# Recycled Pd/C-Catalyzed Heck Reaction of 2-lodoanilines under Ligand-Free Conditions

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**Abstract** Recyclable Pd/C-catalyzed Heck reaction of 2-iodoanilines with acrylate has been developed. The reaction occurred readily in 1,4-dioxane using Pd/C (10 wt%) as catalyst under ligand-free conditions, and the cross-coupling products were obtained with medium to high yield. Gram-scale reactions and recycling of the catalyst were also demonstrated.

**Key words** palladium, heterogeneous catalysis, Heck reaction, ligand-free, 2-iodoaniline

Over the past few decades, there has been a steady growth in the number of palladium-catalyzed crosscoupling reactions that have been used for the construction of carbon–carbon bonds. Among the palladium-catalyzed cross-coupling reactions, Heck, Suzuki, and Negishi crosscoupling reactions are by far the most widely exploited.<sup>1</sup> The Heck reaction is a key technology for converting halogenated aromatics and olefins into useful chemicals.<sup>2</sup> Alkenyl-substituted anilines represent a key building block in organic synthesis, and they are common and important substructures in the synthesis of indoles and quinolines.<sup>3</sup> The most simple and direct method to construct these compounds is C–C coupling reaction of their precursors, because of the high selectivity and efficiency of palladium catalysis systems in these reactions.

Recently, new generations of homogeneous catalysts such as palladacycles,<sup>4</sup> iridium,<sup>5</sup> rhodium,<sup>6</sup> nickel,<sup>7</sup> and copper<sup>8</sup> catalysts have extended the scope of the reaction to almost all aromatic halides. Even the electrochemical Heck reaction has been developed to enhance the efficiency of catalyst.<sup>9</sup> Most recently, a large number of reports have focused on palladium-catalyzed Heck reaction in green solvents,<sup>10</sup> asymmetric Heck reactions,<sup>11</sup> and oxidative Heck

reaction.<sup>12</sup> A great many achievements have been reported for the application of Heck reaction in the synthesis of numerous functionalized molecules.<sup>2</sup>

Among metal catalysts, palladium has often been used to construct C-C bonds in Heck reactions.<sup>13</sup> For economic and environmental reasons, the recovery and the recycling of the expensive palladium catalyst is mandatory. The previous strategies involving Heck reactions mainly employed homogeneous palladium catalysis systems. Unfortunately, homogeneous catalysis suffers several drawbacks with respect to production-practice, such as the low catalytic activity due to the poisoning of active palladium catalyst with the amino group. Furthermore, the necessary ligand used to form the active catalyst may be expensive and the removal of the catalyst from the product can be a challenge because the level of residual palladium in the active pharmaceutical ingredient (API) must be consistently less than 10 ppm. In this context, the development of heterogeneous and ligandfree catalysis is meaningful.

A solution to these problems could be the use of a heterogeneous palladium catalyst, which could be prepared by simple methods and recycled conveniently.<sup>14</sup> During recent years, attention has also focused on the development of catalytic reactions for the manufacture of fine chemicals. Palladium–carbon (Pd/C) catalyst, which is commercially available, has been employed in industries, including for the oxidation of glucose and hydrogenation of nitro compounds and olefins. However, there are few productive practices that involve the Heck reaction with Pd/C catalyst, especially in air atmosphere and under ligand-free conditions.<sup>14g</sup>

The Pd/C catalyst is an interesting alternative for catalysis of the Heck reaction under ligand-free conditions. Herein, we report an efficient process for the Pd/C catalyzed Heck reaction of 2-iodoanilines and acrylate without a ligand, in air (Scheme 1), which takes place in the presence of triethylamine ( $Et_3N$ ). В

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In the course of our continuing research on palladiumcatalyzed reactions of aryl halides, ethyl 3-(2-aminophenyl)acrylate (**3a**) was identified as a cross-coupling product of the Heck reaction. Initial experiments began with 2-iodoaniline (**1a**) and ethyl acrylate (**2a**) as model starting materials, wet Pd/C (10 wt% palladium on activated carbon paste and 50% moisture, 10 wt% wet Pd/C based on starting material **1a**) as catalyst and Et<sub>3</sub>N (2.0 equiv) as base in toluene at 80 °C. The product **3a** was isolated with 59% yield (Table 1, entry 1). This result encouraged us to investigate further our hypothesis that heterogeneous Pd/C can be applied to Heck reaction of aryl halides substituted with an amino group. Other solvents, catalysts and bases were then evaluated to improve the efficiency of the reaction.

Firstly, acetonitrile (MeCN; Table 1, Entry 2), ethanol (EtOH; entry 3), and 1,4-dioxane (entry 4) were tested as solvent to improve the yield of **3a** (53 63, and 61%, respectively) in Pd/C-catalyzed Heck reaction of 2-iodoaniline at 80 °C. Unfortunately, the results were not satisfactory, and the higher yield was desired. When the reaction was performed at 100 °C in toluene, MeCN and EtOH (entries 5-7), higher yields were obtained (56-88%). Pleasingly, the yield was improved to >99% when 1,4-dioxane was used as the solvent and the reaction mixture was heated to 100 °C (entry 8). The results indicated that 1,4-dioxane (at 100 °C) was the best solvent for Pd/C-catalyzed Heck reaction of 2iodoanilines. Homogeneous catalysts Pd(OAc)<sub>2</sub> and PdCl<sub>2</sub> were also tested in 1,4-dioxane, but no more positive results were obtained (52% and 85%; entries 9 and 10). The results indicate that the Pd/C catalyst may be more compatible with the amino group of substrates.

To test whether  $Et_3N$  is necessary for the reaction, other bases and amounts were investigated. The results showed that the reaction was inhibited in the presence of  $K_2CO_3$  (1.0 equiv) or  $Na_2CO_3$  (1.0 equiv) (Table 1, entries 11 and 12). We suggest that the catalyst may be enveloped by the solid inorganic base and the catalytic activity was lost. The phenomenon was also detected in Pd/C catalyzed hydrogenation of olefins. When *N*-ethyl-*N*-isopropylpropan-2-amine (DIPEA; 2.0 equiv) was employed as the organic base, a better result was achieved (90% yield; entry 13). To some extent, the speculation that the catalytic activity was lost in the presence of the solid inorganic base was confirmed. Subsequently, the amount of  $Et_3N$  was tested and the yield decreased dramatically when less  $Et_3N$  (1.0 equiv) was used

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able 1	Optimization	of the S	ynthesis	of 3a
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	↓ + ←	OEt Catalys O Base ( Solver	st (10 wt%) 2.0 equiv) nt, 100 °C	OEt NH <sub>2</sub>
	1a	2a		3a
Entry	Catalyst	Base	Solvent	Yield (%) <sup>b</sup>
1	Pd/C	$Et_3N$	toluenec	59
2	Pd/C	$Et_3N$	MeCN <sup>c</sup>	53
3	Pd/C	$Et_3N$	EtOH <sup>c</sup>	63
4	Pd/C	$Et_3N$	1,4-dioxane <sup>c</sup>	61
5	Pd/C	$Et_3N$	toluene	71
6	Pd/C	$Et_3N$	MeCN	56
7	Pd/C	$Et_3N$	EtOH	88
8	Pd/C	$Et_3N$	1,4-dioxane	>99
9	Pd(OAc) <sub>2</sub> <sup>d</sup>	$Et_3N$	1,4-dioxane	52
10	$PdCl_2^d$	$Et_3N$	1,4-dioxane	85
11	Pd/C	K <sub>2</sub> CO <sub>3</sub> <sup>e</sup>	1,4-dioxane	N/A
12	Pd/C	Na <sub>2</sub> CO <sub>3</sub> <sup>e</sup>	1,4-dioxane	30
13	Pd/C	DIPEA	1,4-dioxane	90
14	Pd/C	$Et_3N^e$	1,4-dioxane	58
15	Pd/C	-	1,4-dioxane	32

 $^{\rm a}$  Reaction conditions (unless noted otherwise): 1a (0.5 mmol), 2a (1.0 mmol), palladium catalyst (10 wt% palladium on activated carbon paste and 50% moisture, 10 wt% wet Pd/C based on starting material 1a), base (2.0 equiv), solvent (3.0 mL), air, 100 °C, 20 h.

<sup>b</sup> Isolated yield. <sup>c</sup> Carried out at 80 °C.

Carried out at 80 °C.

<sup>d</sup> Catalyst (5.0 mol%) was used.

<sup>e</sup> Base (1.0 equiv) was used.

as the base (entry 14). Notably, the Pd/C-catalyzed Heck reaction did occur without base, but only 32% yield of **3a** was isolated (entry 15).

By the optimization of solvents, catalysts, and bases, the best reaction conditions of Pd/C-catalyzed Heck reaction of 2-iodoanilines were established as Pd/C (10 wt%) as catalyst and Et<sub>3</sub>N (2.0 equiv) as base in 1,4-dioxane at 100 °C. Based on the optimized conditions, the substrate scope of the Pd/C-catalyzed Heck reaction of 2-iodoanilines with olefins was tested; the results are summarized in Table 2.

Under the optimal conditions, a variety of 2-iodoanilines **1a–s** were subjected to the Pd/C-catalyzed Heck reaction, as shown in Table 2. The 2-iodoanilines **1a–m** (entries 1–13), with different substituents (Me, CF<sub>3</sub>, Cl, Br, F, NO<sub>2</sub> and CN) on the 4- or 5-position of the 2-iodoanilnes, reacted with ethyl acrylate under the optimal reaction conditions, to give moderate to high isolated yields of **3a–m** (64% to >99%). The results indicated that substrates with Me, Br or Cl gave slightly lower yields and those with electronwithdrawing substituents, such as F, CN, NO<sub>2</sub> and CF<sub>3</sub>, gave higher yields. Substrate 3-chloro-2-iodoaniline (**1k**), with a

bulky substituent *ortho* to the iodine gave the product in 64% yield after 48 hours together with recovered starting material. Furthermore, the starting material 3-iodoaniline (**1n**) reacted with ethyl acrylate under the optimal reaction conditions to give the target product with >99% yield (entry 14). The results indicate that an *ortho*-amino group on the substrate is not required for the reaction. In addition, the reaction system also can be applied to the Heck reaction of 2-iodophenol (**1o**), giving the product in 84% yield (entry 15). The starting material iodobenzene (**1p**) was also tested in the catalysis system and ethyl cinnamate **3p** was prepared with 88% yield (entry 16). The result indicated that the amino group is not necessary for the reaction.





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Table 2 (continued)



<sup>a</sup> Reaction conditions (unless noted otherwise): 1 (0.5 mmol), 2 (1.0 mmol), Pd/C (10 wt% palladium on activated carbon paste and 50% moisture, 10 wt% wet Pd/C based on starting material 1), Et<sub>3</sub>N (2.0 equiv), 1,4dioxane (3.0 mL), air, 100 °C, 20 h. <sup>b</sup> Isolated vield.

<sup>c</sup> The reaction time was 48 h.

Notably, the above optimal conditions were not appropriate for the Heck reaction of bromobenzene (1q), 2-bromobenzene (1r), or 3-iodopyridin-4-amine (1s) (Table 2, entries 17-19), and almost all of the starting material was recovered.

Other acrylates, namely methyl acrylate and tert-butyl acrylate, were investigated under the optimal reaction conditions, and the corresponding products 3t and 3u were isolated in 97% and 98% yield, respectively (Table 2, entries 20 and 21). Other olefins, such as ethyl but-2-enoate and ethyl methacrylate, were tested, but no target products were detected under the optimal conditions (entries 22 and 23). The results may be caused by the low catalytic activity of heterogeneous Pd/C catalysis system and by the low reactivity of this type of starting material.

To test the effect of Pd/C-catalyzed Heck reaction under scale-up conditions, 2-iodoaniline (1a) (5.0 g) was input into the reaction and 3a was attained with 94.0% yield (4.1 g; Table 3, entry 1). Recycling of the Pd/C catalyst was also assessed under the standard reaction conditions. Pleasingly, the catalytic activity of Pd/C catalyst decreased only slightly in the second and third runs (89.6% and 90.6%; entries 2 and 3). The results indicate that the recyclable Pd/C catalyst may be appropriate for the scale-up and industrial production.

#### Table 3 Test of Scale-Up Conditions and Recycling of the Pd/C Catalyst<sup>a</sup>

NH <sub>2</sub>	+ OEt	Pd/C (10 Et <sub>3</sub> N (2.0 1,4-dioxane	equiv) e, 100 °C	O OEt
1a	2a			3a
Recycling run	m (Pd/C)	m ( <b>1a</b> )	m ( <b>3a</b> )	Yield (%) <sup>b</sup>
1st	0.50 g	5.0 g	4.1 g	94.0
2nd	0.46 g	4.6 g	3.6 g	89.6
3rd	0.43 g	4.3 g	3.4 g	90.6

<sup>a</sup> Reaction conditions: 1a (1.0 equiv), 2a (2.0 equiv), Pd/C (10 wt% palladium on activated carbon paste and 50% moisture, 10 wt% wet Pd/C based on starting material 1a), Et<sub>3</sub>N (2.0 equiv), 1,4-dioxane (50 mL), air, 100 °C, 20 h <sup>b</sup> Isolated yield.

In summary, the recyclable Pd/C catalyzed Heck reaction of 2-iodoanilines and acrylate without ligand was developed and afforded 2-alkenylanilines in up to >99% yield. The catalysis system provide a powerful means to develop new applications for heterogeneous palladium-catalyzed C-C, C-N, and C-O cross-coupling reactions. The heterogeneous Pd/C can be recovered and recycled three times.

Commercially available reagents were used throughout without further purification, other than those detailed below. Solvents were purchased and used without further purification. Chemical shifts for <sup>1</sup>H NMR spectra are presented in ppm downfield from tetramethylsilane (TMS) with the solvent resonance as the internal standard. Chemical shifts for <sup>13</sup>C NMR are presented in ppm downfield using the central peak of chloroform-d ( $\delta$  = 77.23 ppm) as the internal standard. Coupling constants (J) are reported in Hz and refer to apparent peak multiplications. Flash column chromatography was performed on silica gel (200-300 mesh). TLC analysis was performed using glass-backed plates coated with 0.2 mm silica.

# Synthesis of Alkenylanilines; Typical Procedure

A mixture of 2-iodoaniline 1 (0.50 mmol) and Pd/C (10 wt% palladium on activated carbon paste and 50% moisture, 10 wt% wet Pd/C based on starting material 1) in 1,4-dioxane (3 mL) was added into a Schlenk

flask (25 mL) and stirred at r.t. Ethyl acrylate (100 mg, 1.0 mmol, 2.0 equiv) and Et<sub>3</sub>N (101 mg, 1.0 mmol, 2.0 equiv) were added and the mixture was stirred at 100 °C until the reaction was complete. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography.

## Ethyl 3-(2-Aminophenyl)acrylate (3a)

Yield: >99% (96.0 mg); light-yellow solid; mp 75-76 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.33 (t, *J* = 7.2 Hz, 3 H), 4.26 (q, *J* = 7.2 Hz, 2 H), 6.35 (d, *J* = 15.8 Hz, 1 H), 6.70–6.79 (m, 2 H), 7.15–7.19 (m, 1 H), 7.37–7.39 (m, 1 H), 7.80–7.85 (m, 1 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.3, 60.4, 116.8, 118.2, 119.0, 120.0, 128.1, 140.0, 145.3, 167.5.

HRMS (EI): *m*/*z* [M]<sup>+</sup> calcd for C<sub>11</sub>H<sub>13</sub>NO<sub>2</sub>: 191.0946; found: 191.0942.

### Ethyl 3-(2-Amino-5-methylphenyl)acrylate (3b)

Yield: 85% (86.9 mg); light-yellow solid; mp 88-90 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.33 (t, J = 7.1 Hz, 3 H), 2.24 (s, 3 H), 4.25 (q, J = 7.1 Hz, 2 H), 6.35 (d, J = 15.8 Hz, 1 H), 6.64 (d, J = 8.1 Hz, 1 H), 6.98–7.00 (m, 1 H), 7.20 (s, 1 H), 7.82 (d, J = 15.8 Hz, 1 H).

 $^{13}C$  NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 14.3, 20.4, 60.4, 117.1, 117.9, 120.1, 128.2, 140.1, 142.8, 167.3.

HRMS (EI): *m*/*z* [M]<sup>+</sup> calcd for C<sub>12</sub>H<sub>15</sub>NO<sub>2</sub>: 205.1103; found: 205.1107.

#### Ethyl 3-(2-Amino-5-(trifluoromethyl)phenyl)acrylate (3c)

Yield: 96% (124.1 mg); light-yellow solid; mp 65-67 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.34 (t, *J* = 7.1 Hz, 3 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 6.40 (d, *J* = 15.8 Hz, 1 H), 6.74 (d, *J* = 8.5 Hz, 1 H), 7.38 (dd, *J* = 8.6, 15.7 Hz, 1 H), 7.61 (s, 1 H), 7.76 (d, *J* = 8.6 Hz, 1 H).

 $^{13}\text{C}$  NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 14.3, 60.7, 116.2, 119.2, 120.0, 120.6, 120.9, 125.3, 125.4, 127.8, 138.5, 147.8, 166.8.

<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>):  $\delta$  = 61.6 (s, 3 F).

HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>12</sub>H<sub>12</sub>F<sub>3</sub>NO<sub>2</sub>: 259.0820; found: 259.0821.

## Ethyl 3-(2-Amino-5-chlorophenyl)acrylate (3d)

Yield: 75% (92.5 mg); light-yellow solid; mp 79-81 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.33 (t, *J* = 7.2 Hz, 3 H), 4.26 (q, *J* = 7.2 Hz, 2 H), 6.34 (d, *J* = 15.8 Hz, 1 H), 6.66 (d, *J* = 8.6 Hz, 1 H), 7.12 (dd, *J* = 2.4, 15.8 Hz, 1 H), 7.35 (d, *J* = 2.4 Hz, 1 H), 7.72 (d, *J* = 15.8 Hz, 1 H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.3, 60.6, 118.0, 119.4, 121.2, 123.8, 127.3, 130.9, 138.5, 143.7, 166.9.

HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>11</sub>H<sub>12</sub>ClNO<sub>2</sub>: 225.0557; found: 225.0559.

## Ethyl 3-(2-Amino-5-bromophenyl)acrylate (3e)

Yield: 76% (102.4 mg); light-yellow solid; mp 80-82 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.33 (t, *J* = 7.2 Hz, 3 H), 4.26 (q, *J* = 7.2 Hz, 2 H), 6.33 (d, *J* = 15.8 Hz, 1 H), 6.59 (d, *J* = 8.5 Hz, 1 H), 7.24 (d, *J* = 8.6 Hz, 1 H), 7.476–7.482 (m, 1 H), 7.68–7.82 (m, 1 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.3, 60.6, 110.6, 118.2, 119.4, 121.7, 130.2, 133.7, 138.4, 144.3, 166.9.

HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>11</sub>H<sub>12</sub>BrNO<sub>2</sub>: 269.0051; found: 269.0049.

Yield: 93% (97.1 mg); light-yellow solid; mp 79-81 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.33 (t, J = 7.1 Hz, 3 H), 4.26 (q, J = 7.1 Hz, 2 H), 6.33 (d, J = 15.8 Hz, 1 H), 6.66–6.70 (m, 1 H), 6.88–6.93 (m, 1 H), 7.07–7.10 (m, 1 H), 7.77 (d, J = 15.8 Hz, 1 H).

 $^{13}C$  NMR (100 MHz, CDCl\_3):  $\delta$  = 14.3, 60.6, 113.2, 113.5, 118.1, 118.2, 118.3, 119.4, 138.75, 138.78, 141.2, 155.2, 157.5, 166.9.

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.3, 60.7, 116.2, 119.2, 120.0, 120.6, 120.9, 125.3, 125.4, 127.8, 138.5, 147.8, 166.8.

<sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>):  $\delta$  = 125.7 (m, 1 F).

HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>11</sub>H<sub>12</sub>FNO<sub>2</sub>: 209.0852; found: 209.0850.

#### Ethyl 3-(2-Amino-5-nitrophenyl)acrylate (3g)

Yield: 93% (109.5 mg); yellow solid; mp 136–138 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.35 (t, *J* = 7.2 Hz, 3 H), 4.28 (q, *J* = 7.2 Hz, 2 H), 6.48 (d, 15.8 Hz, 1 H), 6.70 (d, *J* = 9.0 Hz, 1 H), 7.70 (d, *J* = 15.7 Hz, 1 H), 8.05 (dd, *J* = 2.5, 15.7 Hz, 1 H), 8.31 (d, *J* = 2.5 Hz, 1 H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.3, 60.9, 115.4, 118.6, 121.4, 124.5, 126.7, 137.4, 139.4, 150.5, 166.5.

HRMS (EI): m/z [M]<sup>+</sup> calcd for  $C_{11}H_{12}N_2O_4$ : 236.0797; found: 236.0793.

#### Ethyl 3-(2-Amino-5-cyanophenyl)acrylate (3h)

Yield: >99% (107.8 mg); yellow solid; mp 109-111 °C.

<sup>1</sup>H NMR (400 MHz,  $CDCl_3$ ):  $\delta$  = 1.34 (t, *J* = 7.1 Hz, 3 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 6.36 (d, *J* = 15.8 Hz, 1 H), 6.71 (d, *J* = 8.4 Hz, 1 H), 7.38–7.41 (m, 1 H), 7.63–7.69 (m, 2 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.3, 60.9, 115.4, 118.6, 121.4, 124.5, 126.7, 137.4, 139.4, 150.5, 166.5.

HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>: 216.0899; found: 216.0901.

#### Ethyl 3-(2-Amino-4-chlorophenyl)acrylate (3i)

Yield: 88% (107.5 mg); light-yellow solid; mp 79-81 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.33 (t, *J* = 7.1 Hz, 3 H), 4.25 (q, *J* = 7.1 Hz, 2 H), 6.32 (d, *J* = 15.8 Hz, 1 H), 6.73–6.76 (m, 2 H), 7.30 (d, *J* = 8.2 Hz, 1 H), 7.74 (d, *J* = 15.8 Hz, 1 H).

 $^{13}C$  NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 14.3, 60.6, 116.5, 118.59, 118.63, 119.4, 129.2, 136.8, 138.8, 145.9, 167.1.

HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>11</sub>H<sub>12</sub>ClNO<sub>2</sub>: 225.0557; found: 225.0559.

#### Ethyl 3-(2-Amino-4-bromophenyl)acrylate (3j)

Yield: 86% (116.5 mg); light-yellow solid; mp 80-82 °C.

<sup>1</sup>H NMR (400 MHz,  $CDCI_3$ ):  $\delta$  = 1.33 (t, *J* = 7.1 Hz, 3 H), 4.26 (q, *J* = 7.1 Hz, 2 H), 6.33 (d, *J* = 15.8 Hz, 1 H), 6.87–6.89 (m, 2 H), 7.22 (d, *J* = 8.9 Hz, 1 H), 7.71 (d, *J* = 15.8 Hz, 1 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.3, 60.6, 118.7, 118.8, 119.2, 122.0, 125.1, 129.3, 138.9, 146.4, 167.1.

HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>11</sub>H<sub>12</sub>BrNO<sub>2</sub>: 269.0051; found: 269.0049.

#### Ethyl 3-(2-Amino-6-chlorophenyl)acrylate (3k)

Yield: 64% (71.7 mg); light-yellow solid; mp 108-111 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.34 (t, *J* = 7.1 Hz, 3 H), 4.28 (q, *J* = 7.1 Hz, 2 H), 6.46 (d, *J* = 16.5 Hz, 1 H), 6.62 (d, *J* = 8.1 Hz, 1 H), 6.82 (dd, *J* = 7.9, 0.8 Hz, 1 H), 7.03 (t, *J* = 8.0 Hz, 1 H), 7.87 (d, *J* = 16.5 Hz, 1 H).

 $^{13}C$  NMR (100 MHz, CDCl\_3):  $\delta$  = 14.3, 60.7, 114.6, 118.5, 123.4, 130.3, 135.2, 139.6, 146.3, 166.8.

HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>11</sub>H<sub>12</sub>ClNO<sub>2</sub>: 225.0557; found: 225.0556.

# Ethyl 3-(2-Amino-3,5-dichlorophenyl)acrylate (31)

Yield: 98% (127.4 mg); light-yellow solid; mp 89–91 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.34 (t, J = 7.1 Hz, 3 H), 4.27 (q, J = 7.1 Hz, 2 H), 6.35 (d, J = 15.7 Hz, 1 H), 7.27 (dd, J = 10.4, 2.3 Hz, 2 H), 7.69 (d, J = 15.7 Hz, 1 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.3, 60.8, 120.9, 121.9, 122.8, 126.0, 130.2, 138.1, 140.5, 166.5.

HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>11</sub>H<sub>11</sub>ClNO<sub>2</sub>: 259.0167; found: 259.0165.

## Ethyl 3-(2-Amino-3,5-dimethylphenyl)acrylate (3m)

Yield: 84% (92.3 mg); light-yellow solid; mp 70–73 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.33 (t, J = 7.1 Hz, 3 H), 2.16 (s, 3 H), 2.22 (s, 3 H), 4.26 (q, J = 7.1 Hz, 2 H), 6.34 (d, J = 15.7 Hz, 1 H), 6.92 (s, 1 H), 7.09 (s, 1 H), 7.85 (d, J = 15.7 Hz, 1 H).

 $^{13}\text{C}$  NMR (100 MHz, CDCl\_3):  $\delta$  = 14.3, 17.6, 20.3, 60.4, 118.0, 119.6, 123.4, 125.9, 127.4, 133.4, 140.4, 141.3, 167.4.

HRMS (EI): *m*/*z* [M]<sup>+</sup> calcd for C<sub>13</sub>H<sub>17</sub>NO<sub>2</sub>: 219.1259; found: 219.1262.

# Ethyl 3-(3-Aminophenyl)acrylate (3n)

Yield: >99% (97.2 mg); light-yellow oil.

<sup>1</sup>H NMR (400 MHz,  $CDCI_3$ ):  $\delta$  = 1.33 (t, *J* = 7.1 Hz, 3 H), 4.25 (q, *J* = 7.1 Hz, 2 H), 6.37 (d, *J* = 16.0 Hz, 1 H), 6.71 (m, 1 H), 6.82 (m, 1 H), 6.93 (d, *J* = 7.6 Hz, 1 H), 7.16 (t, *J* = 7.8 Hz, 1 H), 7.59 (d, *J* = 16.0 Hz, 1 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 14.3, 60.4, 114.1, 117.1, 118.0, 118.6, 129.7, 135.4, 144.8, 146.6, 167.1.

HRMS (EI): *m*/*z* [M]<sup>+</sup> calcd for C<sub>11</sub>H<sub>13</sub>NO<sub>2</sub>: 191.0946; found: 191.0947.

#### Ethyl 3-(2-Hydroxyphenyl)acrylate (3o)

Yield: 84% (80.4 mg); light-yellow solid; mp 31-33 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 1.35 (t, J = 7.1 Hz, 3 H), 4.30 (q, J = 7.1 Hz, 2 H), 6.64 (d, J = 16.2 Hz, 1 H), 6.85–6.93 (m, 2 H), 7.21–7.26 (m, 1 H), 7.46–7.48 (m, 1 H), 8.04 (d, J = 16.2 Hz, 1 H).

 $^{13}\text{C}$  NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 14.3, 60.7, 116.4, 118.4, 120.7, 121.7, 129.2, 131.4, 140.6, 155.4, 168.5.

HRMS (EI): *m*/*z* [M]<sup>+</sup> calcd for C<sub>11</sub>H<sub>12</sub>O<sub>3</sub>: 192.0786; found: 192.0782.

## Ethyl Cinnamate (3p)

Yield: 88% (77.1 mg); colorless oil.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.34 (t, *J* = 7.1 Hz, 3 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 6.44 (d, *J* = 15.8 Hz, 1 H), 7.37–7.40 (m, 3 H), 7.51–7.54 (m, 2 H), 7.69 (d, *J* = 16.1 Hz, 1 H).

 $^{13}\text{C}$  NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 14.3, 60.5, 118.2, 128.0, 128.8, 130.2, 134.4, 144.6, 167.0.

HRMS (EI): *m*/*z* [M]<sup>+</sup> calcd for C<sub>11</sub>H<sub>12</sub>O<sub>2</sub>: 176.0837; found: 176.0835.

#### Methyl 3-(2-Aminophenyl)acrylate (3t)

Yield: 97% (85.9 mg); light-yellow solid; mp 55-57 °C.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.80 (s, 3 H), 6.36 (d, *J* = 15.8 Hz, 1 H), 6.70 (dd, *J* = 8.1, 0.7 Hz, 1 H), 6.77 (t, *J* = 7.5 Hz, 1 H), 7.13–7.21 (m, 1 H), 7.38 (dd, *J* = 7.8, 1.2 Hz, 1 H), 7.83 (d, *J* = 15.8 Hz, 1 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 51.7, 116.7, 117.6, 118.9, 119.8, 128.1, 131.3, 140.3, 145.5, 167.7.

HRMS (EI): *m*/*z* [M]<sup>+</sup> calcd for C<sub>10</sub>H<sub>11</sub>NO<sub>2</sub>: 177.0790; found: 177.0792.

## tert-Butyl 3-(2-Aminophenyl)acrylate(3u)

Yield: 98% (107.7 mg); light-yellow solid; mp 68-71 °C.

<sup>1</sup>H NMR (400 MHz,  $CDCI_3$ ):  $\delta$  = 1.53 (s, 9 H), 6.28 (d, *J* = 15.8 Hz, 1 H), 6.69 (d, *J* = 8.1 Hz, 1 H), 6.75 (t, *J* = 7.5 Hz, 1 H), 7.15 (m, 1 H), 7.36 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.73 (d, *J* = 15.8 Hz, 1 H).

 $^{13}\text{C}$  NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 28.2, 80.4, 116.6, 118.9, 120.13, 120.19, 128.1, 130.9, 139.0, 145.3, 166.6.

HRMS (EI): *m*/*z* [M]<sup>+</sup> calcd for C<sub>13</sub>H<sub>17</sub>NO<sub>2</sub>: 219.1259; found: 219.1255.

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### Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1590895.

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