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Dual Role of Acetanilides: Traceless Removal of a Directing Group through Deacetylation/Diazotation and Palladium-Catalyzed C–C-Coupling Reactions

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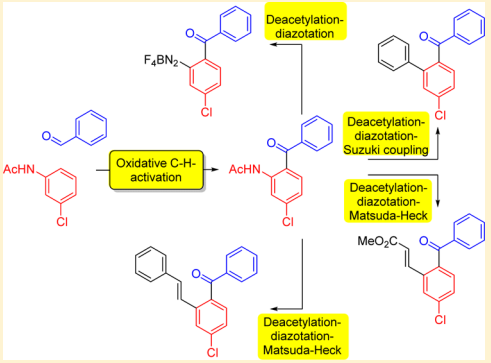
Supporting Information

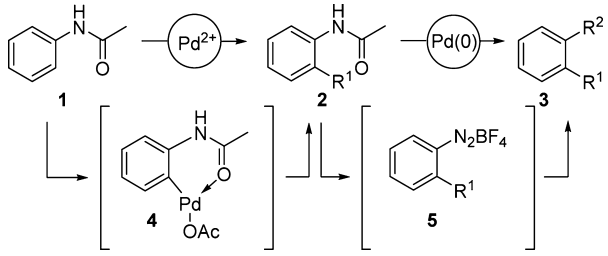
ABSTRACT: The acetamide group enables regioselective oxidative *ortho*-C–H activation reactions, such as Pd-catalyzed acylation. The synthetic utility of these transformations can be significantly enhanced by using the acetamide as a quasi-leaving group in a subsequent conventional Pd-catalyzed coupling or cross-coupling reaction. The concept is illustrated herein for the synthesis of *o*-alkenyl- and *o*-arylphenones, which have potential for the synthesis of arylated aromatic heterocycles.



INTRODUCTION

Since Fujiwara and Moritani's original publication on the Pd-mediated coupling of alkenes and arenes,[1] the field of transition-metal-catalyzed oxidative C–H activation has seen tremendous progress, which has been documented in numerous recent reviews.[2−4] While the coupling between alkenes and arenes[5] has probably been studied in more detail than any other C–H activation reaction, several examples of other transition-metal-catalyzed oxidative C–C bond-forming reactions have recently been published.[6−10] For example, transition-metal-catalyzed oxidative acylation reactions have been explored over the past few years to synthesize benzophenones and alkyl aryl ketones regioselectively. The first report in this regard was a decarboxylative *ortho*-acylation of acetanilides using α-oxocarboxylic acids, an oxidant, and a Pd precatalyst.[11] Shortly afterward, it was demonstrated that the α-oxocarboxylic acids can be replaced by aldehydes,[12−14] benzylic alcohols[15] or ethers,[16] styrenes,[17,18] or toluene derivatives.[19−23] Like most transition-metal-catalyzed aromatic C–H activation reactions, these transformations require the presence of a coordinating functional group which will direct the electrophilic metal (in many cases Pd^{2+}) to the *ortho*-position.[10] Among the first functional groups identified as efficient catalyst directing moieties were acetanilides. For example, Horino and Inoue,[24] and shortly afterward Tremont and Rahman[25] isolated dimeric acetate-bridged Pd–σ-aryl complexes (depicted in monomeric form as structure **4** in Scheme 1) when acetanilides were treated with $Pd(OAc)_2$ and demonstrated that these complexes undergo stoichiometric C–C bond-forming reactions with alkenes or alkyl halides, respectively. Later, the former transformation evolved into a truly catalytic process by reoxidizing Pd(0) to Pd^{2+}, e.g., with benzoquinone.[26]

Scheme 1. Consecutive Pd^{2+}- and Pd(0)-Catalyzed 1,2-Difunctionalization of Acetanilides



Over the past few years, the requirement of a catalyst directing and activating group to ensure mild conditions and good regioselectivities has increasingly been recognized as a severe limitation of aromatic C–H activation reactions, in particular when target structures without the specific functional group or a closely related functional group are addressed.[27−29] Consequently, strategies have been developed to remove a particular directing group, e.g., by hydrolytic cleavage or transesterification, as exemplified by a Rh-catalyzed *ortho*-arylation of phenols in the presence of phosphinite cocatalysts.[30] Hydrolytic removal of a catalyst directing group (CDG) is, however, only facile if the group is attached to the molecular core through a heteroatom. Recently, we described an approach to remove a catalyst directing group by conversion

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to a leaving group suitable for Pd(0)-catalyzed coupling or cross-coupling reactions.[31] In this project, acetanilides **1** were first functionalized at the *ortho*-position via Pd^{2+}-catalyzed Fujiwara–Moritani reactions, and the resulting products **2** were then subjected to the deacetylation–diazotation–coupling sequence previously developed in our group[32−34] to furnish 1,2-disubstituted arenes **3** with high regioselectivity. The deacetylation–diazotation–coupling sequence relies on the in situ formation of arene diazonium salts **5**, which are highly reactive electrophilic reagents in Pd(0)-catalyzed C–C bond-forming reactions (Scheme 1).[35−38]

Parallel to our preliminary communication, a conceptually similar sequence for the 1,2-difunctionalization of arenes was disclosed by Huang and co-workers, who used a triazene as a directing group for a Rh-catalyzed C–H activation. Traceless removal of the triazene and further functionalization were then accomplished by treatment with Brønsted acids (to generate a diazonium cation in situ) and arylation or Pd-catalyzed alkenylation.[39]

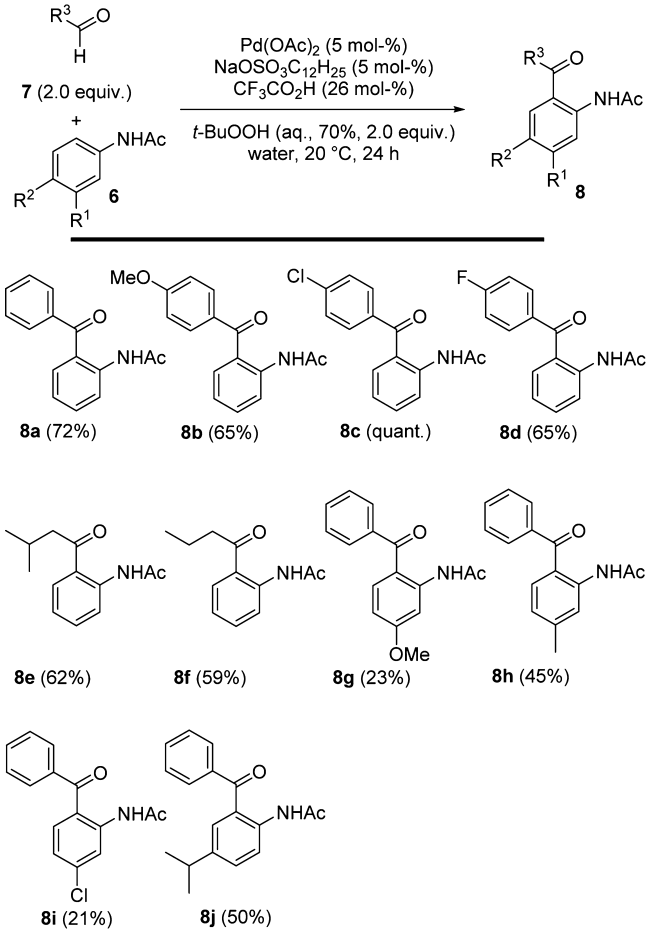
In continuation of our studies on this field, we investigated an extension of the consecutive Pd^{2+}/Pd(0)-catalyzed 1,2-difunctionalization outlined in Scheme 1 to the synthesis of highly functionalized aromatic ketones. These compounds are valuable synthetic intermediates for the synthesis of numerous heterocyclic scaffolds such as xanthones,[40,41] benzodiazepines,[42] or acridones.[43] In addition, aromatic ketones have also been used as selective cyclooxygenase-2 inhibitors[44] and for the synthesis of biologically active natural[45] and non-natural[46] indan derivatives.

RESULTS AND DISCUSSION

Synthesis of *o*-Acylacetanilides 8. We began the investigation with the synthesis of a set of *o*-acylacetanilides **8** from acetanilides **6** and aldehydes **7**, using a protocol recently developed by Novák and co-workers.[14] Under the reaction conditions developed by these authors, a successful and highly regioselective *ortho*-acylation can be accomplished at ambient or slightly elevated temperatures in aqueous medium using a commercially available aqueous solution of *tert*-butyl hydroperoxide as oxidant, $Pd(OAc)_2$ as catalyst, and sodium lauryl sulfate as surfactant (Scheme 2).

Synthesis and Isolation of *o*-Acylarene Diazonium Salts 9. With the *o*-acylacetanilides **8** in hand, we first investigated a deacetylation–diazotation sequence with a view to isolate the functionalized arene diazonium salts **9** as their tetrafluoroborates. We have previously developed a deacetylation–diazotation protocol which relies on a deacetylation promoted by BF_3–methanol complex, followed by in situ diazotation with *tert*-butyl nitrite.[32,47] As crucial parameters for this one-flask sequence were identified the initial substrate concentration, as lower substrate concentrations often prevent the isolation of the diazonium tetrafluoroborate through precipitation, the temperature for the diazotation step, and the number of equivalents of *tert*-butyl nitrite. While low reaction temperatures often retard the diazotation reaction, they reduce the solubility of the diazonium salts in the alcoholic solvent, which in turn facilitates their isolation. The reduced rate of the diazotation step at lower temperatures can be compensated to some extent by increasing the amount of alkyl nitrite. On the other hand, we found that excess of *tert*-butyl nitrite can be disadvantageous if the deacetylation–diazotation sequence is to be extended by a Pd-catalyzed coupling reaction because alkyl nitrites partially inhibit Pd(0)-catalyzed reactions,

Scheme 2. Synthesis of *o*-Acylacetanilides 8[14]



presumably due to their oxidizing properties.[33] For these reasons we aimed at a minimization of the amount of diazotation reagent and used excess *tert*-butyl nitrite only if necessary. The results compiled in Table 1 show that by systematic variation of the above-mentioned parameters suitable conditions for the deacetylation–diazotation sequence were identified for almost all acetanilides **8**, which allow the isolation of the corresponding diazonium salts **9** as microcrystalline powders in synthetically useful yields, with just two exceptions. The isobutyl-substituted derivative **8e** is apparently completely converted to the expected diazonium salt **9e** in the deacetylation–diazotation sequence, as indicated by TLC, but it does not precipitate under any combination of reaction parameters (entry 7). In the case of benzophenone **8j**, TLC analysis shows that the deacetylation proceeds quantitatively, but the intermediate aniline undergoes diazotation only with incomplete conversion (entry 19).

Deacetylation–Diazotation–Coupling (DDC) Sequence of *o*-Acylacetanilides 9. Before investigating the envisaged extension of the one-flask deacetylation–diazotation sequence by a Pd-catalyzed coupling reaction, we decided to investigate the C–C bond-forming reaction separately. To this end, the isolated arene diazonium salts **9** and methyl acrylate were coupled in a Matsuda–Heck[36,48] reaction. The most important parameters for the outcome of Pd-catalyzed coupling reactions involving arene diazonium salts are the solvent and the presence or absence of a base. It is an important requirement for one-flask reactions in general that the

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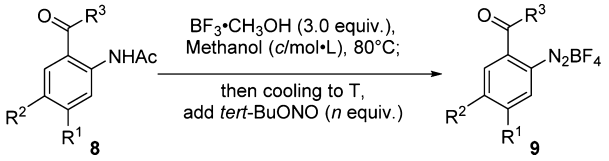
Table 1. Deacetylation–Diazotation Sequence of *o*-Acylacetanilides 8



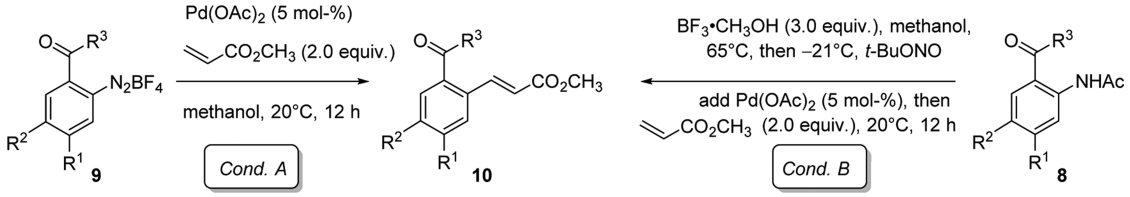
entry	8	T (°C)	c (mol·L^{-1})	n (t-BuONO, equiv)	9 (yield, %)[a]
1	**8a**	0	0.01	1.0	**9a** (n.i.)
2	**8a**	0	0.01	1.5	**9a** (46)
3	**8a**	0	0.02	1.5	**9a** (90)
4	**8b**	0	0.01	1.0	**9b** (95)
5	**8c**	0	0.01	1.0	**9c** (90)
6	**8d**	0	0.01	1.0	**9d** (90)
7[b]	**8e**	0; −21	0.01; 0.02	1.0; 1.5; 2.0	**9e** (n.i.)
8	**8f**	0	0.01; 0.02	1.0; 1.5; 2.0	**9f** (n.(i)
9	**8f**	−21	0.02	1.0	**9f** (n.i.)
10	**8f**	−21	0.02	1.5	**9f** (53)
11	**8f**	−21	0.02	2.0	**9f** (96)
12	**8g**	0	0.02	1.0	**9g** (82)
12	**8g**	0	0.02	1.5	**9g** (91)
13	**8h**	0	0.01; 0.02	1.0; 1.5; 2.0	**9h** (n.i.)
14	**8h**	−21	0.02	1.0	**9h** (n.i.)
15	**8h**	−21	0.02	1.5	**9h** (69)
16	**8h**	−21	0.02	2.0	**9h** (82)
17	**8i**	0	0.02	1.0	**9i** (79)
18	**8i**	0	0.02	2.0	**9i** (66)
19[c]	**8j**	0	0.01; 0.02	1.0; 1.5; 2.0	**9j** (n.i.)

[a]n.i., not isolated. [b]Full conversion to diazonium salt (TLC), but not isolable with any combination of T, c, and n (t-BuONO). [c]Incomplete conversion (TLC) to diazonium salt with any combination of T, c and n (t-BuONO).

conditions chosen for the individual steps are compatible. For this reason, we had to rely on base-free methanol as a solvent because these conditions come closest to those of the preceding deacetylation–diazotation sequence. Commonly used precatalysts for Matsuda–Heck reactions are $Pd_2(dba)_3{\cdot}CHCl_3$ and $Pd(OAc)_2$. For convenience, we started with $Pd(OAc)_2$, which catalyzed gratifyingly in all cases the coupling of arene diazonium salts **9** and methyl acrylate to the expected cinnamates **10** in high yields in methanol under base-free conditions (Table 2, conditions A). *o*-Acyl cinnamates of the general structure **10** have previously been synthesized using, for example, a Wittig olefination,[45] for a single example a Matsuda–Heck reaction,[49] and a Ru-catalyzed *o*-alkenylation of aromatic ketones.[50] With these results in hand, we investigated a synthesis of *o*-acyl cinnamates **10** from *o*-acyl acetanilides **8** via a deacetylation–diazotation–coupling sequence. To this end, acetanilides **8** were treated with BF_3–methanol complex at 65 °C to accomplish the deacetylation, followed by addition of *t*-BuONO at −21 °C for the diazotation. Without removal or exchange of any solvents or byproducts, the Matsuda–Heck reaction of the in situ formed diazonium salts was initiated by simply adding $Pd(OAc)_2$ and methyl acrylate to the mixture, which was then warmed to ambient temperature (conditions B). In all cases, the Matsuda–Heck products **10** could be isolated, mostly in yields exceeding those obtained via the two-step procedure involving isolated arene diazonium salts. Notably, the isobutyl-substituted derivative **10e**, which cannot be synthesized via the two-step procedure as the corresponding arene diazonium salt **9e** could not be isolated, becomes accessible in excellent yield under conditions B (Table 2, entry 5). Compound **10j** was isolated in low yield, which can most likely be attributed to the incomplete formation of the intermediate diazonium salt (Table 2, entry 10; compare Table 1, entry 19).

Investigation into Heterocycle Synthesis from *o*-Acyl Cinnamates. With a view toward the synthesis of phthalazine derivatives we planned a condensation–conjugate addition sequence as outlined in Scheme 3, using hydrazine as a bisnucleophile. Precedence for the formation of phthalazine derivatives through cascade reactions involving a conjugate

Table 2. Comparison of One- And Two-Step Deacetylation–Diazotation Coupling Sequence



	R			conditions A (two-step procedure)				conditions B (one-flask procedure)	
entry	R^1	R^2	R^3	9	10	yield[a] (%)	yield[b] (%)	8	yield[c] (%)
1	H	H	Ph	**9a**	**10a**	93	84	**8a**	quant
2	H	H	*p*-C_6H_4OMe	**9b**	**10b**	88	84	**8b**	68
3	H	H	*p*-C_6H_4Cl	**9c**	**10c**	93	73	**8c**	quant
4	H	H	*p*-C_6H_4F	**9d**	**10d**	84	76	**8d**	quant
5	H	H	$CH_2CH(CH_3)_2$	**9e**	**10e**	*d*	*d*	**8e**	96
6	H	H	$CH_2CH_2CH_3$	**9f**	**10f**	quant	96	**8f**	60
7	OCH_3	H	C_6H_5	**9g**	**10g**	88	80	**8g**	80
8	CH_3	H	C_6H_5	**9h**	**10h**	86	71	**8h**	56
9	Cl	H	C_6H_5	**9i**	**10i**	quant	79	**8i**	quant
10	H	i-Pr	C_6H_5	**9j**	**10j**	*d*	*d*	**8j**	30

[a]Yield of **10** obtained from **9** with conditions A. [b]Calculated yield of **10** based on **8** over two steps. [c]Yield of **10** obtained from **8** with conditions B. [d]Not performed (diazonium salts **9e** and **9j** not isolable).

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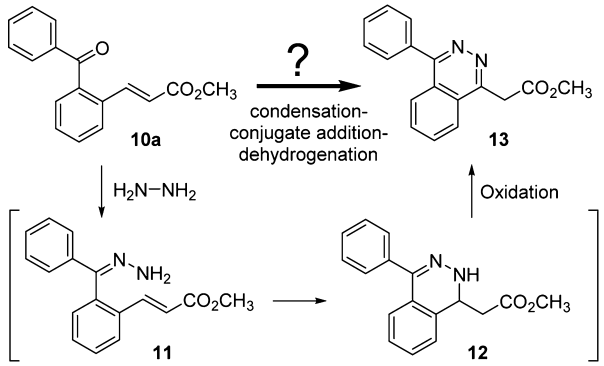
Scheme 3. Proposed Condensation−Conjugate Addition Sequence



addition step has been published by Grigg et al., who reported a Pd-catalyzed carbonylation of iodoarenes, followed by acylation-conjugate addition of the bisnucleophile hydrazine.[51]

Obviously, the C−N bond-forming steps might occur in a reversed order, but in any case one step will involve formation of a hydrazone. For less reactive carbonyl compounds, such as benzophenones, this reaction normally requires acid catalysis and/or elevated temperatures.[52,53] For these reasons, we started our investigation into the proposed condensation−conjugate addition sequence by mixing equimolar amounts of **10a** and hydrazine hydrate in ethanol, which was then heated to reflux for 16 h (Table 3, entry 1). Both TLC and NMR spectroscopy

Table 3. Conditions for Condensation−Conjugate Addition Sequence of 10a and Hydrazine

entry	solvent	heating method (temp, °C)	time (h)	product (yield, %)
1	ethanol	conventional (78)	16	*a*
2	ethanol/water (1:1)	conventional (78)	72	*a*
3	acetic acid	conventional (118)	72	*a*
4	ethanol	μ-wave irradiation (180)	0.5	*a*
5	ethanol/water (1:1)	μ-wave irradiation (180)	0.5	*a*
6	ethyl acetate	μ-wave irradiation (180)	0.5	*a*
7	toluene	μ-wave irradiation (180)	0.3	*a*
8	toluene	μ-wave irradiation (250)	0.5	*a*
9	ethylene glycol	μ-wave irradiation (250)	0.5	**14** (20)[b]
10	ethylene glycol	μ-wave irradiation (250)	1.0	**14** (20)[b]

[a]Complex mixture of products; no major product identified. [b]Major product **14** is formed along with several minor products.

of the crude reaction mixture revealed the formation of a complex mixture of products. The same outcome was observed in ethanol/water and in acetic acid under reflux (entries 2 and 3). Performing reactions under microwave irradiation often reduces reaction times significantly and may lead to higher selectivities.[54] This prompted us to investigate the projected reaction of hydrazine and **10a** in a microwave reactor using various solvents such as ethanol, ethanol/water, ethyl acetate, and toluene (entries 4−8). In all cases, the results were very similar to those observed under conventional heating conditions. In particular, it was not possible to identify a major reaction product. Eventually, ethylene glycol was tested (entries 9 and 10). This solvent has a very high loss factor[55] and should therefore ensure particularly efficient conversion of microwave energy into heat. Indeed, TLC indicated the formation of a main product and a significantly reduced number of side products. Irrespective of the reaction time, the isolated yield of the major product **14**, obtained after column chromatography on silica, is rather low, which might at least in part be explained by loss of material due to the high polarity of the product.

The spectroscopic data of the isolated product **14** were not in agreement with the structure of phthalazine **13** or a dihydrophthalazine **12**. In particular, HRMS leads to a molecular formula of $C_{16}H_{12}O_2N$, which suggests the incorporation of 1 equiv of hydrazine and condensation of 1 equiv of water and methanol. ^{1}H NMR spectroscopy shows the presence of two singlets at 5.83 and 6.22 ppm, which are connected to two tertiary carbon atoms at 82.2 and 65.9 ppm, respectively. Further NMR-spectroscopical analysis, in particular based on two-dimensional ^{1}H−^{13}C correlation spectroscopy, remained ambiguous but pointed toward the structure of a benzoannellated tricyclic pyrazole derivative. Gratifyingly, we succeeded in obtaining a crystal suitable for single-crystal X-ray structure analysis. The molecular structure of product **14** can be described as a pyrazoloisoindole derivative and is shown in Figure 1. Beyond the molecular structure, crystal structure

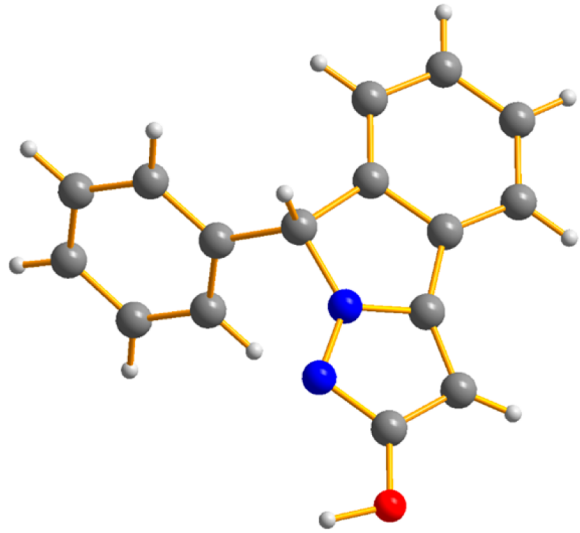


Figure 1. Molecular structure of compound **14** (only *R*-enantiomer shown).

analysis reveals that the two enantiomers of **14** form a centrosymmetric dimer through hydrogen bonding in the solid state. Intermolecular H bonds were observed between the OH group of one molecule and both N atoms of the other molecule, as illustrated in the packing diagram (see the Supporting Information for further details).

A tentative mechanism for the formation of the tricyclic condensation product **14** is outlined below. Cinnamate **10a** reacts with hydrazine in a conjugate addition and subsequent condensation of methanol to the pyrazolidinone **15**. Literature precedence for this type of addition−condensation sequence exists.[56,57] In the next step, **15** cyclizes to a hemiaminal **16**, which eventually undergoes a sequence of deprotonation, 1,3-

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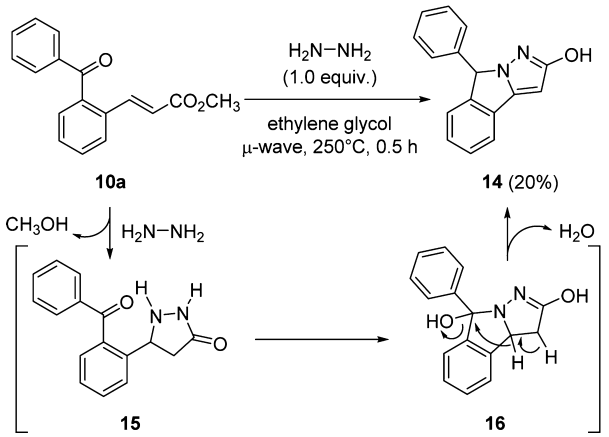
hydride shift, and dehydration. An alternative scenario starting with the formation of a hydrazone from **10a** and subsequent conjugate addition−methanol condensation would also be conceivable. In any case, however, a 1,3-hydride shift must be involved (Scheme 4).

Scheme 4. Tentative Mechanism for the Formation of Pyrazoloisoindole 14

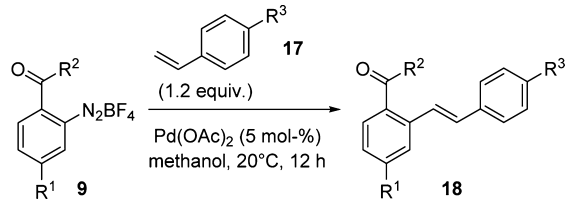


Matsuda−Heck Reaction of *o*-Acylarene Diazonium Salts 9 with Styrenes. The stilbene pattern is present in important bioactive natural products,[58,59] synthetic drugs,[60] and fluorescent dyes.[61] Scattered examples for the synthesis of stilbenes via Matsuda−Heck arylation of styrenes have been reported over the years,[35,62,63] but systematic investigations have not been performed until recently.[34,64,65] For example, Felpin and co-workers reported good yields and high *E*-selectivities of stilbene products at very low catalyst loadings for the Pd-catalyzed arylation of styrenes substituted with an electron-withdrawing group, i.e., aryl acrylates.[64] In contrast, we found that simple styrenes are often surprisingly unreactive toward electron-rich methoxyarene diazonium salts, in particular under base-free conditions, resulting in low yields and undesired side reactions such as hydrodediazonation.[34] This observation prompted us to investigate the Matsuda−Heck reaction of styrenes and electron-deficient *o*-acylarene diazonium salts **9** for comparison. Diazoniums salts **9a−c,f,g,i** and styrene (**17a**), 4-chlorostyrene (**17b**), and 4-methoxystyrene (**17c**), respectively, were chosen for this study. In all experiments, the precatalyst $Pd(OAc)_2$ and the base-free conditions established previously for the coupling with methyl acrylate were used (Table 4).

All Matsuda−Heck reactions of *o*-acylarene diazonium salts **9** and 4-methoxystyrene (**17c**) were unsuccessful and resulted in the formation of complex mixtures. Via GC−MS analysis of the crude reaction mixtures we could identify the hydrodediazonation product as one component. In contrast, the less electron-rich styrene (**17a**) and 4-chlorostyrene (**17b**) underwent the coupling with all *o*-acylarene diazonium salts tested in good to excellent yields and *E*-selectivities higher than 95:5. Notably, the isolated yields of these transformations significantly exceeded those previously reported by us[34] for the reactions of **17a,b** with the more electron-rich *o*-, *m*-, and *p*-methoxyarene diazonium salts.

Suzuki−Miyaura Coupling of *o*-Acylarene Diazonium Salts 9 with Arene Trifluoroborates. Genêt and co-workers described the first Suzuki−Miyaura coupling of arene

Table 4. Matsuda−Heck Reaction of Diazonium Salts 9 and Styrenes 17



entry	9	R^1	R^2	17	R^3	18 (yield, %)
1	**9a**	H	Ph	**17a**	H	**18aa** (96)
2	**9a**	H	Ph	**17b**	Cl	**18ab** (95)
3	**9a**	H	Ph	**17c**	OMe	**18ac** (*a*)
4	**9b**	H	*p*-C_6H_4OMe	**17a**	H	**18ba** (86)
5	**9b**	H	*p*-C_6H_4OMe	**17b**	Cl	**18bb** (86%)
6	**9b**	H	*p*-C_6H_4OMe	**17c**	OMe	**18bc** (*a*)
7	**9c**	H	*p*-C_6H_4Cl	**17a**	H	**18ca** (78)
8	**9c**	H	*p*-C_6H_4Cl	**17b**	Cl	**18cb** (80)
9	**9c**	H	*p*-C_6H_4Cl	**17c**	OMe	**18cc** (*a*)
10	**9f**	H	$CH_2CH_2CH_3$	**17a**	H	**18fa** (57)
11	**9f**	H	$CH_2CH_2CH_3$	**17b**	Cl	**18fb** (63)
12	**9f**	H	$CH_2CH_2CH_3$	**17c**	OMe	**18 fc** (*a*)
13	**9g**	OMe	Ph	**17a**	H	**18ga** (70)
14	**9g**	OMe	Ph	**17b**	Cl	**18gb** (75)
15	**9g**	OMe	Ph	**17c**	OMe	**18gc** (*a*)
13	**9i**	Cl	Ph	**17a**	H	**18ia** (80)
14	**9i**	Cl	Ph	**17b**	Cl	**18ib** (75)
15	**9i**	Cl	Ph	**17c**	OMe	**18ic** (*a*)

[a]Complex mixture of products; hydrodediazonation product detected by GC−MS.

diazonium salts using boronic acids as coupling partners and $Pd(OAc)_2$ as the catalyst under base- and ligand-free conditions.[66] They discovered that high yields can be obtained in dioxane, while the yields in methanol are only mediocre. In contrast, Sengupta and Bhattacharyya reported almost simultaneously that methanol is a suitable solvent for the coupling of arene diazonium salts and arene boronic acids, although significantly higher catalyst loadings had to be applied.[67] Other reports describing the suitability of alcohols as solvents were published later.[68−70] Shortly after their seminal report, Genêt and co-workers found that organotrifluoroborates[71−75] are superior coupling reagents under otherwise identical conditions.[76] More recently, we investigated the Suzuki−Miyaura coupling of organotrifluoroborates and a 4-methoxybenzene diazonium salt in comparison with 4-phenol diazonium salt and found that coupling reactions of the latter were advantageously performed in methanol rather than dioxane.[77]

We started this part of the investigation by comparing the Suzuki−Miyaura coupling of *o*-benzoylbenzene diazonium salt **9a** with phenylboronic acid (**19a′**) and with potassium phenyltrifluoroborate (**19a**), respectively (Scheme 5). With **19a′** in methanol, the expected biphenyl **20aa** was formed together with a considerable amount of methyl ether **21**, which was identified by comparison of its spectroscopic data with those reported previously in the literature.[78] The formation of this solvolysis product was fully suppressed when the analogous potassium organotrifluoroborate **19a** was used. Performing the coupling of **9a** and **19a** in dioxane instead of methanol worked equally well and gave **20aa** in comparable selectivity.

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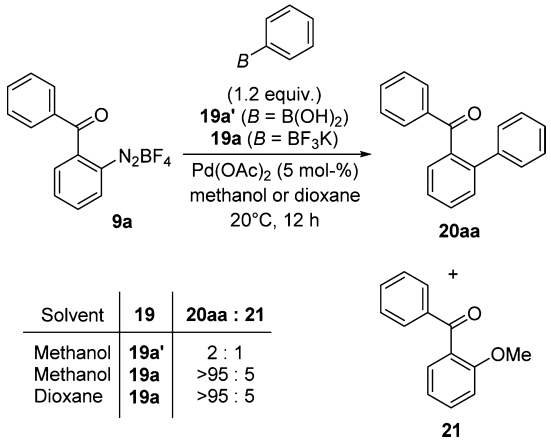
Scheme 5. Suzuki–Miyaura Coupling of 9a and Phenylboron Reagents 19a and 19a′



Solvent	19	20aa : 21
Methanol	19a'	2 : 1
Methanol	19a	>95 : 5
Dioxane	19a	>95 : 5

We applied the conditions established for the cross coupling of **9a** and **19a** to other *o*-acyl diazonium salts **9** and organotrifluoroborates **19** (Table 5). In most cases, good yields and selectivities of biaryl products **20** were obtained in methanol and in dioxane.

CONCLUSIONS

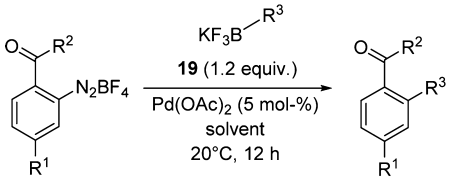
In summary, we report the efficient recycling of a catalyst directing group for oxidative Pd^{2+}-catalyzed C–H activation reactions by conversion into a leaving group for subsequent nonoxidative Pd(0)-catalyzed coupling reactions. Specifically, an acetamide group was used to enable a regioselective *ortho*-acylation through C–H activation, which was then converted into a diazonium group by a deacetylation–diazotation sequence. Pd(0)-catalyzed coupling of the arene diazonium salts thus formed proceeds effectively with styrenes, acrylates, and organotrifluoroborates. The sequence disclosed in this work leads eventually to structurally diverse *ortho*-substituted aromatic ketones from simple acetanilides.

EXPERIMENTAL SECTION

General Methods. All experiments were conducted in dry reaction vessels under an atmosphere of dry nitrogen. Solvents were purified by standard procedures. ^{1}H NMR spectra were obtained at 300 MHz in or at 500 MHz $CDCl_3$ with $CHCl_3$ (δ = 7.26 ppm) as an internal standard. Coupling constants are given in hertz. All ^{13}C NMR spectra were recorded with broadband decoupling at 75 MHz or at 126 MHz in $CDCl_3$ with $CDCl_3$ (δ = 77.0 ppm) as an internal standard. Whenever the solubility of the sample was insufficient in $CDCl_3$, DMSO-d_6 was used (DMSO-d_5 as internal standard for ^{1}H NMR spectroscopy, δ = 2.50 ppm, DMSO-d_6 as internal standard for ^{13}C NMR spectroscopy, δ = 39.5 ppm). IR spectra were recorded as ATR-FTIR spectra. Wavenumbers (ν) are given in cm^{-1}. The peak intensities are defined as strong (s), medium (m), or weak (w). Low- and high-resolution mass spectra were obtained by EI-TOF or ESI-TOF. Microwave reactions were carried out in an Anton-Paar monowave-300 reactor at 150 °C (monowave, maximum power 850 W, temperature control via IR-sensor, vial volume: 20 mL). *o*-Acyl acetanilides **8a–d** and **f–j**[14] and diazonium salt **9h**[79] have previously been described in the literature. Diazonium salts **9a**,[80] **9b**,[81] and **9f**[82] were mentioned in previous publications but not characterized.

*N-(2-(3-Methylbutanoyl)phenyl)acetamide (**8e**).* Acetanilide **6a** (3.00 g, 22.2 mmol) was suspended in water (20 mL), and $Pd(OAc)_2$ (249 mg, 5 mol %), Na–lauryl sulfate (320 mg, 5 mol %), and CF_3COOH (0.44 mL, 5.7 mmol, 0.26 equiv) were added. To this mixture were added isovaleraldehyde (6.30 mL, 44.4 mmol, 2.0 equiv) and *t*-BuOOH (70 wt % solution in water, 5.72 g, 44.4 mmol), and the mixture was stirred for 24 h at ambient temperature and then extracted with ethyl acetate (3×, 20 mL each). The combined organic extracts were washed with water, dried with $MgSO_4$, filtered, and evaporated. The residue was purified by chromatography on silica using a hexane–ethyl acetate mixture (1:1) to furnish **8e** (3.00 g, 13.7 mmol, 62%): colorless solid; mp 73 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.47 (s, 1H), 8.45 (d, J = 8.5 Hz, 1H), 7.58 (dd, J = 8.1, 1.3 Hz, 1H), 7.17 (ddd, J = 8.6, 8.6, 1.3 Hz, 1H), 6.76 (ddd, J = 8.1, 8.1, 1.0 Hz, 1H), 2.55 (d, J = 6.8 Hz, 2H), 1.94 (sept., J = 6.7 Hz, 1H), 1.91 (s, 3H),

Table 5. Suzuki–Miyaura Coupling of *o*-Acyldiazonium Salts 9 and Organotrifluoroborates 19



entry	9	R^1	R^2	19	R^3	solvent	20 (yield, %)
1	**9a**	H	C_6H_5	**19a**	C_6H_5	methanol	**20aa** (91)
2	**9a**	H	C_6H_5	**19a**	C_6H_5	dioxane	**20aa** (93)
3	**9b**	H	*p*-C_6H_4OMe	**19a**	C_6H_5	methanol	**20ba** (78)
4	**9b**	H	*p*-C_6H_4OMe	**19a**	C_6H_5	dioxane	**20ba** (91)
5	**9c**	H	*p*-C_6H_4Cl	**19a**	C_6H_5	methanol	**20ca** (77)
6	**9c**	H	*p*-C_6H_4Cl	**19a**	C_6H_5	dioxane	**20ca** (66)
7	**9f**	H	$CH_2CH_2CH_3$	**19a**	C_6H_5	methanol	**20fa** (79)
8	**9f**	H	$CH_2CH_2CH_3$	**19a**	C_6H_5	dioxane	**20fa** (59)
9	**9g**	OMe	C_6H_5	**19a**	C_6H_5	methanol	**20ga** (87)
10	**9g**	OMe	C_6H_5	**19a**	C_6H_5	dioxane	**20ga** (73)
11	**9i**	Cl	C_6H_5	**19a**	C_6H_5	methanol	**20ia** (55)
12	**9i**	Cl	C_6H_5	**19a**	C_6H_5	dioxane	**20ia** (78)
13	**9c**	H	*p*-C_6H_4Cl	**19b**	*p*-C_6H_4OMe	dioxane	**20cb** (quant)
14	**9c**	H	*p*-C_6H_4Cl	**19c**	*p*-C_6H_4F	dioxane	**20cc** (87)
15	**9c**	H	*p*-C_6H_4Cl	**19d**	2-naphthyl	dioxane	**20cd** (96)

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0.72 (d, J = 6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 169.1, 141.2, 134.7, 131.0, 122.2, 121.8, 120.7, 48.8, 25.5, 25.4, 22.8; IR (ATR) ν 2951 (m), 1518 (s), 1449 (s), 1360 (s), 761 (s); HRMS (EI) calcd for $C_{13}H_{17}O_2N$ [M$^+$] 219.1254, found 219.1259; MS (EI) m/z 219 (18), 162 (100), 144 (18), 120 (74), 92 (21). Anal. Calcd for $C_{13}H_{17}NO_2$ (219.28): C, 71.2; H, 7.8; N, 6.4. Found: C, 71.1; H, 7.7; N, 6.5.

General Procedure for the Synthesis and Isolation of Arene Diazonium Salts 9. To a solution of acetanilide **8** (1.0 mmol) in dry and degassed methanol (5.0 mL) was added $BF_3{\cdot}CH_3OH$ (3.0 mmol). The solution was heated to reflux for 16 h and then cooled to 0 or −21 °C, as indicated in Table 1. *t*-BuONO (103 mg, 1.0 mmol; 155 mg, 1.5 mmol; 206 mg, 2.0 mmol as indicated in Table 1) was added, and stirring at the respective temperature was continued for 2 h. The resulting precipitate of the corresponding arene diazonium salt **9** was filtered through a Büchner funnel, washed with a minimum amount of cold MTBE, and dried in vacuo.

*2-Benzoylbenzenediazonium Tetrafluoroborate (**9a**).*[80] Following the general procedure, **8a** (119 mg, 0.50 mmol) was converted to **9a** (134 mg, 0.46 mmol, 90%): orange solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.03 (dd, J = 8.2, 1.1 Hz, 1H), 8.37 (ddd, J = 7.7, 7.7, 1.1 Hz, 1H), 8.27 (ddd, J = 8.0, 8.0, 1.2 Hz, 1H), 8.19 (dd, J = 7.8, 1.1 Hz, 1H), 7.89 (dm, J = 8.2 Hz, 2H), 7.83 (tm, J = 7.5 Hz), 7.68 (dd, J = 8.2, 7.5 Hz); ^{13}C NMR (126 MHz, DMSO-d_6) δ 189.9, 140.2, 137.1, 136.2, 134.6, 134.3, 133.9, 133.7, 130.7, 128.9, 115.6; IR (ATR) ν 3114 (w), 2290 (m), 1660 (m), 1274 (s), 1036 (s); HRMS (ESI) calcd for $C_{13}H_9N_2O$ [M$^+$] 209.0715, found 209.0721; MS (ESI) m/z 196 (41), 181 (100), 144 (15), 98 (31).

*2-(4-Methoxybenzoyl)benzenediazonium Tetrafluoroborate (**9b**).*[81] Following the general procedure, **8b** (269 mg, 1.00 mmol) was converted to **9b** (309 mg, 0.95 mmol, 95%): yellow solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.00 (dd, J = 8.2, 1.1 Hz, 1H), 8.35 (ddd, J = 7.7, 7.7, 1.2 Hz, 1H), 8.24 (ddd, J = 8.0, 8.0, 1.2 Hz, 1H), 8.19 (dd, J = 7.8, 1.1 Hz, 1H), 7.89 (dm, J = 8.9 Hz, 2H), 7.20 (dm, J = 8.9 Hz), 3.91 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 188.1, 164.4, 140.1, 138.0, 136.1 133.9, 133.4, 133.3, 126.5, 115.7, 114.4, 55.9; IR (ATR) ν 3110 (w), 2293 (m), 1587 (s), 1269 (s), 1041 (s); HRMS (ESI) calcd for $C_{14}H_{11}N_2O_2$ [M$^+$] 239.0821, found 239.0822; MS (ESI) m/z 239 (13), 213 (79), 211 (100), 196 (18).

*2-(4-Chlorobenzoyl)benzenediazonium Tetrafluoroborate (**9c**).* Following the general procedure, **8c** (1.50 g, 5.4 mmol) was converted to **9c** (1.60 g, 4.9 mmol, 90%): colorless solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.02 (dd, J = 8.1, 1.2 Hz, 1H), 8.37 (ddd, J = 7.7, 7.7, 1.3 Hz, 1H), 8.27 (ddd, J = 7.9, 7.9, 1.3 Hz, 1H), 8.20 (dd, J = 7.7, 1.2 Hz, 1H), 7.89 (dm, J = 8.5 Hz, 2H), 7.75 (dm, J = 8.5 Hz, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 188.9, 140.2, 139.5, 136.9, 136.2, 134.4, 133.6, 132.8, 132.6, 129.1, 115.5; IR (ATR) ν 3100 (w), 2284 (m), 1658 (s), 1285 (s), 1027 (s); HRMS (ESI) calcd for $C_{13}H_8N_2OCl$ [M$^+$] 243.0352, found: 243.0331; MS (ESI) m/z 243 (8), 217 (41), 215 (100), 196 (23).

*2-(4-Fluorobenzoyl)benzenediazonium Tetrafluoroborate (**9d**).* Following the general procedure, **9d** (1.50 g, 5.8 mmol) was converted to **9d** (1.65 g, 5.2 mmol, 90%): colorless solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.02 (dd, J = 8.1, 1.1 Hz, 1H), 8.37 (ddd, J = 7.7, 7.7, 1.2 Hz, 1H), 8.26 (ddd, J = 7.9, 7.9, 1.3 Hz, 1H), 8.20 (dd, J = 7.7, 1.2 Hz, 1H), 8.17−7.92 (m, 2H), 7.51 (ddm, J = 8.8, 8.8 Hz, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 188.8, 165.8 (d, J = 254.2 Hz), 140.4, 137.3, 136.4, 134.4, 134.0 (d, J = 9.9 Hz), 133.8, 130.8, 116.3 (d, J = 22.3 Hz), 115.6; ^{19}F NMR (282 MHz, DMSO-d_6) δ −103.3 (s), −148.2 (s); IR (ATR) ν 3100 (w), 2284 (m), 1658 (s), 1285 (s), 1027 (s); HRMS (ESI) calcd for $C_{13}H_8N_2OF$ [M$^+$] 227.0621, found 227.0610; MS (ESI) m/z 227 (10), 201 (26), 199 (100), 196 (36).

*2-Butyrylbenzenediazonium Tetrafluoroborate (**9f**).*[82] Following the general procedure, **8f** (103 mg, 0.50 mmol) was converted to **9f** (126 mg, 0.48 mmol, 96%): colorless solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.94 (dd, J = 8.1, 1.0 Hz, 1H), 8.62 (dd, J = 7.6, 0.7 Hz, 1H), 8.40 (ddd, J = 7.8, 7.8, 1.1 Hz, 1H), 8.23 (ddd, J = 8.1, 8.1, 1.0 Hz, 1H), 3.20 (t, J = 7.0 Hz, 2H), 1.69 (sext, J = 7.3 Hz, 2H), 1.00 (t, J = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 196.5, 140.8, 136.2, 135.9, 134.8, 132.3, 113.9, 16.5, 13.4; IR (ATR) ν 3111 (w), 1700 (m), 1211 (m), 1042 (s), 786 (m); HRMS (ESI) calcd for $C_{10}H_{11}N_2O$ [M$^+$] 175.0871, found 175.0876; MS (ESI) m/z 175 (100), 161 (14), 147 (48), 122 (32).

*2-Benzoyl-5-methoxybenzenediazonium Tetrafluoroborate (**9g**).* Following the general procedure, **8g** (1.00 g, 3.7 mmol) was converted to **9g** (1.20 g, 3.6 mmol, 97%): colorless solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.73 (d, J = 2.7 Hz, 1H), 8.11 (d, J = 8.8 Hz, 1H), 7.9 (dd, J = 8.8, 2.7 Hz, 1H), 7.85−7.78 (m, 3H), 7.67 (dd, J = 7.8, 7.8 Hz, 2H), 4.04 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 189.3, 162.0, 135.4, 134.4, 134.3, 130.4, 129.5, 128.9, 124.7, 121.6, 117.2, 57.5; IR (ATR) ν 3099 (w), 2280 (m), 1654 (m), 1593 (m), 1255 (s); HRMS (ESI) calcd for $C_{14}H_{11}N_2O_2$ [M$^+$] 239.0821, found 239.0828.

*2-Benzoyl-5-methylbenzenediazonium Tetrafluoroborate (**9h**).*[79] Following the general procedure, **8h** (100 mg, 0.40 mmol) was converted to **9h** (100 mg, 0.33 mmol, 82%): colorless solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.87 (s, 1H), 8.18 (dm, J = 8.1 Hz, 1H), 8.09 (d, J = 8.0 Hz, 1H), 7.86 (dm, J = 8.0 Hz, 2H), 7.82 (tm, J = 7.5 Hz, 1H), 7.67 (dd, J = 7.8, 7.8 Hz, 2H), 2.61 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 190.6, 146.5, 141.4, 136.6, 135.6, 135.3, 134.9, 134.5, 131.4, 129.8, 116.3, 21.7; IR (ATR) ν 3111 (w), 2282 (m), 1652 (m), 1274 (m), 1021 (s); HRMS (ESI) calcd for $C_{14}H_{11}N_2O$ [M$^+$] 223.0866, found 223.0864.

*2-Benzoyl-5-chlorobenzenediazonium Tetrafluoroborate (**9i**).* Following the general procedure, **8i** (100 mg, 0.37 mmol) was converted to **9i** (95 mg, 0.29 mmol, 79%): colorless solid; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.24 (d, J = 2.1 Hz, 1H), 8.47 (dd, J = 8.4, 2.2 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 7.88 (dm, J = 8.3 Hz, 2H), 7.83 (tm, J = 7.5 Hz, 1H), 7.68 (dd, J = 8.2, 7.5, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 189.0, 140.2, 137.9, 135.9, 135.0, 134.8, 134.7, 133.7, 130.7, 129.3, 117.4; IR (ATR) ν 3104 (w), 2288 (m), 1653 (m), 1282 (m), 1019 (s); HRMS (ESI) calcd for $C_{13}H_8N_2OCl$ [M$^+$] 243.0320, found 243.0315.

General Procedure for the Synthesis of *o*-Acyl Cinnamates 10 from Arene Diazonium Salts 9 (Conditions A). To a solution of the appropriate arene diazonium salt **9** (1.0 mmol) in anhydrous methanol (3 mL) was added $Pd(OAc)_2$ (11.2 mg, 5 mol %). The solution was stirred for 0.25 h at ambient temperature, followed by addition of methyl acrylate (172 mg, 2.0 mmol). Stirring was continued at this temperature for 12 h. Water (15 mL) was added, and the mixture was extracted three times with ethyl acetate (20 mL for each extraction). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica using hexanes−MTBE mixtures as eluent.

General Procedure for the Synthesis of *o*-Acyl Cinnamates 10 from Acetanilides 8 via Deacetylation−Diazotation−Coupling (Conditions B). To a solution of the appropriate *o*-acyl acetanilide **8** (1.0 mmol) in dry and degassed methanol (6 mL) was added $BF_3{\cdot}CH_3OH$ (3.0 mmol, 324 μL). The solution was stirred at 65 °C for 16 h and then cooled to 0 °C (ice−water bath) or −21 °C (ice−salt bath) as indicated in Table 1. *t*-BuONO (103 mg, 1.0 mmol; 155 mg, 1.5 mmol; 206 mg, 2.0 mmol as indicated in Table 1) was added, and stirring at the respective temperature was continued for 0.5 h, followed by addition of $Pd(OAc)_2$ (5 mol %, 11.2 mg) and warming to ambient temperature. After the mixture was stirred for 0.25 h, methyl acrylate (172 mg, 2.0 mmol) was added, and the solution was stirred for 12 h at ambient temperature. Water (15 mL) was added, and the mixture was extracted three times with ethyl acetate (20 mL for each extraction). The combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica using a hexanes−MTBE mixture as eluent.

*(E)-Methyl 3-(2-Benzoylphenyl)acrylate (**10a**).*[49] Conditions A: Following the general procedure, **9a** (100 mg, 0.34 mmol) was converted to **10a** (84 mg, 0.32 mmol, 93%). Conditions B: following the general procedure, **8a** (239 mg, 1.00 mmol) was converted to **10a** (260 mg, 0.98 mmol, quant): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80−7.68 (m, 4H), 7.57 (tm, J = 7.4 Hz, 1H), 7.50 (m, 1H), 7.47−7.36 (4H), 6.36 (d, J = 15.9 Hz, 1H), 3.69 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.1, 166.7. 142.0, 139.4, 137.3, 133.9,

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133.5, 130.7, 130.3, 129.2, 129.1, 128.5, 127.3, 120.5, 51.7; IR (ATR) ν 3062 (w), 2950 (w), 1715 (s), 1267 (s), 1172 (s); HRMS (ESI) calcd for $C_{17}H_{15}O_3$ $[M + H]^+$ 267.1021, found 267.1022.

*(E)-Methyl 3-(2-Benzoyl-4-methoxyphenyl)acrylate (**10b**).* Conditions A: Following the general procedure, **9b** (100 mg, 0.31 mmol) was converted to **10b** (80 mg, 0.27 mmol, 88%). Conditions B: Following the general procedure, **8b** (269 mg, 1.00 mmol) was converted to **10b** (202 mg, 0.21 mmol, 68%): yellow solid; mp 108 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (dm, J = 9.0 Hz, 2H), 7.78 (d, J = 7.5 Hz, 1H), 7.76 (d, J = 15.9 Hz, 1H), 7.53 (dd, J = 7.5, 7.5 Hz, 1H), 7.47 (ddm, J = 7.5, 7.5 Hz, 1H), 7.41 (dm, J = 7.5 Hz, 1H), 6.95 (dm, J = 9.0 Hz, 2H), 6.40 (d, J = 15.9 Hz, 1H), 3.90 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.9, 166.9, 164.2, 142.2, 140.3, 133.6, 133.0, 130.5, 130.3, 129.4, 128.9, 127.3, 120.6, 114.1, 55.8, 51.9; IR (ATR) ν 2951 (w), 2840 (w), 1595 (s), 1253 (s), 1149 (s); HRMS (ESI) calcd for $C_{18}H_{17}O_4$ $[M + H]^+$ 297.1127, found 297.1100; MS (ESI) m/z 297 (100), 294 (13), 265 (10), 196 (18). Anal. Calcd for $C_{18}H_{16}O_4$ (296.32): C, 73.0; H, 5.4. Found: C, 73.0; H, 5.2.

*(E)-Methyl 3-(2-Benzoyl-4-chlorophenyl)acrylate (**10c**).* Conditions A: Following the general procedure, **9c** (93 mg, 0.28 mmol) was converted to **10c** (79 mg, 0.26 mmol, 93%). Conditions B: Following the general procedure, **8c** (273 mg, 1.00 mmol) was converted to **10c** (294 mg, 0.98 mmol, quant): yellow solid; mp 98–100 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77–7.68 (m, 4H), 7.53 (ddm, J = 7.5, 7.5 Hz, 1H), 7.48–7.34 (m, 4H), 6.36 (d, J = 15.9 Hz, 1H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.1, 166.9, 141.9, 140.4, 139.1, 135.9, 134.1, 131.9, 131.2, 129.5, 129.3, 129.2, 127.6, 121.0, 51.9; IR (ATR) ν 3211 (w), 2951 (w), 1719 (s), 1582 (s), 1163 (s); HRMS (ESI) calcd for $C_{17}H_{14}O_3Cl$ $[M + H]^+$ 301.0631, found 301.0628; MS (ESI) m/z 301 (36), 202 (51), 196 (100), 176 (64). Anal. Calcd for $C_{17}H_{13}ClO_3$ (300.74): C, 67.9; H, 4.4. Found: C, 67.8; H, 4.3.

*(E)-Methyl 3-(2-Benzoyl-4-fluorophenyl)acrylate (**10d**).* Conditions A: Following the general procedure, **9d** (100 mg, 0.32 mmol) was converted to **10d** (76 mg, 0.27 mmol, 84%). Conditions B: Following the general procedure, **9d** (257 mg, 1.00 mmol) was converted to **10d** (280 mg, 0.98 mmol, quant): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87–7.76 (m, 2H), 7.72 (d, J = 15.9 Hz, 1H), 7.72 (d, J = 7.5 Hz, 1H), 7.52 (ddd, J = 7.5, 7.5, 1.6 Hz, 1H), 7.43 (ddd, J = 7.5, 7.5, 1.2 Hz, 1H), 7.38 (dd, J = 7.5, 1.5 Hz, 1H), 7.22 (ddm, J = 9.0, 9.0 Hz, 2H), 6.36 (d, J = 15.9 Hz, 1H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.7, 166.9, 166.2 (J = 255 Hz), 164.5, 141.9, 139.3, 134.0, 133.9, 133.2 (J = 9.0 Hz), 131.0, 129.3 (J = 21.8 Hz), 127.5, 120.9, 116.0 (J = 21.8 Hz), 51.9; IR (ATR) ν 2951 (w), 1716 (s), 1595 (s), 1270 (s), 1148 (s); HRMS (ESI) calcd for $C_{17}H_{13}O_3F$ $[M + H]^+$ 285.0927, found 285.0918; MS (ESI) m/z 383 (100), 294 (20), 285 (72), 196 (59).

*(E)-Methyl 3-(2-(3-Methylbutanoyl)phenyl)acrylate (**10e**).* Conditions B: Following the general procedure, **8e** (100 mg, 0.45 mmol) was converted to **10e** (108 mg, 0.44 mmol, quant): yellow solid; mp 181–184 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, J = 15.9 Hz, 1H), 7.64 (dd, J = 7.5, 1.5 Hz, 1H), 7.57 (dd, J = 7.5, 1.4 Hz, 1H), 7.47 (ddd, J = 7.5, 7.5, 1.4 Hz, 1H), 7.42 (ddd, J = 7.5, 7.5, 1.4 Hz, 1H), 6.27 (d, J = 15.9 Hz, 1H), 3.77 (s, 3H), 2.76 (d, J = 6.9 Hz, 2H), 2.25 (nonet, J = 6.7 Hz, 1H), 0.96 (d, J = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.6, 166.9, 143.8, 139.3, 134.4, 131.5, 129.4, 128.4, 128.2, 120.4, 51.7, 50.5, 25.2, 22.7; IR (ATR) ν 2955 (m), 1716 (s), 1682 (s), 1273 (s), 1170 (s); HRMS (EI) calcd for $C_{15}H_{18}O_3$ $[M^+]$ 246.1256, found 246.1242; MS (EI) m/z 246 (23), 187 (100), 145 (27), 115 (23). Anal. Calcd for $C_{15}H_{18}O_3$ (246.30): C, 73.2; H, 7.4. Found: C, 72.8; H, 7.3.

*(E)-Methyl 3-(2-Butyrylphenyl)acrylate (**10f**).* Conditions A: Following the general procedure, **9f** (70 mg, 0.27 mmol) was converted to **10f** (61 mg, 0.26 mmol, quant). Conditions B: Following the general procedure, **8f** (103 mg, 0.50 mmol) was converted to **10f** (70 mg, 0.30 mmol, 60%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, J = 15.9 Hz, 1H), 7.66 (dd, J = 7.3, 1.4 Hz, 1H), 7.56 (dd, J = 7.3, 1.5 Hz, 1H), 7.48 (ddd, J = 7.3, 7.3, 1.3 Hz, 1H), 7.42 (ddd, J = 7.3, 7.3, 1.4 Hz, 1H), 6.26 (d, J = 15.9 Hz, 1H), 3.78 (s, 3H), 2.87 (t, J = 7.3 Hz, 2H), 1.73 (sext, J = 7.3 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.8, 166.9, 143.9, 138.9, 134.5, 131.5, 129.4, 128.4, 128.2, 120.4, 51.7, 43.5, 17.8, 13.8; IR (ATR) ν 2959 (w), 1716 (s), 1682 (s), 1273 (s), 1169 (s); HRMS (EI) calcd for $C_{14}H_{16}O_3$ $[M^+]$ 232.1099, found 232.1105; MS (EI) m/z 232 (15), 173 (100), 131 (14), 151 (14). Anal. Calcd for $C_{14}H_{16}O_3$ (232.28): C, 72.4; H, 6.9. Found: C, 71.9; H, 6.5.

*(E)-Methyl 3-(2-Benzoyl-5-methoxyphenyl)acrylate (**10g**).* Conditions A: Following the general procedure, **9g** (100 mg, 0.31 mmol) was converted to **10g** (80 mg, 0.27 mmol, 88%). Conditions B: Following the general procedure, **8g** (134 mg, 0.50 mmol) was converted to **10g** (118 mg, 0.40 mmol, 80%): orange-yellow solid; mp 100–104 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 15.9 Hz, 1H), 7.74 (dm, J = 8.5 Hz, 1H), 7.55 (tt, J = 7.4, 1.3 Hz, 1H), 7.51–7.35 (m, 3H), 7.17 (d, J = 2.5 Hz, 1H), 6.91 (dd, J = 8.5, 2.5 Hz, 1H), 6.34 (d, J = 15.9 Hz, 1H), 3.38 (s, 3H), 3.72 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.3, 166.7, 161.6, 142.8, 138.1, 137.1, 132.9, 132.4, 131.5, 130.2, 128.4, 120.6, 114.3, 112.7, 55.6, 51.7; IR (ATR) ν 2949 (w), 1715 (s), 1596 (s), 1227 (s), 1169 (s); HRMS (EI) calcd for $C_{18}H_{16}O_4$ $[M^+]$ 296.1049, found 296.1033; MS (EI) m/z 296 (13), 237 (100), 194 (12), 165 (10). Anal. Calcd for $C_{18}H_{16}O_4$ (296.32): C, 72.9; H, 5.4. Found: C, 72.9; H, 5.4.

*(E)-Methyl 3-(2-Benzoyl-5-methylphenyl)acrylate (**10h**).* Conditions A: Following the general procedure, **9h** (100 mg, 0.32 mmol) was converted to **10h** (77 mg, 0.27 mmol, 86%). Conditions B: Following the general procedure, **8h** (253 mg, 1.00 mmol) was converted to **10h** (158 mg, 0.56 mmol, 56%): yellow solid; mp 118–122 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 15.9 Hz, 1H), 7.75 (dm, J = 8.4 Hz, 2H), 7.55 (tm, J = 7.4 Hz, 1H), 7.51 (s, 1H), 7.43 (dd, J = 8.4, 7.4 Hz, 2H)), 7.32 (d, J = 7.8 Hz, 1H), 7.22 (d, J = 7.8 Hz, 1H), 6.35 (d, J = 15.9 Hz, 1H), 3.71 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.1, 166.8, 142.4, 141.2, 137.7, 136.5, 134.3, 133.3, 130.3, 129.8, 129.7, 128.5, 127.9, 120.2, 51.7, 21.5; IR (ATR) ν 2950 (w), 1716 (s), 1655 (s), 1274 (s), 1170 (s); HRMS (EI) calcd for $C_{18}H_{16}O_3$ $[M^+]$ 280.1099, found 280.1093; MS (EI) m/z 280 (23), 222 (13), 221 (100), 178 (10). Anal. Calcd for $C_{18}H_{16}O_3$ (280.32): C, 77.1; H, 5.8. Found: C, 76.8; H, 5.7.

*(E)-Methyl 3-(2-Benzoyl-5-chlorophenyl)acrylate (**10i**).* Conditions A: Following the general procedure, **9i** (100 mg, 0.30 mmol) was converted to **10i** (89 mg, 0.29 mmol, quant). Conditions B: Following the general procedure, **8i** (273 mg, 1.00 mmol) was converted to **10i** (295 mg, 0.98 mmol, quant): colorless solid; mp 108–113 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 7.5 Hz, 2H), 7.70 (d, J = 15.8 Hz, 1H), 7.68 (s, 1H), 7.59 (t, J = 7.4 Hz, 1H), 7.45 (dd, J = 7.7, 7.7 Hz, 2H), 7.42–7.31 (m, 2H), 6.35 (d, J = 15.9 Hz, 1H), 3.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.2, 166.5, 140.9, 137.7, 137.3, 136.2, 133.9, 130.9, 130.5, 129.3, 128.9, 128.9, 127.5, 121.9, 52.0; IR (ATR) ν 2951 (w), 1721 (s), 1661 (s), 1279 (s), 1196 (s); HRMS (EI) calcd for $C_{17}H_{13}O_3Cl$ $[M^+]$ 300.0553, found 300.0550; MS (EI) m/z 300 (8), 285 (23), 241 (100), 178 (23). Anal. Calcd for $C_{17}H_{13}O_3Cl$ (300.74): C, 67.9; H, 4.4. Found: C,: 67.9; H, 4.1.

*(E)-Methyl 3-(2-Benzoyl-4-isopropylphenyl)acrylate (**10j**).* Conditions B: Following the general procedure, **8j** (100 mg, 0.36 mmol) was converted to **10j** (33 mg, 0.11 mmol, 30%): yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 7.3 Hz, 2H), 7.71 (d, J = 15.9 Hz, 1H), 7.65 (d, J = 8.2 Hz, 1H), 7.58 (tm, J = 7.4 Hz, 1H), 7.46 (dd, J = 7.7, 7.7 Hz, 2H), 7.37 (dm, J = 8.2 Hz, 1H), 7.24 (s, 1H), 6.32 (d, J = 15.9 Hz, 1H), 3.69 (s, 3H), 2.92 (sept., J = 6.9 Hz, 1H), 1.23 (d, J = 6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.5, 166.9, 150.5, 141.9, 139.6, 137.4, 133.5, 131.3, 130.4, 128.9, 128.5, 127.3, 127.2, 119.5, 51.6, 33.9, 23.6; IR (ATR) ν 2960 (m), 1718 (s), 1268 (s), 1170 (s), 721 (s); HRMS (EI) calcd for $C_{20}H_{20}O_3$ $[M^+]$ 308.1412, found 308.1414; MS (EI) m/z 308 (28), 249 (100), 233 (10), 77 (10).

*8-Phenyl-3a,8-dihydro-3H-pyrazolo[5,1-a]isoindol-2-ol (**14**).* Compound **10a** (100 mg, 0.37 mmol) and hydrazine (24 mg of 80 wt % solution in water, 0.37 mmol) were dissolved in ethylene glycol (5 mL) and irradiated for 0.5 h at 250 °C in a dedicated microwave reactor. The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography

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on silica using hexane/ethyl acetate (1:1) to furnish **14** (20 mg, 0.08 mmol, 20%): pale red solid; mp 215 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.99 (s, 1H), 7.66 (d, J = 7.5 Hz, 1H), 7.40 (ddd, J = 8.2, 8.2, 1.8 Hz, 1H), 7.38−7.24 (m, 5H), 7.08 (d, J = 7.0 Hz, 2H), 6.22 (s, 1H), 5.83 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.6, 145.1, 144.9, 138.6, 129.9, 128.7, 128.3, 128.0, 127.3, 126.9, 123.7, 120.1, 82.2, 65.9; IR (ATR) ν 2922 (m), 1489 (s), 1088 (w), 747 (s), 697 (m); HRMS (ESI) calcd for $C_{16}H_{12}ON_2$ [M$^+$] 248.0950, found 248.0947; MS (EI) m/z 248 (100), 220 (21), 189 (22), 165 (18).

General Procedure for the Synthesis of Stilbenes 18. To a solution of the corresponding arene diazonium salt **9** (1.0 equiv) in anhydrous MeOH (15 mL per mmol of **9**) was added $Pd(OAc)_2$ (5.0 mol %). The mixture was stirred at ambient temperature for 0.25 h, and the appropriate styrene **17** (1.2 equiv) was added. The solution was stirred for 16 h at ambient temperature, and water (15 mL) was added. The mixture was extracted three times with ethyl acetate (20 mL each), and the combined organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica using hexanes/MTBE (10:1) as eluent.

*(E)-Phenyl-(2-styrylphenyl)methanone (**18aa**).* Following the general procedure, **9a** (100 mg, 0.34 mmol) and **17a** (47 μL, 0.41 mmol) were converted to **18aa** (93 mg, 0.33 mmol, 96%): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90−7.81 (m, 3H), 7.65−7.21 (m, 12H), 7.08 (d, J = 16.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.5, 138.2, 138.1, 137.3, 136.8, 133.5, 131.5, 130.8, 130.5, 129.3, 128.8, 128.7, 128.1, 127.0, 126.9, 126.2, 126.1; IR (ATR) ν 3059 (w), 1656 (s), 1490 (m), 1268 (s), 1086 (s); HRMS (EI) calcd for $C_{21}H_{16}O$ [M$^+$] 284.1201, found 284.1213; MS (EI) m/z 284 (57), 207 (38), 178 (100), 105 (68), 77 (76).

*(E)-(2-(4-Chlorostyryl)phenyl)(phenyl)methanone (**18ab**).* Following the general procedure, **9a** (100 mg, 0.34 mmol) and **17b** (51 μL, 0.41 mmol) were converted to **18ab** (102 mg, 0.32 mmol, 95%): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85−7.75 (m, 3H), 7.62−7.21 (m, 10H), 7.18 (d, J = 16.2 Hz, 1H), 6.98 (d, J = 16.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.4, 138.1, 138.0, 136.6, 135.8, 133.7, 133.5, 130.9, 130.5, 130.1, 129.4, 128.9, 128.7, 128.1, 127.2, 126.9, 126.2; IR (ATR) ν 3058 (w), 1657 (s), 1596 (m), 1448 (s), 1273 (s); HRMS (EI) calcd for $C_{21}H_{15}OCl$ [M$^+$] 318.0811, found 318.0804; MS (EI) m/z 318 (26), 207 (22), 178 (48), 105 (49), 77 (100).

*(E)-(4-Methoxyphenyl)-(2-styrylphenyl)methanone (**18ba**).* Following the general procedure, **9b** (100 mg, 0.31 mmol) and **17a** (42 μL, 0.37 mmol) were converted to **18ba** (83 mg, 0.26 mmol, 86%): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88−7.80 (m, 3H), 7.52 (ddd, J = 8.0, 8.0, 2.2 Hz, 1H), 7.42−7.20 (m, 7H), 7.20 (d, J = 16.2 Hz, 1H), 7.08 (d, J = 16.2 Hz, 1H), 6.95 (dm, J = 8.9 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.2, 164.0, 138.8, 137.3, 136.3, 132.9, 131.2, 130.9, 130.3, 128.8, 128.7, 128.0, 127.1, 126.9, 126.2, 126.0, 114.0, 55.7; IR (ATR) ν 2956 (w), 1651 (m), 1594 (s), 1252 (s), 1148 (s); HRMS (EI) calcd for $C_{22}H_{18}O_2$ [M$^+$] 314.1307, found 314.1306; MS (EI) m/z 314 (100), 237 (18), 206 (24), 178 (12), 108 (22). Anal. Calcd for $C_{22}H_{18}O_2$ (314.38): C, 84.0; H, 5.8. Found: C, 83.5; H, 5.8.

*(E)-(2-(4-Chlorostyryl)phenyl)-(4-methoxyphenyl)methanone (**18bb**).* Following the general procedure, **9b** (100 mg, 0.31 mmol) and **17b** (47 μL, 0.37 mmol) were converted to **18bb** (92 mg, 0.26 mmol, 86%): colorless solid; mp 95−96 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87−7.77 (m, 3H), 7.51 (ddd, J = 8.0, 8.0, 2.2 Hz, 1H), 7.42−7.20 (m, 6H), 7.18 (d, J = 16.2 Hz, 1H), 7.02 (d, J = 16.2 Hz, 1H), 6.95 (dm, J = 8.9 Hz, 2H), 3.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.0, 164.1, 138.8, 136.1, 135.8, 133.6, 132.9, 130.8, 130.4, 129.9, 128.9, 128.9, 128.1, 127.2, 128.8, 126.0, 113.9, 55.7; IR (ATR) ν 2927 (w), 1651 (m), 1594 (s), 1491 (m), 1253 (s); HRMS (EI) calcd for $C_{22}H_{17}O_2Cl$ [M$^+$] 348.0917, found 348.0925; MS (EI) m/z 348 (100), 240 (18), 108 (46). Anal. Calcd for $C_{22}H_{17}ClO_2$ (348.83): C, 75.7; H, 4.9. Found: C, 75.2; H, 4.8.

*(E)-(4-Chlorophenyl)-(2-styrylphenyl)methanone (**18ca**).* Following the general procedure, **9c** (100 mg, 0.30 mmol) and **17a** (42 μL, 0.36 mmol) were converted to **18ca** (75 mg, 0.24 mmol, 78%):orange-yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86−7.75 (m, 3H), 7.51 (ddd, J = 8.0, 8.0, 2.2 Hz, 1H), 7.45 (dm, J = 8.7 Hz, 2H), 7.42−7.24 (7H), 7.21 (d, J = 16.3 Hz, 1H), 7.07 (d, J = 16.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.2, 140.0, 137.6, 137.1, 136.8, 136.4, 131.8, 131.8, 131.0, 129.1, 129.0, 128.8, 128.2, 127.1, 126.9, 126.4, 125.9; IR(ATR) ν 3058 (w), 1658 (m), 1585 (s), 1271 (m), 1089 (s); HRMS (EI) calcd for $C_{21}H_{15}OCl$ [M$^+$] 318.0811, found 318.0809; MS (EI) m/z 318 (100), 241 (33), 206 (26), 178 (20). Anal. Calcd for $C_{21}H_{15}OCl$ (318.80): C, 79.1; H, 4.7. Found: C, 79.0; H, 4.7.

*(E)-(4-Chlorophenyl)-(2-(4-chlorostyryl)phenyl)methanone (**18cb**).* Following the general procedure, **9c** (100 mg, 0.30 mmol) and **17b** (42 μL, 0.36 mmol) were converted to **18cb** (85 mg, 0.24 mmol, 80%): colorless solid; mp 90−92 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85−7.75 (m, 3H), 7.55 (ddd, J = 8.0, 8.0, 2.4 Hz, 1H), 7.45 (d, J = 8.4 Hz, 2H), 7.42−7.24 (m, 6H), 7.19 (d, J = 16.2 Hz, 1H), 7.01 (d, J = 16.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.1, 140.1, 137.6, 136.6, 136.3, 135.7, 133.8, 131.9, 131.1, 130.5, 129.3, 129.1, 129.0, 128.1, 127.3, 126.6, 126.4; IR (ATR) ν 3058 (w), 1649 (m), 1594 (s), 1262 (s), 700 (s); HRMS (EI) calcd for $C_{21}H_{14}OCl_2$ [M$^+$] 352.0422, found 352.0427; MS (EI) m/z 314 (56), 237 (44), 194 (35), 165 (100), 105 (78). Anal. Calcd for $C_{21}H_{14}OCl_2$ (353.24): C, 71.4; H, 3.9. Found: C, 71.0; H, 4.0.

*(E)-1-(2-Styrylphenyl)butan-1-one (**18fa**).* Following the general procedure, **9f** (85 mg, 0.32 mmol) and **17a** (44 μL, 0.38 mmol) were converted to **18fa** (46 mg, 0.18 mmol, 57%): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J = 7.8 Hz, 1H), 7.63 (m, 1H), 7.59−7.50 (m, 3H), 7.45 (dd, J = 7.6, 1.1 Hz, 1H), 7.43−7.34 (m, 3H), 7.34−7.25 (m, 2H), 7.02 (d, J = 16.2 Hz, 1H), 2.93 (t, J = 7.6 Hz, 2H), 1.78 (sext, J = 7.6 Hz, 2H), 1.02 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.6, 138.5, 137.5, 137.0, 131.8, 131.3, 128.9, 128.4, 128.1, 127.4, 127.4, 127.4 127.0, 44.4, 18.2, 14.1; IR (ATR) ν 2961 (w), 1681 (s), 1494 (m), 1204 (m), 759 (s); HRMS (EI) calcd for $C_{18}H_{18}O$ [M$^+$] 250.1358, found 250.1361; MS (EI) m/z 250 (36), 221 (32), 207 (42), 178 (100), 91 (26).

*(E)-1-(2-(4-Chlorostyryl)phenyl)butan-1-one (**18fb**).* Following the general procedure, **9f** (85 mg, 0.32 mmol) and **17b** (48 μL, 0.38 mmol) were converted to **18fb** (57 mg, 0.20 mmol, 63%): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, J = 7.6 Hz, 1H), 7.69 (dd, J = 7.7, 0.9 Hz, 1H), 7.59 (d, J = 16.2 Hz, 1H), 7.54−7.25 (m, 6H), 6.95 (d, J = 16.2 Hz, 1H), 2.92 (t, J = 7.3 Hz, 2H), 1.78 (sext, J = 7.6 Hz, 2H), 1.01 (t, J = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.2, 138.2, 136.9, 136.0, 133.6, 131.5, 130.3, 129.0, 128.6, 128.2, 128.1, 127.6, 127.4, 44.1, 18.2, 14.1; IR (ATR) ν 2961 (w), 1680 (s), 1490 (m), 1203 (m), 1089 (m); HRMS (EI) calcd for $C_{18}H_{17}OCl$ [M$^+$] 284.0968, found 284.0965; MS (EI) m/z 284 (38), 241 (64), 178 (100), 151 (30), 88 (34).

*(E)-(4-Methoxy-2-styrylphenyl)(phenyl)methanone (**18ga**).* Following the general procedure, **9g** (100 mg, 0.31 mmol) and **17a** (42 μL, 0.37 mmol) were converted to **18ga** (67 mg, 0.21 mmol, 70%): orange-yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (dm, J = 7.8 Hz, 2H), 7.58 (m, 1H), 7.54−7.35 (m, 6H), 7.35−7.20 (m, 4H), 7.06 (d, J = 16.2 Hz, 1H), 6.87 (dd, J = 8.5, 2.4 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.6, 161.8, 140.0, 139.0, 137.3, 132.9, 132.5, 131.5, 130.6, 130.4, 128.8, 128.5, 128.1, 127.0, 126.9, 112.5, 111.5, 55.7; IR (ATR) ν 3058 (w), 1649 (m), 1594 (m), 1263 (m), 700 (s); HRMS (EI) calcd for $C_{22}H_{18}O_2$ [M$^+$] 314.1307, found 314.1311; MS (EI) m/z 314 (50), 237 (40), 165 (100), 105 (70).

*(E)-(2-(4-Chlorostyryl)-4-methoxyphenyl)(phenyl)methanone (**18gb**).* Following the general procedure, **9g** (100 mg, 0.31 mmol) and **17b** (46 μL, 0.37 mmol) were converted to **18gb** (80 mg, 0.23 mmol, 75%): yellow solid; mp 108−110 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 8.0 Hz, 2H), 7.59 (dd, J = 7.3, 7.3 Hz, 1H), 7.52−7.39 (m, 3H), 7.39−7.23 (m, 6H), 7.00 (d, J = 16.2 Hz, 1H), 6.88 (dd, J = 8.6, 2.4 Hz, 1H), 3.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.5, 161.9, 139.7, 138.9, 135.8, 133.7, 132.9, 132.7, 130.5, 130.4, 130.1, 128.9, 128.6, 128.2, 127.5, 112.6, 111.6, 55.7; IR (ATR) ν 3062 (w), 1649 (m), 1594 (s), 1491 (m), 1260 (s); HRMS (EI) calcd for $C_{22}H_{17}O_2Cl$ [M$^+$] 348.0917, found 348.0923; MS (EI) m/z 348 (26), 237 (26), 165 (56), 105 (47), 77 (78). Anal. Calcd for $C_{22}H_{17}O_2Cl$ (348.83): C, 75.7; H, 4.9. Found: C, 75.2; H, 4.9.

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*(E)-(4-Chloro-2-styrylphenyl)(phenyl)methanone (**18ia**).* Following the general procedure, **9i** (100 mg, 0.30 mmol) and **17a** (42 μL, 0.37 mmol) were converted to **18ia** (77 mg, 0.24 mmol, 80%): yellow solid; mp 68−71 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89−7.79 (m, 3H), 7.61 (tm, *J* = 7.5 Hz, 1H), 7.49 (dd, *J* = 7.4, 7.4 Hz, 2H), 7.41−7.22 (m, 7H), 7.19 (d, *J* = 16.2 Hz, 1H), 7.08(d, *J* = 16.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.4, 138.9, 137.8, 137.0, 136.8, 136.3, 133.7, 132.7, 130.8, 130.4, 128.9, 128.8, 128.5, 127.1, 127.0, 126.2, 124.9; IR (ATR) ν 3059 (w), 1658 (s), 1584 (m), 1271 (m), 1243 (m); HRMS (EI) calcd for $C_{21}H_{15}OCl$ [M^+] 318.0811, found 318.00807; MS (EI) *m*/*z* 318 (32), 241 (36), 178 (66), 105 (74), 77 (100). Anal. Calcd for $C_{21}H_{15}OCl$ (318.80): C, 79.1; H, 4.7. Found: C, 78.7; H, 4.7.

*(E)-(4-Chloro-2-(4-chlorostyryl)phenyl(phenyl)methanone (**18ib**).* Following the general procedure, **9i** (100 mg, 0.30 mmol) and **17b** (46 μL, 0.36 mmol) were converted to **18ib** (80 mg, 0.23 mmol, 75%): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87−7.70 (m, 3H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.45 (dd, *J* = 7.4, 7.4 Hz, 2H), 7.36−7.18 (m, 6H), 7.13 (d, *J* = 16.2 Hz, 1H), 6.98 (d, *J* = 16.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.3, 138.6, 137.8, 137.2, 136.2, 135.3, 134.2, 133.7, 131.3, 130.9, 130.4, 129.1, 128.8, 128.2, 127.2, 126.2, 125.6; IR (ATR) ν 3061 (w), 1658 (s), 1583 (m), 1489 (s), 1267 (m); MS (EI) *m*/*z* 354 (6), 352 (10), 176 (60), 105 (45), 77 (100).

General Procedure for the Synthesis of Biaryls 20. To a solution of arene diazonium salt **9** (1.0 equiv) in anhydrous methanol or dioxane (15 mL per mmol of **9**) were added $Pd(OAc)_2$ (5 mol %) and the potassium organotrifluoroborate **19** (1.2 equiv). The reaction mixture was stirred for 12 h at ambient temperature and then filtered through a short pad of Celite, which was washed with MTBE (30 mL). All volatiles were evaporated, and the residue was purified by chromatography on silica, using hexane−MTBE mixtures as eluent.

*Biphenyl-2-yl(phenyl)methanone (**20aa**).*[83] Following the general procedure, **9a** (100 mg, 0.34 mmol) and **19a** (75 mg, 0.41 mmol) were converted to **20aa** (in methanol: 80 mg, 0.31 mmol, 91%; in dioxane: 82 mg, 0.32 mmol, 93%): yellow solid; mp 88 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (dm, *J* = 8.5 Hz, 2H), 7.60−7.34 (m, 5H), 7.30−7.09 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.9, 141.3, 140.4, 139.2, 137.6, 132.9, 130.5, 130.3, 130.1, 129.2, 128.9, 128.4, 128.3, 127.5, 127.3; IR (ATR) ν 3058 (w), 1660 (s), 1448 (m), 1277 (s), 927 (m); HRMS (ESI) calcd for $C_{19}H_{14}O$ [M^+] 258.1045, found 258.1042; MS (EI) *m*/*z* 258 (60), 181 (86), 152 (100), 105 (66), 77 (74).

*Biphenyl-2-yl(4-methoxyphenyl)methanone (**20ba**).* Following the general procedure, **9b** (100 mg, 0.31 mmol) and **19a** (68 mg, 0.37 mmol) were converted to **20ba** (in methanol: 69 mg, 0.24 mmol, 78%; in dioxane: 80 mg, 0.28 mmol, 91%): yellow solid; mp 126−129 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.68−7.46 (m, 5H), 7.42 (dm, *J* = 8.8 Hz, 1H), 7.32−7.15 (m, 5H), 6.92 (d, *J* = 8.8 Hz, 2H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 196.1, 163.2, 139.9, 138.9, 138.8, 131.9, 130.1, 129.9, 129.6, 128.5, 128.3, 127.9, 127.3, 127.2, 113.8, 55.5; HRMS (ESI) calcd for $C_{20}H_{16}O_2$ [M^+] 288.1150, found 288.1136; MS (EI) *m*/*z* 288 (30), 181 (12), 152 (98), 135 (100), 92 (44). Anal. Calcd for $C_{20}H_{16}O_2$ (288.35): C, 83.3; H, 5.6. Found: C, 83.0; H, 5.6.

*Biphenyl-2-yl(4-chlorophenyl)methanone (**20ca**).*[84] Following the general procedure, **9c** (100 mg, 0.30 mmol) and **19a** (66 mg, 0.36 mmol) were converted to **20ca** (in methanol: 68 mg, 0.23 mmol, 77%; in dioxane: 58 mg, 0.20 mmol, 66%): yellow solid; mp 125 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70−7.45 (m, 6H), 7.33−7.15 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.8, 141.3, 140.2, 139.4, 138.7, 135.9, 131.4, 130.8, 130.3, 129.2, 128.9, 128.6, 128.6, 127.7, 127.5; IR (ATR) ν 3059 (w), 1661 (s), 1584 (s), 1276 (s), 1089 (s); HRMS (EI) calcd for $C_{19}H_{13}OCl$ [M^+] 292.0655, found 292.0662; MS (EI) *m*/*z* 292 (18), 181 (36), 152 (80), 139 (82), 57 (100). Anal. Calcd for $C_{19}H_{13}OCl$ (292.76): C, 77.9; H, 4.5. Found: C, 77.4; H, 4.3.

*1-(Biphenyl-2-yl)butan-1-one (**20fa**).* Following the general procedure, **9f** (85 mg, 0.32 mmol) and **19a** (70 mg, 0.38 mmol) were converted to **20fa** (in methanol: 57 mg, 0.25 mmol, 79%; in dioxane: 42 mg, 0.19 mmol, 59%): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52−7.28 (m, 9H), 2.19 (t, *J* = 7.6 Hz, 2H), 1.43 (sext, *J* = 7.6 Hz, 2H), 0.68 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.3, 141.5, 140.9, 140.2, 130.5, 130.3, 129.1, 128.8, 128.0, 127.8, 127.6, 45.0, 18.1, 13.8; IR (ATR) ν 2962 (w), 1685 (s), 1449 (w), 1207 (m), 743 (s); HRMS (ESI) calcd for $C_{16}H_{16}O$ [M^+] 224.1201, found 224.1206; MS (EI) *m*/*z* 224 (18), 181 (100), 152 (74), 127 (22).

*(5-Methoxybiphenyl-2-yl)(phenyl)methanone (**20ga**).* Following the general procedure, **9g** (100 mg, 0.31 mmol) and **19a** (68 mg, 0.37 mmol) were converted to **20ga** (in methanol: 78 mg, 0.27 mmol, 87%; in dioxane: 65 mg, 0.23 mmol, 73%): yellow solid; mp 81−84 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (dm, *J* = 8.4 Hz, 2H), 7.54 (dm, *J* = 8.7 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.35−7.13 (m, 7H), 7.03−6.96 (m, 2H), 3.93 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.2, 161.4, 144.0, 140.6, 138.3, 132.6, 131.7, 131.6, 130.1, 129.1, 128.4, 128.1, 127.6, 115.8, 112.6, 55.7; IR (ATR) ν 3058 (w), 1656 (m), 1596 (s), 1282 (s), 926 (m); HRMS (ESI) calcd for $C_{20}H_{16}O_2$ [M^+] 288.1150, found 288.1155; MS (EI) *m*/*z* 288 (56), 211 (100), 168 (34), 139 (54), 105 (56). Anal. Calcd for $C_{20}H_{16}O_2$ (288.35): C, 83.3; H, 5.6. Found: C, 82.9; H, 5.5.

*(5-Chlorobiphenyl-2-yl)(phenyl)methanone (**20ia**).* Following the general procedure, **9i** (100 mg, 0.30 mmol) and **19a** (66 mg, 0.36 mmol) were converted to **20ia** (in methanol: 48 mg, 0.16 mmol, 55%; in dioxane: 68 mg, 0.23 mmol, 78%): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (dm, *J* = 8.4 Hz, 2H), 7.53−7.40 (m, 4H), 7.33−7.18 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.8, 143.2, 139.1, 137.5, 137.3, 136.5, 133.2, 130.4, 130.3, 130.0, 129.0, 128.6, 128.4, 128.1, 127.4; IR (ATR) ν 3059 (w), 1665 (s), 1589 (m), 1279 (m), 697 (s); HRMS (ESI) calcd for $C_{19}H_{13}OCl$ [M^+] 292.0655, found 292.0667; MS (EI) *m*/*z* 292 (60), 214 (50), 126 (74), 105 (98), 77 (100).

*(4-Chlorophenyl)(4′-methoxybiphenyl-2-yl)methanone (**20cb**).* Following the general procedure, **9c** (100 mg, 0.30 mmol) and **19b** (96 mg, 0.45 mmol) were converted to **20cb** (in dioxane: 96 mg, 0.30 mmol, quant): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58−7.50 (m, 3H), 7.48−7.36 (m, 3H), 7.25−7.18 (m, 2H), 7.14 (dm, *J* = 8.7 Hz, 2H), 6.72 (dm, *J* = 8.7 Hz, 2H), 3.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.0, 159.3, 140.8, 139.4, 138.6, 135.9, 132.6, 131.4, 130.7, 130.3, 130.1, 128.8, 128.6, 127.0, 114.1, 55.4; IR (ATR) ν 2922 (m), 1603 (m), 1273 (s), 1039 (s), 822 (s); HRMS (ESI) calcd for $C_{20}H_{15}O_2Cl$ [M^+] 322.0761, found 322.0762; MS (EI) *m*/*z* 322 (36), 211 (26), 139 (50), 58 (22), 60 (100).

*(4-Chlorophenyl)(4′-fluorobiphenyl-2-yl)methanone (**20cc**).* Following the general procedure, **9c** (100 mg, 0.30 mmol) and **19c** (73 mg, 0.36 mmol) were converted to **20cc** (in dioxane: 81 mg, 0.26 mmol, 87%): colorless solid; mp 120−122 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65−7.42 (m, 6H), 7.30−7.18 (m, 4H), 6.98−6.88 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.6, 162.5 (d, *J* = 247.4 Hz), 140.1, 139.6, 138.7, 136.2 (d, *J* = 3.3 Hz), 135.8, 131.3, 130.8 (d, *J* = 2.7 Hz), 130.7, 130.3, 128.9, 128.7, 127.6, 115.6 (d, *J* = 21.6 Hz); ^{19}F NMR (282 MHz, $CDCl_3$) δ −115.8; IR (ATR) ν 1661 (m), 1586 (m), 1222 (m), 905 (s), 728 (s); HRMS (ESI) calcd for $C_{19}H_{12}OClF$ [M^+] 310.0561, found 310.0562; MS (EI) *m*/*z* 310 (100), 199 (84), 170 (80), 139 (64).

*(4-Chlorophenyl)(2-(naphthalen-2-yl)phenyl)methanone (**20cd**).* Following the general procedure, **9c** (100 mg, 0.30 mmol) and **19d** (85 mg, 0.36 mmol) were converted to **20cd** (in dioxane: 98 mg, 0.28 mmol, 96%): colorless solid; mp 143−145 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80−7.33 (m, 13H), 7.15 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.8, 141.1, 139.4, 138.9, 137.6, 135.9, 133.3, 132.6, 131.3, 130.8, 130.6, 128.9, 128.6, 128.4, 128.3, 128.2, 127.8, 127.5, 127.0, 126.5, 126.4; IR (ATR) ν 3055 (w), 1663 (s), 1586 (s), 1286 (m), 927 (s); HRMS (ESI) calcd for $C_{23}H_{15}OCl$ [M^+] 342.0811, found 342.0819; MS (EI) *m*/*z* 342 (18), 202 (12), 83 (100), 47 (48). Anal. Calcd for $C_{23}H_{15}OCl$ (342.82): C, 80.6; H, 4.4. Found: C, 80.3; H, 4.4.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all compounds; crystallographic details for compound **14** (CCDC-1044259).

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Notes

The authors declare no competing financial interest.

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