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*R. N. Prasad Tulichala, Mallepalli Shankar and K. C. Kumara Swamy**

School of Chemistry, University of Hyderabad, Hyderabad 500 046, Telangana., India.

E-mail: kckssc@uohyd.ac.in; kckssc@yahoo.com

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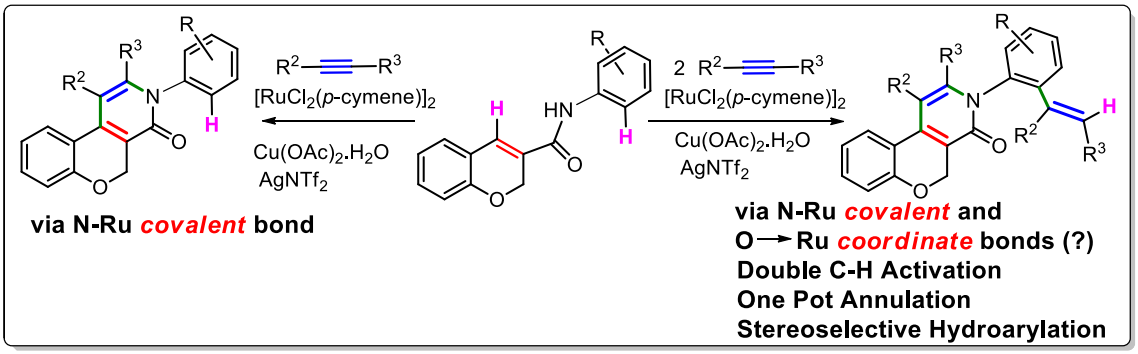


Abstract

Ruthenium-catalyzed oxidative annulation of 2*H*-chromene-3-carboxamides with alkynes has been achieved by using the directing group nature of amide in the presence of $Cu(OAc)_2.H_2O$ as an oxidant and $AgNTf_2$ as an additive. This reaction offers a broad substrate scope, and both symmetrical and unsymmetrical alkynes can be harnessed. High regioselectivity was achieved in the case of unsymmetrical alkynes. In addition, we have also accomplished *double C-H activation* by employing an excess of alkyne, where both annulation and hydroarylation took place regio- and stereo-selectively in one pot, with the catalyst playing a dual role. While the first

C-H functionalization could involve Ru-N *covalent bond*, the second C-H functionalization most likely involves Ru-O *coordinate bond*. The structures of key products are confirmed by X-ray crystallography.

Introduction

Transition-metal-catalyzed organic reactions *via* C-H bond activation[1] and functionalization[2] have been in the forefront of research in recent years. In particular, ruthenium-catalyzed annulation reactions with alkynes *via* C(sp^2)–H bond functionalization[1d,2b,3] with directing group assisted approach has emerged as an important tool for the construction of heterocycles as synthetic targets. Functional groups that include imine, anilide, amide, ester, heterocyclic, amine, carboxylic acid, ketone, and hydroxyl have been employed as directing groups for transition metal-catalyzed direct C–H bond functionalization.[4] The fundamental step involved in these transformations is assumed to be the coordination of nitrogen and/or oxygen atoms with the metal center that directs the metal to a specific proximal C-H bond thus functionalizing the molecule. Among the myriad directing groups evaluated so far, amide has shown distinct reactivity in transition metal-catalyzed C–H bond functionalizations and has served as a crucial platform for the outcome of new transformations *via* C–H activation.[5] Recently, the research groups of Satoh and Miura,[5a] Rovis,[5b] Guimond and Fagnou,[5c,e] and Glorius[5f] established the Cp*Rh-catalyzed annulation of alkynes with various types of benzamides. Later, the first use of less-expensive ruthenium catalysts[6] for oxidative annulation reaction of alkynes with benzamides was reported by Ackermann and coworkers[3a,c] followed by the research groups of Li and Wang.[3d,6a] Huang and co-workers reported the palladium-ctalyzed[7a]

while Chatani's group reported the nickel-catalyzed[7b] annulation reactions of alkynes with benzamides.

C-H hydroarylation of alkynes is also a highly efficient route for the synthesis of alkenyl arenes directly from simple arenes and alkynes.[1,2a,e,8] However, such C-H functionalizations are highly regioselective only when directed by amides, esters, ketones, pyridine and sulfoxide groups. Subsequent to the pioneering work of Murai and co-workers,[9] various transition-metal catalysts such as Ru,[10] Rh,[11] Co[12] and other metals[13] have been developed for alkyne hydroarylation *via* chelation-assisted C–H bond cleavage at the *ortho* position to a directing group. The hydroarylation reactions of alkynes with a combination of ruthenium catalyst and amide directing group has engrossed the recent interest in C-H functionalization reactions.[10a-d,e]

Benzopyran (chromene) ring system is an important structural component in natural products with valuable and diverse biological properties.[14-15] Naturally occurring benzopyran-containing molecules (Figure 1; **1a-f**) show antiproliferative activity against various carcinoma cells,[16] agonistic effect on the cannabinoid receptors, CB_1 and CB_2,[17] inhibitory effect on cellular glucose transport, phytotoxic properties and potent anti-HIV and anti-inflammatory activities.[18,19] The naturally occurring 5,7-dimethoxy-2-methyl-2*H*-chromene shows antifungal activity and was isolated recently from *Calyptranthes tricona*. A large number of these compounds have substituents at pyran-3,4-positions and hence developing methods, like that using C-H functionalization, for substitution at these positions will be of tremendous synthetic value.

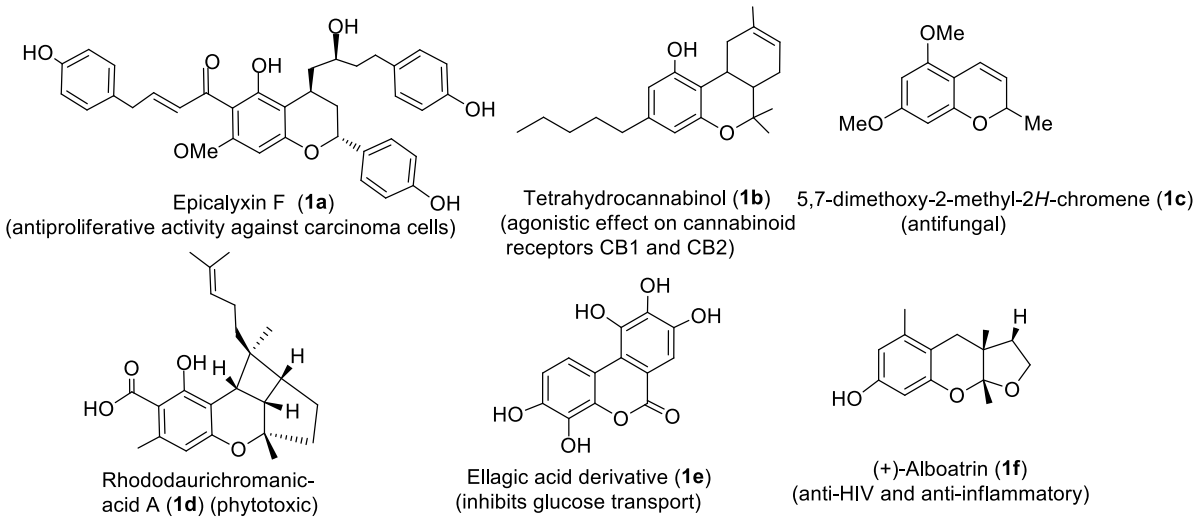
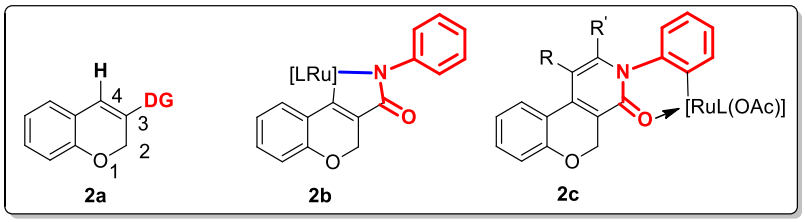


Figure 1. Examples for benzopyran (chromene) containing natural products (**1a-f**)

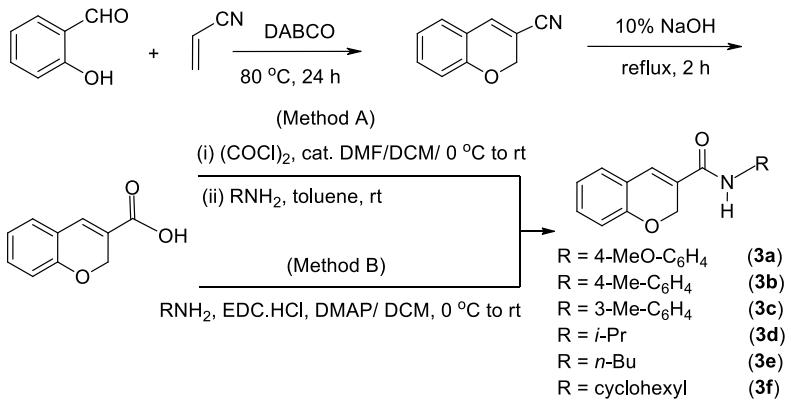
For achieving the above objective, we have chosen the benzopyran moiety with amide directing group (DG, cf. structure **2a**) at the 3-position. To our knowledge, C-H functionalization at C(4)-H position on the benzopyran ring system has not been reported so far. Thus in continuation of our studies on C-H activation/functionalization,[3f,h,20] we report herein Ru-catalyzed C-H functionalization followed by annulation of 2*H*-chromene-3-carboxamides with unactivated alkynes that results in benzopyran fused 2-pyridones (pyrano[3,4-*c*]pyridones). It should be noted that pyridones themselves are also pharmaceutically important.[21-22] More importantly, we have successfully achieved ***double C-H activation*** in the reaction of 2*H*-chromene-3-carboxamides with an excess of alkyne, with the catalyst playing dual role. Here, in an one-pot reaction, one alkyne moiety goes through oxidative annulation *via* C-H and N-H bond cleavage, while the other alkyne undergoes regio- and stereo-selective hydroarylation at the *ortho* position of aryl group attached to nitrogen atom involving amide-C=O directed C-H bond cleavage. While the first C-H functionalization involves Ru-N *covalent bond*, the second one requires Ru-O *coordinate bond* (cf. structures **2b-c**).



Results and Discussion

The precursors for the present work are chromenes (2*H*-chromene-3-carboxamides) with amide functionality on the ring containing the hetero atom. For this purpose, 2*H*-chromene-3-carboxylic acid was prepared in a two-step sequence from salicylaldehyde using Corey's procedure (Scheme 1).[23] The *N*-substituted 2*H*-chromene-3-carboxamides **3** were synthesized *via* the acid chloride obtained by treating the carboxylic acid with oxalyl chloride using a catalytic amount of DMF.[24a,b,c] In the alternative procedure, the 2*H*-chromene-3-carboxylic acids were converted to the corresponding *N*-substituted 2*H*-chromene-3-carboxamides **3** in a single step by using EDC.HCl/DMAP.[24d,e] Amides **3a** and **3e** were prepared by the method A, while **3b-d** and **3f** could be prepared by the method B. The dialkyl or diaryl acetylenes **4a-l** were prepared by following a literature procedure.[25]

Scheme 1. Synthesis of 2*H*-Chromene-3-carboxamide Precursors



We shall first discuss the formation of benzopyran-fused 2-pyridones by Ru-catalyzed oxidative annulation of alkynes by using 2*H*-chromene-3-carboxamides that involves C-H activation. Following this, we shall deliberate on the formation of double C-H activation products *via* Ru-catalyzed annulation followed by hydroarylation.

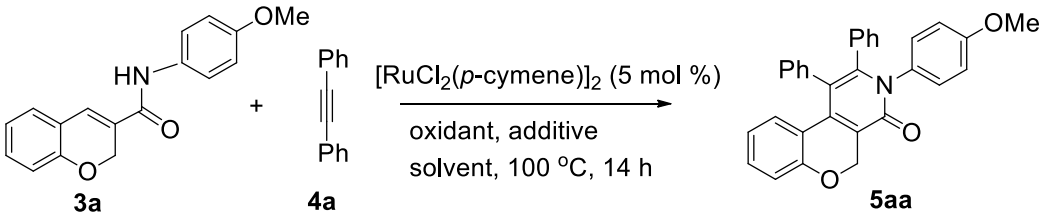
(i) Ruthenium-Catalyzed Synthesis of Benzopyran-fused 2-Pyridones *via* C-H Bond Functionalization

Our investigation began with the reaction of equimolar *N*-(4-methoxyphenyl)-2*H*-chromene-3-carboxamide **3a** with diphenylacetylene **4a** in the presence of $[RuCl_2(p\text{-cymene})]_2$ and $Cu(OAc)_2{\cdot}H_2O$ in *t*AmOH at 100 ^oC. This reaction afforded the desired cyclization product **5aa** in 50% yield (Table 1, entry 1). Other oxidants like Ag_2CO_3, AgOAc and $CuCl_2$ did not improve the yield (entries 2-4). Gratifyingly, additives like NaOAc and KPF_6 improved the yield of **5aa** (entries 5-6). Subsequently, a series of other additives that include $AgSbF_6$, $AgBF_4$, AgOTf and $AgNTf_2$ were examined. Among these, $AgNTf_2$ was the most effective for the annulation (entries 7–10). In this case, we isolated **5aa** in 88% yield.

In the absence of $Cu(OAc)_2{\cdot}H_2O$, the desired product **5aa** (entry 11) was not formed. In the presence of $Cu(OAc)_2{\cdot}H_2O$ but without the Ru-catalyst also, the desired product was not observed (entry 12). Thus both Ru-catalyst and $Cu(OAc)_2{\cdot}H_2O$ are required for the reaction. Changing the solvent to *t*BuOH decreased the yield of **5aa** to 69% (entry 13). Other solvents like *n*BuOH, DCE, DMF and H_2O did not improve the yield (entries 14–17). It is noteworthy that under the same catalytic conditions in open air also the reaction afforded the product in 65% yield (entry 18). Other Ru-catalysts like $[CpRuCl(PPh_3)_2]$, $[Ru(OAc)_2(p\text{-cymene})]$ and $[RuCl_2(benzene)]_2$ were less effective than $[RuCl_2(p\text{-cymene})]_2$ (entries 19–21). Thus, the

combination of 5.0 mol % of $[RuCl_2(p\text{-cymene})]_2$ as the catalyst, 2 equiv of $Cu(OAc)_2{\cdot}H_2O$ as the oxidant and 30 mol % of $AgNTf_2$ as additive in *t*AmOH solvent at 100 °C for 14 h (88% yield; Table 1, entry 10) was found to be the optimum condition.

Table 1: Optimization Study for the Ru-Catalyzed Oxidative Annulation[a]



Entry	Oxidant	Additive	Solvent	Yield of **5aa** (%)[b]
1	$Cu(OAc)_2.H_2O$	-	*t*AmOH	50
2	Ag_2CO_3	-	*t*AmOH	trace
3	AgOAc	-	*t*AmOH	trace
4	$CuCl_2$	-	*t*AmOH	36
5	$Cu(OAc)_2.H_2O$	NaOAc	*t*AmOH	55
6	$Cu(OAc)_2.H_2O$	KPF_6	*t*AmOH	62
7	$Cu(OAc)_2.H_2O$	$AgSbF_6$	*t*AmOH	73
8	$Cu(OAc)_2.H_2O$	$AgBF_4$	*t*AmOH	71
9	$Cu(OAc)_2.H_2O$	AgOTf	*t*AmOH	77
10	**$Cu(OAc)_2.H_2O$**	**$AgNTf_2$**	***t*AmOH**	**88**
11	-	$AgNTf_2$	*t*AmOH	n.d.
12	$Cu(OAc)_2.H_2O$	$AgNTf_2$	*t*AmOH	n.d.[c]
13	$Cu(OAc)_2.H_2O$	$AgNTf_2$	*t*BuOH	69

14	$Cu(OAc)_2.H_2O$	$AgNTf_2$	*n*BuOH	65
15	$Cu(OAc)_2.H_2O$	$AgNTf_2$	DCE	52
16	$Cu(OAc)_2.H_2O$	$AgNTf_2$	DMF	48
17	$Cu(OAc)_2.H_2O$	$AgNTf_2$	H_2O	26
18	$Cu(OAc)_2.H_2O$	$AgNTf_2$	*t*AmOH	65[d]
19	$Cu(OAc)_2.H_2O$	$AgNTf_2$	*t*AmOH	trace[e]
20	$Cu(OAc)_2.H_2O$	$AgNTf_2$	*t*AmOH	75[f]
21	$Cu(OAc)_2.H_2O$	$AgNTf_2$	*t*AmOH	58[g]

[a]Reaction conditions: 2*H*-chromene-3-carboxamide **3a** (0.5 mmol), alkyne **4a** (0.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0 mol %), oxidant (1.0 mmol), additive (30 mol %), solvent (2 mL), 100 °C (oil bath temperature) for 14 h. [b]Isolated yields. [c]No catalyst was added. [d]In open air. [e]5.0 mol % of $[CpRuCl(PPh_3)_2]$ catalyst was used. [f]10.0 mol % of $[Ru(OAc)_2(p\text{-cymene})]$ catalyst was used. [g]5.0 mol % of $[RuCl_2(benzene)]_2$ catalyst was used.

With the optimal catalytic system in hand, we moved on to investigate the scope by employing various 2*H*-chromene-3-carboxamides and alkynes (Table 2). Satisfyingly, the present reaction proved broadly applicable and good to excellent yields of benzopyran fused 2-pyridones were obtained. The scope of alkynes was investigated first using *N*-(4-methoxyphenyl)-2*H*-chromene-3-carboxamide **3a** as the partner. These results indicated that symmetrical diarylacetylenes with electron-donating or electron-withdrawing groups proceeded well and afforded the benzopyran derivatives in excellent yields. The reaction of **3a** with heteroarylalkyne (**3g**) under the same catalytic conditions produced **5ag** in good yield. Moreover, dialkylacetylenes such as 3-hexyne (**4h)** and 1,4-dimethoxybut-2-yne (**4i)** reacted smoothly and

furnished the corresponding 2-pyridone derivatives **5ah-5ai** in good yield. To understand the regioselectivity of the present reaction, unsymmetrical alkyne was employed as the substrate for the reaction with **3a**. Thus, 1-phenyl-1-butyne **4j** gave product **5aj** in 75% yield. Only one isomer in which C-aryl carbon occurred adjacent to amide nitrogen was obtained in a highly ***regioselective*** manner. The regiochemistry of the product **5aj** was confirmed by X-ray crystallography (Figure S1, Supporting Information). Similarly, we also isolated the product **5ak** in 78% yield in a regioselective manner by using **3a** and 1-phenyl-1-propyne (**4k)**. In the reaction using the unsymmetrical alkyne 1-methoxy-4-(phenylethynyl)benzene (**4l**), we observed 1:1 ratio of isomeric mixture of **5al** in 83% overall yield (Table 2). We also evaluated the effect of substituents on the nitrogen atom of amide in the reaction with diphenylacetylene. Amides bearing *N*-aryl or *N*-alkyl substituents were effectively converted to the corresponding benzopyran fused 2-pyridones (**5ba-5fa**) in excellent yields (81-90%). The structure of the product **5ba** was further confirmed by single crystal X-ray analysis (Figure S2, Supporting Information). The annulation reaction also worked well in gram scale, and we isolated the compound **5aa** in 80% yield starting with 1.0 g of the precursor **3a**. Three possible intermediates are **I-III**. A possible mechanistic pathway based on the literature reports[3b,3d,3f,3h,3i,26] is presented in Scheme S1 (Supporting Information).

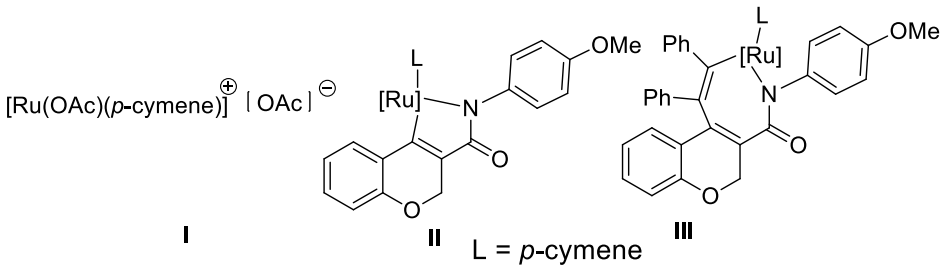
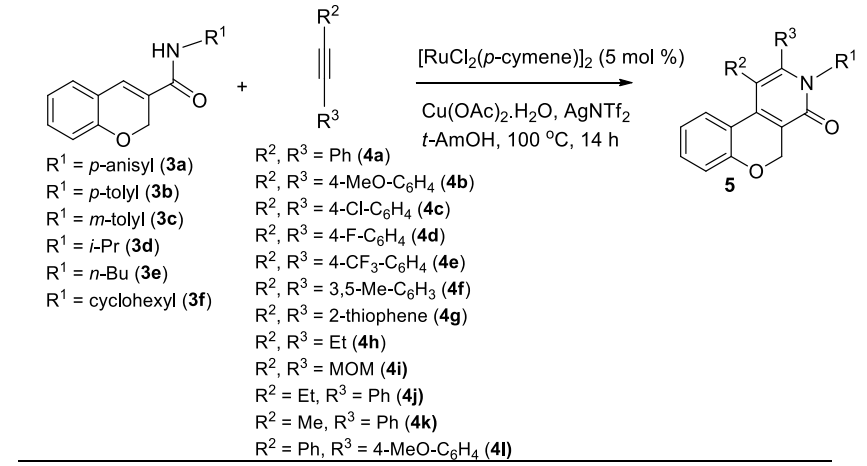
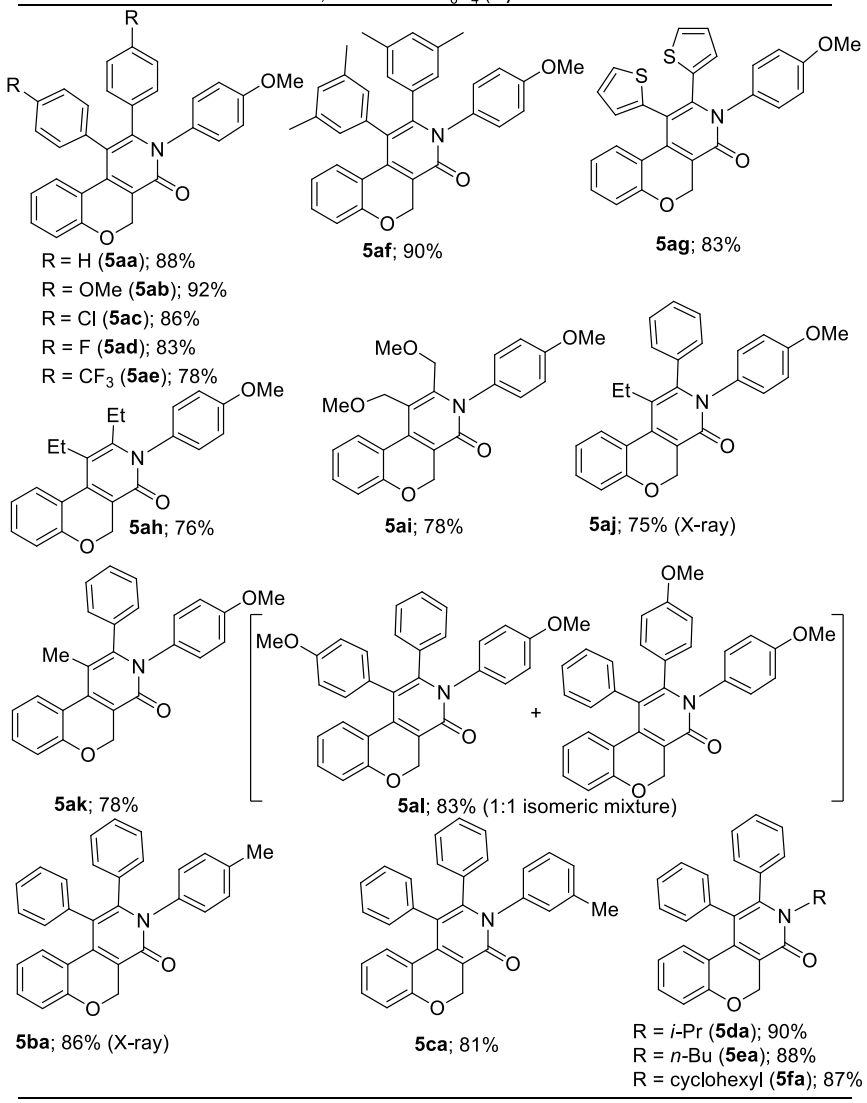


Table 2. Substrate Scope for the Ruthenium-Catalyzed C-H Activation of 2*H*-Chromene-3-carboxamides (3a-f)[a,b,c]





[a]Reaction conditions: 2*H*-chromene-3-carboxamide **3a-f** (0.5 mmol), alkyne **4a-l** (0.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), $Cu(OAc)_2.H_2O$ (1.0 mmol), $AgNTf_2$ (30 mol %), *t*-AmOH (2 mL), 100 °C (oil bath temperature) for 14 h. [b]Isolated yield. [c] Positional assignment (Me/Ph) in the case of **5ak** is based on the structure of **5aj**.

(ii) Ruthenium-Catalyzed One-pot Double C-H Activation of 2*H*-Chromene-3-carboxamides: Annulation Followed by Hydroarylation

In continuation of the above studies, when we treated the 2*H*-chromene-3-carboxamide **3a** with 2.0 equiv of alkyne **4b**, the double C-H activation product **6ab** was isolated in 68% yield (Scheme 2). This is important because here the activation must have come from the carbonyl oxygen coordination to ruthenium rather than a Ru-N covalent bond formation observed in the previous cyclization. Optimization studies revealed that best results could be obtained by using 8 mol % of $[RuCl_2(p\text{-cymene})]_2$, $Cu(OAc)_2\ H_2O$ (2.0 equiv) and $AgNTf_2$ (30 mol %), in *t*-AmOH at 110 °C for 12 h (cf. Table 3).

Scheme 2. Ru-Catalyzed Double C-H Activation Reaction Using 2*H*-Chromene-3-carboxamide 3a

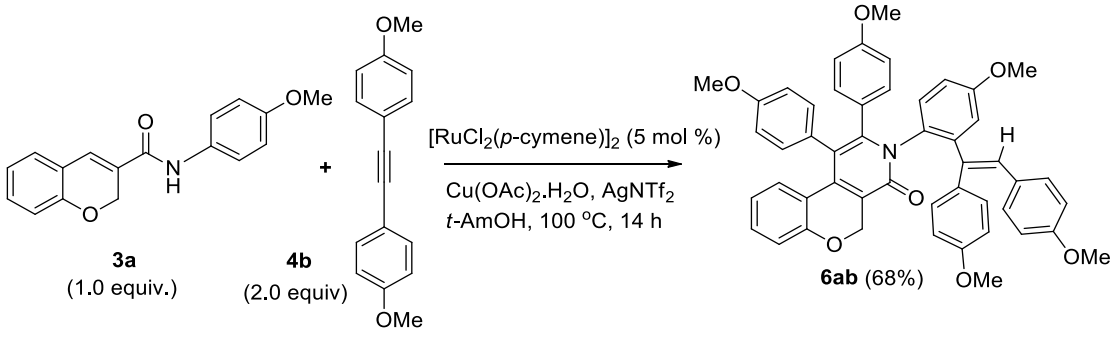


Table 3. Optimization Study for Ruthenium-Catalyzed Double C-H activation[a]

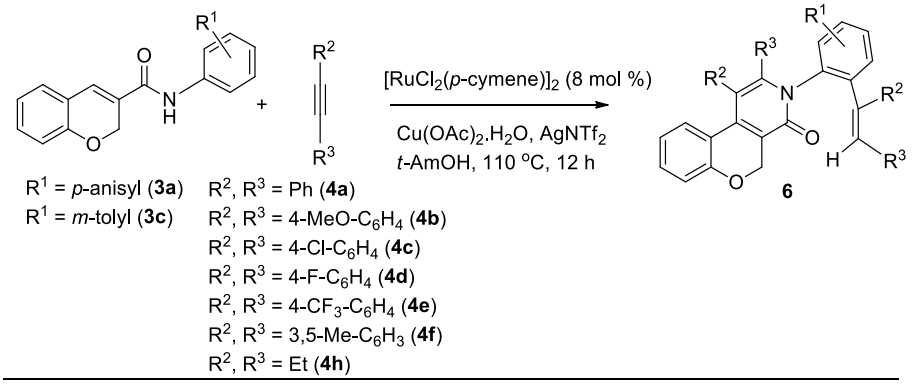
Entry	Ru-catalyst (mol %)[b]	Alkyne **4b** (equiv)	T (^oC)[c]	Time (h)	Yield of **6ab** (%)[d]
1	5	2.0	100	14	68
2	5	2.0	110	14	70
3	5	2.5	110	14	76
4	5	2.5	110	12	75
5	5	2.5	110	10	66
6	**8**	**2.5**	**110**	**12**	**88**
7	8	3.0	110	12	86
8	10	2.5	110	12	88

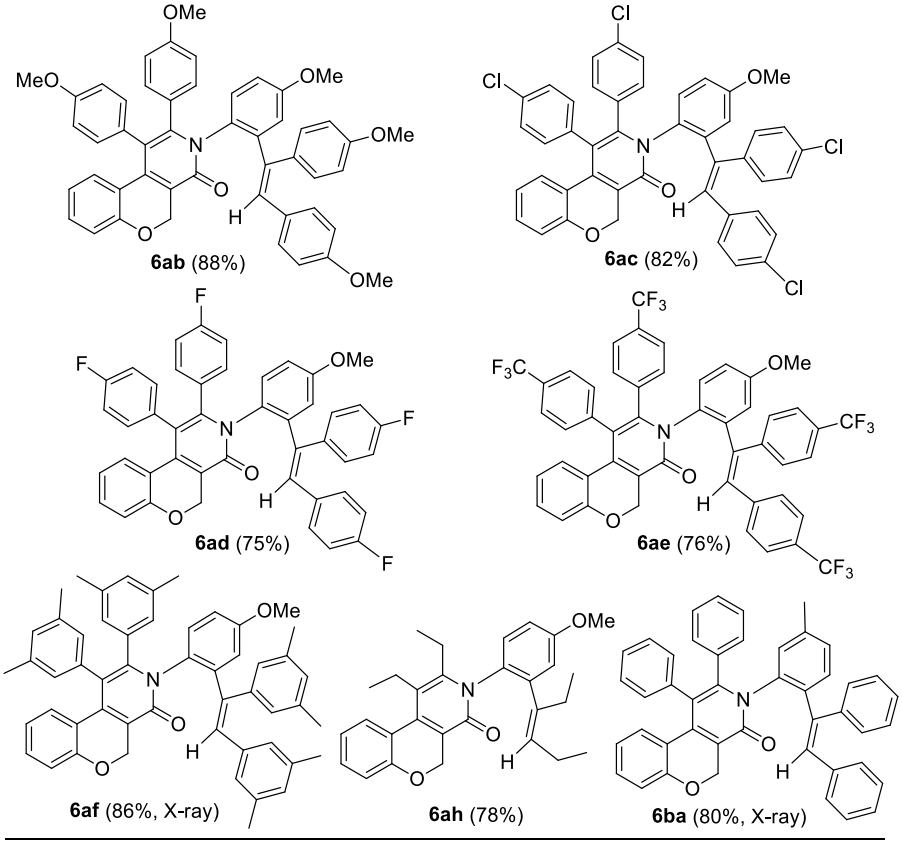
[a]Reaction conditions: 2*H*-chromene-3-carboxamide **3a** (0.5 mmol), alkyne **4b** (1.0-1.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5.0-10 mol %), oxidant (1.0 mmol), additive (30 mol %), solvent (2 mL) for 12-14 h. [b]$[RuCl_2(p\text{-cymene})]_2$. [c]Oil bath temperature. [d]Isolated yields.

Having the optimized reaction conditions in hand, the substrate scope was studied by using differently substituted alkynes (Table 4). Diaryl alkynes bearing electron donating groups as well as withdrawing groups reacted smoothly with chromene-3-carboxamide **3a** and afforded the double C-H activation products **6ab**, **6ae** and **6af** (X-ray, Figure S3, Supporting Information) in excellent yields (76-88%). This protocol was compatible with the presence of synthetically important functional groups such as chloro and fluoro, producing the corresponding double C-H activation products **6ac** and **6ad** in good yields. Moreover, dialkylacetylene such as 3-hexyne (**4h**) was also converted to the corresponding double C-H activation product **6ah** in good yield

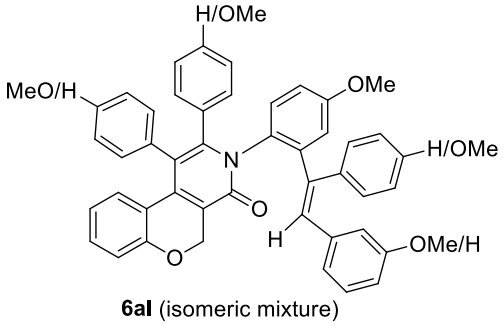
(78%). 3-Methyl substituted chromene-3-carboxamide (**3c**) underwent the C-H functionalization with diphenyl acetylene (**4a**) exclusively at the less hindered position and produced the desired product in good yields (**6ba**, 80%). The structure of compound **6ba** was also confirmed by X-ray crystallography (Figure S4, Supporting Information). Since there is a possibility of regio/stereoisomerism in these hydroarylation products, we treated **5aa** with the unsymmetrical alkyne **4l**, and 1-methyl-4-(phenylethynyl)benzene in separate experiments. As was the case with symmetrical alkynes (*vide infra*), these reactions did not lead to the hydroarylation products. Satisfyingly, though, the one pot reaction of **3a** with two equivalents of unsymmetrical alkyne **4l** produced predominantly (>70%) hydroarylated product **6al**, along with some of the cyclized product **5al**. Since the R_f values were too close, the separation was rather difficult. The NMR data suggested the formation of at least three isomers in this case (see experimental and Supporting Information).

Table 4. Substrate Scope for the Ruthenium-Catalyzed Double C-H Activation of 2*H*-chromene-3-carboxamides (3a or 3c) with alkynes (4a-f and 4h)[a,b]





[a]Reaction conditions: 2*H*-chromene-3-carboxamide **3a** or **3c** (0.5 mmol), alkyne **4a-f** and **4h** (1.25 mmol), $[RuCl_2(p\text{-cymene})]_2$ (8.0 mol %), $Cu(OAc)_2.H_2O$ (1.0 mmol), $AgNTf_2$ (30 mol %), *t*-AmOH (2 mL), 110 °C (oil bath temperature) for 12 h. [b]Isolated yields.



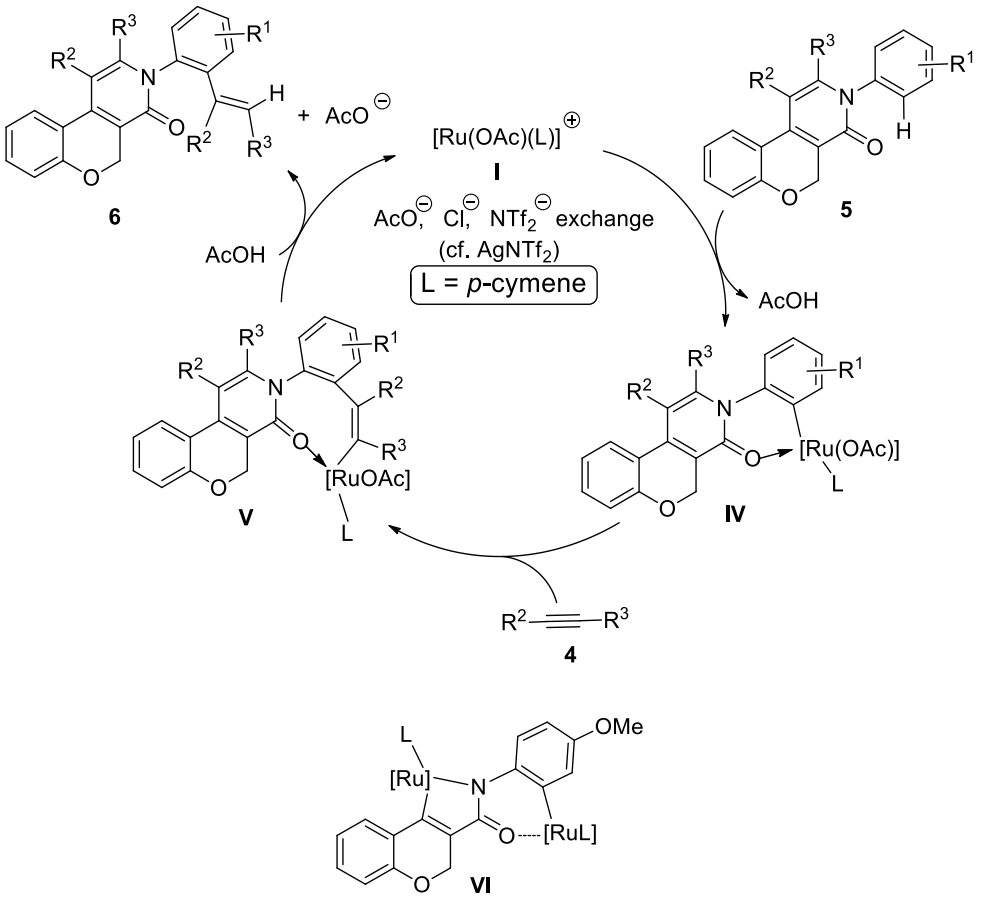
6al (isomeric mixture)

Plausible pathway for the formation of double C-H activation products 6

Formation of double C-H activation products **6** involves annulation followed by hydroarylation. To our knowledge, both of these in a single reaction sequence have not been reported so far. On the basis of previous reports,[3a,c,e,g,4b,6h,27b,28] a possible pathway for the formation of double C-H activation products **6** *via* the annulated products of type **5** is shown in Scheme 3. The active cationic ruthenium species **I** undergoes coordination to Ru via the C=O oxygen atom followed by *ortho* metalation at phenyl ring of amide moiety with subsequent elimination of AcOH providing the ruthenium complex **IV**. Migratory insertion of alkyne moiety into the Ru-C bond furnishes ruthenium intermediate **V**. Finally, intermediate **V** undergoes protonation in the presence of AcOH affording the regio- and stereo-selective formation of double C-H activation products and regenerating the active ruthenium(II) catalyst. However, the tandem annulation/hydroarylation reaction by taking the annulation product **5aa** and alkyne **4a**, **4j**, **4k**, or **4l**) did not work under the conditions employed. Thus experimentally we did not observe such a hydroarylation of **5aa** in the tandem reaction. Hence it is possible that the cyclization/hydroarylation products of type **6** are formed by a different pathway, without the involvement of monocyclized products of type **5**, like that from a doubly activated intermediate like **VI**. The concomitant cyclization/hydroarylation reaction seems to be more facile in a one

pot reaction than in the tandem reaction. Further studies on such hydroarylation in other systems are needed to clarify these observations.

Scheme 3. A Plausible Pathway for the Formation of Double C-H Activation Product (see text also)



Conclusions

We have developed a new protocol of ruthenium-catalyzed oxidative annulation of chromene-3-carboxamides with alkynes for the synthesis of a wide range of benzopyran fused 2-pyridones *via* C-H activation. The reaction features high regioselectivity, good substrate scope, and large functional group tolerance. High regioselectivity was achieved in the case of unsymmetrical alkyne. More significantly, we have also discovered a ***one pot double C-H activation*** process,

involving dual catalytic role for the Ru-complex, when an excess of alkyne is used. In these reactions, one alkyne moiety undergoes annulation with chromene-3-carboxamides and the other alkyne moiety is used up for hydroarylation regio- and stereo-selectively, involving amide- C=O directed C-H bond functionalization.

Experimental Section

General Comments. ^{1}H (400 MHz or 500 MHz), ^{13}C (100 MHz or 125 MHz) and ^{19}F NMR spectra (376 MHz) were recorded in $CDCl_3$ with shifts referenced to $SiMe_4$ (^{1}H, ^{13}C: $\delta = 0$) or $CFCl_3$ ($\delta = 0$). IR spectra were recorded on an FTIR spectrophotometer. Melting points were determined by using a local hot-stage melting point apparatus and are uncorrected. Elemental analyses were carried out on a CHN analyzer. Mass spectra were recorded using LC-MS and HRMS (ESI-TOF analyser) equipment. For column chromatography, silica gel of 100-200 mesh size was used.

(i) Synthesis of 2*H*-Chromene-3-carboxamides (3a-f): General Procedure

Method A: To a stirred solution of 2*H*-chromene-3-carboxylic acid (1.0 equiv) in DCM (50 mL per 6.8 mmol of precursor carboxylic acid) at 0 ^{o}C, oxalyl chloride (2.0 equiv, 13.6 mmol) was added dropwise slowly over a period of 10 min and then catalytic amount (10 drops) of DMF was added. The reaction mixture was kept at 0 ^{o}C for 30 min and then at rt (25 ^{o}C) overnight till complete consumption of the starting material. The solvent was removed by using rotary evaporator. The residue was dissolved in dry toluene (40 mL per 6.8 mmol of precursor carboxylic acid) and DMAP (2.0 equiv) at rt (25 ^{o}C). Alkyl or aryl amine (1.2 equiv) was added after 10 min to this solution and the mixture kept at rt (25 ^{o}C) for 2-3 h. After the completion of the reaction (TLC), the solvent was removed using rotary evaporator and then water (2 x 10 mL

per 6.8 mmol of precursor carboxylic acid) was added. The mixture was extracted with ethyl acetate (2 x 30 mL per 6.8 mmol of precursor carboxylic acid), washed with brine (2 x 10 mL per 6.8 mmol of precursor carboxylic acid), dried over Na_2SO_4, and filtered. The solvent was removed and the crude product was purified by column chromatography by using silica gel with ethyl acetate/hexane mixture (ratio *ca* 1:9) as the eluent to afford the corresponding 2*H*-chromene-3-carboxamides. Amides **3a** and **3e** were prepared by this method. Amide **3e** is known but **3a** is new.

Method B: To a stirred solution of 2*H*-chromene-3-carboxylic acid (1.0 equiv) in DCM (50 mL per 6.8 mmol of precursor carboxylic acid) at 0 ^oC, EDC.HCl (1.2 equiv) and DMAP (2.0 equiv) were added. Alkyl or aryl amine (1.2 equiv) was added after 10 min to this solution and the mixture was kept at 0 ^oC for 1 h and then at rt (25 ^oC) for 2-3 h. After the completion of the reaction (TLC), the solvent was removed using rotary evaporator and then water (2 x 10 mL per 6.8 mmol of precursor carboxylic acid) was added. The mixture was extracted with ethyl acetate (2 x 30 mL per 6.8 mmol of precursor carboxylic acid), washed with brine (2 x 10 mL per 6.8 mmol of precursor carboxylic acid), dried over Na_2SO_4, and filtered. The solvent was removed and the crude product was purified by column chromatography by using silica gel with ethyl acetate/hexane mixture (ratio *ca* 1:9) as the eluent to afford the corresponding 2*H*-chromene-3-carboxamides. Amides **3b-d** and **3f** were prepared by this method and they are new.

*N-(4-methoxyphenyl)-2H-chromene-3-carboxamide (**3a**)*: Yield: 1.65 g (86 %) as pale yellow solid; mp: 145–147 ^oC; R_f = 0.52 (9:1 hexane/ethyl acetate); IR (KBr) 3370, 3215, 3035, 2957, 2828, 1656, 1623, 1538, 1511, 1287, 1251, 1205, 1034, 827, 761 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.50-7.47 (m, 2H), 7.27-7.24 (m, 1H), 7.14 (dd, *J* = 7.5 Hz and *J* = 1.5 Hz, 1H), 7.09 (s, 1H), 6.97-6.94 (m, 1H), 6.92-6.89 (m, 3H), 5.09 (d, *J* = 1.0 Hz, 2H), 3.82 (s,

3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.5, 156.7, 154.9, 131.5, 130.6, 128.4, 127.5, 127.2, 122.4, 121.8, 120.9, 116.2, 114.3, 64.9, 55.5. LC-MS: *m/z* 282 $[M+1]^+$. Anal. Calcd. For $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.43; H, 5.45; N, 4.89.

*N-(p-tolyl)-2H-chromene-3-carboxamide (**3b**)*: Yield: 1.50 g (83 %) as white solid; mp: 152–154 ^oC; R_f = 0.48 (9:1 hexane/ethyl acetate); IR (KBr) 3259, 2970, 2843, 1647, 1599, 1538, 1513, 1407, 1252, 1211, 820, 746 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.24-7.21 (m, 1H), 7.12 (d, *J* = 8.5 Hz, 2H), 7.06 (s, 1H), 7.02 (dd, *J* = 7.5 Hz and *J* = 2.0 Hz, 1H), 6.93-6.89 (m, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 5.03 (d, *J* = 1.5 Hz, 2H), 2.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.6, 154.8, 134.9, 134.4, 131.4, 129.5, 128.4, 127.7, 127.0, 121.8, 120.9, 120.6, 116.1, 64.8, 20.9. LC-MS: *m/z* 266 $[M+1]^+$. Anal. Calcd. For $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.85; H, 5.78; N, 5.23.

*N-(m-tolyl)-2H-chromene-3-carboxamide (**3c**)*: Yield: 1.40 g (78 %) as brown solid; mp: 143–145 ^oC; R_f = 0.50 (9:1 hexane/ethyl acetate); IR (KBr) 3267, 3040, 2828, 1604, 1641, 1538, 1457, 1320, 1299, 1221, 1015 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.0 (s, 1H), 7.43 (s, 1H), 7.37 (d, *J* = 8.5 Hz, 1H), 7.28-7.19 (m, 2H), 7.07-7.04 (m, 2H), 6.96-6.86 (m, 3H), 5.04 (s, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 154.8, 139.0, 137.4, 131.5, 128.9, 128.5, 127.7, 127.1, 125.5 121.8, 121.1, 120.9, 117.5, 116.1, 64.8, 21.5. LC-MS: *m/z* 266 $[M+1]^+$. Anal. Calcd. For $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.85; H, 5.76; N, 5.23.

*N-isopropyl-2H-chromene-3-carboxamide (**3d**)*: Yield: 1.27 g (86 %) as white solid; mp: 108–110 ^oC; R_f = 0.69 (9:1 hexane/ethyl acetate); IR (KBr) 3264, 3070, 2968, 2828, 1650, 1602, 1547, 1460, 1352, 1292, 1208, 1020, 755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 7.2 Hz, 1H), 6.94 (s, 1H), 6.89 (t, *J* = 7.2 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H),

6.04 (s, 1H), 5.0 (s, 2H), 4.20-4.16 (m, 1H), 1.22 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 154.7, 131.1, 128.2, 127.2, 126.6, 121.7, 121.1, 116.0, 64.9, 41.6, 22.7. LC-MS: *m/z* 218 $[M+1]^+$. Anal. Calcd. For $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.69; H, 6.91; N, 6.54.

*N-cyclohexyl-2H-chromene-3-carboxamide (**3f**)*: Yield: 1.31 g (75 %) as white solid; mp: 136–138 ^oC; R_f = 0.67 (9:1 hexane/ethyl acetate); IR (KBr) 3320, 2936, 2853, 1652, 1614, 1529, 1486, 1452, 1325, 1201, 896, 757 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.19 (m, 1H), 7.10 (dd, *J* = 7.6 Hz and *J* = 1.6 Hz, 1H), 6.95-6.91 (m, 2H), 6.86 (d, *J* = 8.4 Hz, 1H), 5.70 (d, *J* = 7.2 Hz, 1H), 5.01 (d, *J* = 1.6 Hz, 2H), 3.93-3.84 (m, 1H), 2.02-1.98 (m, 2H), 1.79-1.65 (m, 3H), 1.48-1.37 (m, 2H), 1.26-1.15 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 159.1, 154.8, 131.2, 128.2, 126.4, 121.8, 121.1, 116.1, 65.1, 48.4, 33.3, 25.6, 25.4, 25.0, 24.8. LC-MS: *m/z* 258 $[M+1]^+$. Anal. Calcd. For $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.52; H, 7.38; N, 5.49.

(ii) Synthesis of Benzopyran fused 2-Pyridone Derivatives 5aa-5al and 5ba-5fa: General Procedure

Into a 10 mL round-bottomed flask, 2*H*-chromene-3-carboxamide (one of **3a-f**, 0.5 mmol), diaryl or dialkyl acetylene (one of **4a-l**, 0.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol %), $Cu(OAc)_2.H_2O$ (1.0 mmol) and $AgNTf_2$ (30 mol %) were added under N_2 atmosphere. To this, *t*AmOH (2 mL) was added and the mixture stirred at 100 ^oC (oil bath temperature) for 14 h. After cooling to rt, saturated NH_4Cl solution (50 mL) was added and the contents extracted with EtOAc (3 x 30 mL). The combined organic phase was washed with brine solution (2 x 25 mL),

dried over anhy. Na_2SO_4 and concentrated *in vacuo.* The crude product was purified by column chromatography on silica gel using *n*-hexane-EtOAc (4:1) mixture as the eluent.

3-(4-methoxyphenyl)-1,2-diphenyl-3H-chromeno[3,4-c]pyridin-4(5H)-one (***5aa***): This compound was prepared by using precursors **3a** and **4a**. Yield: 0.201 g (88%) as pale yellow solid; mp: 228–230 ^oC; R_f = 0.28 (4:1 hexane/ethyl acetate); IR (KBr) 3055, 2828, 1650, 1511, 1490, 1438, 1242, 1025, 839, 798, 762, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.15 (~t, *J* = 7.0 Hz, 2H), 7.10-7.09 (m, 2H), 7.03-6.92 (m, 8H), 6.83-6.82 (m, 2H), 6.73 (d, *J* = 8.8 Hz, 2H), 6.52 (t, *J* = 7.6 Hz, 1H), 6.45 (~d, *J* = 8.0 Hz, 1H), 5.19 (s, 2H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 158.7, 157.5, 147.4, 139.7, 137.4, 134.4, 131.5, 130.8, 130.7, 129.9, 128.9, 128.1, 127.5, 127.3, 126.9, 122.4, 121.4, 120.9, 117.7, 117.5, 114.0, 64.1, 55.3; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{31}H_{24}NO_3$ 458.1756; Found 458.1756.

1,2,3-tris(4-methoxyphenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one (***5ab***): Precursors **3a** and **4b** were used. Yield: 0.238 g (92%) as pale yellow solid; mp: 215–217 ^oC; R_f = 0.20 (4:1 hexane/ethyl acetate); IR (KBr) 3008, 2838, 1644, 1605, 1501, 1293, 1244, 1184, 1041, 838, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.18-7.14 (m, 1H), 7.03-7.01 (m, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.76-6.71 (m, 4H), 6.66 (d, *J* = 8.8 Hz, 2H), 6.59-6.55 (m, 1H), 6.52-6.50 (m, 1H), 6.47 (d, *J* = 8.8 Hz, 2H), 5.18 (s, 2H), 3.74 (s, 3H), 3.73 (s, 3H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 158.6, 158.3, 157.5, 147.5, 139.9, 132.5, 131.9, 131.8, 130.6, 129.9, 129.8, 128.8, 126.9, 122.3, 121.7, 120.9, 117.6, 117.5, 114.1, 113.6, 112.7, 64.2, 55.3, 55.1, 55.0; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{33}H_{28}NO_5$ 518.1967; Found 518.1965.

1,2-bis(4-chlorophenyl)-3-(4-methoxyphenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one ***(5ac)***: Precursors **3a** and **4c** were used. Yield: 0.225 g (86%) as pale yellow solid; mp: 260–262 ^{o}C; R_f = 0.36 (4:1 hexane/ethyl acetate); IR (KBr) 2932, 2833, 2362, 1644, 1595, 1512, 1485, 1392, 1238, 1090, 1008, 762 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.17 (m, 1H), 7.12 (d, *J* = 8.4 Hz, 2H), 7.04 (dd, *J* = 1.2 Hz and *J* = 8.0 Hz, 1H), 6.98-6.94 (m, 4H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.78-6.75 (m, 4H), 6.62-6.58 (m, 1H), 6.44 (dd, *J* = 1.6 Hz and *J* = 8.0 Hz, 1H), 5.17 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 157.5, 146.3, 139.5, 135.8, 133.9, 133.3, 132.8, 132.7, 131.9, 131.2, 131.1, 129.9, 128.6, 127.9, 123.1, 121.1_0, 121.0_8, 117.8, 116.6, 114.3, 64.1, 55.4; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{32}H_{22}Cl_2NO_3$ 526.0976; Found 526.0973.

1,2-bis(4-fluorophenyl)-3-(4-methoxyphenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one ***(5ad)***: Precursors **3a** and **4d** were used. Yield: 0.205g (83%) as pale brown solid; mp: 276–278 ^{o}C; R_f = 0.31 (4:1 hexane/ethyl acetate); IR (KBr) 3052, 2997, 2959, 2833, 1644, 1595, 1496, 1299, 1238, 1211, 1156, 1008, 767 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.16 (m, 1H), 7.04 (dd, *J* = 8.2 Hz and *J* = 0.6 Hz, 1H), 6.97-6.91 (m, 4H), 6.85-6.75 (m, 6H), 6.67 (t, *J* = 8.6 Hz, 2H), 6.61-6.56 (m, 1H), 6.45 (dd, *J* = 8.0 Hz and *J* = 1.2 Hz, 1H), 5.18 (s, 2H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7 (d, *J* = 246.0 Hz), 161.6 (d, *J* = 247.0 Hz), 160.0, 158.9, 157.5, 146.7, 139.6, 133.3 (d, *J* = 3.0 Hz), 133.1 (d, *J* = 8.0 Hz), 131.4, 131.0, 132.5 (d, *J* = 8.0 Hz), 130.4 (d, *J* = 3.0 Hz), 129.9, 128.6, 122.9, 121.2, 121.0, 117.7, 116.9, 115.4 (d, *J* = 21.0 Hz), 114.7 (d, *J* = 22.0 Hz), 114.2, 64.1, 55.4; ^{19}F NMR (376 MHz; proton coupled; $CDCl_3$): δ -112.5, -114.4; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{31}H_{22}F_2NO_3$ 494.1567; Found 494.1563.

3-(4-methoxyphenyl)-1,2-bis(4-(trifluoromethyl)phenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one ***(5ae)***: Precursors **3a** and **4e** were used. Yield: 0.232 g (78%) as brown solid; mp: 241–243 ^{o}C; R_f

= 0.27 (4:1 hexane/ethyl acetate); IR (KBr) 3008, 2953, 2844, 2367, 1644, 1512, 1321, 1249, 1162, 1134, 1068, 1014, 855, 773 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.22-7.17 (m, 1H), 7.11-7.04 (m, 3H), 6.97 (d, *J* = 8.8 Hz, 4H), 6.76 (d, *J* = 9.2 Hz, 2H), 6.58-6.54 (m, 1H), 6.34 (dd, *J* = 1.6 Hz and *J* = 8.0 Hz, 1H), 5.19 (s, 2H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 159.2, 157.6, 146.1, 141.0, 139.4, 137.7, 131.9, 131.3, 131.1, 130.9, 129.9, 129.4, 128.5, 125.2 (qrt, *J* = 3.7 Hz), 124.6 (qrt, *J* = 3.7 Hz), 123.6, 123.7 and 123.3 (two qrt, *J* ~ 272.0 Hz), 121.1, 120.8, 117.9, 116.4, 114.4, 64.0, 55.4; ^{19}F NMR (376 MHz; proton coupled; $CDCl_3$): δ -62.7, -63.0; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{34}H_{22}F_6NO_3$ 594.1504; Found 594.1508.

1,2-bis(3,5-dimethylphenyl)-3-(4-methoxyphenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one (***5af***): Precursors **3a** and **4f** were used. Yield: 0.232g (90%) as pale yellow solid; mp: 216–218 °C; R_f = 0.30 (4:1 hexane/ethyl acetate); IR (KBr) 3057, 2997, 2915, 2838, 1649, 1605, 1512, 1463, 1249, 1030, 822, 844, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18-7.14 (m, 1H), 7.03-6.97 (m, 3H), 6.75-6.71 (m, 3H), 6.60-6.53 (m, 5H), 6.44 (s, 2H), 5.19 (s, 2H), 3.72 (s, 3H), 2.10 (s, 6H), 2.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 158.7, 157.4, 147.7, 139.7, 137.1$_2$, 137.0$_9$, 136.3, 134.1, 131.8, 130.7, 129.9, 129.3, 129.1, 128.8, 128.6, 128.3, 121.7, 121.6, 120.8, 117.9, 117.4, 113.8, 64.1, 55.4, 21.1, 21.0; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{36}H_{32}NO_3$ 514.2382; Found 514.2385.

3-(4-methoxyphenyl)-1,2-di(thiophen-2-yl)-3H-chromeno[3,4-c]pyridin-4(5H)-one (***5ag***): Precursors **3a** and **4g** were used. Yield: 0.195 g (83%) as pale yellow solid; mp: 256–258 °C; R_f

= 0.36 (4:1 hexane/ethyl acetate); IR (KBr) 3074, 2833, 1496, 1436, 1249, 1162, 1123, 1019, 838, 756, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24-7.20 (m, 2H), 7.12 (d, *J* = 4.5 Hz, 1H), 7.05 (t, *J* = 9.5 Hz, 3H), 6.86-6.85 (m, 1H), 6.81 (d, *J* = 8.5 Hz, 2H), 6.72 (d, *J* = 3.0 Hz, 1H), 6.70-6.64 (m, 3H), 6.61 (d, *J* = 3.0 Hz, 1H), 5.17 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.0, 159.1, 157.4, 142.4, 140.0, 138.6, 134.3, 131.4, 131.2, 131.1, 129.9, 129.7, 128.1, 128.0, 127.0, 126.8, 125.8, 123.4, 121.2, 121.1, 117.5, 114.1, 112.4, 64.0, 55.4; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{28}H_{20}NO_3S_2$ 470.0884; Found 470.0887.

1,2-diethyl-3-(4-methoxyphenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one (***5ah***): Precursors **3a** and **4h** were used. Yield: 0.138g (76%) as pale yellow solid; mp: 198–200 °C; R_f = 0.32 (4:1 hexane/ethyl acetate); IR (KBr) 2975, 2844, 2362, 1879, 1638, 1501, 1457, 1293, 1249, 1025, 767 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 1.3 Hz and *J* = 9.8 Hz, 1H), 7.37-7.33 (m, 1H), 7.18 (d, *J* = 11.0 Hz, 2H), 7.12-7.08 (m, 2H), 7.04 (d, *J* = 11.0 Hz, 2H), 5.00 (s, 2H), 3.88 (s, 3H), 2.79 (qrt, *J* = 9.3 Hz, 2H), 2.54 (qrt, *J* = 9.3 Hz, 2H), 1.34 (t, *J* = 9.3 Hz, 3H), 1.00 (t, *J* = 9.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 159.5, 157.9, 148.7, 141.1, 131.5, 130.8, 129.4, 127.4, 122.5, 121.8, 121.6, 118.1, 115.6, 114.8, 55.6, 23.3, 21.6, 15.9, 13.7; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{24}H_{24}NO_3$ 362.1756; Found 362.1759.

1,2-bis(methoxymethyl)-3-(4-methoxyphenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one (***5ai***): Precursors **3a** and **4i** were used. Yield: 0.153 g (78%) as gummy liquid; R_f = 0.29 (4:1 hexane/ethyl acetate); IR (neat) 2921, 2833, 1721, 1644, 1605, 1518, 1463, 1397, 1299, 1244, 1085, 942, 762 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.16-7.10 (m, 2H), 7.04 (d, *J* = 8.8 Hz, 2H), 5.04 (s, 2H), 4.36 (s,

2H), 4.12 (s, 2H), 3.89 (s, 3H), 3.57 (s, 3H), 3.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 159.8, 157.5, 146.1, 141.6, 131.4, 129.6, 127.6, 123.7, 122.2, 121.8, 121.6, 117.9, 114.5, 112.4, 68.2, 67.2, 64.1, 58.7, 58.2, 55.6; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{24}H_{24}NO_5$ 394.1654; Found 394.1652.

1-ethyl-3-(4-methoxyphenyl)-2-phenyl-3H-chromeno[3,4-c]pyridin-4(5H)-one ***(5aj)***: Precursors **3a** and **2j** were used. Yield: 0.153 g (75%) as yellow solid; mp: 216–218 °C; R_f = 0.28 (4:1 hexane/ethyl acetate); IR (KBr) 2964, 2838, 1638, 1551, 1512, 1299, 1244, 1030, 827, 762, 707 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 8.0 Hz and *J* = 1.5 Hz, 1H), 7.39-7.35 (m, 1H), 7.25-7.20 (m, 3H), 7.15 (dd, *J* = 8.3 Hz and *J* = 1.3 Hz, 1H), 7.11-7.08 (m, 3H), 6.92 (d, *J* = 9.0 Hz, 2H), 6.72 (d, *J* = 9.0 Hz, 2H), 5.11 (s, 2H), 3.72 (s, 3H), 2.57 (qrt, *J* = 7.3 Hz, 2H), 0.97 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 158.6, 157.8, 147.3, 140.7, 134.8, 131.9, 131.2, 131.0, 130.2, 130.0, 128.2, 128.0, 127.4, 123.4, 122.5, 121.7, 118.1, 116.9, 114.0, 64.2, 55.3, 22.8, 15.3; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{28}H_{24}NO_3$ 410.1756; Found 410.1758.

3-(4-methoxyphenyl)-1-methyl-2-phenyl-3H-chromeno[3,4-c]pyridin-4(5H)-one ***(5ak)***: Precursors **3a** and **4k** were used. Yield: 0.155 g (78%) as yellow solid; mp: 186–188 °C; R_f = 0.30 (4:1 hexane/ethyl acetate); IR (KBr) 2929, 2838, 1643, 1509, 1297, 1248, 1026, 834, 756, 704 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.8 Hz and *J* = 1.3 Hz, 1H), 7.38-7.34 (m, 1H), 7.24-7.22 (m, 3H), 7.14 (dd, *J* = 8.3 Hz and *J* = 1.0 Hz, 1H), 7.09-7.07 (m, 3H), 6.97-6.94 (m, 2H), 6.75-6.72 (m, 2H), 5.13 (s, 2H), 3.73 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 158.6, 157.8, 147.3, 140.7, 134.8, 131.9, 131.2, 131.0, 130.2, 130.0, 128.2,

128.0, 127.4, 123.4, 122.5, 121.7, 118.1, 116.9, 114.0, 64.2, 55.3, 19.1; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{26}H_{22}NO_3$ 396.1599; Found 396.1598.

*2,3-bis(4-methoxyphenyl)-1-phenyl-3H-chromeno[3,4-c]pyridin-4(5H)-one (**5al**)*: Precursors **3a** and **4l** were used. Yield: 0.202 g (83%, 1:1 isomeric mixture) as yellow solid; mp: 204–206 °C; R_f = 0.32 (4:1 hexane/ethyl acetate); IR (KBr) 2926, 2838, 1645, 1605, 1508, 1294, 1248, 1180, 1029, 761, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.19-7.11 (m, 5H), 7.04-7.02 (m, 2H), 6.99-6.95 (m, 9H), 6.87-6.86 (m, 2H), 6.84-6.82 (m, 2H), 6.77-6.72 (m, 6H), 6.64 (d, *J* = 8.5 Hz, 2H), 6.60-6.51 (m, 3H), 6.47-6.42 (m, 3H), 5.19 (s, 4H), 3.75-3.73 (3 s, 9H), 3.64 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 160.1, 158.8, 158.7, 158.4_1, 158.3_8, 157.5, 147.6, 147.4, 140.0, 139.7, 137.7, 134.6, 132.6, 132.0, 131.8, 131.7, 131.6, 130.7, 130.0, 129.9, 129.7, 128.9, 128.2, 127.4_2, 127.3_5, 126.9, 126.8, 122.4, 121.7, 121.6, 121.0, 120.9, 118.0, 117.6, 117.3, 114.1_3, 114.0_6, 113.6, 112.8, 64.2, 55.3_9, 55.3_8, 55.2, 55.0; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{32}H_{26}NO_4$ 488.1862; Found 488.1863.

*1,2-diphenyl-3-(p-tolyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one (**5ba**)*: Precursors **3b** and **4a** were used. Yield: 0.190 g (86%) as pale yellow solid: mp: 234–236 °C; R_f = 0.30 (4:1 hexane/ethyl acetate); IR (KBr) 2992, 2838, 2236, 1649, 1485, 1441, 1348, 1271, 1238, 1123, 1014, 762 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 7.19-7.14 (m, 1H), 7.11-7.08 (m, 3H), 7.05-7.02 (m, 3H), 6.99-6.97 (m, 3H), 6.96-6.92 (m, 4H), 6.85-6.82 (m, 2H), 6.56-6.51 (m, 1H), 6.46 (dd, *J* = 8.0 Hz and *J* = 1.6 Hz, 1H), 5.20 (s, 2H), 2.25 (s, 3H); ^{13}C NMR (400MHz, $CDCl_3$) δ 159.9, 157.5, 147.2, 139.7, 137.7, 137.4, 136.2, 134.3, 131.6, 130.8, 129.4, 128.8, 128.7, 128.1, 127.4,

127.2, 126.9, 122.5, 121.5, 120.9, 117.6, 117.5, 64.1, 21.1; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{31}H_{24}NO_2$ 442.1807; Found 442.1805.

*1,2-diphenyl-3-(m-tolyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one (**5ca**)*: Precursors **3c** and **4a** were used. Yield: 0.179 g (81%) as yellow solid;. Mp: 246–248 ºC; R_f = 0.30 (4:1 hexane/ethyl acetate); IR (KBr) 3052, 3025, 2921, 2849, 1638, 1485, 1342, 1244, 1205, 1129, 1019, 762 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 7.19-7.15 (m, 1H), 7.13-7.09 (m, 4H), 7.04 (dd, *J* = 8.0 Hz and *J* = 1.2 Hz, 1H), 6.99-6.96 (m, 3H), 6.94-6.87 (m, 5H), 6.85-6.84 (m, 2H), 6.56-6.52 (m, 1H), 6.46 (dd, *J* = 8.0 Hz and *J* = 1.6 Hz, 1H), 5.21 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 159.8, 157.5, 147.1, 139.7, 138.7, 138.6, 137.4, 134.3, 130.8_1, 130.7_6, 129.6, 128.9, 128.7, 128.5, 128.1, 127.5, 127.2, 127.1, 126.9, 126.0, 122.5, 121.5, 120.9, 117.7, 117.6, 64.1, 21.1; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{31}H_{24}NO_2$ 442.1807; Found 442.1801.

*3-isopropyl-1,2-diphenyl-3H-chromeno[3,4-c]pyridin-4(5H)-one (**5da**)*: Precursors **3d** and **4a** were used. Yield: 0.177 g (90%) as yellow solid; mp: 262–264 ºC; R_f = 0.44 (4:1 hexane/ethyl acetate); IR (KBr) 2995, 2843, 1619, 1531, 1469, 1443, 1386, 1237, 1240, 1113, 1012, 890, 760 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.24-7.20 (m, 3H), 7.10-7.04 (m, 6H), 6.97 (dd, *J* = 8.0 Hz and *J* = 1.0 Hz, 1H), 6.91-6.89 (m, 2H), 6.48-6.44 (m, 1H), 6.38 (dd, *J* = 8.0 Hz and *J* = 1.5 Hz, 1H), 5.17 (s, 2H), 4.14-4.09 (m, 1H), 1.56 (d, *J* = 6.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.9, 157.2, 147.4, 138.1, 138.0, 135.2, 131.5, 130.4, 129.4, 128.5, 128.3, 128.1, 127.9, 126.7, 122.8, 121.3, 120.8, 117.9, 117.3, 63.9, 54.5, 19.3; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{27}H_{24}NO_2$ 394.1807; Found 394.1805.

*3-butyl-1,2-diphenyl-3H-chromeno[3,4-c]pyridin-4(5H)-one (**5ea**)*: Precursors **3e** and **4a** were used. Yield: 0.180 g (88%) as pale yellow solid; mp: 196–198 ^{o}C; R_f = 0.38 (4:1 hexane/ethyl acetate); IR (KBr) 2994, 2843, 2235, 1655, 1489, 1445, 1344, 1276, 1243, 1129, 1015, 761 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26-7.23 (m, 3H), 7.15-7.07 (m, 6H), 7.00 (dd, *J* = 8.0 Hz and *J* = 1.0 Hz, 1H), 6.93-6.91 (m, 2H), 6.51-6.48 (m, 1H), 6.41 (dd, *J* = 8.5 Hz and *J* = 1.5 Hz, 1H), 5.20 (s, 2H), 3.82-3.79 (m, 2H), 1.64-1.61 (m, 2H), 1.20-1.12 (m, 2H), 0.75 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 157.3, 147.2, 138.6, 137.7, 134.3, 131.5, 130.6, 129.9, 128.7, 128.4, 128.0, 127.9, 126.8, 121.5, 121.4, 120.8, 117.9, 117.4, 64.1, 46.6, 30.7, 20.1, 13.4; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{28}H_{26}NO_2$ 408.1963; Found 408.1966.

*3-cyclohexyl-1,2-diphenyl-3H-chromeno[3,4-c]pyridin-4(5H)-one (**5fa**)*: Precursors **3f** and **4a** were used; Yield: 0.202 g (93%) as white solid; mp: 218–220 ^{o}C; R_f = 0.60 (4:1 hexane/ethyl acetate); IR (KBr) 2931, 2848, 1634, 1521, 1485, 1443, 1402, 1247, 1113, 1056, 751, 710 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.23 (m, 3H), 7.14-7.06 (m, 6H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.93-6.91 (m, 2H), 6.51-6.47 (m, 1H), 6.38 (dd, *J* = 8.0 Hz and *J* = 1.2 Hz, 1H), 5.17 (s, 2H), 3.62-3.59 (m, 1H), 2.90-2.82 (m, 2H), 1.76-1.63 (m, 4H), 1.53-1.21 (m, 2H), 0.91-0.79 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.1, 159.1, 157.2, 147.6, 138.1, 135.3, 131.5, 130.5, 129.3, 128.5, 128.3, 128.1, 127.9, 126.7, 122.9, 121.4, 120.8, 117.9, 117.4, 64.0, 48.8, 32.6, 26.2, 25.4, 25.0, 24.7; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{30}H_{28}NO_2$ 434.2120; Found 434.2123.

(iii) Synthesis of Annulation cum Hydroarylation Products by the Ru-Catalyzed Double C-H Activation: General Procedure

In a 10 mL round-bottomed flask, a mixture of 2*H*-chromene-3-carboxamide (**3a** or **3c**, 0.5 mmol), diaryl or dialkyl acetylene (one of **4a-f** or **4h** 1.25 mmol), $[RuCl_2(p\text{-cymene})]_2$ (8 mol %), $Cu(OAc)_2.H_2O$ (1.0 mmol) and $AgNTf_2$ (30 mol %) was taken under N_2 atmosphere. To this, *t*AmOH (2 mL) was added and the mixture was stirred at 110 ^oC (oil bath temperature) for 12 h. After cooling to rt, saturated NH_4Cl solution (50 mL) was added and the contents extracted with EtOAc (3 x 30 mL). The combined organic phase was washed with brine solution (2 x 15 mL), dried over anh. Na_2SO_4 and concentrated *in vacuo.* The crude product was purified by column chromatography on silica gel using *n*-hexane-EtOAc (4:1) mixture as the eluent.

*(E)-3-(2-(1,2-bis(4-methoxyphenyl)vinyl)-4-methoxyphenyl)-1,2-bis(4-methoxyphenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one (**6ab**)*: Precursors **3a** and **4b** were used. Yield: 0.332 g (88 %) as brown solid; mp: 166–168 ^oC; R_f = 0.28 (4:1 hexane/ethyl acetate); IR (KBr) 2932, 2827, 2044, 1715, 1638, 1611, 1496, 1348, 1293, 1249, 1030, 833, 745 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.5 Hz, 1H), 7.11-7.08 (m, 1H), 6.98-6.93 (m, 5H), 6.86 (d, *J* = 8.5 Hz, 2H), 6.81-6.78 (m, 3H), 6.71-6.66 (m, 5H), 6.56-6.46 (m, 5H), 6.33 (dd, *J* = 8.0 Hz and *J* = 1.5 Hz, 1H), 6.00 (s, 1H), 4.75-4.66 (m, 2H), 3.80 (s, 3H), 3.77 (s, 3H), 3.75 (s, 3H), 3.73 (s, 3H), 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 159.0, 158.5, 158.4, 158.2, 157.3, 146.8, 142.7, 139.0, 138.3, 132.8, 132.4, 132.3, 131.9, 130.6, 130.2, 130.0, 129.9, 129.8_3, 129.8_0, 128.7, 126.3, 121.6, 120.6, 117.4, 117.3, 116.8, 113.5, 113.2, 113.0, 111.9, 111.7, 63.9, 55.4, 55.2, 55.1, 55.0, 54.9; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{49}H_{42}NO_7$ 756.2961; Found 756.2966.

*(E)-3-(2-(1,2-bis(4-chlorophenyl)vinyl)-4-methoxyphenyl)-1,2-bis(4-chlorophenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one (**6ac**)*: Precursors **3a** and **4c** were used. Yield: 0.317 g (82 %)

as white solid; mp: 264–266 ºC; R_f = 0.32 (4:1 hexane/ethyl acetate); IR (KBr) 2838, 1644, 1595, 1485, 1392, 1288, 1085, 1008, 822, 751 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.17-7.12 (m, 7H), 7.03-6.96 (m, 4H), 6.93 (s, 1H), 6.91-6.88 (m, 4H), 6.83-6.80 (m, 3H), 6.67 (dd, *J* = 8.0 Hz and *J* = 2.0 Hz, 1H), 6.61 (d, *J* = 7.5 Hz, 1H), 6.55-6.52 (m, 1H), 6.27 (dd, *J* = 8.0 Hz and *J* = 1.5 Hz, 1H), 6.14 (s, 1H), 4.75 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 158.7, 157.5, 145.6, 141.8, 139.9, 138.8, 135.9, 135.5, 134.8, 134.2, 134.1, 133.4, 133.3, 132.5, 132.4, 132.3, 132.1, 132.0, 130.9, 130.8, 130.5, 129.4, 128.7, 128.5, 128.3, 127.6, 126.7, 123.3, 120.9, 120.8, 117.8, 117.0, 116.7, 113.8, 63.7, 55.6; HRMS (ESI) *m/z*: $[M+2+H]^+$ Calcd. for $C_{45}H_{32}Cl_4NO_3$ 774.0950; Found 774.0952, 772.0969, 773.0998, 775.0975, 776.0932, 777.0951 and 778.0917 (multiple chlorine pattern).

*(E)-3-(2-(1,2-bis(4-fluorophenyl)vinyl)-4-methoxyphenyl)-1,2-bis(4-fluorophenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one (**6ad**)*: Precursors **3a** and **4d** were used. Yield: 0.266 g (75%) as pale yellow solid; mp: 256-258 ºC; R_f = 0.35 (4:1 hexane/ethyl acetate); IR (KBr) 2838, 2329, 1907, 1644, 1595, 1501, 1227, 1151, 1041, 997, 805 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.17-7.12 (m, 2H), 7.00-6.97 (m, 3H), 6.94-6.85 (m, 10H), 6.83 (d, *J* = 3.0 Hz, 1H), 6.76-6.71 (m, 3H), 6.69-6.65 (m, 2H), 6.53-6.50 (m, 1H), 6.27 (dd, *J* = 8.0 Hz and *J* = 1.0 Hz, 1H), 6.12 (s, 1H), 4.79-4.69 (m, 2H), 3.81 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.4 (d, *J* = 247.5 Hz), 161.8 (d, *J* = 246.3 Hz), 161.7 (d, *J* = 248.8 Hz), 161.6 (d, *J* = 246.3 Hz), 159.5, 158.7, 157.4, 145.9, 142.0, 139.2, 138.9, 133.4 (d, *J* = 3.8 Hz), 133.2 (d, *J* = 8.8 Hz), 133.0 (d, *J* = 3.8 Hz), 132.9 (d, *J* = 3.8 Hz), 132.8 (*J* = 11.2 Hz), 132.5, 131.9, 131.1 (d, *J* = 7.5 Hz), 130.9 (d, *J* = 8.8 Hz), 130.8, 129.6 (d, *J* = 3.8 Hz), 129.4, 128.3, 122.8, 120.9, 120.7, 117.7, 116.8$_4$, 116.81, 115.4 (d, *J* = 13.8 Hz), 115.2 (d, *J* = 13.8 Hz), 114.4 (*J* = 21.2 Hz), 113.5, 113.4 (*J* = 22.5 Hz), 63.7,

55.5; ^{19}F NMR (376 MHz; proton coupled; $CDCl_3$): δ -112.2, -113.1, -113.3, -114.3; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{45}H_{30}F_4NO_3$ 708.2162; Found 708.2164.

*(E)-3-(2-(1,2-bis(4-(trifluoromethyl)phenyl)vinyl)-4-methoxyphenyl)-1,2-bis(4-(trifluoromethyl)phenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one (**6ae**)*: Precursors **3a** and **4e** were used. Yield: 0.345 g (76%) as white solid; mp: 255-258 ^oC; R_f = 0.24 (4:1 hexane/ethyl acetate); IR (KBr) 3068, 3008, 2937, 2838, 1929, 1649, 1605, 1496, 1414, 1315, 1167, 1118, 1063, 1019, 849, 756 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49-7.44 (m, 5H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.30 (d, *J* = 7.0 Hz, 1H), 7.24 (d, *J* = 8.5 Hz, 1H), 7.17-7.13 (m, 4H), 7.07-6.98 (m, 5H), 6.93 (dd, *J* = 8.8 Hz and *J* = 2.8 Hz, 1H), 6.87 (d, *J* = 3.0 Hz, 1H), 6.82 (d, *J* = 6.0 Hz, 1H), 6.77 (d, *J* = 7.5 Hz, 1H), 6.51-6.47 (m, 1H), 6.30 (s, 1H), 6.16 (dd, *J* = 8.0 Hz and *J* = 1.0 Hz, 1H), 4.77-4.69 (m, 2H), 3.83 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$; detailed coupling constant analysis was difficult in this case due to overalapping signals) δ 159.9, 158.7, 157.5, 145.3, 141.4, 141.1, 141.0, 140.6, 139.4, 138.9, 137.0, 132.7, 132.6, 132.1, 131.7, 131.6, 131.3, 130.7, 130.4_7, 130.4_3, 130.2, 129.9, 129.8, 129.5_3, 129.4_9, 129.1, 128.1, 125.5 (qrt, *J* = 3.3 Hz), 125.4 (qrt, *J* = 3.3 Hz), 125.0, 124.2_4, 124.2_1, 123.9 (qrt, *J* ~ 272 Hz), 123.8 (qrt, *J* ~ 272 Hz), 123.7 (qrt, *J* ~ 272 Hz), 123.6_6, 123.4_9, 123.4_7, 123.4_2 (qrt, *J* ~ 272 Hz), 120.9, 120.3, 117.9, 117.2, 116.7, 114.2, 63.4, 55.6; ^{19}F NMR (376 MHz; proton coupled; $CDCl_3$): δ -62.6, -62.7_0, -62.7_1, -62.9; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{49}H_{30}F_{12}NO_3$ 908.2034; Found 908.2030.

*(E)-3-(2-(1,2-bis(3,5-dimethylphenyl)vinyl)-4-methoxyphenyl)-1,2-bis(3,5-dimethylphenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one (**6af**)*: Precursors **3a** and **4f** were used. Yield: 0.321 g (86 %) as pale yellow solid; mp: 242–244 ^oC; R_f = 0.31 (4:1 hexane/ethyl acetate); IR (KBr) 3025, 2964,

2921, 2860, 2356, 1638, 1595, 1507, 1260, 1200, 1030, 1101, 1030, 805 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.12-7.08 (m, 2H), 6.95 (dd, *J* = 8.0 Hz and *J* = 1.0 Hz, 1H), 6.88 (s, 1H), 6.85-6.81 (m, 2H), 6.79 (s, 1H), 6.68 (d, *J* = 9.5 Hz, 5H), 6.59 (s, 1H), 6.56 (d, *J* = 8.0 Hz, 2H), 6.49-6.45 (m, 1H), 6.42-6.40 (m, 2H), 6.26 (s, 1H), 6.17 (s, 1H), 4.84 (d, *J* = 14.0 Hz, 1H), 4.66 (d, *J* = 14.0 Hz, 1H), 3.79 (s, 3H), 2.15-2.14 (m, 15H), 2.06 (s, 6H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 157.2, 147.2, 142.8, 140.8, 138.3, 137.4, 137.2, 136.9, 136.6, 135.5, 135.2, 133.7, 132.5, 132.0, 130.3, 130.2, 129.8, 129.2_3, 129.1_7, 129.1, 128.9, 128.8, 128.7, 128.0, 127.7, 127.1, 121.8, 121.6, 120.3, 117.5, 117.0, 116.6, 112.9, 63.8, 55.4, 21.3, 21.2, 21.1, 21.0; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{53}H_{50}NO_3$ 748.3790; Found 748.3790.

(E)-1,2-diethyl-3-(2-(hex-3-en-3-yl)-4-methoxyphenyl)-3H-chromeno[3,4-c]pyridin-4(5H)-one ***(6ah)***: Precursors **3a** and **4h** were used. Yield: 0.173 g (78 %) as white solid; mp: 125–127 °C; R_f = 0.43 (4:1 hexane/ethyl acetate); IR (KBr) 2970, 2926, 2367, 1742, 1638, 1518, 1447, 1299, 1233, 1036, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.0 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 8.5 Hz, 1H), 7.12-7.08 (m, 2H), 6.93 (dd, *J* = 8.5 Hz and *J* = 3.0 Hz, 1H), 6.84 (d, *J* = 2.5 Hz, 1H), 5.34-5.28 (m, 2H), 4.68 (d, *J* = 7.0 Hz, 1H), 3.88 (s, 3H), 2.85-2.78 (m, 1H), 2.69-2.58 (m, 2H, CHC$H_a$$H_b$), 2.23-2.10 (m, 2H), 2.05-1.99 (m, 2H), 1.97-1.90 (m, 1H, CHC$H_a$$H_b$), 1.33 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.5 Hz, 3H), 0.91-0.85 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 159.4, 157.9, 149.3, 143.0, 140.9, 139.1, 132.8, 130.7, 130.4, 129.3, 127.4, 122.6, 121.8, 121.5, 118.1, 116.2, 115.4, 112.4, 64.4, 55.5, 23.7, 23.3, 21.4_1, 21.3_5, 16.1, 14.3, 13.7, 13.4. HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{29}H_{34}NO_3$ 444.2538; Found 444.2539.

*(E)-3-(2-(1,2-diphenylvinyl)-5-methylphenyl)-1,2-diphenyl-3H-chromeno[3,4-c]pyridin-4(5H)-one (**6ba**)*: Precursors **3b** and **4a** were used. Yield: 0.247 g (80 %) as pale yellow solid; mp: 208–208 ^{o}C; R_f = 0.30 (4:1 hexane/ethyl acetate); IR (KBr) 3052, 3025, 2838, 1737, 1633, 1512, 1490, 1441, 1244, 1025, 756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.22 (m, 1H), 7.19-7.12 (m, 7H), 7.10-7.04 (m, 7H), 7.00-6.86 (m, 9H), 6.65 (d, *J* = 7.2 Hz, 1H), 6.43 (t, *J* = 7.6 Hz, 1H), 6.25 (d, *J* = 8.0 Hz, 1H), 6.08 (s, 1H), 4.71 (s, 2H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 157.3, 146.3, 140.4, 138.8, 138.6, 137.9, 137.8, 137.7, 137.1, 136.6, 133.6, 132.4, 132.1, 131.9, 131.5, 131.2, 131.1, 130.3, 129.6, 129.4, 128.6, 128.1, 128.0, 127.7, 127.6, 127.0, 126.7, 126.5, 126.1, 122.6, 121.3, 120.6, 117.6, 117.4, 63.8, 21.0; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{45}H_{34}NO_2$ 620.2589; Found 620.2586.

*Isomeric mixture **6al***: The R_f values of the monocyclized product **5al** (R_f = 0.32) and this product **6al** (R_f = 0.30; 4:1 hexane/ethyl acetate) were close and hence separation became difficult. The ^{1}H NMR spectrum of the reaction mixture containing **6al** and **5al** (~70:30) ratio) in the –OMe region showed 12 peaks (δ 3.81, 3.79, 3.76_5, 3.76_4, 3.75, 3.74, 3.73, 3.72, 3.71, 3.70, 3.69 and 3.64). Since **5al** had two isomers giving a total of 4-OCH_3 signals (two for each isomer, see Table 2), we surmise that at least three isomers (out of four; each isomer may give three –OCH_3 signals) of **6al** are formed. The ^{1}H NMR spectra of four such fractions along with that of the original reaction mixture are given in the Supporting Information (Figure S66). We were able to isolate a mixture of isomers of **6al** in a fairly pure state (purity >97%). The data for fraction d in Figure S66 is given here. IR (KBr) 2927, 2839, 1635, 1606, 1509, 1462, 1248, 1200, 1138, 1034 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25-6.20 (m, 25H), 6.05 (s, 1H), 4.75-4.60 (m, 2H), 3.81, 3.78, 3.76_6, 3.76_4, 3.72_9, 3.72_7, 3.71_4 and 3.69 (many lines, total 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9, 158.6, 158.2, 157.3, 142.5, 138.9,137.6,133.9, 132.8, 132.6, 132.5,

132.4,132.3,132.2,131.9, 131.5, 131.0, 130.7, 130.6, 130.2, 129.8, 129.5, 129.4, 128.6, 128.1, 128.0, 127.9, 127.7, 127.5, 127.4, 126.9, 126.6, 126.2, 122.4, 121.5, 120.6, 120.5, 117.3, 117.1, 116.9, 116.8, 116.7, 113.5, 113.4, 113.2, 113.0, 111.9, 111.6, 63.9, 55.5, 55.2, 55.1_1, 55.0_6, 54.9; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{47}H_{38}NO_5$ 696.2750; Found 696.2750.

Ruthenium-Catalyzed H/D Exchange in 3a with Isotopically Labelled CD_3ODt

A mixture of *N*-(4-methoxyphenyl)-2*H*-chromene-3-carboxamide **3a** (86 mg, 0.03 mmol), $[RuCl_2(p\text{-cymene})]_2$ (9.4 mg, 5 mol%), $Cu(OAc).H_2O$ (121.2 mg, 2.0 equiv) and $AgNTf_2$ (30 mol %) in CD_3OD (2 mL) was stirred at 70 ºC for 20 h. The reaction mixture was cooled to room temperature and CD_3OD was evaporated under vacuum. Purification was done by column chromatography on silica gel using hexane/EtOAc (9:1) to afford the 3a + $\mathbf{3a}_D$ (yield: 70 mg, 80%) in which only about 13% deuteration occurred at the C(4)-H position as estimated from ^1H NMR spectrum. HRMS for the $\mathbf{3a}_D$: calculated for $[M_D+H]^+$ 283.1193 in addition to $[M_H + H]^+$. Found: 283.1192], but the intensity was low. Since in our experiments we used $Cu(OAc)_2.H_2O$, and the precursor **3a** contained an NHAr group, we did a second experiment by first heating $Cu(OAc)_2.H_2O$ with D_2O and removing most of water to obtain essentially $Cu(OAc)_2.D_2O$. We then tried C-H/C-D exchange using **3a**, the Ru-catalyst, $Cu(OAc)_2.D_2O$ and $AgNTf_2$ over a period of 30 h using the same molar equivalents of the reactants. In this case, we observed 42% C-H/ C-D exchange (^1H NMR) but the NH peak was relatively broad (IR was not helpful because of the low intensity). There is also significant reduction in the intensity of the aromatic multiplet at δ 7.47 that corresponded to only one proton instead of the expected two. The ^1H NMR spectrum in the region δ 6.8-7.8 is shown in Figure S5 (Supporting Information). The $^{13}C\{^1H\}$ NMR spectrum showed some changes around δ 130 and what appears to be a minor

intensity triplet [δ 130.4, J ~ 7.5 Hz}, but the coupling constant is much lower than expected. In the HRMS, we observed peaks at m/z 282. 1123 $[M_H+H]^+$, 283.1192 $[M_D+H]^+$, 284.1249 $[M_{D2}+H]^+$ as well as 305.1008 $[M_D+Na]^+$ and 306.1065 $[M_{D2}+Na]^+$, the latter four being predominant.

(iv) X-ray Data. X-ray data for compounds **5aj, 5ba, 6af** and **6ba** were collected using MoK_α (λ = 0.71073 Å) radiation. The structures were solved and refined by standard methods.[29]

Compound 5aj: $C_{27}H_{23}NO_3$, M = 409.46, Triclinic, Space group *P-1*, a = 11.1487(5), b = 13.6771(7), c = 15.2660(7) Å, α = 71.218(2), β = 75.407(2), γ = 73.308(2), V = 2078.08(17) $Å^3$, Z = 4, μ = 0.130 mm^{-1}, data/restraints/parameters: 9638/0/563, R indices (I> 2σ(I)): R1 = 0.0528, *w*R2 (all data) = 0.1119, CCDC No. 1525145.

Compound 5ba: $C_{31}H_{23}NO_2$, M = 441.52, Monoclinic, Space group $P2_1/n$, a = 10.930(4), b = 14.661(5), c = 14.878(5) Å, β = 98.110(7), V = 2360.2(13) $Å^3$, Z = 4, μ = 0.128 mm^{-1}, data/restraints/parameters: 4156/0/309, R indices (I> 2σ(I)): R1 = 0.0619, *w*R2 (all data) = 0.1285, CCDC No. 1525146.

Compound 6af: $C_{53}H_{49}NO_3$, M = 747.96, Monoclinic, Space group $P2_1/c$, a = 11.300(2), b = 23.294(6), c = 16.578(4) Å, β = 94.778(8), V = 4348.4(18) $Å^3$, Z = 4, μ = 0.128 mm^{-1}, data/restraints/parameters: 9941/0/523, R indices (I> 2σ(I)): R1 = 0.0668, *w*R2 (all data) = 0.1364, CCDC No. 1525147.

Compound 6ba: $C_{45}H_{33}NO_2$, M = 619.75, Monoclinic, Space group $P2_1/c$, a = 10.3589(5), b = 17.6488(6), c = 36.7182(15) Å, β = 91.708(2), V = 6709.9(5) $Å^3$, Z = 8, μ = 0.128 mm^{-1}, data/restraints/parameters: 14825/0/867, R indices (I> 2σ(I)): R1 = 0.0758, *w*R2 (all data) = 0.1354, CCDC No. 1525148.

ASSOCIATED CONTENT

Supporting Information

Figures and CIF files giving ORTEP drawings as shown by X-ray crystallography, and copies of $^{1}H/^{13}C$ NMR spectra of all new products. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: kckssc@uohyd.ac.in; kckssc@yahoo.com

Notes

The authors declare no competing financial interest.

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