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Acetamidoarenediazonium Salts: Opportunities for Multiple Arene Functionalization

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Unlike their *ortho* counterparts, *meta*- and *para*-acetamidoanilines can be converted into the corresponding acetamidoarenediazonium salts. These offer various opportunities for multiple Pd-catalyzed arene functionalization reactions, such as Matsuda–Heck-, Suzuki–Miyaura- or Fujiwara–Moritani couplings.

Introduction

Substituted aromatic rings are core structures in many drugs,[1] agrochemicals,[2] azo dyes with applications in materials chemistry,[3] and sensitizers for dye-sensitized solar cells.[4,5] In particular, dyes for advanced optoelectronic applications are often characterized by extended π-systems with alkenyl or polyalkenyl arenes as central structural elements.[4] The interest in such aromatic compounds has led to a continuous development of synthetic methods and strategies for the regioselective functionalization of arenes,[6] with the Pd-catalyzed Mizoroki–Heck[7] and cross-coupling reactions[8] being the most important tools. More recently, transition-metal-catalyzed C–H activation reactions have been attracting increasing attention for arene functionalizations. In these transformations, synthetically useful regioselectivities are normally accomplished with the aid of catalyst-directing groups.[9–13]

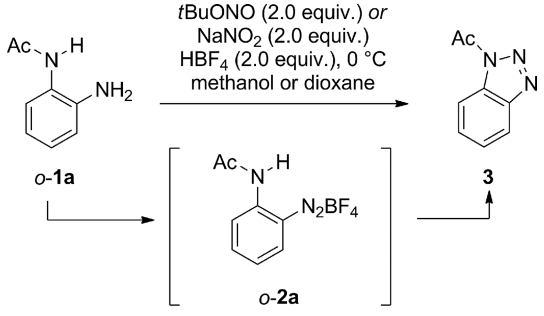
Although first described in the late 1970s, by Matsuda and co-workers,[14] the potential for use of arenediazonium salts as electrophilic arylating agents for Pd-catalyzed coupling reactions has only recently been more intensively investigated.[15–20] Our main contribution to the field is the development of a deacetylation/diazotization (DD) sequence for the one-flask synthesis of arenediazonium salts from acetanilides,[21–25] and the extension of this synthesis through a Pd-catalyzed coupling or cross-coupling reaction to a deacetylation/diazotization/coupling (DDC) sequence.[26] In previous contributions we demonstrated that DD and DDC sequences have the potential to broaden the scope and synthetic utility of oxidative Pd-catalyzed C–H activation reactions of the Fujiwara–Moritani type, because they allow efficient recycling of the catalyst-directing acetamido group by conversion into a diazonium leaving group.[27,28]

In continuation of our previous investigations, we report here that bis(acetamido)arenes and acetamidoanilines offer interesting opportunities for Pd-catalyzed multiple arene functionalization reactions.

Results and Discussion

Acetamidobenzenediazonium Salts

At the beginning of this investigation, we aimed at the synthesis, isolation and characterization of the regioisomeric acetamidobenzenediazonium tetrafluoroborates (**2**). It has been known for several decades that the diazotization of *o*-acetamidoaniline (*o*-**1a**) leads to the formation of *N*-acetylbenzotriazole (**3**), due to unavoidable cyclization of the intermediate diazonium salt *o*-**2a**.[29,30] We checked these reports by subjecting *o*-**1a** to various diazotization conditions, and were indeed unable to detect any diazonium salt, variously in water, methanol or dioxane, which are commonly used solvents for diazotization reactions (Scheme 1).



Scheme 1. Diazotation of *o*-**1a** and cyclization to benzotriazole **3**.[30]

We then turned our attention to the diazotization of *m*-acetamido aniline (*m*-**1a**, Scheme 2). Attempted diazotiza-

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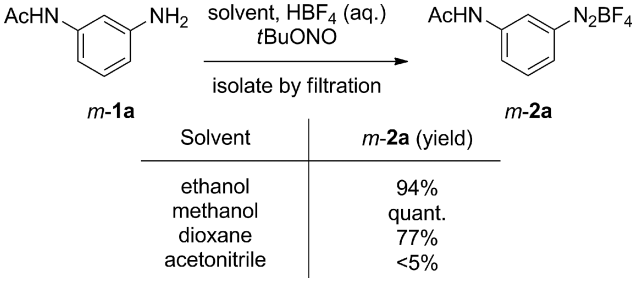
tion in analogy to Doyle's method[31] (*tert*-butyl nitrite, BF_3·methanol complex) resulted, surprisingly, in no conversion. Equally surprisingly, the same result was obtained on using classical diazotization conditions with $NaNO_2$ and aqueous HBF_4, although these conditions had previously been successfully applied to the synthesis of *m*-**2a**.[32,33] We then investigated an adaptation of a method described by Whetsel et al.,[30] who accomplished a selective monodiazotization of *p*-phenylenediamine by passing ethyl nitrite into a solution of the corresponding aniline in tetrafluoroboric acid. Instead of ethyl nitrite, we used *tert*-butyl nitrite and carefully adjusted the initial substrate concentration and the relative amounts of reagents to ensure maximum conversion and, ideally, quantitative precipitation of the arenediazonium tetrafluoroborate. Eventually, *m*-**2a** was obtained as a powder (from ethanol) in 94% yield. In previous studies on the deacetylation/diazotization sequence for the synthesis of diazonium salts from acetanilides we had found that a switch from ethanol to methanol can have a significant effect on the solubilities of arenediazonium tetrafluoroborates.[21] The main difference from the optimized conditions in ethanol is a preferable reaction temperature of 0 °C, which allows the isolation of *m*-**2a** in quantitative yield, if the substrate concentration and relative amounts of reagents are appropriately adjusted.



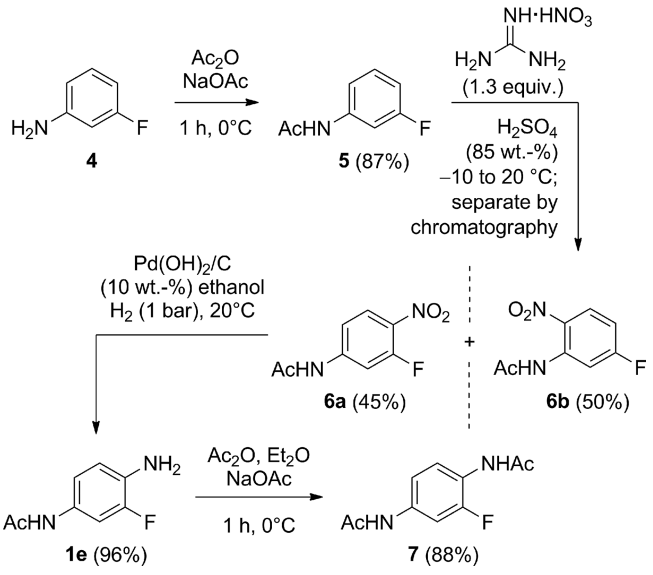
Solvent	*m*-**2a** (yield)
ethanol	94%
methanol	quant.
dioxane	77%
acetonitrile	<5%

Scheme 2. Yields of isolated *m*-**2a** in different solvents.

After completion of the experimental work reported in this contribution, Goossen and co-workers produced a manuscript that described the Sandmeyer-type difluoromethylation of various arenediazonium salts, including *p*-acetamido diazonium salt *p*-**2a**.[34] These authors performed the diazotization of various anilines in ethanol, under conditions similar to those shown in Scheme 2.

One of the reasons for choosing methanol as a solvent was the potential for extension of the diazotization with a Matsuda–Heck reaction, which has often been performed under base-free conditions in methanol or acetonitrile. In contrast, Suzuki–Miyaura coupling reactions with arenediazonium salts have advantageously been conducted in dioxane,[35] which prompted us to include this solvent in the present investigation. Under optimized conditions, *m*-**2a** was isolated in a slightly lower, but still synthetically useful yield of 77%. As mentioned above, acetonitrile is also a common and sometimes superior solvent for Matsuda–Heck reactions, because it can stabilize Pd intermediates,[36,37] and was therefore also tested. Unfortunately, no conversion of the starting material was observed with the reagent combinations investigated, so further optimization did not appear promising (Scheme 2).

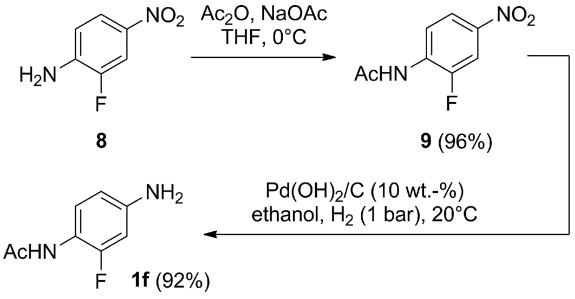
The optimized conditions for each solvent were then applied to the *para* isomer *p*-**1a** and a variety of other substituted acetamido anilines with *m*- or *p*-arrangement of amino and acetamido groups. The acetamido anilines **1b**–**d** are commercially available at moderate cost, but the fluorine-containing compounds **1e** and **1f** had to be synthesized from affordable precursors. The synthesis of **1e** (Scheme 3) started from *m*-fluoroaniline (**4**), which was first acetylated to produce **5**. Nitration of **5** with nitrous acid had previously been reported to afford primarily the unwanted regioisomer **6b** in moderate yield,[38,39] so this prompted us to test guanidinium nitrate, a reagent introduced by Ramana et al.[40] and subsequently used successfully by us for regioselective nitration.[21] Treatment of **5** with guanidinium nitrate furnished regioisomers **6a** and **6b** in a 1:1 ratio; they were easily separated by column chromatography and isolated in good yield. Structure assignment of **6a** and **6b** was not straightforward, but could be accomplished with the aid of 2D-NMR experiments, in particular HMBC. Pd-catalyzed hydrogenation of **6a** gave **1e** in nearly quantitative yield. To test the possibility of a dual deacetylation/diazotization sequence in a later stage of the project, the bisacetanilide **7** was synthesized by acetylation of **1e** (Scheme 3).



Scheme 3. Synthesis of acetamido aniline **1e** from *m*-fluoroaniline (**4**).

The synthesis of **1f** started from commercially available nitroaniline **8**, which was quantitatively acetylated to afford **9**, followed by Pd-catalyzed hydrogenation to furnish **1f** (Scheme 4).

The isolated yields of acetamidoarenediazonium salts **2** depend to some extent on the solvents chosen for the diazotization and precipitation. Except in the syntheses of **2d** and **2e**, methanol was found to be the solvent of choice, leading to yields higher than 80% in almost all cases. The *o*-chloro-substituted derivative **2d** is advantageously synthesized in



Scheme 4. Synthesis of acetamido aniline **1f** from **8**.

dioxane, whereas the *o*-fluoro-substituted diazonium salt **2e** is preferably isolated from ethanol (Figure 1).

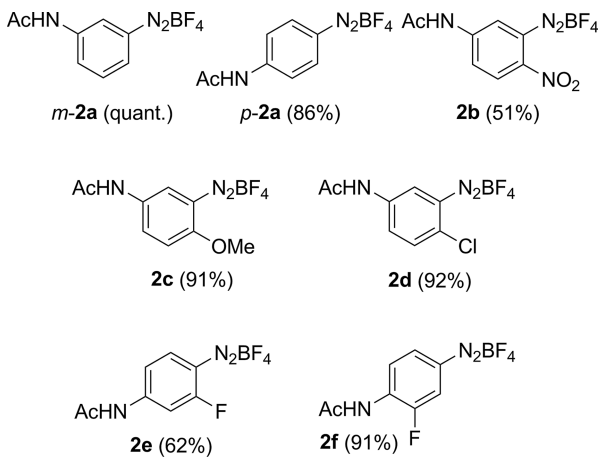


Figure 1. Acetamido arenediazonium salts **2**.

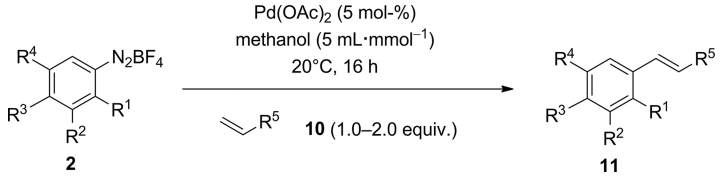
Matsuda–Heck Reactions of Acetamidobenzene Diazonium Salts

To the best of our knowledge, Pd-catalyzed coupling reactions have not previously been investigated for arenediazonium salts substituted with acetamide groups. However, diazonium salts *m*- and *p*-**2a** have been used in the Balz–Schiemann reaction,[32] inter alia for the synthesis of radiolabelled fluoroarenes,[33] in Cu-catalyzed difluoromethylations[34] and perfluoroalkylations,[41] and for the site-selective modification of genetically engineered proteins through azo coupling.[42]

As well as the solvent and the precatalyst, the presence or absence of a base is a crucial parameter in a Matsuda–Heck reaction. To investigate the effect of the acetamido substituent on the efficiency of the reaction, we started with the Pd-catalyzed coupling of *m*-**2a** and *p*-**2a** with the benchmark olefin methyl acrylate (**10a**) under various sets of conditions, using $Pd(OAc)_2$ as the precatalyst, and in some cases $Pd_2(dba)_3{\cdot}CHCl_3$ for comparison. The results obtained under optimized conditions for each pair of reactants are shown in Table 1. An extensive summary describing the variation of solvents, precatalyst and basic additive in detail can be found in the Supporting Information.

In the case of *m*-**2a**, notable levels of conversion to the cinnamate *m*-**11aa** were only observed in methanol under base-free conditions; however, the yields of isolated product remained moderate, irrespective of the precatalyst (Entry 1). The reactivity of the *para* isomer *p*-**2a** was strikingly different. Even under those conditions that had not resulted in any conversion in the case of *m*-**2a**, *p*-**2a** and methyl acrylate reacted to afford the expected Matsuda–Heck product *p*-**11aa** in synthetically useful yields under almost all condi-

Table 1. Matsuda–Heck reactions of acetamidobenzenediazonium salts **2**.[a]

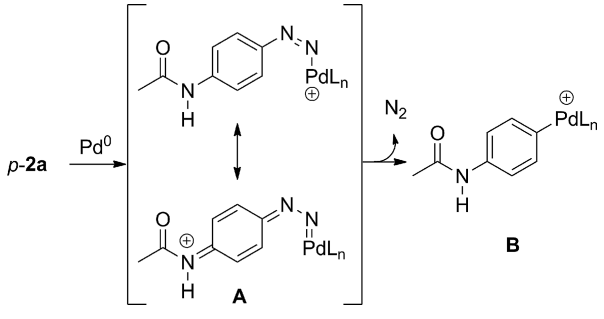


Entry	Diazonium salt	R^1	R^2	R^3	R^4	**10**	R^5	Product	Yield
1[b]	*m*-**2a**	H	H	H	NHAc	**10a**	CO_2Me	*m*-**11aa**	45%
2	*p*-**2a**	H	H	NHAc	H	**10a**	CO_2Me	*p*-**11aa**	quant.
3	**2b**	NO_2	H	H	NHAc	**10a**	CO_2Me	**11ba**	< 5%
4	**2c**	OMe	H	H	NHAc	**10a**	CO_2Me	**11ca**	65%
5	**2d**	Cl	H	H	NHAc	**10a**	CO_2Me	**11da**	< 5%
6	**2e**	F	H	NHAc	H	**10a**	CO_2Me	**11ea**	51%
7	**2f**	H	F	NHAc	H	**10a**	CO_2Me	**11fa**	76%
8	*p*-**2a**	H	H	NHAc	H	**10b**	C_6H_5	*p*-**11ab**	66%
9	*p*-**2a**	H	H	NHAc	H	**10c**	4-MeC_6H_4	*p*-**11ac**	51%
10	*p*-**2a**	H	H	NHAc	H	**10d**	3-MeC_6H_4	*p*-**11ad**	50%
11[c]	*p*-**2a**	H	H	NHAc	H	**10e**	4-$MeOC_6H_4$	*p*-**11ae**	66%
12	*p*-**2a**	H	H	NHAc	H	**10f**	4-ClC_6H_4	*p*-**11af**	51%
13[d]	*p*-**2a**	H	H	NHAc	H	**10g**	4-$NO_2C_6H_4$	*p*-**11ag**	quant.

[a] See the Supporting Information for a comprehensive tabular survey of conditions tested for Matsuda–Heck coupling. [b] With $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol-%) as precatalyst. [c] With NaOAc (3.0 equiv.) as basic additive. [d] Stilbene *p*-**11ag** isolated as *E*/*Z* mixtures in ratios of 3:1–4:1.

tions tested. Under base-free conditions and in methanol as a solvent, the yields of coupling product were quantitative (Entry 2). Remarkably, in acetonitrile basic conditions were found to be advantageous, giving *p*-**11aa** in quantitative yield, whereas only a moderate yield of 41% was observed in the absence of a base (see the Supporting Information). These results are to some extent in line with observations previously published by us on Matsuda–Heck reactions of arenediazonium salts bearing hydroxy or methoxy substituents in the *meta* or *para* position relative to the diazonium group.[22,25] We reason that in this and in the present case the electron-donating substituent has an overall beneficial effect on the Pd-catalyzed coupling by enhancing the electron density on the *ipso*-C and the diazonium group. In view of previous investigations into the mechanisms of Pd-catalyzed coupling reactions with aryl halides, this result is somewhat counterintuitive. Normally, one would expect a faster oxidative addition of the electrophilic arylating reagent Ar–X to Pd^0 if electron-withdrawing substituents were present in the *o*- or *p*-position of the leaving group. This has been explained in terms of lower energies of σ* and π* orbitals of the C–X bond and hence a smaller HOMO–LUMO gap.[43–45]

In the particular case of the Matsuda–Heck reaction a two-step process has been proposed for the formation of the σ-aryl-Pd complex.[46,47] In the first step, a Pd-diazenido complex of type **A** (Scheme 5) is formed,[48] and this then decomposes with extrusion of nitrogen to afford the cationic Pd-σ-aryl complex **B**.[49] Although the short-lived Pd-diazenido complexes were not detected by ESI-MS in Correia's pioneering study of the mechanism,[47] their involvement in the Matsuda–Heck reaction appears likely, on the basis of earlier studies describing the isolation and reactivity of metal-diazenido complexes formed through reactions between arenediazonium salts and electron-rich metal complexes.[50–54] Some of these early studies suggest a notable stabilization of the metal-diazenido complexes by electron-donating substituents in the *para*-position, whereas electron-withdrawing groups result in fast decomposition to the σ-aryl metal complex, along with other, unidentified products.[52,54] Although these substituent effects cannot conclusively explain the strikingly different reactivities of *p*- and *m*-acetamidoarenediazonium salts in Matsuda–Heck reactions, our results suggest – in light of the literature reports – that diazenido complex formation and subsequent nitrogen extrusion to afford the σ-aryl metal complex might play a more important role in the mechanism, and this might contribute to a better understanding of the varying reactivities of differently substituted arenediazonium salts (Scheme 5).



Scheme 5. Electron-donating effect of acetamide on the diazonium group.

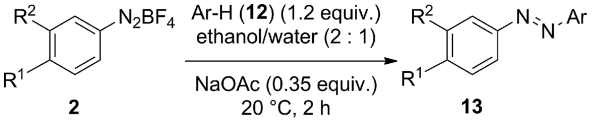
The results obtained for the coupling of *o*-substituted diazonium salts **2b**–**d** with methyl acrylate are in line with this presumed substituent effect. A synthetically useful yield was only observed with **2c** (Entry 4), whereas the presence of the more or less strongly electron-withdrawing nitro or chloro substituents in **2b** and **2d** (Entries 3 and 5) resulted in complete failure of the coupling.

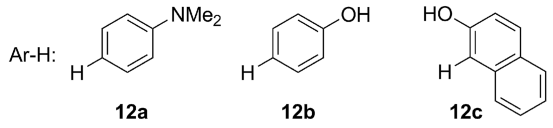
Notably, the fluoro-substituted diazonium salts **2e** and **2f** underwent Matsuda–Heck coupling with methyl acrylate in acceptable yields (Entries 6 and 7). Unlike in **2b** and **2d**, the acetamido group is located *para* to the diazonium group, and its stabilizing effect might (over)compensate for the detrimental effect of the fluoro substituents.

This part of the study was concluded by investigating the Matsuda–Heck coupling of *p*-acetamido-substituted diazonium salt *p*-**2a** with styrenes **10b**–**g** (Entries 8–13). Base-free conditions were found to be advantageous in all cases, except that of the electron-rich styrene **10e** (Entry 11). The electron-deficient styrene **10g** was the most reactive coupling partner, giving stilbene *p*-**11ag** in quantitative yield (Entry 13). In this particular case, inseparable mixtures of *E* and *Z* isomers were obtained irrespective of the conditions; this has previously also been observed by us for Matsuda–Heck reactions between *p*-nitrostyrene (**10g**) and other diazonium salts.[25]

If the higher yields in Matsuda–Heck reactions of *p*-**2a**, relative to those of *m*-**2a**, can indeed be attributed to higher nucleophilicity at the terminal nitrogen and hence to improved stabilization of the cationic Pd·diazenido complex (see Scheme 5), one would expect a reversed order of reactivity with nucleophiles. To test this hypothesis, we investigated the azo coupling of *m*- and *p*-**2a** with three electron-

Table 2. Azo coupling of *m*- and *p*-**2a** with electron-rich arenes **12**.





Entry	2	R^1	R^2	12	13	Yield
1[a]	*m*-**2a**	H	NHAc	**12a**	*m*-**13aa**	82%
2	*p*-**2a**	NHAc	H	**12a**	*p*-**13aa**	40%
3	*m*-**2a**	H	NHAc	**12b**	*m*-**13ab**	46%
4	*p*-**2a**	NHAc	H	**12b**	*p*-**13ab**	16%
5	*m*-**2a**	H	NHAc	**12c**	*m*-**13ac**	43%
6	*p*-**2a**	NHAc	H	**12c**	*p*-**13ac**	30%

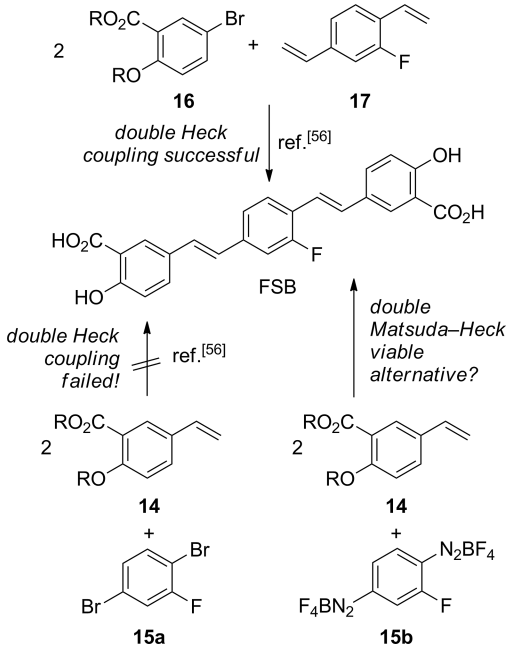
[a] Compound *m*-**13aa** was also obtained in 67% yield from *m*-**1a** by one-flask diazotization/azo coupling.

rich arenes – *N*,*N*-dimethylaniline (**12a**), phenol (**12b**) and 2-naphthol (**12c**) – under otherwise identical conditions. In all cases, substantially lower yields were obtained for *p*-**2a**, indicating a notably reduced electrophilicity of the diazo moiety due to the electron-donating character of the acetamido group in the *para*-position (Table 2).

Investigations Directed towards the Synthesis of FSB – Limitations of Matsuda–Heck Reactions

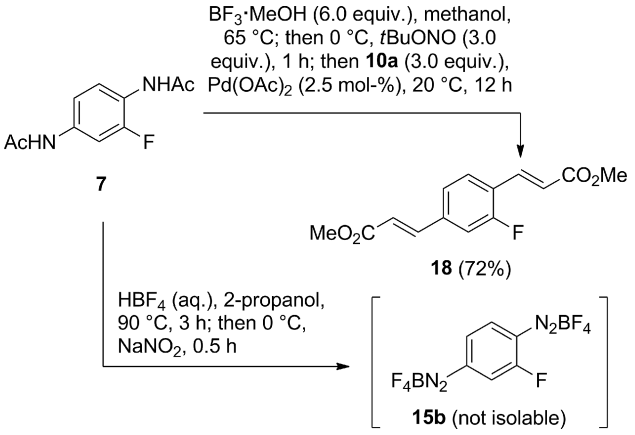
The bisstilbene (*E*,*E*)-1-fluoro-2,5-bis[4-hydroxy-3-(hydroxycarbonyl)styryl]benzene (FSB) (Scheme 6, below) has emerged as a potential marker for amyloid fibrils and is expected to become a useful diagnostic agent for detecting Alzheimer's disease and monitoring its treatment.[55] The first synthesis of FSB relied on Wittig olefination chemistry for constructing the C=C double bonds.[56] A second synthesis used a double Heck reaction,[57] whereas syntheses of isotopically labelled FSB derivatives proceeded through a bis-Sonogashira coupling with subsequent *E*-selective deuteration of the triple bond.[58,59] Intriguingly, Skrydstrup and co-workers reported that a double Heck coupling of the dibromide **15a** (Scheme 6, below) with two equivalents of fully protected styrene **14** failed completely under a variety of different conditions.[57]

This prompted these authors to reverse the role of alkene and aryl halide coupling partner by first converting **15a** into 2-fluoro-1,4-divinylbenzene (**17**), which was then successfully coupled with protected aryl bromide **16** in a double Heck reaction.[57] We wondered whether Skrydstrup's unsuccessful disconnection could become synthetically viable with the apparently more reactive bisdiazonium salt **15b** (Scheme 6).



Scheme 6. Structure of FSB and alternative Heck or Matsuda–Heck approaches.

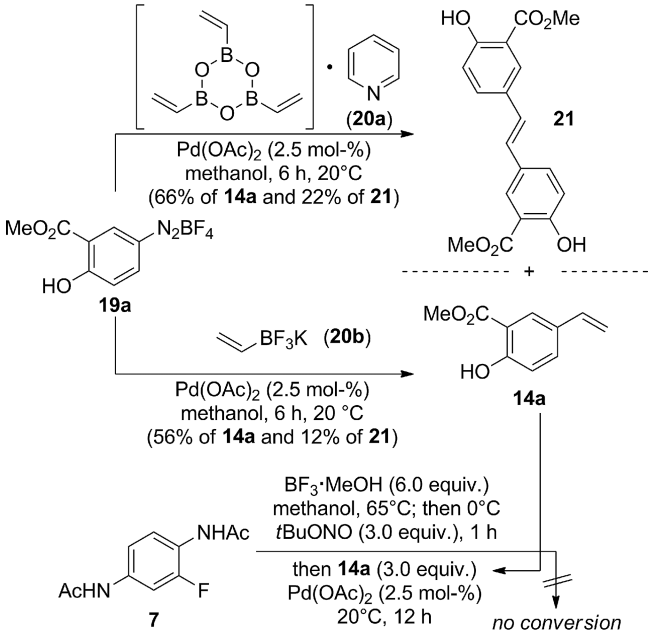
Encouraged by literature reports describing the synthesis and isolation of arenebis-diazonium salts and their dual Matsuda–Heck coupling,[60–63] we investigated the synthesis of **15b** from **7** (see Scheme 3) by the deacetylation/diazotization sequence. Apparently, this transformation was successful, because **7** was completely consumed and a precipitate was formed. All attempts to isolate this precipitate, presumably the bis-diazonium salt **15b**, failed due to spontaneous decomposition with gas evolution. To check whether the bis-diazonium salt **15b** was indeed formed under deacetylation/diazotization conditions, we conducted coupling in the same flask by adding methyl acrylate (**10a**) and a catalytic amount of $Pd(OAc)_2$.[26] This deacetylation/diazotization/coupling (DDC) sequence was indeed successful and led to the isolation of **18** in 72% yield (Scheme 7).



Scheme 7. DDC sequence with **7**.

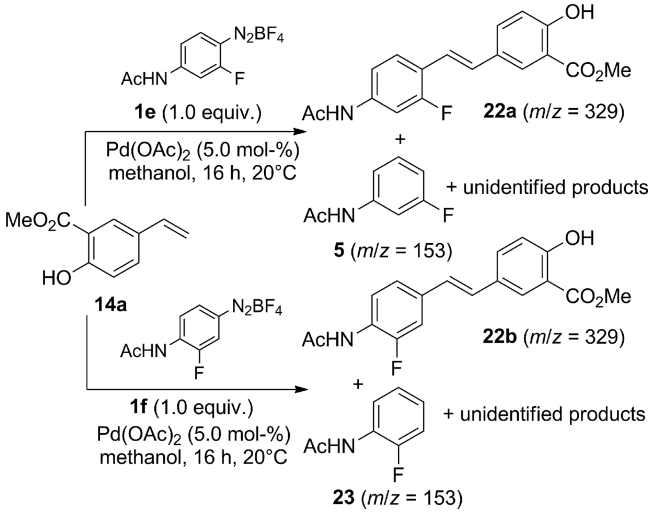
With this positive result in hand, we investigated the DDC sequence of bisacetamide **7** and styrene **14a** under the same conditions. For the synthesis of **14a**, Suzuki–Miyaura coupling of phenol-diazonium salt **19a**[22]was investigated. To this end, **19a** was treated either with 0.33 equiv. of 2,4,6-trivinylcycloboroxane·pyridine complex (**20a**) or with one equivalent of potassium vinyltrifluoroborate (**20b**) in methanol under base-free conditions (Scheme 8). With both reagents, **14a** was obtained in synthetically useful yields; however, notable amounts of symmetric stilbene **21** were obtained as a byproduct. Gratifyingly, **21** could be conveniently separated from the desired **14a** through column chromatography. The formation of **21** can be explained in terms of a Suzuki–Miyaura coupling/Matsuda–Heck reaction sequence. Assignment of the double bond configuration is not straightforward from routine spectra, due to the symmetrical structure. A one-dimensional HMQC spectrum, however, revealed a vicinal coupling constant of 16.5 Hz, which confirms the expected *E* configuration.

We then applied the previously established deacetylation/diazotization/coupling conditions to **7** and **14a**, unfortunately to no avail. In all experiments the styrene **14a** was recovered from the reaction mixture, whereas the fate of the fluoroarene building block could not be clarified. Possible decomposition pathways of arenediazonium salts in slow Pd-catalyzed coupling reactions are solvolysis or hydrodediazonation, but neither fluorobenzene nor its methoxy derivatives were detected in the reaction mixture.



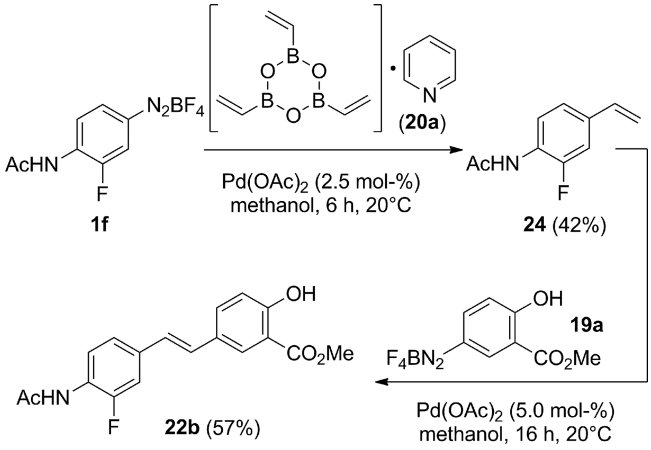
Scheme 8. Synthesis of styrene **14a** and attempted DDC sequence with **7**.

In light of this rather disappointing result, we decided to investigate a stepwise approach by treating diazonium salts **1e** or **1f** with styrene **14a**. We then planned to convert the expected truncated FSB derivatives **22a** and **22b** further to FSB methyl ester, by means of a deacetylation/diazotization/coupling sequence with a second equivalent of styrene **14a**. Although **22a** and **22b** were detected by GC–MS from the reactions with diazonium salts **1e** and **1f**, respectively, both transformations were slow and sluggish, and large amounts of the corresponding hydrodediazonation products **5** and **23** were formed, along with other unidentified byproducts (Scheme 9).



Scheme 9. Unsuccessful stepwise approach to FSB.

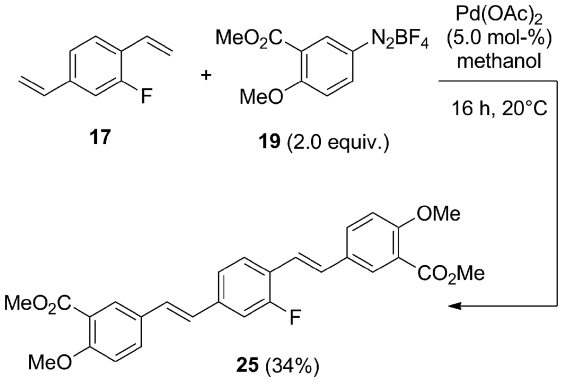
Although our previous investigations (see Table 1) had already indicated a considerably lower reactivity of styrenes in Matsuda–Heck reactions, in relation to electron-deficient acrylates, we were surprised that the desired transformations failed completely. Out of curiosity we investigated whether truncated FSB derivative **22** would become accessible if the roles of arenediazonium and styrene coupling partner were reversed (Scheme 10). To this end, **1f** and vinylboron reagent **20a** were coupled under the same conditions as previously employed for the synthesis of **14a** (see Scheme 7). The resulting styrene **24** and phenol-diazonium salt **19a** underwent Matsuda–Heck coupling to give a fair yield of stilbene **22b**, which is, as mentioned above, not accessible from **1f** and **14a**. All attempts to obtain FSB from **22b** by deacetylation, diazotization and Pd-catalyzed coupling with one equivalent of styrene **14a** resulted in the formation of complex mixtures of products.



Scheme 10. Synthesis of truncated FSB derivative **22b**.

To conclude the studies directed towards a diazonium-salt-based synthesis of FSB, we resumed to Skrydstrup's successful strategy and tested a double Matsuda–Heck reaction of 2-fluoro-1,4-divinylbenzene (**17**).[57] Firstly, a protecting-group-free approach was tested by use of a diazonium salt[22] with a free carboxylic acid and phenol functionality. Although this diazonium salt had previously been successfully used by us in Matsuda–Heck[22] and Suzuki–Miyaura couplings,[23] its reaction with **17** failed completely. Under basic conditions, compound **17** was quantitatively recovered, whereas the fate of the diazonium salt could not be clarified. In the absence of base, the bisstyrene **17** was completely consumed as indicated by TLC, but a complex mixture of products was obtained. Essentially the same outcome was observed for semiprotected diazonium salt **19a**.[22] Only in the case of bismethylated diazonium salt **19b** did significant conversion into the FSB derivative **25** occur under base-free conditions, leading to a yield of 34% for the one-pot double Matsuda–Heck reaction. In previous investigations, basic conditions had been found to be disadvantageous for 4-methoxyarenediazonium salts and so were not tested in this reaction (Scheme 11).[25]

The investigations into the synthesis of FSB show that Pd-catalyzed coupling reactions involving arenediazonium salts clearly have limitations, in particular when the Pd-catalyzed step is slow in relation to solvolysis, hydrodediazonation or other decomposition reactions of the arenedi-



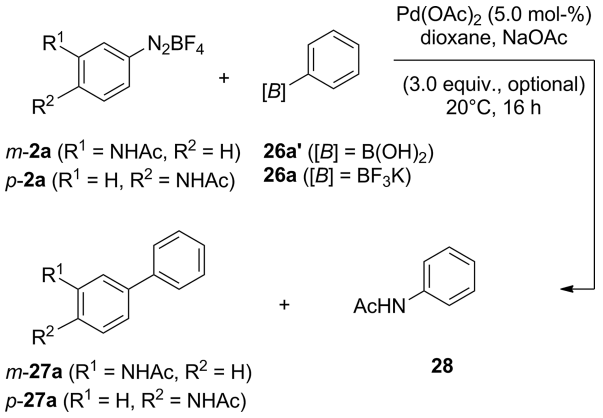
Scheme 11. FSB derivative **25** through a double Matsuda–Heck reaction.

azonium salt. In these cases aryl halides or triflates are preferable coupling partners.

Suzuki–Miyaura Reactions of Acetamidobenzene Diazonium Salts

Boronic acids,[35,64–68] boronates[69,70] and organotrifluoroborates[23,25,26,71] have previously been used as cross-coupling partners in Suzuki–Miyaura reactions with other arenediazonium salts. As a test reaction for the coupling with acetamidobenzenediazonium salts, we investigated the reactions of *m*-**2a** and *p*-**2a** with phenylboronic acid (**26a′**, Table 3). Since Genêt's seminal work, 1,4-dioxane has commonly been used as a solvent for Suzuki–Miyaura reactions of arenediazonium salts and it was therefore also tested for this transformation. Normally, Suzuki–Miyaura coupling reactions involving boronic acids require the presence of a base to facilitate the transmetallation step through the so-called hydroxy-Pd pathway[72] and to increase the nucleophilicity of the boronic acid by quaternization.[73] Although base-free conditions are normally preferred for arenediazonium salts, we tested the addition of the base NaOAc for comparison (Table 3).

Table 3. Optimization of Suzuki–Miyaura coupling of *m*- and *p*-**2a**.



Entry	**2**	**26** [equiv.]	Product [s] (ratio)[a]	Yield[b]
1[c]	*m*-**2a**	**26a′** (1.2)	*m*-**27a**/**28** (1.0:2.5)	n.d.
2	*m*-**2a**	**26a′** (1.2)	*m*-**27a**/**28** (1.0:3.6)	n.d.
3[c]	*p*-**2a**	**26a′** (1.2)	*m*-**27a**/**28** (1.0:2.0)	n.d.
4	*p*-**2a**	**26a′** (1.2)	**28**	n.d.
5	*m*-**2a**	**26a** (1.0)	*m*-**27a**	46%
6	*p*-**2a**	**26a** (1.0)	*p*-**27a**	55%
7	*m*-**2a**	**26a** (1.5)	*m*-**27a**	79%
8	*p*-**2a**	**26a** (1.5)	*p*-**27a**	89%
9[d]	*m*-**2a**	**26a** (1.5)	*m*-**27a**	18%
10[d]	*p*-**2a**	**26a** (1.5)	*p*-**27a**	69%

[a] Ratio determined by GC–MS. If no ratio is given, the product was formed with high selectivity. [b] n.d.: not determined. [c] With added NaOAc (3.0 equiv.). [d] Reduced catalyst loading of 2.5 mol-%.

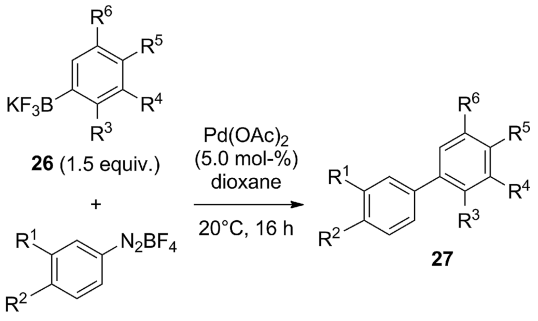
With diazonium salt *m*-**2a** and boronic acid **26a′**, mixtures of the desired biphenyl *m*-**27a** and the hydrodediazonation product acetanilide (**28**) were obtained both under basic and under base-free conditions (Entries 1 and 2). With *p*-**2a** the hydrodediazonation pathway was even more pronounced, with acetanilide being the only detectable product under base-free conditions (Entry 4).

These disappointing results prompted us to replace the boronic acid with organotrifluoroborate **26a**.[74–76] When equimolar amounts of both coupling partners were allowed to react in the presence of 5 mol-% of Pd acetate, the expected biaryls *m*-**27a** and *p*-**27a** could be obtained in fair yields of 46% and 54%, respectively (Entries 5 and 6). Increasing the amount of phenyltrifluoroborate (**26a**) to 1.5 equiv. (Entries 7–8) resulted in an improved yield of cross-coupling products *m*-**27a** (79%) and *p*-**27a** (89%). We then checked the possibility of reducing the catalyst loading to 2.5 mol-% under otherwise identical conditions. For *p*-**2a** the yield of coupling product *p*-**27a** was lower but still synthetically useful (Entry 10). For *m*-**2a**, however, the yield of the cross coupling product *m*-**27a** declined significantly to 18% (Entry 9). These results show that the *para*-acetamido-substituted diazonium salt *p*-**2a** is significantly more reactive in Suzuki–Miyaura coupling reactions than the *meta* isomer *m*-**2a**, which is in line with the results for Matsuda–Heck reactions of these arenediazonium salts.

The optimized conditions were then applied to Suzuki–Miyaura coupling reactions of *m*- and *p*-**2a** and some other arene trifluoroborates (Table 4). With the nitro- and difluoro-substituted organotrifluoroborates **26c** and **26d** better results were again obtained for *p*-**2a** (Entries 5–8). The bis(trifluoromethyl)-substituted organotrifluoroborate **26b** gave unsatisfactory results for both diazonium salts (Entries 3 and 4). In particular, we were surprised to find that a complex mixture of products reproducibly resulted from the attempted coupling with *p*-**2a**, whereas *m*-**2a** gave the expected biaryl in a moderate yield of 25%. The reasons for this unusual behaviour of **26c** are unclear.

To demonstrate the utility of acetamidoarenediazonium salts in multiple, selective arene functionalization reactions, *p*-**2a** was chosen as a starting point. As outlined above (Table 4, Entry 2), under optimised conditions the Suzuki–Miyaura coupling with **26a** furnished the acetamido-substituted biaryl *p*-**27a**. The acetamido group in *p*-**27a** was then exploited as a catalyst-directing group in a Fujiwara–Moritani reaction[77,78] under conditions previously reported by Youn and co-workers[79] and by ourselves,[27] to give the substituted cinnamate **29**. As mentioned in the Introduc-

Table 4. Examples of Suzuki–Miyaura couplings of *m*- and *p*-**2a** under optimized conditions.

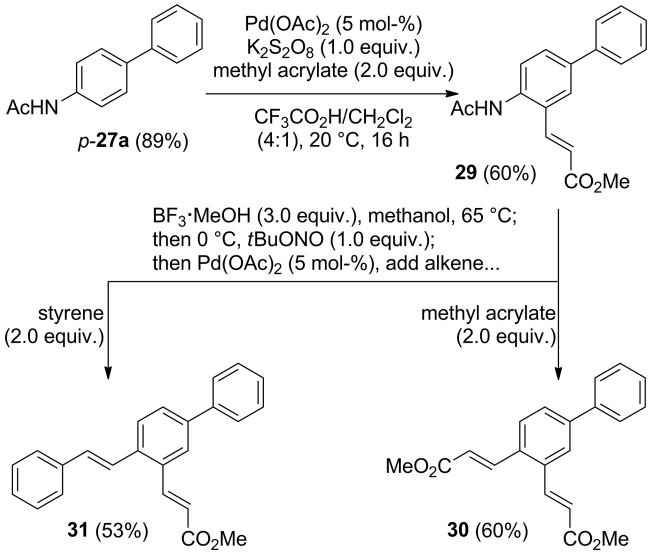


m-**2a** (R^1 = NHAc, R^2 = H)
p-**2a** (R^1 = H, R^2 = NHAc)

Entry	2	26	R^3	R^4	R^5	R^6	27 (yield)[l]
1	*m*-**2a**	**26a**	H	H	H	H	*m*-**27a** (79%)
2	*p*-**2a**	**26a**	H	H	H	H	*p*-**27a** (89%)
3	*m*-**2a**	**26b**	H	CF_3	H	CF_3	*m*-**27b** (25%)
4[a]	*p*-**2a**	**26b**	H	CF_3	H	CF_3	*p*-**27b** (n.d.)
5	*m*-**2a**	**26c**	H	NO_2	H	H	*m*-**27c** (29%)
6	*p*-**2a**	**26c**	H	NO_2	H	H	*p*-**27c** (79%)
7	*m*-**2a**	**26d**	F	H	F	H	*m*-**27d** (71%)
8	*p*-**2a**	**26d**	F	H	F	H	*p*-**27d** (80%)
9	*p*-**2a**	**26e**	H	H	F	H	*p*-**27e** (59%)

[a] Complex mixture of products.

tion, we have recently developed protocols for deacetylation/diazotization/coupling (DDC) sequences that allow the dual exploitation of acetamides as a catalyst-directing group and subsequently as a virtual leaving group in a Pd^0-catalyzed C–C bond-forming reaction.[27,28] By subjecting **29** to the conditions of a DDC sequence, we were able to synthesize **30** with methyl acrylate as a coupling partner, as well as stilbene **31** with styrene (Scheme 12).



Scheme 12. Triple functionalization of acetamidoarenediazonium salt *p*-**2a**.

Conclusions

In summary, we have demonstrated that *meta*- and *para*-acetamidoarenediazonium salts can be synthesized and isolated, whereas the *ortho* isomers remain elusive. The diazonium salts undergo Pd-catalyzed coupling and cross-coupling reactions to afford cinnamates, stilbenes and biaryls, proceeding in significantly higher yields for the *para*-substituted derivatives. Although our investigations into the synthesis of the potential amyloid marker FSB clearly show the limitations of the Matsuda–Heck coupling of acetamido arenediazonium salts, we believe that these reagents offer interesting opportunities for the site-selective multiple functionalization of arenes.

Experimental Section

General Methods: All experiments were conducted in dry reaction vessels under dry nitrogen. Solvents were purified by standard procedures. ^{1}H NMR spectra were obtained at 300 MHz or 500 MHz in $CDCl_3$ with $CHCl_3$ (δ = 7.26 ppm) as an internal standard. Coupling constants are given in Hz. ^{13}C NMR spectra were recorded at 75 MHz or at 125 MHz in $CDCl_3$ with $CDCl_3$ (δ = 77.0 ppm) as an internal standard. Whenever the solubility of the sample in $CDCl_3$ was insufficient, [D_6]DMSO ([D_5]DMSO as internal standard for ^{1}H NMR spectroscopy, δ = 2.50 ppm, [D_6]DMSO as internal standard for ^{13}C NMR spectroscopy, δ = 39.5 ppm) or [D_4]-MeOH (CD_2HOD as internal standard for ^{1}H NMR spectroscopy, δ = 3.31 ppm, CD_3OD as internal standard for ^{13}C NMR spectroscopy, δ = 49.2 ppm) were used. 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.

3-Fluoroacetanilide (5):[32] A suspension of 3-fluoraniline (**4**, 5.00 g, 45.0 mmol) and NaOAc (3.70 g, 45.0 mmol) in water (200 mL) was cooled to 0 °C. Acetic anhydride (25.0 mL) was added dropwise. The reaction mixture was stirred for 1 h at 0 °C, and then extracted six times with methyl *tert*-butyl ether (MTBE, 600 mL total volume). The combined organic layers were dried with $MgSO_4$, filtered and concentrated under reduced pressure to give **5** (6.00 g, 39.0 mmol, 87%): colourless solid, m.p. 80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00 (br. s, 1 H), 7.47 (d, J = 11.0 Hz, 1 H), 7.23 (m, 1 H), 7.13 (d, J = 8.3 Hz, 1 H), 6.78 (dd, J = 8.7, 8.7 Hz, 1 H), 2.16 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.9, 162.9 (d, J = 244 Hz), 139.8 (d, J = 10.8 Hz), 130.0 (d, J = 9.4 Hz), 115.6 (d, J = 2.8 Hz), 111.1 (d, J = 21.3 Hz), 107.7 (d, J = 26.1 Hz), 24.3 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –114.59 (m) ppm. MS (EI): *m*/*z* (%) = 153 (21), 111 (100), 83 (15), 43 (36). HRMS (EI): calcd. for C_8H_8NOF $[M]^+$ 153.0590; found 153.0585.

3-Fluoro-4-nitroacetanilide (6a) and 3-Fluoro-6-nitroacetanilide (6b): Compound **5** (3.84 g, 25.1 mmol) was dissolved in sulfuric acid (85 wt.-%, 90 mL) and the solution was cooled to –10 °C. Guanidinium nitrate (3.98 g, 32.6 mmol) was added portionwise, and the mixture was stirred for 6 h at –10 °C, allowed to warm to ambient temperature and poured onto ice-water (300 mL). The aqueous phase was extracted repeatedly with ethyl acetate (150 mL total volume), MTBE (100 mL total volume) and hexane (400 mL total volume). The combined organic layers were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was chromatographed on silica with MTBE/ethyl acetate (1:1) as eluent to

furnish **6a** (more polar, second fraction, 2.24 g, 11.3 mmol, 45%) and **6b** (less polar, first fraction, 2.48 g, 12.6 mmol, 50%).

Analytical Data for 6a: Colourless solid, m.p. 173–175 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.69 (s, 1 H), 8.15 (dd, J = 9.0, 9.0 Hz, 1 H), 7.84 (dd, J = 14.5, 2.1 Hz, 1 H), 7.42 (dd, J = 9.1, 1.4 Hz, 1 H), 2.12 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 169.6, 155.7 (d, J = 258.0 Hz), 146.3 (d, J = 12.0 Hz), 130.9 (d, J = 3.0 Hz), 127.4 (d, J = 2.3 Hz), 114.3 (d, J = 3.0 Hz), 106.6 (d, J = 25.5 Hz), 24.2 ppm. ^{19}F NMR (282 MHz, [D$_6$]DMSO): δ = –115.3 (dd, J = 14.9, 8.9 Hz) ppm. IR (ATR): $\tilde{\nu}$ = 3084 (w), 1680 (m), 1600 (m), 1540 (m), 1485 (s) cm^{-1}. MS (EI): m/z (%) = 198 (10), 156 (100), 126 (15). $C_8H_7FN_2O_3$ (198.15): calcd. C 48.5, H 3.6, N 14.1; found C 48.8, H 3.6, N 13.8. HRMS (EI): calcd. for $C_8H_7N_2O_3F$ [M]$^+$ 198.0441; found 198.0446.

Analytical Data for 6b: Yellowish solid, m.p. 85 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.54 (s, 1 H), 8.62 (dd, J = 11.4, 2.8 Hz, 1 H), 8.27 (dd, J = 9.4, 5.8 Hz, 1 H), 6.85 (ddd, J = 9.5, 6.8, 2.8 Hz, 1 H), 2.30 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.1, 166.6 (d, J = 257.8 Hz), 137.4 (d, J = 14.1 Hz), 132.3 (d, J = 5.1 Hz), 128.5 (d, J = 11.4 Hz) 110.7 (d, J = 24.1 Hz), 108.6 (d, J = 29.9 Hz), 25.6 ppm.

4-Amino-3-fluoroacetanilide (1e): A suspension of **6a** (0.60 g, 2.9 mmol) and $Pd(OH)_2$/C (10 wt.-%, 25 mg) in ethanol (20 mL) was stirred for 12 h under hydrogen (1 bar). The mixture was then concentrated under reduced pressure, the residue was mixed with a minimum amount of MTBE, and the slurry was filtered through a short pad of celite. The solvent was removed in vacuo and the residue was purified by column chromatography on silica with MTBE/ethyl acetate (1:1) as eluent to furnish **1e** (0.47 g, 2.8 mmol, 96%): slightly purple solid, m.p. 107–109 °C. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 9.67 (s, 1 H), 7.39 (dd, J = 13.7, 2.2 Hz, 1 H), 6.95 (dd, J = 8.5, 1.4 Hz, 1 H), 6.68 (dd, J = 10.1, 8.6 Hz, 1 H), 4.84 (s, 2 H), 1.97 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 167.5, 149.8 (d, J = 235.0 Hz), 131.8 (d, J = 13.2 Hz), 128.9 (d, J = 9.4 Hz), 115.9 (d, J = 5.5 Hz), 115.5 (d, J = 2.9 Hz), 107.1 (d, J = 23.1 Hz), 23.7 ppm. ^{19}F NMR (282 MHz, [D$_6$]DMSO): δ = –135.5 (dd, J = 13.4, 10.3 Hz) ppm. IR (ATR): $\tilde{\nu}$ = 3276 (w), 1640 (w), 1514 (w), 1425 (w), 1267 (w) cm^{-1}. MS (EI): m/z (%) = 168 (56), 126 (100), 98 (15). $C_8H_9FN_2O$ (168.17): calcd. C 57.1, H 5.4, N 16.7; found C 57.3, H 5.4, N 16.7. HRMS (EI): calcd. for $C_8H_9N_2OF$ [M]$^+$ 168.0699; found 168.0708.

***N,N′*-(2-Fluoro-1,4-phenylene)diacetamide (7):** Acetic acid anhydride (250 µL, 2.74 mmol) was added to a suspension of **1e** (230 mg, 1.37 mmol) and NaOAc (224 mg, 2.74 mmol) in diethyl ether (25 mL). The mixture was stirred for 2 h at ambient temperature and concentrated, and the residue was suspended in acetone (50 mL). The resulting slurry was filtered through a short pad of celite, and the filtrate was dried with $MgSO_4$. After filtration, the solvent was evaporated to give **7** (252 mg, 1.20 mmol, 88%): colourless solid, m.p. 266–268 °C. ^{1}H NMR (300 MHz, [D$_4$]-MeOH): δ = 7.72 (t, J = 8.7 Hz, 1 H), 7.63 (dd, J = 13.0, 2.3 Hz, 1 H), 7.15 (ddd, J = 8.8, 2.2, 1.2 Hz, 1 H), 2.14 (s, 3 H), 2.11 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_4$]MeOH): δ = 172.2, 171.8, 155.8 (d, J = 244.0 Hz), 138.2 (d, J = 10.6 Hz), 126.2 (d, J = 2.5 Hz), 122.71 (d, J = 12.1 Hz), 116.2 (d, J = 3.2 Hz), 108.50 (d, J = 25.0 Hz), 23.9, 23.4 ppm. ^{19}F NMR (282 MHz, [D$_4$]MeOH): δ = –126.1 (dd, J = 12.5, 8.8 Hz) ppm. MS (EI): m/z (%) = 210 (35), 168 (32), 126 (100). HRMS (EI): calcd. for $C_{10}H_{11}FN_2O_2$ [M]$^+$ 210.0799; found 210.0791.

2-Fluoro-4-nitroacetanilide (9): A suspension of **8** (2.50 g, 16.0 mmol) and NaOAc (1.30 g, 16.0 mmol) in THF (100 mL) was cooled to 0 °C. Acetic acid anhydride (4.5 mL) was added dropwise. The reaction mixture was stirred for 12 h at ambient temperature and then concentrated under reduced pressure. The residue was mixed with MTBE (30 mL), and the mixture was washed with water. The aqueous layer was separated and extracted with MTBE, and the combined organic layers were dried with $MgSO_4$. After filtration, all volatiles were removed in vacuo to give **9** (3.10 g, 15.6 mmol, quant.): yellow solid, m.p. 203–205 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.25 (s, 1 H), 8.41 (dd, J = 8.5, 8.5 Hz, 1 H), 8.17 (dd, J = 11.0, 2.5 Hz, 1 H), 8.10 (dd, J = 9.5, 1.9 Hz, 1 H), 2.18 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 169.6, 151.1 (d, J = 248.9 Hz), 142.1 (d, J = 8.5 Hz), 133.4 (d, J = 11.2 Hz), 121.6 (d, J = 2.5 Hz), 120.5 (d, J = 3.1 Hz), 111.4 (d, J = 24.6 Hz), 23.9 ppm. ^{19}F NMR (282 MHz, [D$_6$]DMSO): δ = –122.5 (dd, J = 10.6, 8.4 Hz) ppm. IR (ATR): $\tilde{\nu}$ = 3217 (w), 1683 (m), 1491 (s), 1327 (s), 740 (s) cm^{-1}. MS (EI): m/z (%) = 198 (36), 156 (100), 126 (62), 43 (31). HRMS (EI): calcd. for $C_8H_7N_2O_3F$ [M]$^+$ 198.0441; found 198.0449.

4-Amino-2-fluoroacetanilide (1f):[80] A suspension of **9** (3.00 g, 15.1 mmol) and $Pd(OH)_2$/C (10 wt.-%, 106 mg) in methanol (20 mL) was stirred for 12 h under hydrogen (1 bar). The mixture was concentrated in vacuo, taken up in MTBE (10 mL) and filtered through a short pad of celite. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica with MTBE/ethyl acetate (1:1) as eluent to furnish **1f** (2.30 g, 13.7 mmol, 92%): colourless solid, m.p. 140–141 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.20 (s, 1 H), 7.16 (dd, J = 8.7, 8.7 Hz, 1 H), 6.42–6.26 (2 H), 5.24 (s, 2 H), 1.97 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.2, 155.9 (d, J = 242.1 Hz), 147.6 (d, J = 10.8 Hz), 127.0 (d, J = 3.6 Hz), 113.7 (d, J = 13.0 Hz), 109.2, 100.3 (d, J = 22.8 Hz), 22.9 ppm. ^{19}F NMR (282 MHz, [D$_6$]-DMSO): δ = –126.3 (dd, J = 12.7, 9.1 Hz) ppm. IR (ATR): $\tilde{\nu}$ = 3254 (w), 1661 (m), 1514 (s), 1270 (m), 808 (m) cm^{-1}. MS (EI): m/z (%) = 168 (56), 126 (100), 98 (10). HRMS (EI): calcd. for $C_8H_9N_2OF$ [M]$^+$ 168.0699; found 168.0695.

General Procedure for the Synthesis of Acetamidobenzendiazonium Tetrafluoroborates: HBF_4 (50 wt.-% solution in water, 250 mg, 1.40 mmol) and *tert*-BuONO (206 mg, 2.00 mmol) were dissolved in methanol (1.0 mL) and cooled to 0 °C. A solution of HBF_4 (50 wt.-% solution in water, 105 mg, 0.60 mmol) and the appropriate aniline **1** (1.00 mmol) in methanol (1.0 mL) was added at 0 °C, resulting in the formation of a precipitate. Stirring was continued for 1 h at 0 °C, followed by filtration of the mixture through a Büchner funnel. The product was washed with a minimum amount of cold MTBE and dried in vacuo at ambient temperature. An analogous procedure can be used for the diazotization in ethanol; in this case cooling to 0 °C is not mandatory. In dioxane the solvent volume should be increased to 4.0 mL mmol^{-1} and the total amount of HBF_4 should be increased to 4.0 mmol per mmol of **1**.

3-Acetamidobenzenediazonium Tetrafluoroborate (*m*-2a):[32] Compound *m*-**1a** (150 mg, 1.00 mmol) was converted into *m*-**2a** (in methanol: 243 mg, 0.98 mmol, quant.; in ethanol: 234 mg, 0.94 mmol, 94%; in dioxane: 192 mg, 0.77 mmol, 77%) by the General Procedure: colourless solid. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 10.81 (s, 1 H), 9.16 (dd, J = 2.1, 2.1 Hz, 1 H), 8.33 (ddd, J = 8.2, 2.0, 0.9 Hz, 1 H), 8.00 (ddd, J = 8.4, 2.0, 0.9 Hz, 1 H), 7.88 (dd, J = 8.3, 8.3 Hz, 1 H), 2.14 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 170.5, 141.5, 132.5, 131.1, 128.1, 120.9, 117.2, 24.9 ppm. IR (ATR): $\tilde{\nu}$ = 3355 (w), 3085 (w), 2299 (m), 1527 (s), 1006 (s) cm^{-1}. HRMS (ESI): calcd. for $C_8H_8N_3O$ [M]$^+$ 162.0662; found 162.0663.

4-Acetamidobenzenediazonium Tetrafluoroborate (*p*-2a): Compound *p*-**1a** (150 mg, 1.00 mmol) was converted into *p*-**2a** (in methanol:

214 mg, 0.86 mmol, 86%; in ethanol: 199 mg, 0.80 mmol, 80%; in dioxane: 159 mg, 0.64 mmol, 64%) by the General Procedure: red solid. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 11.14 (s, 1 H), 8.54 (d, J = 9.1 Hz, 2 H), 8.02 (d, J = 9.2 Hz, 2 H), 2.18 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 170.5, 149.8, 135.2, 119.6, 104.5, 24.6 ppm. IR (ATR): $\tilde{\nu}$ = 3341 (w), 3099 (w), 2249 (m), 1720 (s), 1525 (s) cm^{-1}. HRMS (ESI): calcd. for $C_8H_8N_3O$ [M]$^+$ 162.0662; found 162.0665.

5-Acetamido-2-nitrobenzenediazonium Tetrafluoroborate (2b): Compound **1b** (500 mg, 2.56 mmol) was converted into **2b** (in methanol: 387 mg, 1.32 mmol, 51%; in ethanol: 371 mg, 1.26 mmol, 49%) by the General Procedure: yellow solid. ^{1}H NMR (500 MHz, [D$_6$]-DMSO): δ = 11.39 (s, 1 H), 9.58 (d, J = 2.4 Hz, 1 H), 8.70 (d, J = 9.2 Hz, 1 H), 8.16 (dd, J = 9.2, 2.4 Hz, 1 H), 2.22 (s, 3 H) ppm. ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 171.2, 145.9, 139.2, 129.9, 129.3, 124.3, 113.5, 25.2 ppm. IR (ATR): $\tilde{\nu}$ = 3329 (w), 3114 (w), 2292 (w), 1720 (m), 1015 (s) cm^{-1}. HRMS (ESI): calcd. for $C_8H_7N_4O_3$ [M]$^+$ 207.0513; found 207.0506.

5-Acetamido-2-methoxybenzenediazonium Tetrafluoroborate (2c): Compound **1c** (500 mg, 2.78 mmol) was converted into **2c** (in methanol: 705 mg, 2.53 mmol, 91%; in ethanol: 430 mg, 1.54 mmol, 55%) by the General Procedure: colourless solid. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.56 (s, 1 H), 8.99 (d, J = 2.5 Hz, 1 H), 8.00 (d, J = 9.4, 2.6 Hz, 1 H), 7.66 (d, J = 9.5 Hz, 1 H), 4.15 (s, 3 H), 2.18 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 169.9, 159.6, 135.4, 134.1, 119.7, 116.2, 102.5, 59.5, 24.6 ppm. IR (ATR): $\tilde{\nu}$ = 3349 (w), 3101 (w), 2261 (m), 1692 (m), 1063 (s) cm^{-1}. HRMS (ESI): calcd. for $C_9H_{10}N_3O_2$ [M]$^+$ 192.0773; found 192.0783.

5-Acetamido-2-chlorobenzenediazonium Tetrafluoroborate (2d): Compound **1d** (500 mg, 2.71 mmol) was converted into **2d** (in methanol: 574 mg, 2.03 mmol, 75%; in ethanol: 490 mg, 1.72 mmol, 64%; in dioxane: 709 mg, 2.50 mmol, 92%) by the General Procedure: brown-red solid. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 10.90 (s, 1 H), 9.38 (d, J = 2.4 Hz, 1 H), 8.08 (d, J = 9.0 Hz, 1 H), 7.99 (dd, J = 9.0, 2.5 Hz, 1 H), 2.18 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 170.6, 140.3, 133.2, 132.3, 129.8, 122.6, 117.6, 24.9 ppm. IR (ATR): $\tilde{\nu}$ = 3354 (w), 3079 (w), 2288 (m), 1702 (m), 1004 (s) cm^{-1}. HRMS (ESI): calcd. for $C_8H_7N_3OCl$ [M]$^+$ 196.0278; found 196.0295.

4-Acetamido-2-fluorobenzenediazonium Tetrafluoroborate (2e): Compound **1e** (100 mg, 0.60 mmol) was converted into **2e** (in methanol: 62 mg, 0.23 mmol, 39%; in ethanol: 100 mg, 0.37 mmol, 62%; in dioxane: 70 mg, 0.26 mmol, 44%) by the General Procedure: yellow solid. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 11.40 (s, 1 H), 8.57 (dd, J = 9.3, 7.0 Hz, 1 H), 8.13 (dd, J = 12.6, 1.9 Hz, 1 H), 7.65 (dd, J = 9.3, 1.9 Hz, 1 H), 2.21 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 170.9, 162.3 (d, J = 269.0 Hz), 152.6 (d, J = 12.9 Hz), 134.6, 116.5, 106.0 (d, J = 20.9 Hz), 94.3 (d, J = 12.8 Hz), 24.7 ppm. ^{19}F NMR (282 MHz, [D$_6$]DMSO): δ = –100.0 (dd, J = 12.6, 7.0 Hz), –148.4 (m) ppm. IR: $\tilde{\nu}$ = 3575 (w), 2250 (w), 1591 (m), 1324 (m), 1042 (s) cm^{-1}. HRMS (ESI): calcd. for $C_8H_7N_3OF$ [M]$^+$ 180.0568; found 180.0566.

4-Acetamido-3-fluorobenzenediazonium Tetrafluoroborate (2f): Compound **1f** (425 mg, 2.50 mmol) was converted into **2f** (in methanol: 609 mg, 2.30 mmol, 91%; in ethanol: 306 mg, 1.80 mmol, 51%) by the General Procedure: yellow solid. ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 10.81 (s, 1 H), 8.76 (dd, J = 8.9, 8.9 Hz, 1 H), 8.65 (dd, J = 10.0, 1.9 Hz, 1 H), 8.52 (dm, J = 9.1 Hz, 1 H), 2.26 (s, 3 H) ppm. ^{13}C NMR (126 MHz, [D$_6$]DMSO): δ = 170.8, 149.4 (d, J = 252.3 Hz), 139.4 (d, J = 10.6 Hz), 132.3, 121.8 (d, J = 2.9 Hz), 119.6 (d, J = 28.2 Hz), 105.3 (d, J = 7.5 Hz), 24.5 ppm. ^{19}F NMR (282 MHz, [D$_6$]DMSO): δ = –119.4 (dd, J = 8.6, 8.6 Hz), –148.1 (m) ppm. IR (ATR): $\tilde{\nu}$ = 3574 (w), 2271 (m), 1586 (m), 1489 (m), 1035 (s) cm^{-1}. HRMS (ESI): calcd. for $C_8H_7N_3OF$ [M]$^+$ 180.0568; found 180.0567.

General Procedure for the Matsuda–Heck Coupling: $Pd(OAc)_2$ (5 mol-%) was added to a solution of the appropriate diazonium salt **2** (1.00 mmol) in anhydrous methanol (3 mL) or an alternate solvent as listed in Table 3. For basic conditions (see Table 3), NaOAc (3.00 mmol, 246 mg) was added. After 0.2 h, methyl acrylate (**10a**, 180 μL, 2.00 mmol) or one of the styrenes **10b**–**g** (2.00 mmol) was added. The solution was stirred for 16 h at ambient temperature. The reaction was quenched by addition of water (15 mL) and the mixture was extracted three times with ethyl acetate (60 mL total volume). The combined organic layers were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography.

Methyl (*E*)-3-(3-Acetamidophenyl)acrylate (*m*-11aa): Compounds *m*-**2a** (500 mg, 2.28 mmol) and **10a** (410 μL, 4.56 mmol) were converted into *m*-**11aa** (176 mg, 0.80 mmol, 38%) by the General Procedure: colourless solid, m.p. 103 °C. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 10.03 (s, 1 H), 7.85 (s, 1 H), 7.60 (d, J = 16.0 Hz, 1 H), 7.60 (dm, J = 7.7 Hz, 1 H), 7.40 (d, J = 7.7 Hz, 1 H), 7.34 (dd, J = 7.7, 7.7 Hz, 1 H), 6.50 (d, J = 16.0 Hz, 1 H), 3.72 (s, 3 H), 2.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.9, 166.9, 144.9, 140.3, 134.8, 129.8, 123.4, 121.6, 118.9, 118.3, 51.9, 24.5 ppm. IR (ATR): $\tilde{\nu}$ = 3180 (m), 3118 (m), 1706 (s) 1645 (s) 1004 (s), 765 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 219 (56), 177 (100), 146 (74), 118 (23). HRMS (EI): calcd. for $C_{12}H_{13}NO_3$ [M]$^+$ 219.0895; found 219.0886.

Methyl (*E*)-3-(4-Acetamidophenyl)acrylate (*p*-11aa):[81] Compounds *p*-**2a** (100 mg, 0.40 mmol) and **10a** (72 μL, 0.80 mmol) were converted into *p*-**11aa** (86 mg, 0.40 mmol, quant) by the General Procedure: colourless solid, m.p. 169–171 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.14 (s, 1 H), 7.65–7.63 (m, 4 H), 7.59 (d, J = 16.1 Hz, 1 H), 6.51 (d, J = 16.0 Hz, 1 H), 3.71 (s, 3 H), 2.02 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 169.1, 167.3, 144.7, 141.8, 129.6, 129.0, 119.3, 116.2, 51.8, 24.6 ppm. MS (EI): *m*/*z* (%) = 219 (41), 177 (67), 146 (100), 118 (31). HRMS (EI): calcd. for $C_{12}H_{13}NO_3$ [M]$^+$ 219.0895; found 219.0886.

Methyl (*E*)-3-(5-Acetamido-2-methoxyphenyl)acrylate (11ca):[82] Compounds **2c** (100 mg, 0.36 mmol) and **10a** (65 μL, 0.72 mmol) were converted into **11ca** (58 mg, 0.23 mmol, 65%) by the General Procedure: colourless solid, m.p. > 240 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.86 (s, 1 H), 7.83 (d, J = 16.1 Hz, 1 H), 7.83 (d, J = 2.5 Hz, 1 H), 7.57 (dd, J = 8.9, 2.5 Hz, 1 H), 7.05 (d, J = 9.0 Hz, 1 H), 6.42 (d, J = 16.2 Hz, 1 H), 3.83 (s, 3 H), 3.72 (s, 3 H), 2.02 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.6, 167.2, 154.3, 139.7, 133.1, 123.8, 119.5, 118.3, 118.2, 112.6, 56.3, 51.9, 24.2 ppm. IR (ATR): $\tilde{\nu}$ = 3370 (w), 1666 (m), 1496 (s), 1243 (s), 985 (m) cm^{-1}. MS (EI): *m*/*z* (%) = 249 (100), 207 (46), 176 (28), 120 (16). HRMS (EI): calcd. for $C_{13}H_{15}NO_4$ [M]$^+$ 249.1001; found 249.1006.

Methyl (*E*)-3-(4-Acetamido-2-fluorophenyl)acrylate (11ea): Compounds **2e** (100 mg, 0.37 mmol) and **10a** (67 μL, 0.74 mmol) were converted into **11ea** (45 mg, 0.19 mmol, 51%) by the General Procedure: colourless solid, m.p. 177–180 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.36 (s, 1 H), 7.61 (d, J = 16.2 Hz, 1 H), 7.52 (dd, J = 13.1, 1.2 Hz, 1 H), 7.31 (dd, J = 8.3, 8.3 Hz, 1 H), 7.17 (d, J = 8.5 Hz, 1 H), 6.31 (d, J = 16.2 Hz, 1 H), 3.67 (s, 3 H), 2.03 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.2, 167.4, 161.5 (d, J = 251.3 Hz), 142.3 (d, J = 12 Hz), 137.2, 129.1 (d, J = 4.5 Hz), 118.2 (d, J = 6.8 Hz), 117.1, 115.1, 106.9 (d, J = 48.0 Hz), 51.6,

24.3 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –112.7 (dd, J = 12.9, 8.3 Hz) ppm. IR (ATR): $\tilde{\nu}$ = 3341 (w), 1690 (s), 1419 (s), 1275 (s), 1176 (s) cm^{-1}. MS (EI): m/z (%) = 237 (35), 195 (57), 163 (100), 136 (35), 106 (13). HRMS (EI): calcd. for $C_{12}H_{12}NO_3F$ $[M]^+$ 237.0796; found 237.0796.

Methyl (*E*)-3-(4-Acetamido-3-fluorophenyl)acrylate (11fa): Compounds **2f** (100 mg, 0.37 mmol) and **10a** (67 μL, 0.74 mmol) were converted into **11fa** (67 mg, 0.28 mmol, 76%) by the General Procedure: colourless solid, m.p. 188 °C. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 9.89 (s, 1 H), 8.04 (dd, J = 8.3, 8.3 Hz, 1 H), 7.70 (dd, J = 12.3, 1.7 Hz, 1 H), 7.60 (d, J = 16.0 Hz, 1 H), 7.50 (dd, J = 8.4, 1.5 Hz, 1 H), 6.62 (d, J = 16.0 Hz, 1 H), 3.72 (s, 3 H), 2.11 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.9, 166.6, 152.8 (d, J = 245.6 Hz), 143.0, 130.6 (d, J = 7.1 Hz), 128.4 (d, J = 11.8 Hz), 125.0 (d, J = 2.9 Hz), 143.0, 117.8, 114.8 (d, J = 20.5 Hz), 51.4, 23.6 ppm. ^{19}F NMR (282 MHz, [D$_6$]DMSO): δ = –125.0 (dd, J = 9.3, 9.3 Hz) ppm. IR (ATR): $\tilde{\nu}$ = 3258 (w), 1703 (s), 1521 (s), 1427 (s), 1178 (s) cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{12}NO_3F$ $[M + H]^+$ 238.0874; found 238.0876.

(*E*)-*N*-(4-Styrylphenyl)acetamide (*p*-11ab):[83] Compounds *p*-**2a** (80 mg, 0.32 mmol) and **10b** (37 μL, 0.32 mmol) were converted into *p*-**11ab** (50 mg, 0.21 mmol, 66%) by the General Procedure: yellow solid, m.p. 230 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.01 (s, 1 H), 7.65–7.50 (m, 6 H), 7.36 (dd, J = 7.5, 7.5 Hz, 2 H), 7.25 (tm, J = 7.5 Hz, 1 H), 7.20 (d, J = 16.1 Hz, 1 H), 7.13 (d, J = 16.5 Hz, 1 H), 2.06 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.7, 139.4, 137.7, 132.3, 129.1, 128.5, 127.8, 127.4, 127.3, 126.7, 119.5, 24.5 ppm. IR (ATR): $\tilde{\nu}$ = 3299 (w), 1663 (m), 1321 (m), 969 (s), 823 (s) cm^{-1}. MS (EI): m/z (%) = 237 (56), 195 (65), 165 (31), 43 (100). HRMS (EI): calcd. for $C_{16}H_{15}NO$ $[M]^+$ 237.1154; found 237.1141. $C_{16}H_{15}NO$ (237.30): calcd. C 76.4, H 6.4, N 5.2; found C 76.1, H 6.4, N 5.3.

(*E*)-*N*-[4-(4-Methylstyryl)phenyl]acetamide (*p*-11ac):[84] Compounds *p*-**2a** (80 mg, 0.32 mmol) and **10c** (42 μL, 0.32 mmol) were converted into *p*-**11ac** (41 mg, 0.16 mmol, 51%) by the General Procedure: yellow solid, m.p. 242–244 °C. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 9.99 (s, 1 H), 7.59 (d, J = 8.5 Hz, 2 H), 7.51 (d, J = 8.6 Hz, 2 H), 7.46 (d, J = 8.0 Hz, 2 H), 7.17 (d, J = 7.9 Hz, 2 H), 7.08 (d, J = 16.8 Hz, 1 H), 7.14 (d, J = 16.8 Hz, 1 H), 2.30 (s, 3 H), 2.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.7, 139.2, 137.1, 134.9, 132.4, 129.7, 127.5, 127.3, 127.2, 126.6, 119.5, 24.5, 21.3 ppm. IR (ATR): $\tilde{\nu}$ = 3296 (w), 1662 (s), 1593 (s), 1315 (s), 1260 (m) cm^{-1}. MS (EI): m/z (%) = 251 (97), 209 (100), 194 (28), 165 (28). HRMS (EI): calcd. for $C_{17}H_{17}NO$ $[M]^+$ 251.1310; found 251.1324.

(*E*)-*N*-[4-(3-Methylstyryl)phenyl]acetamide (*p*-11ad): Compounds *p*-**2a** (80 mg, 0.32 mmol) and **10d** (42 μL, 0.32 mmol) were converted into *p*-**11ad** (40 mg, 0.16 mmol, 50%) by the General Procedure: yellow solid, m.p. 142–143 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.00 (s, 1 H), 7.64 (d, J = 8.6 Hz, 2 H), 7.56 (d, J = 8.6 Hz, 2 H), 7.43 (s, 1 H), 7.39 (d, J = 7.9 Hz, 1 H), 7.28 (dd, J = 7.6, 7.6 Hz, 1 H), 7.21 (d, J = 16.5 Hz, 1 H), 7.13 (d, J = 16.6 Hz, 1 H), 7.10 (d, J = 7.1 Hz, 1 H), 2.32 (s, 3 H), 2.07 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.7, 139.3, 138.2, 137.6, 132.3, 129.0, 128.5, 128.3, 127.4, 127.3, 127.2, 124.0, 119.5, 24.5, 21.5 ppm. IR (ATR): $\tilde{\nu}$ = 3277 (w), 1660 (s), 1526 (s), 1369 (m), 1261 (m) cm^{-1}. MS (EI): m/z (%) = 251 (97), 209 (87), 165 (33), 43 (100). HRMS (EI): calcd. for $C_{17}H_{17}NO$ $[M]^+$ 251.1310; found 251.1315.

(*E*)-*N*-[4-(4-Methoxystyryl)phenyl]acetamide (*p*-11ae):[85] Compounds *p*-**2a** (80 mg, 0.32 mmol) and **10e** (43 μL, 0.32 mmol) were converted into *p*-**11ae** (56 mg, 0.21 mmol, 66%) by the General Procedure under basic conditions: yellow solid, m.p. 93 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.98 (s, 1 H), 7.58 (d, J = 8.6 Hz, 2 H), 7.51 (d, J = 8.5 Hz, 2 H), 7.47 (d, J = 8.5 Hz, 2 H), 7.09 (d, J = 16.5 Hz, 1 H), 7.01 (d, J = 16.5 Hz, 1 H), 6.93 (d, J = 8.8 Hz, 1 H), 3.77 (s, 3 H), 2.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.7, 139.4, 137.7, 132.3, 129.1, 128.5, 127.8, 127.4, 127.3, 126.7, 119.5, 55.6, 24.5 ppm. IR (ATR): $\tilde{\nu}$ = 3283 (w), 1659 (m), 1509 (s), 1243 (s), 1031 (s) cm^{-1}. MS (EI): m/z (%) = 267 (100), 225 (33), 135 (49), 43 (90). HRMS (EI): calcd. for $C_{17}H_{17}NO_2$ $[M]^+$ 267.1259; found 267.1250. $C_{17}H_{17}NO_2$ (267.33): calcd. C 76.4, H 6.4, N 5.2; found C 76.1, H 6.4, N 5.3.

(*E*)-*N*-[4-(4-Chlorostyryl)phenyl]acetamide (*p*-11af): Compounds *p*-**2a** (80 mg, 0.32 mmol) and **10f** (41 μL, 0.32 mmol) were converted into *p*-**11af** (44 mg, 0.16 mmol, 51%) by the General Procedure: yellow solid, m.p. > 250 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.01 (s, 1 H), 7.60 (d, J = 8.3 Hz, 2 H), 7.58 (d, J = 8.6 Hz, 2 H), 7.52 (d, J = 8.6 Hz, 2 H), 7.40 (d, J = 8.4 Hz, 2 H), 7.21 (d, J = 16.5 Hz, 1 H), 7.12 (d, J = 16.5 Hz, 1 H), 2.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.7, 139.6, 136.7, 132.0, 129.4, 129.1, 129.1, 128.3, 127.5, 126.0, 119.5, 24.5 ppm. IR (ATR): $\tilde{\nu}$ = 3291 (w), 1660 (s), 1595 (s), 1510 (s), 1316 (m) cm^{-1}. MS (EI): m/z (%) = 271 (77), 229 (70), 165 (30), 43 (100). HRMS (EI): calcd. for $C_{16}H_{14}NOCl$ $[M]^+$ 271.0758; found 271.0749. $C_{16}H_{14}ClNO$ (271.74): calcd. C 70.7, H 5.2, N 5.2; found C 70.5, H 5.1, N 5.3.

(*E*/*Z*)-*N*-[4-(4-Nitrostyryl)phenyl]acetamide (*p*-11ag): Compounds *p*-**2a** (80 mg, 0.32 mmol) and **10g** (48 mg, 0.32 mmol) were converted into *p*-**11ag** (90 mg, 0.32 mmol, quant) by the General Procedure: inseparable mixtures of *E* and *Z* isomers (ratios 3:1–4:1); yellow oil.

NMR Data for the Major Isomer (*E*)-*p*-11ag: ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.08 (s, 1 H), 8.21 (d, J = 8.8 Hz, 2 H), 7.82 (d, J = 8.8 Hz, 2 H), 7.65 (d, J = 8.9 Hz, 2 H), 7.58 (d, J = 8.9 Hz, 2 H), 7.44 (d, J = 16.6 Hz, 1 H), 7.29 (d, J = 16.4 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.9, 146.4, 144.8, 140.3, 133.4, 131.5, 129.6, 128.2, 127.4, 125.2, 119.5, 24.5 ppm.

Selected ^{1}H-NMR Data for the Minor Isomer (*Z*)-*p*-11ag: ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.00 (s, 1 H), 8.13 (d, J = 8.8 Hz, 2 H), 7.15 (d, J = 8.6 Hz, 2 H), 6.78 (d, J = 12.3 Hz, 1 H), 6.64 (d, J = 12.3 Hz, 1 H) ppm.

General Procedure for the Azo Coupling of Acetamidoarene Diazonium Salts 2a: The appropriate coupling partner **12** (1.20 mmol) and NaOAc (30 mg, 0.35 mmol) were added to a solution of one of the arenediazonium salts *m*-**2a** or *p*-**2a** (237 mg, 1.00 mmol) in methanol (6 mL) and water (3 mL). The solution was stirred at ambient temperature for 2 h, diluted with water (15 mL) and extracted three times with ethyl acetate (60 mL total volume). The combined organic layers were dried with Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica.

(*E*)-*N*-(3-{[4-(Dimethylamino)phenyl]diazenyl}phenyl)acetamide (*m*-13aa):[86] Compounds *m*-**2a** (249 mg, 1.00 mmol) and **12a** (145 mg, 1.20 mmol) were converted into *m*-**13aa** (230 mg, 0.82 mmol, 82%) by the General Procedure: red solid, m.p. 189 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.12 (s, 1 H), 8.05 (s, 1 H), 7.78 (d, J = 9.1 Hz, 2 H), 7.62 (ddd, J = 7.3, 2.1, 2.1 Hz, 1 H), 7.44–7.39 (m, 2 H), 6.83 (d, J = 9.2 Hz, 2 H), 3.06 (s, 6 H), 2.07 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.9, 153.3, 152.9, 142.9, 140.6, 129.8, 125.2, 120.4, 117.9, 112.0, 111.9, 24.5 ppm. IR (ATR): $\tilde{\nu}$ = 3301 (w), 2926 (w), 1598 (s), 1360 (s), 1148 (s) cm^{-1}. MS (EI): m/z (%) = 282 (23), 148 (100), 120 (20), 105 (18). HRMS (EI):

calcd. for $C_{16}H_{18}N_4O$ $[M]^+$ 282.1481; found 282.1470. $C_{16}H_{18}N_4O$ (282.35): calcd. C 68.1, H 6.4, N 19.8; found C 67.6, H 6.4, N 19.2.

(*E*)-*N*-(4-{[4-(Dimethylamino)phenyl]diazenyl}phenyl)acetamide (*p*-13aa): Compounds *p*-**2a** (125 mg, 0.50 mmol) and **12a** (73 mg, 0.60 mmol) were converted into *p*-**13aa** (57 mg, 0.20 mmol, 40%) by the General Procedure: red solid, m.p. 229 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.17 (s, 1 H), 7.78–7.72 (m, 6 H), 6.82 (d, J = 9.2 Hz, 2 H), 3.06 (s, 6 H), 2.10 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 169.4, 153.1, 148.8, 143.5, 141.6, 125.2, 123.4, 120.0, 112.5, 24.1 ppm. IR (ATR): $\tilde{\nu}$ = 2924 (w), 1664 (m), 1596 (s), 1365 (s), 1318 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 282 (100), 148 (23), 120 (92), 105 (18), 77 (23). HRMS (EI): calcd. for $C_{16}H_{18}N_4O$ $[M]^+$ 282.1481; found 282.1486.

(*E*)-*N*-{3-[(4-Hydroxyphenyl)diazenyl]phenyl}acetamide (*m*-13ab):[87] Compounds *m*-**2a** (125 mg, 0.50 mmol) and **12b** (56 mg, 0.60 mmol) were converted into *m*-**13ab** (59 mg, 0.23 mmol, 46%) by the General Procedure: colourless solid, m.p. 127 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.30 (br. s, 1 H), 10.15 (s, 1 H), 8.08 (s, 1 H), 7.79 (d, J = 8.8 Hz, 2 H), 7.67 (d, J = 7.4 Hz, 1 H), 7.57–7.41 (2 H), 6.94 (d, J = 8.8 Hz, 2 H), 2.08 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 169.4, 161.8, 153.3, 146.1, 141.1, 130.3, 125.7, 121.7, 118.6, 116.8, 112.5, 24.9 ppm. IR (ATR): $\tilde{\nu}$ = 3398 (w), 1649 (m), 1603 (s), 1537 (s), 1283 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 255 (1), 161 (13), 121 (10), 93 (13), 45 (100). HRMS (EI): calcd. for $C_{14}H_{13}N_3O_2$ $[M]^+$ 255.1008; found 255.1017.

(*E*)-*N*-{4-[(4-Hydroxyphenyl)diazenyl]phenyl}acetamide (*p*-13ab):[87] Compounds *p*-**2a** (125 mg, 0.50 mmol) and **12b** (56 mg, 0.60 mmol) were converted into *p*-**13ab** (21 mg, 0.08 mmol, 16%) by the General Procedure: colourless solid, m.p. 197 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 10.22 (s, 1 H), 7.80–7.70 (m, 6 H), 6.92 (d, J = 8.7 Hz, 1 H), 2.09 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 169.5, 161.3, 148.4, 146.2, 142.3, 125.3, 123.9, 120.0, 116.7, 25.0 ppm. IR (ATR): $\tilde{\nu}$ = 3396 (w), 1584 (m), 1528 (s), 1370 (s), 1227 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 255 (44), 134 (54), 121 (31), 93 (67), 65 (100). HRMS (EI): calcd. for $C_{14}H_{13}N_3O_2$ $[M]^+$ 255.1008; found 255.1006.

(*E*)-*N*-{3-[(2-Hydroxynaphthalen-1-yl)diazenyl]phenyl}acetamide (*m*-13ac): Compounds *m*-**2a** (125 mg, 0.50 mmol) and **12c** (86 mg, 0.60 mmol) were converted into *m*-**13ac** (71 mg, 0.23 mmol, 47%) by the General Procedure: red solid, m.p. 227 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 15.84 (s, 1 H), 10.17 (s, 1 H), 8.47 (d, J = 8.1 Hz, 1 H), 8.15 (s, 1 H), 7.93 (d, J = 9.5 Hz, 1 H), 7.76 (d, J = 7.6 Hz, 1 H), 7.65–7.52 (m, 2 H), 7.49–7.39 (m, 3 H), 6.89 (d, J = 9.4 Hz, 1 H), 2.10 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]-DMSO): δ = 170.4, 169.5, 145.9, 141.6, 140.9, 133.6, 130.9, 130.0, 129.9, 129.8, 128.7, 126.7, 124.9, 121.9, 119.2, 115.1, 108.9, 24.1 ppm. IR (ATR): $\tilde{\nu}$ = 3288 (w), 2924 (w), 1652 (s), 1446 (s), 1209 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 305 (64), 253 (77), 212 (31), 143 (100), 115 (72). HRMS (EI): calcd. for $C_{18}H_{15}N_3O_2$ $[M]^+$ 305.1164; found 305.1157. $C_{18}H_{15}N_3O_2$ (305.34): calcd. C 70.8, H 5.0, N 13.8; found C 70.7, H 4.9, N 13.5.

(*E*)-*N*-{4-[(2-Hydroxynaphthalen-1-yl)diazenyl]phenyl}acetamide (*p*-13ac):[42] Compounds *p*-**2a** (100 mg, 0.40 mmol) and **12c** (69 mg, 0.48 mmol) were converted into *p*-**13ac** (37 mg, 0.12 mmol, 30%) by the General Procedure: red solid, m.p. 265 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 15.35 (s, 1 H), 10.26 (s, 1 H), 8.67 (d, J = 8.2 Hz, 1 H), 7.97 (d, J = 9.2 Hz, 1 H), 7.93 (d, J = 9.0 Hz, 2 H), 7.85 (d, J = 8.2 Hz, 1 H), 7.80 (d, J = 9.0 Hz, 2 H), 7.63 (ddm, J = 7.7, 7.7 Hz, 1 H), 7.47 (ddm, J = 7.5, 7.5 Hz, 1 H), 7.08 (d, J = 9.2 Hz, 1 H), 2.09 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 169.5, 161.5, 143.6, 141.6, 138.2, 133.3, 129.7, 129.5, 129.4, 128.7, 125.9, 122.8, 122.1, 122.1, 120.5, 25.0 ppm. IR (ATR): $\tilde{\nu}$ = 3304 (w), 2924 (w), 1599 (s), 1315 (s), 1266 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 305 (100), 276 (23), 143 (61), 134 (36), 115 (51). HRMS (EI): calcd. for $C_{18}H_{15}N_3O_2$ $[M]^+$ 305.1164; found 305.1167. $C_{18}H_{15}N_3O_2$ (305.34): calcd. C 70.8, H 4.9, N 13.8; found C 70.5, H 4.8, N 13.7.

Dimethyl (2*E*,2′*E*)-3,3′-(2-Fluoro-1,4-phenylene)diacrylate (18): BF_3·methanol (50 wt.-% solution in methanol, 0.68 mL, 6.00 mmol) was added to a solution of **7** (210 mg, 1.00 mmol) in anhydrous methanol (4 mL). The solution was heated to 65 °C until the starting material was fully consumed (TLC), and then cooled to 0 °C. *tert*-Butyl nitrite (310 mg, 3.00 mmol) was added, and the mixture was stirred at 0 °C for one hour, followed by addition of $Pd(OAc)_2$ (6 mg, 2.5 mol-%). Stirring was continued for another 0.25 h. Methyl acrylate (**10a**, 0.27 mL, 3.00 mmol) was added, and the solution was allowed to warm to ambient temperature and then stirred for 12 h. After this time, water (10 mL) was added and the mixture was repeatedly extracted with ethyl acetate (40 mL total volume). The combined organic layers were dried with $MgSO_4$ and filtered, and all volatiles were evaporated. The residue was purified by column chromatography on silica, with hexane/MTBE 5:1 as eluent, to furnish **18** (190 mg, 0.72 mmol, 72%): colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, J = 16.2 Hz, 1 H), 7.59 (d, J = 16.0 Hz, 1 H), 7.52 (dd, J = 7.8, 7.8 Hz, 1 H), 7.29 (dd, J = 8.1, 1.5 Hz, 1 H), 7.23 (dd, J = 11.4, 1.5 Hz, 1 H), 6.55 (d, J = 16.2 Hz, 1 H), 6.44 (d, J = 16.0 Hz, 1 H), 3.80 (s, 3 H), 3.80 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.9, 166.7, 161.3 (d, J = 254.7 Hz), 142.4 (d, J = 2.5 Hz), 138.0 (d, J = 8.5 Hz), 136.4 (d, J = 2.5 Hz), 129.4 (d, J = 3.4 Hz), 124.2 (d, J = 3.3 Hz), 124.0 (d, J = 12.2 Hz), 121.3 (d, J = 6.7 Hz), 120.1, 115.1 (d, J = 22.9 Hz), 51.9, 51.8 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –115.0 (dd, J = 11.3, 7.5 Hz) ppm. MS (EI): *m*/*z* (%) = 264 (82), 233 (100). HRMS (EI): calcd. for $C_{14}H_{13}FO_4$ $[M]^+$ 264.0792; found 264.0786.

Methyl 2-Hydroxy-5-vinylbenzoate (14a): Trivinyltriboroxine·pyridine complex **20a** (82 mg, 0.34 mmol) was added to a solution of **19a** (266 mg, 1.00 mmol) and $Pd(OAc)_2$ (6 mg, 2.5 mol-%) in dry and degassed methanol (10 mL). The mixture was stirred for 6 h at ambient temperature, diluted with MTBE (100 mL) and washed with dilute hydrochloric acid (1 M, 25 mL). The aqueous layer was separated and extracted repeatedly with MTBE, and the combined organic extracts were dried with $MgSO_4$. After filtration, all volatiles were removed in vacuo, and the residue was purified by chromatography on silica, with hexane/MTBE (1:1) as eluent, to furnish **14a** (118 mg, 0.66 mmol, 66%) as a colourless liquid. A second fraction was identified as stilbene **21** (72 mg, 0.22 mmol, 22%).

Alternatively, **19a** (266 mg, 1.00 mmol) and $Pd(OAc)_2$ (6 mg, 2.5 mol-%) were dissolved in methanol (10 mL), and K-vinyltrifluoroborate **20b** (134 mg, 1.00 mmol) was added. The mixture was stirred for 6 h at ambient temperature, diluted with MTBE (100 mL) and washed with dilute hydrochloric acid (1 M, 25 mL). The aqueous layer was separated and extracted repeatedly with MTBE, and the combined organic extracts were dried with $MgSO_4$. After filtration, all volatiles were removed in vacuo, and the residue was purified by chromatography on silica, with hexane/MTBE (1:1) as eluent, to furnish **14a** (100 mg, 0.56 mmol, 56%) as a colourless liquid. A second fraction was identified as stilbene **21** (40 mg, 0.12 mmol, 12%).

Analytical Data for 14a: Colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.75 (s, 1 H), 7.84 (d, J = 2.3 Hz, 1 H), 7.55 (dd, J = 8.7, 2.3 Hz, 1 H), 6.95 (d, J = 8.7 Hz, 1 H), 6.63 (dd, J = 17.6, 10.9 Hz, 1 H), 5.63 (dd, J = 17.6, 0.6 Hz, 1 H), 5.18 (dd, J = 10.9, 0.5 Hz, 1 H), 3.96 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ =

170.4, 161.2, 135.4, 133.1, 129.1, 127.8, 117.8, 112.5, 112.2, 52.3 ppm. IR (ATR): $\tilde{\nu}$ = 3168 (w), 2954 (w), 1675 (s), 1491 (m), 1441 (m), 1305 (m), 1205 (s) cm^{-1}. MS (EI): *m/z* (%) = 178 (41), 163 (53), 146 (100). HRMS (EI): calcd. for $C_{10}H_{10}O_3$ $[M]^+$ 178.0630; found 178.0632. $C_{10}H_{10}O_3$ (178.18): calcd. C 67.4, H 5.7; found C 67.3, H 5.7.

Analytical Data for 21: Colourless solid, m.p. 159–162 °C. ^1H NMR (500 MHz, $CDCl_3$): δ = 10.74 (s, 2 H), 7.93 (d, *J* = 2.3 Hz, 2 H), 7.61 (dd, *J* = 8.7, 2.3 Hz, 2 H), 6.98 (d, *J* = 8.6 Hz, 2 H), 6.90 (s, 2 H), 3.98 (s, 6 H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.8, 161.5, 133.6, 129.2, 128.2, 126.5, 118.4, 112.9, 52.7 ppm. IR (ATR): $\tilde{\nu}$ = 3158 (w), 2954 (w), 1673 (s), 1590 (m), 1490 (m), 1438 (m), 1296 (m), 1205 (s) cm^{-1}. MS (EI): *m/z* (%) = 328 (5), 215 (34), 115 (100). HRMS (EI): calcd. for $C_{18}H_{16}O_6$ $[M]^+$ 328.0947; found 328.0943.

***N*-(2-Fluoro-4-vinylphenyl)acetamide (24):** Arenediazonium salt **1f** (267 mg, 1.00 mmol) was suspended in methanol (3 mL). $Pd(OAc)_2$ (6 mg, 2.5 mol-%) was added, followed by vinylboron compound **20a** (82 mg, 0.34 mmol). The reaction mixture was stirred for 6 h at ambient temperature, and then diluted with MTBE (50 mL). The resulting solution was washed with HCl (aq., 1 M), and the aqueous phase was separated and extracted with MTBE (100 mL). The combined organic layers were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica, with hexane/MTBE mixtures as eluent, to furnish **24** (76 mg, 0.42 mmol, 42%): colourless solid, m.p. 149 °C. ^1H NMR (300 MHz, $[D_6]$DMSO): δ = 9.75 (s, 1 H), 7.89 (dd, *J* = 8.3, 8.3 Hz, 1 H), 7.39 (dd, *J* = 12.4, 1.7 Hz, 1 H), 7.23 (d, *J* = 8.4 Hz, 1 H), 6.67 (dd, *J* = 17.6, 10.9 Hz, 1 H), 5.82 (d, *J* = 17.6 Hz, 1 H), 5.26 (d, *J* = 11.0 Hz, 1 H), 2.09 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $[D_6]$DMSO): δ = 168.7, 153.5 (d, *J* = 243.5 Hz), 135.2 (d, *J* = 2.2 Hz), 134.3 (d, *J* = 7.0 Hz), 125.8 (d, *J* = 11.9 Hz), 123.7 (d, *J* = 1.0 Hz), 122.3 (d, *J* = 2.9 Hz), 114.7, 112.4 (d, *J* = 20.2 Hz), 23.5 ppm. ^{19}F NMR (282 MHz, $[D_6]$-DMSO): δ = –125.2 (dd, *J* = 11.7, 8.9 Hz) ppm. IR (ATR): $\tilde{\nu}$ = 3245 (w), 1525 (s), 1369 (m), 993 (m), 708 (m) cm^{-1}. MS (EI): *m/z* (%) = 179 (69), 137 (100), 109 (15). HRMS (EI): calcd. for $C_{10}H_{10}ONF$ $[M]^+$ 179.0746; found 179.0741.

Methyl (*E*)-5-(4-Acetamido-3-fluorostyryl)-2-hydroxybenzoate (22b): Arenediazonium salt **19a** (100 mg, 0.38 mmol) was suspended in methanol (3 mL). $Pd(OAc)_2$ (4 mg, 5 mol-%) was added and the mixture was stirred for 10 min, followed by addition of **24** (68 mg, 0.38 mmol). The reaction mixture was stirred at ambient temperature for 16 h and then filtered through a short pad of celite and silica. The pad was washed with MTBE, and all volatiles were evaporated. The residue was purified by chromatography on silica, with hexane/MTBE mixtures as eluent, to furnish **22b** (71 mg, 0.22 mmol, 57%): off-white solid, m.p. 191–193 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 10.77 (s, 1 H), 8.27 (dd, *J* = 8.2, 8.2 Hz, 1 H), 7.91 (s, 1 H), 7.60 (dd, *J* = 8.7, 1.9 Hz, 1 H), 7.37 (br. s, 1 H), 7.20 (d, *J* = 10.4 Hz, 1 H), 6.96 (d, *J* = 8.6 Hz, 1 H), 6.92 (d, *J* = 16.3 Hz, 1 H), 6.85 (d, *J* = 16.3 Hz, 1 H), 3.96 (s, 3 H), 2.21 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6, 168.3, 161.5, 150.9 (d, *J* = 12.8 Hz), 134.2 (d, *J* = 5.8 Hz), 133.6, 128.7, 128.3, 127.9, 126.0 (d, *J* = 2.3 Hz), 125.7 (d, *J* = 10.6 Hz), 123.1 (d, *J* = 3.0 Hz), 121.8, 118.3, 112.7, 112.0 (d, *J* = 20.3 Hz), 52.6, 24.9 ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –127.2 (dd, *J* = 11.7, 8.9 Hz) ppm. IR (ATR): $\tilde{\nu}$ = 2915 (w), 1730 (m), 1459 (s), 1377 (s), 1180 (s) cm^{-1}. MS (EI): *m/z* (%) = 329 (11), 255 (16), 85 (36), 71 (66), 57 (100). HRMS (EI): calcd. for $C_{18}H_{16}O_4NF$ $[M]^+$ 329.1063; found 329.1069.

Dimethyl 5,5′-[(1*E*,1′*E*)-(2-Fluoro-1,4-phenylene)bis(ethene-2,1-diyl)]bis(2-methoxybenzoate) (25c): Arenediazonium salt **19c** (100 mg, 0.357 mmol) was suspended in methanol (3 mL). $Pd(OAc)_2$ (5 mg, 5 mol-%) was added, and the mixture was stirred for 10 min, followed by addition of **17** (26 mg, 0.176 mmol). The reaction mixture was stirred for 16 h at ambient temperature, and then filtered through a short pad of celite and silica. The pad was washed with MTBE, and all volatiles were evaporated under reduced pressure. The residue was purified by chromatography on silica, with hexane/MTBE mixtures as eluent, to furnish **25c** (28 mg, 0.059 mmol, 34%): yellow solid, m.p. 178–180 °C (reported in the literature:[59] m.p. 179–182 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.97–7.92 (m, 2 H), 7.63–7.55 (m, 2 H), 7.51 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.24–6.90 (m, 8 H), 3.91 (s, 12 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.9, 166.8, 159.2, 159.2, 138.7 (d, *J* = 8.3 Hz), 131.9, 131.8, 130.3, 130.2, 130.1, 129.7, 129.5 (d, *J* = 5.0 Hz), 128.6, 127.5 (d, *J* = 4.2 Hz), 126.7 (d, *J* = 2.5 Hz), 124.6 (d, *J* = 12.6 Hz), 122.9 (d, *J* = 2.9 Hz), 120.7 (d, *J* = 2.6 Hz), 120.2 (d, *J* = 3.0 Hz), 113.6, 113.3, 112.8, 112.7, 56.6, 56.6, 52.5, 52.5 [*ipso*-C(F) obscured due to low intensity and coupling with ^{19}F] ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –118.2 (dd, *J* = 11.9, 7.9 Hz) ppm. IR (ATR): $\tilde{\nu}$ = 2927 (w), 1698 (s), 1309 (s), 1252 (s), 809 (s) cm^{-1}. MS (EI): *m/z* (%) = 476 (100), 312 (23), 183 (16), 207 (75). HRMS (EI): calcd. for $C_{28}H_{25}O_6F$ $[M]^+$ 476.1635; found 476.1630.

General Procedure for the Suzuki–Miyaura Coupling: $Pd(OAc)_2$ (4.5 mg, 5.0 mol-%) was added to a solution of the appropriate diazonium salt *m*- or *p*-**2a** (100 mg, 0.40 mmol) in 1,4-dioxane (4 mL). The corresponding K-organotrifluoroborate **26** (0.6 mmol) was added, and the solution was stirred for 16 h at ambient temperature. The reaction mixture was filtered through a short pad of celite, which was then washed with MTBE. All volatiles were evaporated, and the residue was purified by chromatography on silica, with hexane/MTBE mixtures as eluent, to furnish the biaryls **27**.

3-Phenylacetanilide (*m*-27a):[88] Compounds *m*-**2a** (100 mg, 0.40 mmol) and **26a** (110 mg, 0.60 mmol) were converted into *m*-**27a** (67 mg, 0.32 mmol, 79%) by the General Procedure: colourless solid, m.p. 145 °C. ^1H NMR (300 MHz, $[D_6]$DMSO): δ = 10.04 (s, 1 H), 7.89 (m, 1 H), 7.59 (dm, *J* = 8.2, 1.1 Hz, 2 H) 7.56 (dm, *J* = 8.0 Hz, 1 H), 7.47 (dd, *J* = 8.0, 8.0 Hz, 2 H), 7.41–7.34 (m, 2 H), 7.31 (dm, *J* = 7.8 Hz, 1 H), 2.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $[D_6]$DMSO): δ = 169.3, 141.6, 141.6, 141.1, 140.7, 130.1, 129.8, 128.4, 127.5, 122.3, 118.1, 24.9 ppm. MS (EI): *m/z* (%) = 211 (42), 169 (100), 141 (13), 115 (15). HRMS (EI): calcd. for $C_{14}H_{13}NO$ $[M]^+$ 211.0992; found 211.0988.

4-Phenylacetanilide (*p*-27a):[89] Compounds *p*-**2a** (100 mg, 0.40 mmol) and **26a** (110 mg, 0.60 mmol) were converted into *p*-**27a** (74 mg, 0.35 mmol, 89%) by the General Procedure: colourless solid, m.p. 163 °C. ^1H NMR (300 MHz, $[D_6]$DMSO): δ = 10.03 (s, 1 H), 7.67 (d, *J* = 8.7 Hz, 2 H), 7.65–7.55 (m, 4 H), 7.43 (dd, *J* = 7.7, 7.7 Hz, 2 H), 7.32 (tm, *J* = 7.5 Hz, 1 H), 2.06 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $[D_6]$DMSO): δ = 169.2, 140.6, 139.7, 135.5, 129.7, 127.8, 127.7, 127.1, 120.2, 24.9 ppm. MS (EI): *m/z* (%) = 211 (40), 169 (100), 141 (14), 115 (20). HRMS (EI): calcd. for $C_{14}H_{13}NO$ $[M]^+$ 211.0992; found 211.0993.

***N*-[3′,5′-Bis(trifluoromethyl)biphenyl-3-yl]acetamide (*m*-27b):** Compounds *m*-**2a** (96 mg, 0.39 mmol) and **26b** (187 mg, 0.59 mmol) were converted into *m*-**27b** (34 mg, 0.10 mmol, 25%) by the General Procedure: colourless solid, m.p. 73–75 °C. ^1H NMR (300 MHz, $[D_6]$DMSO): δ = 8.02–7.98 (m, 2 H), 7.92–7.82 (m, 2 H), 7.60–7.50 (m, 2 H), 7.45 (dd, *J* = 7.8, 7.8 Hz, 1 H), 7.35 (d, *J* = 7.7 Hz, 1 H), 2.24 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $[D_6]$DMSO): δ = 168.9, 143.2, 139.5, 139.2, 132.5 (q, *J* = 33.0 Hz), 130.3, 127.6 (quint., *J*

= 3.5 Hz), 123.7 (q, J = 272.6 Hz), 123.5, 121.5 (m, 1 H), 120.5, 119.0, 24.9 ppm. ^{19}F NMR (282 MHz, [D$_6$]DMSO): δ = –62.8 (s) ppm. IR (ATR): $\tilde{\nu}$ = 3301 (w), 1668 (m), 1376 (m), 1274 (s), 1126 (s) cm^{-1}. MS (EI): m/z (%) = 347 (18), 305 (100), 149 (5), 43 (38). HRMS (EI): calcd. for $C_{16}H_{11}NOF_6$ [M]$^+$ 347.0745; found 347.0761.

***N*-(3′-Nitrobiphenyl-3-yl)acetamide (*m*-27c):** Compounds *m*-**2a** (100 mg, 0.40 mmol) and **26c** (140 mg, 0.60 mmol) were converted into *m*-**27c** (30 mg, 0.12 mmol, 29%) by the General Procedure: colourless solid, m.p. 167–170 °C. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 10.10 (s, 1 H), 8.36 (dd, J = 1.9, 1.9 Hz, 1 H), 8.22 (dm, J = 8.2 Hz, 1 H), 8.08 (dm, J = 8.3 Hz, 1 H), 7.98 (s, 1 H), 7.77 (dd, J = 8.0, 8.0 Hz, 1 H), 7.65 (m, 1 H), 7.50–7.40 (m, 2 H), 2.08 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.9, 148.8, 142.1, 140.6, 138.7, 131.0, 130.1, 122.7, 122.0, 121.3, 119.5, 117.8, 24.5 ppm. IR (ATR): $\tilde{\nu}$ = 3298 (w), 1666 (m), 1567 (s), 1523 (s), 1281 (m) cm^{-1}. MS (EI): m/z (%) = 256 (38), 214 (100), 167 (28), 139 (23). HRMS (EI): calcd. for $C_{14}H_{12}N_2O_3$ [M]$^+$ 256.0848; found 256.0852.

***N*-(3′-Nitrobiphenyl-4-yl)acetamide (*p*-27c):** Compounds *p*-**2a** (100 mg, 0.40 mmol) and **26c** (140 mg, 0.60 mmol) were converted into *p*-**27c** (81 mg, 0.32 mmol, 79%) by the General Procedure: colourless solid, m.p. 185–188 °C. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 10.10 (s, 1 H), 8.40 (dd, J = 1.9, 1.9 Hz, 1 H), 8.16 (dm, J = 8.2 Hz, 1 H), 8.11 (dm, J = 7.9 Hz, 1 H), 7.79–7.68 (m, 5 H), 2.08 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.9, 148.9, 141.8, 140.3, 133.1, 132.6, 130.9, 127.8, 122.0, 119.9, 24.5 ppm. IR (ATR): $\tilde{\nu}$ = 3298 (w), 1666 (m), 1567 (s), 1523 (s), 1281 (m) cm^{-1}. MS (EI): m/z (%) = 256 (51), 214 (100), 168 (64), 139 (41). HRMS (EI): calcd. for $C_{14}H_{12}N_2O_3$ [M]$^+$ 256.0848; found 256.0860. $C_{14}H_{12}N_2O_3$ (256.26): calcd. C 65.6, H 4.7, N 10.9; found C 65.1, H 4.9, N 10.6.

***N*-(2′,4′-Difluorobiphenyl-3-yl)acetamide (*m*-27d):** Compounds *m*-**2a** (80 mg, 0.32 mmol) and **26d** (106 mg, 0.48 mmol) were converted into *m*-**27d** (56 mg, 0.23 mmol, 71%) by the General Procedure: colourless solid, m.p. 119 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 7.65–7.58 (m, 2 H), 7.50 (d, J = 8.6 Hz, 1 H), 7.40–7.30 (m, 2 H), 7.20 (d, J = 7.7 Hz, 1 H), 6.95–6.80 (m, 2 H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 169.1, 162.7 (dd, J = 249.2, 12.0 Hz), 160.07 (dd, J = 250.6, 11.9 Hz), 138.5, 136.1, 131.9, 129.5, 125.3, 120.8, 120.4, 119.7, 111.9, 104.7, 24.9 ppm. ^{19}F NMR (282 MHz, CDCl$_3$): δ = –111.1, –113.4 ppm. IR (ATR): $\tilde{\nu}$ = 3265 (w), 1502 (s), 1409 (s), 1264 (s), 843 (s) cm^{-1}. MS (EI): m/z (%) = 247 (38), 205 (100), 189 (78), 71 (17). HRMS (EI): calcd. for $C_{14}H_{11}NOF_2$ [M]$^+$ 247.0809; found 247.0803.

***N*-(2′,4′-Difluorobiphenyl-4-yl)acetamide (*p*-27d):** Compounds *p*-**2a** (80 mg, 0.32 mmol) and **26d** (106 mg, 0.48 mmol) were converted into *p*-**27d** (63 mg, 0.26 mmol, 80%) by the General Procedure: colourless solid, m.p. 155–158 °C. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 10.06 (s, 1 H), 7.68 (d, J = 8.6 Hz, 2 H), 7.61–7.50 (2 H), 7.55 (ddd, J = 8.8, 8.8, 6.6 Hz, 1 H), 7.46 (dm, J = 8.6 Hz, 2 H), 7.33 (ddd, J = 11.0, 9.3, 2.6 Hz, 1 H), 7.17 (dddm, J = 8.3, 8.3, 2.3 Hz, 1 H), 2.07 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.9, 161.9 (dd, J = 246.5, 12.1 Hz), 159.5 (dd, J = 248.3, 12.3 Hz), 139.5, 132.0 (dd, J = 9.6, 4.9 Hz), 129.5 (d, J = 3.0 Hz), 129.1, 125.0 (dd, J = 13.3, 3.8 Hz), 119.5, 112.4 (dd, J = 21.1, 3.7 Hz), 104.9 (dd, J = 26.0, 26.0 Hz), 24.5 ppm. ^{19}F NMR (282 MHz, [D$_6$]DMSO): δ = –111.8 (m), –113.8 (m) ppm. IR (ATR): $\tilde{\nu}$ = 3288 (w), 1659 (m), 1493 (s), 1397 (m), 809 (s) cm^{-1}. MS (EI): m/z (%) = 247 (61), 205 (100), 177 (13), 151 (10). HRMS (EI): calcd. for $C_{14}H_{11}NOF_2$ [M]$^+$ 247.0809; found 247.0805.

***N*-(4′-Fluorobiphenyl-4-yl)acetamide (*p*-27e):** Compounds *p*-**2a** (100 mg, 0.40 mmol) and **26e** (122 mg, 0.60 mmol) were converted into *p*-**27e** (54 mg, 0.24 mmol, 59%) by the General Procedure: colourless solid, m.p. 198–203 °C. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 10.03 (s, 1 H), 7.72–7.62 (m, 4 H), 7.58 (d, J = 8.7 Hz, 2 H), 7.26 (ddm, J = 8.9, 8.9 Hz, 2 H), 2.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.3, 161.5 (d, J = 243.9 Hz), 138.7, 136.2 (d, J = 3.1 Hz), 133.6, 128.1 (d, J = 8.1 Hz), 126.8, 119.3, 115.6 (d, J = 21.3 Hz), 24.0 ppm. ^{19}F NMR (282 MHz, [D$_6$]-DMSO): δ = –116.1 (m) ppm. IR (ATR): $\tilde{\nu}$ = 3288 (w), 1657 (m), 1537 (s), 1496 (s), 1217 (m) cm^{-1}. MS (EI): m/z (%) = 229 (21), 187 (100), 159 (13), 133 (10). HRMS (EI): calcd. for $C_{14}H_{12}NOF$ [M]$^+$ 229.0903; found 229.0911.

Methyl (*E*)-3-(4-Acetamido-1,1′-biphenyl-3-yl)acrylate (29):[27] Biphenyl *p*-**27a** (211 mg, 1.00 mmol) was dissolved in a mixture of CH_2Cl_2 (1 mL) and CF_3CO_2H (4 mL). $K_2S_2O_8$ (270 mg, 1.00 mmol) and Pd(OAc)$_2$ (11 mg, 5.0 mol-%) were added, followed by methyl acrylate (172 mg, 2.00 mmol). The mixture was stirred at ambient temperature for 20 h, diluted with CH_2Cl_2 (2 mL) and neutralized with an aqueous solution of Na_2CO_3. The resulting mixture was extracted with CH_2Cl_2 (3 times 15 mL), and the organic layer was separated and dried with $MgSO_4$. After filtration, all volatiles were evaporated and the residue was purified by column chromatography on silica, with hexane/ethyl acetate mixtures as eluent, to furnish **28** (176 mg, 0.60 mmol, 60%): colourless solid, m.p. 195–200 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 9.90 (s, 1 H), 8.07 (d, J = 1.8 Hz, 1 H), 7.84 (d, J = 16.0 Hz, 1 H), 7.76 (d, J = 7.2 Hz, 2 H), 7.71 (dd, J = 8.4, 2.0 Hz, 1 H), 7.55 (d, J = 8.4 Hz, 1 H), 7.47 (dd, J = 7.2, 7.2 Hz, 2 H), 7.38 (t, J = 7.2 Hz, 1 H), 6.80 (d, J = 16.0 Hz, 1 H), 3.75 (s, 3 H), 2.09 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.8, 166.7, 140.2, 139.0, 137.4, 137.4, 136.4, 128.8, 128.6, 127.5, 126.8, 126.7, 124.8, 119.1, 51.4, 23.2 ppm. IR (ATR): $\tilde{\nu}$ = 3273 (w), 1719 (s), 1660 (s), 1294 (m), 1169 (s), 760 (s), 698 (s) cm^{-1}. MS (EI): m/z (%) = 295 (58), 253 (22), 222 (100), 193 (38), 165 (28). HRMS (EI): calcd. for $C_{18}H_{17}NO_3$ [M]$^+$ 295.1208; found 295.1216. $C_{18}H_{17}NO_3$ (295.34): calcd. C 73.2, H 5.8, N 4.7; found C 73.1, H 5.6, N 4.9.

Dimethyl (2*E*,2′*E*)-3,3′-(1,1′-Biphenyl-3,4-diyl)diacrylate (30):[27] BF_3·CH_3OH (324 μL, 3.00 mmol) was added to a solution of *p*-**27a** (295 mg, 1.00 mmol) in anhydrous methanol (6.0 mL). The solution was heated to reflux for 16 h and then cooled to 0 °C, and *tert*-BuONO (120 μL, 1.00 mmol) was added. The mixture was stirred for 0.5 h, followed by addition of Pd(OAc)$_2$ (5 mol-%) and stirring for another 0.25 h. Methyl acrylate (1.20 mmol) was then added, and the mixture was stirred for 16 h at ambient temperature. Water (15 mL) was added, the mixture was extracted three times with ethyl acetate (60 mL total volume), the organic layer was separated, dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by chromatography on silica to furnish **29** (193 mg, 0.60 mmol, 60%): colourless solid, m.p. 115–118 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 8.08 (d, J = 15.8 Hz, 1 H), 8.04 (d, J = 15.8 Hz, 1 H), 7.75 (d, J = 1.6 Hz, 1 H), 7.66–7.55 (m, 4 H), 7.45 (dd, J = 7.5, 7.5 Hz, 2 H), 7.37 (t, J = 7.5 Hz, 1 H), 6.41 (d, J = 15.8 Hz, 1 H), 6.39 (d, J = 15.8 Hz, 1 H), 3.81 (s, 3 H), 3.81 (s, 3 H) ppm. ^{13}C NMR (75 MHz, CDCl$_3$): δ = 167.1, 166.9, 143.2, 141.7, 141.2, 139.8, 134.9, 133.1, 129.2, 128.9, 128.4, 128.3, 127.2, 126.4, 122.0, 121.3, 52.1, 52.1 ppm. IR (ATR): $\tilde{\nu}$ = 2950 (w), 1712 (s), 1633 (m), 1434 (m), 1272 (m), 1168 (s), 976 (s), 762 (s), 698 (s) cm^{-1}. MS (EI): m/z (%) = 322 (20), 262 (100), 231 (95), 204 (64), 101 (18). HRMS (EI): calcd. for $C_{20}H_{18}O_4$ [M]$^+$ 322.1205; found 322.1208. $C_{20}H_{18}O_4$ (322.36): calcd. C 74.5, H 5.6; found C 74.2, H 5.8.

(*E*)-Methyl 3-[(*E*)-4-Styrylbiphenyl-3-yl]acrylate (31): Compound *p*-**27a** (295 mg, 1.00 mmol) and styrene (1.20 mmol) were converted into **30** (180 mg, 0.53 mmol, 53%) by the procedure given above for **29**: colourless solid, m.p. 135 °C. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 8.12 (d, J = 15.9 Hz, 1 H), 8.02 (s, 1 H), 7.85–7.72 (m, 3 H), 7.66 (d, J = 7.3 Hz, 2 H), 7.57 (d, J = 16.2 Hz, 1 H), 7.52–7.25 (m, 7 H), 7.16 (d, J = 16.1 Hz, 1 H), 6.75 (d, J = 15.8 Hz, 1 H), 3.75 (s, 3 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 166.5, 141.7, 139.5, 138.9, 136.8, 136.1, 132.7, 132.4, 128.9, 128.7, 128.4, 128.1, 127.7, 127.5, 126.8, 126.7, 125.4, 124.7, 120.5, 51.5 ppm. IR (ATR): $\tilde{\nu}$ = 3028 (w), 2924 (w), 1715 (s), 1169 (s), 760 (s), 694 (s) cm^{-1}. MS (EI): *m*/*z* (%) = 340 (64), 281 (100), 203 (51). HRMS (EI): calcd. for $C_{24}H_{20}O_2$ [M]$^+$ 340.1463; found 340.1469.

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