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Article

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Palladium-Catalyzed/Norbornene-Mediated *ortho*-amination/*N*-Tosylhydrazone Insertion Reaction: An Approach to the Synthesis of *ortho*-amination Vinylarenes

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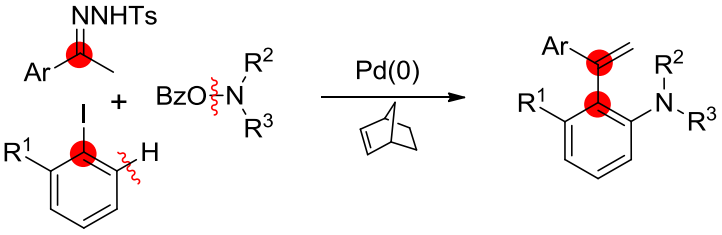


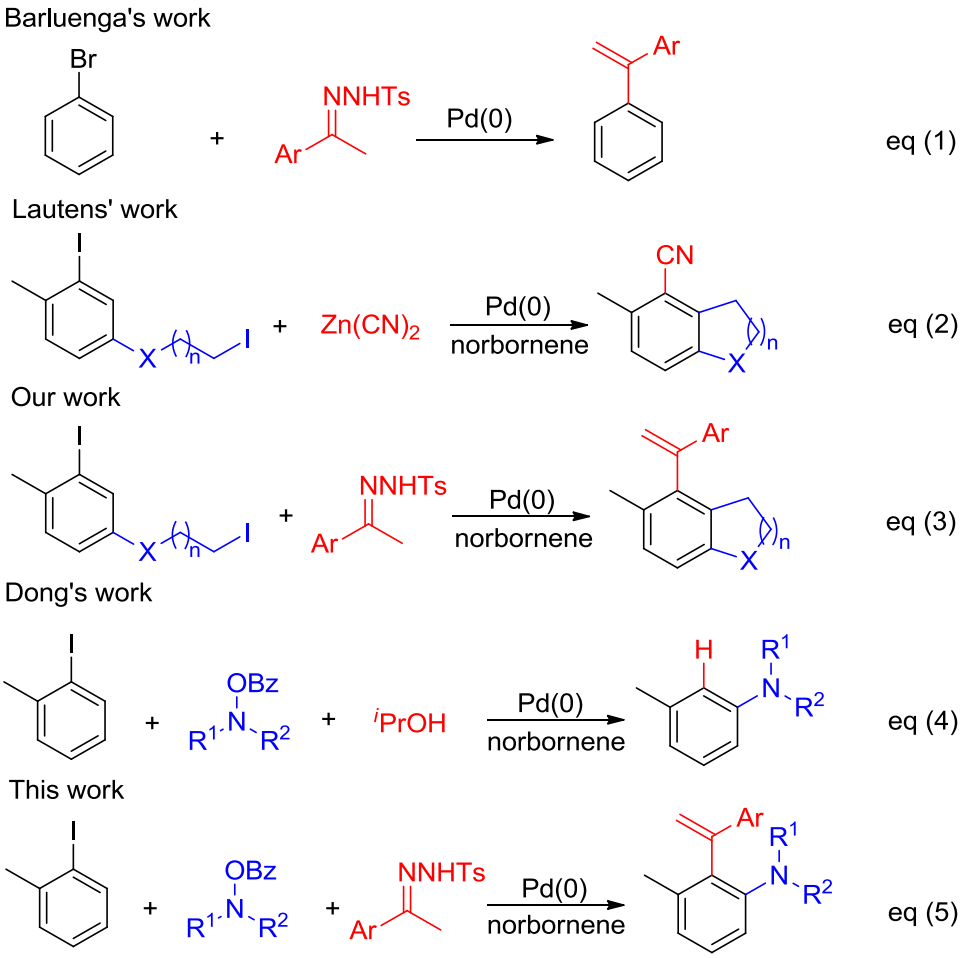
ABSTRACT: *Ortho*-amination vinylarene derivatives are obtained via a reaction of aryl iodides, *N*-benzoyloxyamines and *N*-tosylhydrazones. This approach involves a palladium-catalyzed, norbornene-mediated ortho-amination/*N*-tosylhydrazone insertion reaction. In this transformation, one C-N bond and one C-C bond are formed and an amine group is introduced at the *ortho*-position successfully.

INTRODUCTION

Palladium catalyzed cross-coupling reactions, which represent one of the most reliable and powerful tools for the organic synthesis and natural product total synthesis, have attracted the interest of several groups.[1] More recently, considerable attention has been focused on the utility of *N*-tosylhydrazones as the new cross-coupling partners in palladium catalyzed transformations, which was initially reported by Barluenga in 2007 (eq 1)[2] and further developed by Wang, Van Vranken, our group and others.[3] Despite the variety of possibilities offered by this transformation, it still needs to develop new chemical transformations based on this unique coupling to further increase its effectiveness and usefulness.

Combining multistep process into a one-step protocol is an important goal of transition-metal-catalyzed reactions. A remarkable type of this reaction was firstly reported by Catellani and further modified by Lautens. This strategy provided a way to synthesize highly substituted aromatic compounds and fused aromatic rings from easily accessible starting materials in an efficient, atom economic way by the palladium-catalyzed norbornene mediated ortho C-H functionalization, followed by terminal cross-coupling processes. The scope of this reaction has been broadened considerably since its discovery.[4] For example, Lautens reported a palladium-catalyzed intramolecular alkylation/intermolecular cyanation reaction to afford polycyclic benzonitriles (eq 2).[5] We successfully modified this sequence by using *N*-tosylhydrazones as a terminal reagent to give polycyclic vinylarenes via intramolecular alkylation/*N*-tosylhydrazones insertion reaction (eq 3).[6]

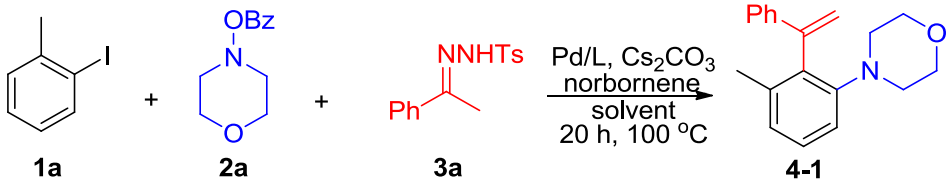
Recently, Dong and co-worker developed the first example of forming C-N bonds at the *ortho* position of aryl iodides via Catellani-Lautens type C-H activation (eq 4).[7] Inspired by Dong's work and in connection with our interest in using *N*-tosylhydrazones as a new coupling partner in Catellani-Lautens reaction[6, 8] and our interest in palladium-catalyzed insertion of *N*-tosylhydrazones [3m, 3n, 3o, 9], we wish to report a palladium-catalyzed, norbornene-mediated ortho-amination/*N*-tosylhydrazone insertion reaction to obtain the *ortho*-amination vinylarenes (eq 5).



RESULTS AND DISCUSSION

Initially, we employed the 1-iodo-2-methylbenzene **1a**, *N*-benzoyloxyamine **2a** and *N*-tosylhydrazone **3a** as the substrates. To our delight, the product **4-1** was afforded in 17% yield when the reaction were catalyzed by $Pd(OAc)_2$ (10 mol%)/TFP (20 mol%)/norbornene (1.0 equiv) in the presence of Cs_2CO_3 in CH_3CN (Table 1, entry 1). A further investigation of the solvent revealed that the reaction proceeded more efficiently in nonpolar solvents than in polar solvents (Table 1, entries 2-6).

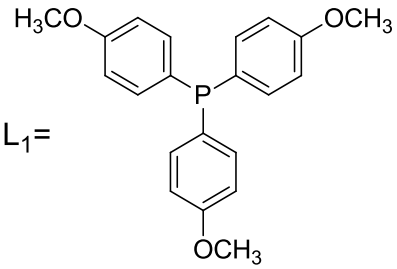
Table 1. Optimization of reaction conditions[a]

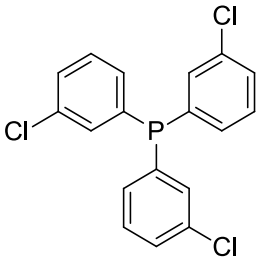


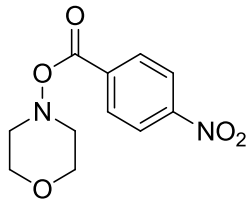
1a **2a** **3a** **4-1**

Entry	Catalyst	ligand	Solvent	Yield
1	$Pd(OAc)_2$	TFP	CH_3CN	17
2	$Pd(OAc)_2$	TFP	dioxan	23
3	$Pd(OAc)_2$	TFP	DME	18
4	$Pd(OAc)_2$	TFP	DMF	<10%
5	$Pd(OAc)_2$	TFP	DCE	trace
6	$Pd(OAc)_2$	TFP	toluene	47
7	$Pd(OAc)_2$	Xphos	toluene	trace
8	$Pd(OAc)_2$	dppe	toluene	16
9	$Pd(OAc)_2$	dppb	toluene	35
10	$Pd(OAc)_2$	PPh_3	toluene	62
11	$Pd(OAc)_2$	L_1	toluene	50
12	$Pd(OAc)_2$	L_2	toluene	49

13	$PdCl_2$	PPh_3	toluene	53
14	$Pd(CH_3CN)_2Cl_2$	PPh_3	toluene	61
15	$Pd(PPh_3)_4$	PPh_3	toluene	38
16	$Pd_2(dba)_3{\cdot}CHCl_3$	PPh_3	toluene	37
17	$Pd_2(dba)_3$	PPh_3	toluene	32
18	$Pd(OAc)_2$	PPh_3	toluene	50[b]
19	none	PPh_3	toluene	0
20	$Pd(OAc)_2$	PPh_3	toluene	0[c]

L_1= 

L_2= 



2a'

[a].**1a** (0.3 mmol, 1.0 equiv), **2a** (0.33 mmol, 1.1 equiv), **3a** (0.75 mmol, 2.5 equiv), Pd (10 mol %), ligand (20 mol %), norbornene (0.3 mmol, 1.0 equiv), Cs_2CO_3 (1.5 mmol, 5.0 equiv), solvent (4.5 mL), 100 °C, 20 h. [b]. 5 mol % of $Pd(OAc)_2$ and 10 mol% PPh_3 were employed. [c].The reaction was carried out in the absence of norbornene.

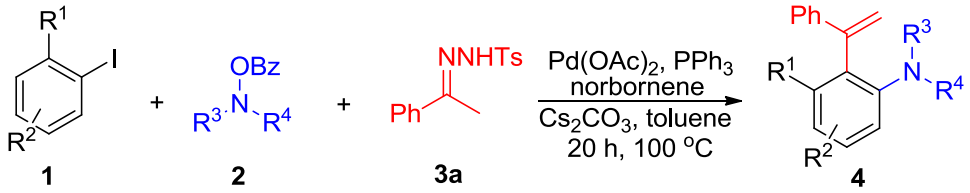
The yield was slightly improved when the solvent was replaced by dioxane (Table 1, entry 2). However, DCE and DMF were found to be less effective for this reaction (Table 1, entries 4-5). Using nonpolar toluene gave a better yield (Table 1, entry 6). According to previous reports, it may be due to that the more polar solvents increased the decomposition of *N*-benzoyloxyamine **2a**.[7, 10] A series of mono- and bidentate phosphine ligands were envisioned. Only a trace amount of

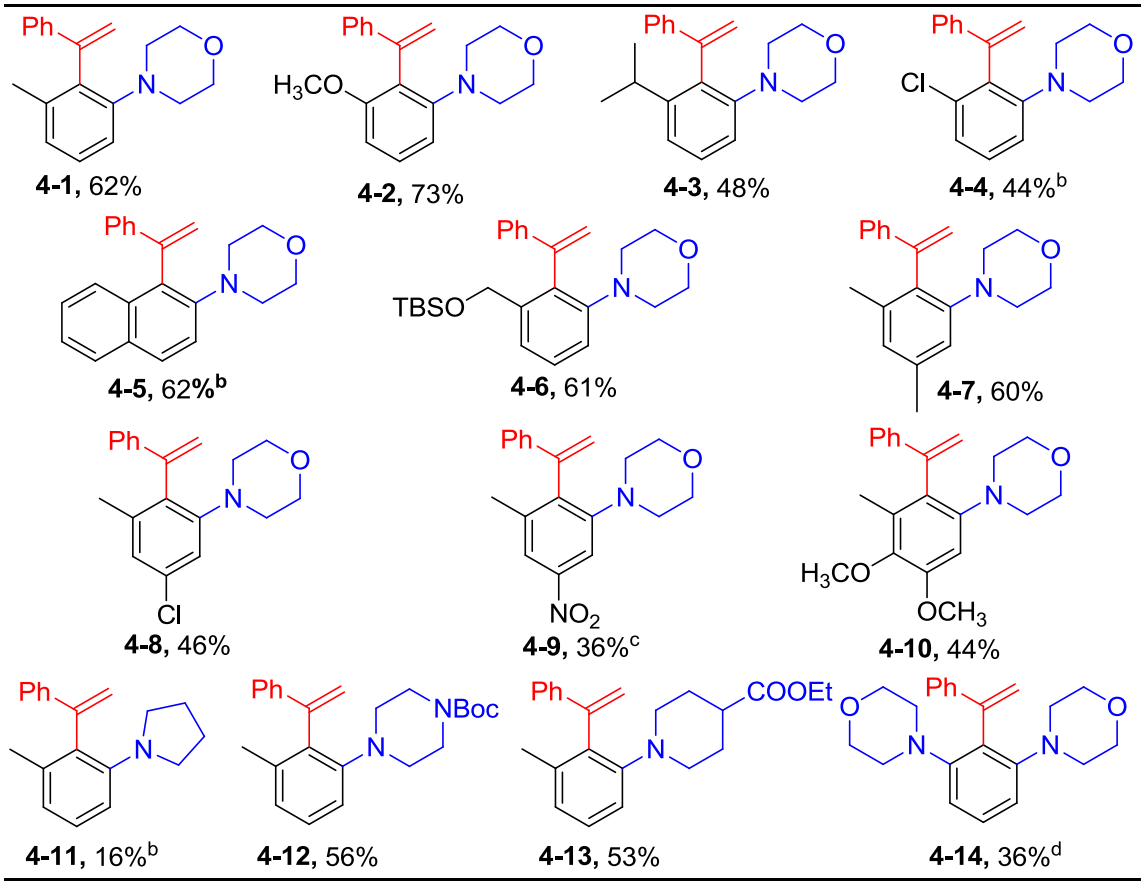
product was detected when Xphos was used and a lower yield was obtained with dppe (Table 1, entries 7-8). Switching the ligand to dppb could not further improve the yield (Table 1, entry 9). PPh_3 gave a better result compared with L_1 and L_2 (Table 1, entries 10-12). Different palladium catalysts, including Pd(II) and Pd(0) were surveyed, and it was found that $Pd(OAc)_2$ could catalyzed this reaction more effectively (Table 1, entries 13-17). Lowering the catalyst loading to 5 mol % diminished the product yield (Table 1, entry 18). Further inspection of the reaction conditions indicated that norbornene was essential for this reaction (Table 1, entry 20). Decreasing the amount of norbornene relative to **1a** led to a decreased yield (data not shown in Table 1). In previous studies, Wang has indicated that using triethylamine as co-base was beneficial for the palladium-catalyzed insertion of *N*-tosylhydrazone.[3p, 11] Addition of 2.0 equivalents of NEt_3, however, led to a slight reduction in yield (data not shown in Table 1). Glorius has demonstrated that more electron-deficient electrophilic amination reagent was found to be effective in Rh-catalyzed C-H amination reaction.[12] Nevertheless, an attempt to further improve the yield by employing electron-deficient **2a'** in this reaction was not successful (data not shown in Table 1). Finally, none of the desired product was detected without palladium catalyst or norbornene in the control experiment (Table 1, entries 19 and 20).

With the optimal conditions, we turned out to explore the scope of this reaction with a variety of substituted aryl iodides and *N*-benzoyloxyamines. The

results are summarized in Table 2. Both electron-donating and electron-withdrawing groups on the aromatic ring could be compatible with the reaction. Highly sterically hindered 1-iodo-2-isopropylbenzene could also lead to the coupling product **4-3** in 48% yields. 2-Iodonaphthalene also worked, providing the amination vinylarene in moderate yield (Table 2, **4-5**). It was noteworthy that chloro substituted product could be achieved successfully, which allowed further metal-catalyzed coupling reaction (Table 2, **4-4**). Furthermore, the reactions demonstrated high functional group tolerance. For instance, TBS ether and nitro

Table 2. Scope of aryl iodides **1** and *N*-benzoyloxyamines **2** [a]





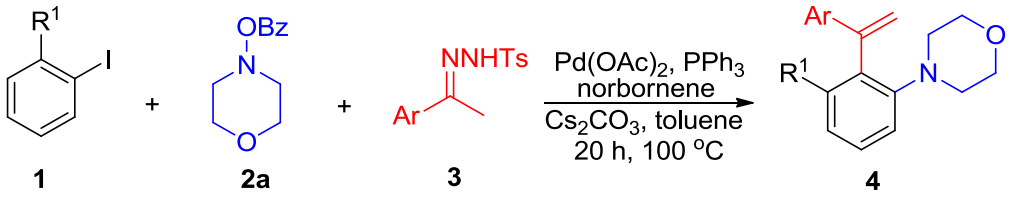
[a].Reaction conditions as in Table 1. [b]. NMR yield. [c]. TFP was used as ligand. [d]. 2.5 equiv of **2a**, 2.0 equiv of norbornene and 6.0 equiv of Cs_2CO_3 were employed.

groups were all compatible (Table 2, **4-6**, **4-9**). Next, we studied the scope of the electrophilic amine partners. Pyrrolidine gave the desired product in a low yield (Table 2, **4-11**). *N*-benzoyloxyamines containing the ester or Boc protecting group were also compatible and afforded the corresponding amination products in moderate yields (Table 2, **4-12**, **4-13**). Finally, we were pleased to find that the 1, 3-diamination product could be afforded in 36% yield by a double C-H activation

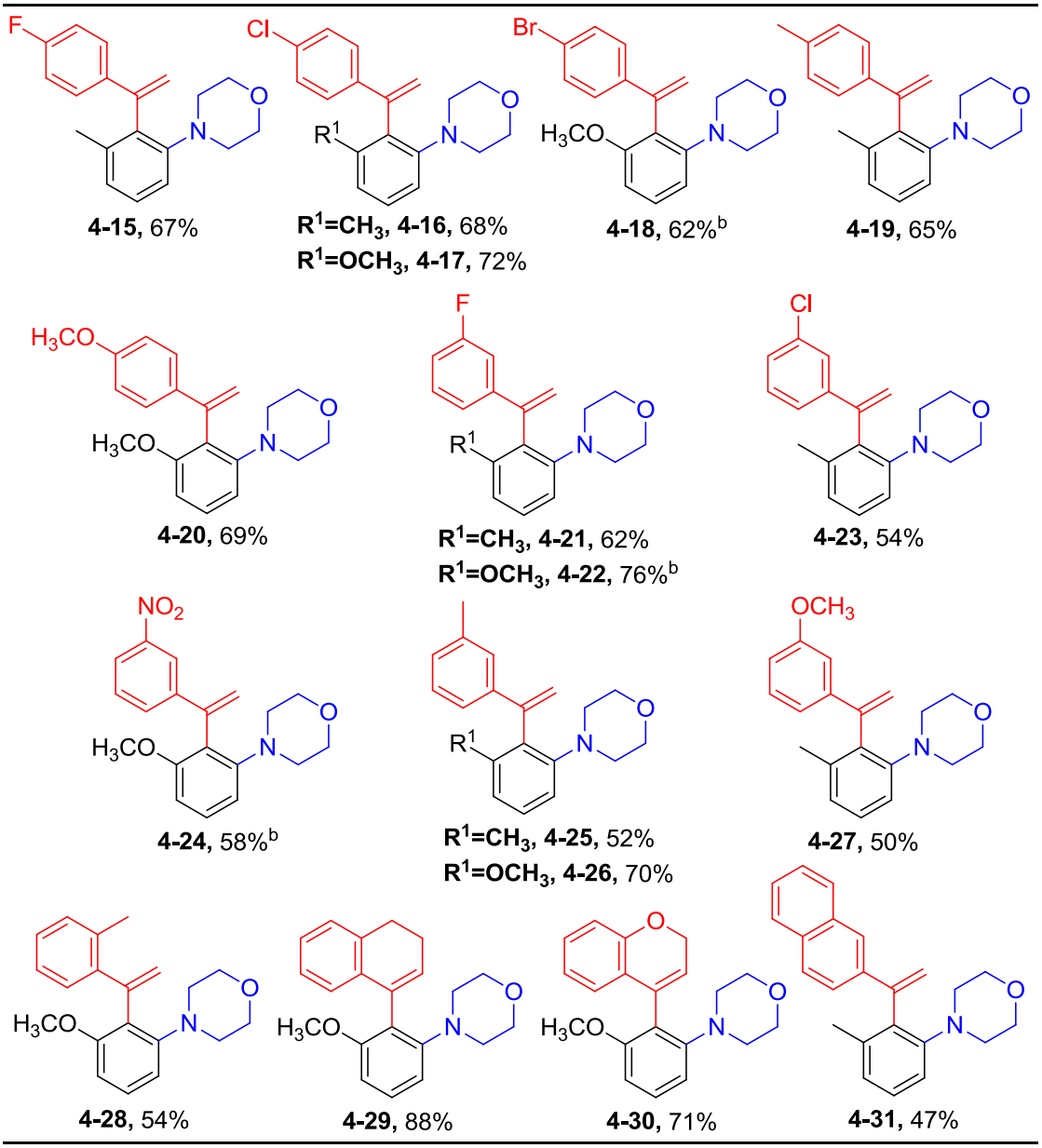
of two ortho positions of aryl iodide (Table 2, **4-14**). The low yield of **4-14** may be attributed to the steric hindrance of two morpholine groups.

The scope of this reaction was subsequently explored with various *N*-tosylhydrazones **3**. *Ortho*-, *para*-, and *meta*-substituted *N*-tosylhydrazones were all good coupling partners in this reaction, resulting in the corresponding products in moderate to good yields (Table 3). Cyclic *N*-tosylhydrazones led to a good yield of **4-29** and **4-30**. The naphthyl *N*-tosylhydrazone also worked efficiently (Table 3, **4-31**).

Table 3. Scope of *N*-tosylhydrazones **3**[a]

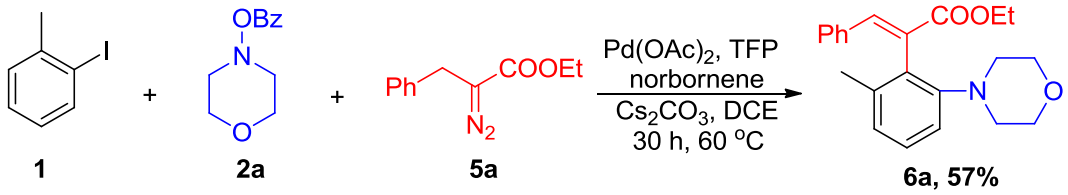


1 **2a** **3** **4**



[a]. Reaction conditions as in Table 1. [b]. NMR yield.

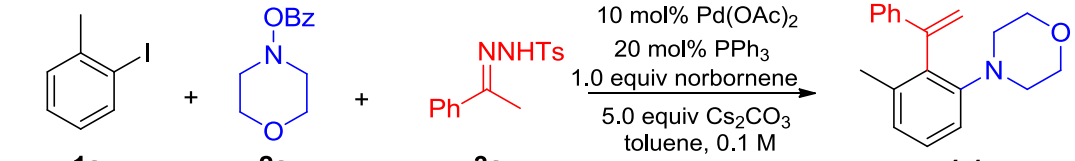
To further demonstrate the generality of this reaction, *α*-diazocarbonyl compound **5a** was employed as substrate under slightly modified conditions. To our delight, the desired product **6a** was given in moderate yield.



1 **2a** **5a** **6a, 57%**

To further demonstrate the practical utility of this protocol, we carried this reaction on a gram scale. Gratifyingly, the desired product **4-1** could also be afforded in moderate yield.

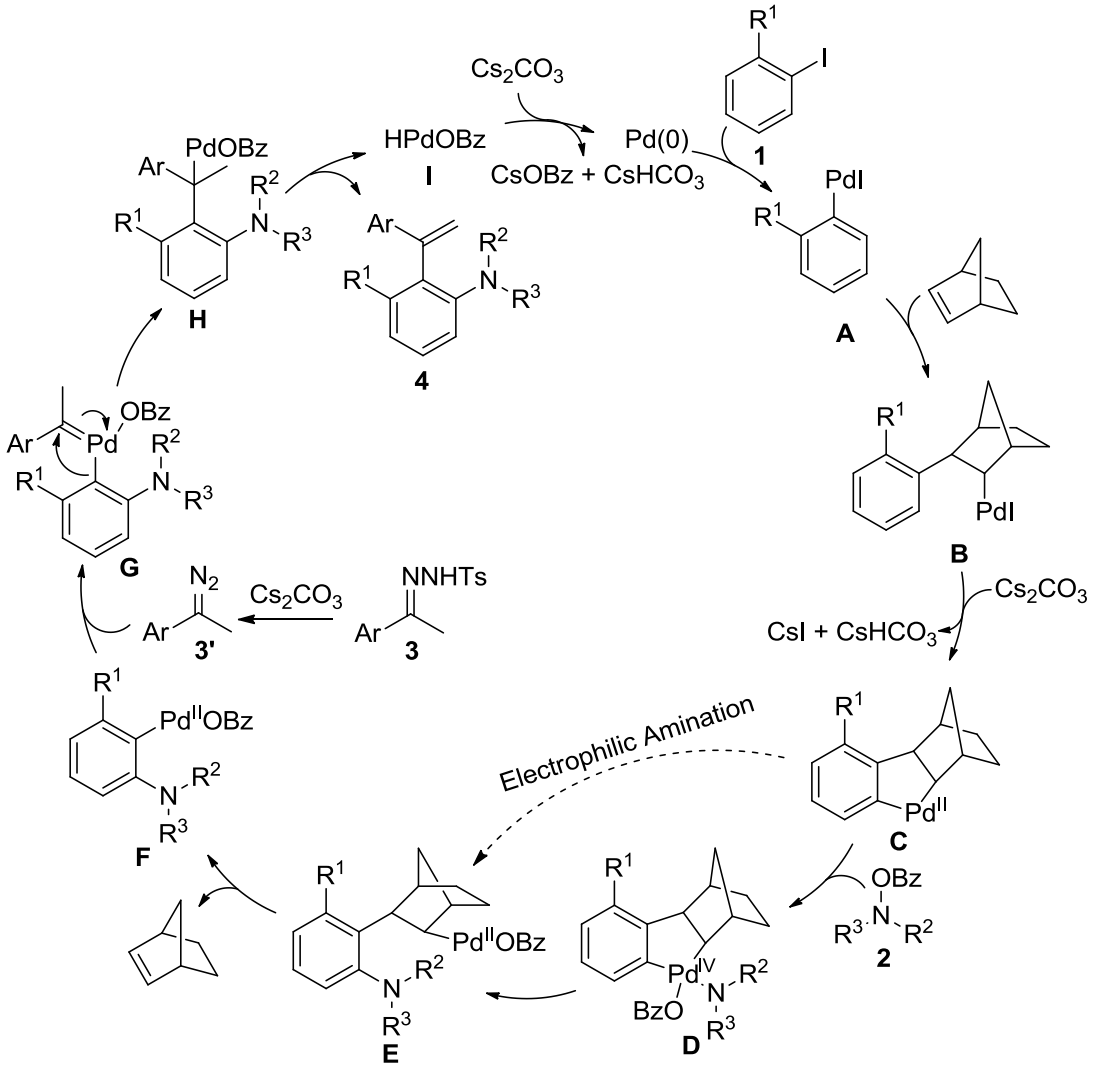
Gram scale



1a 1.09 g, 5.0 mmol **2a** 1.1 equiv **3a** 2.5 equiv **4-1** 50%

According to previous reports, [3, 4, 7, 13] we envisioned a possible catalytic cycle for this palladium-catalyzed transformation. A oxidative addition of substrate **1** to Pd(0) would occur to produce the intermediated **A**. Then, the norbornene insertion into the intermediated **A** would proceed to finish intermediate **B**. An electrophilic metalation at the ortho position occurs and further elimination of HI delivers **C**. A further oxidative addition of *N*-benzoyloxyamine **2** to species **C** result in the formation of cyclic Pd(IV) complex **D**, followed by reductive elimination to produce the Pd(II) complex **E**. Alternatively, direct electrophilic amination of the intermediate **C** to give the Pd(II) complex **E**. Intermediated **F**, resulting from norbornene release, undergoes

palladium carbene formation and migratory insertion, followed by *β*-H elimination to yield the 4.



CONCLUSION

In conclusion, we have developed a palladium-catalyzed norbornene-mediated *ortho*-amination/*N*-tosylhydrazone insertion reaction to synthesize ortho-amination vinylarenes. In this approach, it afforded a C-N bond and a C-C bond by using the electron-deficient *N*-benzoyloxyamines as an efficient electrophilic nitrogen source and with *N*-tosylhydrazones as nucleophilic

coupling partners in the termination steps. This transformation is complementary to the Catellani-Lautens reaction, Dong's work and Barluenga's work. Importantly, this reaction further demonstrates the possibility of utility *N*-tosylhydrazones as a coupling partner in Catellani-Lautens reaction and the possibility of incorporation of C-H activation in the palladium-catalyzed insertion of *N*-tosylhydrazone, which opens a new avenue for the development of more novel Pd-catalyzed insertion of *N*-tosylhydrazone.

EXPERIMENTAL SECTION

General procedure for the preparation of the products 4. An dried Schlenk tube under argon atmosphere was charged with aryl iodide **1** (0.3 mmol, 1.0 equiv), *N*-benzoyloxyamines **2** (0.33 mmol, 1.1 equiv), *N*-tosylhydrazones **3** (0.75 mmol, 2.5 equiv), $Pd(OAc)_2$ (6.7mg, 0.03mmol, 10 mol %), PPh_3 (15.7mg, 0.06mmol, 20 mol %), norbornene (28mg, 0.3 mmol, 1.0 equiv), Cs_2CO_3 (487mg, 1.5 mmol, 5.0 equiv) and toluene (4.5 mL). The mixture was stirred at room temperature for 15 minutes and then stirred at 100°C for 20 h. The resulting mixture was cooled to room temperature and filtered through celite with EtOAc as eluents. The solvents were evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel using petroleum ether/ethyl acetate to afford **4** in over 90% purity.

General procedure for the preparation of the products 6a. An dried Schlenk tube under argon atmosphere was charged with aryl iodide **1a** (65.4mg, 0.3 mmol, 1.0 equiv), *N*-benzoyloxyamines **2a** (124mg, 0.45 mmol, 1.5 equiv), *α*-diazocarbonyl compounds **5a** (73.4mg, 0.36 mmol, 1.2 equiv), $Pd(OAc)_2$ (6.7mg, 0.03mmol, 10 mol%), TFP (14mg, 0.06mg, 20 mol%), norbornene (56mg, 0.60 mmol, 2.0 equiv), Cs_2CO_3 (215mg, 0.66 mmol, 2.2 equiv) and DCE (3.0 mL). The mixture was stirred at room temperature for 15 minutes and then stirred at 60°C for 30 h. The resulting mixture was cooled to room temperature and filtered through celite with EtOAc as eluents. The solvents were evaporated under reduced pressure and the residue was purified by flash chromatography on silica gel using petroleum ether/ethyl acetate to afford pure **6a**.

4-(3-methyl-2-(1-phenylvinyl)phenyl)morpholine (4-1): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to affored **4-1** (52 mg, 62% yield); coreless oil, slowly solidifying to a white solid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.26-7.21(m, 6H), 7.04(d, J = 7.2Hz, 1H), 6.94(d, J = 8.0Hz, 1H), 5.94(d, J = 1.2Hz, 1H), 5.16(d, J = 1.2Hz, 1H), 3.50(s, 2H), 3.34(s, 2H), 3.01(s, 2H), 2.58(s, 2H), 2.25(s, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 151.1, 146.4, 141.2, 137.8, 137.6, 128.0, 127.9, 127.1, 125.8, 125.7, 117.9, 115.5, 67.1, 52.3, 20.7; HRMS (ESI) m/z: calcd for $C_{19}H_{21}NO$: M+H=280.1696; found: 280.1699.

4-(3-methoxy-2-(1-phenylvinyl)phenyl)morpholine(4-2): Flash chromatography

on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-2** (65 mg, 73% yield); yellow solid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.30-7.19(m, 6H), 6.75-6.70(m, 2H), 5.95(d, *J* = 1.2Hz, 1H), 5.31(d, *J* = 1.2Hz, 1H), 3.71(s, 3H), 3.43(t, *J* = 4.4Hz, 4H), 2.83(s, 4H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm:158.1, 152.2, 142.9, 141.3, 128.8, 127.9, 127.0, 125.8, 125.7, 116.6, 112.5, 106.7, 67.1, 56.0, 51.8; HRMS (ESI) m/z: calcd for $C_{19}H_{21}NO_2$: M+H=296.1645; found: 296.1648.

4-(3-isopropyl-2-(1-phenylvinyl)phenyl)morpholine (4-3): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-3** (44 mg, 48% yield); colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.35-7.31(m, 1H), 7.24-7.15(m, 6H), 6.96 (d, *J* =7.6Hz, 1H), 5.95(d, *J* = 1.2Hz, 1H), 5.11(d, *J* = 1.2Hz, 1H), 3.53-3.48(m, 2H), 3.33-3.27(m, 2H), 3.25-3.20(m, 1H), 3.02-2.97(m, 2H), 2.54-2.50(m, 2H), 1.22(d, *J* = 6.8Hz, 3H), 1.11(d, *J* = 6.8Hz, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 150.8, 148.7, 146.1, 141.6, 137.1, 130.4, 127.9, 127.1, 125.8, 121.6, 118.3, 114.9, 67.2, 52.5, 29.8, 25.0, 24.1; HRMS (ESI) m/z: calcd for $C_{21}H_{25}NO$: M+H=308.2009; found: 308.2011.

4-(3-chloro-2-(1-phenylvinyl)phenyl)morpholine (4-4): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-4** (44% yield) as colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.22(d, *J* = 9.2Hz, 7H), 6.96(dd, *J* = 6.8 Hz, 2.0Hz,

1H), 6.02(s, 1H), 5.32(s, 1H), 3.50(s, 2H), 3.36(s, 2H), 3.01(s, 2H), 2.63(s, 2H); $^{13}C\{H\}$ NMR (100MHz, $CDCl_3$) δ ppm: 152.6, 144.3, 140.1, 136.1, 134.7, 128.9, 128.1, 127.3, 125.7, 124.7, 118.6, 117.4, 66.9, 51.9; HRMS (ESI) m/z: calcd for $C_{18}H_{18}ClNO$: M+H=300.1150; found: 300.1151.

4-(1-(1-phenylvinyl)naphthalen-2-yl)morpholine (4-5): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-5** (62% yield) as white liquid; ^1H NMR (400MHz, $CDCl_3$) δ ppm: 8.08-8.06(m, 1H), 7.87-7.82(m, 2H), 7.41-7.37(m, 3H), 7.25-7.20(m, 5H), 6.14(d, *J* =1.2 Hz, 1H), 5.29(d, *J* =1.2 Hz, 1H), 3.59-3.54(m, 2H), 3.40-3.36(m, 2H), 3.13-3.08(m, 2H), 2.69-2.65(m, 2H); $^{13}C\{H\}$ NMR (100MHz, $CDCl_3$) δ ppm: 147.3, 145.4, 141.7, 133.8, 133.5, 131.0, 128.9, 128.0, 127.8, 127.2, 126.2, 126.1, 125.8, 124.7, 120.3, 116.9, 67.2, 52.1; HRMS (ESI) m/z: calcd for $C_{22}H_{21}NO$: M+H=316.1696; found: 316.1699.

4-(3-(((tert-butyldimethylsilyl)oxy)methyl)-2-(1-phenylvinyl)phenyl)morpholine (4-6): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-6** (75 mg, 61% yield); colorless liquid; ^1H NMR (400MHz, $CDCl_3$) δ ppm: 7.49-7.38(m, 2H), 7.25-7.24(m, 5H), 7.07(d, *J* = 7.2Hz, 1H), 5.96(d, *J* = 1.6Hz, 1H), 5.22(d, *J* = 1.2Hz, 1H), 4.83(d, *J* = 13.6Hz, 1H), 4.64(d, *J* = 13.6Hz, 1H), 3.57-3.53(m, 2H), 3.35(s, 2H), 3.09(d, *J* = 8.8Hz, 2H), 2.62-2.58(m, 2H), 0.97(s, 9H), 0.09(s, 3H), 0.07(s, 3H); $^{13}C\{H\}$ NMR (100MHz, $CDCl_3$) δ ppm: 150.5, 145.4, 141.0, 140.8,

135.6, 128.3, 128.0, 127.2, 125.8, 122.5, 119.1, 115.7, 67.1, 63.1, 52.3, 26.0, 18.4, -5.4; HRMS (ESI) m/z: calcd for $C_{25}H_{35}NO_2Si$: M+H=410.2510; found: 410.2513; EA: calcd for C: 73.30%, H: 8.61%, N:3.42%; found: C: 73.10%, H: 8.42%, N: 2.95%.

4-(3,5-dimethyl-2-(1-phenylvinyl)phenyl)morpholine (4-7): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-7** (53 mg, 60% yield); colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.20(d, J = 11.2Hz, 5H), 6.87(s, 1H), 6.74(s, 1H), 5.92(d, J = 1.2Hz, 1H), 5.14(d, J = 0.8Hz, 1H), 3.49(s, 2H), 3.33(s, 2H), 3.00(s, 2H), 2.57(s, 2H), 2.34(s, 3H), 2.21(s, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 151.0, 146.4, 141.4, 137.6, 137.5, 134.6, 128.0, 127.1, 126.4, 125.8, 118.6, 115.6, 67.1, 52.3, 21.3, 20.6; HRMS (ESI) m/z: calcd for $C_{20}H_{23}NO$: M+H=294.1852; found: 294.1854.

4-(5-chloro-3-methyl-2-(1-phenylvinyl)phenyl)morpholine (4-8): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-8** (43 mg, 46% yield); white liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.26-7.19(m,5H), 7.02(d, J = 1.6Hz, 1H), 6.88(d, J = 1.6Hz, 1H), 5.96(s, 1H), 5.16(s, 1H), 3.49(s, 2H), 3.33(s, 2H), 3.00(s, 2H), 2.59(s, 2H), 2.21(s, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 152.2, 145.5, 140.5, 139.4, 135.6, 133.2, 128.1, 127.4, 125.7, 125.3, 118.2, 116.2, 66.9, 52.0, 20.7; HRMS (ESI) m/z: calcd for $C_{19}H_{20}ClNO$: M+H=314.1306; found: 314.1307;

EA: calcd for C: 72.72%, H: 6.42%, N:4.46%; found: C: 72.58%, H: 6.58%, N: 4.00%.

4-(3-methyl-5-nitro-2-(1-phenylvinyl)phenyl)morpholine (4-9): Flash chromatography on silica using petroleum ether/ethyl acetate (5% ethyl acetate in petroleum ether) as eluent to affored **4-9** (35 mg, 36% yield); yellow liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.89(d, J = 2.0Hz, 1H), 7.75(d, J = 2.0Hz, 1H), 7.29-7.26(m, 3H), 7.20-7.18(m, 2H), 6.05(s, 1H), 5.24(s, 1H), 3.53(s, 2H), 3.39(s, 2H), 3.08(s, 2H), 2.69(s, 2H), 2.32(s, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 152.1, 147.6, 144.9, 143.7, 139.5, 139.4, 128.4, 127.9, 125.5, 120.0, 116.6, 112.7, 66.8, 51.9, 21.0; HRMS (ESI) m/z: calcd for $C_{19}H_{20}N_2O_3$: M+H=325.1547; found: 325.1550.

4-(4,5-dimethoxy-3-methyl-2-(1-phenylvinyl)phenyl)morpholine (4-10): Flash chromatography on silica using petroleum ether/ethyl acetate (5% ethyl acetate in petroleum ether) as eluent to affored **4-10** (45 mg, 44% yield); colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.26-7.20(m, 5H), 6.56(s, 1H), 5.91(d, J = 1.6Hz, 1H), 5.10(d, J = 1.6Hz, 1H), 3.88(s, 3H), 3.81(s, 3H), 3.50(d, J =8.0Hz, 2H), 3.32(s, 2H), 2.95(s, 2H), 2.54(s, 2H), 2.19(s, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 152.1, 147.0, 146.2, 143.9, 141.7, 131.7, 131.3, 127.9, 127.1, 125.8, 115.7, 102.9, 67.1, 60.3, 55.7, 52.5, 13.6; HRMS (ESI) m/z: calcd for $C_{21}H_{25}NO_3$: M+H=340.1907; found: 340.1912.

1-(3-methyl-2-(1-phenylvinyl)phenyl)pyrrolidine (4-11): Flash chromatography

on silica using petroleum ether/ethyl acetate (1% ethyl acetate in petroleum ether) as eluent to afforded **4-11** (16% yield) as colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.38-7.36(m, 2H), 7.29-7.22(m, 3H), 7.15-7.11(m, 1H), 6.70(dd, *J* =7.2 Hz, 15.6 Hz, 2H), 6.01(d, *J* =0.8 Hz, 1H), 5.20(d, *J* =0.8 Hz, 1H), 3,21(s, 2H), 3.11(s, 2H), 2.06(s, 3H), 1.71(t, *J* =6.4 Hz, 4H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 148.5, 147.0, 140.7, 137.9, 128.2, 127.6, 127.2, 126.0, 125.6, 120.2, 115.5, 112.9, 50.6, 25.3, 21.0; HRMS (ESI) m/z: calcd for $C_{19}H_{21}N$: M+H=264.1747; found: 264.1750.

Tert-butyl 4-(3-methyl-2-(1-phenylvinyl)phenyl)piperazine-1-carboxylate (4-12): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-12** (64 mg, 56% yield); colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.23-7.19(m, 6H), 7.05(d, *J* = 7.6 Hz, 1H), 6.91(d, *J* = 8.0 Hz,1H), 5.94(s, 1H), 5.14(s, 1H), 3.26-3.22(m, 2H), 3.02-2.94(m, 4H), 2.50(s, 2H), 2.27(s, 3H), 1.42(s, 9H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 154.7, 151.1, 146.3, 141.1, 137.9, 137.8, 128.0, 127.9, 127.1, 125.9, 125.6, 118.1, 115.4, 79.4, 51.9, 28.4, 20.7; HRMS (ESI) m/z: calcd for $C_{24}H_{30}N_2O_2$: M+H=379.2380; found: 379.2383.

Ethyl 1-(3-methyl-2-(1-phenylvinyl)phenyl)piperidine-4-carboxylate (4-13): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-13** (55 mg, 53% yield); colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.22-7.17(m, 6H), 7.01(d, *J* =

7.2 Hz, 1H), 6.92(d, *J* = 8.0Hz, 1H), 5.93(d, *J* = 1.2Hz, 1H), 5.13(d, *J* = 1.2Hz, 1H), 4.09(q, *J* = 7.2 Hz, 2H), 3.28(d, *J* = 10.4Hz, 1H), 2.74-2.66(m, 2H), 2.49-2.39(m, 1H), 2.23 (s, 3H), 2.21-2.15(m, 1H), 1.67(d, *J* = 17.6Hz, 4H), 1.23-1.20(m, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) *δ* ppm: 175.2, 152.0, 146.4, 141.1, 137.9, 137.5, 127.9, 127.7, 127.0, 125.7, 125.4, 118.1, 115.1, 60.0, 53.0, 50.9, 41.0, 28.5, 20.7, 14.2; HRMS (ESI) m/z: calcd for $C_{23}H_{27}NO_2$: M+H=350.2115; found: 350.2118. EA: calcd for C: 79.05%, H: 7.79%, N: 4.01%; found: C: 79.03%, H: 7.86%, N: 3.70%.

4,4'-(2-(1-phenylvinyl)-1,3-phenylene)dimorpholine (4-14): Flash chromatography on silica using petroleum ether/ethyl acetate (5% ethyl acetate in petroleum ether) as eluent to afforded **4-14** (38 mg, 36% yield); white solid; ^{1}H NMR (400MHz, $CDCl_3$) *δ* ppm: 7.30-7.21(m, 6H), 6.84(d, *J* = 8.0Hz, 2H), 5.94(s, 1H), 5.51(s, 1H), 3.46(s, 8H), 2.84(s, 8H); ^{13}C{H} NMR (100MHz, $CDCl_3$) *δ* ppm: 152.2, 144.1, 142,1, 131.7, 128.8, 127.9, 126.9, 125.5, 116.2, 115.4, 67.0, 51.8; HRMS (ESI) m/z: calcd for $C_{22}H_{26}N_2O_2$: M+H=351.2067; found: 351.2072.

4-(2-(1-(4-fluorophenyl)vinyl)-3-methylphenyl)morpholine (4-15): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-15** (59 mg, 67% yield; white solid); ^{1}H NMR (400MHz, $CDCl_3$) *δ* ppm: 7.25-7.16(m, 3H), 7.04(d, *J* = 7.6Hz, 1H), 6.96-6.91(m, 3H), 5.88(d, *J* =0.4Hz, 1H), 5.13(s, 1H), 3.51(s, 2H),

3.35(s, 2H), 3.03(s, 2H), 2.56(s, 2H), 2.25(s, 3H); $^{13}C\{H\}$ NMR (100MHz, $CDCl_3$) δ ppm: 163.4, 161.0, 151.0, 145.4, 137.7, 137.4, 137.3, 137.2, 128.1, 127.3, 127.2, 125.8, 118.0, 115.3, 114.9, 114.7, 67.1, 52.3, 20.6; HRMS (ESI) m/z: calcd for $C_{19}H_{20}FNO$: M+H=298.1602; found: 298.1601. EA: calcd for C: 76.74%, H: 6.78%, N:4.71%; found: C: 76.61%, H: 7.05%, N: 4.28%.

4-(2-(1-(4-chlorophenyl)vinyl)-3-methylphenyl)morpholine (4-16): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-16** (64 mg, 68% yield); colorless liquid; ^1H NMR (400MHz, $CDCl_3$) δ ppm: 7.25-7.20(m, 3H), 7.15-7.13(m, 2H), 7.04(d, J = 7.6Hz, 1H), 6.94(d, J = 7.6Hz, 1H), 5.93(s, 1H), 5.17(s, 1H), 3.51(s, 2H), 3.35(s, 2H), 3.02(d, J = 8.8Hz, 2H), 2.56(s, 2H), 2.24(s, 3H); $^{13}C\{H\}$ NMR (100MHz, $CDCl_3$) δ ppm: 151.0, 145.3, 139.7, 137.7, 137.1, 132.8, 128.2, 128.1, 127.0, 125.9, 118.0, 116.0, 67.1, 52.3, 20.6; HRMS (ESI) m/z: calcd for $C_{19}H_{20}ClNO$: M+H=314.1306; found: 314.1308. EA: calcd for C: 72.72%, H: 6.42%, N:4.46%; found: C: 72.59%, H: 6.25%, N: 4.07%.

4-(2-(1-(4-chlorophenyl)vinyl)-3-methoxyphenyl)morpholine (4-17): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-17** (72% yield) as colorless liquid; ^1H NMR (400MHz, $CDCl_3$) δ ppm: 7.29(d, J =8.4 Hz, 1H), 7.26(s, 4H), 6.74-6.70(m, 2H), 5.93(s, 1H), 5.33(s, 1H), 3.72(s, 3H), 3.46-3.44(m, 4H), 2.83(s, 4H); $^{13}C\{H\}$ NMR (100MHz, $CDCl_3$) δ ppm: 158.1, 152.1, 141.8, 139.9,

132.6, 129.0, 128.0, 127.0, 125.0, 117.1, 112.5, 106.7, 67.0, 56.0, 51.9; HRMS (ESI) m/z: calcd for $C_{19}H_{20}ClNO_2$: M+H=330.1255; found: 330.1258.

4-(2-(1-(4-bromophenyl)vinyl)-3-methoxyphenyl)morpholine (4-18): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-18** (62% yield) as white liquid; HRMS (ESI) m/z: calcd for $C_{19}H_{20}BrNO_2$: M+H=374.0750; found: 374.0752.

4-(3-methyl-2-(1-(p-tolyl)vinyl)phenyl)morpholine (4-19): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-19** (57 mg, 65% yield); white solid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.24-7.20(m, 1H), 7.12(d, *J* = 8.4Hz, 2H), 7.05-7.01(m, 3H), 6.93(d, *J* = 7.6Hz, 1H), 5.90(d, *J* = 1.2Hz, 1H), 5.10(d, *J* = 1.2Hz, 1H), 3.54-3.50(m, 2H), 3.37(s, 2H), 3.02(d, *J* = 8.8 Hz, 2H), 2.63-2.59(m, 2H), 2.32(s, 3H), 2.22(s, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 151.1, 146.1, 138.1, 137.8, 137.6, 136.9, 128.7, 127.8, 125.6, 125.5, 117.7, 114.6, 67.2, 52.3, 21.1, 20.6; HRMS (ESI) m/z: calcd for $C_{20}H_{23}NO$: M+H=294.1852; found: 294.1855.

4-(3-methoxy-2-(1-(4-methoxyphenyl)vinyl)phenyl)morpholine (4-20): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-20** (67 mg, 69% yield); white solid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.28-7.24(m, 1H), 7.21(d, *J* = 9.2 Hz, 2H), 6.77(d, *J* = 9.2Hz, 2H), 6.73-6.69(m, 2H), 5.86(d, *J* = 1.6Hz, 1H), 5.20(d,

J = 1.2Hz, 1H), 3.78(s, 3H), 3.70(s, 3H), 3.48-3.46(m, 4H), 2.85(s, 4H); ^{13}C{H} NMR (100MHz, $CDCl_3$) *δ* ppm: 158.8, 158.1, 152.1, 142.2, 133.7, 128.6, 126.9, 125.7, 114.6, 113.2, 112.3, 106.6, 67.1, 56.0, 55.2, 51.8; HRMS (ESI) m/z: calcd for $C_{20}H_{23}NO_3$: M+H=326.1751; found: 326.1754. EA: calcd for C: 73.82%, H: 7.12%, N:4.30%; found: C: 73.45%, H: 7.02%, N: 3.88%.

4-(2-(1-(3-fluorophenyl)vinyl)-3-methylphenyl)morpholine (4-21): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-21** (55 mg, 62% yield); white solid; ^{1}H NMR (400MHz, $CDCl_3$) *δ* ppm: 7.25-7.17(m, 2H), 7.05-7.01(m, 2H), 6.96-6.88(m, 3H), 5.95(d, *J* = 0.6 Hz, 1H), 5.20(s, 1H), 3.51(s, 2H), 3.34(s, 2H), 3.01(s, 2H), 2.56(s, 2H), 2.25(s, 3H), ^{13}C{H} NMR (100MHz, $CDCl_3$) *δ* ppm: 164.1, 161.7, 151.0, 145.5, 145.4, 143.8, 143.7, 137.7, 137.1, 129.4, 129.3, 128.2, 125.9, 121.4, 121.3, 118.0, 116.6, 114.0, 113.7, 112.6, 112.4, 67.1, 52.3, 20.6; HRMS (ESI) m/z: calcd for $C_{19}H_{20}FNO$: M+H=298.1602; found: 298.1603. EA: calcd for C: 76.74%, H: 6.78%, N:4.71%; found: C: 77.15%, H: 6.82%, N: 4.32%.

4-(2-(1-(3-fluorophenyl)vinyl)-3-methoxyphenyl)morpholine (4-22): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-22** (76% yield) as white solid; HRMS (ESI) m/z: calcd for $C_{19}H_{20}FNO_2$: M+H=314.1551; found: 314.1553.

4-(2-(1-(3-chlorophenyl)vinyl)-3-methylphenyl)morpholine (4-23): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl

acetate in petroleum ether) as eluent to afforded **4-23** (50 mg, 54% yield); yellow solid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.26-7.15(m, 4H), 7.10-7.04(m, 2H), 6.96(d, *J* = 15.6 Hz, 1H), 5.95(s, 1H), 5.20(s, 1H), 3.51(s, 2H), 3.35(s, 2H), 3.01(s, 2H), 2.56(s, 2H), 2.25(s, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 151.0, 145.3, 143.2, 137.7, 137.0, 134.0, 129.2, 128.2, 127.1, 126.0, 125.8, 123.9, 118.1, 116.8, 67.1, 52.3, 20.7; HRMS (ESI) m/z: calcd for $C_{19}H_{20}ClNO$: M+H=314.1306; found: 314.1308.

4-(3-methoxy-2-(1-(3-nitrophenyl)vinyl)phenyl)morpholine (4-24): Flash chromatography on silica using petroleum ether/ethyl acetate (5% ethyl acetate in petroleum ether) as eluent to afforded **4-24** (58% yield) as yellow oil; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 8.13-8.06(m, 2H), 7.58(d, *J* =15.6 Hz, 1H), 7.41(t, *J* =8.0 Hz, 1H), 7.34-7.30(m, 1H), 6.79-6.74(m, 2H), 6.08(s, 1H), 5.50(s, 1H), 3.74(s, 3H), 3.41-3.39(m, 4H), 2.83(s, 4H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 157.9, 151.9, 148.2, 143.3, 140.8, 131.6, 129.5, 128.6, 123.9, 121.6, 120.6, 119.4, 112.6, 106.8, 66.8, 55.8, 51.8; HRMS (ESI) m/z: calcd for $C_{19}H_{20}N_2O_4$: M+H=341.1496; found: 341.1499.

4-(3-methyl-2-(1-(m-tolyl)vinyl)phenyl)morpholine (4-25): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-25** (46 mg, 52% yield); colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.24-7.20(m, 1H), 7.12(dd, *J* = 7.6Hz, 1H), 7.09(dd, *J* = 8.4Hz, 1H), 7.03(d, *J* = 7.6Hz, 2H), 6.99(d, *J* = 7.6Hz, 1H),

6.94(d, *J* = 8.0Hz, 1H), 5.92(d, *J* = 1.2Hz, 1H), 5.14(d, *J* = 1.2Hz, 1H), 3.52(s, 2H), 3.36(s, 2H), 3.00(s, 2H), 2.60(s, 2H), 2.30(s, 3H), 2.24(s, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 151.1, 146.4, 141.1, 137.8, 137.7, 137.4, 127.9, 127.8, 127.8, 126.4, 125.7, 123.1, 117.9, 115.4, 67.2, 52.3, 21.5, 20.7; HRMS (ESI) m/z: calcd for $C_{20}H_{23}NO$: M+H=294.1852; found: 294.1851.

4-(2-(1-(3-fluorophenyl)vinyl)-3-methoxyphenyl)morpholine (4-26): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-26** (70% yield) as solid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.26(d, *J* =8.8Hz, 1H), 7.13-7.10(m, 2H), 7.04-7.01(m, 2H), 6.74-6.70(m, 2H), 5.94(s, 1H), 5.29(s, 1H), 3.71(s, 3H), 3.47-3.45(m, 4H), 2.84(s, 4H), 2.30(s, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 158.1, 152.1, 142.9, 141.2, 137.2, 128.7, 127.8, 126.4, 125.8, 123.1, 116.3, 112.4, 106.7, 67.1, 56.1, 51.8, 21.5; HRMS (ESI) m/z: calcd for $C_{20}H_{23}NO_2$: M+H=310.1802; found: 310.1804.

4-(2-(1-(3-methoxyphenyl)vinyl)-3-methylphenyl)morpholine (4-27): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-27** (46 mg, 50% yield); colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.25-7.14(m, 2H), 7.02(d, *J* = 7.6 Hz, 1H), 6.93(d, *J* = 8.0 Hz, 1H), 6.83-6.76(m, 3H), 5.94(d, *J* =1.6 Hz, 1H), 5.16(d, *J* =1.2 Hz, 1H), 3.75(s, 3H), 3.55(d, *J* =15.2Hz, 2H), 3.38(s, 2H), 3.00(s, 2H), 2.61(s, 2H), 2.24(s, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 159.5, 151.1,

146.2, 142.8, 137.8, 137.5, 128.9, 128.0, 125.7, 118.6, 117.9, 115.8, 112.2, 111.9, 67.2, 55.2, 52.3, 20.7; HRMS (ESI) m/z: calcd for $C_{20}H_{23}NO_2$: M+H=310.1802; found: 310.1805.

4-(3-methoxy-2-(1-(o-tolyl)vinyl)phenyl)morpholine (4-28): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-28** (50 mg, 54% yield); colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.27-7.23(m, 1H), 7.20-7.18(m, 1H), 7.08-7.07(m, 3H), 6.77-6.72(m, 2H), 5.64(d, *J* = 2.0Hz, 1H), 5.50(d, *J* = 2.0 Hz, 1H), 3.78(s, 3H), 3.45(t, *J* = 4.4 Hz, 4H), 2.73-2.71(m, 4H), 2.14(s, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 157.8, 152.1, 142.5, 142.3, 134.7, 130.5, 129.1, 128.6, 128.1, 126.3, 125.1, 121.0, 113.1, 107.4, 66.8, 55.8, 52.3, 20.8; HRMS (ESI) m/z: calcd for $C_{20}H_{23}NO_2$: M+H=310.1802; found: 310.1805.

4-(2-(3,4-dihydronaphthalen-1-yl)-3-methoxyphenyl)morpholine (4-29): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-29** (85 mg, 88% yield); white solid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.28-7.24(m, 1H), 7.13(d, *J* = 7.6 Hz, 1H), 7.09-7.05(m, 1H), 7.00-6.96(m, 1H), 6.71-6.68(m, 2H), 6.64(d, *J* = 7.6 Hz, 1H), 6.08-6.06(m, 1H), 3.66(s, 3H), 3.48-3.39(m, 4H), 2.99-2.94(m, 2H), 2.89-2.85(m, 2H), 2.78-2.74(m, 2H), 2.53-2.33(m,2H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 158.4, 152.4, 135.7, 135.6, 133.1, 129.2, 128.5, 127.1, 126.2, 125.9, 124.0, 123.4, 111.8, 106.4, 67.1, 56.0, 51.6, 28.1, 23.5; HRMS (ESI) m/z:

calcd for $C_{21}H_{23}NO_2$: M+H=322.1802; found: 322.1804. EA: calcd for C: 78.47%, H: 7.21%, N:4.36%; found: C: 78.03%, H: 6.97%, N: 4.04%.

4-(2-(2H-chromen-4-yl)-3-methoxyphenyl)morpholine (4-30): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-30** (69 mg, 71% yield); colorless liquid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.30-7.26(m, 1H), 7.09-7.05(m, 1H), 6.85(dd, *J* = 1.2 Hz, *J* = 8.0 Hz, 1H), 6.75-6.67(m, 3H), 6.64-6.62(m, 1H), 5.83-5.81(m, 1H), 4.94-4.90(m, 1H), 4.86-4.81(m, 1H), 3.70(s, 3H), 3.48-3.46(m, 4H), 2.99-2.94(m, 2H), 2.82-2.77(m,2H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 158.3, 154.6, 152.3, 130.8, 129.1, 128.4, 125.1, 124.0, 122.4, 120.8, 120.6, 115.7, 111.8, 106.1, 67.1, 65.3, 55.9, 51.7; HRMS (ESI) m/z: calcd for $C_{20}H_{21}NO_3$: M+H=324.1594; found: 324.1592.

4-(3-methyl-2-(1-(naphthalen-2-yl)vinyl)phenyl)morpholine (4-31): Flash chromatography on silica using petroleum ether/ethyl acetate (4% ethyl acetate in petroleum ether) as eluent to afforded **4-31** (46 mg, 47% yield); white solid; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 7.79-7.73(m, 2H), 7.69-7.66(m, 1H), 7.54-7.50(m, 2H), 7.40-7.38(m, 2H), 7.28-7.24(m, 1H), 7.07(d, *J* = 7.6 Hz, 1H), 6.97(d, *J* = 7.6 Hz, 1H), 6.07(d, *J* = 1.2 Hz, 1H), 5.26(d, *J* = 1.2 Hz, 1H), 3.45(s, 2H), 3.29(s, 2H), 3.01(s, 2H), 2.60(s, 2H), 2.27(s, 3H); ^{13}C{H} NMR (100MHz, $CDCl_3$) δ ppm: 151.2, 146.2, 138.4, 137.8, 137.5, 133.3, 132.8, 128.1, 128.0, 127.6, 127.5, 125.9, 125.8, 125.6, 124.4, 124.3, 118.0, 116.1, 67.1, 52.3, 20.7;

HRMS (ESI) m/z: calcd for $C_{23}H_{23}NO$: M+H=330.1852; found: 330.1854. EA: calcd for C: 83.85%, H: 7.04%, N:4.25%; found: C: 83.80%, H: 6.93%, N: 3.90%.

(E)-ethyl 2-(2-methyl-6-morpholinophenyl)-3-phenylacrylate (6a): Flash chromatography on silica using petroleum ether/ethyl acetate (5% ethyl acetate in petroleum ether) as eluent to afforded **6a** (60 mg, 57% yield); colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.74(s, 1H), 7.31-7.26(m, 1H), 7.23-7.16(m, 3H), 7.08(d, *J* = 7.2 Hz, 2H), 7.00-6.98(m, 2H), 4.26-4.18(m, 2H), 3.68-3.63(m, 2H), 3.60-3.55(m, 2H), 2.91-2.86(m, 2H), 2.74-2.68(m, 2H), 2.00(s, 3H), 1.25-1.21(m, 3H); ^{13}C{H} NMR (100 MHz, $CDCl_3$) δ: 168.8, 151.5, 138.9, 137.5, 135.4, 132.6, 130.8, 129.4, 129.1, 128.8, 128.5, 126.1, 117.7, 67.4, 60.8, 52.3, 19.7, 14.4; HRMS (ESI) m/z: calcd for $C_{22}H_{25}NO_3$: M+H=352.1907; found: 352.1891.

ASSOCIATED CONTENT

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Supporting Information

The copies of ^{1}H, ^{13}C spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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