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Note

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Palladium-Catalyzed Chemoselective Synthesis of 2-Aminocinnamyl Esters via Sequential Amination and Olefination of Aryl Iodides

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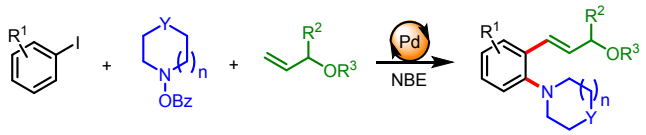
Supporting Information Placeholder



ABSTRACT: We report a highly chemoselective palladium-catalyzed Catellani-type amination of aryl iodides terminated by Heck reaction using allylic esters as terminating reagents. 2-Aminocinnamyl esters were formed exclusively via β-H elimination rather than β-OAc elimination without the assistance of a silver salt. This protocol represents a useful extension of Catellani-type transformations.

The introduction of functional groups into aromatics is a fundamental strategy for the synthesis of multisubstituted arenes. Traditional methods, including nucleophilic aromatic substitutions (S_NAr) and transition metal-catalyzed cross-couplings, have limitation that generally introduces only one substituent in a single procedure. During the past decades, the Pd/NBE-catalyzed *ortho*-functionalization of aryl halides with concomitant *ipso*-termination reaction, namely Catellani reaction, has emerged as a powerful method for the construction of multisubstituted arenes (Scheme 1a).[1,2] A wide range of terminating reagents has been proved to be suitable for this reaction. Among them, α,β-unsaturated olefins and styrenes are commonly used reagents in Catellani reaction terminated by Heck reaction.[3,4] In 2008, Jiao and co-workers reported a stoichiometric Ag(I)-promoted Heck reaction, which proceeded through β-H elimination to form cinnamyl acetate derivatives (Scheme 1b, path a).[5,6] However, to the best of our knowledge, the application of allylic esters as terminating reagents in Catellani reaction to form cinnamyl esters has not been realized (Scheme 1b, path b). Probably because there are two possible competitive pathways in Pd-catalyzed Heck reaction between aryl halides and allylic esters: (1) β-OAc elimination. Lautens and co-workers had obtained the allylbenzene products from Heck reaction of aryl iodides and allylic esters *via* β-OAc elimination (Scheme 1b, path b).[7] (2) Tsuji–Trost reaction.[8] The allylic ester could form a π-allyl Pd^{II} species through oxidative addition to Pd^0, which could be captured by nucleophiles (Scheme 1b, path c).

As a part of our ongoing interest in Catellani reaction,[9] we now describe an efficient and highly selective Catellani reaction of aryl iodides with allylic esters as new terminating reagents (Scheme 1c). Inspired by Dong's Pd/NBE-catalyzed arene C–H amination,[10] we chose *N*-benzoyloxy amine as an *ortho* electrophile to begin our research.

Scheme 1. The Pd/NBE-Catalyzed Reaction of Iodobenzenes and Allyl Esters

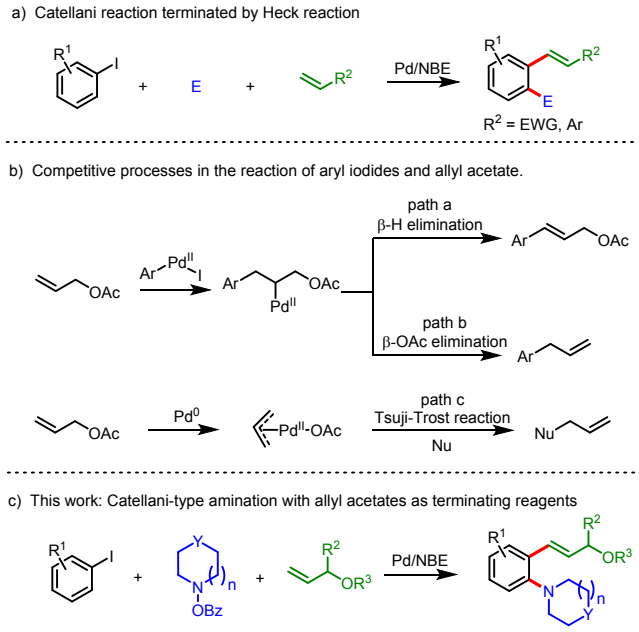
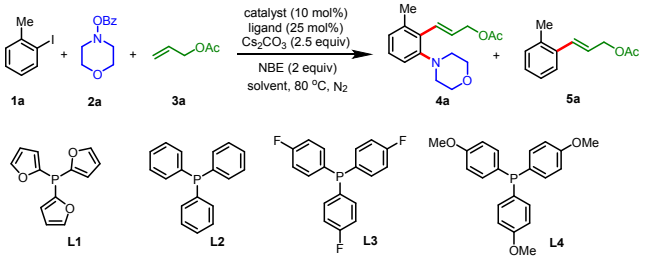


Table 1. Optimization of the Reaction Conditions[a]

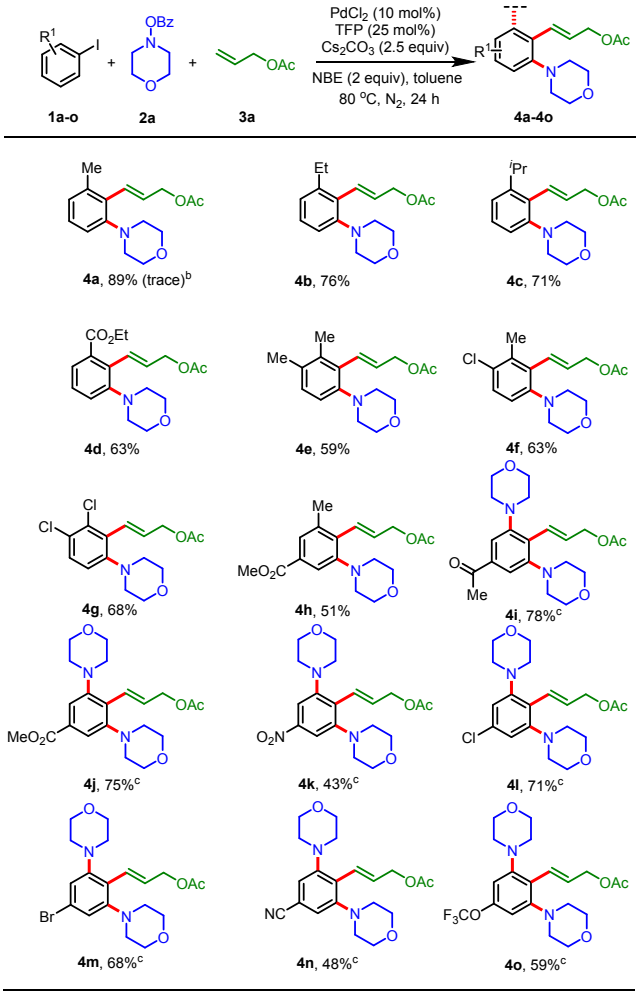


entry	catalyst	solvent	ligand	yield (%)[b]	
				4a	5a
1	$Pd(OAc)_2$	THF	**L1**	22	12
2	$Pd(OAc)_2$	MTBE	**L1**	50	34
3	$Pd(OAc)_2$	1,4-dioxane	**L1**	46	32
4	$Pd(OAc)_2$	DMF	**L1**	trace	0
5	$Pd(OAc)_2$	DMSO	**L1**	trace	0
6	$Pd(OAc)_2$	CH_3CN	**L1**	trace	trace
7	$Pd(OAc)_2$	toluene	**L1**	66	6
8	$[(allyl)PdCl]_2$	toluene	**L1**	33	trace
9	$(dppf)PdCl_2$	toluene	**L1**	66	7
10	$PdCl_2$	toluene	**L1**	75	trace
11	$PdCl_2$	toluene	**L2**	56	<5
12	$PdCl_2$	toluene	**L3**	trace	trace
13	$PdCl_2$	toluene	**L4**	46	<5
14[c]	$PdCl_2$	toluene	**L1**	40	<5
15[d]	$PdCl_2$	toluene	**L1**	92	trace
16[e]	$PdCl_2$	toluene	**L1**	86	trace
17[f]	$PdCl_2$	toluene	**L1**	80	trace
18[g]	$PdCl_2$	toluene	**L1**	0	78

[a]**1a** (0.1 mmol), **2a** (1.5 equiv), **3a** (2.0 equiv), catalyst (10 mol%), ligand (25 mol%), base (2.5 equiv), NBE (2.0 equiv), solvent (1 mL) at 80 °C under nitrogen atmosphere for 24 h. [b]The yields were determined by ^1H NMR analysis of the crude product using CH_2Br_2 as the internal standard. [c]K_2CO_3 was used instead of Cs_2CO_3 [d]1.8 equiv of **2a** were used. [e]2.0 equiv of **2a** were used.. [f]At 100 °C. [g]without NBE. MTBE = Methyl tertiary butyl ether. DMF = *N*,*N*-Dimethylformamide. DMSO = Dimethylsulfoxide.

Initially, we employed 1-iodo-2-methylbenzene (**1a**), morpholino benzoate (**2a**), and allyl acetate (**3a**) as model substrates to optimize the reaction conditions. To our delight, we got the desired product (**4a**) in 22% yield on our first try, by using $Pd(OAc)_2$ (10 mol%), tri(2-furyl)phosphane (TFP, 25 mol%), NBE (2.0 equiv) in the presence of Cs_2CO_3 (2.0 equiv) in THF (Table 1, entry 1). Then, a series of solvents were screened (Table 1, entries 2–7). MTBE and 1,4-dioxane could provide the desired product in moderate yields (Table 1, entries 2, 3), while a trace amount of **4a** was obtained using DMF, DMSO, and CH_3CN (Table 1, entries 4–6). To our delight, 66% yield of **4a** was achieved when toluene was used (Table 1, entry 7). The effect of the catalysts was subsequently investigated (Table 1, entries 8–10), and a 75% yield was obtained in the presence of $PdCl_2$ (Table 1, entry 10). A further evaluation of phosphine ligands revealed that no better result was achieved than TFP (Table 1, entries 11–13). Switching the base to K_2CO_3 could give 40% yield of product (Table 1, entry 14). Remarkably, 1.8 equiv of **2a** could promote this reaction to afford **4a** in 92% yield (Table 1, entry 15), whereas the yield was reduced to 86% when the loadings of **2a** were further increased to 2.0 equiv (Table 1, entry 16). A lower yield was observed when the reaction was conducted at a higher temperature (Table 1, entry 17). No **4a** was detected and cinnamyl ester (**5a**) was formed in 78% yield in the absence of NBE (Table 1, entry 18). Through systematic conditional screening, the optimum reaction conditions were determined as follows: $PdCl_2$ (10 mol%), TFP (25 mol%), Cs_2CO_3 (2.5 equiv), and NBE (2.0 equiv) in toluene (1 mL) under N_2 at 80 °C (Table 1, entry 15).

Scheme 2. Scope of Aryl Iodides[a]



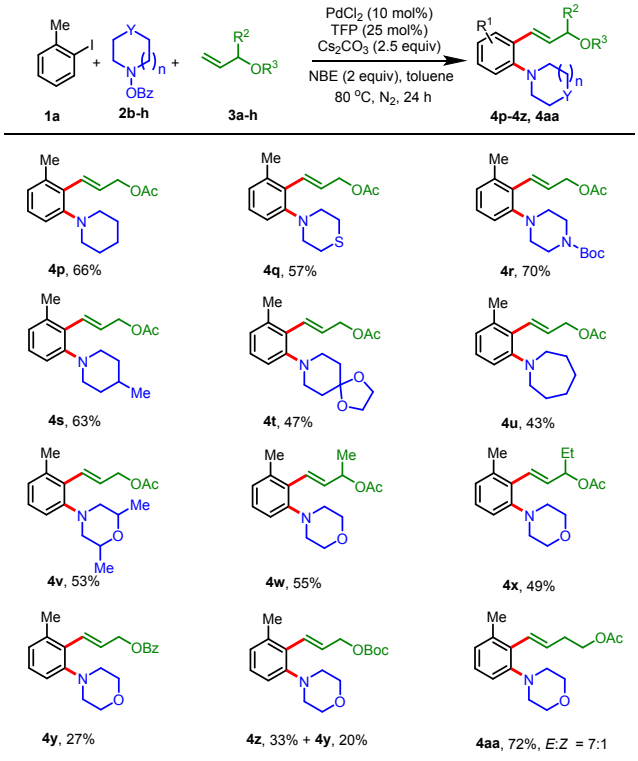
[a]**1** (0.1 mmol), **2a** (1.8 equiv), **3a** (2.0 equiv), $PdCl_2$ (10 mol%), TFP (25 mol%), Cs_2CO_3 (2.5 equiv), NBE (2.0 equiv), toluene (1 mL) at 80 °C under nitrogen atmosphere for 24 h. [b]1-Bromo-2-methylbenzene was used as substrate. [c]**2a** (3.0 equiv) was used.

With the established optimal reaction conditions in hand, we first investigated the substrate scope of aryl iodides by using **2a** and **3a** as coupling partners (Scheme 2). In the process, we used a variety of *ortho*-, *para*-, and disubstituted iodobenzenes to extend the reaction. The corresponding target products (**4a**–**o**) were obtained, and the yields ranged from 43% to 89%. However, **4a** was formed in trace amount when 1-bromo-2-methylbenzene was used. Aryl iodides with a large variety of functional groups could be applied to the reaction system, such as alkyl, ester, halogen, ketone, nitro, cyano, and trifluoromethoxyl. Notably, diamination products were observed as the only products when *para*-substituted iodobenzenes (**4i**–**o**) were subjected to the reaction. It is

noteworthy that the coordinative cyano group gave the desired product (**4n**) without obstacle. It should be noted that the structure of **4j** was confirmed by single-crystal X-ray crystallography.

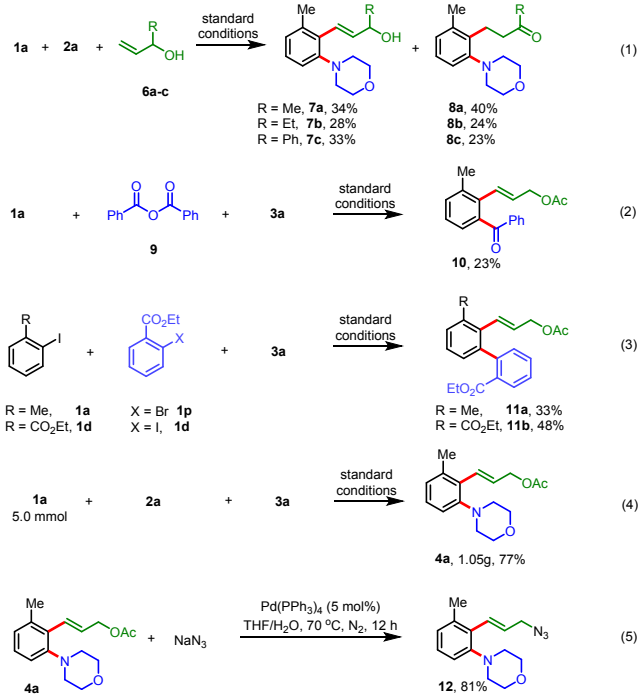
And then, we continued to use 1-iodo-2-methylbenzene (**1a**) and allyl acetate (**3a**) as the model substrates to explore the scope of the amination reagents (**2**) (Scheme 3). Piperidine, thiomorpholine, *tert*-butyl piperazine-1-carboxylate, 4-methylpiperidine, 1,4-dioxa-8-azaspiro[4,5]decane, azepane, and 2,6-dimethylmorpholine-derived cyclic amination reagents were proved to be viable substrates, producing the desired products (**4p**–**v**) in moderate to good yields. However, noncyclic amination reagents, such as O-benzoyl-*N*,*N*-dimethylhydroxylamine, was not tolerated. Dimethyl benzoyl hydroxylamine was completely decomposed, and only cinnamyl esters (**5a**) were detected. Our further investigations that expanded the scope of allyl acetates indicated that the desired products (**4w**–**z**) could be formed in moderate yields by using but-3-en-2-yl acetate (**3b**), pent-1-en-3-yl acetate (**3c**), allyl benzoate (**3d**), and allyl *tert*-butyl carbonate (**3e**) as the substrates. In the case of **3e**, 33% yield of the desired product (**4z**) and 20% yield of **4y** were isolated. However, only **4y** was detected when allyl trifluoriacetate (**3f**) and allyl dimethyl phosphate (**3g**) were used. Probably, **4y** was formed through transesterification. Importantly, homoallylic esters (**3h**) could deliver the desired product (**4aa**) in 72% yield (*E*:*Z*=7:1).

Scheme 3. Scope of Amination Reagents[a]

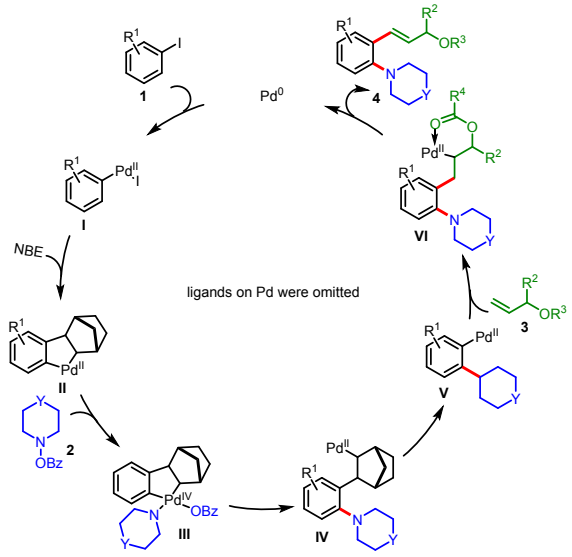


[a]**1a** (0.1 mmol), **2** (1.8 equiv), **3** (2.0 equiv), $PdCl_2$ (10 mol%), TFP (25 mol%), Cs_2CO_3 (2.5 equiv), NBE (2.0 equiv), toluene (1 mL) at 80 °C under nitrogen atmosphere for 24 h.

We also evaluated the reactivity of allyl alcohol (**6a**–**c**) in our reaction system. The cinnamyl alcohol product (**7a**–**c**) and ketone product (**8a**–**c**) were isolated in 23% to 40% yields (eq. 1). These control experiments indicated that the acetate moiety plays an important role in directing the reaction pathways and products distribution. 2-Acylcinnamyl ester (**10**) and 2-arylcinnamyl esters (**11a** and **11b**) were also formed under the standard reaction conditions, albeit in lower yields (eq. 2 and eq. 3). It should be noted that aryl iodide substrates were consumed completely in all cases of the above mentioned reactions, and cinnamyl esters (**5**) and 2-arylcinnamyl esters (**11**) could be detected as the byproducts. A gram-scale experiment was performed using **1a**, **2a**, and **3a** as starting substrates, and the desired product **4a** was isolated in 77% yield (eq. 4). It is worth mentioning that cinnamyl acetate is versatile synthetic intermediate. For example, **4a** could lead to azidesubstituted product **12** in 81% yield (eq. 5).



Scheme 4. Proposed Reaction Pathway



We propose a mechanism of this transformation (Scheme 4).[1] After the formation of aryl Pd(II) species (**I**) from the

oxidative addition of aryl iodides (**1**) to Pd^0 catalyst, the Catellani-type C–H activation takes place, giving the palladacycle (**II**). Subsequently, another oxidative addition of *N*-benzoyloxy amine (**2**) to palladacycle (**II**) occurs, leading to palladacycle (**III**), which further transforms to intermediate (**IV**) via reductive elimination. Then, intermediate (**V**) is generated via β-C elimination. Finally, Heck-type carbopalladation of allylic esters generates a palladium species (**VI**), which could undergo β-H elimination to form the final products (**4**).[5]

In conclusion, we have described the efforts of developing a Catellani-type amination of aryl iodides terminated by a highly chemoselective Heck reaction. The use of allylic esters as terminating reagents could give a range of 2-aminocinnamyl esters chemoselectively, which is a good extension of Catellani-type reactions.

EXPERIMENTAL SECTION

General Information. All commercially available solvents were of analytical grade and used as received.The other commercial chemicals were used without further purification. All reactions were performed under an inert atmosphere of nitrogen in flame-dried glassware, unless otherwise stated. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light and Vogel's permanganate. Preparative TLC was performed on 1.0 mm silica gel. ^{1}H NMR spectra were recorded on a Bruker Avance III instrument (500 MHz). ^{13}C NMR spectra were recorded on a Bruker Avance III instrument (126 MHz) were fully decoupled by broad band proton decoupling. High-resolution mass spectra (HRMS) were recorded on an Agilent 1290 Mass spectrometer using ESI-TOF (electrospray ionization-time of flight). NMR spectra were recorded in $CDCl_3$. ^{1}H NMR spectra were referenced to residual $CHCl_3$ at 7.26 ppm, and ^{13}C NMR spectra were referenced to the central peak of $CDCl_3$ at 77.0 ppm. Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

General procedure 1.[12]

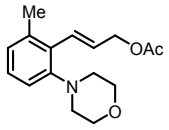
Benzoyl peroxide (2.9 g, 12 mmol, 1.2 equiv), dipotassium hydrogen phosphate trihydrate (4.5 g, 20 mmol, 2.0 equiv), and DMF (35 ml) were added to a dry round bottom flask. The resultant reaction mixture was stirred at room temperature for 30 minutes, and then amine (10 mmol, 1.0 equiv) was added. After reaction mixture was stirred for 24 hours, water (100 mL) was added to quench the reaction, and the aqueous phase was extracted with CH_2Cl_2. The organic phase was washed with brine, dried over $MgSO_4$, and filtered. The organic phase was concentrated under vacuum, and purified by chromatography on silica gel with hexanes/ethyl acetate (4:1) to afford **2**.

General procedure 2.

A dried 15 ml Schlenk tube was charged with aryl iodide **1** (0.1 mmol, 1.0 equiv), amine benzoate **2** (0.18 mmol, 1.8 equiv), allyl esters **3** (2.0 mmol, 2.0 equiv), $PdCl_2$ (1.8 mg, 0.01 mmol, 10 mol%), TFP (5.8 mg, 0.025 mmol, 25 mol%), Cs_2CO_3 (81.5 mg, 0.25 mmol, 2.5 equiv), norbornene (18.9 mg, 0.2 mmol, 2.0 equiv), and toluene (1 mL). The reaction mixture was heated to 80 °C for 24 hours on a heating plate under nitrogen atmosphere. Upon completion, the reaction mixture was cooled to room temperature, and filtered. The mixture was concentrated under vacuum, and purified by preparative thin layer chromatography (PTLC) with hexanes/ethyl acetate to give the corresponding products (**4a**–**h, 4p**–**z**, and **4aa**).

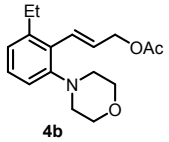
General procedure 3.

A dried 15 ml Schlenk tube was charged with aryl iodide **1** (0.1 mmol, 1.0 equiv), amine benzoate **2** (0.3 mmol, 3.0 equiv), allyl acetate **3a** (2.0 mmol, 2.0 equiv), $PdCl_2$ (1.8 mg, 0.01 mmol, 10 mol%), TFP (5.8 mg, 0.025 mmol, 25 mol%), Cs_2CO_3 (81.5 mg, 0.25 mmol, 2.5 equiv), norbornene (18.9 mg, 0.2 mmol, 2.0 equiv), and toluene (1 mL). The reaction mixture was heated to 80 °C for 24 hours on a heating plate under nitrogen atmosphere. Upon completion, the reaction mixture was cooled to room temperature, and filtered. The mixture was concentrated under vacuum, and purified by preparative thin layer chromatography (PTLC) with hexanes/ethyl acetate to give the corresponding products (**4i-o**).



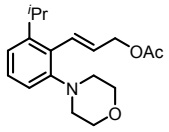
4a

(*E*)-3-(2-methyl-6-morpholinophenyl)allyl acetate (4a) (24.4 mg, 89%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (t, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.80 (d, *J* = 16.4 Hz, 1H), 6.12 (dt, *J* = 16.4, 6.4 Hz, 1H), 4.76 (dd, *J* = 6.4, 1.1 Hz, 2H), 3.82 – 3.78 (m, 4H), 2.95 – 2.91 (m, 4H), 2.36 (s, 3H), 2.10 (s, 3H); ^{13}C{1H} NMR (126 MHz, CDCl3) δ 170.7, 151.3, 137.0, 130.9, 130.1, 127.7, 127.5, 125.5, 115.9, 67.2, 65.7, 52.3, 21.4, 20.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{22}NO_3^+$ 276.1594; Found 276.1597.



4b

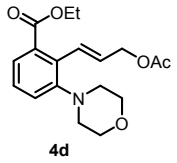
(*E*)-3-(2-ethyl-6-morpholinophenyl)allyl acetate (4b) (21.9 mg, 76%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.8 Hz, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 7.9 Hz, 1H), 6.78 (d, *J* = 16.4 Hz, 1H), 6.14 (dt, *J* = 16.3, 6.4 Hz, 1H), 4.75 (dd, *J* = 6.4, 1.2 Hz, 2H), 3.92 – 3.61 (m, 4H), 3.09 – 2.88 (m, 4H), 2.71 (q, *J* = 7.5 Hz, 2H), 2.11 (s, 3H), 1.19 (t, *J* = 7.5 Hz, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.8, 151.3, 143.3, 130.7, 129.8, 128.0, 127.2, 123.9, 116.0, 67.2, 65.7, 52.3, 26.6, 21.0, 15.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{24}NO_3^+$ 290.1751; Found 290.1753.



4c

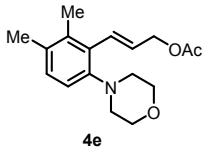
(*E*)-3-(2-isopropyl-6-morpholinophenyl)allyl acetate (4c) (21.4 mg, 71%) was prepared from general procedure 2 as

yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.9 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.87 (d, *J* = 7.9 Hz, 1H), 6.77 (d, *J* = 16.3 Hz, 1H), 6.00 (dt, *J* = 16.3, 6.4 Hz, 1H), 4.76 (d, *J* = 6.4 Hz, 2H), 4.00 – 3.66 (m, 4H), 3.44 – 3.19 (m, 1H), 2.97 – 2.89 (m, 4H), 2.11 (s, 3H), 1.20 (d, *J* = 6.9 Hz, 6H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.9, 151.1, 147.9, 130.7, 129.9, 128.2, 127.6, 120.5, 115.9, 67.3, 65.6, 52.4, 29.2, 24.1, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{26}NO_3^+$ 304.1907; Found 304.1908.



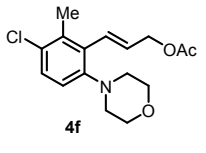
4d

ethyl (*E*)-2-(3-acetoxyprop-1-en-1-yl)-3-morpholinobenzoate (4d) (21.1 mg, 63%) was prepared from general procedure 2 as yellow solid, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1). Mp: 58−59 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 – 7.27 (m, 2H), 7.13 – 7.05 (m, 1H), 6.95 (d, *J* = 16.2 Hz, 1H), 6.07 (dt, *J* = 16.2, 6.2 Hz, 1H), 4.71 (dd, *J* = 6.2, 1.3 Hz, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 3.97 – 3.83 (m, 4H), 2.96– 2.92 (m, 4H), 2.10 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.6, 169.3, 151.3, 133.4, 130.4, 129.7, 128.1, 127.5, 123.4, 121.0, 77.3, 77.0, 76.8, 67.1, 65.2, 61.2, 52.2, 20.9, 14.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{24}NO_5^+$ 334.1649; Found 334.1652.



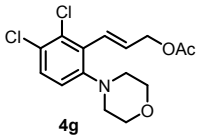
4e

(*E*)-3-(2,3-dimethyl-6-morpholinophenyl)allyl acetate (4e) (17.1 mg, 59%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06 (d, *J* = 8.1 Hz, 1H), 6.94 – 6.61 (m, 2H), 5.99 (dt, *J* = 16.4, 6.4 Hz, 1H), 4.76 (dd, *J* = 6.4, 1.2 Hz, 2H), 3.81– 3.75 (m, 4H), 2.93 – 2.85 (m, 4H), 2.26 (s, 3H), 2.25 (s, 3H), 2.11 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.8, 149.3, 135.4, 132.1, 131.5, 131.0, 129.2, 128.0, 115.7, 67.3, 65.6, 52.4, 21.0, 20.5, 17.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{24}NO_3^+$ 290.1751; Found 290.1754.



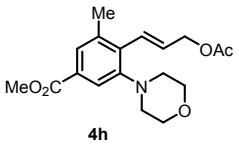
4f

(*E*)-3-(3-chloro-2-methyl-6-morpholinophenyl)allyl acetate (4f) (20.1 mg, 63%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 1H), 6.82 (d, *J* = 8.6 Hz, 1H), 6.74 (d, *J* = 16.4 Hz, 1H), 6.02 (dt, *J* = 16.4, 6.2 Hz, 1H), 4.76 (dd, *J* = 6.2, 1.2 Hz, 2H), 3.81 – 3.77 (m, 4H), 2.91 – 2.86 (m, 4H), 2.39 (s, 3H), 2.11 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.7, 149.8, 134.6, 132.5, 130.5, 129.9, 129.0, 128.4, 117.1, 67.2, 65.2, 52.2, 21.0, 18.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{21}ClNO_3^+$ 310.1204; Found 310.1207.



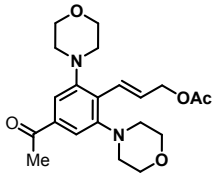
4g

(*E*)-3-(2,3-dichloro-6-morpholinophenyl)allyl acetate (4g) (23.1 mg, 68%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.7 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 1H), 6.70 (d, *J* = 16.4 Hz, 1H), 6.60 – 6.51 (m, 1H), 4.78 (dd, *J* = 6.0, 1.2 Hz, 2H), 3.81 – 3.77 (m, 4H), 2.95 – 2.89 (m, 4H), 2.12 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.6, 150.9, 132.1, 130.9, 130.3, 129.1, 127.9, 127.8, 117.7, 67.0, 65.1, 51.0, 20.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{18}Cl_2NO_3^+$ 330.0658; Found 330.0658.



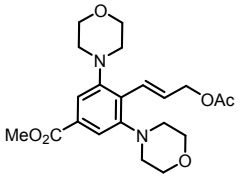
4h

methyl (*E*)-4-(3-acetoxyprop-1-en-1-yl)-3-methyl-5-morpholinobenzoate (4h) (16.9 mg, 51%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.52 (s, 1H), 6.79 (d, *J* = 16.5 Hz, 1H), 6.21 (dt, *J* = 16.5, 6.2 Hz, 1H), 4.78 (dd, *J* = 6.2, 1.2 Hz, 2H), 3.91 (s, 3H), 3.84 – 3.80 (m, 4H), 2.98 – 2.96 (m, 4H), 2.40 (s, 3H), 2.12 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.7, 167.0, 151.4, 137.3, 134.8, 130.0, 129.1, 126.7, 117.2, 67.2, 65.4, 52.3, 52.1, 21.5, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{24}NO_5^+$ 334.1649; Found 334.1650.



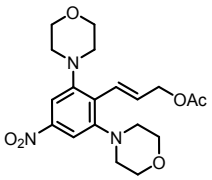
4i

(*E*)-3-(4-acetyl-2,6-dimorpholinophenyl)allyl acetate (4i) (21.0 mg, 54%) was prepared from general procedure 3 as yellow solid, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1). Mp: 106−108 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (s, 2H), 7.09 – 7.02 (m, 1H), 6.89 (d, *J* = 16.4 Hz, 1H), 4.77 (dd, *J* = 6.2, 1.2 Hz, 2H), 3.86 – 3.80 (m, 8H), 2.99 – 2.93 (m, 8H), 2.59 (s, 3H), 2.13 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 197.6, 170.7, 152.4, 137.0, 129.1, 128.5, 127.7, 114.5, 67.0, 66.0, 52.3, 26.6, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{29}N_2O_5^+$ 389.2071; Found 389.2073.



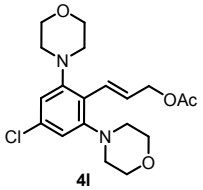
4j

methyl (*E*)-4-(3-acetoxyprop-1-en-1-yl)-3,5-dimorpholinobenzoate (4j) (23.1 mg, 57%) was prepared from general procedure 3 as yellow solid, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1). Mp: 128−129 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (s, 2H), 7.08 – 7.01 (m, 1H), 6.89 (d, *J* = 16.4 Hz, 1H), 4.77 (dd, *J* = 6.2, 1.2 Hz, 2H), 3.92 (s, 3H), 3.85 – 3.79 (m, 8H), 2.98 – 2.91 (m, 8H), 2.11 (d, *J* = 18.7 Hz, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.7, 166.8, 152.2, 129.9, 128.9, 128.3, 127.8, 115.8, 67.0, 66.0, 52.3, 52.2, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{29}N_2O_6^+$ 405.2020; Found 405.2022.



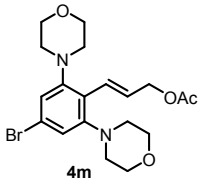
4k

(*E*)-3-(2,6-dimorpholino-4-nitrophenyl)allyl acetate (4k) (10.0 mg, 26%) was prepared from general procedure 3 as yellow solid, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1). Mp: 101-102 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (s, 2H), 7.05 (dt, *J* = 16.4, 6.1 Hz, 1H), 6.83 (d, *J* = 16.4 Hz, 1H), 4.78 (dd, *J* = 6.1, 1.3 Hz, 2H), 3.90 – 3.77 (m, 8H), 3.03 – 2.92 (m, 8H), 2.14 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.6, 152.9, 147.8, 130.7, 129.6, 126.9, 109.8, 66.9, 65.6, 52.2, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{26}N_3O_6^+$ 392.1816; Found 392.1817.



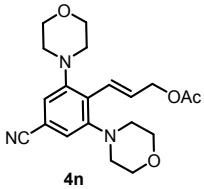
4l

(*E*)-3-(4-chloro-2,6-dimorpholinophenyl)allyl acetate (4l) (16.2 mg, 43%) was prepared from general procedure 3 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 – 6.85 (m, 1H), 6.81 – 6.76 (m, 3H), 4.73 (d, J = 6.2 Hz, 2H), 3.84 – 3.78 (m, 8H), 2.93 – 2.87 (m, 8H), 2.11 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.7, 153.2, 134.1, 127.9, 127.0, 122.8, 115.2, 67.0, 66.2, 52.4, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{26}ClN_2O_4^+$ 381.1576; Found 381.1577.



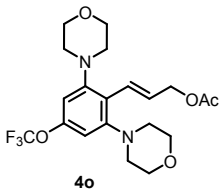
4m

(*E*)-3-(4-bromo-2,6-dimorpholinophenyl)allyl acetate (4m) (12.9 mg, 30%) was prepared from general procedure 3 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92 (s, 2H), 6.92 – 6.86 (m, 1H), 6.77 (d, *J* = 16.4 Hz, 1H), 4.73 (dd, *J* = 6.2, 1.1 Hz, 2H), 3.82 – 3.78 (m, 8H), 2.92 – 2.88 (m, 8H), 2.11 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.7, 153.3, 127.9, 127.1, 123.3, 122.3, 118.2, 67.0, 66.2, 52.4, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{26}BrN_2O_4^+$ 425.1070; Found 425.1073.



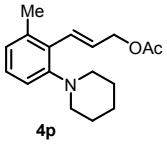
4n

(*E*)-3-(4-cyano-2,6-dimorpholinophenyl)allyl acetate (4n) (13.4 mg, 36%) was prepared from general procedure 3 as white solid, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1). Mp: 110−113 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (s, 2H), 7.00 (dt, *J* = 16.4, 6.1 Hz, 1H), 6.81 (dt, *J* = 16.4, 1.3 Hz, 1H), 4.76 (dd, *J* = 6.1, 1.4 Hz, 2H), 3.85 – 3.77 (m, 8H), 2.96 – 2.89 (m, 8H), 2.13 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.6, 152.8, 129.3, 129.1, 127.0, 118.8, 118.2, 111.9, 66.9, 65.7, 52.2, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{26}N_3O_4^+$ 372.1918; Found 372.1919.



4o

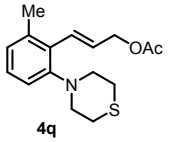
(*E*)-3-(2,6-dimorpholino-4-(trifluoromethoxy)phenyl)allyl acetate (4o) (17.3 mg, 40%) was prepared from general procedure 3 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.88 (dt, *J* = 16.4, 6.2 Hz, 1H), 6.79 (d, *J* = 16.5 Hz, 1H), 6.64 (s, 2H), 4.74 (d, *J* = 6.1 Hz, 2H), 3.84 – 3.78 (m, 8H), 2.94 – 2.89 (m, 8H), 2.11 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.7, 153.4, 149.4, 127.8, 127.2, 122.8, 120.5 (q, *J* = 257.4Hz), 107.2, 67.0, 66.1, 52.3, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{26}F_3N_2O_5^+$ 431.1788; Found 431.1786.



4p

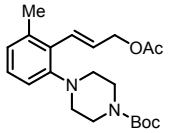
(*E*)-3-(2-methyl-6-(piperidin-1-yl)phenyl)allyl acetate (4p) (18.1mg, 66%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer

chromatography (PTLC) (hexane/ ethyl acetate (4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (t, *J* = 7.8 Hz, 1H), 6.89 – 6.84 (m, 2H), 6.81 (d, *J* = 16.4 Hz, 1H), 6.13 (dt, *J* = 16.4, 6.5 Hz, 1H), 4.77 (dd, *J* = 6.5, 1.2 Hz, 2H), 2.92 – 2.77 (m, 4H), 2.37 (s, 3H), 2.10 (s, 3H), 1.68 – 1.62 (m, 4H), 1.57 – 1.50 (m, 2H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.9, 153.1, 136.8, 131.5, 130.2, 127.6, 126.9, 125.0, 116.3, 66.0, 53.5, 26.4, 24.3, 21.5, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{24}NO_2^+$ 274.1802; Found 274.1803.



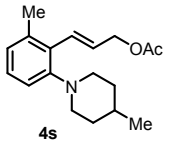
4q

(*E*)-3-(2-methyl-6-thiomorpholinophenyl)allyl acetate (4q) (16.5mg, 57%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (t, *J* = 7.8 Hz, 1H), 6.93 (d, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.77 (d, *J* = 16.4 Hz, 1H), 6.07 (dt, *J* = 16.4, 6.4 Hz, 1H), 4.77 (dd, *J* = 6.4, 1.2 Hz, 2H), 3.22 – 3.12 (m, 4H), 2.81 – 2.70 (m, 4H), 2.36 (s, 3H), 2.11 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.9, 152.7, 137.1, 131.0, 130.9, 127.7, 125.9, 117.1, 65.7, 54.6, 28.3, 21.4, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{22}NO_2S^+$ 292.1366; Found 292.1369.



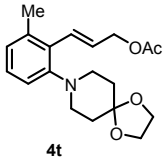
4r

***tert*-butyl (E)-4-(2-(3-acetoxyprop-1-en-1-yl)-3-methylphenyl)piperazine-1-carboxylate (4r)** (26.1mg, 70%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (t, *J* = 7.8 Hz, 1H), 6.93 (d, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 7.9 Hz, 1H), 6.80 (d, *J* = 16.4 Hz, 1H), 6.12 (dt, *J* = 16.4, 6.4 Hz, 1H), 4.75 (dd, *J* = 6.4, 1.1 Hz, 2H), 3.56 – 3.47 (m, 4H), 2.92 – 2.83 (m, 4H), 2.37 (s, 3H), 2.11 (s, 3H), 1.48 (s, 9H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.8, 154.9, 151.4, 137.1, 131.0, 130.4, 127.8, 127.7, 125.8, 116.3, 79.7, 65.7, 51.9, 28.5, 21.4, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{31}N_2O_4^+$ 375.2278; Found 375.2279.



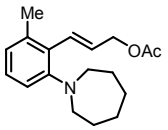
4s

(*E*)-3-(2-methyl-6-(4-methylpiperidin-1-yl)phenyl)allyl acetate (4s) (18.3mg, 63%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (t, *J* = 7.8 Hz, 1H), 6.90 – 6.84 (m, 2H), 6.80 (d, *J* = 16.4 Hz, 1H), 6.13 (dt, *J* = 16.4, 6.5 Hz, 1H), 4.76 (dd, *J* = 6.4, 0.9 Hz, 2H), 3.17 (d, *J* = 11.8 Hz, 2H), 2.57 (td, *J* = 11.8, 1.8 Hz, 2H), 2.37 (s, 3H), 2.11 (s, 3H), 1.72 – 1.63 (m, 2H), 1.51 – 1.41 (m, 1H), 1.36 – 1.29 (m, 2H), 0.98 (d, *J* = 6.5 Hz, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.9, 152.8, 136.8, 131.4, 130.2, 127.6, 126.9, 124.9, 116.3, 66.0, 52.8, 34.8, 30.7, 22.0, 21.5, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{26}NO_2^+$ 288.1958; Found 288.1961.



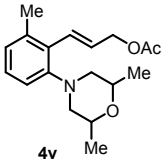
4t

(*E*)-3-(2-methyl-6-(1,4-dioxa-8-azaspiro[4.5]decan-8-yl)phenyl)allyl acetate (4t) (16.5mg, 47%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (t, *J* = 7.8 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 2H), 6.80 (d, *J* = 16.4 Hz, 1H), 6.13 (dt, *J* = 16.4, 6.4 Hz, 1H), 4.75 (dd, *J* = 6.4, 0.9 Hz, 2H), 3.99 (s, 4H), 3.05 – 2.96 (m, 4H), 2.36 (s, 3H), 2.10 (s, 3H), 1.86 – 1.81 (m, 4H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.9, 151.9, 136.9, 131.0, 130.3, 127.6, 127.3, 125.3, 116.5, 107.1, 65.9, 64.3, 50.3, 35.4, 21.5, 21.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{26}NO_4^+$ 332.1856; Found 332.1857.



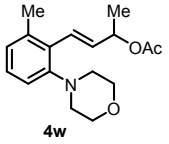
4u

(*E*)-3-(2-(azepan-1-yl)-6-methylphenyl)allyl acetate (4u) (13.1mg, 43%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (t, *J* = 7.8 Hz, 1H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.88 – 6.79 (m, 2H), 5.97 (dt, *J* = 16.4, 6.4 Hz, 1H), 4.77 (dd, *J* = 6.4, 1.2 Hz, 2H), 3.12 – 3.05 (m, 4H), 2.36 (s, 3H), 2.10 (s, 3H), 1.74 – 1.67 (m, 8H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.9, 154.7, 136.8, 132.2, 130.8, 127.4, 126.8, 124.6, 118.1, 65.9, 56.1, 29.4, 27.1, 21.6, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{26}NO_2^+$ 288.1958; Found 288.1957.



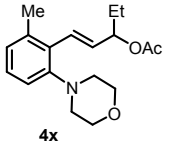
4v

(*E*)-3-(2-(2,6-dimethylmorpholino)-6-methylphenyl)allyl acetate (4v) (16.4 mg, 53%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (t, *J* = 7.8 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 16.4 Hz, 1H), 6.14 (dt, *J* = 16.4, 6.4 Hz, 1H), 4.75 (dd, *J* = 6.4, 1.1 Hz, 2H), 3.83 – 3.75 (m, 2H), 3.05 (d, *J* = 11.1 Hz, 2H), 2.39 (d, *J* = 11.4 Hz, 2H), 2.36 (s, 3H), 2.10 (s, 3H), 1.19 (d, *J* = 6.3 Hz, 6H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.7, 151.1, 137.1, 131.3, 130.1, 127.8, 127.5, 125.5, 116.2, 72.1, 65.8, 58.0, 21.4, 21.0, 18.9; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{26}NO_3^+$ 304.1907; Found 304.1909.



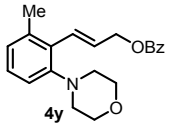
4w

(*E*)-4-(2-methyl-6-morpholinophenyl)but-3-en-2-yl acetate (4w) (15.8mg, 55%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (t, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 16.5 Hz, 1H), 6.00 (dd, *J* = 16.5, 6.8 Hz, 1H), 5.53 (p, *J* = 6.5 Hz, 1H), 3.84 – 3.79 (m, 4H), 2.99 – 2.89 (m, 4H), 2.35 (s, 3H), 2.08 (s, 3H), 1.43 (d, *J* = 6.5 Hz, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.3, 151.3, 137.0, 133.4, 130.3, 128.2, 127.6, 125.6, 115.9, 71.7, 67.3, 52.3, 21.4, 21.4, 20.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{24}NO_3^+$ 290.1751; Found 290.1753.



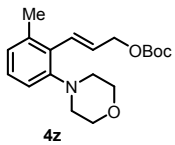
4x

(*E*)-1-(2-methyl-6-morpholinophenyl)pent-1-en-3-yl acetate (4x) (14.9mg, 49%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (t, *J* = 7.8 Hz, 1H), 6.93 (d, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.75 (d, *J* = 16.5 Hz, 1H), 5.92 (dd, *J* = 16.5, 7.3 Hz, 1H), 5.33 (q, *J* = 6.8 Hz, 1H), 3.86 – 3.76 (m, 4H), 2.99 – 2.88 (m, 4H), 2.36 (s, 3H), 2.09 (s, 3H), 1.82 – 1.69 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.3, 151.3, 137.0, 132.1, 130.5, 129.3, 127.6, 125.7, 116.0, 77.0, 67.3, 52.3, 27.8, 21.5, 21.3, 9.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{26}NO_3^+$ 304.1907; Found 304.1906.



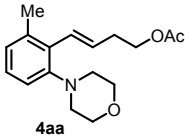
4y

(E)-3-(2-methyl-6-morpholinophenyl)allyl benzoate (4y) (9.1 mg, 27%) was prepared from general procedure 2 as colorless oil, after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1).^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.15 (t, *J* = 7.8 Hz, 1H), 6.96 – 6.85 (m, 3H), 6.25 (dt, *J* = 16.4, 6.2 Hz, 1H), 5.02 (dd, *J* = 6.3, 1.4 Hz, 2H), 3.82 – 3.73 (m, 4H), 2.94 (dd, *J* = 5.5, 3.5 Hz, 4H), 2.39 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 166.3, 151.4, 137.1, 133.0, 131.2, 130.3, 130.3, 129.6, 128.4, 127.8, 127.6, 125.7, 116.1, 67.3, 66.1, 52.4, 21.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{24}NO_3^+$ 338.1751; Found 338.1748.



4z

(E)-tert-butyl (3-(2-methyl-6-morpholinophenyl)allyl) carbonate (4z) (10.4 mg, 33%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexane/DCM (2:1).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (t, *J* = 7.8 Hz, 1H), 6.93 (d, *J* = 7.5 Hz, 1H), 6.89 – 6.80 (m, 2H), 6.14 (dt, *J* = 16.4, 6.5 Hz, 1H), 4.75 (dd, *J* = 6.4, 1.3 Hz, 2H), 3.84 – 3.77 (m, 4H), 2.98 – 2.89 (m, 4H), 2.37 (s, 3H), 1.50 (s, 9H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 153.5, 151.5, 137.2, 131.4, 130.1, 127.8, 127.4, 125.7, 116.0, 82.1, 68.3, 67.3, 52.4, 27.8, 21.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{28}NO_4^+$ 334.2013; Found 334.2015.

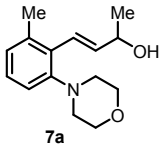


4aa

(E)-4-(2-methyl-6-morpholinophenyl)but-3-en-1-yl acetate (4aa) (22.1 mg, 72%) was prepared from general procedure 2 as yellow oil, after purification by preparative thin layer chromatography (PTLC) (hexanes/ethyl acetate (10:1).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (t, *J* = 7.8 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.59 (d, *J* = 16.4 Hz, 1H), 5.93 (dt, *J* = 16.4, 6.9 Hz, 1H), 4.20 (t, *J* = 6.7 Hz, 2H), 3.87 – 3.77 (m, 4H), 2.99 – 2.92 (m, 4H), 2.62 – 2.55 (m, 2H), 2.35 (s, 3H), 2.05 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 171.0, 151.1, 136.9, 131.4, 129.9, 129.1, 127.2, 125.7, 115.9, 67.3, 64.0, 52.2, 33.1, 21.5, 21.0; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{24}NO_3^+$ 290.1751; Found 290.1755.

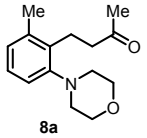
Preparation of 7 and 8.

A dried 15 ml Schlenk tube was charged with iodobenzene **1** (0.1 mmol, 1.0 equiv), morpholino benzoate **2a** (37.4 mg, 0.18 mmol, 1.8 equiv), allyl alcohol **6** (2.0 mmol, 2.0 equiv), $PdCl_2$ (1.8 mg, 0.01 mmol, 10 mol%), TFP (5.8 mg, 0.025 mmol, 25 mol%), Cs_2CO_3 (81.5 mg, 0.25 mmol, 2.5 equiv), norbornene (18.9 mg, 0.2 mmol, 2.0 equiv), and toluene (1 mL). The reaction mixture was heated to 80 °C for 24 hours on a heating plate under nitrogen atmosphere. Upon completion, the reaction mixture was cooled to room temperature, and filtered. The mixture was purified by thin layer chromatography to give **7** and **8**.



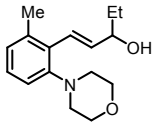
7a

(*E*)-4-(2-methyl-6-morpholinophenyl)but-3-en-2-ol (7a) (8.4 mg, 34%) was prepared as colorless oil after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (t, *J* = 7.8 Hz, 1H), 6.93 (d, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.70 (d, *J* = 16.5 Hz, 1H), 6.08 (dd, J = 16.5, 6.4 Hz, 1H), 4.56 – 4.46 (m, 1H), 3.83 – 3.78 (m, 4H), 2.98 – 2.90 (m, 4H), 2.37 (s, 3H), 1.38 (d, *J* = 6.4 Hz, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 151.2, 138.0, 137.0, 130.7, 127.4, 125.9, 125.7, 116.0, 69.5, 67.3, 52.3, 23.7, 21.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{22}NO_2^+$ 248.1645; Found 248.1649.



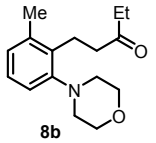
8a

4-(2-methyl-6-morpholinophenyl)butan-2-one (8a) (9.9 mg, 40%) was prepared as colorless oil after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (t, *J* = 7.7 Hz, 1H), 7.03 (d, *J* = 7.8 Hz, 1H), 6.97 (d, *J* = 7.4 Hz, 1H), 3.86 – 3.77 (m, 4H), 3.02 – 2.95 (m, 2H), 2.88 – 2.82 (m, 4H), 2.67 – 2.60 (m, 2H), 2.31 (s, 3H), 2.18 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 208.5, 151.6, 137.4, 135.9, 127.1, 126.8, 119.1, 67.6, 53.8, 43.8, 29.8, 22.0, 19.9; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{15}H_{22}NO_2^+$ 248.1645; Found 248.1653.



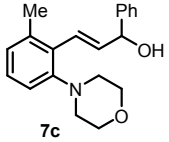
7b

(E)-1-(2-methyl-6-morpholinophenyl)pent-1-en-3-ol (7b) (7.3 mg, 28%) was as colorless oil after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1)). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (t, *J* = 7.8 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 16.5 Hz, 1H), 6.02 (dd, *J* = 16.5, 6.8 Hz, 1H), 4.28 – 4.20 (m, 1H), 3.81 (t, *J* = 4.6 Hz, 4H), 3.00 – 2.89 (m, 4H), 2.38 (s, 3H), 1.74 – 1.61 (m, 2H), 0.98 (t, *J* = 7.5 Hz, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 151.2, 137.0, 136.7, 130.8, 127.4, 127.1, 125.8, 116.1, 75.2, 67.3, 52.3, 30.4, 21.6, 9.8; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{16}H_{24}NO_2^+$ 262.1802; Found 262.1800.



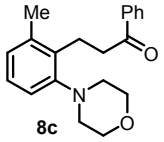
8b

1-(2-methyl-6-morpholinophenyl)pentan-3-one (8b) (6.4 mg, 24%) was prepared as colorless oil after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1)). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 – 7.10 (m, 1H), 7.06 – 7.01 (m, 1H), 6.99 – 6.94 (m, 1H), 3.87 – 3.78 (m, 4H), 3.01 – 2.95 (m, 2H), 2.90 – 2.81 (m, 4H), 2.67 – 2.58 (m, 2H), 2.46 (q, *J* = 7.3 Hz, 2H), 2.31 (s, 3H), 1.09 (t, *J* = 7.3 Hz, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 211.2, 151.5, 137.4, 136.0, 127.1, 126.7, 119.1, 67.6, 53.8, 42.3, 35.9, 22.1, 19.9, 7.9; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{16}H_{24}NO_2^+$ 262.1802; Found 262.1806.



7c

(E)-3-(2-methyl-6-morpholinophenyl)-1-phenylprop-2-en-1-ol (7c) (11.5 mg, 33%) was prepared as colorless oil after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (4:1)). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.40 (m, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.31 – 7.26 (m, 1H), 7.11 (t, *J* = 7.8 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.77 (d, *J* = 16.4 Hz, 1H), 6.23 (dd, *J* = 16.4, 6.6 Hz, 1H), 5.39 (d, *J* = 6.6 Hz, 1H), 3.70 – 3.61 (m, 4H), 2.88 – 2.79 (m, 4H), 2.36 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 151.2, 143.3, 137.0, 136.2, 130.5, 128.6, 127.7, 127.5, 126.9, 126.1, 125.7, 116.0, 76.0, 67.1, 52.2, 21.6; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{20}H_{24}NO_2^+$ 310.1802; Found 310.1800.

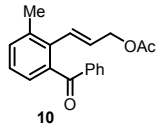


8c

3-(2-methyl-6-morpholinophenyl)-1-phenylpropan-1-one (8c) (7.0 mg, 23%) was prepared as colorless oil after purification by preparative thin layer chromatography (PTLC) (hexane/ ethyl acetate (10:1)). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 – 7.97 (m, 2H), 7.59 – 7.54 (m, 1H), 7.50 – 7.44 (m, 2H), 7.18 – 7.12 (m, 1H), 7.05 (d, *J* = 7.5 Hz, 1H), 7.00 (d, *J* = 7.4 Hz, 1H), 3.82 – 3.72 (m, 4H), 3.22 – 3.10 (m, 4H), 2.92 – 2.80 (m, 4H), 2.36 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 199.9, 151.7, 137.6, 136.8, 136.1, 133.0, 128.6, 128.1, 127.2, 126.8, 119.0, 67.5, 53.8, 38.9, 22.8, 20.0; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{20}H_{24}NO_2^+$ 310.1802; Found 310.1805.

Preparation of 10.

A dried 15 ml Schlenk tube was charged with iodobenzene **1** (0.1 mmol, 1.0 equiv), benzoic anhydride **9** (45.2 mg, 2.0 mmol, 2.0 equiv), allyl acetate **3a** (20.0 mg, 2.0 mmol, 2.0 equiv), $PdCl_2$ (1.8 mg, 0.01 mmol, 10 mol%), TFP (5.8 mg, 0.025 mmol, 25 mol%), Cs_2CO_3 (81.5 mg, 0.25 mmol, 2.5 equiv), norbornene (18.9 mg, 0.2 mmol, 2.0 equiv), and toluene (1 mL). The reaction mixture was heated to 80 °C for 24 hours on a heating plate under nitrogen atmosphere. Upon completion, the reaction mixture was cooled to room temperature, and filtered. The mixture was purified by thin layer chromatography to give **10**.



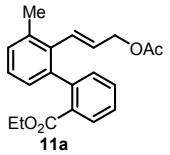
10

(E)-3-(2-benzoyl-6-methylphenyl)allyl acetate (10) (6.7 mg, 23%) was prepared as yellow oil after purification by preparative thin layer chromatography (PTLC) (hexanes/ethyl acetate (10:1).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 6.7 Hz, 1H), 7.53 (t, *J* = 7.3 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.33 – 7.27 (m, 2H), 7.26 – 7.23 (m, 1H), 6.58 (d, *J* = 16.0 Hz, 1H), 5.64 (dt, *J* = 16.0, 6.2 Hz, 1H), 4.39 (dd, *J* = 6.2, 1.4 Hz, 2H), 2.35 (s, 3H), 1.96 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 199.1, 170.4, 139.4, 137.9, 136.7, 134.9, 132.9, 131.7, 130.8, 130.1, 129.6, 128.4, 127.2, 126.1, 64.5, 20.9, 20.2; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{19}H_{19}NO_3^+$ 295.1329; Found 295.1326.

Preparation of 11a.

A dried 15 ml Schlenk tube was charged with iodobenzene **1a** (0.1 mmol, 1.0 equiv), ethyl 2-bromobenzoate **1p** (45.8 mg, 2.0 mmol, 2.0 equiv), allyl acetate **3a** (20.0 mg, 2.0 mmol, 2.0

equiv), $PdCl_2$ (1.8 mg, 0.01 mmol, 10 mol%), TFP (5.8 mg, 0.025 mmol, 25 mol%), Cs_2CO_3 (81.5 mg, 0.25 mmol, 2.5 equiv), norbornene (18.9 mg, 0.2 mmol, 2.0 equiv), and toluene (1 mL). The reaction mixture was heated to 80 °C for 24 hours on a heating plate under nitrogen atmosphere. Upon completion, the reaction mixture was cooled to room temperature, and filtered. The mixture was purified by thin layer chromatography to give **11a**.

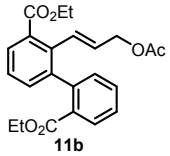


11a

ethyl (E)-2'-(3-acetoxyprop-1-en-1-yl)-3'-methyl-[1,1'-biphenyl]-2-carboxylate (11a) (11.2 mg, 33%) was prepared as yellow oil after purification by preparative thin layer chromatography (PTLC) (hexanes/ethyl acetate (10:1).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 7.7 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 7.37 (t, J = 7.9 Hz, 1H), 7.22 – 7.15 (m, 3H), 7.00 (d, J = 126.1 Hz, 2H), 6.40 (d, J = 16.2 Hz, 1H), 5.44 (dt, J = 16.1, 6.4 Hz, 1H), 4.47 – 4.35 (m, 2H), 4.09 – 3.99 (m, 2H), 2.36 (s, 3H), 1.97 (s, 3H), 0.99 (t, J = 7.1 Hz, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.5, 167.6, 142.9, 141.1, 135.7, 134.5, 131.5, 131.5, 131.2, 131.1, 129.8, 129.3, 129.1, 127.0, 126.8, 126.6, 65.0, 60.6, 20.9, 20.9, 13.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{21}H_{23}O_4^+$ 339.1591; Found 339.1586.

Preparation of 11b.

A dried 15 ml Schlenk tube was charged with ethyl 2-iodobenzoate **1d** (0.2 mmol, 1.0 equiv), allyl acetate **3a** (40.0 mg, 4.0 mmol, 2.0 equiv), $PdCl_2$ (3.6 mg, 0.02 mmol, 10 mol%), TFP (11.6 mg, 0.05 mmol, 25 mol%), Cs_2CO_3 (163.0 mg, 0.5 mmol, 2.5 equiv), norbornene (37.7 mg, 0.4 mmol, 2.0 equiv), and toluene (2 mL). The reaction mixture was heated to 80 °C for 24 hours on a heating plate under nitrogen atmosphere. Upon completion, the reaction mixture was cooled to room temperature, and filtered. The mixture was purified by thin layer chromatography to give **11b**.

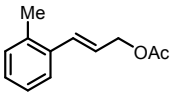


11b

diethyl (E)-2'-(3-acetoxyprop-1-en-1-yl)-[1,1'-biphenyl]-2,3'-dicarboxylate (11b) (18.7 mg, 48%) was prepared as yellow oil after purification by preparative thin layer chromatography (PTLC) (hexanes/ethyl acetate (10:1).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.92 (m, 1H), 7.81 – 7.77 (m, 1H), 7.54 – 7.48 (m, 1H), 7.44 – 7.38 (m, 1H), 7.36 – 7.28 (m, 2H), 7.19 (dd, J = 7.6, 1.3 Hz, 1H), 6.71 (d, J = 16.1 Hz, 1H), 5.36 (dt, J = 16.1, 6.4 Hz, 1H), 4.40 – 4.30 (m, 4H), 4.08 – 4.01 (m, 2H), 1.95 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H), 0.99 (t, J = 7.2 Hz, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$)δ 170.4, 168.2, 167.2, 142.1, 141.8, 135.9, 132.4, 131.5, 131.4, 131.4, 130.9, 130.8, 130.1, 128.8, 128.7, 127.2, 126.6, 64.6, 61.1, 60.7, 20.9, 14.2, 13.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{25}O_6^+$ 397.1646; Found 397.1649.

Preparation of 5a.

A dried 15 ml Schlenk tube was charged with iodobenzene **1a** (0.1 mmol, 1.0 equiv), allyl acetate **3a** (20.0 mg, 2.0 mmol, 2.0 equiv), $PdCl_2$ (1.8 mg, 0.01 mmol, 10 mol%), TFP (5.8 mg, 0.025 mmol, 25 mol%), Cs_2CO_3 (81.5 mg, 0.25 mmol, 2.5 equiv), norbornene (18.9 mg, 0.2 mmol, 2.0 equiv), and toluene (1 mL). The reaction mixture was heated to 80 °C for 24 hours on a heating plate under nitrogen atmosphere. Upon completion, the reaction mixture was cooled to room temperature, and filtered. The mixture was purified by chromatography with hexanes/ethyl acetate (20:1) to give **5a**.



5a

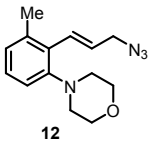
(E)-3-(o-tolyl)allyl acetate (5a) (13.2 mg, 76%) was prepared from preparation of product 5a as colorless oil, after purification by preparative thin layer chromatography (PTLC) (hexanes/ethyl acetate (20:1).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.41 (m, 1H), 7.20 – 7.12 (m, 3H), 6.92 – 6.82 (m, 1H), 6.17 (dt, J = 15.7, 6.5 Hz, 1H), 4.75 (dd, J = 6.5, 1.3 Hz, 2H), 2.35 (s, 3H), 2.10 (s, 3H); ^{13}C{1H} NMR (126 MHz, $CDCl_3$) δ 170.8, 135.6, 135.3, 132.1, 130.3, 127.9, 126.1, 125.8, 124.5, 65.3, 21.0, 19.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{15}O_2^+$ 191.1067; Found 191.1069.

Gram-Scale Synthesis of 4a.

A dried 15 ml Schlenk tube was charged with iodobenzene **1** (1.08 g, 5.0 mmol, 1.0 equiv), morpholino benzoate **2a** (1.87 g, 0.18 mmol, 1.8 equiv), allyl acetate **3a** (1.0 g, 2.0 mmol, 2.0 equiv), $PdCl_2$ (90 mg, 0.01 mmol, 10 mol%), TFP (292 mg, 0.025 mmol, 25 mol%), Cs_2CO_3 (4.10 g, 0.25 mmol, 2.5 equiv), norbornene (0.94 g, 0.2 mmol, 2.0 equiv), and toluene (50 mL). The reaction mixture was heated to 80 °C for 24 hours on a heating plate under nitrogen atmosphere. Upon completion, the reaction mixture was cooled to room temperature, and filtered. The mixture was purified by chromatography with hexanes/ethyl acetate (10:1) to give product **4a** (1.05 g, 77%).

Preparation of product 12.

A dried 15 ml Schlenk tube was charged with **4a** (26.5 mg, 0.096 mmol, 1.0 equiv), NaN_3 (8.9 mg, 0.137 mmol, 1.4 equiv), and $Pd(PPh_3)_4$ (5.4 mg, 5 mol%), THF (0.75 mL), and H_2O (0.25 mL). The reaction mixture was heated to 70 °C for 12 hours on a heating plate under nitrogen atmosphere. Upon completion, the reaction mixture was cooled to room temperature, and filtered. The mixture was purified by chromatography with hexanes/ethyl acetate (10:1) to give **12**.



12

(*E*)-4-(2-(3-azidoprop-1-en-1-yl)-3-methylphenyl)morpholine (12) (20 mg, 81%) was prepared as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (t, J = 7.8 Hz, 1H), 6.96 (d, J = 7.5 Hz, 1H), 6.90 (d, J = 8.0 Hz, 1H), 6.84 (d, J = 16.3 Hz, 1H), 6.10 (dt, J = 16.2, 6.7 Hz, 1H), 3.96 (d, J = 6.6 Hz, 2H), 3.83 – 3.79 (m, 4H), 2.98 – 2.92 (m, 4H),

2.39 (s, 3H); $^{13}C\{1H\}$ NMR (126 MHz, $CDCl_3$) δ 151.5, 137.2, 131.7, 130.2, 129.0, 126.7, 125.9, 116.3, 67.3, 54.0, 52.4, 21.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{14}H_{19}N_4O^+$ 259.1553; Found 259.1558.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

General experimental procedures, characterization data, and ^{1}H and ^{13}C NMR spectra of new compounds (PDF)

Accession Codes

CCDC 1959971 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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The authors declare no competing financial interest.

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REFERENCES

(1) For selected reviews, see: (a) Wang, J.; Dong, G. Palladium/Norbornene Cooperative Catalysis. *Chem. Rev.* **2019,** *119*, 7478-7528. (b) Cheng, H.-G.; Chen, S.; Chen, R.; Zhou, Q. Palladium(II)-Initiated Catellani-Type Reactions. *Angew. Chem. Int. Ed.* **2019,** *58*, 5832-5844. (c) Zhao, K.; Ding, L.; Gu, Z. Development of New Electrophiles in Palladium/Norbornene-Catalyzed ortho - Functionalization of Aryl Halides. *Synlett* **2019,** *30*, 129-140. (d) Liu, Z.-S.; Gao, Q.; Cheng, H.-G.; Zhou, Q. Alkylating Reagents Employed in Catellani-Type Reactions. *Chem Eur. J.* **2018,** *24*, 15461-15476. (e) Wegmann, M.; Henkel, M.; Bach, T. C-H alkylation reactions of indoles mediated by Pd(ii) and norbornene: applications and recent developments. *Org. Biom. Chem.* **2018,** *16*, 5376-5385. (f) Della Ca, N.; Fontana, M.; Motti, E.; Catellani, M. Pd/Norbornene: A Winning Combination for Selective Aromatic Functionalization via C-H Bond Activation. *Acc. Chem. Res.* **2016,** *49*, 1389-1400. (g) Ye, J.; Lautens, M. Palladium-catalysed norbornene-mediated C-H functionalization of arenes. *Nature Chem.* **2015,** *7*, 863-870.

(2) For selected recent examples see: (a) Zhang, B.-S.; Li, Y.; Zhang, Z.; An, Y.; Wen, Y.-H.; Gou, X.-Y.; Quan, S.-Q.; Wang, X.-G.; Liang, Y.-M. Synthesis of C4-Aminated Indoles via a Catellani and Retro-Diels-Alder Strategy. *J. Am. Chem. Soc.* **2019,** *141*, 9731-9738. (b) Gao, Q.; Shang, Y.; Song, F.; Ye, J.; Liu, Z.-S.; Li, L.; Cheng, H.-G.; Zhou, Q. Modular Dual-Tasked C-H Methylation via the Catellani Strategy. *J. Am. Chem. Soc.* **2019,** *141*, 15986-15993. (c) Shi, G.; Shao, C.; Ma, X.; Gu, Y.; Zhang, Y. Pd(II)-Catalyzed Catellani-Type Domino Reaction Utilizing Arylboronic Acids as Substrates. *ACS Catal.* **2018,** *8*, 3775-3779. (d) Cheng, G.; Wang, P.; Yu, J.-Q. *meta*-C-H Arylation and Alkylation of Benzylsulfonamide Enabled by a Palladium(II)/Isoquinoline Catalyst. *Angew. Chem. Int. Ed.* **2017,** *56*, 8183-8186. (e) Sun, F.; Li, M.; He, C.; Wang, B.; Li, B.; Sui, X.; Gu, Z. Cleavage of the C(O)-S Bond of Thioesters by Palladium/Norbornene/Copper Cooperative Catalysis: An Efficient Synthesis of 2-(Arylthio)aryl Ketones. *J. Am. Chem. Soc.* **2016,** *138*, 7456-7459. (f) Wang, X.-C.; Gong, W.; Fang, L.-Z.; Zhu, R.-Y.; Li, S.; Engle, K. M.; Yu, J.-Q. Ligand-enabled *meta*-C-H activation using a transient mediator. *Nature* **2015,** *519*, 334-338. (g) Dong, Z.; Wang, J.; Ren, Z.; Dong, G. Ortho C-H Acylation of Aryl Iodides by Palladium/Norbornene Catalysis. Angew. Chem. Int. Ed. **2015**, *54*, 12664-12668.

(3) (a) Heck, R. F.; Nolley, J. P. Palladium-Catalyzed Vinylic Hydrogen Substitution Reactions with Aryl,Benzyl, and Styryl Halides. *J.Org. Chem.* 1972, 37, 2320. (b) Mizoroki, T.; Mori, K.; Ozaki, A. Arylation of Olefin with Aryl Iodide Catalyzed by Palladium *Bull. Chem. Soc. Jpn.* 1971, 44, 581.

(5) Pan, D.; Chen, A.; Su, Y.; Zhou, W.; Li, S.; Jia, W.; Xiao, J.; Liu, Q.; Zhang, L.; Jiao, N., Ligand-Free Pd-Catalyzed Highly Selective Arylation of Allylic Esters with Retention of the Traditional Leaving Group. *Angew. Chem. Int. Ed.* **2008,** *47*, 4729-4732.

(6) (a) Li, Z.; Zhang, Y.; Liu, Z.-Q., Pd-Catalyzed Olefination of Perfluoroarenes with Allyl Esters. *Org. Lett.* **2012,** *14*, 74-77. (b) Zhang, Y.; Li, Z.; Liu, Z.-Q., Pd-Catalyzed Olefination of Furans and Thiophenes with Allyl Esters. *Org. Lett.* **2012,** *14*, 226-229. (c) Shang, X.; Xiong, Y.; Zhang, Y.; Zhang, L.; Liu, Z., Pd(II)-Catalyzed Direct Olefination of Arenes with Allylic Esters and Ethers. *Synlett* **2012,** 259-262. (d) Shang, X.; Liu, Z., Recent Developments in Pd-Catalyzed Oxidative Heck Cross Coupling Reaction of Arenes/Alkenes with Allylic Esters. *Chin. J. Org. Chem.* **2015,** *35*, 522-527.

(4) For selected examples of Catellani reaction terminated by Heck reaction, see: (a) Catellani, M.; Frignani, F.; Rangoni, A. A complex catalytic cycle leading to a regioselective synthesis of o,o'-disubstituted vinylarenes. *Angew. Chem. Int. Ed.* **1997,** *36*, 119-122. (b) Casnati, A.; Gemoets, H. P. L.; Motti, E.; Della Ca, N.; Noël, T., Homogeneous and Gas–Liquid Catellani-Type Reaction Enabled by Continuous-Flow Chemistry. *Chem. Eur.J.* **2018,** *24*, 14079-14083.

(7) (a) Lautens, M.; Tayama, E.; Herse, C., Palladium-Catalyzed Intramolecular Coupling between Aryl Iodides and Allyl Moieties via Thermal and Microwave-Assisted Conditions. *J. Am. Chem. Soc.* **2005,** *127*, 72-73. (b) Mariampillai, B.; Herse, C.; Lautens, M., Intermolecular Heck-Type Coupling of Aryl Iodides and Allylic Acetates. *Org. Lett.* **2005,** *7*, 4745-4747.

(8) (a) Tsuji, J.; Takahashi, H.; Morikawa, M., Organic syntheses by means of noble metal compounds XVII. Reaction of π-allylpalladium chloride with nucleophiles. *Tetrahedron Lett.* **1965,** *6*, 4387-4388. (b) Trost, B. M.; Fullerton, T. J., New synthetic reactions. Allylic alkylation. *J. Am. Chem. Soc.* **1973,** *95*, 292-294. (c) Trost, B. M., New rules of selectivity: allylic alkylations catalyzed by palladium. *Acc. Chem. Res.* **1980,** *13*, 385-393. (d) Trost, B. M.; Van Vranken, D. L., Asymmetric Transition Metal-Catalyzed Allylic Alkylations. *Chem. Rev.* **1996,** *96*, 395-422. (e) Tsuji, J., Recollections of organopalladium chemistry. *Pure Appl. Chem.* **1999,** *71*, 1539-1547. (f) Trost, B. M.; Crawley, M. L., Asymmetric Transition-Metal-Catalyzed Allylic Alkylations: Applications in Total Synthesis. *Chem. Rev.* **2003,** *103*, 2921-2944.

(9) (a) Lv, W.; Chen, Y.; Wen, S.; Ba, D.; Cheng, G. Modular and Stereoselective Synthesis of C-Aryl Glycosides via Catellani Reaction. *J. Am. Chem. Soc.* **2020**, *142*, 14864-14870. (b) Lv, W.; Wen, S.; Yu, J.; Cheng, G. Palladium-Catalyzed *Ortho*-Silylation of Aryl Iodides with Concomitant Arylsilylation of Oxanorbornadiene: Accessing Functionalized (*Z*)-beta-Substituted Vinylsilanes and Their Analogues. *Org. Lett.* **2018**, *20*, 4984-4987. (c) Lv, W.; Yu, J.; Ge, B.; Wen, S.; Cheng, G. Palladium-Catalyzed Catellani-Type Bis-silylation and Bis-germanylation of Aryl Iodides and Norbornenes. *J. Org. Chem.* **2018,** *83*, 12683-12693.

(10) (a) Dong, Z.; Dong, G. Ortho vs Ipso: Site-Selective Pd and Norbornene-Catalyzed Arene C-H Amination Using Aryl Halides. *J. Am. Chem. Soc.* **2013,** *135*, 18350-18353. (b) Sun, F.; Gu, Z., Decarboxylative Alkynyl Termination of Palladium-Catalyzed Catellani Reaction: A Facile Synthesis of α-Alkynyl Anilines via Ortho C–H Amination and Alkynylation. *Org. Lett.* **2015,** *17*, 2222-2225. (c) Majhi, B.; Ranu, B. C., Palladium-Catalyzed Norbornene-

Mediated Tandem ortho-C–H-Amination/ipso-C–I-Cyanation of Iodoarenes: Regiospecific Synthesis of 2-Aminobenzonitrile. *Org. Lett.* **2016,** *18*, 4162-4165. (d) Fu, W. C.; Zheng, B.; Zhao, Q.; Chan, W. T. K.; Kwong, F. Y., Cascade Amination and Acetone Monoarylation with Aryl Iodides by Palladium/Norbornene Cooperative Catalysis. *Org. Lett.* **2017,** *19*, 4335-4338. (e) Chen, Z.-Y.; Ye, C.-Q.; Zhu, H.; Zeng, X.-P.; Yuan, J.-J., Palladium/Norbornene-Mediated Tandem C□H Amination/C□I Alkenylation Reaction of Aryl Iodides with Secondary Cyclic O-Benzoyl Hydroxylamines and Activated Terminal Olefins. *Chem. Eur.J.* **2014,** *20*, 4237-4241. (f) Shi, H.; Babinski, D. J.; Ritter, T., Modular C–H Functionalization Cascade of Aryl Iodides. *J. Am. Chem. Soc.* **2015,** *137*, 3775-3778. (g) Zhou, P.-X.; Ye, Y.-Y.; Ma, J.-W.; Zheng, L.; Tang, Q.; Qiu, Y.-F.; Song, B.; Qiu, Z.-H.; Xu, P.-F.; Liang, Y.-M., Palladium-Catalyzed/Norbornene-Mediated ortho-Amination/N-Tosylhydrazone Insertion Reaction: An Approach to the Synthesis of ortho-Aminated Vinylarenes. *J. Org. Chem.* **2014,** *79*, 6627-6633. (h) Ye, C.; Zhu, H.; Chen, Z., Synthesis of Biaryl Tertiary Amines through Pd/Norbornene Joint Catalysis in a Remote C–H Amination/Suzuki Coupling Reaction. *J. Org. Chem.* **2014,** *79*, 8900-8905. (i) Pan, S.; Ma, X.; Zhong, D.; Chen, W.; Liu, M.; Wu, H., Palladium-Catalyzed One-Pot Consecutive Amination and Sonogashira Coupling for Selective Synthesis of 2-Alkynylanilines. *Adv. Synth. Catal.* **2015,** *357*, 3052-3056. (j) Wang, J.; Gu, Z., Synthesis of 2-(1-Alkoxyvinyl)anilines by Palladium/Norbornene-Catalyzed Amination Followed by Termination with Vinyl Ethers. *Adv. Synth. Catal.* **2016,** *358*, 2990-2995. (k) Gao, Q.; Liu, Z.-S.; Hua, Y.; Li, L.; Cheng, H.-G.; Cong, H.; Zhou, Q., A palladium/norbornene cooperative catalysis to access N-containing bridged scaffolds. *Chem. Commun*., **2019**, *55*, 8816-8819.

(11) (a) Liu, Z.-S.; Qian, G.; Gao, Q.; Wang, P.; Cheng, H.-G.; Wei, Q.; Liu, Q.; Zhou, Q., Palladium/Norbornene Cooperative Catalysis To Access Tetrahydronaphthalenes and Indanes with a Quaternary Center. *ACS Catal.* **2018,** *8*, 4783-4788. (b) Catellani, M.; Deledda, S.; Ganchegui, B.; Hénin, F.; Motti, E.; Muzart, J., A new catalytic method for the synthesis of selectively substituted biphenyls containing an oxoalkyl chain. *J. Organomet. Chem.* **2003,** *687*, 473-482.

(12) (1) Graßl, S.; Chen, Y.-H.; Hamze, C.; Tüllmann, C. P.; Knochel, P., Late Stage Functionalization of Secondary Amines via a Cobalt-Catalyzed Electrophilic Amination of Organozinc Reagents. *Org. Lett.* **2019**, *21*, 494-497.