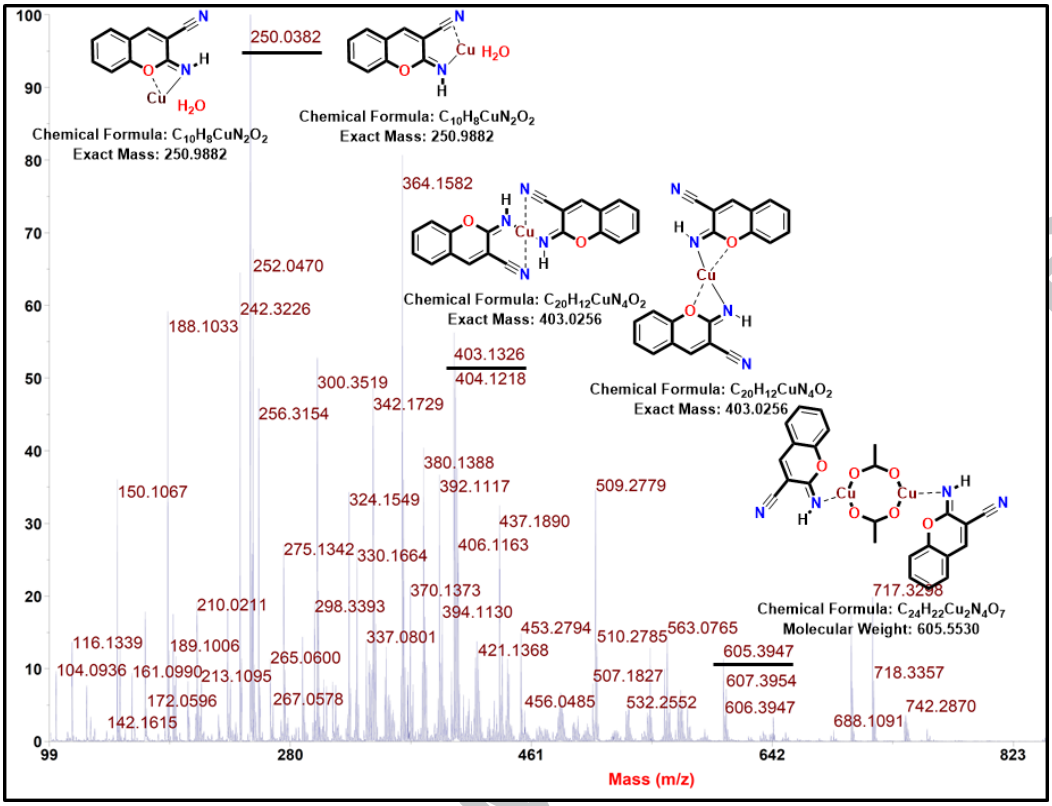

Figure 4. MALDI-ESI mass spectra (2, 4-Dihydroxybenzoic acid as the matrix) of $Cu(OAc)_2.H_2O$ and 2-imino-2H-chromene-3-carbonitrile stirred at room temperature in 2-MeTHF solvent for 24 h.

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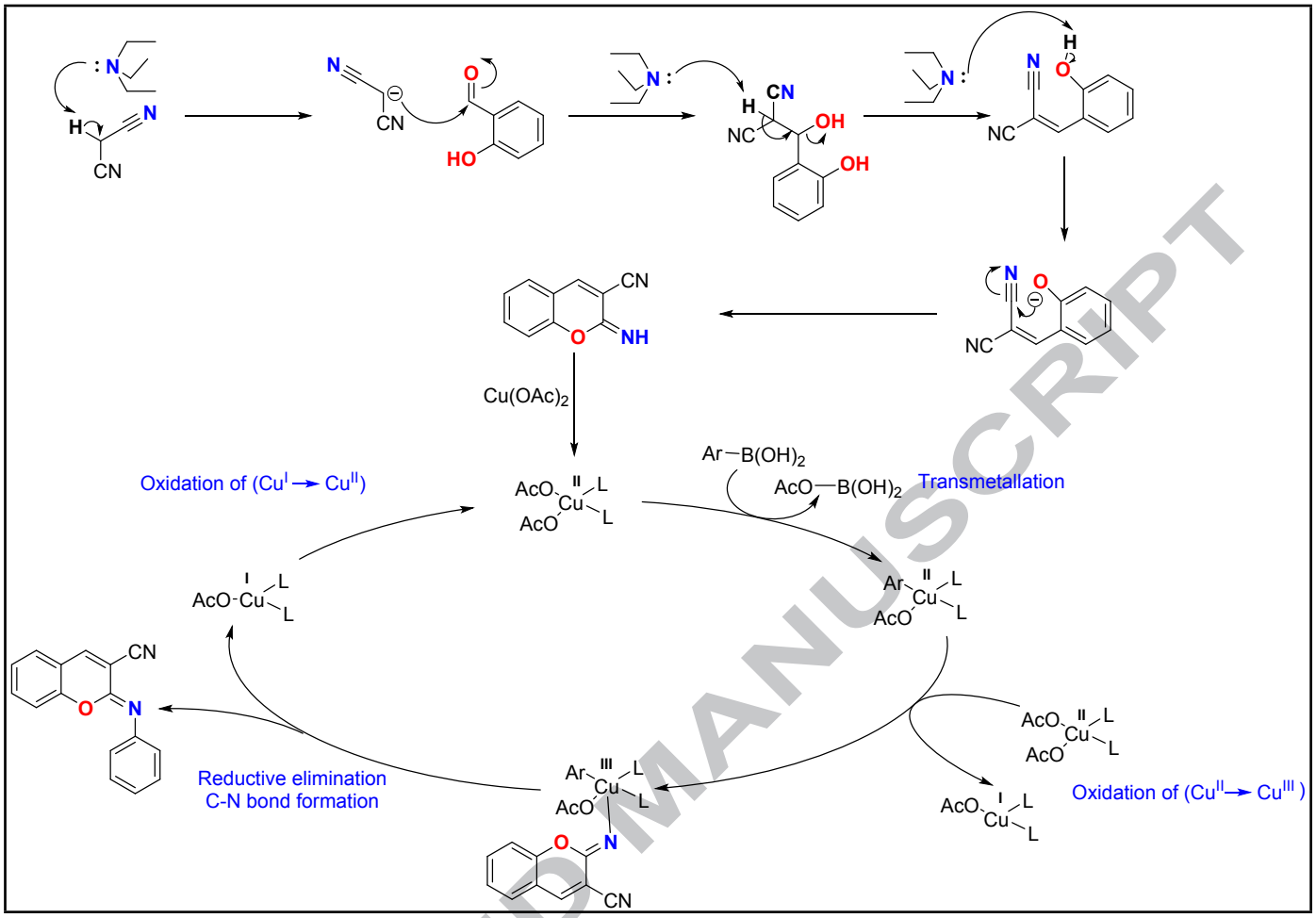

Scheme 2. Plausible mechanistic pathway.

4. Experimental

4.1. General information

NMR spectra were recorded with tetramethylsilane as the internal standard. TLC was performed on glass-backed silica plates. Column chromatography was performed using silica gel (200-300 mesh) eluting with ethyl acetate and petroleum ether. ^{1}H-NMR spectra were recorded at 400 MHz, and ^{13}C- NMR spectra were recorded at 100 MHz. Chemical shifts (δ) are reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) or DMSO-D_6 (δ = 2.49 ppm) for ^{1}H-NMR and relative to the central $CDCl_3$ resonance (δ = 77.0 ppm) or DMSO-D_6 (δ = 39.5 ppm) for ^{13}C-NMR spectroscopy. Coupling constants (J) are given in Hz. Commercial grade solvents were dried and purified by standard procedures as specified in Purification of Laboratory Chemicals.

4.2. General procedure for the synthesis of Iminochromene derivatives.

A solution of aldehyde (0.81 mmol), base (0.081), malononitrile (0.81 mmol) in 2-MeTHF (3 mL) was stirred for 30 min. The progress of reaction was monitored by TLC analysis. After complete conversion of both the starting material, the arylboronic acid derivatives (1.22 mmol) and $Cu(OAc)_2.H_2O$ (10 mol%) was added. The reaction completed within 2h. After completion of the reaction, the organic phase was concentrated under reduced pressure and the crude residue was purified by column chromatography with ethyl acetate/petroleum ether (5:95) to give the compound.

Experimental Procedure for synthesis of (Z)-2-(phenylimino)-2H-chromene-3-carbonitrile: 4aa

To a solution of 2-imino-2*H*-chromene-3-carbonitrile **2a** (0.81 mmol) with phenylboronic acid (1.22 mmol) and $Cu(OAc)_2.H_2O$ (10 mol%) in 2-MeTHF solvent. The reaction mixture was stirred for 1h and then the solvent was removed and crude crude residue was purified by column chromatography with ethyl acetate/petroleum ether (5:95) to give the compound **4aa** with 95% yield.

Experimental Procedure for synthesis of N-Arylimino derivative from different aniline derivatives: 4ab-4ac

To a solution of 2-imino-2*H*-chromene-3-carbonitrile **2a** (0.81 mmol), aniline derivatives (0.81 mmol) and base NH_4OAc (0.81 mmol) in glacial acetic acid and the reaction mixture was reflux for 12h. After completion of the reaction, the organic phase was concentrated under reduced pressure and the crude residue was purified by column chromatography with ethyl acetate/petroleum ether (5:95) to give the compound.

4.2.1 (Z)-2-(Phenylimino)-2H-chromene-3-carbonitrile 4a, 4aa, 4ab [34]

Yield 92%, 95%, 55% (yellow solid, 184 mg, 137 mg, 80 mg); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.59 (t, J = 7.8 Hz, 1H), 7.49 (t, J = 8.6 Hz, 3H), 7.41 – 7.27 (m, 4H), 7.19 (d, J = 8.3 Hz, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.69, 144.75, 144.68, 144.58, 134.07, 128.84, 128.80, 125.02, 124.86, 123.18, 117.73, 116.44, 114.76, 107.40.

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4.2.2 (Z)-2-(p-Tolylimino)-2H-chromene-3-carbonitrile 4b

Yield 90% (yellow solid, 192 mg); m.p. 130-131ºC; IR (ν/cm^{-1}): 2231, 1650, 1595, 1566, 1455, 1380, 1291, 1218, 1193, 1044, 1017.^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.48 (ddd, J = 8.4, 7.5, 1.6 Hz, 1H), 7.38 (dd, J = 7.7, 1.6 Hz, 1H), 7.22 (ddd, J = 4.8, 3.8, 1.5 Hz, 3H), 7.18 (d, J = 8.5 Hz, 2H), 7.10 (d, J = 8.3 Hz, 1H), 2.37 (s, 3H).^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.69, 144.25, 144.16, 141.73, 134.80, 133.86, 129.31, 128.69, 124.69, 123.39, 117.73, 116.32, 114.75, 107.60, 21.11; HRMS Mass Chemical Formula: $C_{17}H_{13}N_2O$ $[M + H]^+$: 261.1022; Found: 261.1005.

4.2.3 (Z)-2-((4-Methoxyphenyl)imino)-2H-chromene-3-carbonitrile 4c and 4ac

Yield 88%, 62% (yellow solid, 198 mg, 102 mg); m.p. 150-151ºC; IR (ν/cm^{-1}): 2231, 1651, 1604, 1504, 1379, 1293, 1218, 1192, 1168, 1033; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.46 (s, 1H), 7.35 (t, J = 7.5 Hz, 3H), 7.19 (d, J = 7.5 Hz, 1H), 7.11 (d, J = 8.2 Hz, 1H), 6.89 (d, J = 8.8 Hz, 2H), 3.82 (s, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 157.23, 153.68, 143.45, 137.26, 133.66, 128.54, 125.41, 124.57, 117.80, 116.21, 114.70, 113.83, 107.94, 55.39; HRMS Mass Chemical Formula: $C_{17}H_{13}N_2O_2$ $[M + H]^+$: 277.0972; Found: 277.0965.

4.2.4 (Z)-2-((4-Fluorophenyl)imino)-2H-chromene-3-carbonitrile 4d

Yield 86% (yellow solid, 185 mg); m.p. 137-138ºC; IR (ν/cm^{-1}): 2231, 1651, 1605, 1563, 1454, 1382, 1223, 1194, 1123, 1095, 1051; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.57 – 7.50 (m, 1H), 7.43 (dd, J = 7.7, 1.5 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.26 (td, J = 7.6, 0.9 Hz, 1H), 7.14 (d, J = 8.3 Hz, 1H), 7.11 – 7.05 (m, 2H); ^{13}C-NMR (126 MHz, $CDCl_3$) δ 161.12, 159.18, 153.54, 144.69, 144.44, 140.42, 134.02, 128.77, 125.01, 124.95, 124.89, 117.68, 116.32, 115.50, 115.32, 114.58, 107.42; HRMS Mass Chemical Formula: $C_1H_{10}FN_2O$ $[M + H]^+$: 265.0772; Found: 265.0744.

4.2.5 (Z)-2-((4-Chlorophenyl)imino)-2H-chromene-3-carbonitrile 4e

Yield 84% (yellow solid, 193 mg); m.p. 148-149ºC; IR (ν/cm^{-1}): 2231, 1647, 1604, 1580, 1567, 1482, 1454, 1382, 1290, 1215, 1122, 1010; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.57 – 7.52 (m, 1H), 7.52 – 7.48 (m, 2H), 7.43 (dd, J = 7.7, 1.3 Hz, 1H), 7.29 – 7.26 (m, 1H), 7.18 (d, J = 8.6 Hz, 2H), 7.13 (d, J = 8.3 Hz, 1H); ^{13}C-NMR (126 MHz, $CDCl_3$) δ 153.49, 145.17, 144.81, 143.55, 134.16, 131.77, 128.82, 124.99, 124.92, 118.00, 117.63, 116.36, 114.47, 107.19; HRMS Mass Chemical Formula: $C_{16}H_{10}ClN_2O$ $[M + H]^+$: 281.0476; Found: 281.0468.

4.2.6 (Z)-2-((4-Bromophenyl)imino)-2H-chromene-3-carbonitrile 4f

Yield 80% (yellow solid, 152 mg); m.p. 160-161ºC; IR (ν/cm^{-1}): 2231, 1644, 1602, 1567, 1455, 1380, 1290, 1196, 1121, 1072, 1045; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.56 – 7.35 (m, 4H), 7.23 (d, J = 7.7 Hz, 1H), 7.11 (dd, J = 19.8, 8.0 Hz, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.44, 145.10, 144.74, 143.50, 134.09, 131.71, 128.77, 124.93, 124.87, 117.95, 117.59, 116.30, 114.42, 107.14; HRMS Mass Chemical Formula: $C_{16}H_{10}BrN_2O$ $[M + H]^+$: 324.9971; Found: 324.9952.

4.2.7 (Z)-2-((4-(Trifluoromethyl)phenyl)imino)-2H-chromene-3-carbonitrile 4g

Yield 78% (yellow solid, 200 mg); m.p. 162-163ºC; IR (ν/cm^{-1}): 2233, 1656, 1600, 1567, 1510, 1455, 1321, 1218, 1155, 1061; ^{1}H- NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 3H), 7.60 (d, J = 8.2 Hz, 6H), 7.55 – 7.38 (m, 7H), 7.31 – 7.24 (m, 8H), 7.08 (d, J = 8.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.37, 147.90, 145.33, 134.27, 128.86, 125.93, 125.89, 125.07, 122.78, 117.51, 116.36, 114.30, 106.76; HRMS Mass Chemical Formula: $C_{17}H_{10}F_3N_2O$ $[M + H]^+$: 315.0740; Found: 315.0719.

4.2.8 (Z)-2-((4-Nitrophenyl)imino)-2H-chromene-3-carbonitrile 4h

Yield 55%, 34% (yellow solid, 132 mg, 59 mg); m.p. 204-205ºC; IR (ν/cm^{-1}): 2235, 1657, 1605, 1582, 1506, 1488, 1464, 1366, 1337, 1256, 1185, 1111, 1051; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 8.15 (d, J = 8.3 Hz, 3H), 7.65 (d, J = 51.6 Hz, 1H), 7.40 (s, 1H), 6.90 (d, J = 7.4 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 156.45, 154.61, 151.85, 135.58, 134.64, 129.30, 125.73, 125.43, 124.74, 123.04, 117.47, 117.15, 113.53, 103.37; HRMS Mass Chemical Formula: $C_{16}H_{10}N_3O_3$ $[M + H]^+$: 292.0717; Found: 292.0727.

4.2.9 (Z)-2-(m-Tolylimino)-2H-chromene-3-carbonitrile 4i

Yield 75% (yellow solid, 160 mg); m.p. 120-121ºC; IR (ν/cm^{-1}): 2230, 1725, 1644, 1604, 1508, 1488, 1447, 1369, 1337, 1257, 1186, 1050; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.27 (d, J = 4.1 Hz, 1H), 8.26 (d, J = 9.1 Hz, 1H), 7.73 (ddd, J = 8.5, 7.4, 1.6 Hz, 1H), 7.61 (dd, J = 8.0, 1.6 Hz, 1H), 7.58 – 7.53 (m, 1H), 7.44 – 7.39 (m, 2H), 7.32 – 7.26 (m, 1H), 7.11 (d, J = 8.4 Hz, 1H), 1.60 (s, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 154.62, 151.79, 143.89, 135.55, 129.27, 125.70, 124.73, 123.03, 117.47, 117.15, 116.48, 114.46, 113.51, 103.40, 20.47; HRMS Mass Chemical Formula: $C_{17}H_{13}N_2O$ $[M + H]^+$: 261.1022; Found: 261.1005.

4.2.10 (Z)-2-((3-Methoxyphenyl)imino)-2H-chromene-3-carbonitrile 4j

Yield 78% (yellow solid, 177 mg); m.p. 151-153ºC;
IR (ν/cm^{-1}): 2232, 1733, 1655, 1606, 1590, 1566, 1480, 1387, 1289, 1255, 1217, 1150, 1048; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.71 (t, J = 7.1 Hz, 1H), 7.64 – 7.56 (m, 1H), 7.51 – 7.34 (m, 3H), 7.24 (dd, J = 15.6, 8.4 Hz, 1H), 7.08 (d, J = 8.2 Hz, 1H), 6.90 – 6.67 (m, 1H), 3.80 (s, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 156.38, 154.56, 151.79, 144.59, 135.51, 133.95, 129.26, 128.69, 125.67, 124.75, 117.40, 115.29, 113.49, 110.85, 108.62, 55.27; HRMS Mass Chemical Formula: $C_{17}H_{13}N_2O_2$ $[M + H]^+$: 277.0972; Found: 277.0965.

4.2.11 (Z)-2-(Naphthalen-1-ylimino)-2H-chromene-3-carbonitrile 4k

Yield 70% (yellow solid, 169 mg); m.p. 135-136ºC; IR (ν/cm^{-1}): 2230, 1650, 1614, 1563, 1502, 1453, 1395, 1341, 1288, 1214, 1191, 1059; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.32 (dd, J = 5.4, 4.3 Hz, 1H), 7.90 – 7.85 (m, 2H), 7.71 (d, J = 8.0 Hz, 1H), 7.54 – 7.42 (m, 6H), 7.24 (td, J = 7.6, 1.0 Hz, 1H), 7.06 (d, J = 8.3 Hz, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.65, 145.04, 144.48, 140.60, 134.20, 133.98, 128.71, 127.72, 126.47, 126.15, 125.80, 125.46, 125.09, 124.79, 124.18, 117.73, 117.08, 116.47; HRMS Mass Chemical Formula: $C_{20}H_{13}N_2O$ $[M + H]^+$: 297.1022; Found: 297.1008.

4.2.12 (Z)-7-Methoxy-2-(phenylimino)-2H-chromene-3-carbonitrile 4aa [34]

Yield 85% (yellow solid, 155 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.43 – 7.37 (m, 2H), 7.29 (d, J = 5.3 Hz, 1H), 7.28 – 7.23 (m, 2H), 7.21 – 7.15 (m, 1H), 6.79 (dd, J = 8.6, 2.4 Hz, 1H), 6.59 (d, J = 2.3 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.69, 155.59, 144.82, 144.52, 135.65, 129.75, 128.71, 128.01, 124.61, 122.91, 112.52, 111.20, 103.39, 100.95, 56.03.

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4.2.13 (Z)-7-(Diethylamino)-2-(phenylimino)-2H-chromene-3-carbonitrile 4ab [34]

Yield 82% (yellow solid, 135 mg); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.44 – 7.36 (m, 2H), 7.27 – 7.22 (m, 2H), 7.19 – 7.12 (m, 2H), 6.48 (dd, J = 8.9, 2.5 Hz, 1H), 6.20 (d, J = 2.3 Hz, 1H), 3.41 (q, J = 7.1 Hz, 4H), 1.21 (t, J = 7.1 Hz, 6H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 156.30, 152.38, 146.46, 145.58, 144.68, 129.96, 128.64, 123.91, 122.96, 116.40, 108.47, 106.86, 98.01, 97.15, 44.85, 12.53.

4.2.14 (Z)-6-Chloro-2-(phenylimino)-2H-chromene-3-carbonitrile 4ac [34]

Yield 80% (yellow solid, 145 mg); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.77 (m, 1H), 7.61 – 7.44 (m, 4H), 7.43 – 7.27 (m, 3H), 7.22 – 7.09 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 152.04, 144.17, 143.22, 133.64, 130.03, 128.84, 127.94, 125.30, 123.17, 118.79, 117.80, 114.32, 108.73.

4.2.15 (Z)-6,8-Dibromo-2-(phenylimino)-2H-chromene-3-carbonitrile 4ad

Yield 75% (yellow solid, 108 mg); m.p. 210-211ºC IR (ν/cm^{-1}): 2238, 1653, 1582, 1548, 1486, 1410, 1230, 1199, 1046; ^{1}H - NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 2.2 Hz, 1H), 7.66 (s, 1H), 7.53 (dd, J = 8.4, 1.0 Hz, 2H), 7.49 (d, J = 2.2 Hz, 1H), 7.45 – 7.39 (m, 2H), 7.26 – 7.21 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.37, 147.90, 145.33, 134.27, 128.86, 125.93, 125.89, 125.07, 122.78, 117.51, 116.36, 114.30, 106.76; HRMS Mass Chemical Formula: $C_{16}H_9Br_2NO_2O$ $[M + H]^+$: 402.9076; Found: 402.9049.

4.2.16 (Z)-6,8-Di-tert-butyl-2-(phenylimino)-2H-chromene-3-carbonitrile 4ae [34]

Yield 65% (yellow solid, 199 mg); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.48 (d, J = 2.4 Hz, 1H), 7.37 – 7.30 (m, 2H), 7.18 (d, J = 2.3 Hz, 1H), 7.13 – 7.06 (m, 1H), 7.00 – 6.95 (m, 2H), 1.31 (s, 9H), 1.04 (s, 9H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 150.50, 147.08, 146.69, 146.61, 146.05, 137.40, 129.57, 128.82, 123.86, 123.63, 121.14, 117.37, 114.86, 105.12, 34.61, 34.55, 31.24, 29.21.

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Supplementary Material

^{1}H and ^{13}C-NMR of all the compounds

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Highlights

- One-pot Aryliminocoumarins synthesis without isolating intermediates is showcased
- Use of bio-mass-derived solvent 2-methyltetrahydrofuran is more environ-friendly
- Mass spectrometry studies reveal formation of iminocoumarin-copper complex

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