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Palladium-Catalyzed Heck Reaction of Aryl Chlorides under Mild Conditions Promoted by Organic Ionic Bases

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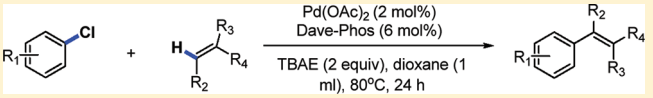
Supporting Information

ABSTRACT: An efficient Pd-catalyzed Heck reaction of aryl chlorides with olefins under mild conditions is described. High yields of products were achieved with *n*-$Bu_4N^+OAc^-$ as base. Significantly, the temperature of the Heck reaction of diverse nonactivated aryl chlorides can be lowered to 80 °C. The new reaction system can also tolerate a wider range of olefins.



The palladium-catalyzed Heck reaction of aryl/vinyl halides with olefins is arguably one of the most important carbon−carbon bond-forming processes in synthetic organic chemistry.[1] Besides the standard aryl halides, various aryl sources such as aryl triflates,[2] diazonium salts,[3] sulfonyl halides,[4] aroyl halides,[5] and aromatic sulfinic acid sodium[6] have been utilized, and highly efficient catalytic systems have been developed. Because aryl chlorides are more readily available and cheaper than other substrates, more attention had been attracted to develop efficient catalyst systems for the Heck reaction of aryl chlorides. Although studies on Heck reaction of both activated aryl chlorides[7] and unactivated aryl chlorides[8] have made significant progress in the past few years, most of these catalytic systems for Heck reaction of unactivated aryl chlorides require relatively harsh conditions (T > 100 °C). Moreover, these reactions are inefficient for the reaction of some aryl chlorides (e.g., 4-chlorobenzaldehyde) with unactivated olefins (e.g., 1,1-disubstituted olefins, 1,2-disubstituted olefins, and alkyl monosubstituted alkenes). Therefore, there is still a need to explore milder and more efficient catalyst systems to improve the scope and utility of the Heck coupling reaction of the aryl chloride substrates.

In 2009, Liu et al. reported that Cu-catalyzed carbon−nitrogen cross-couplings of aryl iodides and aryl bromides could be promoted by organic ionic bases at room temperature.[9] These organic ionic bases are composed of tetraalkylammonium or tetraalkylphosphonium cations and basic anions (e.g., *n*-$Bu_4N^+OAc^-$). In comparison to the traditionally used inorganic bases (e.g., K_3PO_4 and Cs_2CO_3), the organic ionic bases have good solubility and are fully ionized in organic solvents. Therefore, they can show much better performance as compared to the inorganic bases in the transformations carried out in organic solvents. In this context, it should be noted that the choice of base has been found to have a crucial effect on the rate and the yield of Heck reaction.[8c,f] The reason is that reductive elimination of hydrogen halide from the Pd(II) center is the last step in the Heck reaction catalytic cycle to regenerate the Pd(0) catalyst.[10] This step is promoted by the base, and that is why a base must be used in the Heck coupling reaction. As a result, we decided to test the application of the organic ionic bases on the Heck reactions. Herein, we reported an efficient palladium-catalyzed Heck reaction of both unactivated and activated aryl chlorides promoted by an organic ionic base *n*-$Bu_4N^+OAc^-$ (TBAE) under mild conditions. In particular, our reaction temperature can now reach 80 °C for the coupling with unactivated aryl chlorides. To the best of our knowledge, the reaction temperature of 80 °C is the lowest so far reported Heck reaction of unactivated aryl chlorides (see the Supporting Information for a compilation of recently described reaction conditions).[11] Moreover, because of the promotion of the organic ionic base, the new reaction system can tolerate a wider range of olefins as compared to many previously reported systems.

Initially, the reaction conditions were optimized starting from chlorobenzene and styrene catalyzed by $Pd(OAc)_2$ in 1,4-dioxane at 60 °C with various organic ionic bases under Ar as shown in Table 1. It was observed that TBAE gave the best result in 60% yield (Table 1, entries 1−4). Other solvents gave a lower yield (Table 1, entries 5−8). To our surprise, 99% yield of the desired product was obtained when the temperature was increased to 80 °C (Table 1, entry 10), but the yields only ranged from trace to 29% when traditional inorganic bases were used at the same temperature (Table 1, entries 11−13). Comparison of different ligands and catalysts indicated that Dave-Phos was superior to X-Phos and S-Phos (Table 1, entries 14−15) and $Pd(OAc)_2$ was superior to $PdCl_2$ and $Pd_2(dba)_3$ (Table1, entries 16−17). Optimization of the amount of TBAE and styrene showed that an excess of TBAE (2.0 equiv) and styrene (1.5 equiv) (with comparison of 1.0 equiv of aryl halides) are necessary to achieve high yields (Table 1, entries 19 and 20). The reaction was also sensitive to air (Table 1, entry 21).

To explore the scope of the catalytic system, the reaction of different aryl chlorides with styrene were carried out under optimized conditions (2 mol % of $Pd(OAc)_2$, 6 mol % of Dave-Phos, 2 equiv of TBAE, 1,4-dioxane, 80 °C), and the

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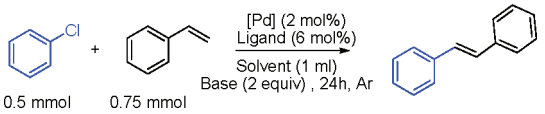
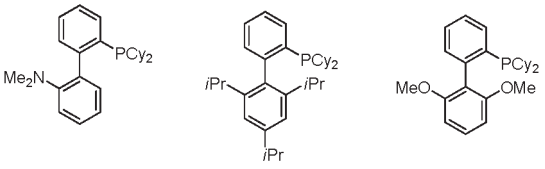
Table 1. Optimization of the Reaction Conditions[a]



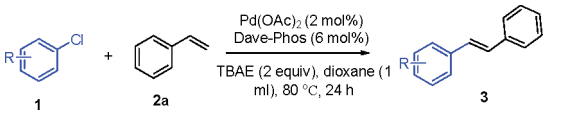
Entry	Cat.	Ligand	Base	Solvent	T/°C	Yield (%)[b]
1	$Pd(OAc)_2$	Dave-Phos	TBPE	1,4-dioxane	60	30
2	$Pd(OAc)_2$	Dave-Phos	TBPM	1,4-dioxane	60	trace
3	$Pd(OAc)_2$	Dave-Phos	TBAP	1,4-dioxane	60	12
4	$Pd(OAc)_2$	Dave-Phos	TBAE	1,4-dioxane	60	60
5	$Pd(OAc)_2$	Dave-Phos	TBAE	toluene	60	11
6	$Pd(OAc)_2$	Dave-Phos	TBAE	THF	60	47
7	$Pd(OAc)_2$	Dave-Phos	TBAE	DMF	60	24
8	$Pd(OAc)_2$	Dave-Phos	TBAE	DMSO	60	18
9	$Pd(OAc)_2$	Dave-Phos	TBAE	1,4-dioxane	70	90
10	**$Pd(OAc)_2$**	**Dave-Phos**	**TBAE**	**1,4-dioxane**	**80**	**99**
11	$Pd(OAc)_2$	Dave-Phos	NaO*t*Bu	1,4-dioxane	80	29
12	$Pd(OAc)_2$	Dave-Phos	Cs_2CO_3	1,4-dioxane	80	5
13	$Pd(OAc)_2$	Dave-Phos	K_3PO_4	1,4-dioxane	80	trace
14	$Pd(OAc)_2$	X-Phos	TBAE	1,4-dioxane	80	92
15	$Pd(OAc)_2$	S-Phos	TBAE	1,4-dioxane	80	73
16	$PdCl_2$	Dave-Phos	TBAE	1,4-dioxane	80	90
17	$Pd_2(dba)_3$	Dave-Phos	TBAE	1,4-dioxane	80	67
18[c]	$Pd(OAc)_2$	Dave-Phos	TBAE	1,4-dioxane	80	64
19[d]	$Pd(OAc)_2$	Dave-Phos	TBAE	1,4-dioxane	80	65
20[e]	$Pd(OAc)_2$	Dave-Phos	TBAE	1,4-dioxane	80	83
21[f]	$Pd(OAc)_2$	Dave-Phos	TBAE	1,4-dioxane	80	trace

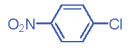
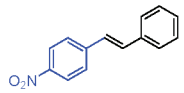
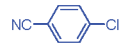
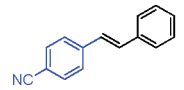
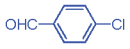
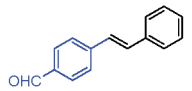
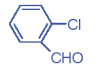
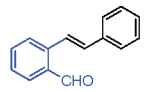
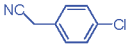
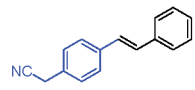
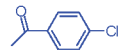
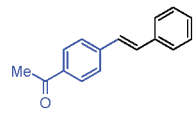
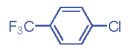
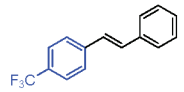
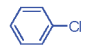
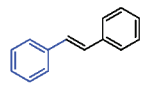
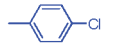
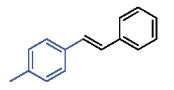
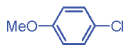
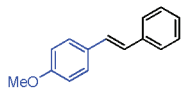
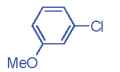
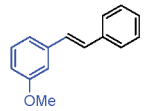


Dave-Phos X-Phos S-Phos

[a] Unless otherwise noted, the reactions were carried out with chlorobenzene (0.5 mmol), styrene (0.75 mmol), base (2.0 equiv), catalyst (2 mol %), ligand (6 mol %), and solvent (1 mL) under Ar for 24 h. [b] Determined by GC. [c] 1 mol % of $Pd(OAc)_2$ and 3 mol % of Dave-Phos were used. [d] With 1.5 equiv of TBAE. [e] 1.2 equiv of styrene was used. [f] Under air. TBPE = tetrabutylphosphonium acetate, TBPM = tetrabutylphosphonium malonate, TBAP = tetrabutylammonium phosphate, Cy = cyclohexyl.

Table 2. Heck Couplings of Different Aryl Chlorides with Styrene[a]



Entry	aryl chloride		Product		Yield (%)[b]
1		1a		3a	98
2		1b		3b	98
3		1c		3c	92
4		1d		3d	95[c]
5		1e		3e	40[c]
6		1f		3f	74
7		1g		3g	55
8		1h		3h	99
9		1i		3i	99
10		1j		3j	95
11		1k		3k	95

[a] Reactions were carried out using Ar-Cl (0.5 mmol) and styrene (0.75 mmol) at 80 °C under Ar for 24 h. [b] Yields are given for isolated products. [c] At 100 °C, 48 h.

results were summarized in Table 2. It was observed that the couplings of activated aryl chlorides with styrene proceeded in excellent yields. The examples include 1-chloro-4-nitrobenzene, 4-chlorobenzonitrile, and 4-chlorobenzaldehyde (**3a**−**c**). Even sterically hindered substrates such as 2-chlorobenzaldehyde were also successfully coupled in excellent yields (**3d**), although a higher temperature and a longer reaction time were required. However, the reaction of 4-chlorobenzyl cyanide, 4-chloroacetophenone, and 4-chlorobenzotrifluoride with styrene only gave moderate yields (**3e**−**g**). Interestingly, reactions of unactivated aryl chlorides bearing a methyl or methoxy group with styrene gave higher yields than activated aryl chlorides (**3i**−**k**).

The reactions of different alkenes with 4-chlorobenzaldehyde were subsequently investigated. It was clear that the reactions of methyl-, ethyl-, n-butyl, and *tert*-butyl acrylate with 4-chlorobenzaldehyde all gave the desired products in excellent yields (**3l**−**o**) in Table 3. Even styrene derivatives also reacted nicely with 4-chlorobenzaldehyde. For example, 4-methystyrene and

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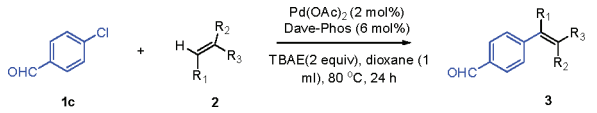
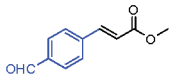
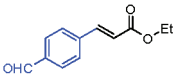
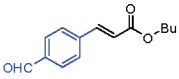
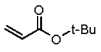
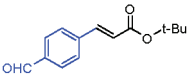
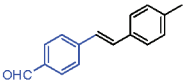
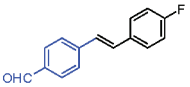
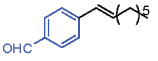
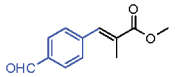
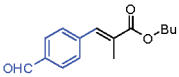
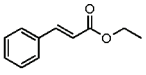
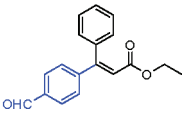
Table 3. Heck Couplings of 4-Chlorobenzaldehyde with Different Olefins[a]



1c 2 3

Entry	olefin		Product		Yield (%)[b]
1		2b		3l	94
2		2c		3m	89
3		2d		3n	96
4		2e		3o	85
5		2f		3p	94
6		2g		3q	95
7		2h		3r	90
8		2i		3s	60
9		2j		3t	51
10		2k		3u	70[c]

[a] Reactions were carried out using 4-chlorobenzaldehyde (0.5 mmol) and olefins (0.75 mmol) at 80 °C under Ar for 24 h. [b] Yields are given for isolated products. [c] At 100 °C, 48 h.

4-flourostyrene, respectively, gave the corresponding products in 94% and 95% yield (**3p**−**q**).

Note that alkyl-substituted terminal olefins are usually found to have low reactivity in the documented Heck reactions.[8j,12] However, it is gratifying that high reactivity was also observed for the coupling of octene with 4-chlorobenzaldehyde (Table 3, entry 7) in our newly developed protocol. Furthermore, 1,1-disubstituted and 1,2-disubstituted olefins also gave moderate yields in this catalytic system (**3s**,**t**).

In summary, we have developed an efficient protocol for the Heck reaction of various aryl chlorides with a wide range of olefins promoted by TBAE under mild conditions. TBAE was shown to play an important role in these processes. High yields were achieved with the organic ionic base. Significantly, the reaction temperature of Heck reaction of unactivated aryl chlorides can be lowered to 80 °C, and 4-chlorobenzaldehyde can also react with various olefins to give desired products with high yields.

EXPERIMENTAL SECTION

Experimental Procedures for Preparing Organic Ionic Bases.[9a] *Tetrabutylphosphonium Malonate (TBPM).* A half-equimolar quantity of malonic acid was allowed to react with aqueous tetra-*n*-alkylphosphonium hydroxide (40%) in water by stirring for 3 h under a nitrogen atmosphere. Dry salts were obtained after evaporation of the solvent and finally dried in vacuo at least 24 h at 50 °C without further purification. The sample was sealed in a vessel under N_2 atmosphere: ^{1}H NMR (300 MHz, D_2O) δ 3.00 (s, 2H), 2.27−1.86 (m, 16H), 1.66−1.15 (m, 32H), 0.82 (t, J = 7.2 Hz, 24H); ^{13}C NMR (75 MHz, D_2O) δ 177.1, 47.6, 23.3 (d, J = 15.2 Hz), 22.7 (d, J = 4.4 Hz), 17.3 (d, J = 48.2 Hz), 12.6.

Tetrabutylammonium Phosphate (TBAP). Phosphoric acid (85%) (3.7028 g, 0.0321 mol) was allowed to react with aqueous tetrabutylammonium hydroxide (25%) (100 g, 0.0964 mol) in water by stirring for 3 h under a nitrogen atmosphere. A white solid was obtained by lyophilization. The product was dried in vacuo for at least 24 h at 30 °C without further purification. The sample was sealed off in a vessel under N_2 atmosphere: ^{1}H NMR (300 MHz, D_2O) δ 3.15−3.10 (m, 24H), 1.63−1.53 (m, 24H), 1.35−1.23 (m, 24H), 0.90−0.85 (t, J = 7.3 Hz, 36H); ^{13}C NMR (75 MHz, D_2O, δ ppm) δ 58.1, 23.1, 19.1, 12.8.

Tetrabutylammonium Acetate (TBAE). KOAc (17.6562 g, 0.1800 mol) was allowed to react with tetrabutylammonium chloride (50 g, 0.1800 mol) in methanol (200 mL) by stirring for 1 day under a nitrogen atmosphere and then passed through a fritted glass filter to remove the inorganic salts (KCl) generated by the ion-exchange reaction. A white solid was obtained by drying in vacuo for at least 24 h at 30 °C without further purification. The sample was sealed off in a vessel under N_2 atmosphere: ^{1}H NMR (300 MHz, D_2O) δ 3.20−2.83 (m, 8H), 1.80 (s, 3H), 1.54 (dt, J = 15.7, 7.9 Hz, 8H), 1.35−1.09 (m, 8H), 0.84 (t, J = 7.3 Hz, 12H); ^{13}C NMR (75 MHz, D_2O) δ 181.1, 58.1, 48.8, 23.1, 19.1, 12.8.

General Procedure for Heck Coupling of Different Aryl Chlorides with Styrene (A). After standard cycles of evacuation and backfilling with dry and pure argon, an oven-dried Schlenk tube equipped with a magnetic stirring bar was charged with $Pd(OAc)_2$ (2 mol %, 2.2 mg), Dave-Phos (6 mol %, 11.8 mg), the aryl chlorides if a solid (0.5 mmol, 1 equiv), and TBAE (1 mmol, 0.301 g). The tube was evacuated and backfilled with argon (this procedure was repeated three times). Under a counter flow of argon, styrene (0.75 mmol, 86 μL), aryl chlorides (if liquid), and 1,4-dioxane (1.0 mL) were added by syringe. The tube was sealed, and the mixture was allowed to stir under argon at 80 °C for 24 h. Upon completion of the reaction, the mixture was diluted with ethyl acetate and filtered through silica gel (which was rinsed with EtOAc), and solvent was removed with the aid of a rotary evaporator. The residue was purified by column chromatography on silica gel and the product was dried under high vacuum for at least 0.5 h.

General Procedure for Heck Coupling of 4-Chlorobenzaldehyde with Different Olefins (B). After standard cycles of evacuation and backfilling with dry and pure argon, an oven-dried Schlenk tube equipped with a magnetic stirring bar was charged with $Pd(OAc)_2$ (2 mol %, 2.2 mg), Dave-Phos (6 mol %, 11.8 mg), 4-chlorobenzaldehyde (0.5 mmol, 70.3 mg), and TBAE (1 mmol, 0.301 g). The tube was evacuated and backfilled with argon (this procedure was repeated three times). Under a counter flow of argon, olefins (0.75 mmol) and 1,4-dioxane (1.0 mL) were added by syringe. The tube was sealed, and the mixture was allowed to stir under argon at 80 °C for 24 h. Upon completion of the reaction, the mixture was diluted with ethyl acetate and filtered through silica gel (which was rinsed with

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EtOAc), and solvent was removed with the aid of a rotary evaporator. The residue was purified by column chromatography on silica gel, and the product was dried under high vacuum for at least 0.5 h.

*(E)-4-Nitrostilbene (**3a**).*[13] Following general procedure A, 1-chloro-4-nitrobenzene (0.5 mmol, 78.8 mg) was allowed to react with styene (0.75 mmol, 86 μL) for 24 h. The product was isolated as a yellow solid (111 mg, 98% yield): mp 154.2−155.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 8.8 Hz, 2H), 7.60 (d, J = 8.8 Hz, 2H), 7.54 (d, J = 7.3 Hz, 2H), 7.41−7.37 (m, 2H), 7.34−7.32 (m, 1H), 7.25 (d, J = 16.3 Hz, 1H), 7.12 (d, J = 16.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.7, 143.8, 136.2, 133.3, 128.9, 128.8, 127.0, 126.8, 126.3, 124.1; EI-MS m/z = 225 (M^+).

*(E)-4-Styrylbenzonitrile (**3b**).*[14] Following general procedure A, 4-chlorobenzonitrile (0.5 mmol, 68.8 mg) was allowed to react with styene (0.75 mmol, 86 μL) for 24 h. The product was isolated as a white solid (101 mg, 98% yield): mp 114.9−115.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51−7.49 (m, 2H), 7.45−7.41 (m, 4H), 7.28 (t, J = 7.4 Hz, 1H), 7.24−7.18 (m, 1H), 7.09 (d, J = 16.3 Hz, 1H), 6.96 (d, J = 16.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.9, 136.3, 132.5, 132.4, 128.9, 128.7, 127.0, 126.9, 126.7, 119.1, 110.6; EI-MS m/z = 205 (M^+).

*(E)-4-Formylstilbene (**3c**).*[14] Following general procedure A, 4-chlorobenzaldehyde (0.5 mmol, 70.3 mg) was allowed to react with styene (0.75 mmol, 86 μL) for 24 h. The product was isolated as a white solid (96 mg, 92% yield): mp 116.0−116.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.97 (s, 1H), 7.85 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 7.2 Hz, 2H), 7.38 (t, J = 7.4 Hz, 2H), 7.32−7.28 (m, 1H), 7.24 (d, qJ = 16.3 Hz, 1H), 7.12 (d, J = 16.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.7, 143.4, 136.6, 135.3, 132.2, 130.3, 128.9, 128.6, 127.4, 126.9; EI-MS m/z = 208 (M^+).

*(E)-2-Formylstilbene (**3d**).*[15] Following general procedure A, 2-chlorobenzaldehyde (0.5 mmol, 70.3 mg) was allowed to react with styene (0.75 mmol, 86 μL) for 48 h. The product was isolated as yellow oil (100 mg, 95% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.30 (s, 1H), 8.03 (d, qq$J$ = 16.2 Hz, 1H), 7.81 (d, J = 8.7 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.57−7.54 (m, 3H), 7.42−7.35 (m, 3H), 7.27−7.30 (m, 1H), 7.03 (d, J = 16.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.7, 140.0, 137.0, 134.0, 133.7, 133.0, 132.4, 128.8, 128.4, 127.7, 127.2, 127.0, 124.8; EI-MS m/z = 208 (M^+).

*(E)-2-(4-Styrylphenyl)acetonitrile (**3e**).*[16] Following general procedure A, 4-chlorobenzyl cyanide (0.5 mmol, 64 μL) was allowed to react with styene (0.75 mmol, 86 μL) for 48 h. The product was isolated as a white solid (44 mg, 40% yield): mp 121.6−122.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53−7.50 (m, 4H), 7.36 (t, J = 7.5 Hz, 2H), 7.32−7.25 (m, 3H), 7.10 (m, 2H), 3.75 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.3, 137.0, 129.6, 129.0, 128.8, 128.3, 127.9, 127.6, 127.2, 126.6, 117.8, 23.4; EI-MS m/z = 219 (M^+).

*(E)-4-Acetylstilbene (**3f**).*[8i] Following general procedure A, 4-chloroacetophenone (0.5 mmol, 64 μL) was allowed to react with styene (0.75 mmol, 86 μL) for 24 h. The product was isolated as a white solid (82 mg, 74% yield): mp 141.3−142.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 7.4 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.32−7.29 (m, 1H), 7.24 (d, J = 16.5 Hz, 1H), 7.13 (d, J = 16.3 Hz, 1H), 2.61 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.4, 142.0, 136.7, 136.0, 131.5, 128.9, 128.8, 128.3, 127.5, 126.8, 126.5, 26.6; EI-MS m/z = 222 (M^+)

*(E)-1-Styryl-4-(trifluoromethyl)benzene (**3g**).*[9b] Following general procedure A, 4-chlorobenzotrifluoride (0.5 mmol, 66.8 μL) was allowed to react with styene (0.75 mmol, 86 μL) for 24 h. The product was isolated as a white solid (68 mg, 55% yield): mp 132.1−133.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.56 (m, 4H), 7.52 (d, J = 7.4 Hz, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.29 (t, J = 7.3 Hz, 1H), 7.18 (d, J = 16.4 Hz, 1H), 7.10 (d, J = 16.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9, 136.7, 131.2, 129.5, 129.1, 128.8, 128.3, 127.2, 126.7, 126.8, 125.7 (q, ^3J (C, F) = 3.7 Hz), 123.0; EI-MS m/z = 248 (M^+).

*(E)-Stilbene (**3h**).*[13] Following general procedure A, chlorobenzene (0.5 mmol, 52 μL) was allowed to react with styene (0.75 mmol) for 24 h. The product was isolated as a white solid (89 mg, 99% yield). Spectral data matched the literature description: mp 123.9−124.6 °C; ^{1}H NMR (400 MHz, CDCl) δ 7.51 (d, J = 7.2 Hz, 4H), 7.37−7.33 (m, 4H), 7.27−7.22 (m, 2H), 7.10 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.4, 128.8, 128.7, 127.7, 126.6; EI-MS m/z = 180 (M^+).

*(E)-4-Methylstilbene (**3i**).*[17] Following general procedure A, 4-methylchlorobenzene (0.5 mmol, 59 μL) was allowed to react with styene (0.75 mmol, 86 μL) for 24 h. The product was isolated as a white solid (96 mg, 99% yield). Spectral data matched the literature description: mp 121.7−122.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.4 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.33 (t, J = 7.6 Hz, 2H), 7.24−7.20 (m, 1H), 7.14 (d, J = 7.9 Hz, 2H), 7.08 (d, J = 16.5 Hz, 1H), 7.03 (d, J = 16.4 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.6, 137.6, 134.6, 129.5, 128.7, 127.8, 127.5, 126.5, 126.5, 21.3; EI-MS m/z = 194 (M^+).

*(E)-4-Methoxystilbene (**3j**).*[17] Following general procedure A, 4-chloroanisole (0.5 mmol, 62 μL) was allowed to react with styene (0.75 mmol, 86 μL) for 24 h. The product was isolated as a white solid (100 mg, 95% yield): mp 135.3−135.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.43 (m, 4H), 7.33 (t, J = 7.6 Hz, 2H), 7.24−7.20 (m, 1H), 7.06 (d, J = 16.3 Hz, 1H), 6.96 (d, J = 16.3 Hz, 1H), 6.89 (d, J = 8.8 Hz, 2H), 3.81 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 137.7, 130.2, 128.7, 128.3, 127.8, 127.3, 126.7, 126.3, 114.2, 55.4; EI-MS m/z = 210 (M^+).

*(E)-3-Methoxystilbene (**3k**).*[17] Following general procedure A, 3-chloroanisole (0.5 mmol, 61 μL) was allowed to react with styene (0.75 mmol, 86 μL) for 24 h. The product was isolated as a white solid (100 mg, 95% yield): mp 31.3−32.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J = 7.3 Hz, 2H), 7.27 (t, J = 7.4 Hz, 2H), 7.22−7.16 (m, 2H), 7.04−6.97 (m, 4H), 6.74 (d, J = 10.1 Hz, 1H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.0, 138.8, 137.3, 129.7, 129.1, 129.7, 128.7, 127.7, 126.6, 119.3, 113.4, 111.8, 55.3; EI-MS m/z = 210 (M^+).

*(E)-Methyl-3-(4-formylphenyl)acrylate (**3l**).*[18] Following general procedure B, 4-chlorobenzaldehyde (0.5 mmol, 70.3 mg) was allowed to react with methyl acrylate (0.75 mmol, 68 μL) for 24 h. The product was isolated as a yellow solid (89.4 mg, 94% yield): mp 82.7−83.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.90 (d, J = 8.0 Hz, 2H), 7.74−7.66 (m, 3H), 6.55 (d, J = 16.0 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 166.8, 143.1, 140.0, 137.2, 130.1, 128.5, 121.0, 51.9; EI-MS m/z = 190 (M^+).

*(E)-Ethyl-3-(4-formylphenyl)acrylate (**3m**).*[19] Following general procedure B, 4-chlorobenzaldehyde (0.5 mmol, 70.3 mg) was allowed to react with ethyl acrylate (0.75 mmol, 82 μL) for 24 h. The product was isolated as a yellow solid (91 mg, 89% yield): mp 39.4−40.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.02 (s, 1H), 7.89 (d, J = 7.3 Hz, 2H), 7.71−7.66 (m, 3H), 6.54 (d, J = 16.1 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.3, 166.2, 142.7, 140.1, 137.1, 130.1, 128.4, 121.4, 60.8, 14.2; EI-MS m/z = 204 (M^+).

*(E)-n-Butyl-3-(4-formylphenyl)acrylate (**3n**).*[14] Following general procedure B, 4-chlorobenzaldehyde (0.5 mmol, 70.3 mg) was allowed to react with *n*-butyl acrylate (0.75 mmol, 108 μL) for 24 h. The product was isolated as a yellow solid (111 mg, 96% yield): mp 35.2−36.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.90 (d, J = 8.1 Hz, 2H), 7.72−7.67 (m, 3H), 6.56 (d, J = 16.1 Hz, 1H), 4.23 (t, J = 6.7 Hz, 2H), 1.74−1.67 (m, 2H), 1.49−1.40 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 166.4, 142.8, 140.1, 137.1, 130.1, 128.5, 121.5, 64.7, 30.7, 19.2, 13.7; EI-MS m/z = 232 (M^+).

*(E)-tert-Butyl-3-(4-formylphenyl)acrylate (**3o**).*[20] Following general procedure B, 4-chlorobenzaldehyde (0.5 mmol, 70.3 mg) was allowed to react with *tert*-butyl acrylate (0.75 mmol, 109 μL) for 24 h. The product was isolated as a blue solid (99 mg, 85% yield): mp 108.7−109.5 °C; ^{1}H

NMR (400 MHz, $CDCl_3$) δ 10.02 (s, 1H), 7.89 (d, J = 8.2 Hz, 2H), 7.67−7.59 (m, 3H), 6.48 (d, J = 16.0 Hz, 1H), 1.55 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 165.6, 141.8, 140.4, 137.0, 130.1, 128.4, 123.4, 81.0, 28.1; EI-MS m/z = 232 (M^+).

*(E)-4-(4-Methylstyryl)benzaldehyde (**3p**).*[21] Following general procedure B, 4-chlorobenzaldehyde (0.5 mmol, 70.3 mg) was allowed to react with 4-methylphenylene (0.75 mmol, 98 μL) for 24 h. The product was isolated as a yellow solid (105 mg, 94% yield): mp 182.1−182.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.85 (d, J = 6.8 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H), 7.25−7.18 (m, 3H), 7.08 (d, J = 16.3 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.6, 143.7, 138.6, 135.2, 133.8, 132.2, 130.2, 129.6, 126.9, 126.8, 126.4, 21.0; EI-MS m/z = 222 (M^+).

*(E)-4-(4-Fluorostyryl)benzaldehyde (**3q**).*[22] Following general procedure B, 4-chlorobenzaldehyde (0.5 mmol, 70.3 mg) was allowed to react with 4-fluorophenylene (0.75 mmol, 89 μL) for 24 h. The product was isolated as a yellow solid (103 mg, 95% yield): mp 119.9−120.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 7.86 (d, J = 8.2 Hz, 2H), 7.63 (d, J = 8.2 Hz, 2H), 7.51 (dd, J = 8.6, 5.4 Hz, 2H), 7.21 (d, J = 16.3 Hz, 1H), 7.10 − 7.02 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.6, 162.8, (d, ^1J (C, F) = 248.8 Hz), 143.3, 135.4, 132.8, 132.8, 130.9, 130.3, 128.5, 128.5, 127.1, 127.1, 126.9, 116.0, 115.8; EI-MS m/z = 226 (M^+).

*(E)-4-(Oct-1-enyl)benzaldehyde (**3r**).*[23] Following general procedure B, 4-chlorobenzaldehyde (0.5 mmol, 70.3 mg) was allowed to react with 1-octene (0.75 mmol, 118 μL) for 24 h. The product was isolated as liquid (97 mg, 90% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 7.79 (d, J = 8.3 Hz, 2H), 7.46 (d, J = 8.3 Hz, 2H), 6.42−6.40 (m, 2H), 2.24 (dd, J = 11.6, 8.3 Hz, 2H), 1.52−1.44(m, 2H), 1.34−1.26 (m, 6H), 0.89 (t, J = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.6, 143.1, 134.4, 133.9, 129.1, 127.9, 125.7, 125.3, 32.2, 30.7, 28.1, 27.9, 21.6, 13.1; EI-MS m/z = 216 (M^+).

*(E)-Methyl-3-(4-formylphenyl)-2-methylacrylate (**3s**).*[7h] Following general B, 4-chlorobenzaldehyde (0.5 mmol, 70.3 mg) was allowed to react with methyl methacrylate (0.75 mmol, 80 μL) for 24 h. The product was isolated as a yellow solid (61 mg, 60% yield): mp 41.2−42.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.91 (d, J = 8.1 Hz, 2H), 7.71 (s, 1H), 7.54 (d, J = 8.1 Hz, 2H), 3.84 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.6, 167.6, 140.9, 136.4, 134.7, 130.0, 129.0, 128.7, 51.3, 13.2; EI-MS m/z = 204 (M^+).

*(E)-Butyl-3-(4-formylphenyl)-2-methylacrylate (**3t**).*[24] Following general procedure B, 4-chlorobenzaldehyde (0.5 mmol, 70.3 mg) was allowed to react with *n*-butyl methacrylate (0.75 mmol, 120 μL) for 24 h. The product was isolated as a yellow liquid (63 mg, 51% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.02 (s, 1H), 7.90 (d, J = 8.0 Hz, 2H), 7.69 (s, 1H), 7.54 (d, J = 7.9 Hz, 2H), 4.23 (t, J = 6.6 Hz, 2H), 2.12 (s, 3H), 1.76−1.67 (m, 2H), 1.51−1.39 (m, 2H), 0.97 (t, J = 7.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.6, 168.2, 142.1, 137.1, 135.6, 131.4, 130.1, 129.7, 126.9, 65.1, 30.7, 19.3, 14.2, 13.8; EI-MS m/z = 246 (M^+).

*(E)-Ethyl-3-(4-formylphenyl)-3-phenylacrylate (**3u**).*[25] Following general procedure B, 4-chlorobenzaldehyde (0.5 mmol, 70.3 mg) was allowed to react with ethyl cinnamate (0.75 mmol, 126 μL) for 48 h. The product was isolated as yellow liquid (98 mg, 70% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.84 (d, J = 8.2 Hz, 2H), 7.48−7.40 (m, 5H), 7.22 (d, J = 2.2 Hz, 2H), 6.43 (s, 1H), 4.07 (q, J = 7.1 Hz, 2H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.7, 165.7, 154.8, 146.7, 138.2, 136.6, 129.7, 129.1, 128.9, 128.5, 128.1, 119.9, 60.4, 14.0; EI-MS m/z = 280 (M^+).

■ ASSOCIATED CONTENT

Supporting Information. References reported of chlorobenzene with styrene and copies of ^{1}H and ^{13}C NMR spectra for the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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