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Synthesis of 4-Alkenyl Benzoxazoles via Pd-catalyzed *ortho* C-H Functionalization of 2-Amidophenols

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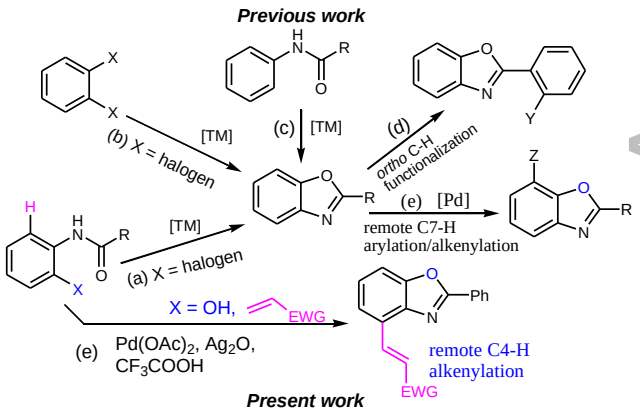
Abstract. A one-pot direct transformation to remotely C-H alkene functionalized 2-aryl benzoxazoles from the reaction of amidophenol and electronically deficient olefin was reported. Control experiments confirm that the Pd-catalyzed regioselective C−H activation/alkenylation occurs at the first step by leading to *ortho*-alkenylated amidophenol; which subsequently underwent tandem intramolecular annulation to afford C4-alkenylated 2-arylbenzoxazole derivatives.

Keywords: C-H activation; Benzoxazole; Pd-catalysis; C-H alkenylation ; 2-amidophenol.

Introduction

The diverse biological activities of functionalized benzoxazoles make them an ideal pharmacophore in drug discovery research.[1] The unique chromophoric property of the 2-aryl benzoxazoles renders them as a useful scaffold in broader applications such as optical brighteners, blue LED, etc.[2] Further, benzoxazoles also serve as potential ligands in transition metal-catalyzed coupling reactions.[3] As such, rapid access to a broad range of benzoxazoles with different substituents at the benzene ring is synthetically fascinating. Plethora of methods for the synthesis of benzoxazole core has been reported over the past years. The condensation of *ortho*-aminophenol and carboxylic acid or its surrogates represent a classical approach to construct the benzoxazole unit.[1b] Traditionally, this process requires harsh reaction conditions such as high temperature, strong acids, strong oxidative conditions, etc. To circumvent these pitfalls, several transition metal catalyzed methods with enhanced substrate scope and several degrees of flexibility have been developed.[4] These strategies are mainly: (i) transition-metal-catalyzed C−O cross-coupling of 2-haloanilides leading to benzoxazole motif (Scheme 1a);[5-7] (ii) copper-catalyzed intermolecular domino C−N/C-O cross-coupling of 1,2-dihalobenzene with benzamides (Scheme 1b);[8] and (iii) aromatic C−H functionalization followed by C−O bond formation (Scheme 1c).[9] Besides, the coordinating ability of the nitrogen has been exploited for the regioselective *ortho* C−H arylation,[11] acylation,[11] hydroxylation,[12] fluorination[13] and alkenylation at the C2-aryl group of 2-aryl benzoxazoles[14] (Scheme 1d). Contrastingly, the synthesis of benzoxazole framework with C-H functionalization at the fused-benzene ring is less literature precedent. To the best of our knowledge, so far, there are only two methods have been reported for the synthesis of such functionalized heterocyclic-core (functionalization at C7-position only) (Scheme 1d).[15] These methods include: (i) Pd-catalyzed regioselective C-H arylation of the 2-aryl benzoxazoles at the remote C7 position,[15a] and (ii) bifunctional nitrile templet driven remote C-H alkenylation of 2-methyl benzoxazole (one example only).[15b] Considering the pharmacological potential of the functionalized benzoxazoles,[16] the synthesis of remotely functionalized benzoxazole-core deemed to be important. In continuation to our recent interest

Scheme 1. Synthesis of 2-aryl benzoxazoles



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on transition-metal catalyzed C-C and C-heteroatom bond formation reactions in heterocycle synthesis,[17] we herein, report a Pd-catalyzed protocol for the tandem synthesis 4-alkenyl benzoxazoles directly from the reaction *ortho*-hydroxy *N*-aryl amides and electronically deficient terminal alkenes *via ortho* C-H alkenylation and subsequent intramolecular annulation under ligand-free conditions (Scheme 1f).

Results and Discussion

To access the C4-H functionalized benzoxazole motif, we anticipated that the *N*-(2-hydroxy-phenyl)benzamide (**1a**) might undergo transition-metal catalyzed Fujiwara-Moritani *ortho*-alkenylation and subsequent annulation to afford C4-alkenylated 2-phenyl benzoxazole (**3aa**). With this in mind, when **1a** was treated with methyl acrylate (**2a**) under a similar Pd-catalyzed reaction conditions as reported by us for the *N*-tosyl benzoxazolidine synthesis,[17i] 2-phenyl benzoxazole (**4a**) was produced exclusively (25%) along with a trace (< 10%) of a new product (from TLC) and the remaining unreacted starting material (Scheme 2). However, at higher temperature (i.e., 110°C), 2-phenyl benzoxazole (70%) was produced along with a 16% of the previously new product with a molecular weight of 279 (as shown by the ESI-MS). The appearance of a singlet at δ 3.84 ppm in ^{1}H NMR spectrum indicates the presence of methyl ester substituents in the new product. Presence of doublets at δ 8.02 and 7.37 (with J = 16 Hz) suggests for the existence of an *E*-double bond. Considering the ^{1}H and 15 signals from the ^{13}C NMR spectra, we presumed that the structure of the new compound would be (*E*)-methyl 3-(2-phenylbenzo[d]oxazol-4-yl)acrylate (**3aa**). The exact molecular structure of **3aa** was further confirmed by X-ray crystallography (Figure 1).[18] To a side note, sequential C-H activation and annulation leading to the remotely C4-alkene functionalized benzoxazole were not reported earlier though there are limited pioneering efforts have been made on Pd- and Rh-catalyzed aromatic C-H olefination of anilides (Fujiwara-Moritani reaction).[19] Notably, due to the steric reason, the Pd-catalyzed Fujiwara–Moritani olefination of *ortho*-substituted substrates traditionally unsuccessful or results in poor yield.[19, 20] Also, the hydroxyl group *ortho* to the directing group usually has the deleterious effect in transition metal catalyzed C-H activation reaction, and the O-alkenylation would be the potential reaction. Indeed, the alkenylation of phenol in the presence of Pd-catalyst was reported recently by Cai and co-workers.[21] Thus, selective C-alkenylation of 2-amidophenol (e.g., **1a)** in the presence of transition metal catalyst is considered to be challenging. Intriguingly, when **1a** was treated with methyl acrylate under the similar reaction conditions as reported by van Leeuwen,[20a] C-alkenylated product (e.g., **3aa´**) was obtained only in 21% yield along with a trace amount of **3aa** and 2-phenyl benzoxazole (**4a**, 24% yield). Thus, we intended to develop an efficient protocol for the regioselective synthesis of remotely alkene functionalized benzoxazole (e.g., **3aa**) from 2-amidophenol (e.g., **1a)** via the sequential regioselective C-alkenylation and subsequent intramolecular annulation.

Scheme 2. Reactions of amide with alkene

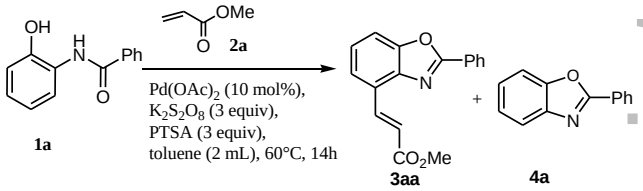
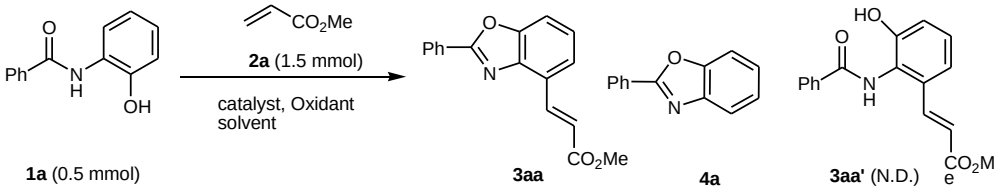


Figure 1. ORTEP of **3aa**

At the onset, we intended to optimize the reaction condition (Table 1) for the efficient synthesis of **3aa** from the model substrate **1a** and methyl acrylate (**2a**) in the presence of Pd-catalyst. Treatment of 1a with 2a the presence of $Pd(OAc)_2$, oxidant ($K_2S_2O_8$) and additive (PTSA) at room temperature did not show any change in the starting materials (entry 1). By increasing the reaction temperature to 110°C, a mixture of **3aa** (16%) and **4a** (70%) was produced (entry 3). In the absence of oxidant, **3aa** was not formed, rather the annulated product **4a** was isolated quantitatively (entry 4). From a similar reaction in the absence of any additive (entry 5), almost no reaction occurred (**4a** was isolated in <10% yield). Solvent screening to get a better yield of **3aa** was unsuccessful (entries 6-11). In the presence of a basic additive such as NaOAc and Et_3N the reaction did not proceed (entries 12, 13). Interestingly, by changing the additive from PTSA to CF_3COOH (1 equiv) in the presence of terminal oxidant $K_2S_2O_8$ (1 equiv), benzoxazole **4a** was not identified, instead the desired benzoxazole **3aa** was produced, albeit in low yield (only 20%) with the recovery of remaining starting material (entry 14). While employing CF_3COOH, both as an additive and the solvent in the presence of $K_2S_2O_8$, **3aa** was formed in 55% yield (entry 15).

Among the tested oxidants (e.g., oxone, BQ, $Cu(OAc)_2$, AgOAc, Ag_2O, $AgOCOCF_3$ and $Cu(OAc)_2$) Ag_2O (1 equiv.) served as the best oxidant

Table 1. Optimization of reaction conditions[a]



1a (0.5 mmol) **3aa** **4a** **3aa'** (N.D.)

Entry	catalyst (10 mol%)	oxidant (equiv)	additive (equiv)	solvent (2 mL)	temperature	yield (%) **3aa**	**4a**
1	$Pd(OAc)_2$	$K_2S_2O_8$ (5)	PTSA (3)	toluene	rt	0	0
2	$Pd(OAc)_2$	$K_2S_2O_8$(5)	PTSA(3)	toluene	60°C	<10	25
3	$Pd(OAc)_2$	$K_2S_2O_8$ (5)	PTSA(3)	toluene	110°C	16	70
4	$Pd(OAc)_2$	-	PTSA(3)	toluene	110°C	0	100
5	$Pd(OAc)_2$	$K_2S_2O_8$ (5)	-	toluene	110°C	0	<10
6	$Pd(OAc)_2$	$K_2S_2O_8$ (1)	PTSA(3)	toluene	110°C	35	30
7	$Pd(OAc)_2$	$K_2S_2O_8$ (1)	PTSA(3)	methanol	60°C	15	30
8	$Pd(OAc)_2$	$K_2S_2O_8$ (1)	PTSA(3)	DCE	60°C	10	20
9	$Pd(OAc)_2$	$K_2S_2O_8$ (1)	PTSA(3)	THF	60°C	0	0
10	$Pd(OAc)_2$	$K_2S_2O_8$ (1)	PTSA(3)	CH_3CN	60°C	0	0
11	$Pd(OAc)_2$	$K_2S_2O_8$ (1)	PTSA(3)	1,4-dioxane	60°C	0	0
12	$Pd(OAc)_2$	$K_2S_2O_8$ (1)	Et_3N (3)	toluene	60°C	0	0
13	$Pd(OAc)_2$	$K_2S_2O_8$(1)	NaOAc (3)	toluene	60°C	0	0
14	$Pd(OAc)_2$	$K_2S_2O_8$ (1)	CF_3COOH(1)	toluene	60°C	20	0
15	$Pd(OAc)_2$	$K_2S_2O_8$ (1)	-	CF_3COOH	60°C	55	trace
16	$Pd(OAc)_2$	BQ (1)	-	CF_3COOH	60°C	46	0
17	$Pd(OAc)_2$	AgOAc (1)	-	CF_3COOH	60°C	60	0
18	$Pd(OAc)_2$	AgOAc (3)	-	CF_3COOH	60°C	65	0
19	$Pd(OAc)_2$	Ag_2CO_3 (1)	-	CF_3COOH	60°C	52	0
20	$Pd(OAc)_2$	Ag_2O (1)	-	CF_3COOH	60°C	90	0
21	$Pd(OAc)_2$	$AgOCOCF_3$ (1)	-	CF_3COOH	60°C	78	0
22	$Pd(OAc)_2$	Ag_2O (1)	CF_3COOH(1)	toluene	60°C	20	0
23	$Pd(OAc)_2$	$Cu(OAc)_2$ (1)	-	CF_3COOH	60°C	35	0
24	$Pd(OAc)_2$	Ag_2O (1)	-	CF_3COOH	rt	0	0

[a]Reaction conditions: A mixture of **1a**, **2a** and additive in solvent was stirred in a closed round bottom for 14h.

to afford **3aa** in optimum yield (90%) with complete conversion of starting material over a period of 14h at 60°C (entry 20). At room temperature, no reaction occurred (entry 24). Besides, by lowering the catalyst loading to 5 mol% as well as oxidant concentration to 0.5 equiv., incomplete conversion occured by offering a lower yield of **3aa** (47% and 42% respectively) even after 24h.

During our investigation to exploit the scope and limitations of this reaction process, we noticed that the reaction of 2-chloro-*N*-(2-hydroxyphenyl)-benzamide (**1c**) with **2a**, under optimized reaction conditions affords 25% of the desired product (**3ca**) along with the intermediate **3ca´** (50%) (Scheme 3). Formation of **3ca´** was evident from ^1H and ^{13}C NMR data. On heating the intermediate **3ca´** at 90°C in CF_3COOH, **3ca** was produced smoothly with a combined yield of 65% from **1c**. Additionally, when 2-phenyl benzoxazole (**4a**) was treated with the methyl acrylate in the presence of $Pd(OAc)_2$ (10 mol%) and Ag_2O (1 equiv) in TFA, **3aa** was not formed with complete recovery of the starting material. Hence, the possibility for weakly coordinating oxazole nitrogen-directed remote C4-H alkenylation to access **3aa** was disregarded. On the other hand, we predict that the overall transformation occurs with the initial C-alkenylation through C-H activation (Fujiwara-Moritani reaction) followed by an acid catalyzed annulation. In line with the reported literature,[21, 22] the catalytic cycle is presented in Scheme 4. We presumed that electronically more deficient and more reactive Pd-catalyst ($Pd(OCOCF_3)_2$) is forming initially from the reaction of $Pd(OAc)_2$ and CF_3COOH.[21e] The electrophilic

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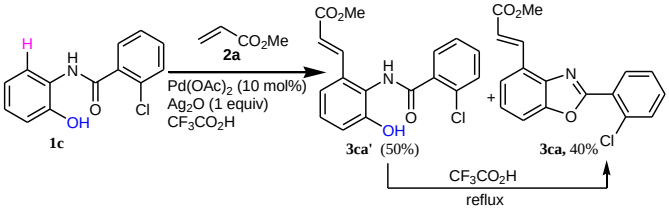
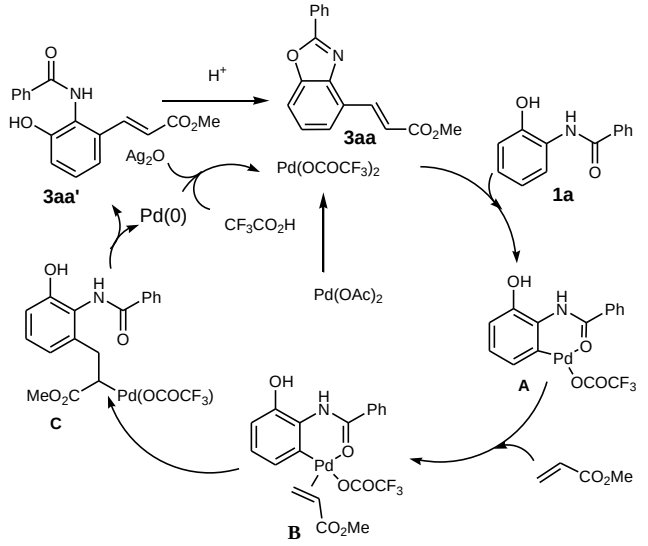
attack at the palladium center by the anilide forms the palladocycle (e.g., A) through *ortho*-palladation. The carbopalladation of methyl acrylate (A → B → C) followed by reductive elimination enables the *ortho* C-H alkenated amidophenol (**3aa´**). In the presence of terminal oxidant (i.e., Ag_2O), the newly generated Pd(0) oxidizes to Pd(II) for the next catalytic cycle. Finally, the cross-coupled hydroxy anilide **3aa´** undergoes acid-catalyzed annulation[22] to afford the desired benzoxazole **3aa**.

Scheme 3. Control experiment

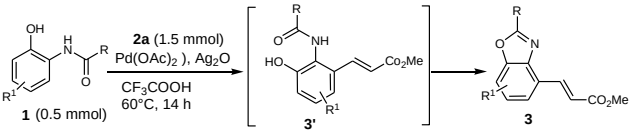


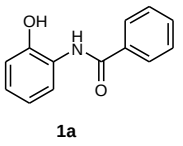
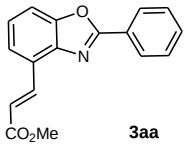
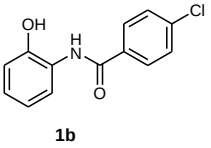
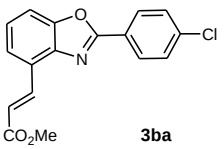
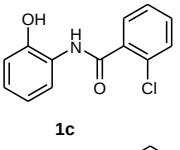
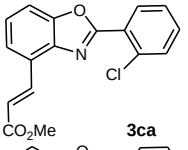
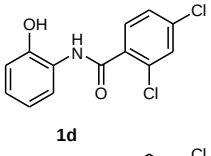
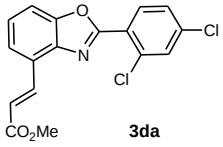
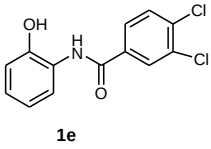
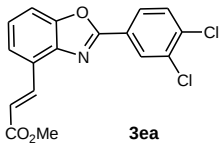
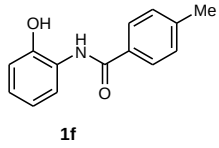
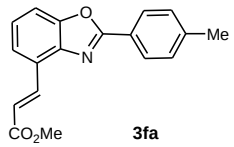
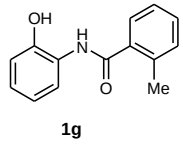
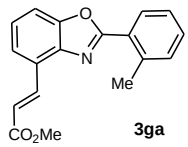
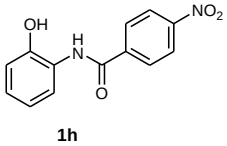
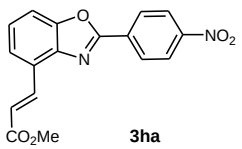
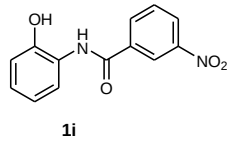
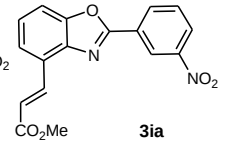
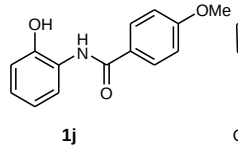
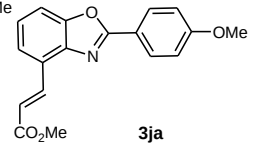
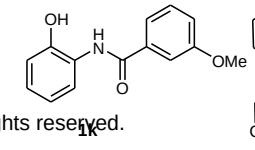
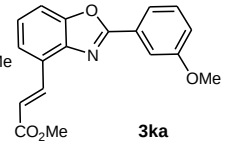
Scheme 4. Reaction pathway



Next, we turned our attention to study the compatibility of this tandem C-H functionalization and annulation protocol to form a series of C4-functionalized benzoxazole derivatives (**3**) by varying the substituents at the aromatic rings. To our pleasure, the coupling of differently substituted amidophenols (**1a-u**) with methyl acrylate (**2a**) gave the desired derivatives (**3aa-3ua)** in moderate to good yield. Worthy to mention that the *ortho*-substituents (e.g., **1c, 1d, 1g**) to the aromatic ring cause masking for acid catalyzed annulation (e.g., **3ca´** → **3ca**) due to steric shield. As a result, the intermediate **3ca´** was formed via dehydrogenative C-H alkenylation along with the annulated product **3ca**. Moreover, when **3ca´**was heated at 90°C in TFA, C4-alkenylated benzoxazole was formed smoothly. The reaction of *para*-fluoro amidophenol, i.e., **1u** with **2a** procceds with partial conversion and the desired C4-alkenylated benzoxazole **3ua** was isolated in 44% yield. Unfortunately, similar reaction with other *para*-substituted amidophenols (entries 22-24) gave only the benzoxazoles **4v-x** with the recovery of unreacted starting materials (**1v-x**). Probably, due to

Table 2. Synthesis of substituted C4-alkenylated benzoxazoles[a]



Entry	amide (**1**)	benzoxazole (**3**)	% yield
1	 **1a**	 **3aa**	90
2	 **1b**	 **3ba**	88
3	 **1c**	 **3ca**	85
4	 **1d**	 **3da**	77
5	 **1e**	 **3ea**	52
6	 **1f**	 **3fa**	82
7	 **1g**	 **3ga**	62
8	 **1h**	 **3ha**	56
9	 **1i**	 **3ia**	47
10	 **1j**	 **3ja**	79
11	 **1k**	 **3ka**	57

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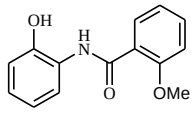
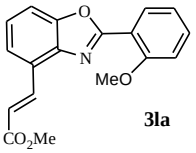
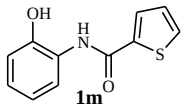
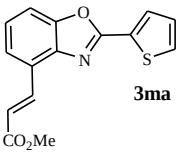
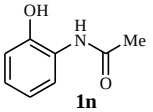
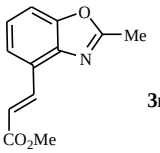
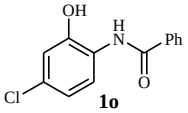
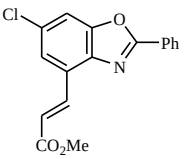
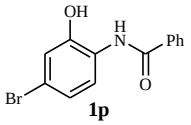
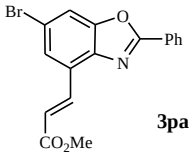
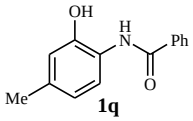
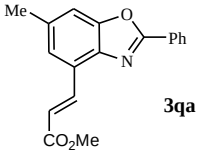
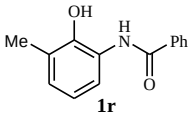
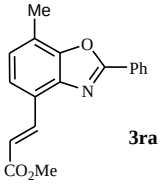
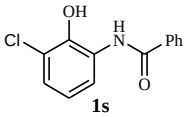
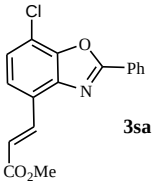
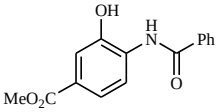
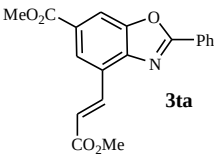
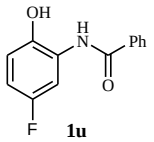
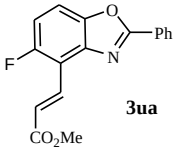
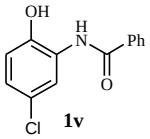
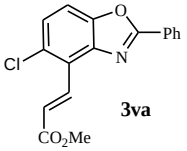
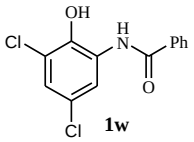
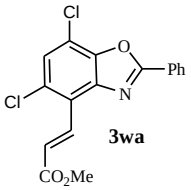
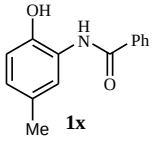
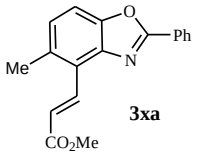
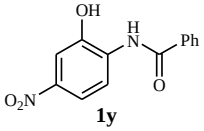
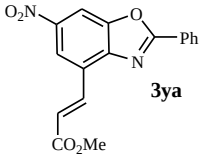
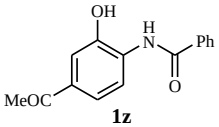
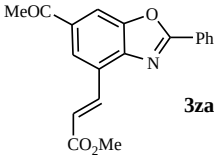
Entry	Amide (**1**)	benzoxazole (**3**)	% yield
12	 **1l**	 **3la**	68
13	 **1m**	 **3ma**	55
14	 **1n**	 **3na**	35
15	 **1o**	 **3oa**	76
16	 **1p**	 **3pa**	75
17	 **1q**	 **3qa**	62
18	 **1r**	 **3ra**	55
19	 **1s**	 **3sa**	57
20	 **1t**	 **3ta**	40
21	 **1u**	 **3ua**	44
22	 **1v**	 **3va**	0[b]
23	 **1w**	 **3wa**	0[c]
24	 **1x**	 **3xa**	0[d]
25	 **1y**	 **3ya**	0[e]
26	 **1z**	 **3za**	trace[f]

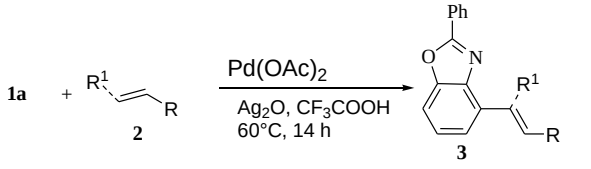
[a] *Reaction conditions*: Amide (0.5 mmol), alkene (1.5 mmol), $Pd(OAc)_2$ (10 mol%), Ag_2O (0.5 mmol) in CF_3CO_2H (2 mL) at 60°C, 14h. [b-f] Benzoxazoles **4v-4z** were formed with recovery starting material.

steric reason, the initial anilide directed C-H alkenylation did not occur and so the subsequent annulation. Amidophenol with an ester substituent (i.e., **1t**) also underwent the coupling reaction with **2a**, and **3ta** was formed (entry 20). Worthy to mention here that while amidophenols with strong electron-withdrawing groups were treated with **2a** under optimized reaction conditions, the aromatic ring gets deactivated substantially, and the alkenylation did not occur (entries 25 & 26), rather the benzoxazoles such as 5-nitro and 5-acyl -2-phenylbenzo[d]oxazole (**4y** and **4z** respectively) were produced from the acid-catalyzed annulation in 40% and 31% yield respectively, with the recovery of unreacted amidophenol.

Coupling of **1a** with different alkenes to enable the C4-alkenated benzoxazole was also investigated (Scheme 5). It has been observed that the acrylates are the most suitable coupling partners to afford the desired C4-alkenylated benzoxazoles (e.g., **3aa**, **3ab, 3ac, 3ae**) under our Pd-catalyzed reaction conditions. Notably, when benzyl acrylate was employed, the benzyl 3-(2-phenyl-benzoxazol-4-yl)-acrylate (**3ae**) was formed (28% yield) along with **3ad** (60%), that resulted from the hydrolysis of **3ae**. Surprisingly, the reaction of acrylic acid with **1a** gave **3ad** (28%) along with (*E*)-3-(5-benzoyl-4-oxo-2,3,4,5-tetrahydro-

benzo[*b*][1,4]-oxazepin-6-yl)acrylic acid (**5**) (40% yield). Acrylonitrile and acrylamide were also underwent coupling reaction by enabling the corresponding alkenylated benzoxazole **3af** and **3ag** respectively with the concordant formation of 2-phenyl benzoxazole (**4a**) in a reasonable amount (42% and 35% yield respectively) from the acid-catalyzed intramolecular annulation of **1a**. Unfortunately, the initial anilide directed Pd-catalyzed C-H alkenylation by vinyl acetate, methyl cinnamate, methyl methacrylate, styrene, *N*,*N*-dimethyl acrylamide as well as acrylophenone did not occur[19e] under the optimized reaction conditions. Moreover, under forcing reaction conditions, i.e., at a higher temperature (90°C), **4a** was isolated in reasonable yield.

Scheme 5. Coupling of 1a with alkenes (2)



3aa; R^1 = H, R = CO_2Me (90%)
3ab; R^1 = H, R = CO_2n-Bu (72%)
3ac; R^1 = H, R = CO_2Ph (59%)
3ad; R^1 = H, R = CO_2H (28%)[b]
3ae; R^1 = H, R = CO_2Bz (28%)[c]
3af; R^1 = H, R = CN (42%)
3ag; R^1 = H, R = $CONH_2$ (47%)

[a] *Reaction conditions*: **1a** (0.5 mmol), alkene (1.5 mmol), $Pd(OAc)_2$ (10 mol%), Ag_2O (0.5 mmol) in CF_3CO_2H (2 mL) at 60°C, 14h. [b](*E*)-3-(5-benzoyl-4-oxo-2,3,4,5-tetrahydrobenzo[*b*][1,4]oxaze-pin-6-yl) acrylic acid (**5**) was formed in 40% yield along with **3ad**. [c]In addition to **3ae**, **3ad** was also formed in 60% yield.

Conclusion

In conclusion, a strategically simple method for the synthesis of C4-H alkene functionalized benzoxazole from the reaction of 2-amidophenol and electronically deficient olefin was developed. The said transformation proceeds through the initial Pd-catalyzed N-acyl assisted tandem C4-H alkenylation and subsequent acid catalyzed annulation to afford a series of 4-alkenylated 2-arylbenzoxazoles. This protocol was found to be most successful with the acrylates. Other alkenes having –COOH, CN and $CONH_2$ were also underwent coupling reaction under optimized reaction condition. Study on biological activities and photophysical properties of these benzoxazoles are going on in our laboratory.

Experimental Section

General Information

Unless otherwise noted, the reagents (chemicals) were purchased from commercial sources and used without further purification. 2-Amidophenols (**1**) were prepared from the reaction of aroyl chloride and 2-amino phenol by following the procedure reported elsewhere.[23] Reactions were monitored by TLC, and the residue was chromatographed on a silica gel (100 - 200 mesh), using ethyl acetate-petroleum ether (60-80°C) mixture as an eluent. All NMR spectra were recorded on a 400 MHz (for ^{1}H NMR) and 100 MHz (for ^{13}C NMR) NMR spectrometer, and chemical shifts were expressed in δ units relative to the TMS signal as an internal reference in $CDCl_3$. Multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet, when multiplicity is complex) for ^{1}H NMR. Coupling constants, J were reported in Hz. IR spectra were recorded on an FTIR spectrometer (IR Affinity 1S W/L with quest ATR). High-resolution mass spectrometry (ESI-HRMS) (Agilent 6520 Q-TOF) was used to determine the elemental composition.

General Procedure for the synthesis of benzoxazolyl acrylate (3)

A mixture of 2-amidophenol (**1,** 0.5 mmol), $Pd(OAc)_2$ (10 mol%) and silver oxide (0.5 mmol) in trifluoroacetic acid (2 mL) was stirred at room temperature for 1h. Then, alkene (**2**, 1.5 mmol) was added and then heated at 60°C for 14h during which colour of the solution changes from dark brown to black. After completion of the reaction (from TLC) the reaction mixture was triturated with EtOAc (5 mL) and neutralized with 5% aq. $NaHCO_3$ solution. Next, the two layers were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was washed with aq. $NaHCO_3$ (5 mL) solution and dried over anhydrous Na_2SO_4. Then solvent was removed under reduced pressure and the crude reaction mixture was purified by column chromatography using EtOAc: pet. ether (2:98) to enable the desired benzoxazoles.

Synthesis and analytical data

(E)-methyl 3-(2-phenylbenzo[d]oxazol-4-yl)acrylate (3aa): Compound **3aa** was obtained from the reaction of 2-benzamidophenol (**1a**) and methyl acrylate (**2a**) as a white crystalline solid (125 mg, 90% yield); mp 88 - 90ºC; IR: 2924, 2854, 2358, 1710, 1627, 1550, 1431, 1355, 790, 746, 686 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 - 8.31(2H, m), 8.04 (d, 1H, J = 16 Hz), 7.62 - 7.54 (m, 6H), 7.48 (m, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 163.5, 151.1, 141.0, 140.6, 31.7, 128.8, 127.8, 126.8, 126.6, 125.7, 124.8, 121.9, 111.8, 51.7. MS (ESI, +ve) m/z (relative intensity) 302.079 $[M+Na]^+$, 100%

(E)-Methyl 3-(2-(4-chlorophenyl)benzo[d]oxazol-4-yl)acrylate (3ba): Compound **3ba** was obtained from the reaction of 4-chloro-*N*-(2-hydroxyphenyl)benzamide **(1b**) and methyl acrylate as a white crystalline solid (137 mg, 88% yield); mp 120 - 122ºC; IR: 2958, 2924, 2880, 1714, 1635, 1558, 1473, 1431, 1321, 1024, 985, 746 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 - 8.24 (m, 2H), 8.01 (d,

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1H, J = 16 Hz), 7.59 (d, 1H, J = 7.6 Hz), 7.53(d, 2H, J = 8.8 Hz), 7.47 (d, 1H, J = 7.6 Hz), 7.49 - 7.34 (m, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 162.5, 151.0, 140.8, 140.5, 138.0, 129.2, 129.0, 126.7, 125.8, 125.3, 125.1, 122.0, 111.8, 51.7 HRMS (ESI-TOF) m/z calcd for $C_{17}H_{13}ClNO_3$ $[M+H]^+$ 314.0589; Found 314.0584.

(E)-Methyl 3-(2-(2-chlorophenyl)benzo[d]oxazol-4-yl)acrylate (3ca): Compound **3ca** was obtained from the reaction of 2-chloro-*N*-(2-hydroxyphenyl)benzamide **(1c)** and methyl acrylate as a white crystalline solid (42 mg, 25%) along with the intermediate (*E*)-methyl 3-(2-(2-chlorobenzamido)-3-hydroxyphenyl) acrylate (**3ca´**) (112 mg,) as a gummy liquid. [IR: 3600 - 3200 (b), 2940, 2395, 1714, 1646, 1556,1430, 1328, 1260, 1250, 1000, 863 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.63 (s, 1H), 8.03 (d, 1H, J = 16 Hz), 7.90 (d, 1H, J = 7.2 Hz), 7.51 - 7.43 (m, 3H), 7.43 - 7.37 (m, 1H), 7.38 - 7.28 (m, 1H), 7.29 - 7.25 (m, 1H), 7.25 - 7.13 (m, 1H) 6.39 (d, 1H, J = 16 Hz), 3.78 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 166.9, 166.3, 151.3, 139.7, 132.5, 131.2, 130.8, 130.5, 129.9, 128.3, 127.4, 123.8, 121.9, 121.1, 119.3, 51.8, 31.6. MS (ESI, +ve) m/z (relative intensity) 332.06 $[M+H]^+$, 100%].
Treatment of **3ca´** with TFA (2 mL) at 90°C produces **3ca** (60 mg) with an overall yield of 65% from **1c**; mp 115-118 ºC; IR: 2949, 2924, 2850, 1714, 1635, 1558, 1473, 1431, 1321, 1172, 1024, 985, 746 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 8.28 - 8.24 (m, 1H), 8.03 (d, 1H, J = 16 Hz), 7.67 – 7.59 (m, 2H), 7.53 – 7.39 (m, 5H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 161.5, 150.9, 140.3, 140.2, 133.5, 132.0, 131.9, 131.4, 126.9, 126.8, 125. 9, 125.7, 125.3, 122.1, 111.9, 51.6. HRMS (ESI-TOF) m/z calcd for $C_{17}H_{13}ClNO_3$ $[M+H]^+$ 314.0581; Found 314.0584.

(E)-Methyl 3-(2-(3,4-dichlorophenyl)benzo[d]oxazol-4-yl)acrylate (3da): Compound **3da** was obtained from the reaction of 2,4-dichloro-*N*-(2-hydroxyphenyl)benzamide **(1d)** and methyl acrylate as a white crystalline solid (134 mg, 77%); mp 135 - 138ºC; IR: 2962, 1716, 1635, 1558, 1257, 1012, 869, 788 cm^{-1}. ^{1}H NMR (400 MHz $CDCl_3$): δ 8.24 (d, 1H, J = 8.4 Hz), 8.01 (d, 1H, J = 16 Hz), 7.66 - 7.62 (m, 2H), 7.50 (d, 1H, J = 7.2 Hz), 7.47 – 7.40 (m, 3H), 3.87 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 167.7, 160.6, 150.8, 140.2, 140.1 137.7, 134.3, 132.6, 131.3, 127.3, 127.0, 126.0, 125.5, 124.2, 122.2, 111.9, 51.6. HRMS (ESI-TOF) m/z calcd for $C_{17}H_{12}Cl_2NO_3$ $[M+H]^+$ 348.0188; Found 348.0194.

(E)-Methyl 3-(2-(3,4-dichlorophenyl)benzo[d]oxazol-4-yl)acrylate (3ea): Compound **3ea** was obtained from the reaction of 3,4-dichloro-*N*-(2-hydroxy-phenyl)-benzamide **(1e)** and methyl acrylate as a white crystalline solid (90 mg, 52% yield); mp 148-150ºC; IR: 2926, 2848, 1701, 1558, 1458, 1288, 1265, 1028, 748 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.4 (d, 1H, J = 2 Hz), 8.19-8.14 (m, 1H), 8.01 (d, 1H, J = 16 Hz), 7.66 – 7.59 (m, 2H), 7.49 (d, 1H, J = 7.2 Hz), 7.43 – 7.36 (m, 2H), 3.89 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 167.6, 161.2, 151.0, 140.6, 140.2, 136.1, 133.4, 131.0, 129.3, 126.8, 126.7, 126.6, 125.9, 125.4, 122.1, 111.8, 51.7. HRMS (ESI-TOF) m/z calcd for $C_{17}H_{12}Cl_2NO_3$ $[M+H]^+$ 348.0191; Found 348.0194.

(E)-Methyl 3-(2-p-tolylbenzo[d]oxazol-4-yl)acrylate (3fa): The desired compound was obtained from the reaction of *N*-(2-hydroxy-phenyl)-4-methyl benzamide **(1f)** and methyl acrylate as a white crystalline solid (120 mg, 82% yield); mp 104 – 106 ºC; IR 2956, 2920, 1699, 1626, 1498, 1426, 1316, 1234, 1180, 979, 760 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, 2H, J = 8 Hz), 8.04 (d, 1H, J = 16 Hz), 7.58 (dd, 1H, J_1 = 8.4 Hz, J_2 = 0.4 Hz), 7.45 (d, 1H, J = 6.4 Hz), 7.43 (d, 1H, J = 15.6 Hz), 7.38 - 7.32 (m, 3H), 3.88 (s, 3H), 2.47(s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 167.9, 163.9, 151.0, 142.4, 141.2, 140.7, 129.6, 127.8, 126.4, 125.7, 124.6, 124.1, 121.8, 111.8, 51.7, 21.7. HRMS (ESI-TOF) m/z calcd for $C_{18}H_{16}NO_3$ $[M+H]^+$ 294.1126; Found 294.1130.

(E)-methyl 3-(2-o-tolylbenzo[d]oxazol-4-yl)acrylate (3ga): The desired compound was obtained from the reaction of *N*-(2-hydroxy-phenyl)-2-methyl- benzamide **(1g)** and methyl acrylate as a white crystalline solid (88 mg, 60% yield) mp 115-118ºC; IR: 2963, 2927, 2827, 1724, 1634, 1532, 1419, 1317, 1169, 987, 761 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (d, 2H, J = 8 Hz), 8.04 (d, 1H, J = 16 Hz), 7.59 (d, 1H, J = 8 Hz), 7.47 - 7.40 (m, 2H), 7.38 – 7.32 (m, 3 H), 3.88 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 163.7, 150.4, 140.8, 140.6, 139.2, 131.8, 131.0, 129.8, 126.5, 126.0, 125.7, 125.6, 124.7, 121.9, 111.6, 51.0, 22.4. HRMS (ESI-TOF) m/z calcd for $C_{18}H_{16}NO_3$ $[M+H]^+$ 294.1124; Found 294.1130.

(E)-methyl 3-(2-(4-nitrophenyl)benzo[d]oxazol-4-yl)acrylate (3ha): The desired compound was obtained was obtained from the reaction of N-(2-hydroxy-phenyl)-4 nitro-benzamide **(1h)** and methyl acrylate as a white crystalline solid (91 mg, 56% yield); mp 158 – 160 ºC, IR: 2958, 2953, 1718, 1521, 1340, 1259, 1012, 852, 790 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, 2H, J = 8.8 Hz), 8.42 (d, 2H, J = 8.8 Hz), 8.03 (d, 1H, J = 16.4 Hz), 7.65(d, 1H, J = 8 Hz), 7.52 (d, 1H, J = 7.2 Hz), 7.48 – 7.39 (m, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 161.1, 151.3, 149.4, 140.6, 140.1, 132.3, 128.6, 127.3, 126.2, 126.1, 124.1, 122.4, 112.1, 51.8. HRMS (ESI-TOF) m/z calcd for $C_{17}H_{13}N_2O_5$ $[M+H]^+$ 325.0824; Found 325.0822.

(E)-methyl 3-(2-(3-nitrophenyl)benzo[d]oxazol-4-yl)acrylate (3ia): Compound **3ia** was obtained from the reaction of *N*-(2-hydroxy-phenyl)-3-nitrobenzamide **(1i)** and methyl acrylate as a white crystalline solid (76 mg, 47% yield); mp 150 – 153 ºC; IR: 2958, 2924, 1714, 1520, 1340, 1257, 1012, 852, 790 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.15 - 9.13 (m, 1H), 8.69 (d, 1H, J = 6 Hz), 8.46 - 8.41 (m, 1H), 8.04 (d, 1H J = 16 Hz), 7.81 - 7.66 (t, 1H, J = 8 Hz), 7.66 (d, 1H, J = 8 Hz), 7.52 (d, 1H, J = 7.6 Hz), 7.48 - 7.37 (m, 2H), 3.90 (s, 3H). ^{13}C NMR (100MHz, $CDCl_3$): δ 167.6, 161.0, 151.2, 148.6, 140.5, 140.1, 133.3, 130.1, 128.6, 127.2, 126.1, 126.0, 125.9, 122.5, 122.3, 112.0, 51.8. HRMS (ESI-TOF) m/z calcd for $C_{17}H_{13}N_2O_5$ $[M+H]^+$ 325.0824; Found 325.0819.

(E)-Methyl 3-(2-(4-methoxyphenyl)benzo[d]oxazol-4-yl)acrylate (3ja): Compound **3ja** was obtained from the reaction of *N*-(2-hydroxy-phenyl)-4-methoxy benzamide **(1j)** and methyl acrylate as a white crystalline solid (121

mg, 79% yield); mp 128 - 130ºC; IR: 2924, 2848, 1701, 1608, 1498, 1423, 1290, 1172, 1020, 839, 744 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.30 - 8.26 (m, 2H), 8.03 (d, 1H, J = 16.4 Hz), 7.57 (d, 1H, J = 8 Hz), 7.45 – 7.31 (m, 3H), 7.06 (d, 2H, J = 8.8 Hz), 3.93 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (100MHz, $CDCl_3$): δ 167.8, 163.6, 162.4, 150.9, 141.2, 140.7, 129.6, 126.1, 125.4, 124.2, 121.6, 119.3, 114.2, 111.5, 55.3, 51.5. HRMS (ESI-TOF) m/z calcd for $C_{18}H_{16}NO_4$ $[M+H]^+$ 310.1074; Found 310.1079.

(E)-Methyl 3-(2-(3-methoxyphenyl)benzo[d]oxazol-4-yl)acrylate (3ka): **3ka** was obtained from the reaction of *N* -(2-hydroxy-phenyl)-3-methoxy benzamide **(1k)** and methyl acrylate as a white crystalline solid (88 mg, 57% yield); mp 118 - 120ºC; IR: 2922, 2854, 1699, 1558, 1458, 1267, 1028, 983, 748 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): 8.06 (d, 1H, J = 16 Hz), 7.92 (d, 1H, 7.6 Hz), 7.84 (s, 1H), 7.60 (d, 1H, J = 8 Hz), 7.49 -7.43 (m, 2H), 7.41 - 7.33 (m, 2H), 7.14- 7.10(m, 1H), 3.96 (s, 3H), 3.88(s, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 167.7, 163.3, 159.8, 151.0, 140.9, 140.4, 129.9, 127.9, 126.6, 125.4, 124.8, 121.7, 120.2, 118.1, 112.2, 111.7, 55.4, 51.6. HRMS (ESI-TOF) m/z calcd for $C_{18}H_{16}NO_4$ $[M+H]^+$ 310.1077; Found 310.1079.

(E)-Methyl 3-(2-(2-methoxyphenyl)benzo[d]oxazol-4-yl)acrylate (3la): Following the general procedure, compound **3la** was obtained from the reaction of 2-benzamidophenol **(1l)** and methyl acrylate (**2a**) as a white crystalline solid (62 mg, 47% yield); mp 112 - 115°C. IR : 2902, 2857, 1708, 1626, 1616, 1544, 1435, 1297, 1234, 1170, 1006, 760 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.24 (dd, 1H, J_1 = 8 Hz, J_2 = 2 Hz), 8.08 (d, 2H, J = 16 Hz), 7.65 – 7.61 (m, 1H), 7.58-7.52 (m, 1H), 7.47 (d, 1H, J = 7.2 Hz), 7.42 -7.33 (m, 2H), 7.17-7.09 (m, 2H), 4.05 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9, 162.7, 158.6, 150.9, 140.9, 140.7, 133.1, 131.7, 126.5, 125.3, 124.7, 121.7, 120.8, 115.9, 112.2, 111.9, 56.1, 51.7. HRMS (ESI-TOF) m/z calcd for $C_{18}H_{16}NO_4$ $[M+H]^+$ 310.1074; Found 310.1078.

(E)-methyl 3-(2-(thiophen-2-yl)benzo[d]oxazol-4-yl)acrylate (3ma): **3ma** was obtained from the reaction of thiophene 2-carboxylic acid (2-hydroxyl-phenyl)amide **(1m)** and methyl acrylate as a white crystalline solid (65 mg, 46% yield), mp 100 - 102ºC; IR: 2924, 1703, 1637, 1564, 1419, 1240, 790, 744 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 - 7.96 (m, 2H), 7.62 - 7.59 (m, 1H), 7.55 (d, 1H, J = 8 Hz), 7.45 (d, 1H, J = 7.6 Hz), 7.37- 7.30 (m, 2H), 7.24 - 7.20 (m, 1H). 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 159.4, 150.6, 140.9, 140.3, 130.7, 130.4, 129.2, 128.2, 126.3, 125.5, 124.7, 121.7, 111.5, 51.6. HRMS (ESI-TOF) m/z calcd for $C_{15}H_{12}NO_3S$ $[M+H]^+$ 286.0538; Found 286.0539.

(E)-methyl 3-(2-methylbenzo[d]oxazol-4-yl)acrylate (3na): Following the general procedure, **3na** was obtained from the reaction of *N* -(2-hydroxy-phenyl)acetamide (**1n**) and methyl acrylate as a white crystalline solid (38 mg, 35% yield); mp 90 - 92ºC; IR 2953, 2924, 2852, 1712, 1425, 1319, 989, 923, 869, 748 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, 1H, J = 16 Hz), 7.49 (d, 1H, J = 8 Hz), 7.42 (d, 1H, J = 7.6 Hz), 7.33 - 7.22 (m, 2H), 3.84 (s, 3H), 2.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 164.4, 151.7, 140.3, 140.2, 126.1, 124.9, 124.2, 121.7, 111.4, 51.5, 14.5. HRMS (ESI-TOF) m/z calcd for $C_{12}H_{12}NO_3$ $[M+H]^+$ 218.0812; Found 218.0817.

(E)-Methyl 3-(6-chloro-2-phenylbenzo[d]oxazol-4-yl)acrylate (3oa): Following the general procedure, **3oa** was obtained from the reaction of *N* -(4-chloro-2-hydroxy-phenyl)benzamide **(1o)** and methyl acrylate as a white crystalline solid (49 mg, 31% yield), mp 138 - 140ºC; IR 3100, 2951, 2861, 1726, 1624, 1566, 1442, 1158, 987, 840, 653 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.31 - 8.27 (m, 2H), 7.93 (d, 1H, J = 8 Hz), 7.56 - 7.55 (m, 4H), 7.45 - 7.42 (m, 1H), 7.38 (d, 1H, J = 8 Hz), 3.88 (s,1H); ^{13}C NMR (100MHz, $CDCl_3$): δ 167.2, 164.0, 151.1, 139.0, 131.9, 130.4, 128.8, 127.8, 127.1, 126.3, 125.5, 123.2, 111.9, 51.7. HRMS (ESI-TOF) m/z calcd for $C_{17}H_{13}ClNO_3$ $[M+H]^+$ 314.0581; Found 314.0584.

(E)-Methyl 3-(6-bromo-2-phenylbenzo[d]oxazol-4-yl)acrylate (3pa): Following the general procedure, **3pa** was obtained from the reaction of *N* -(4-Bromo-2-hydroxy-phenyl)benzamide **(1p)** and methyl acrylate as a white crystalline solid (65 mg, 37% yield); mp 148 – 150 ºC; IR 3100, 2930, 2838, 1703, 1624, 1556, 1453, 1160, 932, 718 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.32 - 8.27 (m, 2H), 7.92 (d, 1H, J = 8 Hz), 7.74 (d, 1H, 1.6 Hz), 7.61 - 7.52 (m, 4H), 7.38 (d, 1H, J = 8 Hz), 3.88 (s, 1H); ^{13}C NMR (100MHz, $CDCl_3$): δ 167.4, 164.0, 151.5, 140.2, 139.1, 132.1, 129.0, 128.4, 127.9, 127.7, 126.4, 123.3, 117.7, 114.9, 51.8. HRMS (ESI-TOF) m/z calcd for $C_{17}H_{13}BrNO_3$ $[M+H]^+$ 358.0082; Found 358.0079.

(E)-methyl 3-(6-methyl-2-phenylbenzo[d]oxazol-4-yl)acrylate (3qa): Following the general procedure, **3qa** was obtained from the reaction of N-(2-hydroxy 4-methylphenyl)benzamide **(1q)** and methyl acrylate as a white crystalline solid (91 mg, 62% yield); mp 135 - 138 ºC; IR, 2930, 2372, 1703, 1634, 1544, 1419, 1342, 1181, 1012, 829, 738 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.33 - 8.28 (m, 2H), 7.98 (d, 1H, J = 16 Hz), 7.57 - 7.52 (m, 3H), 7.44 - 7.38(m, 2H), 7. 27 (s, 1H), 3.88 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7 163.0, 151.3, 140.6, 138.8, 135.2, 131.4, 128.7, 127.6, 126.9, 126.8, 125.9, 121.7, 112.0, 51.5, 21.5. HRMS (ESI-TOF) m/z calcd for $C_{18}H_{16}NO_3$ $[M+H]^+$ 294.1125; Found 294.1130.

(E)-methyl 3-(7-methyl-2-phenylbenzo[d]oxazol-4-yl)-acrylate (3ra): Following the general procedure, **3ra** was obtained from the reaction of N-(2-hydroxy-3-methylphenyl)benzamide **(1r)** and methyl acrylate as a white crystalline solid (80 mg, 55% yield); mp 92 - 94°C; IR: 2372, 2304, 1720, 1634, 1531, 1514, 1445, 1326, 759 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.37 - 8.32 (m, 2H), 8.0 (d, 1H, J = 16 Hz), 7.59 - 7.53 (m, 3H), 7.38 (d, 1H, J = 16 Hz), 7.37 - 7.34 (m, 1H), 7.17 - 7.13 (m, 1H), 3.88 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.0, 163.3, 150.2, 140.9, 140.5, 131.6, 128.8, 127.8, 127.0, 126.0, 125.9, 124.2, 123.1, 120.7, 51.6, 15.4. HRMS (ESI-TOF) m/z calcd for $C_{18}H_{16}NO_3$ $[M+H]^+$ 294.1125; Found 294.1129.

(E)-methyl 3-(7-chloro-2-phenylbenzo[d]oxazol-4-yl)acrylate (3sa):
Following the general procedure, **3sa** was obtained from the reaction of N-(3-chloro-2-hydroxyphenyl)benzamide **(1s)** and methyl acrylate as a white crystalline solid (89 mg, 57% yield); mp 150-152ºC; IR: 2939, 1703, 1531, 1308, 1205, 1188, 1068, 707 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.35 (dd, 2H, J_1 = 8 Hz, J_2 = 1.2 Hz), 7.59 (d, 1H, J = 16 Hz), 7.61-7.54 (m, 3H), 7.82 (d, 1H, J = 16 Hz), 7.37-7.32 (m, 2H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 163.9, 147.6, 141.9, 139.7, 132.2, 129.0, 128.1, 126.4, 126.2, 125.3, 125.3, 122.1, 117.3, 51.8. HRMS (ESI-TOF) m/z calcd for $C_{17}H_{13}ClNO_3$ $[M+H]^+$ 314.0578; Found 314.0583.

(E)-methyl 4-(3-methoxy-3-oxoprop-1-enyl)-2-phenylbenzo[d]oxazole-6-carboxylate (3ta): The desired compound **3ta** was obtained from the reaction of methyl 4-benzamido-3-hydroxybenzoate **(1t)** and methyl acrylate as a white crystalline solid (67 mg, 40% yield); mp 167-170ºC; IR: 3059, 2955, 1857, 1737, 1703, 1634, 1549, 1428, 1326, 1290, 1153, 1051, 759, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.35 (dd, 2H, J_1 = 8 Hz, J_2 = 1.2 Hz), 8.04 (d, 1H, 16 Hz), 8.23 (dd, 1H, J_1 = 24 Hz, J_2 = 0.8 Hz), 7.63-7.54 (m, 3H), 7.44 (d, 1H, J = 16 Hz), 4.00 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 166.2, 166.0, 150.8, 144.6, 139.7, 132.5, 129.0, 128.2, 127.2, 127.0, 126.3, 126.2, 122.9, 113.0, 52.6, 51.8. HRMS (ESI-TOF) m/z calcd for $C_{19}H_{16}NO_5$ $[M+H]^+$ 338.1023; Found 338.1029.

(E)-methyl 3-(5-fluoro-2-phenylbenzo[d]oxazol-4-yl)acrylate (3ua): The desired compound **3ua** was obtained from the reaction of N-(5-fluoro-2-hydroxyphenyl)benzamide **(1u)** and methyl acrylate as a white crystalline solid (65 mg, 44% yield); mp: 97 - 99°C; 2921, 2853, 1720, 1686, 1634, 1549, 1463, 1428, 1290, 1205, 1171, 1051, 914, 793, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.32 (dd, 2H, J_1 = 8 Hz, J_2 = 1.6 Hz), 8.14 (d, 1H, J = 16 Hz), 7.62 (d, 1H, J = 16 Hz), 7.59-7.51 (m, 4H), 7.12 (dd, 1H, J_1 = 10.8 Hz, J_2 = 8.8 Hz), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, F-coupled): δ 167.7, 165.1, 159.9, 157.4, 147.1, 141.7, 133.2, 133.1, 132.0, 129.0, 127.9, 126.6, 124.1, 124.0, 114.5, 114.4, 112.7, 112.5, 112.0, 111.9, 51.8. HRMS (ESI-TOF) m/z calcd for $C_{17}H_{13}FNO_3$ $[M+H]^+$ 298.0874; Found 298.0879.

(E)-Butyl 3-(2-phenylbenzo[d]oxazol-4-yl)acrylate (3ab): Following the general procedure, **3ab** was obtained from the reaction of 2-benzamidophenol **(1a)** and *n*-butyl acrylate (**2b**) as a white crystalline solid (112 mg, 70 % yield); mp 58 - 60ºC; IR: 2958, 2934, 2926, 2922, 1703, 1629, 1541, 1473, 1417, 985, 790 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.36 – 8.32 (m, 2H), 8.02 (d, 1H, J = 16 Hz), 7.62 - 7.54 (m, 4H), 7.48 - 7.33 (m, 3H), 429 (t, 2H, J = 6.8 Hz), 1.76 (m, 2H), 1.51 (m, 2H), 1.01 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 163.5, 151.0, 140.9, 140.3, 131.7, 128.8, 127.8, 126.8, 126.7, 125.7, 124.8, 122.4, 111.7, 64.4, 30.8, 19.2, 13.7. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{20}NO_3$ $[M+H]^+$ 322.1443; Found 322.1445.

(E)-phenyl 3-(2-phenylbenzo[d]oxazol-4-yl)acrylate (3ac): Following the general procedure, compound **3ac** was obtained from the reaction of 2-benzamidophenol **(1a)** and phenyl acrylate (**2c**) as a white crystalline solid (99 mg, 59% yield); mp 108 – 110 °C; IR 1717, 1626, 1553, 1489, 1416, 1134, 751, 696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.39 – 8.34 (m, 2H), 8.20 (d, 1H, J = 16 Hz), 7.69 – 7.63 (m, 2H), 7.60 – 7.55 (m, 3H), 7.52 (d, 1H, J = 7.6 Hz), 7.49 – 7.40 (m, 3H), 7.32 – 7.23 (m, 3H); ^{13}C NMR (100MHz, $CDCl_3$): δ 165.9, 163.8, 151.2, 150.9, 142.4, 141.2, 131.9, 129.4, 129.0, 127.9, 126.8, 126.4, 126.2, 125.7, 125.0, 121.7, 121.5, 112.3. HRMS (ESI-TOF) m/z calcd for $C_{22}H_{16}NO_3$ $[M+H]^+$ 342.1125; Found 342.1130.

(E)-3-(2-Phenylbenzo[d]oxazol-4-yl)acrylic acid (3ad): The desired compound **3ad** was obtained from the reaction of 2-benzamidophenol **(1a)** and acylic acid (**2d**) as a white crystalline solid (37 mg, 28% yield) mp 198 - 200ºC (decomposition); IR: 2924, 1703, 1637, 1564, 1419, 1240, 790, 744 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.38 - 8.33(m, 1H), 8.18 - 8.10 (m, 1H), 7.65 - 7.48 (m, 4H), 7.47 – 6.95 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 163.6, 151.0, 142.5, 141.1, 131.7, 128.8, 127.8, 126.7, 126.2, 125.9, 124.8, 121.2, 112.1. HRMS (ESI-TOF) m/z calcd for $C_{16}H_{12}NO_3$ $[M+H]^+$ 266.0817; Found 266.0814.

(E)-Benzyl 3-(2-phenylbenzo[d]oxazol-4-yl)acrylate (3ae): **3ae** was obtained from the reaction of 2-benzamidophenol **(1a)** and benzyl acrylate (**2e**) as a white crystalline solid (50 mg, 28% yield, mp 92 - 94°C) along with **3da** (60%); IR 2975, 1708, 1635, 1544, 1462, 1407, 1325, 1207, 1142, 1006, 733, 678 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.34 – 8.31 (m, 2H), 8.07 (d, 1H, J = 16 Hz), 7.63 – 7.53 (m, 6H), 7.54 – 7.33 (m, 6H), 5.34 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 163.6, 151.1, 141.0, 136.2, 131.8, 128.9, 128.6, 128.4, 128.3, 128.2, 127.9, 126.8, 126.6, 125.9, 124.9, 122.0, 111.9, 66.4. HRMS (ESI-TOF) m/z calcd for $C_{23}H_{18}NO_3$ $[M+H]^+$ 356.1287; Found 356.1282.

(E)-3-(2-Phenylbenzo[d]oxazol-4-yl)acrylonitrile (3af): The desired compound **3af** was obtained from the reaction of 2-benzamidophenol **(1a)** and acrylonitrile (**2f**) as a white crystalline solid (52 mg, 42% yield); mp 148 - 150ºC; IR: 2958, 2954, 2848, 2208, 1541, 1419, 1240, 1060, 744, 702 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.34 – 8.29 (m 2H), 7.67 – 7.57, (m, 5H), 7.40- 7.36 (m, 2H), 7.22 (d, 1H, J = 16 Hz); ^{13}C NMR (100MHz, $CDCl_3$): δ 164.2, 151.1, 146.6, 140.6, 132.0, 129.0, 127.8, 126.5, 125.9, 125.5, 124.9, 118.6, 112.6, 101.2. HRMS (ESI-TOF) m/z calcd for $C_{16}H_{11}N_2O$ $[M+H]^+$ 247.0871; Found 247.0868.

(E)-3-(2-phenylbenzo[d]oxazol-4-yl)acrylamide (3ag): Following the general procedure, compound **3ag** was obtained from the reaction of 2-benzamidophenol **(1a)** and acryl amide (**2g**) as a white crystalline solid (62 mg, 47% yield); mp 190 – 192 °C (decomposition); IR 3348, 3139, 1663, 1599, 1489, 1398, 1271, 1225, 1035, 970, 715 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.35 - 8.31 (m, 2H), 7.93 (d, 1H, J = 16 Hz), 7.62 - 7.52 (m, 5H), 7.45 (d, 1H, J = 7.2

Hz), 7.38 (d, 1H, J = 8 Hz), 5.8 – 5.5 (b, 2H); ^{13}C NMR (100MHz, $CDCl_3$): δ 168.2, 163.5, 151.1, 140.7, 138.5, 131.8, 128.9, 127.8, 126.9, 126.8, 126.4, 125.0, 123.9, 111.6. HRMS (ESI-TOF) m/z calcd for $C_{16}H_{13}N_2O_2$ $[M+H]^+$ 265.0977; Found 265.0972.

(E)-3-(5-benzoyl-4-oxo-2,3,4,5-tetrahydro-benzo[b][1,4]-oxazepin-6-yl)acrylic acid (5)

From the reaction of **1a** and **2d**, **5** was formed as a white crystaline in 40% (68 mg) yield; mp 118 – 120 ºC; IR 2930, 2975, 2857, 1689, 1635, 1562, 1407, 1325, 1207, 1142, 988, 742, 705 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 - 8.29 (m, 2H), 8.02 (d, 1H, J = 16 Hz), 7.60 - 753(m, 4H), 7.44 (d, 1H, J = 7.6 Hz), 7.39 (s, 1H), 7.37 - 7.31 (m, 1H), 4.56 (t, 3H, J = 6 Hz), 2.87 (t, 3H, J = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.7, 167.0, 163.5, 151.0, 141.0, 140.9, 131.7, 128.8, 127.7, 126.7, 126.4, 125.7, 124.7, 121.5, 111.8, 59.4, 33.5. HRMS (ESI-TOF) m/z calcd for $C_{19}H_{16}NO_5$ $[M+H]^+$ 338.1028; Found 338.1025.

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Synthesis of 4-alkenyl benzoxazoles via Pd-catalyzed *ortho* C-H functionalization of 2-amidophenols

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