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# Room-Temperature, Ligand- and Base-Free Heck Reactions of Aryl Diazonium Salts at Low Palladium Loading: Sustainable Preparation of Substituted Stilbene Derivatives

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**Abstract:** The $Pd(OAc)_2$-catalyzed Heck reaction of aryl diazonium salts with 2-arylacrylates led to *cis*-stilbenes with good to excellent stereoselectivity. The environmentally friendly protocol developed in this work features low palladium loading in technical-grade methanol at room temperature under base-, additive-, and ligand-free conditions. The same protocol applied to simple Heck coupling of aryl diazonium salts with methyl acrylate allows astonishingly low palladium loading, down to 0.005 mol%. The stereoselectivity experimentally observed for the synthesis of *cis*-stilbenes has been rationalized by DFT calculations. Moreover, the role of methanol in promoting the reaction has been clarified by a computational study.

**Keywords:** diazo compounds · density functional calculations · Heck reaction · palladium · sustainable chemistry

## Introduction

The Mizoroki–Heck reaction, arguably one of the most important methods for the creation of carbon–carbon bonds, allows the coupling of aryl or vinyl halides with olefins.[1] Since its discovery in the early 1970s,[2] an impressive amount of work has been devoted to its development that culminated in industrial applications.[3]

A variant of this coupling, involving the use of aryl diazonium salts as aryl halide surrogates and known as the Matsuda–Heck reaction,[4] has been much less explored in spite of several advantages including energy, cost, and waste benefits. Indeed, the high reactivity of diazonium salts, which can be classified as "super-electrophiles" allows coupling under mild conditions (25–70 °C), sometimes under ligand-free and even base-free conditions.[5]

We recently reported a novel approach for the preparation of 3-benzyl-2-oxindoles using a tandem Heck–reduction–cyclization (HRC) sequence catalyzed with a Pd/C catalyst generated in situ[6] under ligand-, base-, and additive-free conditions at only 40 °C. It features a number of advantages to the organic chemist: in particular, the reduced number of operations results in significant atom-economy and waste-generation benefits. As a key step, the HRC process[7] required coupling of aryl diazonium salts with 2-arylacrylates, furnishing functionalized stilbenes. At that time we were not concerned with the stereoselectivity of the reaction, since the newly created double bond was further reduced during the tandem process. Although diazonium salts have been coupled with a variety of olefins including acrylates, styrenes,[8] heterocycles,[9] and others[10] we were surprised to find that the use of 2-arylacrylates has been largely ignored even under classical Heck conditions.[11]

Here we present our results on the palladium-catalyzed coupling of aryl diazonium salts with acrylates with a special emphasis on 2-arylacrylates. Experimental conditions were carefully optimized in order to decrease the palladium loading and minimize waste and energy costs according to a sustainable approach.[12] Moreover, theoretical calculations were conducted to better understand the high stereoselectivity observed for the formation of *cis*-stilbenes.[13,14]

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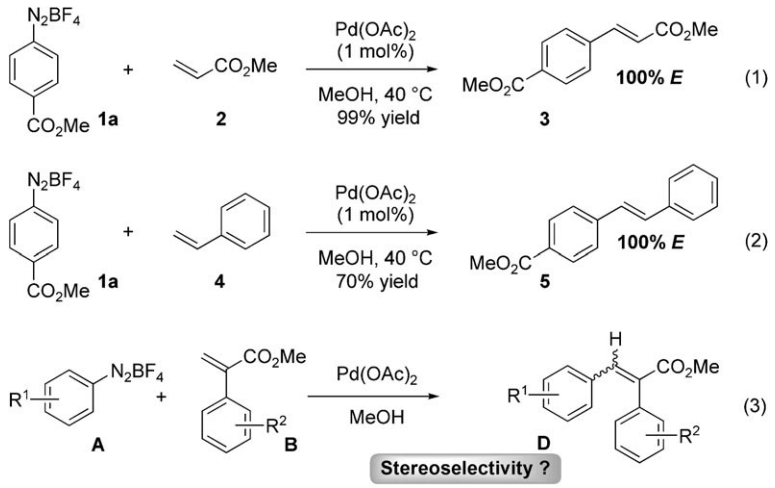
## Results and Discussion

During our previous studies on the Heck reactions of diazonium salts with olefins including acrylate and styrene derivatives,[15] we consistently observed perfect control of the double-bond geometry in favor of the *E* isomers (Scheme 1, Eqs. (1) and (2)). When we began this study we were unable to predict the stereoselectivity of Heck arylation for the synthesis of compounds **D** (Scheme 1, Eq. (3)).



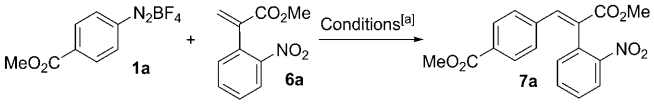

Scheme 1. Heck reactions with aryl diazonium salts.

**Optimization**: Initially, coupling was optimized on a model reaction involving methyl 2-(2-nitrophenyl)acrylate (**6a**) and 4-(methoxycarbonyl)benzenediazonium tetrafluoroborate (**1a**) as coupling partners (Table 1). We arbitrarily started with $Pd(OAc)_2$ as catalyst. With a loading of 1 mol% of palladium at 40°C in technical-grade methanol, the reaction evolved rapidly to give a high yield of the coupled product **7a** (Table 1, entry 1). Although not presented here, the effect of concentration on the reaction outcome was also evaluated. We found that a concentration of 0.2 M is the best compromise in terms of yield and ease of stirring with highly crystalline diazonium salts. Indeed, more diluted conditions (0.1 M) increased the reaction time and diminished the yield (<90%), while concentrated solutions (0.5 M) were problematic for magnetic stirring (diazonium salts are highly crystalline) and would require mechanical stirring.

At 40°C the palladium loading could be reduced to 0.50 mol% with consistent activity (Table 1, entry 2), but a further decrease to 0.25 mol% gave incomplete conversion (Table 1, entry 3). Surprisingly, when the temperature was raised to 60°C, the reaction suddenly stopped after 30 min with formation of palladium black and conversion was incomplete (Table 1, entry 4). We explained that result in terms of rapid aggregation into large colloids of unstable palladium(0) nanoparticles under ligand-free conditions. This assumption was confirmed by the observation that under milder conditions (25°C) a high yield of **7a** was obtained with only 0.25 mol% palladium and no observable formation of palladium black (Table 1, entry 5). A further decrease of the palladium loading to 0.10 mol% (Table 1, entry 6) and even 0.05 mol% (Table 1, entry 7) resulted in slightly lower but still remarkable yields (88–89%) due to incomplete conversion (ca. 91–92%). Importantly, we consistently obtained (*E*)-**7a** (corresponding to a *cis*-stilbene) as the sole observable isomer in the $^1H$ NMR spectrum of the crude product. This unanticipated result opens the way for stereoselective preparation of stilbene derivatives under mild conditions (vide infra).

Solvent screening revealed that methanol is the best solvent for this kind of coupling. Other solvents tested, including $CH_3CN$, PhCN, THF, dioxane, and $CH_3COOH$, proved to inhibit completely the reaction (Table 1, entries 8–12). In order to understand the crucial role of the solvent, we performed DFT calculations. We compared the coordination energy of $PhPd^+$ with both the solvent (e.g., MeOH, $CH_3CN$, and THF) and methyl 2-(2-nitrophenyl)acrylate (**6a**).[15] Indeed, the solvent should stabilize the $PhPd^+$ complex enough by coordination but not too much in order to allow reaction with acrylate **6a**. Theoretical results are coherent with the experimental data, since formation of the $PhPd^+$–acrylate complex is exoergic with MeOH, iso-

Table 1. Optimization studies for substrates **1a** and **6a**: variation of palladium source and solvent.




| Entry | Pd source | Loading [mol%] | Solvent | *T* [°C] | *t* [h] | Yield [%][b] |
|---|---|---|---|---|---|---|
| 1 | $Pd(OAc)_2$ | 1 | MeOH | 40 | 0.5 | 95 |
| 2 | $Pd(OAc)_2$ | 0.5 | MeOH | 40 | 0.5 | 98 |
| 3 | $Pd(OAc)_2$ | 0.25 | MeOH | 40 | 5 | (84) |
| 4 | $Pd(OAc)_2$ | 0.25 | MeOH | 60 | 5 | (63) |
| 5 | $Pd(OAc)_2$ | 0.25 | MeOH | 25 | 12 | 98 |
| 6 | $Pd(OAc)_2$ | 0.10 | MeOH | 25 | 12 | 88 |
| 7 | $Pd(OAc)_2$ | 0.05 | MeOH | 25 | 12 | 89 |
| 8 | $Pd(OAc)_2$ | 0.25 | $CH_3CN$ | 25 | 12 | 0 |
| 9 | $Pd(OAc)_2$ | 0.25 | PhCN | 25 | 12 | 0 |
| 10 | $Pd(OAc)_2$ | 0.25 | THF | 25 | 12 | 0 |
| 11 | $Pd(OAc)_2$ | 0.25 | dioxane | 25 | 12 | 0 |
| 12 | $Pd(OAc)_2$ | 0.25 | $CH_3COOH$ | 25 | 12 | 0 |
| 13 | $[Pd_2(dba)_3]$[c] | 0.25 | MeOH | 25 | 12 | (5) |
| 14 | $PdCl_2$ | 0.25 | MeOH | 25 | 12 | 0 |
| 15 | $[\{(C_3H_5)PdCl\}_2]$ | 0.25 | MeOH | 25 | 12 | 0 |
| 16 | $Pd(TFA)_2$[d] | 0.25 | MeOH | 25 | 12 | 85 |
| 17 | $Pd(TFA)_2$ | 0.10 | MeOH | 25 | 12 | 0 |

[a] Arylacrylate **6a** (1 mmol) and aryl diazonium salt **1a** (1.2 mmol) were mixed in MeOH (5 mL) with $Pd(OAc)_2$ and stirred at 25°C for 12 h. [b] Yield of isolated product. Conversion in parentheses. [c] dba = *trans*,*trans*-dibenzylideneacetone. [d] TFA = trifluoroacetate.

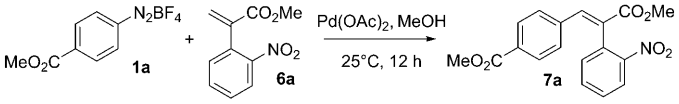
energetic with THF, and endoergic with $CH_3CN$,[17] that is, $PhPd^+$–MeOH can easily dissociate in favor of formation of the $PhPd^+$–acrylate complex. Solvents having considerable coordination energy with $PhPd^+$ such as $CH_3CN$ stabilize too much $PhPd^+$ and inhibit the reaction. On the other hand, we also found that other sources of palladium were not as effective as $Pd(OAc)_2$ under the developed reaction conditions (Table 1, entries 13–17).

We further studied the influence of various additives for their ability to stabilize generated palladium nanoparticles (Table 2). Strong inhibition of coupling was observed when a base was used to trap the $HBF_4$ liberated by the diazonium salt (Table 2, entries 1 and 2). This observation was in sharp contrast with usual Heck reactions, for which a base is mandatory. The use of stabilizing agents for nanosized palladium colloids gave contrasting results.[18] While the use of tetrabutylammonium bromide (TBAB, 1 equiv) clearly prevented any catalytic activity (Table 2, entry 5), PEG-400 (5% w/w) seemed to act as a spectator on the reaction outcome (Table 2, entries 3 and 4).

Lastly, we screened a variety of ligands **L1**–**L7** (Scheme 2) including ferrocenyl phosphines[19] and biphenyl phosphines, with or without the presence of $CaCO_3$ as base. We observed that ligands were at the best only spectators of the reaction outcome but more frequently detrimental for the success of the coupling. We believe that without a base, the phosphine ligands would be rapidly protonated with generation of $HBF_4$, resulting in its inability to stabilize palladium species. In the presence of a base, we consistently observed decreased activity, which could be attributed to the joint effect of the base itself (Table 2, entries 1 and 2) and the phosphine. Indeed, it has been reported that phosphines and phosphites give rise to de-diazonization pathway through formation of aryl free radicals.[20]

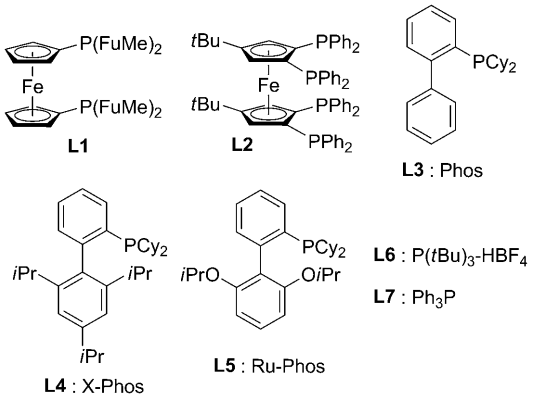
In summary: Heck type reactions with diazonium salts are best performed, in the majority of cases, at room temperature, under base-, ligand- and additive-free conditions in methanol.

Table 2. Optimization studies for substrates **1a** and **6a**: base and ligand variations.[a]




| Entry | Loading [mol%] | Base | Additive | Ligand | Yield [%][b] |
|---|---|---|---|---|---|
| 1 | 0.25 | $CaCO_3$ | – | – | (50) |
| 2 | 0.25 | NaOAc | – | – | 0 |
| 3 | 0.25 | – | PEG-400 | – | 98 |
| 4 | 0.25 | – | PEG-400 | – | 88 |
| 5 | 0.25 | – | TBAB | – | 0 |
| 6 | 0.25 | – | – | **L1** | (50) |
| 7 | 0.25 | $CaCO_3$ | – | **L1** | (30) |
| 8 | 0.25 | – | – | **L2** | 83 |
| 9 | 0.25 | $CaCO_3$ | – | **L2** | (5) |
| 10 | 0.25 | – | - | **L3** | (5) |
| 11 | 0.25 | – | – | **L4** | 91 |
| 12 | 0.10 | – | – | **L4** | 81 |
| 13 | 0.25 | $CaCO_3$ | – | **L4** | (50) |
| 14 | 0.10 | – | – | **L5** | 80 |
| 15 | 0.25 | – | – | **L6** | 0 |
| 16 | 0.25 | $CaCO_3$ | – | **L6** | 0 |
| 17 | 0.25 | – | – | **L7** | (75) |
| 18 | 0.25 | $CaCO_3$ | – | **L7** | (5) |

[a] 2-Acrylacrylate **6a** (1 mmol) and aryl diazonium salt **1a** (1.2 mmol) were mixed in MeOH (5 mL) with $Pd(OAc)_2$ and stirred at 25°C for 12 h. [b] Yield of isolated product. Conversion in parentheses.

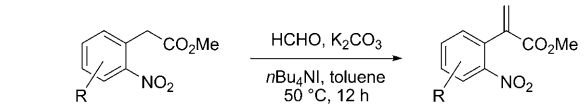



Scheme 2. Ligands screened in the optimization studies. Fu = Furyl.

**Scope**: Substituted 2-arylacrylates **6a**–**6k** employed in this study were easily accessed by methylenation of the corresponding methyl phenylacetates (Table 3). These compounds proved to be stable for months when stored in the freezer (−20°C), except compound **6i**, for which we detected a tendency to polymerization.

Having successfully optimized the coupling on a model reaction, we next explored its scope with various coupling partners (Table 4). Initially, we selected 2-arylacrylates

Table 3. Preparation of 2-arylacrylates.



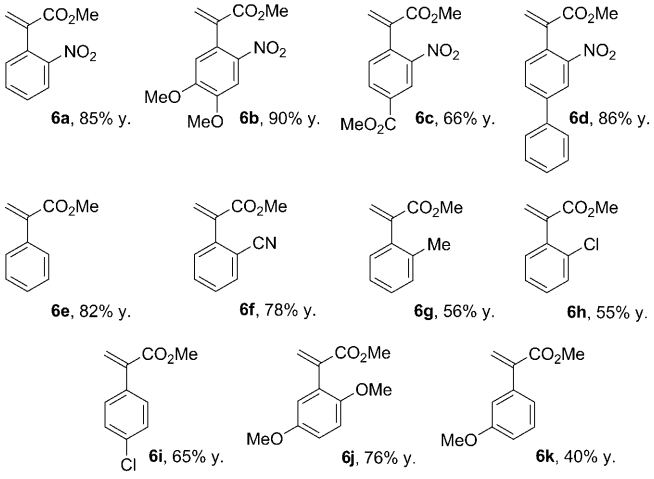
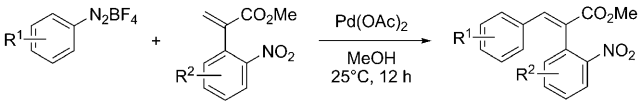



Table 4. Preparation of variously substituted stilbenes by Heck-type coupling.[a]



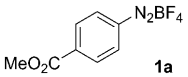
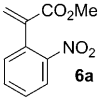
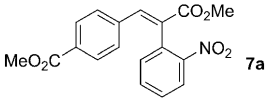
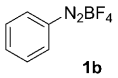
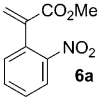
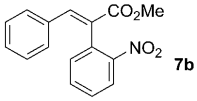
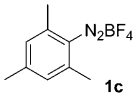
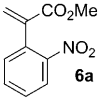
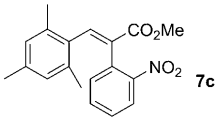
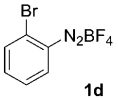
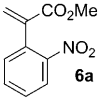
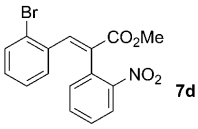
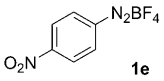
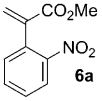
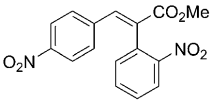
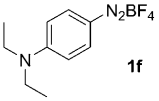
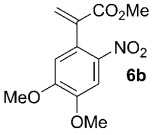
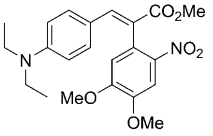
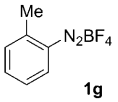
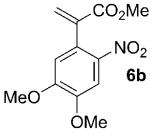
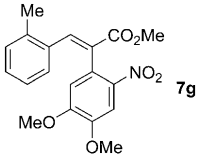
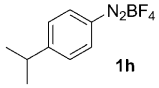
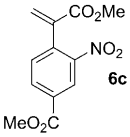
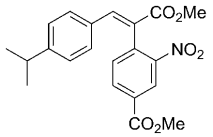
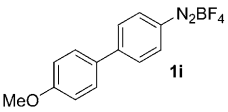
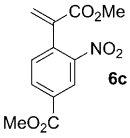
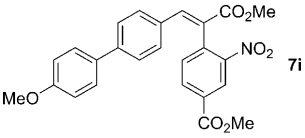
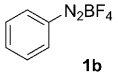
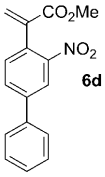
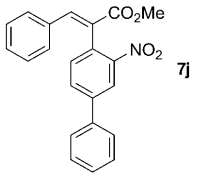
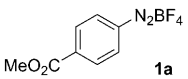
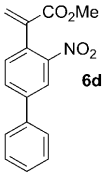
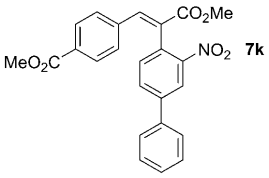
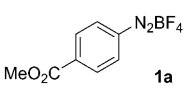
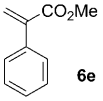
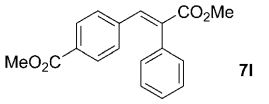
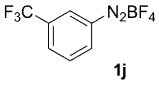
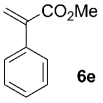
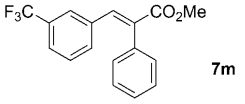
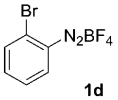
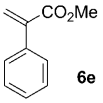
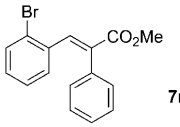
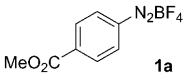
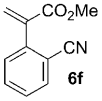
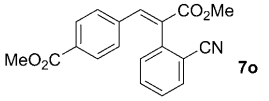
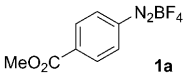
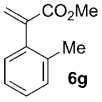
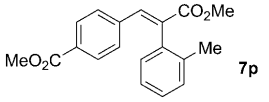
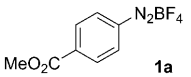
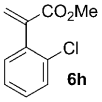
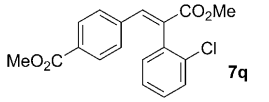
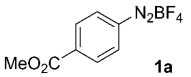
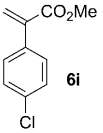
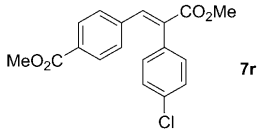
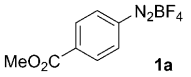
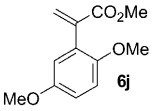
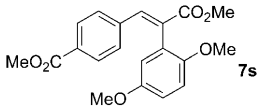
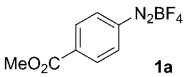
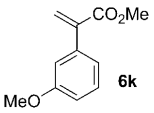
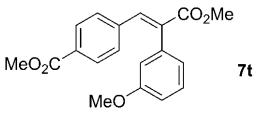

| Entry | Diazonium salt | Olefin | Product | $Pd(OAc)_2$ [mol%] | *E*/*Z* | Yield [%][b] |
|---|---|---|---|---|---|---|
| 1 |  **1a** |  **6a** |  **7a** | 0.25 | >98:2 | 98 |
| 2 |  **1b** |  **6a** |  **7b** | 0.25 | >98:2 | 99 |
| 3 |  **1c** |  **6a** |  **7c** | 0.5 | >98:2 | 52 |
| 4 |  **1d** |  **6a** |  **7d** | 0.25 | >98:2 | 83 |
| 5 |  **1e** |  **6a** |  **7e** | 0.1 | >98:2 | 93 |
| 6 |  **1f** |  **6b** |  **7f** | 0.5 | >98:2 | 98 |
| 7 |  **1g** |  **6b** |  **7g** | 0.5 | >98:2 | 81 |
| 8 |  **1h** |  **6c** |  **7h** | 0.5 | >98:2 | 92 |
| 9 |  **1i** |  **6c** |  **7i** | 0.5 | >98:2 | 93 |
| 10 |  **1b** |  **6d** |  **7j** | 0.5 | >98:2 | 92 |
| 11 |  **1a** |  **6d** |  **7k** | 0.5 | >98:2 | 95 |

Table 4. (Continued)

| Entry | Diazonium salt | Olefin | Product | $Pd(OAc)_2$ [mol%] | *E*/*Z* | Yield [%][b] |
|---|---|---|---|---|---|---|
| 12 |  **1a** |  **6e** |  **7l** | 0.5 | 80:20 | 86 |
| 13 |  **1j** |  **6e** |  **7m** | 0.5 | 80:20 | 81 |
| 14 |  **1d** |  **6e** |  **7n** | 0.5 | 85:15 | 88 |
| 15 |  **1a** |  **6f** |  **7o** | 0.9 | >98:2 | 73 |
| 16 |  **1a** |  **6g** |  **7p** | 0.5 | 95:5 | 97 |
| 17 |  **1a** |  **6h** |  **7q** | 0.25 | 97:3 | 89 |
| 18 |  **1a** |  **6i** |  **7r** | 0.5 | 85:15 | 91 |
| 19 |  **1a** |  **6j** |  **7s** | 0.5 | 96:4 | 92 |
| 20 |  **1a** |  **6k** |  **7t** | 1.5 | 86:14 | 74 |

[a] 2-Acrylacrylate **6a** (1 mmol) and aryl diazonium salt **1a** (1.2 mmol) were mixed in MeOH (5 mL) with $Pd(OAc)_2$ and stirred at 25 °C for 12 h. [b] Yield of isolated product.

having a nitro group on the aromatic ring at C2, since they are valuable synthetic intermediates for the preparation of oxindoles and related heterocycles.[6] As anticipated, the coupling proceeded at low catalyst loading (0.1–0.5 mol%) under mild conditions (25 °C) to furnish *cis*-stilbenes with perfect control of the double-bond geometry (Table 4, entries 1–10). Interestingly, the high stereoselectivity observed does not seem to be related to any stereoelectronic effect on the acrylate or the diazonium salt. Moreover, even highly congested stilbenes such as **7c** were isolated exclusively in their *E* form; the modest yield in this case (Table 4, entry 3) is attributed to the low reactivity of mesityl diazonium salt **1c** leading to incomplete conversion. The *E* geometry of *cis*-stilbenes prepared in this study was assigned by means of the $^1$H NMR shift of the olefinic proton at ~8 ppm (vs. ca. 7 ppm for the *Z* isomer). Moreover, this assignment was confirmed by X-ray analysis of **7c** (Figure 1).

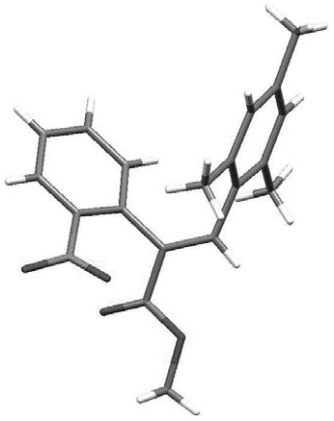


Figure 1. X-ray crystal structure of **7c**.

To extend the scope of this method, we studied a variety of 2-arylacrylates that do not bear a nitro group on the aro-

matic ring at C2. We were surprised to find that 2-arylacrylates **6e**, **6i**, and **6k** led to a less selective reaction giving an isomeric mixture of stilbenes ($E/Z \approx 80/20$) whatever the position of the substituents on the diazonium salt counterpart (Table 4, entries 12–14, 18, 20). On the other hand, 2-chloro-, 2-cyano-, 2-methyl-, and 2,5-dimethoxy-2-phenylacrylates gave *cis*-stilbenes in high isomeric purity (Table 4, entries 15–17, 19), while reactions of 4-chloro-, and 3-methoxy-2-phenylacrylates were less selective (Table 4, entries 18 and 20).

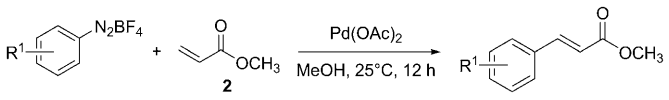
A careful analysis of all these couplings led to the establishment of an unanticipated rule. 2-Arylacrylates having at least one substituent on the aromatic ring at C2 react with diazonium salts under palladium catalysis to give almost exclusively *cis*-stilbenes. Moreover, additional experiments, not shown in Table 4, showed that the *E*/*Z* ratio was not dependent on the palladium loading. These results could be extremely relevant for medicinal purposes, since compounds **7a**–**7t** can all be viewed as synthetic analogues of the anticancer natural products Combretastatin A1 and A4.[21]

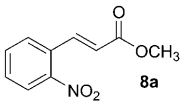
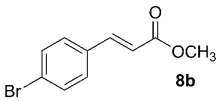
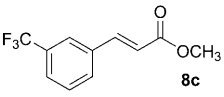
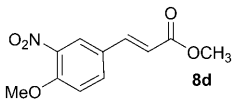
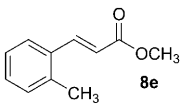
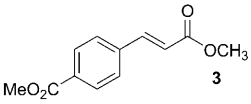
Although the primary interest of this work focused on the preparation of stilbenes, we also examined our conditions for simple Heck-type reactions involving methyl acrylate (**2**) and diazonium salts for comparison with substrates usually screened in the literature (Table 5). We were surprised to find that astonishingly low palladium loading could be used (0.005–0.05 % Pd) at room temperature in methanol. Such low loadings have no literature precedent under base-, ligand-, and additive-free conditions.

These results highlight the prodigious reactivity of diazonium salts under palladium catalysis in methanol. This is all the more relevant since most aryl diazonium tetrafluoroborate salts are very stable in crystalline form (for several years at −20 °C) and many are now commercially available. Such an approach allows the development of a more environmental friendly chemistry with significant atom economy and waste reduction.

As previously demonstrated,[6] 2-(2-nitrophenyl)acrylates are valuable synthetic intermediates for the preparation of oxindoles (Table 6). Indeed, when treated with Pd/C under $H_2$ (1 atm) stilbenes **7a**, **7c**, and **7j** were smoothly reduced to give the corresponding oxindoles **9a**–**9c** in good yield.

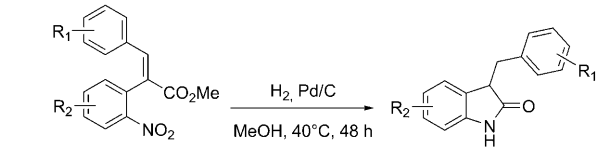
Table 5. Coupling reactions at very low palladium loading.[a]

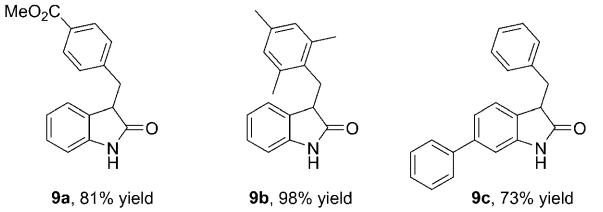



| Entry | Product | Pd [mol %] | Yield [%][b] |
|---|---|---|---|
| 1 |  **8a** | 0.05 | 98 |
| 2 |  **8b** | 0.05 | 98 |
| 3 |  **8c** | 0.01 | 96 |
| 4 |  **8d** | 0.005 | 93 |
| 5 |  **8e** | 0.05 | 81 |
| 6 |  **3** | 0.05 | 93 |

[a] Methyl acrylate (1 mmol) and aryl diazonium salt (1.2 mmol) were mixed in MeOH (5 mL) with $Pd(OAc)_2$ and stirred at 25 °C for 12 h. [b] Yield of isolated product.

Table 6. Preparation of oxindoles from stilbenes.

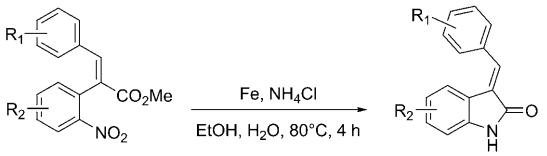


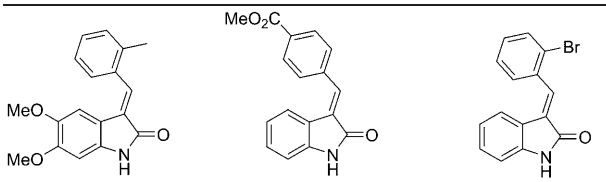




**9a**, 81% yield **9b**, 98% yield **9c**, 73% yield

On the other hand, selective reduction of the nitro group led to novel arylidenoxindoles with perfect control of the double-bond geometry (Table 7). A brief survey of literature precedents showed that these compounds are important synthetic intermediates for the preparation of alkaloids and biologically active compounds, such as those shown in Scheme 3.[22] Moreover, recent papers testify to the growing interest in arylidenoxindoles by medicinal chemists in oncology.[23]

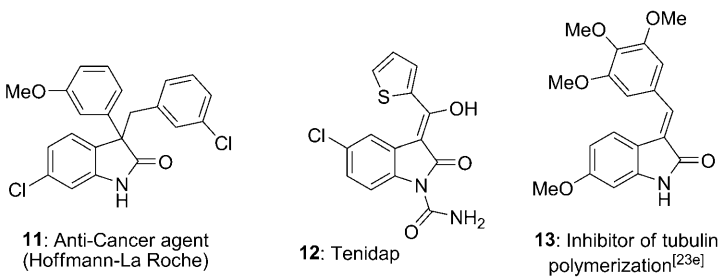
Table 7. Preparation of arylidenoxindoles from stilbenes




**10a**, 98% yield **10b**, 45% yield **10c**, 60% yield

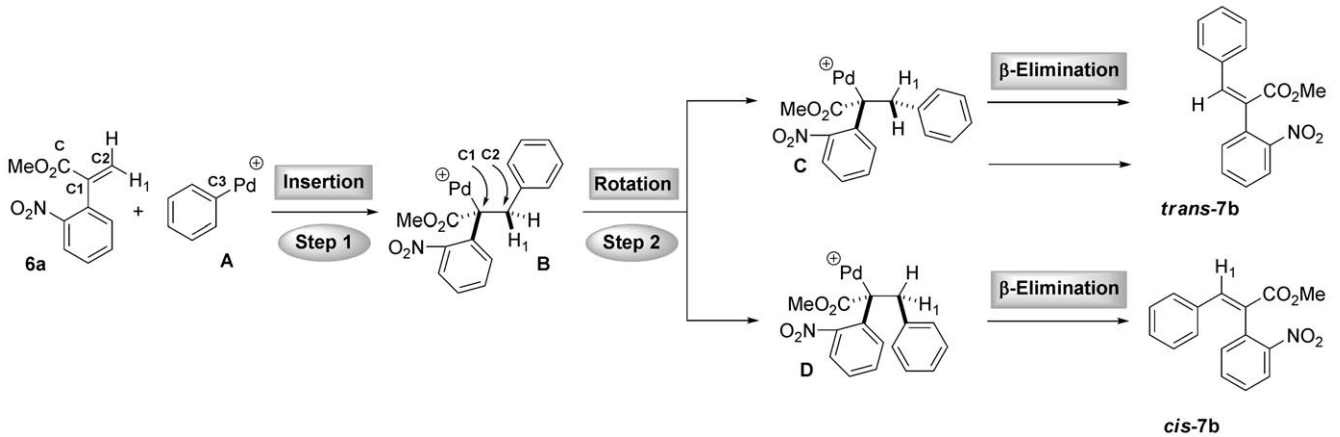



Scheme 3. Representative oxindole-containing biologically active compounds.

**Computational study**: A computational study was undertaken on a model reaction to understand the stereoselectivity observed. We assumed that the arylation of **6a** with diazonium salts proceeds in two important steps: 1) *cis* addition of $PhPd^+$ (**A**) to acrylate **6a** and 2) rotation around the C1–C2 bond followed by PdH *syn* β-elimination to give stilbenes *trans*-**7b** or *cis*-**7b** (Scheme 4).

Two energy profiles based on two conformations of intermediate **B** were studied according to the position of the $NO_2$ substituent on the phenyl group [*ortho* (o, Figure 2) or *ortho′* (o′, Figure 3)]. The reaction starts with formation of π-PdPh complex $\mathbf{1}_{NO2}$ (o and o′), in which the C1–C2 and Pd–C1/C2 bond lengths are respectively about 1.4 and 2.2 Å.[24] We calculated that the first step (Step 1), corresponding to *cis* addition of **A** to acrylate **6a** has small activation barriers for $\mathbf{1TS}_{NO2o}$ and $\mathbf{1TS}_{NO2o'}$ of 11.4 kcal mol$^{-1}$ (Figure 2) and 5.8 kcal mol$^{-1}$ (Figure 3) to give respectively $\mathbf{2}_{NO2o}$ and $\mathbf{2}_{NO2o'}$. In complexes $\mathbf{2}_{NO2o}$ and $\mathbf{2}_{NO2o'}$, the C2–C3 bond is definitively formed (C2–C3: 1.5 Å vs. 2.7–3 Å in $\mathbf{1}_{NO2o'}$). The second step requires either a clockwise or an anticlockwise rotation around the C1–C2 bond followed by migration of a benzylic hydrogen atom (H or $H^1$) on palladium to give the pro-*cis* ($\mathbf{2TS}^{c}_{NO2}$) or the pro-*trans* ($\mathbf{2TS}^{t}_{NO2}$) complex.[25] Our calculations on the two energy profiles (Figures 2 and 3) unambiguously show that this process (i.e., rotation around C1–C2 followed by H migration) is the limiting step of the reaction with the highest activation barrier. Whatever the conformation of the phenyl ring bearing the nitro group, the lower activation barrier is predicted for structures in the transition state having the two phenyl groups in a *cis* relation and leading to the corresponding *cis*-stilbene (25.7 vs. 28.2 kcal mol$^{-1}$ in Figure 2 or 23.0 vs. 26.5 kcal mol$^{-1}$ in Figure 3). It is also noteworthy that all of the cationic Pd complexes (minima or TSs) involved in Figure 3 are far more stable than their analogues presented in Figure 2, by 12–23 kcal mol$^{-1}$ (see Table 8 in the Supporting Information). This interesting observation can be explained by the short Pd–O distance and $n_O \rightarrow 4d(Pd)$ stabilizing interactions in the NBO calculations of conformations reported in Figure 3 compared to conformations in which the $NO_2$ group has no influence (Figure 2). Therefore, the high *E* selectivity (leading to the *cis*-stilbene) experimentally observed with acrylates bearing a $NO_2$ group at the *ortho* position can be rationalized by our calculations. The Pd–O interaction also contributes to favor the discrimination of $\mathbf{2TS}^{t}_{NO2}$ and $\mathbf{2TS}^{c}_{NO2}$ ($\Delta G = 3.5$ kcal mol$^{-1}$, Figure 3 vs. $\Delta G =$ 2.5 kcal mol$^{-1}$, Figure 2).

Since all of these results were obtained in the gas phase, the role of methanol in the reaction outcome was also studied. We carried out PCM calculations considering methanol, acetonitrile, tetrahydrofuran for the energy profile with the $NO_2$ group at the ortho′ position (Figure 2). PCM calculations show clearly that the presence of methanol better promotes the two steps of the reaction (Steps 1 and 2) than acetonitrile and THF (see Figure 6 in the Supporting Information) and strongly diminishes the activation barrier of the second step (by around half), which is the limiting step in the gas-phase calculations. These data confirm that the solvent helps the reaction to occur. As previously described, the formation of the palladium acrylate complex is more or less favored by the solvent.[1,17] Thus, both stabilization of the palladium acrylate complex and the low activation energy for H migration from carbon to palladium play a role in the feasibility of the reaction. For methanol, these two factors allow the reaction to occur easily.




Scheme 4. Mechanistic interpretation leading to *cis*- and *trans*-stilbenes

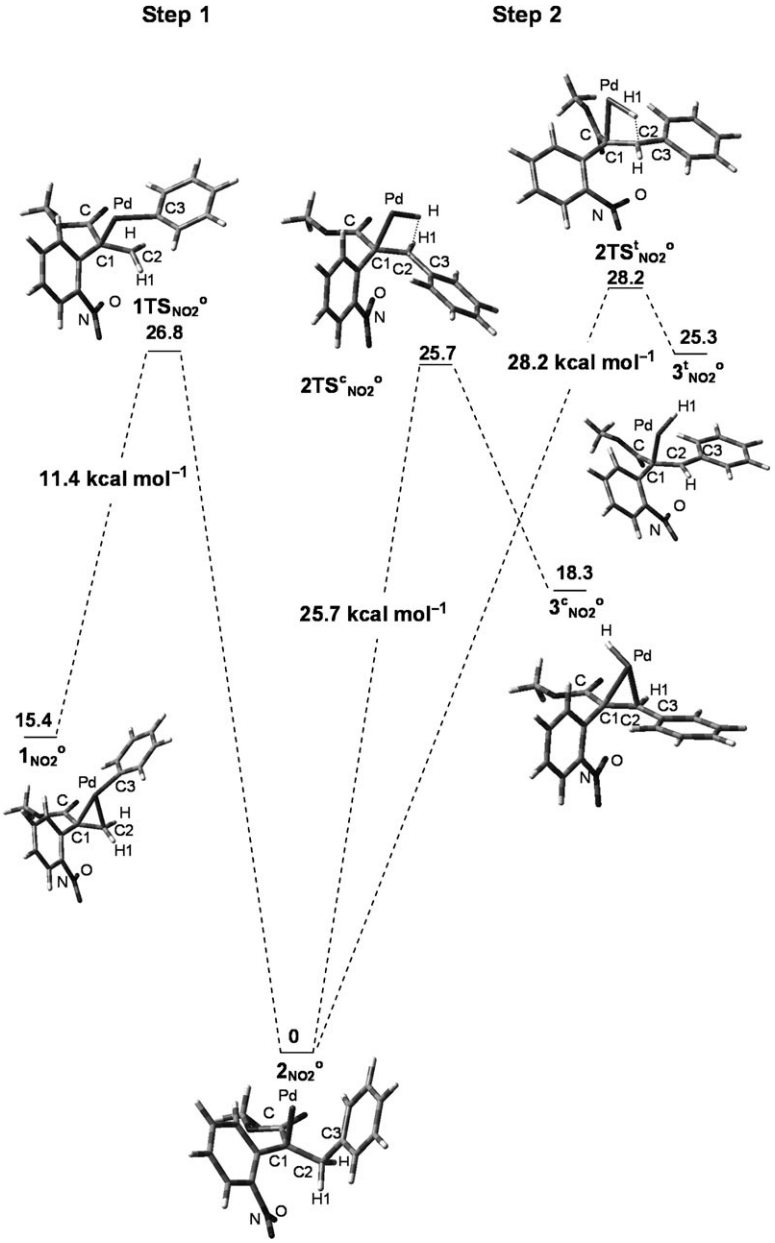



Figure 2. Energy profile in the gas phase ($\Delta G$ in kcal mol$^{-1}$) of the reaction involving the $NO_2$-substituted 2-phenyl-2-nitroacrylate ($NO_2$ group in *ortho* position). Step 1: *cis* addition of the acrylate on $PhPd^+$; Step 2: rotation around the C1–C2 bond, H migration from C2 to Pd leading to a PdH complex. **3$^{c}_{NO2o}$** can be described as a palladium complex involving a three-center interaction, consistent with the short Pd–C1 and Pd–C2 distances and NBO calculations ($4d_{Pd} \rightarrow 2p^{\pi}_{C2}$: 30.1 kcal mol$^{-1}$, $4d_{Pd} \rightarrow 2p^{\pi}_{C1}$: 20.1 kcal mol$^{-1}$, and $\sigma_{C1C2} \rightarrow 4d_{Pd}$: 6.6 kcal mol$^{-1}$).

## Conclusion

We have described highly efficient Heck coupling of aryl diazonium salts with 2-arylacrylates leading to *cis*-stilbenes with good to excellent *E* stereoselectivity. The coupling reported herein features extremely mild conditions and a particularly simple and environmentally friendly experimental protocol at low palladium loading. The high *E* stereoselectivity observed has been explained and discussed on the basis of DFT calculations. Lastly, the synthetic utility of the stilbene derivatives prepared in this work has been evidenced with the synthesis of oxindoles and arylidenoxindoles. We believe that such a simple methodology that fits in with many principles of sustainable chemistry[12] could be of interest for synthetic and medicinal chemists.

## Experimental Section

**General remarks**: Chemical shifts from proton and carbon NMR spectra are reported in ppm relative to the $CDCl_3$ peak at 7.26 ppm ($^1$H) or 77.0 ppm ($^{13}$C). Infrared (IR) spectra were recorded as neat samples on NaCl plates or as KBr pellets. Yields refer to isolated material determined to be pure by NMR spectroscopy and thin layer chromatography (TLC), unless specified otherwise in the text. Diazonium salts used in this study were all known and prepared as described in the literature.

**General procedure for the methylenation of esters (**Table 3**)**: HCHO (28 mmol, 2.8 equiv), $Bu_4NI$ (0.2 mmol, 0.04 equiv), and $K_2CO_3$ (30 mmol, 3 equiv) were added to a solution of ester (10 mmol, 1 equiv) in toluene (13 mL) at room temperature. The resulting mixture was stirred for 12 h at 50 °C. After cooling to room temperature, water (10 mL) was added and the aqueous phase was extracted with toluene (2×20 mL). The collected organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give the corresponding methylene ester, which was purified by flash chromatography.

**Methyl 2-(2-nitrophenyl)acrylate (6a)**: Purification by flash chromatography (25% EtOAc/petroleum ether) gave **6a** as a pale yellow oil (1.76 g, 85% yield). IR (KBr): $\tilde{\nu}$ = 1608, 1730, 2954, 3001 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 250 MHz): $\delta$ = 3.72 (s, 3H), 5.88 (s, 1H), 6.54 (s, 1H), 7.39 (dd, 1H, $J$ = 1.6, 7.5 Hz), 7.53 (dt, 1H, $J$ = 1.6, 8.1 Hz), 7.65 (dt, 1H, $J$ = 1.4, 7.5 Hz), 8.12 ppm (dd, 1H, $J$ = 1.4, 8.1 Hz); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.3, 124.6, 127.5, 129.3, 132.1, 132.9, 133.6, 139.8, 147.8, 165.2 ppm; HRMS (electrospray) calcd for $C_{10}H_9NO_4Na$ [$M$+Na]$^+$: 230.0423, found: 230.0427.

**Methyl 2-(4,5-dimethoxy-2-nitrophenyl)acrylate (6b)**: Purification by flash chromatography (40% EtOAc/petroleum ether) gave **6b** as a yellow solid (2.40 g, 90% yield). M.p. 105 °C; IR (KBr): $\tilde{\nu}$ = 1632, 1726, 2950, 3014, 3068 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 250 MHz): $\delta$ = 3.71 (s, 3H), 3.96 (s, 6H), 5.78 (d, 1H, $J$ = 1.0 Hz), 6.54 (d, 1H, $J$ = 1.0 Hz), 6.73 (s, 1H), 7.71 ppm (s, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.2, 56.4, 56.4, 107.7,

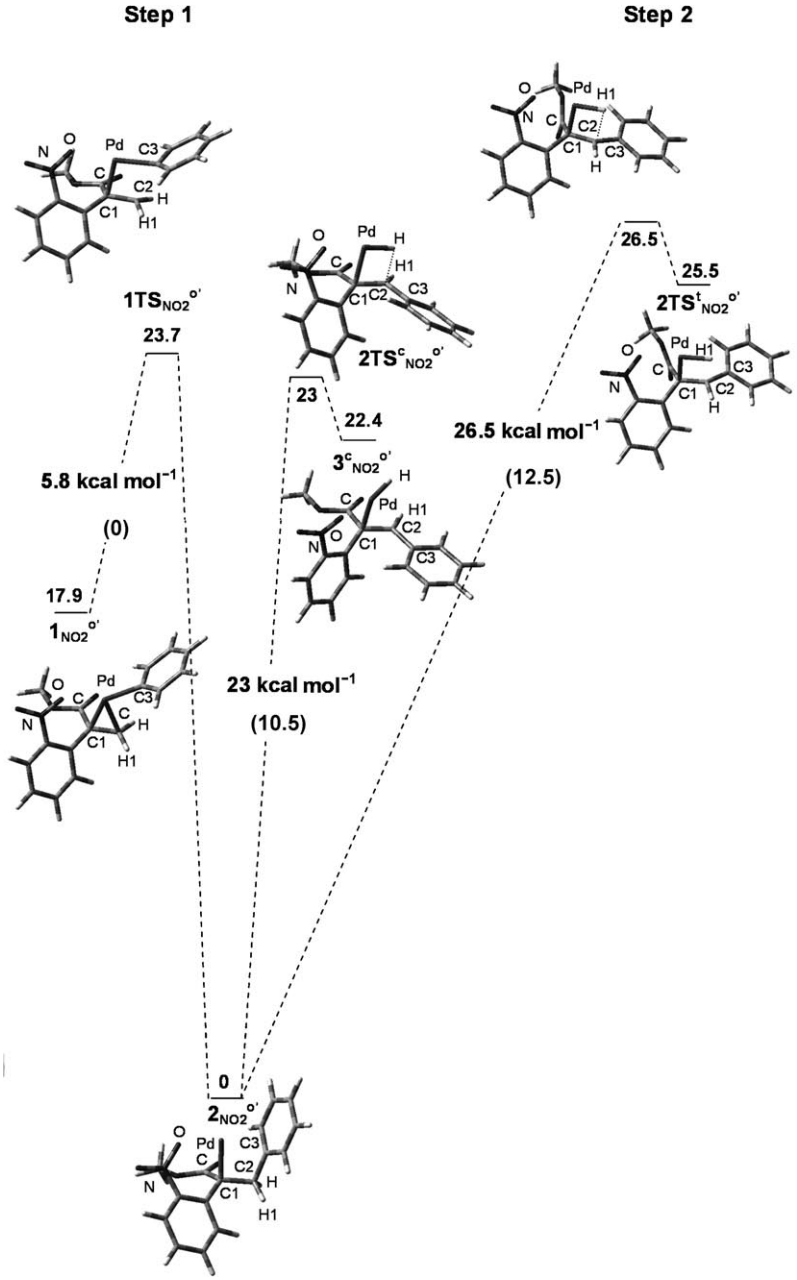



Figure 3. Energy profile in the gas phase ($\Delta G$ in kcal mol$^{-1}$) of the reaction involving the $NO_2$-substituted 2-phenyl-2-nitroacrylate ($NO_2$ group in *ortho*' position). Step 1: *cis* addition of the acrylate on PhPd$^+$. Step 2: rotation around the C1−C2 bond, H migration from C2 to Pd leading to a PdH complex. PCM values are given in parentheses.

113.4, 126.4, 127.5, 140.0, 140.3, 148.7, 153.2, 165.5 ppm; HRMS (electrospray) calcd for $C_{12}H_{13}NO_6Na$ $[M+Na]^+$: 290.0635, found: 290.0633.

**Methyl 2-(4-methoxycarbonyl-2-nitrophenyl)acrylate (6c)**: Purification by flash chromatography (20% EtOAc/petroleum ether) gave **6c** as a white solid (1.75 g, 66% yield). M.p. 55°C; IR (KBr): $\tilde{\nu}$ = 1617, 1731, 2956, 3004, 3092 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 3.71 (s, 3H), 3.97 (s, 3H), 5.93 (s, 1H), 6.59 (s, 1H), 7.48 (d, 1H, $J$ = 7.9 Hz), 8.27 (dd, 1H, $J$ = 1.5, 7.9 Hz), 8.71 ppm (d, 1H, $J$ = 1.5 Hz); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.3, 52.8, 125.6, 128.4, 131.5, 132.4, 134.1, 136.8, 139.0, 147.9, 164.6, 164.7 ppm; HRMS (electrospray) calcd for $C_{12}H_{11}NO_6Na$ $[M+Na]^+$: 288.0478, found: 288.0476.

**Methyl 2-(2-nitro-4-phenylphenyl)acrylate (6d)**: Purification by flash chromatography (6% EtOAc/toluene) gave **6d** as a colorless oil (2.43 g, 86% yield). IR (KBr): $\tilde{\nu}$ = 1614, 1732, 2953, 3032, 3062 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 3.75 (s, 3H), 5.93 (s, 1H), 6.57 (s, 1H), 7.43–7.53 (m, 4H), 7.62–7.64 (m, 2H), 7.85 (dd, 1H, $J$ = 1.9, 7.9 Hz), 8.33 ppm (d, 1H, $J$ = 1.9 Hz); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.3, 128.9, 127.0, 127.5, 128.6, 129.1, 131.3, 131.8, 132.5, 138.0, 139.5, 142.7, 148.2, 165.3 ppm; HRMS (electrospray) calcd for $C_{16}H_{13}NO_4Na$ $[M+Na]^+$: 306.0736, found: 306.0736.

**Methyl 2-phenylacrylate (6e)**: Purification by flash chromatography (5% EtOAc/toluene) gave **6e** as a colorless oil (82% yield). IR (neat): $\tilde{\nu}$ = 1614, 1722, 2953 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 250 MHz): $\delta$ = 3.82 (s, 3H), 5.92 (d, 1H, $J$ = 1.2 Hz), 6.41 (d, 1H, $J$ = 1.4 Hz), 7.35–7.50 ppm (m, 5H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.1, 126.8, 128.0, 128.1, 128.2, 136.6, 141.3, 167.2 ppm.

**Methyl 2-(2-cyanophenyl)acrylate (6f)**: Purification by flash chromatography (25% EtOAc/petroleum ether) gave **6f** as a white solid (1.47 g, 78% yield). M.p. 57°C; IR (KBr): $\tilde{\nu}$ = 1625, 1725, 2228, 2954, 3002, 3069 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 250 MHz): $\delta$ = 3.83 (s, 3H), 5.99 (s, 1H), 6.71 (s, 1H), 7.40 (d, 1H, $J$ = 7.7 Hz), 7.44 (app t, 1H, $J$ = 7.5 Hz), 7.60 (app t, 1H, $J$ = 7.7 Hz), 7.69 ppm (d, 1H, $J$ = 7.7 Hz); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.5, 112.4, 117.7, 128.4, 130.1, 131.4, 132.4, 132.8, 138.5, 140.7, 165.6 ppm; HRMS (electrospray) calcd for $C_{11}H_9NO_2Na$ $[M+Na]^+$: 210.0525, found: 210.0528.

**Methyl 2-(2-methylphenyl)acrylate (6g)**: Purification by flash chromatography (5% EtOAc/petroleum ether) gave **6g** as a colorless oil (986 mg, 56% yield); $^1$H NMR ($CDCl_3$, 200 MHz): $\delta$ = 2.23 (s, 3H), 3.78 (s, 3H), 5.73 (d, 1H, $J$ = 1.6 Hz), 6.54 (d, 1H, $J$ = 1.6 Hz), 7.13–7.33 ppm (m, 4H); $^{13}$C NMR ($CDCl_3$, 50 MHz): $\delta$ = 19.8, 52.2, 125.6, 128.1, 128.6, 129.4, 129.8, 136.1, 137.1, 141.7, 167.1 ppm; HRMS (electrospray) calcd for $C_{11}H_{12}O_2Na$ $[M+Na]^+$: 199.0734, found: 199.0735.

**Methyl 2-(2-chlorophenyl)acrylate (6h)**: Purification by flash chromatography (10% EtOAc/petroleum ether) gave **6h** as a colorless oil (1.08 g, 55% yield). IR (neat): $\tilde{\nu}$ = 1626, 1728, 2845, 2952, 2998, 3002, 3027, 3060 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 3.79 (s, 3H), 5.80 (d, 1H, $J$ = 1.5 Hz), 6.54 (d, 1H, $J$ = 1.1 Hz), 7.26–7.32 (m, 3H), 7.39–7.42 ppm (m, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.3, 126.7, 129.2, 129.3, 129.5, 130.8, 133.3, 136.5, 140.1, 166.4 ppm; HRMS (electrospray) calcd for $C_{10}H_{10}O_2Cl$ $[M+H]^+$: 197.0369, found: 197.0360.

**Methyl 2-(4-chlorophenyl)acrylate (6i)**: Purification by flash chromatography (10% EtOAc/petroleum ether) gave **6i** as a colorless oil (1.28 g, 65% yield). IR (neat): $\tilde{\nu}$ = 1615, 1724, 2845, 2953, 2999, 3032 cm$^{-1}$;

$^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 3.82 (s, 3H), 5.90 (s, 1H), 6.39 (s, 1H), 7.31–7.38 ppm (m, 4H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.3, 127.3, 128.3, 129.6, 134.2, 135.1, 140.1, 166.8 ppm; HRMS (electrospray) calcd for $C_{10}H_9O_2NaCl$ $[M+Na]^+$: 219.0183, found: 219.0182.

**Methyl 2-(2,5-dimethoxyphenyl)acrylate (6j)**: Purification by flash chromatography (20% EtOAc/petroleum ether) gave **6j** as a white solid (1.69 g, 76% yield). M.p. 52°C; IR (KBr): $\tilde{\nu}$ = 1626, 1715, 2835, 2956, 3005 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 3.74 (s, 3H), 3.76 (s, 3H), 3.78 (s, 3H), 5.75 (d, 1H, $J$ = 1.4 Hz), 6.28 (d, 1H, $J$ = 1.4 Hz), 6.78–6.85 ppm (m, 3H); $^{13}$C NMR ($CDCl_3$, 50 MHz): $\delta$ = 52.0, 55.7, 56.3, 111.9, 114.1, 116.0, 126.5, 127.8, 139.6, 151.1, 153.5, 167.7 ppm; HRMS (electrospray) calcd for $C_{12}H_{14}O_4Na$ $[M+Na]^+$: 245.0784, found: 245.0784.

**Methyl 2-(3-methoxyphenyl)acrylate (6k)**: Purification by flash chromatography (10% EtOAc/petroleum ether) gave **6k** as a yellow oil (768 mg, 40% yield). IR (neat): $\tilde{\nu}$ = 1600, 1724, 2837, 2952, 3001 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 3.83 (s, 6H), 5.90 (s, 1H), 6.37 (s, 1H), 6.87–6.91 (m, 1H), 6.96–7.02 (m, 2H), 7.28 ppm (app t, 1H, $J$ = 7.9 Hz); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.2, 55.2, 113.7, 114.0, 120.7, 127.0, 129.1, 138.0, 141.1, 159.2, 167.1 ppm; HRMS (electrospray) calcd for $C_{11}H_{12}O_3Na$ $[M+Na]^+$: 215.0678, found: 215.0678.

**General procedure for the Heck cross-coupling reaction (Table 4)**: Acrylate (1 mmol) and $Pd(OAc)_2$ (0.1–1.5 mol%, see Table 4) were added to a solution of diazonium salt (1.2 mmol) in MeOH (2.5 mL) at 25°C. The resulting mixture was stirred for 12 h at 25°C and then concentrated under reduced pressure. The crude product was purified by flash chromatography to give the corresponding product.

**Methyl (2*E*)-2-(2-nitrophenyl)-3-(4-methoxycarbonylphenyl)acrylate (7a)**: The crude product was purified by flash chromatography (30% EtOAc/petroleum ether) to give **7a** as a white solid (334 mg, 98% yield). M.p. 80°C; IR (KBr): $\tilde{\nu}$ = 1633, 1717, 1733, 2846, 2904, 2953, 3001, 3033, 3068 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 200 MHz): $\delta$ = 3.75 (s, 3H), 3.85 (s, 3H), 7.06 (d, 2H, $J$ = 8.3 Hz), 7.11–7.15 (m, 1H), 7.46–7.59 (m, 2H), 7.82 (d, 2H, $J$ = 8.4 Hz), 7.94 (s, 1H), 8.19–8.27 ppm (m, 1H); $^{13}$C NMR ($CDCl_3$, 50 MHz): $\delta$ = 52.2, 52.6, 125.0, 129.5, 129.5, 129.9, 130.3, 131.4, 132.1, 132.5, 133.9, 138.4, 138.7, 148.6, 165.9, 166.3 ppm; HRMS (electrospray) calcd for $C_{18}H_{15}NO_6Na$ $[M+Na]^+$: 364.0791, found: 364.0792.

**Methyl (2*E*)-2-(2-nitrophenyl)-3-(4-methoxycarbonylphenyl)acrylate (7b)**: The crude product was purified by flash chromatography (20% EtOAc/petroleum ether) to give **7b** as a white solid (280 mg, 99% yield). M.p. 99–100°C; IR (KBr): $\tilde{\nu}$ = 1525, 1628, 1708, 2952, 3023, 3073 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 3.75 (s, 3H), 7.00 (d, 2H, $J$ = 9.1 Hz), 7.14–7.22 (m, 4H), 7.50–7.56 (m, 2H), 7.94 (s, 1H), 8.19–8.25 ppm (m, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.4, 124.9, 128.4, 129.2, 129.3, 129.8, 130.2, 132.0, 132.7, 133.8, 133.9, 140.1, 148.8, 166.4 ppm; HRMS (electrospray) calcd for $C_{16}H_{13}NO_4Na$ $[M+Na]^+$: 306.0736, found: 306.0749.

**Methyl (2*E*)-2-(2-nitrophenyl)-3-(2,4,6-trimethylphenyl)acrylate (7c)**: The crude product was purified by flash chromatography (10% EtOAc/petroleum ether) to give **7c** as a white solid (169 mg, 52% yield). M.p. 173°C; IR (KBr): $\tilde{\nu}$ = 1520, 1712, 2855, 2924, 2956 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 2.05 (s, 6H), 2.22 (s, 3H), 3.75 (s, 3H), 6.74 (s, 2H), 6.84 (dd, 1H, $J$ = 1.5, 7.5 Hz), 7.30 (dt, 1H, $J$ = 1.5, 7.5 Hz), 7.38 (dt, 1H, $J$ = 1.5, 7.5 Hz), 8.00 (s, 1H), 8.12 ppm (dd, 1H, $J$ = 1.5, 7.9 Hz); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 19.9, 20.9, 52.3, 124.7, 128.4, 128.8, 130.4, 131.4, 132.4, 132.7, 133.0, 135.8, 137.8, 140.8, 147.9, 165.9 ppm; HRMS (electrospray) calcd for $C_{19}H_{19}NO_4Na$ $[M+Na]^+$: 348.1206, found: 348.1215.

**Methyl (2*E*)-2-(2-nitrophenyl)-3-(2-bromophenyl)acrylate (7d)**: The crude product was purified by flash chromatography (15% EtOAc/petroleum ether) to give **7d** as a white solid (300 mg, 83% yield). M.p. 143°C; IR (KBr): $\tilde{\nu}$ = 1527, 1709, 2956, 3064 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 3.77 (s, 3H), 6.39 (dd, 1H, $J$ = 1.1, 7.5 Hz), 6.95 (t, 1H, $J$ = 7.9 Hz), 7.01–7.09 (m, 2H), 7.38–7.48 (m, 2H), 7.56 (d, 1H, $J$ = 7.9 Hz), 8.05 (s, 1H), 8.16 ppm (dd, 1H, $J$ = 2.3, 6.8 Hz); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.5, 124.6, 127.0, 129.1, 130.1, 130.8, 131.2, 132.6, 132.9, 133.6, 135.2, 139.5, 149.0, 165.6 ppm; HRMS (electrospray) calcd for $C_{16}H_{12}NO_4NaBr$ $[M+Na]^+$: 383.9841, found: 383.9848.

**Methyl (2*E*)-2-(2-nitrophenyl)-3-(4-nitrophenyl)acrylate (7e)**: The crude product was purified by flash chromatography (25% EtOAc/petroleum ether) to give **7e** as a white solid (305 mg, 93% yield). M.p. 118°C; IR (KBr): $\tilde{\nu}$ = 1520, 1711, 2955 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 3.77 (s, 3H), 7.11 (dd, 1H, $J$ = 1.9, 7.1 Hz), 7.18 (d, 2H, $J$ = 8.7 Hz), 7.52–7.62 (m, 2H), 7.96 (s, 1H), 8.03 (d, 1H, $J$ = 9.0 Hz), 8.26 ppm (dd, 1H, $J$ = 1.9, 7.9 Hz); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.8, 123.6, 125.2, 129.9, 130.6, 130.8, 132.3, 133.8, 134.1, 137.1, 140.5, 147.5, 148.7, 165.5 ppm; HRMS (electrospray) calcd for $C_{16}H_{12}N_2O_6Na$ $[M+Na]^+$: 351.0587, found: 351.0580.

**Methyl (2*E*)-2-(2-nitro-4,5-dimethoxyphenyl)-3-(4-*N*,*N*-diethylaminophenyl)acrylate (7f)**: The crude product was purified by flash chromatography (30% EtOAc/1% $Et_3N$/petroleum ether) to give **7f** as a yellow solid (406 mg, 98% yield). M.p. 169°C; IR (KBr): $\tilde{\nu}$ = 1521, 1588, 1702, 2942, 2968 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 1.12 (t, 6H, $J$ = 7.2 Hz), 3.31 (q, 4H, $J$ = 7.2 Hz), 3.71 (s, 3H), 3.82 (s, 3H), 4.02 (s, 3H), 6.42 (d, 2H, $J$ = 9.0 Hz), 6.70 (s, 1H), 6.85 (d, 2H, $J$ = 9.0 Hz), 7.76 (s, 1H), 7.83 ppm (s, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 12.5, 44.3, 52.1, 56.3, 56.4, 107.9, 110.8, 113.8, 120.5, 123.2, 127.7, 132.6, 140.1, 141.0, 148.3, 148.5, 153.5, 167.5 ppm; HRMS (electrospray) calcd for $C_{22}H_{27}N_2O_6$ $[M+H]^+$: 415.1863, found: 415.1871.

**Methyl (2*E*)-2-(2-nitro-4,5-dimethoxyphenyl)-3-(2-methylphenyl)acrylate (7g)**: The crude product was purified by flash chromatography (20% EtOAc/petroleum ether) to give **7g** as a white solid (289 mg, 81% yield). M.p. 50°C; IR (KBr): $\tilde{\nu}$ = 1521, 1718, 2840, 2951 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 2.36 (s, 3H), 3.57 (s, 3H), 3.76 (s, 3H), 3.96 (s, 3H), 6.32 (s, 1H), 6.72 (d, 1H, $J$ = 7.9 Hz), 6.86–6.91 (m, 1H), 7.08–7.15 (m, 2H), 7.74 (s, 1H), 8.04 ppm (s, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 19.9, 52.4, 56.1, 56.3, 103.6, 114.1, 125.7, 126.2, 128.8, 129.1, 130.1, 132.0, 133.7, 137.2, 138.7, 141.4, 148.4, 152.9, 166.4 ppm; HRMS (electrospray) calcd for $C_{19}H_{19}NO_6Na$ $[M+Na]^+$: 380.1104, found: 380.1111.

**Methyl (2*E*)-2-(2-nitro-4-methoxycarbonylphenyl)-3-(4-isopropylphenyl)acrylate (7h)**: The crude product was purified by flash chromatography (20% EtOAc/petroleum ether) to give **7h** as a yellow oil (352 mg, 92% yield). IR (neat): $\tilde{\nu}$ = 1538, 1732, 2958 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 1.17 (d, 6H, $J$ = 7.1 Hz), 2.82 (quint, 1H, $J$ = 7.1 Hz), 3.73 (s, 3H), 3.99 (s, 3H), 6.92 (d, 2H, $J$ = 8.3 Hz), 7.04 (d, 2H, $J$ = 8.3 Hz), 7.33 (d, 1H, $J$ = 7.9 Hz), 7.95 (s, 1H), 8.19 (d, 1H, $J$ = 8.6 Hz), 8.85 ppm (s, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 23.6, 33.9, 52.5, 52.8, 126.0, 126.7, 127.7, 130.5, 131.0, 131.3, 133.2, 134.2, 136.7, 141.0, 148.9, 151.1, 164.8, 166.0 ppm; HRMS (electrospray) calcd for $C_{21}H_{21}NO_6Na$ $[M+Na]^+$: 406.1261, found: 406.1253.

**Methyl (2*E*)-2-(2-nitro-4-methoxycarbonylphenyl)-3-(4-methoxybiphenyl)acrylate (7i)**: The crude product was purified by flash chromatography (20% EtOAc/petroleum ether) to give **7i** as a yellow solid (416 mg, 93% yield). M.p. 148°C; IR (KBr): $\tilde{\nu}$ = 1533, 1601, 1610, 1717, 1729, 2842, 2955, 3012 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ = 3.75 (s, 3H), 3.82 (s, 3H), 3.99 (s, 3H), 6.93 (d, 2H, $J$ = 8.6 Hz), 7.05 (d, 2H, $J$ = 8.3 Hz), 7.33–7.39 (m, 3H), 7.46 (d, 2H, $J$ = 8.7 Hz), 8.00 (s, 1H), 8.19 (dd, 1H, $J$ = 1.5, 7.9 Hz), 8.87 ppm (d, 1H, $J$ = 1.5 Hz); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ = 52.5, 52.8, 55.3, 114.3, 126.1, 126.6, 128.0, 128.4, 130.8, 131.3, 131.7, 132.1, 133.2, 134.2, 136.6, 140.7, 142.0, 148.9, 159.6, 164.7, 165.9 ppm; HRMS (electrospray) calcd for $C_{25}H_{21}NO_7Na$ $[M+Na]^+$: 470.1210, found: 470.1221.

**Methyl (2*E*)-2-(2-nitro-4-phenylphenyl)-3-phenylacrylate (7j)**: The crude product was purified by flash chromatography (10% EtOAc/petroleum) to give **7j** as a cream-colored solid (330 mg, 92% yield). M.p. 149°C; IR (KBr): $\tilde{\nu}$ = 1527, 1703, 2951, 3030, 3067 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 200 MHz): $\delta$ = 3.78 (s, 3H), 7.07–7.12 (m, 2H), 7.18–7.29 (m, 4H), 7.44–7.56 (m, 3H), 7.66–7.79 (m, 3H), 7.99 (s, 1H), 8.48 ppm (d, 1H, $J$ = 2.4 Hz); $^{13}$C NMR ($CDCl_3$, 50 MHz): $\delta$ = 52.5, 123.2, 127.0, 128.4, 128.7, 129.1, 129.3, 129.5, 130.2, 130.5, 131.9, 133.1, 133.9, 137.9, 140.2, 142.3, 149.1, 166.4 ppm; HRMS (electrospray) calcd for $C_{22}H_{17}NO_4Na$ $[M+Na]^+$: 382.1049, found: 382.1047.

**Methyl (2*E*)-2-(2-nitro-4-phenylphenyl)-3-(4-methoxycarbonylphenyl)acrylate (7k)**: The crude product was purified by flash chromatography (20% EtOAc/petroleum ether then 70% $CH_2Cl_2$/petroleum ether) to give **7k** as a white solid (396 mg, 95% yield). M.p. 169°C; IR (KBr): $\tilde{\nu}$ =

1528, 1722, 2951, 2996, 3028, 3047 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 200 MHz): $\delta =$ 3.78 (s, 3H), 3.86 (s, 3H), 7.15 (d, 2H, $J=7.9$ Hz), 7.19 (d, 1H, $J=$ 7.8 Hz), 7.42–7.54 (m, 3H), 7.65 (dd, 2H, $J=1.7$, 8.1 Hz), 7.74 (dd, 1H, $J=1.8$, 7.9 Hz), 7.86 (d, 2H, $J=8.4$ Hz), 7.99 (s, 1H), 8.47 ppm (d, 1H, $J=1.8$ Hz); $^{13}C$ NMR ($CDCl_3$, 50 MHz): $\delta =$ 52.2, 52.6, 123.2, 127.0, 128.7, 129.1, 129.6, 129.8, 130.0, 130.3, 131.8, 132.0, 133.0, 137.8, 138.5, 138.8, 142.7, 149.1, 166.0, 166.3 ppm; HRMS (electrospray) calcd for $C_{24}H_{19}NO_6Na$ $[M+Na]^+$: 440.1104, found: 440.1096.

**Methyl (2*E*)-2-phenylphenyl-3-(4-methoxycarbonylphenyl)acrylate (7l)**: The crude product was purified by flash chromatography (10% EtOAc/petroleum ether) to give **7l** as a white solid (255 mg, 86% yield) in the form of two inseparable isomers (*E*/*Z*: 80/20). M.p. 97°C; IR (KBr): $\tilde{\nu} =$ 1717, 2949, 3032 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta =$ 3.78 (s, 3H×0.2), 3.80 (s, 3H×0.8), 3.86 (s, 3H×0.8), 3.92 (s, 3H×0.2), 7.06 (s, 1H×0.2), 7.09 (d, 2H×0.8, $J=8.3$ Hz), 7.18–7.22 (m, 2H×0.8), 7.34–7.36 (m, 3H× 0.8), 7.34–7.37 (m, 3H×0.2), 7.43 (d, 2H×0.2, $J=8.7$ Hz), 7.46–7.79 (m, 2H×0.2), 7.81 (d, 2H×0.8, $J=8.3$ Hz), 7.86 (s, 1H×0.8), 8.03 ppm (d, 2H×0.2, $J=8.3$ Hz); $^{13}C$ NMR ($CDCl_3$, 50 MHz): $\delta =$ 52.1, 52.1, 52.3, 52.5, 126.5, 128.0, 128.1, 128.7, 128.8, 129.3, 129.6, 129.7, 130.0, 130.2, 130.3, 134.6, 135.2, 136.3, 136.8, 139.1, 140.2, 166.4, 166.6, 167.9, 169.6 ppm; HRMS (electrospray) calcd for $C_{18}H_{16}O_4Na$ $[M+Na]^+$: 319.0940, found: 319.0940.

**Methyl (2*E*)-2-phenylphenyl-3-(3-trifluoromethylphenyl)acrylate (7m)**: The crude product was purified by flash chromatography (10% EtOAc/petroleum ether) to give **7m** as a colorless oil (233 mg, 76% yield) in the form of two inseparable isomers (*E*/*Z*: 80/20). IR (neat): $\tilde{\nu} =$ 1717, 2953, 3026, 3060 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta =$ 3.78 (s, 3H×0.2), 3.81 (s, 3H×0.8), 7.04 (s, 1H×0.2), 7.17–7.21 (m, 3H×0.8), 7.23–7.28 (m, 2H×0.8), 7.36–7.40 (m, 3H×0.8), 7.39–7.50 (m, 6H×0.2), 7.42–7.46 (m, 2H×0.8), 7.53–7.57 (m, 2H×0.2), 7.63 (s, 1H×0.2), 7.85 ppm (s, 1H× 0.8); HRMS (electrospray) calcd for $C_{17}H_{14}O_2F_3$ $[M+H]^+$: 307.0940, found: 307.0948.

**Methyl (2*E*)-2-phenylphenyl-3-(2-bromophenyl)acrylate (7n)**: The crude product was purified by flash chromatography (15% EtOAc/petroleum ether) to give **7n** as a white solid (317 mg, 88% yield). M.p. 143°C; IR (KBr): $\tilde{\nu} =$ 1527, 1709, 2957, 3064 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta =$ 3.77 (s, 3H), 6.75 (d, 1H, $J=7.5$ Hz), 6.95 (t, 1H, $J=7.9$ Hz), 7.02–7.09 (m, 2H), 7.39–7.48 (m, 2H), 7.56 (d, 1H, $J=7.9$ Hz), 8.05 (s, 1H), 8.16 ppm (dd, 1H, $J=2.3$, 6.8 Hz); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta =$ 52.5, 124.6, 127.0, 129.1, 130.1, 130.8, 131.2, 132.6, 132.9, 133.6, 135.2, 139.5, 149.0, 165.6 ppm; HRMS (electrospray) calcd for $C_{16}H_{12}NO_4NaBr$ $[M+Na]^+$: 383.9841, found: 383.9815.

**Methyl (2*E*)-2-(2-cyanophenyl)-3-(4-methoxycarbonylphenyl)acrylate (7o)**: The crude product was purified by flash chromatography (20% EtOAc/petroleum ether) to give **7o** as a yellow oil (234 mg, 73% yield). IR (neat): $\tilde{\nu} =$ 1631, 1715, 2847, 2952, 2996 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 250 MHz): $\delta =$ 3.82 (s, 3H), 3.86 (s, 3H), 7.03 (d, 2H, $J=8.5$ Hz), 7.30 (d, 1H, $J=7.7$ Hz), 7.48 (dt, 1H, $J=1.4$, 7.7 Hz), 7.59 (dt, 1H, $J=1.4$, 7.7 Hz), 7.71 (dd, 1H, $J=1.4$, 7.7 Hz), 7.83 (d, 2H, $J=8.5$ Hz), 8.07 ppm (s, 1H); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta =$ 52.2, 52.7, 113.5, 117.2, 128.7, 129.5, 130.0, 130.7, 130.9, 132.9, 133.2, 138.0, 139.4, 142.2, 166.2 ppm; HRMS (electrospray) calcd for $C_{19}H_{15}NO_4Na$ $[M+Na]^+$: 344.0893, found: 344.0898.

**Methyl (2*E*)-2-(2-methylphenyl)-3-(4-methoxycarbonylphenyl)acrylate (7p)**: The crude product was purified by flash chromatography (10% EtOAc/petroleum ether) to give **7p** as a white solid (301 mg, 97% yield) in the form of two inseparable isomers (*E*/*Z*: 95/05). M.p. 63°C; IR (KBr): $\tilde{\nu} =$ 1721, 2924, 2953, 3006 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, major isomer): $\delta =$ 2.12 (s, 3H), 3.79 (s, 3H), 3.86 (s, 3H), 7.04 (d, 2H, $J=8.3$ Hz), 7.04–7.07 (m, 1H), 7.18–7.33 (m, 3H), 7.81 (d, 2H, $J=$ 8.3 Hz), 7.90 ppm (s, 1H); $^{13}C$ NMR ($CDCl_3$, 75 MHz, major isomer): $\delta =$ 19.5, 52.1, 52.5, 126.4, 128.4, 129.2, 129.4, 130.0, 130.2, 130.4, 133.9, 135.0, 136.3, 139.0, 139.2, 166.4, 167.9 ppm; HRMS (electrospray) calcd for $C_{19}H_{18}O_4$ $[M+H]^+$: 311.1277, found: 311.1276.

**Methyl (2*E*)-2-(2-chlorophenyl)-3-(4-methoxycarbonylphenyl)acrylate (7q)**: The crude product was purified by flash chromatography (10% EtOAc/petroleum ether) to give **7q** as a white solid (294 mg, 89% yield) in the form of two inseparable isomers (*E*/*Z*: 97/03). M.p. 91°C; IR (KBr): $\tilde{\nu} =$ 1605, 1633, 1719, 2844, 2925, 2952, 3001 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, major isomer): $\delta =$ 3.79 (s, 3H), 3.86 (s, 3H), 7.08 (d, 2H, $J=8.3$ Hz), 7.10 (dd, 1H, $J=1.5$, 7.8 Hz), 7.23 (app dt, 1H, $J=1.1$, 7.5 Hz), 7.33 (app dt, 1H, $J=1.9$, 7.5 Hz), 7.47 (dd, 1H, $J=1.0$, 7.9 Hz), 7.83 (d, 2H, $J=8.7$ Hz), 7.94 ppm (s, 1H); $^{13}C$ NMR ($CDCl_3$, 75 MHz, major isomer): $\delta =$ 52.1, 52.6, 127.2, 129.5, 129.7, 129.7, 129.9, 130.3, 131.0, 132.1, 134.0, 134.7, 138.6, 140.3, 166.3, 167.0 ppm; HRMS (electrospray) calcd for $C_{18}H_{16}O_4Cl$ $[M+H]^+$: 331.0731, found: 331.0734.

**Methyl (2*E*)-2-(4-chlorophenyl)-3-(4-methoxycarbonylphenyl)acrylate (7r)**: The crude product was purified by flash chromatography (10% EtOAc/petroleum ether) to give **7r** as a white solid (301 mg, 91% yield) in the form of two inseparable isomers (*E*/*Z*: 85/15). M.p. 104°C; IR (KBr): $\tilde{\nu} =$ 1608, 1623, 1724, 2842, 2947, 2993 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta =$ 3.76 (s, 3H×0.15), 3.80 (s, 3H×0.85), 3.86 (s, 3H×0.85), 3.91 (s, 3H×0.15), 7.04 (s, 1H×0.15), 7.10 (d, 2H×0.85, $J=8.7$ Hz), 7.13 (d, 2H×0.85, $J=8.3$ Hz), 7.32 (d, 2H×1, $J=8.3$ Hz), 7.38 (d, 2H×0.15, $J=7.8$ Hz), 7.40 (d, 2H×0.15, $J=8.7$ Hz), 7.84 (d, 2H×0.85, $J=8.3$ Hz), 7.86 (s, 1H), 8.02 ppm (d, 2H×0.85, $J=8.3$ Hz); $^{13}C$ NMR ($CDCl_3$, 75 MHz, *E*/*Z* mixture): $\delta =$ 52.2, 52.5, 52.6, 127.2, 127.9, 128.1, 129.0, 129.5, 129.8, 130.2, 130.9, 131.2, 133.4, 133.6, 134.2, 134.7, 134.9, 135.6, 138.8, 139.7, 139.9, 166.4, 167.5, 169.2 ppm; HRMS (electrospray) calcd for $C_{18}H_{16}O_4Cl$ $[M+H]^+$: 331.0731, found: 331.0732.

**Methyl (2*E*)-2-(2,5-dimethoxyphenyl)-3-(4-methoxycarbonylphenyl)acrylate (7s)**: The crude product was purified by flash chromatography (20% EtOAc/petroleum ether) to give **7s** as a yellow solid (328 mg, 92% yield) in the form of two inseparable isomers (*E*/*Z*: 96/04). M.p. 99°C; IR (KBr): $\tilde{\nu} =$ 1617, 1709, 2839, 2951, 3079 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, major isomer): $\delta =$ 3.66 (s, 3H), 3.66 (s, 3H), 3.78 (s, 3H), 3.86 (s, 3H), 6.58 (s, 1H), 6.88 (app s, 2H), 7.15 (d, 2H, $J=8.3$ Hz), 7.81 (s, 1H), 7.83 ppm (d, 2H, $J=8.1$ Hz); $^{13}C$ NMR ($CDCl_3$, 75 MHz, major isomer): $\delta =$ 52.1, 52.4, 55.6, 56.2, 112.4, 114.5, 116.2, 125.3, 129.3, 129.8, 131.5, 139.1, 139.3, 151.5, 153.6, 166.5, 167.9 ppm; HRMS (electrospray) calcd for $C_{20}H_{20}O_6Na$ $[M+Na]^+$: 379.1152, found: 379.1155.

**Methyl (2*E*)-2-(3-methoxyphenyl)-3-(4-methoxycarbonylphenyl)acrylate (7t)**: The crude product was purified by flash chromatography (20% EtOAc/petroleum ether) to give **7t** as a colorless oil (261 mg, 80% yield) in the form of two inseparable isomers (*E*/*Z*: 86/14). IR (neat): $\tilde{\nu} =$ 1606, 1716, 2839, 2952, 3001 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, mixture isomers): $\delta =$ 3.75 (s, 3H×0.86), 3.77 (s, 3H×0.14), 3.80 (s, 3H×0.86), 3.83 (s, 3H×0.14), 3.86 (s, 3H×0.86), 3.92 (s, 3H×0.14), 6.75 (s, 1H×0.86), 6.76 (d, 1H×0.86, $J=10.6$ Hz), 6.87–6.93 (m, 1H×0.86, 1H×0.14), 7.00–7.09 (m, 3H×0.14), 7.05 (s, 1H×0.14), 7.11 (d, 2H×0.86, $J=8.3$ Hz), 7.28 (app t, 1H×0.86, $J=7.8$ Hz), 7.42 (d, 2H×0.14, $J=8.3$ Hz), 7.82 (d, 2H× 0.86, $J=8.3$ Hz), 7.83 (s, 1H×0.86), 8.02 ppm (d, 2H×0.14, $J=8.4$ Hz); $^{13}C$ NMR ($CDCl_3$, 75 MHz, mixture of isomers): $\delta =$ 52.1, 52.4, 52.5, 55.1, 55.3, 104.5, 112.1, 113.6, 114.2, 115.0, 119.0, 121.8, 128.0, 129.3, 129.8, 130.0, 130.3, 134.3, 136.5, 136.7, 137.7, 138.9, 139.1, 140.0, 159.7, 166.4, 167.8, 169.5 ppm; HRMS (electrospray) calcd for $C_{19}H_{18}O_5Na$ $[M+Na]^+$: 349.1046, found: 349.1047.

**General procedure for Heck cross-coupling reaction with methyl acrylate** (Table 5): Acrylate (1 mmol) and $Pd(OAc)_2$ (0.005–0.05 mol%, see Table 5) were added to a solution of diazonium salt (1.2 mmol) in MeOH (2.5 mL) at 25°C. The resulting mixture was stirred for 12 h at 25°C and then concentrated under reduced pressure. The crude product was purified by flash chromatography to give the corresponding product.

**(*E*)-Methyl 2-nitrocinnamate (8a)**: Purification by flash chromatography (70% $CH_2Cl_2$/petroleum ether) gave **8a** as a yellow solid (203 mg, 98%). M.p. 72°C (Lit.[26] 71–72°C); IR (KBr): $\tilde{\nu} =$ 1637, 1719, 2953, 3024 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 250 MHz): $\delta =$ 3.80 (s, 3H), 6.34 (d, 1H, $J=15.9$ Hz), 7.49–7.68 (m, 4H), 8.01 (d, 1H, $J=7.9$ Hz), 8.08 ppm (d, 1H, $J=$ 15.9 Hz); $^{13}C$ NMR ($CDCl_3$, 50 MHz): $\delta =$ 51.9, 122.7, 124.8, 129.0, 130.3, 130.4, 133.5, 140.0, 148.2, 166.1 ppm; MS (EI): *m*/*z* 207 [*M*], 176 $[M-OCH_3]$.

**(*E*)-Methyl 4-bromoocinnamate (8b)**: Purification by flash chromatography (20% AcOEt/petroleum ether) gave **8b** as a white solid (235 mg, 98%). M.p. 88°C [Lit.[27] 88–93°C]; IR (KBr): $\tilde{\nu} =$ 1643, 1711, 1959, 3033, 3049 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta =$ 3.80 (s, 3H), 6.42 (d, 1H, $J=$ 15.8 Hz), 7.38 (d, 2H, $J=8.3$ Hz), 7.51 (d, 1H, $J=8.6$ Hz), 7.62 ppm (d,

1H, $J=16.2$ Hz); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta=51.8$, 118.5, 124.5, 129.4, 132.1, 133.3, 143.5, 167.1 ppm; MS (EI): *m/z* 240 [*M*, $^{79}$Br], 242 [*M*, $^{81}$Br], 161 [*M*−Br].

**(*E*)-Methyl 3-trifluoromethylcinnamate (8c)**: Purification by flash chromatography (10% AcOEt/petroleum ether) gave **8c** as a white solid (221 mg, 96%). M.p. 41 °C [Lit.[28] 36.5 °C]; IR (KBr): $\tilde{\nu}=1634$, 1713, 2948, 2997, 3032 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 250 MHz): $\delta=3.82$ (s, 3H), 6.50 (d, 1H, $J=16.2$ Hz), 7.52 (app t, 1H, $J=7.9$ Hz), 7.62–7.76 (m, 3H), 7.71 ppm (d, 1H, $J=16.2$ Hz); MS (EI): *m/z* 230 [*M*], 161 [*M*−$CF_3$].

**(*E*)-Methyl 4-methoxy-3-nitrocinnamate (8d)**: Purification by flash chromatography (10% AcOEt/petroleum ether) gave **8d** as a yellow solid (220 mg, 93%). M.p. 128 °C [Lit.[29] 130–130.5 °C]; IR (KBr): $\tilde{\nu}=1639$, 1702, 2952, 2983, 3062 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 250 MHz): $\delta=3.80$ (s, 3H), 4.00 (s, 3H), 6.38 (d, 1H, $J=16.1$ Hz), 7.11 (d, 1H, $J=8.5$ Hz), 7.61 (d, 1H, $J=15.9$ Hz), 7.68 (dd, 1H, $J=2.1$, 8.8 Hz), 8.00 ppm (d, 1H, $J=2.1$ Hz); $^{13}$C NMR ($CDCl_3$, 50 MHz): $\delta=51.8$, 56.7, 113.8, 118.4, 124.9, 127.0, 133.4, 141.7, 154.0, 166.8 ppm; MS (EI): *m/z* 237 [*M*], 206 [*M*−$OCH_3$].

**(*E*)-Methyl 2-methylcinnamate (8e)**: Purification by flash chromatography (10% AcOEt- petroleum ether) gave **8e** as a colorless oil (143 mg, 81%). IR (neat): $\tilde{\nu}=1634$, 1718, 2950 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 250 MHz): $\delta=2.44$ (s, 3H), 3.81 (s, 3H), 6.36 (d, 1H, $J=15.9$ Hz), 7.18–7.31 (m, 3H), 7.55 (d, 1H, $J=7.3$ Hz), 7.99 ppm (d, 1H, $J=15.9$ Hz); $^{13}$C NMR ($CDCl_3$, 50 MHz): $\delta=51.8$, 120.6, 125.3, 127.8, 127.7, 131.2, 133.4, 134.4, 143.1, 166.8 ppm; MS (EI): *m/z* 176 [*M*], 145 [*M*−$OCH_3$].

**(*E*)-Methyl 4-methoxycarbonylcinnamate (3)**: Purification by flash chromatography (15% AcOEt/petroleum ether) gave **3** as a white solid (205 mg, 93%). M.p. 124 °C (Lit.[30] 122–123 °C). IR (KBr): $\tilde{\nu}=1641$, 1720, 2958 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 250 MHz): $\delta=3.81$ (s, 3H), 3.92 (s, 3H), 6.51 (d, 1H, $J=15.9$ Hz), 7.57 (d, 2H, $J=8.5$ Hz), 7.70 (d, 1H, $J=16.1$ Hz), 8.04 ppm (d, 1H, $J=8.2$ Hz); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta=51.8$, 52.2, 120.1, 127.9, 130.0, 131.3, 138.5, 143.4, 166.4, 166.9 ppm; MS (EI): *m/z* 220 [*M*], 189 [*M*−$OCH_3$].

**General procedure for the preparation of oxindoles from acrylates (Table 6)**: 10% Pd/C was added to a solution of the corresponding acrylate (1 mmol) in MeOH (2.5 mL) (5 mol%), and the resulting mixture stirred at 40 °C under $H_2$ for 48 h. After filtration, the crude product was purified by flash chromatography to give the corresponding oxindoles.

**3-(4-Methoxycarbonylbenzyl)oxindole (9a)**: Purification by flash chromatography (40% EtOAc/petroleum ether) gave **9a** as a white solid (228 mg, 81% yield). M.p. 156 °C; IR (KBr): $\tilde{\nu}=1701$, 1719, 2956, 3035, 3080, 3179 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 250 MHz): $\delta=3.05$ (dd, 1H, $J=8.7$, 13.8 Hz), 3.51 (dd, 1H, $J=4.8$, 13.7 Hz), 3.78 (dd, 1H, $J=4.8$, 8.7 Hz), 3.89 (s, 3H), 6.76–6.94 (m, 3H), 7.14–7.26 (m, 3H), 7.91 (d, 2H, $J=8.1$ Hz), 8.94 ppm (br s, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta=36.4$, 47.1, 52.0, 109.8, 122.1, 124.6, 128.1, 128.4, 128.6, 129.5, 129.6, 141.4, 143.1, 167.0, 179.2 ppm; HRMS (electrospray) calcd for $C_{17}H_{15}NO_3Na$ [*M*+Na]$^+$: 304.0944, found: 304.0942.

**3-(2,4,6-Trimethylbenzyl)oxindole (9b)**: Purification by flash chromatography (30% EtOAc/petroleum ether) gave **9b** as a white solid (260 mg, 98% yield). M.p. 206 °C; IR (KBr): $\tilde{\nu}=1622$, 1707, 2961, 3002, 3031, 3079, 3176 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta=2.18$ (s, 3H), 2.32 (s, 3H), 2.90 (dd, 1H, $J=11.7$, 13.9 Hz), 3.45 (dd, 1H, $J=5.6$, 13.9 Hz), 3.71 (dd, 1H, $J=5.6$, 11.7 Hz), 6.33 (d, 1H, $J=7.5$ Hz), 6.80 (t, 1H, $J=7.5$ Hz), 6.89 (s, 2H), 6.95 (t, 1H, $J=7.5$ Hz), 7.18 (t, 1H, $J=7.7$ Hz), 9.26 ppm (br s, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta=20.2$, 20.9, 30.6, 44.8, 109.7, 121.9, 125.0, 127.8, 128.9, 129.2, 131.8, 136.0, 137.0, 141.4, 180.4 ppm; HRMS (electrospray) calcd for $C_{18}H_{19}NONa$ [*M*+Na]$^+$: 288.1358, found: 288.1356.

**3-Benzyl-6-phenyloxindole (9c)**: Purification by flash chromatography (15% EtOAc/$CH_2Cl_2$) gave **9c** as a white solid (218 mg, 73% yield). M.p. 155 °C; IR (KBr): $\tilde{\nu}=1627$, 1698, 3027, 3061, 3089, 3159 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 250 MHz): $\delta=2.95$ (dd, 1H, $J=9.5$, 13.7 Hz), 3.56 (dd, 1H, $J=4.3$, 13.9 Hz), 3.81 (dd, 1H, $J=4.6$, 9.5 Hz), 6.77 (d, 1H, $J=7.5$ Hz), 7.11–7.15 (m, 2H), 7.25–7.45 (m, 9H), 7.54 (d, 2H, $J=7.9$ Hz), 9.05 ppm (br s, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta=36.7$, 47.5, 108.6, 120.9, 125.0, 126.7, 127.0, 127.4, 128.0, 128.4, 128.7, 129.4, 137.8, 140.7, 141.3, 142.1, 180.3 ppm; HRMS (electrospray) calcd for $C_{23}H_{16}NO$ [*M*] 322.1226, found: 322.1219.

**General procedure for the preparation of arylidenoxindoles from acrylates (Table 7)**: Fe (168 mg, 3 mmol) and $NH_4Cl$ (32.1 mg, 0.6 mmol) were added to a solution of the corresponding acrylate (1 mmol) in EtOH (8 mL) and $H_2O$ (2 mL). After being stirred for 4 h at 80 °C, the resulting mixture was diluted with water (8 mL) and extracted with $CH_2Cl_2$ (3×). The collected organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure.

**(*E*)-3-(2-Methylbenzylidene)-5,6-dimethoxyoxindole (10a)**: After workup, **10a** was obtained as a yellow solid (289 mg, 98%). M.p. 152 °C; IR (KBr): $\tilde{\nu}=1620$, 1695, 2836, 2959, 3006, 3164 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta=2.37$ (s, 3H), 3.57 (s, 3H), 3.87 (s, 3H), 6.52 (s, 1H), 6.83 (s, 1H), 7.23–7.35 (m, 3H), 7.60 (d, 1H, $J=7.5$ Hz), 7.74 (s, 1H), 9.21 ppm (s, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta=19.9$, 56.1, 56.3, 95.4, 107.6, 112.5, 125.5, 128.5, 128.6, 129.4, 130.5, 133.6, 134.1, 136.5, 137.4, 144.1, 151.1, 171.1 ppm; HRMS (electrospray) calcd for $C_{18}H_{18}NO_3$ [*M*+H]$^+$: 296.1281, found: 296.1281.

**(*E*)-3-(4-methoxycarbonylbenzylidene)oxindole (10b)**: Purification by flash chromatography (5% EtOAc/$CH_2Cl_2$ then 10% EtOAc/$CH_2Cl_2$) gave **10b** (126 mg, 45%) as a yellow solid. M.p. 234–236 °C (Lit.[31] 238–239 °C); IR (KBr): $\tilde{\nu}=1609$, 1625, 1701, 1715, 2953, 3021, 3077, 3141 cm$^{-1}$; $^1$H NMR (DMSO, 300 MHz): $\delta=3.88$ (s, 3H), 6.81–6.88 (m, 2H), 7.24 (app t, 1H, $J=7.9$ Hz), 7.42 (d, 1H, $J=7.5$ Hz), 7.64 (s, 1H), 7.81 (d, 2H, $J=7.9$ Hz), 8.07 (d, 2H, $J=8.3$ Hz), 10.7 ppm (s, 1H); $^{13}$C NMR (DMSO, 75 MHz): $\delta=52.3$, 110.3, 120.5, 121.3, 122.7, 129.2, 129.5, 130.0, 130.7, 134.1, 139.3, 143.3, 165.7, 168.3 ppm; HRMS (electrospray) calcd for $C_{17}H_{14}NO_3$ [*M*+H]$^+$: 280.0973, found: 280.0977.

**(*E*)-3-(2-Bromobenzylidene)oxindole (10c)**: Purification by flash chromatography (5% EtOAc/$CH_2Cl_2$ then 10% EtOAc/$CH_2Cl_2$) gave **10c** (180 mg, 60%) as a yellow solid. M.p. 182 °C (Lit.[32] 166–167 °C); IR (KBr): $\tilde{\nu}=1615$, 1714, 2840, 2900, 3006, 3027, 3081, 3145 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta=6.82$ (app t, 1H, $J=7.9$ Hz), 6.96 (d, 1H, $J=7.9$ Hz), 7.19–7.34 (m, 3H), 7.41 (app t, 1H, $J=7.1$ Hz), 7.71 (d, 2H, $J=7.9$ Hz), 7.82 (s, 1H), 9.37 ppm (s, 1H); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta=110.5$, 121.3, 121.8, 123.1, 124.2, 127.2, 129.0, 130.2, 130.8, 133.2, 135.4, 135.8, 142.0, 170.1 ppm; HRMS (electrospray) calcd for $C_{15}H_{11}NOBr$ [*M*+H]$^+$: 300.0018, found: 300.0013.

**Computational details**: Calculations were performed with the Gaussian 03 suite of programs[33] using the hybrid functional B3LYP,[34,35] which is a three-parameter functional developed by Becke that combines the Becke gradient-corrected exchange functional and the Lee–Yang–Parr and Vosko–Wilk–Nusair correlation functionals with the exact part of the HF exchange energy. Pd was treated with a Stuttgart–Dresden pseudopotential in combination with its adapted basis set.[36] Oxygen, nitrogen, carbon, and hydrogen atoms were described with a 6-31G(d,p) double-ζ basis set.[37] Geometry optimizations were carried out without any symmetry restrictions, the nature of the extrema (minimum or TS) was verified with analytical frequency calculations. All total energies and Gibbs free energies were corrected for zero-point energy (ZPE) and temperature by using unscaled density functional frequencies. The connection between the transition states and the corresponding minima was confirmed by IRC calculations.[38] The electronic structure was studied by natural bond orbital (NBO) analysis.[39] Molecular structures were drawn with Molekel 4.3.[40] Energies in solution reported in Figure 3 result from single-point energy calculations with the solvent (methanol) effect taken into account through the polarisable continuum model (PCM) implemented in Gaussian 03.[41]

**X-ray crystallography**: CCDC-753309 (**7c**) contains the crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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