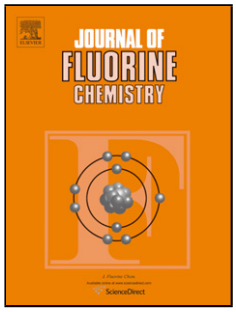

Title: Simultaneous exploration of TBAF·$3H_2O$ as a base as well as a solvating agent for the palladium catalyzed Suzuki cross-coupling of 4-methyl-7-nonafluorobutylsulfonyloxy coumarins under microwave irradiation

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Simultaneous exploration of TBAF·3H_2O as a base as well as a solvating agent for the palladium catalyzed Suzuki cross-coupling of 4-methyl-7-nonafluorobutylsulfonyloxy coumarins under microwave irradiation

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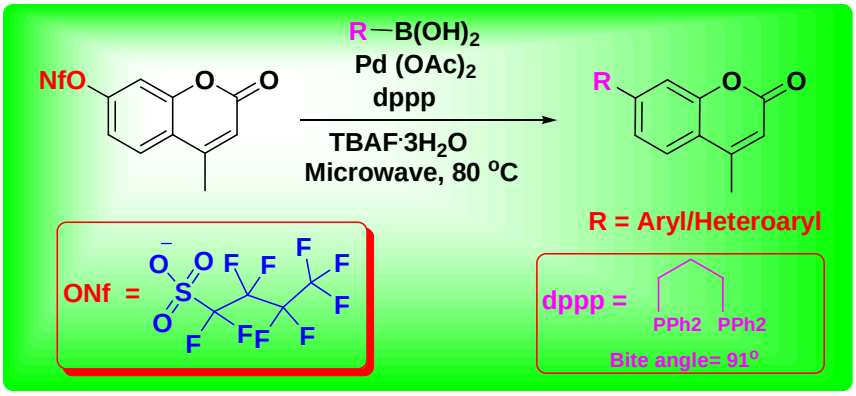
GRAPHICAL ABSTRACT



A concise, efficient and facile protocol for the synthesis of a variety of 4-methyl-7-aryl/heteroaryl coumarins has been developed by utilizing the palladium catalyzed Suzuki cross-coupling reaction of 4-methyl-7-nonafluorobutylsulfonyloxy coumarin with a wide range of electronically diverse boronic acids under microwave irradiation.

Highlights

1. An efficient protocol for the palladium catalyzed Suzuki coupling of 4-methyl-7-nonafluorobutylsulfonyloxy coumarins has been achieved.
2. The dual role of TBAF·$3H_2O$ as a base and a solvating was found to be instrumental for the success of the reaction.
3. An assortment of 4-methyl-7-aryl coumarins were successfully synthesized using the optimized conditions.

Abstract

A concise, efficient and facile protocol for the synthesis of a variety of 4-methyl-7-aryl/heteroaryl coumarins has been developed by utilizing the palladium catalyzed Suzuki cross-coupling reaction of 4-methyl-7-nonafluorobutylsulfonyloxy coumarin with a wide range of electronically diverse boronic acids under microwave irradiation. In the presence of a suitable catalyst, ligand and base, the coupling reaction proceeded smoothly to give the biaryls in satisfactory to exceptional yields. The dual role of $TBAF{\cdot}3H_2O$ as a base as well as a solvating agent and the utilization of dppp as a ligand with moderate bite angle (91°) were found to be instrumental for the success of the reaction. Prominent features of this optimization conditions include: shorter reaction times, good to excellent yield and exceptional tolerance to a wide variety of functional groups.

Keywords: Coumarin; Nonaflates; Suzuki coupling; Microwave.

1. Introduction

The Suzuki–Miyaura cross-coupling reaction between organoboranes and organic halides or pseudohalides has emerged as one of the foremost methods for the creation of carbon–carbon bonds under mild conditions [1]. The reaction provides an efficient pathway to a range of pharmaceuticals, herbicides, natural products, polymers and liquid crystalline materials and hence has significantly extended its scope in recent years [2]. Salient features of these reactions are the availability, stability and non-toxicity of a variety of boronic acids, extensive functional group tolerance and easy access for product isolation [3]. These features evidently reveal its significance in synthetic chemistry and hence this reaction has found widespread use in pharmaceutical industries. The microwave assisted organic synthesis (MAOS) has gained remarkable importance in drug discovery laboratories these days mostly due to their superior reaction rates, selectivity and product yields as compared to standard thermal conditions [4]. Transition metal catalyzed cross-coupling reactions usually take hours or days for completion by conventional heating whereas the use of microwave irradiation will complete those reactions in minutes with excellent reproducibility and lesser side-reactions [5].

Coumarins are an important class of benzopyrones that are essentially found in green plants either in free or combined state [6]. They represent one of the most active classes of compounds and possess a wide spectrum of biological activity [7]. Coumarin derivatives have numerous therapeutic applications including photo chemotherapy, anti-tumor therapy, anti-HIV therapy [8], and are also active as anti-bacterial [9], anti-inflammatory [10] and anti-coagulating agents [11]. In addition, coumarins are known to be lipid lowering agents with moderate triglyceride lowering activity [12] whereas hydroxycoumarins are powerful chain breaking anti-oxidants and can prevent free radical injury [13,14]. The coumarin core is present within the chemical structure of several pharmaceutical drugs such as warfarin, acenocoumarol, carbochromen etc. and in antibiotics such as novobiocin, clorobiocin and coumermycin A1 [15]. In view of these varied applications, the investigation of facile and efficient methods for the synthesis of diversely substituted coumarin derivatives has been the aim of many researchers for the past 20 years [16].

The diverse applications of coumarins in various fields of chemistry have been extensively reported in the literature. Furthermore, the structure activity relationship (SAR) studies of various aryl/heteroaryl coumarins have revealed the fact that the presence of substituted

heteroaryl/aryl groups in the coumarin moiety is an indispensable characteristic for their pharmacological action [17]. Coumarin derivatives with substitution at 7th position are known to possess various bioactive applications [18]. 4-Methyl-7-substituted coumarins are reported to have diverse applications in the field of medicinal chemistry such as Monoamine Oxidase Inhibitory Potency and DNA binding capacity [19]. Even though the synthesis of various 3,4,6,7 and 8 substituted coumarins have been extensively reported in the literature [20], the synthesis of 7-substituted coumarins require the conversion of its triflate to corresponding boronic ester which took 17 hours for completion and the further biaryl coupling was quite unclear [21]. Furthermore, the methodology for the synthesis of 7-arylcoumarins was reported to be time consuming over night reactions with relatively lower yields [22]. Moreover, the instability (lactone ring cleavage) of the coumarin scaffold in basic as well as under prolonged heating conditions was broadly reported in literatures [17,23]. These observations prompted us to utilize the microwave irradiation for the synthesis of coumarin derivatives by considering the fact that the reactions could reach to completion within minutes as compared to conventional heating methodologies.

As a continuation of our ongoing research program in the synthesis of biologically active molecules [24], we were interested in synthesizing some 7-substituted coumarins which may possess considerable pharmacological activities. On continuation of our ongoing research on palladium catalyzed cross-coupling reactions [25], it has been planned to apply the Suzuki coupling reaction for the synthesis of various coumarin analogues under microwave irradiation. Among the pseudohalides, the stability and reactivity of nonaflates over corresponding triflates in the palladium catalyzed cross-coupling reactions has been recently reported from our laboratory [26]. In this letter, we report a facile and reliable protocol for the synthesis of a variety of 4-methyl-7-aryl/heteroaryl coumarins by utilizing the Suzuki cross-coupling reaction of 4-methyl-7-nonafluorobutylsulfonyloxy coumarin with various aryl/heteroaryl boronic acids under microwave irradiation. To the best of our knowledge, the exploration of the 7th position of coumarins for direct arylation by Suzuki coupling under microwave irradiation is few.

2. Results and discussion

The parent 4-methyl-7-hydroxycoumarin molecule **2** was prepared by the modified Pechmann cyclization of resorcinol **1** with ethyl acetoacetate in 1-butyl-3-methylimidazolium chloroaluminate at 30 °C for 20 minutes [27] (Scheme 1). The obtained hydroxy coumarin **2** was then converted to corresponding triflate **3a** by treating it with trifluoromethanesulfonic anhydride in dichloromethane (DCM) and pyridine at −10 °C for 2 h. The intermediate thus obtained was then subjected to Suzuki coupling with the intention of synthesizing an array of novel 4-methyl-7-aryl/heteroaryl coumarins of considerable pharmacological relevance (Scheme 2).

As a model reaction, we selected the triflate **3a** and phenylboronic acid in various solvents under microwave irradiation for optimizing the reaction conditions. We decided to optimize the reaction by employing $TBAF{\cdot}3H_2O$ as a base as it has been reported to have significant effect in suppressing the hydrolysis of pseudohalides by increasing its solvation in the reaction medium [26,28]. To our disappointment, we obtained the detriflated product **5** as the major product in all the explored conditions (Table 1). The triflate proved to be highly unstable in the reaction conditions which could be presumably due to the unstable nature of the intermediate Pd(II) complex that is expected to form during its preliminary oxidative addition to Pd(0).

Our subsequent efforts were to optimize the reaction conditions by changing the substrate to corresponding nonaflates. The hydroxycoumarin intermediate **2** was converted to the corresponding nonaflate by treating it with 1.5 equivalent of nonafluorobutanesulfonic anhydride at −10 °C in dichloromethane (DCM) and pyridine as base for 2 hours. The obtained nonaflate intermediate **3b** was found to be highly stable than the corresponding triflates and didn't decompose even after storing for a longer period of time. The intermediate **3b** was then subjected to Suzuki coupling with various boronic acids with the objective of synthesizing a variety of novel 4-methyl-7-substituted coumarins (Scheme 3).

As a model reaction, we selected the nonaflate **3b** and phenylboronic acid in order to optimize the reaction conditions in view of the fact that the products and impurities could be easily identified by TLC and LC-MS. A series of palladium catalysts like $Pd_2(dba)_3$, $Pd(OAc)_2$, $Pd(dppf)Cl_2$, $Pd(dppf)CH_2Cl_2$, $PdCl_2.(CH_3CN)_2$ etc. were screened at the initial stage with $TBAF{\cdot}3H_2O$ (2 equiv) in various solvents like DME, DMF and 1,4-dioxane at 100 °C for 30 min.

in a 110 W microwave oven (Table 2). Disappointingly, under most of the reaction conditions examined, the formation of product was not observed as only a trace amount of the required biaryl was formed (Table 2, entries 1 to 7). However, we observed the formation of biaryls in considerably better yield (45 %) when $Pd(OAc)_2$ was used as a catalyst in DME as solvent (Table 2, entry 8). On the basis of our assumption that the improvement of solubility of reagents in the solvent system could facilitate the coupling more effectively, we added water and methanol as a co-solvent with DME and the reaction was carried out at 100 °C for 30 min. in a 110 W microwave oven. The hypothesis proved to be true as we observed the formation of desired product in reasonable yield when DME-MeOH in 3:1 ratio (Table 2, entry 10) was used along with $TBAF{\cdot}3H_2O$ and $Pd(OAc)_2$. DME-H_2O mixture yielded the biaryls in comparatively lower yield (Table 2, entry 9) which could be rationalized by the fact that DME-MeOH improved the overall solubility of the reagents when compared to that of DME-H_2O [29]. A significant improvement in the yield of the desired product could not be realized either by decreasing reaction temperature and reaction time or by increasing the amount of the base (Table 2, entries 11,12 and 13).

In our continuous efforts to improve the yield of the desired product, we screened the reaction by adding some diphosphine ligands (Figure 1) to the catalyst [$Pd(OAc)_2$] which are known to enhance the catalytic activity in the reaction system. The results are summarized in Table 3. These catalytic systems generated *in situ* were treated with the nonaflate **3b**, phenylboronic acid and $TBAF{\cdot}3H_2O$ in DME-MeOH (3:1) at 100 °C for 30 min. in a 110 W microwave oven. We observed that the reaction conditions and the nature of the ligand have a crucial influence in the formation of desired product. Ligands with moderate bite angle that could accomplish chelation and form a cis complex in the reaction medium [30] were found to be necessary for better conversions. To our delight, we obtained the biaryl coupled product in satisfactory yield when 1,3-bis(diphenylphosphino)propane (dppp) was used as the ligand (Table 3, entry 3). Ligands with bite angle less than that of dppp (91°) furnished the product in lower yields and the ligands with bite angle greater than that of dppp produced unwanted side products which caused a decrease in the yield of the desired product (Table 3, entries 1, 2 and 4, 5). Finally, addition of one more equivalent of base and decreasing the temperature to 80 °C rendered the required biaryl in 98 % yield with 93 % of isolated yield (Table 3, entry 6).

In the present study, the ligand with moderate bite angle (dppp) is assumed to increase the stability of the catalyst in the reaction medium [30]. Presumably, it could be accounted that the dppp ligand with moderate bite angle immediately initiated the catalytic reaction without an incubation period. This would bring about an increase in the electron density and hence the stability of the catalyst by forming a divalent square planar complex which in turn enhanced the reductive elimination and procured the biaryls as a major product rather than competitive side products [31]. In the current study, it is speculated that the ligands with wider bite angles might have involved in side reactions by β-hydride elimination or substitution reactions [32].

In order to investigate the effect of various bases in the developed strategy, the Suzuki coupling reaction was carried out using a variety of bases while keeping all the other parameters unchanged (Table 4). Among the various bases screened, $TBAF{\cdot}3H_2O$ gave outstanding yield and proved to be superior to K_3PO_4, CsF and Cs_2CO_3. The plausible reasons for this superiority might be the moderate basicity of $TBAF{\cdot}3H_2O$ and its increase in solvation in the reaction medium when its stoichiometric equivalence was increased [28,33]. Moreover, it is assumed that the presence of a nucleophilic activator like $TBAF{\cdot}3H_2O$ facilitated the decomposition of divalent $Pd(OAc)_2$ to a catalytically active Pd(0) species and the stabilization of the oxidative adduct complex thereby increasing the rate of the reaction to a greater extent [33,34]. The dual role of $TBAF{\cdot}3H_2O$ as a base as well as a solvating agent is greatly acknowledged in the present study.

Next, we focused our attention to evaluate the generality of the developed protocol (Scheme 4). Keeping this in mind, we applied the optimized condition [1.5 equiv. boronic acid, 3 equiv. $TBAF{\cdot}3H_2O$, 5 mol % $Pd(OAc)_2$, 0.1 equiv. dppp, DME-MeOH (3:1), 80 °C, 30 min, microwave] to a wide range of sterically and electronically different boronic acids (Table 5). All the boronic acids furnished the required biaryls in acceptable to excellent yields. The methodology showed exceptional functional group tolerance and almost all the reactions were completed within 30 min. with a smaller amount of side products. Electron rich boronic acids provided excellent yield (Table 5, entries 10 to 12 and 21 to 23), whereas electronically poor boronic acids gave slightly lower yields (Table 5, entries 5 to 9) even after increasing the reaction time to 1 hour. Furthermore, sterically hindered boronic acids gave moderate yields **(**Table 5, entries 14 to 20).

A plausible mechanism of the Suzuki coupling reaction of nonaflates with boronic acids has been proposed (Scheme 5). In the first step, coordination of dppp to divalent palladium acetate results in the formation of a Pd(0) species which subsequently undergoes oxidative addition with the nonaflate **3b** to form an organo palladium complex. This oxidative adduct was stabilized by $TBAF{\cdot}3H_2O$ which subsequently facilitated transmetallation. Meanwhile, the boron atom of the boronic acid also forms a borate complex with $TBAF{\cdot}3H_2O$ which is assumed to have a crucial role to facilitate the transmetallation step. Finally, it undergoes reductive elimination to give the coupled product and completes the catalytic cycle.

3. Conclusion

In summary, a rapid, facile and modified approach for the synthesis of an array of 4-methyl-7-aryl/heteroaryl coumarins has been developed under microwave irradiation. This method paved the way for an assortment of pharmacologically relevant coumarins with exceptional functional group tolerance, shorter reaction times and higher yields. The biological screening of the synthesized molecules will be done in due course and will be communicated shortly.

4. Experimental

4.1. General information

All solvents and reagents were obtained from commercial suppliers and used without any further purification unless otherwise noted. Analytical TLC was performed on pre-coated aluminum sheets of silica (60 F254 nm) and visualized by short-wave UV light at λ 254. Melting points were determined on an EZ - Melt automated melting point apparatus. ^{1}H NMR spectra were recorded at 400 MHz and 300 MHz using an internal deuterium lock. Chemical shifts were measured in δ (ppm). Data is presented as follows: chemical shift, multiplicity, coupling constant (*J*) in Hz, and integration. The following abbreviations were used for the splitting patterns: s for singlet, d for doublet, t for triplet, m for multiplet and br for broad. ^{13}C NMR spectra were recorded at 100 MHz using an internal deuterium lock. LC-MS analyses were performed using ESI/APCI, with an ATLANTIS C18 (50X4.6 mm - 5µm) column and a flow rate of 1.2 mL/min.

*4.2. Procedure for the synthesis of 4-methyl-7-hydroxy coumarin intermediate **2***

To the weighed quantity of phenol (1 equiv.) and ethyl acetoacetate (1.1 equiv.), the ionic liquid [bmim]Cl·2$AlCl_3$ (1.1 equiv.) was added and the reaction mixture was stirred at 30 °C for 20 min. All additions were carried out in an inert atmosphere. The reaction was quenched by adding 6 M HCl in cold conditions. The resultant product was filtered and further purified by column chromatography to obtain the titled compound **2** as off white solid in 88 % yield. MP : 70-72 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.68 Hz, 3H, CH_3), 6.1 (s, 1H, ArH), 6.69 (d, *J*=2.32 Hz, 1H, ArH), 6.77-6.80 (dd, J_1=2.24 Hz J_2=8.6 Hz, 1H, ArH), 7.57 (d, *J*=8.68 Hz, 1H, ArH), 10.51 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 112.3, 117.5, 130.5, 154.5, 161.1, 160.4 (CO); LC-MS: Calculated 176.2, Observed 177.2; Analysis calculated for $C_{10}H_8O_3$: C, 68.18, H, 4.58 %, found: C, 68.21, H, 4.57 %.

*4.3.Procedure for the synthesis of 4-methyl-7-nonafluorobutylsulfonyloxy coumarin **3b***

To a solution of 4-methyl-7-hydroxy coumarin (**2**, 1 equiv.) in DCM, was added pyridine (2 equiv.) at −10 °C, followed by the addition of nonafluorobutane sulfonic anhydride (1.5 equiv.) drop wise. Reaction mixture was warmed to 0 °C and stirred for 2 h. Reaction mass was then diluted with DCM, bi-phased with water and extracted, organic layer was washed with $NaHCO_3$, brine solution and dried over Na_2SO_4 and distilled under reduced pressure. The obtained crude compound was purified by column chromatography packed with 60-120 silica gel and eluted with 15 to 20 % ethyl acetate in petroleum ether to obtain the titled compound **3** as colorless solid in 87 % yield. MP : 86-88 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.47 (d, *J*=1.08 Hz, 3H, CH_3), 6.37 (d, *J*=1.08 Hz, 1H, ArH), 7.23-7.29 (m, 2H, ArH), 7.69 (d, *J*=8.67 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 115.3, 116.5, 116.9 (m, CF_2), 118.9 (m, CF_2), 126.7 (m, CF_3), 132.2, 154.1-154.7 (2 peaks), 156.3 (m, SO_2CF_2), 160.6 (CO); ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −125.32 to −125.22 (m), −120.77 to −120.68 (m), −112.97 to −112.87 (m), −80.59 to −80.52 (m); LC-MS: Calculated 458.3, Observed 459.3; Analysis calculated for $C_{14}H_7F_9O_5S$: C, 36.69, H, 1.54 %, found: C, 36.74, H, 1.51 %.

4.4.General procedure of the coupling reaction

To a solution of 4-methyl-7-nonafluorobutylsulfonyloxy coumarin (**3b**, 1 equiv.) in DME-MeOH (3:1), were added $Pd(OAc)_2$ (0.05 equiv.) and dppp (0.1 equiv.). The solution was purged with nitrogen and stirred at room temperature for 10 min, at which time boronic acid (1.5 equiv.) and TBAF·3H_2O (3 equiv.) was added. The reaction solution was purged again with nitrogen and

then placed in the microwave and heated for 20–30 min at 80 °C at 110 W. When TLC and LC-MS showed full consumption of starting materials, the reaction mixture was diluted with ethyl acetate, separated the organic layer, given water wash, brine wash and was dried over anhydrous sodium sulfate and distilled under reduced pressure to get the crude material. The crude product was further purified by column chromatography and eluted in varying polarities to obtain the diaryls **4a-x**.

*4.4.1. 4-Methyl-7-(pyridin-3-yl)-2H-chromen-2-one (**4a**)*: White solid. MP : 88-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=2.04 Hz, 3H, CH_3), 6.31 (s, 1H, ArH), 7.43-7.51 (m, 3H, ArH), 8.22-8.25 (dd, J_1=1.96 Hz J_2=7.92 Hz, 1H, ArH), 8.42-8.45 (dd, J_1=2.24 Hz J_2=8.08 Hz, 1H, ArH), 8.71-8.75 (dd, J_1=1.76 Hz J_2=7.84 Hz, 1H, ArH), 9.12 (d, *J*=8.92 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 115.3, 116.5, 117.1, 119.7, 136.2, 138.3, 145.1, 147.6, 154.1, 156.3, 157.6, 157.9, 160.6 (CO); LC-MS: Calculated 237.2, Observed 238.2; Analysis calculated for $C_{15}H_{11}NO_2$: C, 75.94, H, 4.67, N, 5.90 %, found: C, 75.91, H, 4.68, N, 5.93 %.

*4.4.2. 7-(5-Chloropyridin-3-yl)-4-methyl-2H-chromen-2-one (**4b**)*: White solid. MP : 92-95 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.16 Hz, 3H, CH_3), 6.31 (d, *J*=1.12 Hz, 1H, ArH), 7.43-7.49 (m, 3H, ArH), 8.44 (d, *J*=8.12 Hz, 1H, ArH), 9.08 (s, 1H, ArH), 9.14 (d, *J*=7.84 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 115.3, 120.5, 121.1, 123.7, 125.2, 135.3, 135.8, 138.1, 149.6, 150.5, 154.1, 156.3, 157.6, 160.6 (CO); LC-MS: Calculated 271.2, Observed 272.2; Analysis calculated for $C_{15}H_{10}ClNO_2$: C, 66.31, H, 3.71, N, 5.16 %, found: C, 66.35, H, 3.69, N, 5.14 %.

*4.4.3. 4-Methyl-7-(2-methylpyridin-4-yl)-2H-chromen-2-one (**4c**)*: White solid. MP : 90-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.44 Hz, 3H, CH_3), 3.34 (s, 3H, CH_3), 6.31 (d, *J*=1.08 Hz, 1H, ArH), 7.38-7.46 (m, 5H, ArH), 9.08-9.11 (dd, J_1=1.88 Hz J_2=8.24 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 27.1 (CH_3), 111.3, 114.5 (2C), 116.8, 120.1, 123.4, 126.2, 129.3, 139.8, 143.4, 151.1 (2C), 152.6, 154.5, 160.4 (CO); LC-MS: Calculated 251.2, Observed 252.2; Analysis calculated for $C_{16}H_{13}NO_2$: C, 76.48, H, 5.21, N, 5.57 %, found: C, 76.52, H, 5.20, N, 5.55 %.

*4.4.4. 4-Methyl-7-phenyl-2H-chromen-2-one (**4d**)*: Off white solid. MP : 78-80 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.28 Hz, 3H, CH_3), 6.49 (s, 1H, ArH), 7.59-7.61 (dd, J_1=1.72 Hz J_2=8.12 Hz, 1H, ArH), 7.64-7.67 (dd, J_1=1.08 Hz J_2=8.48 Hz, 2H, ArH), 7.71-7.73 (d, *J*=7.8

Hz, 1H, ArH), 7.82-7.86 (m, 1H, ArH), 7.92-8.05 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 107.7, 110.5, 113.5, 117.9, 124.7, 125.6, 131.4, 132.7, 140.8, 142.7, 146.4, 151.3, 160.4 (CO); LC-MS: Calculated 236.2, Observed 237.2; Analysis calculated for $C_{16}H_{12}O_2$: C, 81.34, H, 5.12 %, found: C, 81.36, H, 5.11 %.

*4.4.5. 4-(4-Methyl-2-oxo-2H-chromen-7-yl)benzonitrile (**4e**)*: Brown solid. MP : 101-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.36 Hz, 3H, CH_3), 6.47 (s, 1H, ArH), 7.56-7.64 (m, 2H, ArH), 7.71 (d, *J*=7.44 Hz, 1H, ArH), 7.77-7.82 (m, 2H, ArH), 7.91 (d, *J*=8.04 Hz, 1H, ArH), 7.99 (d, *J*=7.52, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 114.2, 115.1, 118.6 (CN), 121.5, 123.1, 127.2, 130.4, 131.7, 132.0, 136.1, 137.2, 140.3, 146.3, 154.5, 156.1, 160.4 (CO); LC-MS: Calculated 261.2, Observed 262.2; Analysis calculated for $C_{17}H_{11}NO_2$: C, 78.15, H, 4.24, N, 5.36 %, found: C, 78.19, H, 4.22, N, 5.32 %.

*4.4.6. 7-(4-Fluorophenyl)-4-methyl-2H-chromen-2-one (**4f**)*: White solid. MP : 85-88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.47 (d, *J*=1.56 Hz, 3H, CH_3), 6.33 (d, *J*=1.16 Hz, 1H, ArH), 7.24-7.29 (m, 2H, ArH), 7.44-7.47 (m, 2H, ArH), 7.76-7.80 (m, 2H, ArH), 8.04 (d, *J*=8.20 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.7 (CH_3), 110.6, 113.8, 118.0, 121.5, 125.8, 131.7, 134.2, 138.6, 141.9, 143.7, 146.5, 148.5, 154.9 (m, CF), 160.4 (CO); ^{19}F NMR (376.5 MHz, $CDCl_3$): δ − 121.7; LC-MS: Calculated 254.2, Observed 255.2; Analysis calculated for $C_{16}H_{11}FO_2$: C, 75.58, H, 4.36 %, found: C, 75.61, H, 4.35 %.

*4.4.7. Methyl 4-(4-methyl-2-oxo-2H-chromen-7-yl)benzoate (**4g**)*: Brown solid. MP : 98-100 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.17 Hz, 3H, CH_3), 3.9 (s, 3H, OCH_3), 6.34 (d, *J*=1.14 Hz, 1H, ArH), 7.47-7.56 (m, 2H, ArH), 7.64-7.72 (m, 3H, ArH), 8.14-8.17 (dd, J_1=1.68 Hz J_2=6.51 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 53.8 (OCH_3), 115.3, 122.5, 123.7, 127.1, 128.2, 131.1, 131.8 (2C), 132.1, 133.3 (2C), 139.1, 143.6, 153.1, 155.3, 163.1 (CO), 165.3 (CO, Ester); LC-MS: Calculated 294.3, Observed 295.3; Analysis calculated for $C_{18}H_{14}O_4$: C, 73.46, H, 4.79 %, found: C, 73.49, H, 4.78 %.

*4.4.8. 2-(4-Methyl-2-oxo-2H-chromen-7-yl)benzonitrile (**4h**)*: Brown solid. MP : 102-104 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.52 Hz, 3H, CH_3), 6.49 (s, 1H, ArH), 7.59-7.67 (m, 2H, ArH), 7.73 (d, *J*=7.8 Hz, 1H, ArH), 7.82-7.86 (m, 2H, ArH), 7.94 (d, *J*=8.16 Hz, 1H, ArH), 8.01 (d, *J*=7.76, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 114.4, 115.3, 118.7 (CN),

121.7, 123.1, 127.2, 130.6, 131.9, 132.1, 136.3, 137.1, 140.6, 146.5, 154.7, 156.1, 160.6 (CO); LC-MS: Calculated 261.2, Observed 262.2; Analysis calculated for $C_{17}H_{11}NO_2$: C, 78.15, H, 4.24, N, 5.36 %, found: C, 78.19, H, 4.22, N, 5.32 %.

*4.4.9. 4-Methyl-7-(4-nitrophenyl)-2H-chromen-2-one (**4i**)*: Yellow solid. MP : 95-97 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.60 Hz, 3H, CH_3), 6.36 (d, *J*=1.24 Hz, 1H, ArH), 7.28-7.33 (m, 2H, ArH), 7.48-7.53 (m, 2H, ArH), 7.81-7.85 (m, 2H, ArH), 8.16 (d, *J*=8.32 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.1 (CH_3), 111.6, 114.9, 118.0, 121.7, 125.8, 132.7, 135.4, 138.9, 142.4, 144.2, 146.5, 148.7, 160.4 (CO); LC-MS: Calculated 281.0, Observed 282.0; Analysis calculated for $C_{16}H_{11}NO_4$: C, 68.32, H, 3.94, N, 4.98 %, found: C, 68.36, H, 3.93, N, 4.97 %.

*4.4.10. 7-(4-Methoxyphenyl)-4-methyl-2H-chromen-2-one (**4j**)*: Light yellow solid. MP : 89-91 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.56 Hz, 3H, CH_3), 3.93 (s, 3H, OCH_3), 6.34 (s, 1H, ArH), 7.54-7.59 (m, 3H, ArH), 7.64-7.72 (m, 3H, ArH), 8.14-8.17 (dd, J_1=2.24 Hz J_2=8.68 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.6 (CH_3), 55.8 (OCH_3), 110.2, 117.9, 118.8, 125.9, 129.8, 132.9, 136.8, 141.6, 141.8, 146.0, 146.6, 155.5, 156.3, 160.4 (CO); LC-MS: Calculated 266.3, Observed 267.3; Analysis calculated for $C_{17}H_{14}O_3$: C, 76.68, H, 5.30 %, found: C, 76.71, H, 5.28 %.

*4.4.11. 4-Methyl-7-p-tolyl-2H-chromen-2-one (**4k**)*: White solid. MP : 85-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.64 Hz, 3H, CH_3), 3.14 (s, 3H, CH_3), 6.49 (s, 1H, ArH), 6.84-6.89 (m, 2H, ArH), 6.96-6.99 (dd, J_1=1.24 Hz J_2=7.76 Hz, 2H, ArH), 7.46-7.49 (dd, J_1=1.36 Hz J_2=7.92 Hz, 2H, ArH), 7.78 (d, *J*=7.76 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.4 (CH_3), 26.2 (CH_3), 111.1, 112.2, 114.3, 117.8, 121.8, 129.7 (2C), 131.1, 133.2, 139.6, 142.4, 154.3, 155.8, 160.6 (CO); LC-MS: Calculated 250.3, Observed 251.3; Analysis calculated for $C_{17}H_{14}O_2$: C, 81.58, H, 5.64 %, found: C, 81.62, H, 5.63 %.

*4.4.12. 7-(4-Ethylphenyl)-4-methyl-2H-chromen-2-one (**4l**)*: White solid. MP : 88-91 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.82-1.86 (m, 3H, CH_3), 2.47 (d, *J*=1.24 Hz, 3H, CH_3), 2.85-2.90 (m, 2H, CH_2), 6.31 (s, 1H, ArH), 7.46-7.51 (m, 4H, ArH), 7.67 (d, *J*=7.64 Hz, 1H, ArH), 7.78-7.81 (dd, J_1=1.92 Hz J_2=8.36 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.4 (CH_3), 23.2 (CH_3), 34.4 (CH_2), 115.3, 121.6, 125.7, 129.7, 130.1 (2C), 130.6 (2C), 135.6, 138.1, 140.3,

152.1, 154.3, 160.4 (CO); LC-MS: Calculated 264.3, Observed 265.3; Analysis calculated for $C_{18}H_{16}O_2$: C, 81.79, H, 6.10 %, found: C, 81.82, H, 6.08 %.

*4.4.13. 7-(Furan-3-yl)-4-methyl-2H-chromen-2-one (**4m**)*: Brown solid. MP : 87-89 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.46 (d, *J*=1.16 Hz, 3H, CH_3), 6.29 (d, *J*=1.16 Hz, 1H, ArH), 6.54-6.56 (dd, J_1=1.76 Hz J_2=3.36 Hz, 1H, ArH), 6.84 (d, *J*=3.36 Hz, 1H, ArH), 7.27-7.29 (m, 2H, ArH), 7.56-7.61 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 111.2, 115.3, 121.5, 124.6, 127.7, 130.8, 132.3, 139.1, 140.1, 141.3, 146.4, 154.3, 158.9, 160.6 (CO); LC-MS: Calculated 226.2, Observed 227.2; Analysis calculated for $C_{14}H_{10}O_3$: C, 74.33, H, 4.46 %, found: C, 74.37, H, 4.44 %.

*4.4.14. 7-(3-(Dimethylamino)phenyl)-4-methyl-2H-chromen-2-one (**4n**)*: Light yellow solid. MP : 102-104 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.32 Hz, 3H, CH_3), 3.44 (s, 6H, NMe_2), 6.31 (s, 1H, ArH), 6.82 (d, *J*=7.48 Hz, 1H, ArH), 7.03-7.07 (m, 2H, ArH), 7.29-7.34 (m, 3H, ArH), 7.64-7.67 (dd, J_1=1.84 Hz J_2=8.32 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 43.6 (NMe_2), 115.3, 115.5, 120.6, 122.7, 124.7, 129.3, 132.1, 134.3, 140.1, 141.8, 151.8, 156.1, 156.9, 160.4 (CO); LC-MS: Calculated 279.3, Observed 280.3; Analysis calculated for $C_{18}H_{17}NO_2$: C, 77.4, H, 6.13, N, 5.01 %, found: C, 77.43, H, 6.12, N, 4.99 %.

*4.4.15. 7-(3,5-Difluorophenyl)-4-methyl-2H-chromen-2-one (**4o**)*: White solid. MP : 92-94 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.36 Hz, 3H, CH_3), 6.31 (d, *J*=1.04 Hz, 1H, ArH), 7.06-7.10 (m, 1H, ArH), 7.54-7.59 (m, 2H, ArH), 7.77-7.81 (m, 2H, ArH), 7.92-7.95 (dd, J_1=1.68 Hz J_2=8.08 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 105.3, 114.6, 115.3, 121.6, 125.7, 129.7, 132.1, 141.3, 144.1, 155.8, 157.5, 160.6 (CO), 165.5 (m, CF); ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −109.2; LC-MS: Calculated 272.2, Observed 273.2; Analysis calculated for $C_{16}H_{10}F_2O_2$: C, 70.59, H, 3.70 %, found: C, 70.63, H, 3.68 %.

*4.4.16. 4-Methyl-7-(1-methyl-1H-indol-5-yl)-2H-chromen-2-one (**4p**)*: Light green solid. MP : 120-122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.08 Hz, 3H, CH_3), 3.86 (s, 3H, NCH_3), 6.30 (d, *J*=1.08 Hz, 1H, ArH), 6.60 (d, *J*=3.12 Hz, 1H, ArH), 7.14 (d, *J*=3.08 Hz, 1H, ArH), 7.28 (s, 1H, ArH), 7.45 (s, 1H, ArH), 7.52-7.55 (dd, J_1=1.72 Hz J_2=8.52 Hz, 1H, ArH), 7.62-7.68 (m, 2H, ArH), 7.93 (s, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 46.2 (NCH_3), 106.3, 114.5, 115.3, 120.1, 122.3, 122.9, 129.3, 130.1, 134.5, 137.6, 139.1 (2C), 146.4, 147.2, 153.8,

156.4, 157.1, 160.4 (CO); LC-MS: Calculated 289.2, Observed 290.2; Analysis calculated for $C_{19}H_{15}NO_2$: C, 78.87, H, 5.23, N, 4.84 %, found: C, 78.91, H, 5.21, N, 4.83 %.

*4.4.17. 7-(4-(Dimethylamino)phenyl)-4-methyl-2H-chromen-2-one (**4q**)*: Light yellow solid. MP : 103-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.36 Hz, 3H, CH_3), 3.52 (s, 6H, NMe_2), 6.33 (s, 1H, ArH), 6.82 (d, *J*=7.52 Hz, 2H, ArH), 7.73-7.84 (m, 5H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.6 (CH_3), 43.6 (NMe_2), 115.6, 115.9, 119.7, 122.8, 124.9, 129.8, 132.5, 134.7, 140.3, 151.8, 156.3, 156.9, 160.6 (CO); LC-MS: Calculated 279.3, Observed 280.3; Analysis calculated for $C_{18}H_{17}NO_2$: C, 77.4, H, 6.13, N, 5.01 %, found: C, 77.44, H, 6.11, N, 4.99 %.

*4.4.18. 7-(3,5-Dichlorophenyl)-4-methyl-2H-chromen-2-one (**4r**)*: White solid. MP : 99-101 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.36 Hz, 3H, CH_3), 6.29 (d, *J*=1.00 Hz, 1H, ArH), 7.03-7.07 (m, 1H, ArH), 7.50-7.54 (m, 2H, ArH), 7.71-7.76 (m, 2H, ArH) 7.86-7.89 (dd, J_1=1.52 Hz J_2=7.96 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 105.1, 114.2, 115.3, 121.6, 125.4, 129.7, 132.1, 137.9, 138.1, 141.0, 155.4, 157.3, 160.4 (CO); LC-MS: Calculated 304.0, Observed 305.0; Analysis calculated for $C_{16}H_{10}Cl_2O_2$: C, 62.97, H, 3.30 %, found: C, 62.99, H, 3.31 %.

*4.4.19. 7-(3,5-bis(Trifluoromethyl)phenyl)-4-methyl-2H-chromen-2-one (**4s**)*: White solid. MP : 110-112 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.48 Hz, 3H, CH_3), 6.34 (d, *J*=1.08 Hz, 1H, ArH), 7.13-7.17 (m, 1H, ArH), 7.58-7.62 (m, 2H, ArH), 7.75-7.79 (m, 2H, ArH), 7.96-7.99 (dd, J_1=1.64 Hz J_2=8.08 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 105.6, 114.6, 115.7, 121.9, 125.6, 126.9 (m, CF_3), 129.8, 132.6, 138.3, 138.5, 141.2, 155.5, 157.6, 160.6 (CO); ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −58.6; LC-MS: Calculated 372.2, Observed 373.2; Analysis calculated for $C_{18}H_{10}F_6O_2$: C, 58.08, H, 2.71 %, found: C, 58.13, H, 2.69 %.

*4.4.20. tert-Butyl-4-(4-methyl-2-oxo-2H-chromen-7-yl)phenylcarbamate (**4t**)*: Off white solid. MP : 106-108 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.56 (s, 9H, *t*-Bu), 2.49 (d, *J*=1.52 Hz, 3H, CH_3), 6.31 (s, 1H, ArH), 7.51-7.55 (m, 3H, ArH), 7.68-7.73 (m, 3H, ArH), 8.08-8.11 (dd, J_1=2.08 Hz J_2=8.56 Hz, 1H, ArH), 8.31 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.6 (CH_3), 30.7 (Boc CH_3), 81.9 (Boc C), 109.8, 117.5, 118.4, 125.3, 129.5, 132.1, 136.7, 141.2, 141.5, 145.8, 146.4, 155.2, 155.9, 160.2 (CO); LC-MS: Calculated 351.2, Observed 252.2; Analysis calculated for $C_{21}H_{21}NO_4$: C, 71.78, H, 6.02, N, 3.99 %, found: C, 71.84, H, 5.99, N, 3.97 %.

*4.4.21. 7-(4-Hydroxyphenyl)-4-methyl-2H-chromen-2-one (**4u**)*: Brown solid. MP : 86-88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.68 Hz, 3H, CH_3), 5.23 (s, 1H, OH), 6.31 (s, 1H, ArH), 7.01-7.04 (dd, J_1=1.96 Hz J_2=8.44 Hz, 2H, ArH), 7.68-7.77 (m, 5H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.6 (CH_3), 110.2, 117.9, 118.8, 125.9, 129.8, 130.1 (2C), 132.9, 136.6, 137.8, 152.5, 155.3, 158.6, 160.4 (CO); LC-MS: Calculated 252.1, Observed 253.1; Analysis calculated for $C_{16}H_{12}O_3$: C, 76.18, H, 4.79 %, found: C, 76.23, H, 4.77 %.

*4.4.22. 4-Methyl-7-(4-(methylamino)phenyl)-2H-chromen-2-one (**4v**)*: Yellow solid. MP : 93-95 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.28 Hz, 3H, CH_3), 3.02 (s, 3H, NCH_3), 6.31 (s, 1H, ArH), 6.77 (d, *J*=7.24 Hz, 2H, ArH), 7.66-7.72 (m, 5H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.6 (CH_3), 31.6 (NCH_3), 115.5, 115.7, 119.7, 122.8, 124.7, 127.8 (2C), 132.3, 134.2, 140.1, 151.4, 156.3, 156.5, 160.4 (CO); LC-MS: Calculated 265.1, Observed 266.1; Analysis calculated for $C_{17}H_{15}NO_2$: C, 76.96, H, 5.70, N, 5.28 %, found: C, 76.99, H, 5.69, N, 5.27 %.

*4.4.23. 7-(6-Methoxypyridin-3-yl)-4-methyl-2H-chromen-2-one (**4w**)*: White solid. MP : 92-94 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (d, *J*=1.32 Hz, 3H, CH_3), 4.08 (s, 3H, OCH_3), 6.29 (s, 1H, ArH), 7.03-7.06 (dd, J_1=2.04 Hz J_2=8.52 Hz, 1H, ArH), 7.61-7.66 (m, 3H, ArH), 8.24-8.29 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.8 (CH_3), 57.5 (OCH_3), 112.2, 114.9, 120.4, 122.9, 124.8, 125.9, 129.8, 136.6, 138.8, 143.0, 151.6, 154.5, 160.6 (CO), 162.1; LC-MS: Calculated 267.1, Observed 268.1; Analysis calculated for $C_{16}H_{13}NO_3$: C, 71.90, H, 4.90, N, 5.24 %, found: C, 71.94, H, 4.89, N, 5.22 %.

*4.4.24. 4-Methyl-7-(thiophen-3-yl)-2H-chromen-2-one (**4x**)*: Off white solid. MP : 90-92 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.47 (d, *J*=1.08 Hz, 3H, CH_3), 6.31 (d, *J*=1.08 Hz, 1H, ArH), 6.42-6.44 (dd, J_1=1.68 Hz J_2=3.24 Hz, 1H, ArH), 6.78 (d, *J*=3.28 Hz, 1H, ArH), 7.19-7.33 (m, 2H, ArH), 7.44-7.48 (m, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.2 (CH_3), 111.2, 117.3, 120.5 (2C), 124.6, 127.7, 128.3, 129.3 (2C), 137.4, 151.3, 154.6, 160.4,CO; LC-MS: Calculated 242.3, Observed 243.3; Analysis calculated for $C_{14}H_{10}O_2S$: C, 69.40, H, 4.16 %, found: C, 69.44, H, 4.15 %.

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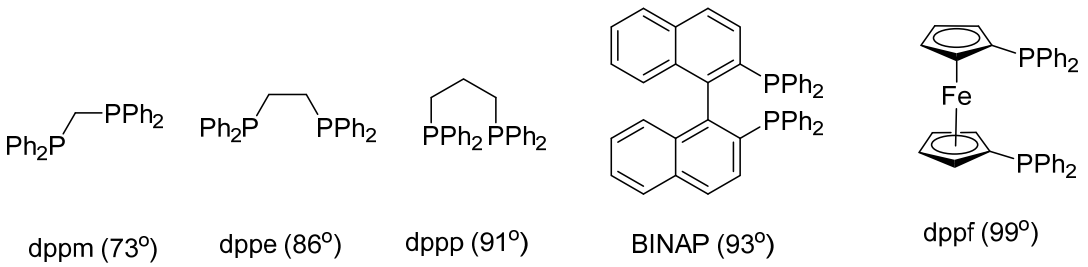
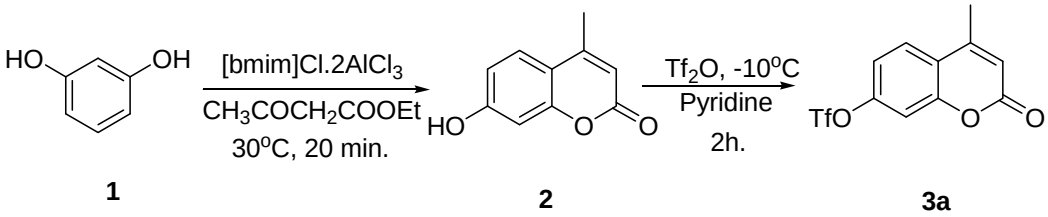
Figure Captions



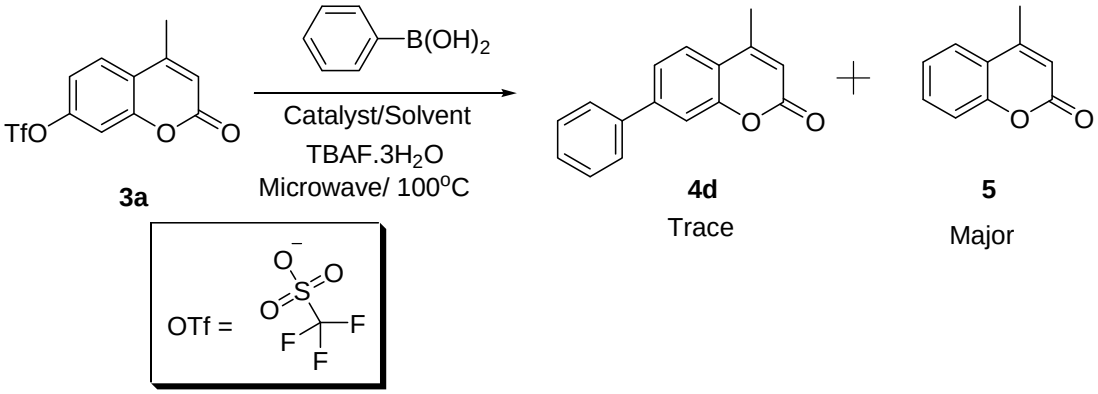
dppm (73°) dppe (86°) dppp (91°) BINAP (93°) dppf (99°)

Figure 1: Structure of various ligands used and their bite angles

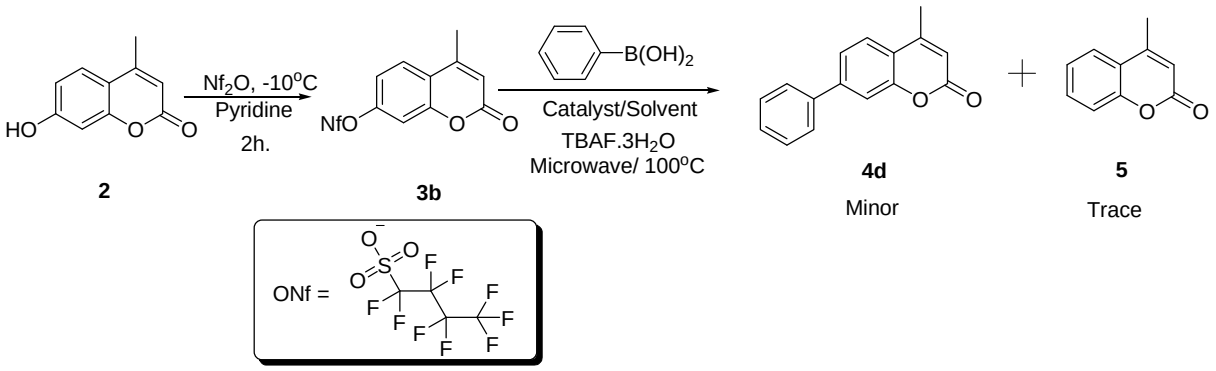


1 **2** **3a**

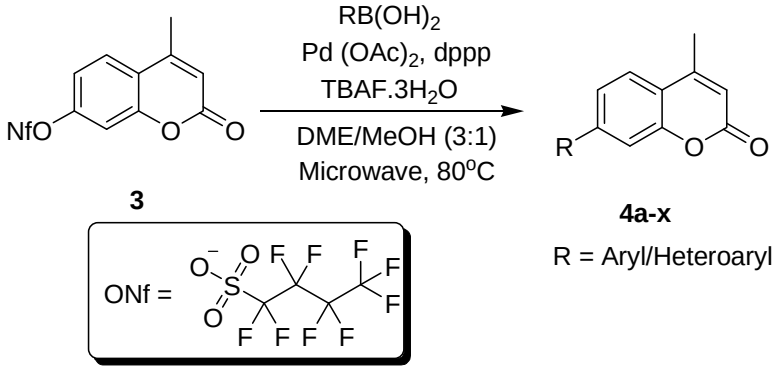
Scheme 1: Synthesis of 4-methyl-7-trifluoromethylsulfonyloxy coumarin intermediate



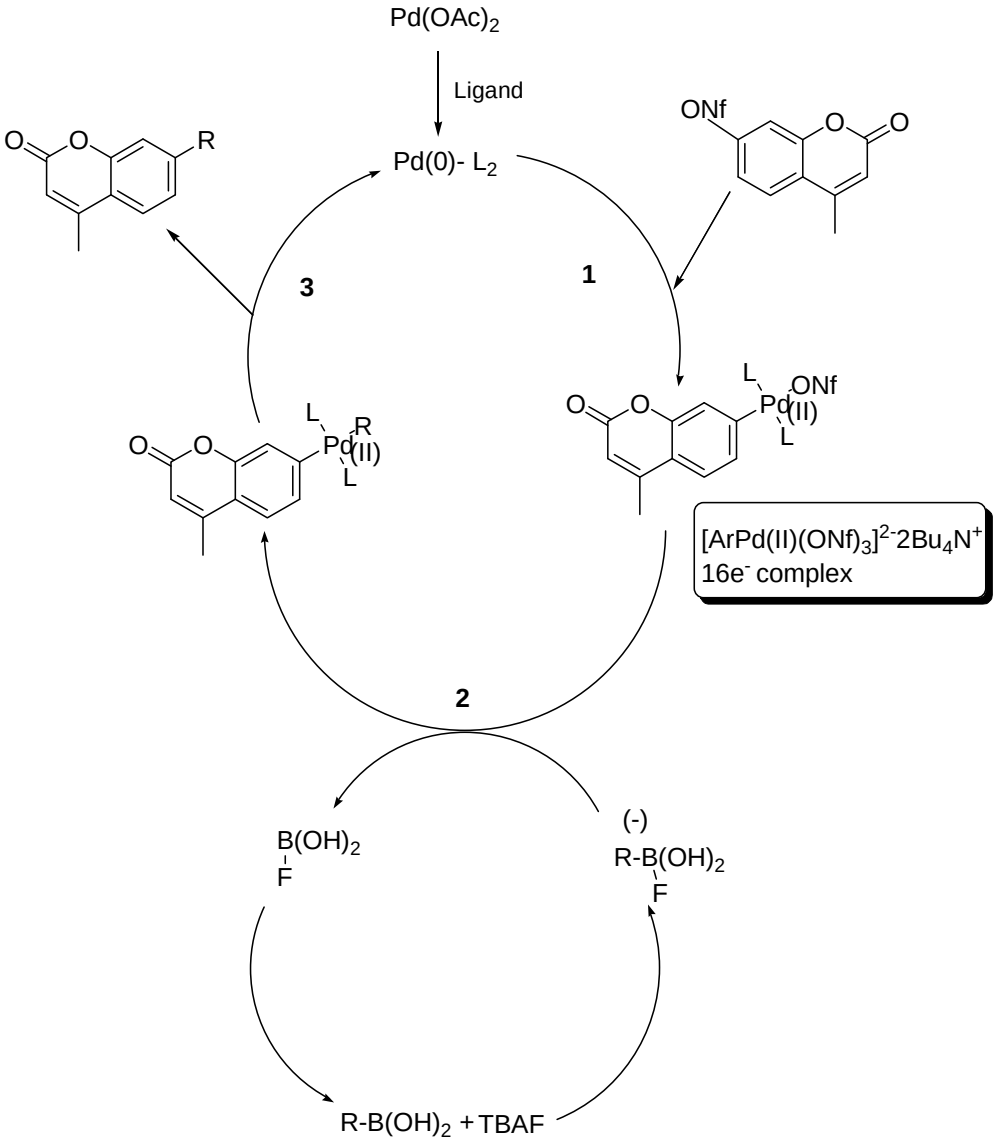
Scheme 2: Suzuki coupling of 4-methyl-7-trifluoromethylsulfonyloxy coumarin intermediate with phenylboronic acid



Scheme 3: Synthesis of 4-methyl-7-nonafluorobutylsulfonyloxycoumarin intermediate and its Suzuki coupling with phenylboronic acid



Scheme 4: Synthesis of 4-methyl-7-aryl/heteroaryl coumarins



Scheme 5: Proposed mechanism of the coupling reaction

Tables

Table 1: Effect of various catalysts and solvents in the Suzuki coupling of **3a** with phenylboronic acid

Entry	Catalyst	Base	Solvent	Yield 4d (%)	Yield 5 (%)
1	$Pd_2(dba)_3$	$TBAF{\cdot}3H_2O$	DMF	trace	90
2	$Pd(dppf)Cl_2$	$TBAF{\cdot}3H_2O$	DMF	trace	88
3	$PdCl_2.(CH_3CN)_2$	$TBAF{\cdot}3H_2O$	DMF	trace	90
4	$Pd(dppf)CH_2Cl_2$	$TBAF{\cdot}3H_2O$	DMF	trace	92
5	$PdCl_2(PCy_3)_2$	$TBAF{\cdot}3H_2O$	DMF	trace	87
6	$Pd(OAc)_2$	$TBAF{\cdot}3H_2O$	DMF	4	82
7	$Pd(OAc)_2$	$TBAF{\cdot}3H_2O$	1,4- Dioxane	5	80
8	$Pd(OAc)_2$	$TBAF{\cdot}3H_2O$	DME	8	75

Reaction conditions: 4-methyl-7-trifluoromethylsulfonyloxy coumarin (1 mmol), phenylboronic acid (1.5 mmol), catalyst (0.05 mmol), $TBAF{\cdot}3H_2O$ (2 mmol), solvent, microwave irradiated at 110 W at 100 °C for 30 min.

Table 2: Effect of various catalysts and solvents in the Suzuki coupling of **3b** with phenylboronic acid

Entry	Catalyst	Base	Solvent	Yield 4d (%)
1	$Pd_2(dba)_3$	$TBAF{\cdot}3H_2O$	DMF	trace
2	$Pd(dppf)Cl_2$	$TBAF{\cdot}3H_2O$	DMF	10
3	$PdCl_2.(CH_3CN)_2$	$TBAF{\cdot}3H_2O$	DMF	trace
4	$Pd(dppf)CH_2Cl_2$	$TBAF{\cdot}3H_2O$	DMF	trace
5	$PdCl_2(PCy_3)_2$	$TBAF{\cdot}3H_2O$	DMF	16
6	$Pd(OAc)_2$	$TBAF{\cdot}3H_2O$	DMF	20
7	$Pd(OAc)_2$	$TBAF{\cdot}3H_2O$	1,4- Dioxane	25
8	$Pd(OAc)_2$	$TBAF{\cdot}3H_2O$	DME	45
9	$Pd(OAc)_2$	$TBAF{\cdot}3H_2O$	DME- H_2O (3:1)	50
10	$Pd(OAc)_2$	$TBAF{\cdot}3H_2O$	DME-MeOH (3:1)	65
11	$Pd(OAc)_2$	$TBAF{\cdot}3H_2O$	DME-MeOH (3:1)	68[c]
12	$Pd(OAc)_2$	$TBAF{\cdot}3H_2O$	DME-MeOH (3:1)	40[d]
13	$Pd(OAc)_2$	$TBAF{\cdot}3H_2O$	DME-MeOH (3:1)	50[e]

Reaction conditions: 4-methyl-7-nonafluorobutylsulfonyloxy coumarin (1 mmol), phenylboronic acid (1.5 mmol), catalyst (0.05 mmol), $TBAF{\cdot}3H_2O$ (2 mmol), solvent, microwave irradiated at 110 W at 100 °C for 30 min.

[c]3 mmol of base used.

[d]Reaction carried out for 15 min.

[e]Reaction carried out at 80 °C.

Table 3: Screening of various ligands used for the Suzuki coupling of **3b** with phenylboronic acid and their bite angles

Entry	Catalyst	Ligand	Bite Angle	Yield[b] 4d (%)
1	$Pd(OAc)_2$	dppm	71°	73
2	$Pd(OAc)_2$	dppe	86°	80
3	$Pd(OAc)_2$	dppp	91°	92
4	$Pd(OAc)_2$	dppf	99°	78
5	$Pd(OAc)_2$	BINAP	93°	82
6	$Pd(OAc)_2$	dppp	91°	98[c,d]

Reaction conditions: 4-methyl-7-nonafluorobutylsulfonyloxy coumarin (1 mmol), phenylboronic acid (1.5 mmol), $Pd(OAc)_2$ (0.05 mmol), ligand (0.1 mmol), $TBAF{\cdot}3H_2O$ (2 mmol), DME-MeOH (3:1), microwave irradiated at 110 W at 100 °C for 30 min.

[b]LC-MS yield.

[c]3 mmol of base used.

[d]Reaction carried out at 80 °C.

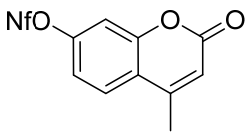
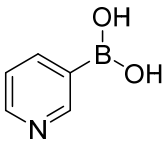
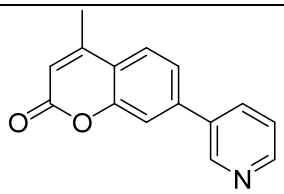
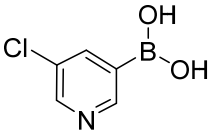
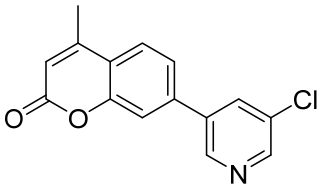
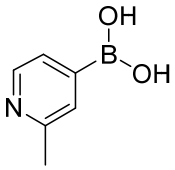
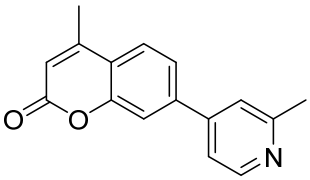
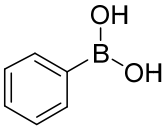
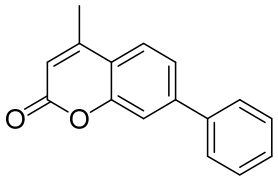
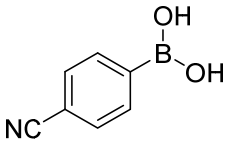
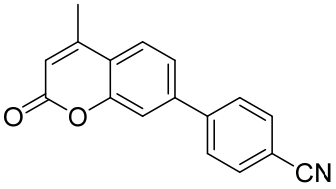
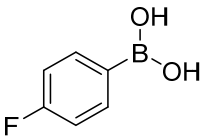
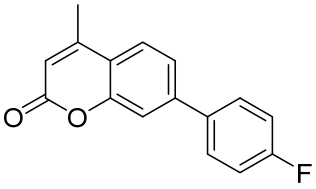
Table 4: Effect of various bases in the Suzuki coupling of nonaflate **3b** with phenylboronic acid

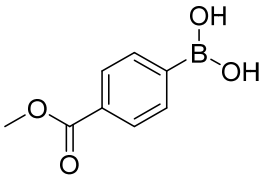
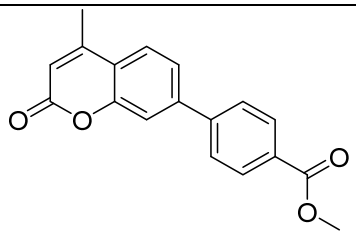
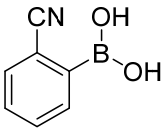
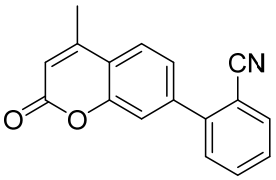
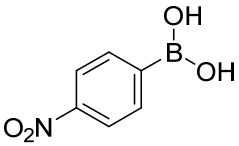
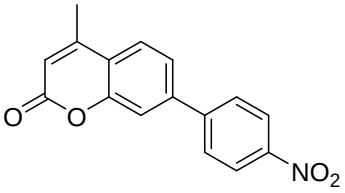
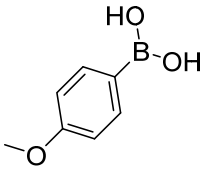
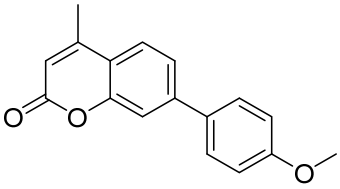
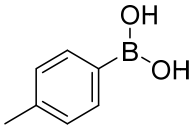
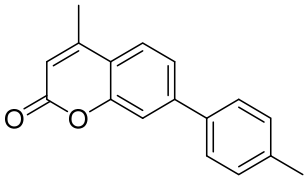
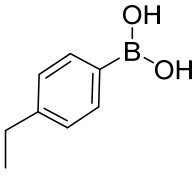
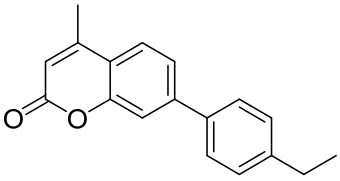
Entry	Base	Yield[b] 4d (%)
1	K_2CO_3	15
2	NaOH	traces
3	Na_2CO_3	18
4	CsF	60
5	Cs_2CO_3	65
6	K_3PO_4	48
7	$TBAF{\cdot}3H_2O$	93

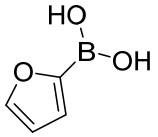
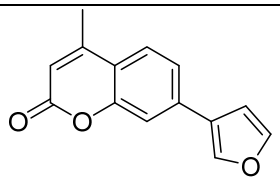
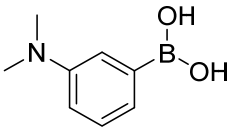
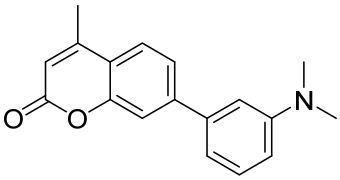
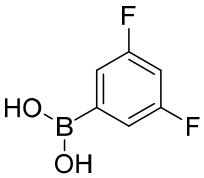
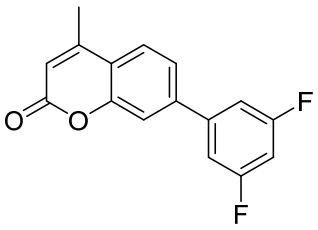
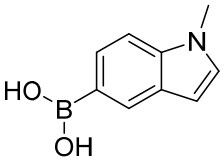
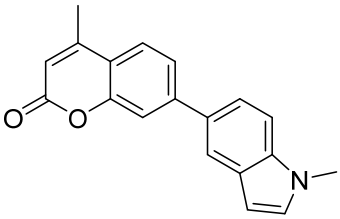
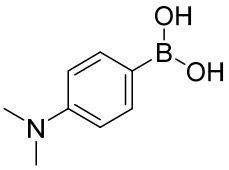
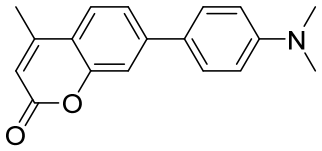
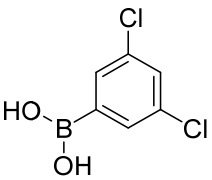
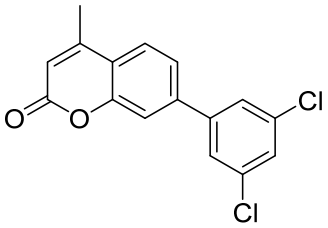
Reaction conditions: 4-methyl-7-nonafluorobutylsulfonyloxy coumarin (1 mmol), phenylboronic acid (1.5 mmol), $Pd(OAc)_2$ (0.05 mmol), dppp (0.1 mmol), base (3 mmol), DME-MeOH (3:1), microwave irradiated at 110 W at 80 °C for 30 min.

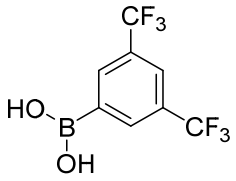
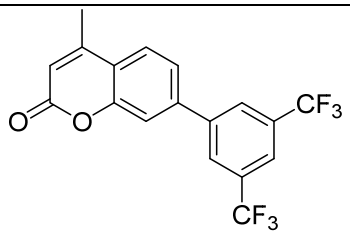
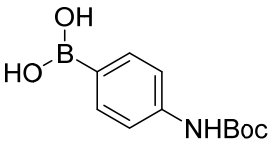
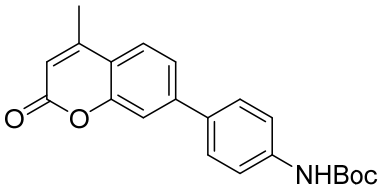
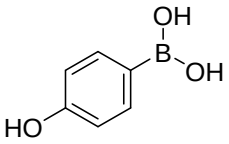
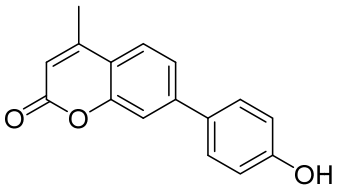
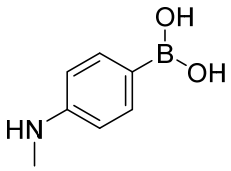
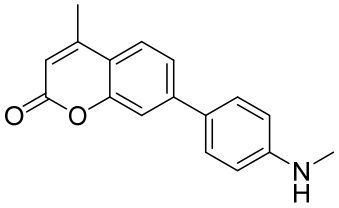
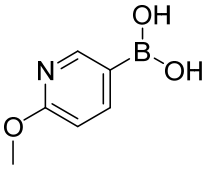
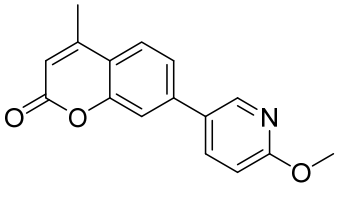
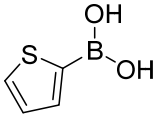
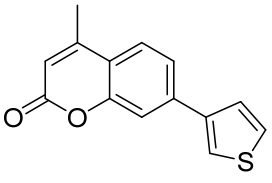
[b] Isolated yield.

Table 5: Suzuki coupling of 4-methyl-7-nonafluorobutylsulfonyloxy coumarin **3b** with various boronic acids

Entry	Nonaflate (3)	Boronic acid	Product (4a-x)	Yield[b] (%)
1			 **4a**	92
2	**3**		 **4b**	90
3	**3**		 **4c**	92
4	**3**		 **4d**	93
5	**3**		 **4e**	82
6	**3**		 **4f**	84

7	**3**		 **4g**	85
8	**3**		 **4h**	77
9	**3**		 **4i**	86
10	**3**		 **4j**	95
11	**3**		 **4k**	97
12	**3**		 **4l**	94

13	**3**		 **4m**	90
14	**3**		 **4n**	80
15	**3**		 **4o**	82
16	**3**		 **4p**	85
17	**3**		 **4q**	82
18	**3**		 **4r**	82

19	**3**		 **4s**	80
20	**3**		 **4t**	84
21	**3**		 **4u**	93
22	**3**		 **4v**	90
23	**3**		 **4w**	95
24	**3**		 **4x**	92

Reaction conditions: 4-methyl-7-nonafluorobutylsulfonyloxy coumarin (1 mmol), boronic acid (1.5 mmol), $Pd(OAc)_2$ (0.05 mmol), dppp (0.1 mmol), $TBAF{\cdot}3H_2O$ (3 mmol), DME-MeOH (3:1), microwave irradiated at 110 W at 80 °C for 30 min.
[b]Isolated yield.