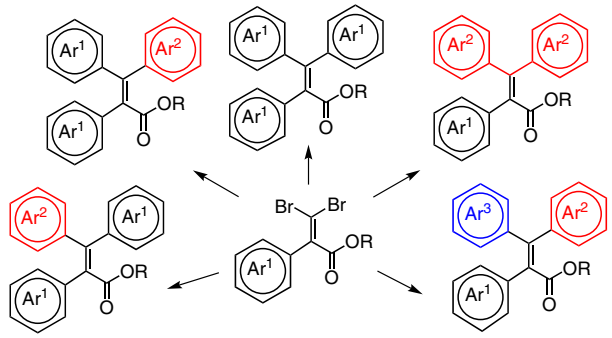
Synthesis S. Cardinal, N. Voyer Paper

# Preparation of 2,3,3-Triarylacrylic Acid Esters Using Suzuki–Miyaura Coupling Reactions

**Sébastien Cardinal**
**Normand Voyer***

Département de Chimie and PROTEO, Université Laval, 1045 avenue de la Médecine, Québec, QC, G1V OA6, Canada
Normand.voyer@chm.ulaval.ca




Received: 11.01.2016
Accepted: 24.01.2016
Published online: 17.02.2016
DOI: 10.1055/s-0035-1560419; Art ID: ss-2016-m0021-op

**Abstract** We report here a new strategy to produce 2,3,3-triarylacrylic acid esters, a class of 1,2,2-triarylethene compounds with an α,β-unsaturated ester functionality. Our approach requires the preparation of a *gem*-dibromoalkene precursor from an α-keto ester, followed by the installation of two aryl groups by Suzuki–Miyaura coupling reactions on the two C–Br bonds. Many 2,3,3-triarylacrylic acid esters with one, two, or three different aryl groups were obtained with complete regio- and stereocontrol in most cases.

**Key words** triarylethene, triarylacrylic acid, *gem*-dibromoalkene, double Suzuki–Miyaura coupling, stereoselective Suzuki–Miyaura coupling

Triarylethene compounds have been widely studied.[1] Tamoxifen, an antagonist of the estrogen receptor and a commonly used anticancer agent, is surely the most famous compound with the triarylethene moiety. Many synthetic pathways for it have been developed, facilitating reactions to produce various analogues.[2] The 1,2,2-triarylethene π-system has also been studied as a potential scaffold for the design of functional materials with useful photophysical properties.[3] In the course of a project directed toward the total synthesis of quebecol (**1**) [Figure 1 (a)], a natural product found in maple syrup, we devised a synthetic strategy to access efficiently the 1,2,2-triarylethene compound **2** [Figure 1 (b)], a key intermediate in the synthesis of natural polyphenol **1**.[4]

While working on the construction of the 2,3,3-triarylacrylic acid ester scaffold, a particular 1,2,2-triarylethene moiety conjugated with an α,β-unsaturated ester functionality [Figure 1 (c)], we realized that there was a scarcity of published synthetic methods for these compounds. Some of the methods are only useful to prepare a limited number of compounds. Most described synthetic pathways use alkynes as starting materials, and form the 2,3,3-triarylacrylic acid ester moiety by strategies such as the double addition of an organometallic reagent or the coupling with an aryl iodide and an arylboronic acid.[5–7] The latter strategy, developed by Larock, showed good yields and compatibility with a range of substrates and has been used to prepare different 2,3,3-triarylacrylic acid esters.[6] However, this multicomponent reaction often leads to moderate regioselectivity, showing that it is challenging to control the geometry when preparing tetrasubstituted alkenes with four C–C bonds on the olefin scaffold.[8] Recently, the Sawamura group reported the synthesis of some 2,3,3-triarylacrylic acid esters with stereocontrol over the olefin via an elegant method that require the preparation of particular β-boryl-α-silyl or α,β-diboryl acrylate templates.[7a]

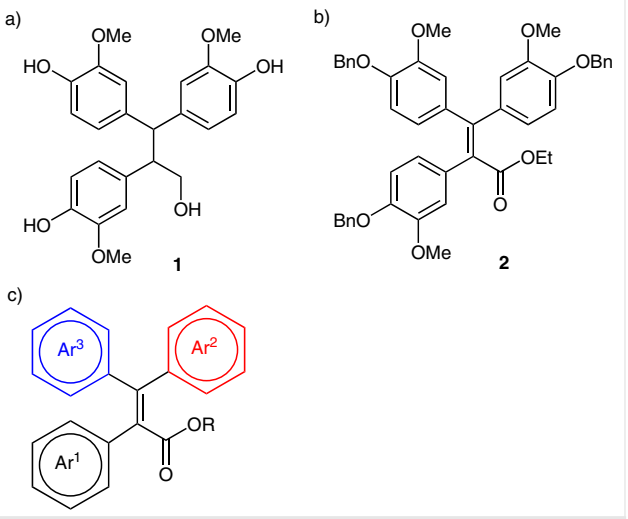



**Figure 1** Structure of (a) quebecol (**1**), (b) its key precursor **2**, and (c) the general structure of the 2,3,3-triarylacrylic acid ester scaffold

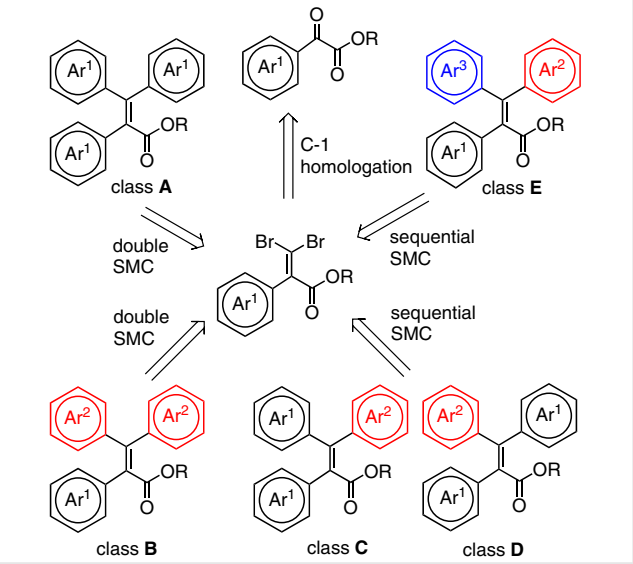
Herein, we report our most recent results aimed at the preparation of various 2,3,3-triarylacrylic acid esters [Figure 1 (c)] with one, two, or even three different aryl groups, in a way to access all possible arrangements of the aromatic rings.

Our retrosynthetic approach towards 2,3,3-triarylacrylic acid esters is presented in Scheme 1. It uses an α-keto ester as an easily accessible starting material. The key sequence involves the formation of a *gem*-dibromoalkene (Corey–Fuchs template)[9] by a Wittig-like C-1 homologation reaction, followed by Suzuki–Miyaura coupling (SMC) reactions. As previously mentioned, we recently used this approach to prepare the symmetrically substituted 2,3,3-triarylacrylic acid ethyl ester **2** (Figure 1).[4] However, we sought to prepare 2,3,3-triarylacrylic acid ester analogues with various arrangements of aryl rings on the 1,2,2-triarylethene scaffold exploiting a single α-keto ester compound, as shown in Scheme 1. For the sake of clarity, the five possible classes of compounds have been grouped in classes denoted **A** to **E** (Scheme 1).

The 2,3,3-triarylacrylic acid ester compounds with one type of aryl group (Class **A**) can be prepared by a double SMC reaction on the two C–Br bonds of the *gem*-dibromoalkene precursor, using an identically substituted arylboronic acid.[4] The use of two equivalents of a boronic acid with an aromatic substituent different from the substrate could lead to the preparation of triaryl compounds of Class **B**.

Three other classes of compounds could potentially be accessed by two consecutive SMC reactions with distinct boronic acids. These transformations require the development of efficient conditions for the preparation of 1,2-diaryl-2-bromoethene compounds with control over the stereochemical outcome of the first coupling. Such reaction, followed by another coupling, would open the way to the preparation of 2,3,3-triarylacrylic acid esters with two (Class **C** and **D**) or, most interestingly, three (Class **E**) types of aryl groups with complete regio- and diastereocontrol (Scheme 1).

The sequence involving for the formation of a *gem*-dibromoalkene followed by one or two SMC reactions has attracted some interest in the past years, particularly in medicinal chemistry and material science.[10,11] Some triarylalkenes, other than 2,3,3-triarylacrylic acid esters, have previously been prepared from *gem*-dibromoalkenes.[3b,10c,12] However, few applications of this strategy starting from an α-keto ester have been reported. Lu's group has prepared a series of ethyl esters of 3,3-diaryl-2-(trifluoromethyl)acrylic acid from ethyl trifluoropyruvate, which is so far the closest reported example of this reaction sequence to our synthetic plan.[13]

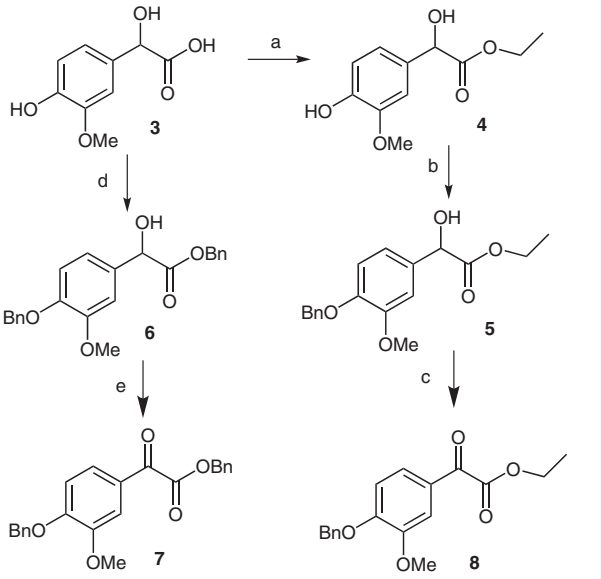



**Scheme 1** Retrosynthetic approach towards the five possible classes of 2,3,3-triarylacrylic acid esters involving Suzuki–Miyaura coupling (SMC) reactions

As mentioned, preparing compounds of classes **C**, **D**, and **E** (Scheme 1) requires a diastereoselective reaction for the installation of the first boronic acid on a *gem*-dibromoalkene. Such stereoselective reactions have been reported, which shows that it is possible to discriminate between the two C–Br bonds. Most of these have involved *gem*-dibromoalkenes derived from aldehydes and lead to (*Z*)-monobromoalkenes as products of the first SMC.[14] A second coupling results in trisubstituted alkenes.

Few examples of these sequences, which involve more substituted *gem*-dibromoalkenes and lead to the diastereoselective preparation of tetrasubstituted alkenes, have been reported.[1b,10a,12a,15] Shimizu and co-workers synthesized panomifene and other $CF_3$-substituted triarylethenes by a stereoselective threefold cross-coupling reaction, the first two couplings proceeding on 1,1-dibromo-3,3,3-trifluoro-2-(tosyloxy)propene.[1b] According to the authors, the trifluoromethyl group is essential for the stereoselectivity of the first coupling.[15] Chapleur's group prepared bioactive 1,1-diarylalkenes by two consecutive cross-couplings on a *gem*-dibromoalkene functionality installed on a carbohydrate scaffold.[10a] Recently, Tobrman reported stereoselective cross-coupling reactions on a enolphosphate dibromide template.[12a] Then, a coupling on the remaining C–Br bond and further activation and coupling on the C–O bond provided access to all-carbon tetrasubstituted alkenes. Some systems have also been developed using the opposite strategy, where aryl bromides were selectively coupled on an alkene with multiple metallic groups, leading to some tri- and tetraarylethenes.[7a,16]

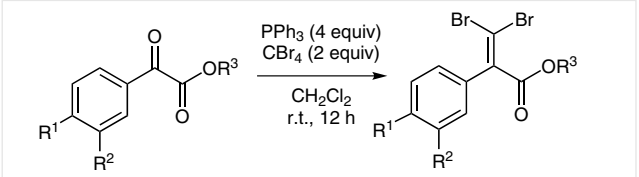
As a first step, our strategy towards the desired 1,2,2-triarylethene scaffold requires the preparation of *gem*-dibromoalkenes. These compounds can usually be obtained with a $PPh_3/CBr_4$ Wittig-like C-1 homologation reaction on the corresponding activated carbonyl precursor.[17] Two aryl-functionalized α-keto esters were prepared for this study and chosen for their relevance in our synthetic plan towards polyphenolic natural products.[4] Scheme 2 presents the synthesis of compounds **7** and **8**[4,18] from a commercially available mandelic acid analogue.




**Scheme 2** Preparation of carbonyl compounds **7**,**8**. *Reagents and conditions*: (a) MeOH/$H_2O$ (10:1), $Cs_2CO_3$, pH 7, then EtBr (1.2 equiv), DMF, r.t., 96 h, 77%; (b) BnBr (1.7 equiv), $K_2CO_3$ (1.7 equiv), acetone, reflux, 20 h, 84%; (c) Dess–Martin periodinane (2 equiv), $CH_2Cl_2$, 0 °C, 2 h, 99%; (d) BnBr (3.4 equiv), $K_2CO_3$ (3.4 equiv), acetone, reflux, 72 h, 54%; (e) Dess–Martin periodinane (2 equiv), $CH_2Cl_2$, 0 °C, 2 h, 94%.

Only a few examples of $PPh_3/CBr_4$ C-1 homologation have been previously reported for α-keto esters.[13,19] Knochel's work, in which ethyl 3,3-dibromo-2-phenylpropenoate (**10**) is prepared by this strategy, was of particular interest.[19b] The conditions they described were tested on model compound **9** and allowed us to obtain **10** efficiently. Applying the same conditions to **7** and **8** led to the preparation of our desired *gem*-dibromoalkenes **11** and **12**[4,18] in excellent yields (Scheme 3).

With *gem*-dibromoalkene compounds **10**–**12** in hand, we investigated the preparation of a first series of 2,3,3-triarylacrylic acid esters using a double coupling reaction to unite three identical aromatic rings. Reported examples of double SMC reactions on *gem*-dibromoalkenes used various catalytic systems and conditions.[1b,3b,10,11,12b,13,19] We chose to adapt conditions used successfully in a natural product synthesis related to our previous work on the synthesis of

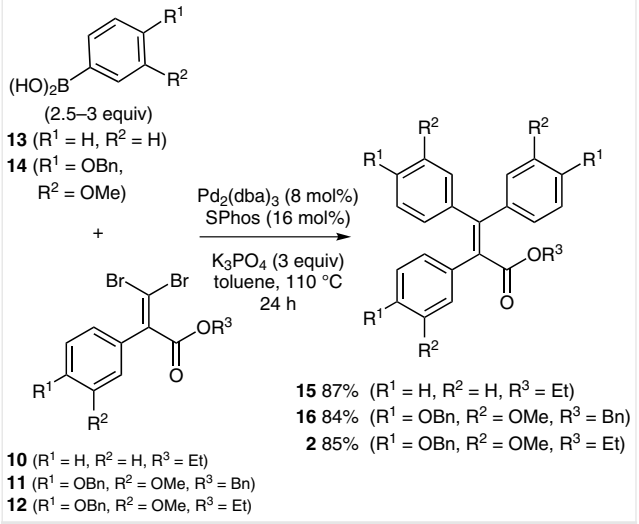



**9** ($R^1$ = H, $R^2$ = H, $R^3$ = Et)
**7** ($R^1$ = OBn, $R^2$ = OMe, $R^3$ = Bn)
**8** ($R^1$ = OBn, $R^2$ = OMe, $R^3$ = Et)

**10** 85% ($R^1$ = H, $R^2$ = H, $R^3$ = Et)
**11** 91% ($R^1$ = OBn, $R^2$ = OMe, $R^3$ = Bn)
**12** 91% ($R^1$ = OBn, $R^2$ = OMe, $R^3$ = Et)

**Scheme 3** Preparation of *gem*-dibromoalkene compounds **10**–**12**

hindered *o*-(aminomethyl)biaryl systems.[20] For this double coupling, $Pd_2(dba)_3$ serves as the catalyst and 2-(dicyclohexylphosphino)-2′,6′-dimethoxybiphenyl (Buchwald's SPhos ligand) promotes coupling efficiently for this hindered system.[21] Scheme 4 shows the results of the SMC reactions on *gem*-dibromoalkenes **10**–**12** with such conditions. As coupling partners, we used phenylboronic acid (**13**) and 4-(benzyloxy)-3-methoxyphenylboronic acid (**14**), which we have previously reported.[4] Satisfying yields of **2**, **15**, and **16** were obtained when using 2.5 to 3 equivalents of the boronic acids, proving the viability of the approach to access Class **A** compounds (Scheme 4).[18]

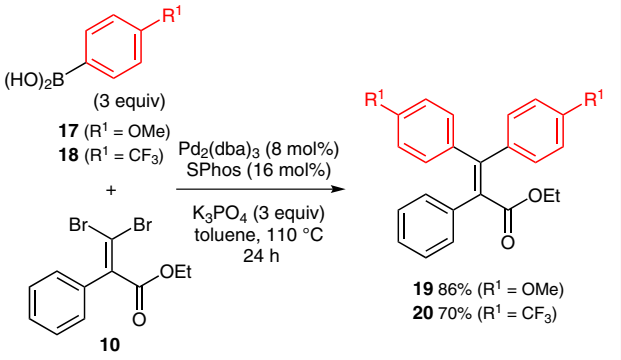



**10** ($R^1$ = H, $R^2$ = H, $R^3$ = Et)
**11** ($R^1$ = OBn, $R^2$ = OMe, $R^3$ = Bn)
**12** ($R^1$ = OBn, $R^2$ = OMe, $R^3$ = Et)

**15** 87% ($R^1$ = H, $R^2$ = H, $R^3$ = Et)
**16** 84% ($R^1$ = OBn, $R^2$ = OMe, $R^3$ = Bn)
**2** 85% ($R^1$ = OBn, $R^2$ = OMe, $R^3$ = Et)

**Scheme 4** Preparation of Class **A** compounds **2**, **15**, and **16**

The efficient double SMC reaction conditions were used for the preparation of Class **B** compounds with two types of aryl groups. We reacted the *gem*-dibromoalkene **10** with both an electron-rich, and an electron-poor, arylboronic acids **17** and **18**, respectively, to explore the versatility of our method. These two reactions, presented in Scheme 5, led to compounds **19** and **20** in good isolated yields. Hence, it can be concluded that these coupling conditions will allow the synthesis of a variety of triarylethenes.




**Scheme 5** Preparation of Class **B** compounds **19** and **20**

The extension of our synthetic strategy to the preparation of 2,3,3-triarylacrylic acid esters of Classes **C**, **D**, and **E** (Scheme 1) requires, as first step, the efficient preparation of 1,2-diaryl-2-bromoethenes by a single SMC reaction, ideally by a diastereoselective reaction.

Since the SPhos/$Pd_2(dba)_3$ catalytic system worked well in the preparation of the first 2,3,3-triarylacrylic acid esters, we tried the same conditions for the single coupling reactions. Table 1 presents the results of those coupling experiments, using 1.1 equivalents of boronic acid. First, boronic acid **14** was used at room temperature, leading exclusively to a low yield of double addition product **27** (Table 1, entry 1). The use of reflux heating with the same boronic acid only led to an increased yield in **27** (Table 1, entry 2). We also tried boronic acids **17** and **21**, but could not isolate the product of single addition (Table 1, entries 3 and 4). Products **19** and **28** were observed instead in good yield, considering that the boronic acid was the limiting reagent for their formation.

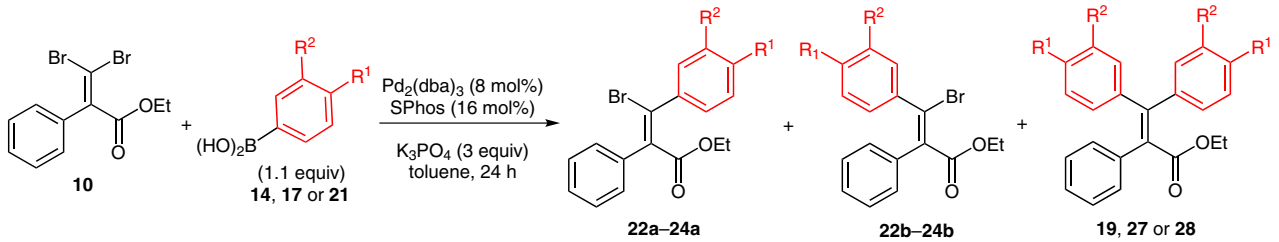
Due to the undesired preference of the SPhos/$Pd_2(dba)_3$ catalytic system for the double addition product, we investigated other reaction conditions inspired by the reported examples of diastereoselective coupling on a *gem*-dibromoalkene moiety.[1b,10a,14,15] The $PdCl_2(PPh_3)_2$/tri(2-furyl)phosphine (TFP) catalytic system reported by Chapleur[10a] lead us to prepare bromodiarylethene **26a** in a satisfying yield and with good diastereoselectivity (Table 2, entry 1).

These conditions were also applicable to other boronic acids [both a typical electron-rich one (Table 2, entry 3) and a model electron-poor one (Table 2, entry 4)]. In all cases, the (*E*)-single addition product was prepared as the major product, but the formation of the double addition product could not be avoided, suggesting that the monobromoalkenes undergo a second addition easily.

The best yield of single addition product was observed when using boronic acid **18**, followed by **21**, **13**, and **17**, illustrating a clear connection between the electron-withdrawing character of the *para* substituent on the boronic acid and the formation of the desired bromodiarylethenes ($CF_3$ > F > H > OMe).[22] This behavior might also be a consequence of the greater tendency of electron-rich boronic acids to form double coupling products, as illustrated in Table 2.

The X-ray structure of compound **24a** was obtained and clearly establishes the stereochemical outcome of the single coupling process for boronic acid **17** (Figure 2) Comparison of the $^1$H NMR spectra for **24a** and **24b** (which differ in the chemical shifts for *E* and *Z* ethyl groups) and the other pairs of isomers of **23**, **25**, and **26** confirmed that the same stereoselectivity was found for all four boronic acid single addition products. Preference for the coupling under an *anti* configuration regarding the phenyl groups present on the

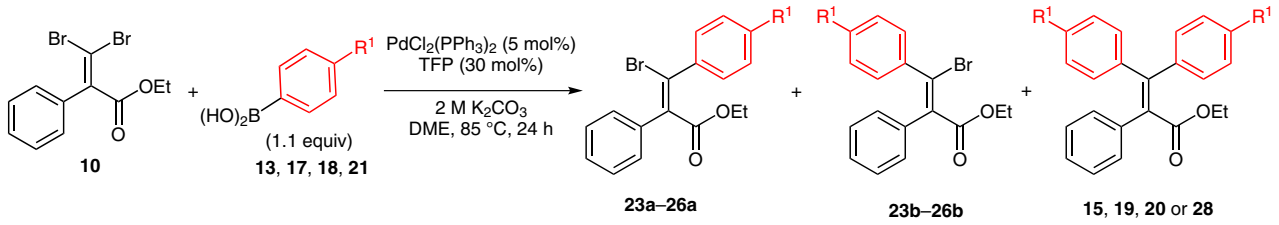
**Table 1** Single Coupling Attempts on **10** Using a SPhos/$Pd_2(dba)_3$ Catalytic System




| Entry | Boronic acid | $R^1$ | $R^2$ | Temp (°C) | (*E*)-Single addition product/ yield (%) | (*Z*)-Single addition product/ yield (%) | Double addition product/ yield (%) |
|---|---|---|---|---|---|---|---|
| 1 | **14** | OBn | OMe | 25 | **22a**/–[a] | **22b**/–[a] | **27**/18 |
| 2 | **14** | OBn | OMe | 110 | **22a**/–[a] | **22b**/–[a] | **27**/27 |
| 3 | **21** | F | H | 110 | **23a**/–[a] | **23b**/–[a] | **28**/41 |
| 4 | **17** | OMe | H | 110 | **24a**/–[a] | **24b**/–[a] | **19**/38 |

[a] Product could not be isolated.

**Table 2** Single Coupling Attempts on **10** Using a $PdCl_2(PPh_3)_2$/TFP Catalytic System




| Entry | Boronic acid | $R^1$ | Single addition products | | | Double addition product |
|---|---|---|---|---|---|---|
| | | | Isolated yield[a] (%) | (*E*)-Product/yield[b] (%) | (*Z*)-Product/yield[b] (%) | isolated yield (%) |
| 1 | **13** | H | 60 | **26a**/52 | **26b**/8 | **15**/20 |
| 2 | **21** | F | 64 | **23a**/54 | **23b**/10 | **28**/26 |
| 3 | **17** | OMe | 45 | **24a**/39 | **24b**/6 | **19**/32 |
| 4 | **18** | $CF_3$ | 80 | **25a**/70 | **25b**/10 | **20**/14 |

[a] Pure isolated yield of (*E*) + (*Z*) isomers.
[b] Determined by NMR analysis.

*gem*-dibromoalkene follows the same tendency as previously reported for stereoselective single couplings on such moieties.[14]

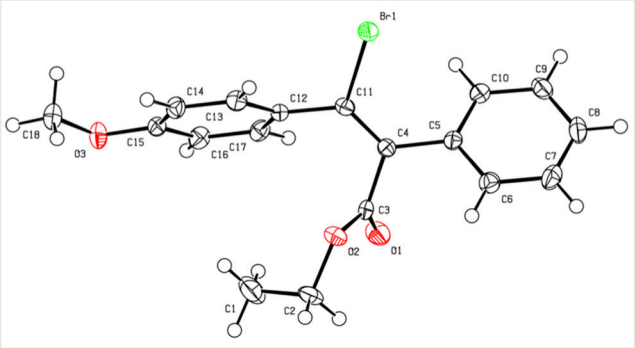
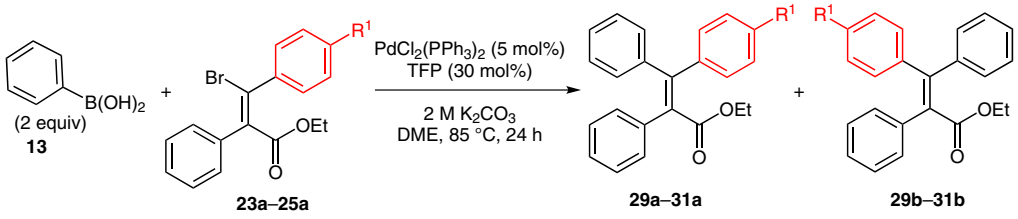



**Figure 2** X-ray diffraction structures of compound **24a**

With compounds **23a**–**26a** in hand, we performed second SMC reactions to investigate the preparation of other classes of 1,2,2-triarylethene compounds. Class **C** compounds, with two identically substituted aryl groups in a *syn* relationship, can be synthesized by using, as partner for the second coupling reaction, a boronic acid with the same substituents as the *gem*-dibromoalkene precursor. Likewise, 2,3,3-triarylacrylic acid esters of Class **C** can be obtained from **23a**–**25a** by a SMC reaction with phenylboronic acid, considering **23a**–**25a** were all synthesized from α-keto ester **9**. The results of the preparation of compounds **29a**–**31a** are presented in Table 3.

Good conversions were obtained using the $PdCl_2(PPh_3)_2$/TFP catalytic system with an excess of boronic acid, showing that this system was also efficient for the second coupling. This matches what we expected due to our previous obtention of undesirable double coupling products (Table 2).

**Table 3** Second SMC on Compound **23a**–**25a** To Prepare 2,3,3-Triarylacrylic Acid Esters of Class **C** **29a**–**31a**




| Entry | Bromine compound | $R^1$ | (*Z*)-Product/yield (%) | (*E*)-Product/yield (%) |
|---|---|---|---|---|
| 1 | **23a**/**b** (*E*/*Z* 96:4) | F | **29a**/85 | **29b**/4 |
| 2 | **24a** | OMe | **30a**/36 | **30b**/53 |
| 3 | **25a** | $CF_3$ | **31a**/84 | **31b**/0 |

Due to its ease of use and efficiency, this system was chosen for the second SMC on 1,2-diaryl-2-bromoethene compounds. Using the same catalytic system for the first and the second coupling is also advantageous, because it opens the way to the one-pot preparation of 2,3,3-triarylacrylic acid esters directly from a *gem*-dibromoalkene precursor.

The preparation of compounds **29**–**31** established the isomerization behavior of the functionalized 1,2-diaryl-2-bromoethene compounds in the context of a second palladium-catalyzed cross-coupling. As shown in Table 3, no isomerization occurs in the case of **23a**/**b** (Table 3, entry 1) and **25a** (Table 3, entry 3). Compound **31b** was not formed from **25a**. The low yield of product **29b** is due to the conversion of **23b** and parallels the amount of (*Z*) isomer present in the starting material. A very different reactivity was observed with 1,2-diaryl-2-bromoethene compound **24a**, for which the presence of **30b** as the major second coupling product indicates an undeniable case of isomerization. For the structure of **24a**, the conjugation of the electron-donating methoxy group with the ester functionality might significantly reduce the double bond character of the olefin,[23] thus permitting rotation at some point in the coupling mechanism and facilitating the migration of the electron-rich aryl group to a thermodynamically favored antiperiplanar position from the electron-withdrawing ester.

To investigate the source of this isomerization event, we performed two sets of control experiments with substrate **24a** and product **30a**. We solubilized **24a** and **30a** in DME and heated the solutions at 85 °C for 16 hours. We also exposed them to the single SMC conditions, but without the presence of a boronic acid coupling partner. No isomerization was observed for either experiment. This suggests that isomerization occurs at a later stage of the catalytic cycle, following the transmetalation step.

Other groups have also reported undesired erosion of the double bond geometry of allyl halide compounds in the context of cross-coupling reactions.[12a,24] An extensive screening of catalysts was necessary to reduce or avoid this problem in these cases. Negishi even used these isomerization phenomena to perform coupling reactions with complete inversion of stereochemistry on dienylpalladium intermediates generated via oxidative addition.[25] To the best of our knowledge, there has been no extensive studies of the isomerization of alkenyl halides in cross-coupling reactions.

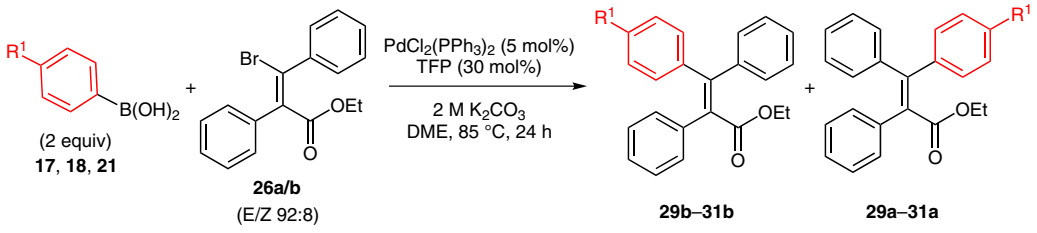
All the pairs of isomers of 2,3,3-triarylacrylic acid esters are separable by chromatography. Consequently, our method provides access to **30a** and to the other triarylethene compounds with the 4-methoxyphenyl group in the *syn* configuration with the ester, though the yield is compromised by the isomerization of compound **24a** in the context of a second SMC.

Compounds of Class **D** can be synthesized from the 1,2-diaryl-2-bromoethane compound **26a**, a precursor that already has phenyl groups as two of the future three aryl groups.[26] Table 4 presents the preparation of 2,3,3-triarylacrylic acid esters **29b**–**31b**. We obtained excellent yields and no isomerization of the double bond for all three products. In all three cases, the amount of (*Z*)-products **29a**–**31a** obtained was due to the presence of a minor amount of (*Z*)-isomer **26b** in the starting material. These results establish the stability of compound **26a** towards isomerization under these SMC conditions, and illustrate that the nature of the boronic acid chosen does not influence the geometry of the second coupling product.

The preparation of 1,2,2-triarylethene moieties with three differently substituted aryl groups provide a synthetic challenge. We were particularly interested in preparing such compounds to demonstrate the potential of our method, in terms of molecular diversity. Table 5 present the synthesis of six different 2,3,3-triarylacrylic acid esters of Class **E** from 1,2-diaryl-2-bromoethenes **23**–**25**.

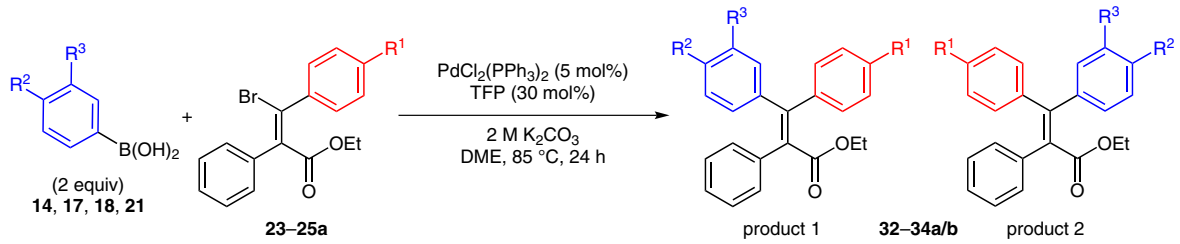
As previously observed, excellent conversions were obtained when using 2 equivalents of any of the arylboronic acid (Table 5, entries 1–4). Compounds **23a** and **25a** reacted

**Table 4** Second SMC on Compound **26a** To Prepare 2,3,3-Triarylacrylic Acid Esters of Class **D** **29b**–**31b**




| Entry | Boronic acid | $R^1$ | (*E*)-Product/yield (%) | (*Z*)-Product/yield (%) |
|---|---|---|---|---|
| 1 | **21** | F | **29b**/91 | **29a**/8 |
| 2 | **17** | OMe | **30b**/86 | **30a**/7 |
| 3 | **18** | $CF_3$ | **31b**/92 | **31a**/8 |

**Table 5** Preparation of 2,3,3-Triarylacrylic Acid Esters **32**–**34** of Class **E**




| Entry | Boronic Acid | $R^2$ | $R^3$ | Bromine compound | $R^1$ | Product 1/yield (%) | Product 2/yield (%) |
|---|---|---|---|---|---|---|---|
| 1 | **17** | OMe | H | **23a**/**b** (*E*/*Z* 96:4) | F | **32a**/96 | **32b**/4 |
| 2 | **21** | F | H | **24a** | OMe | **32b**/39 | **32a**/56 |
| 3 | **18** | $CF_3$ | H | **24a** | OMe | **33a**/38 | **33b**/57 |
| 4 | **17** | OMe | H | **25a** | $CF_3$ | **33b**/99 | **33a**/0 |
| 5[a] | **14** | OBn | OMe | **23a**/**b** (*E*/*Z* 96:4) | F | **34a**/74 | **34b**/4 |

[a] Coupling reaction proceeded with 1.5 equiv of boronic acid.

once again in a second SMC with complete retention of geometry (Table 5, entries 1, 4, and 5). Compound **24a** showed consistent isomerization behavior with all the arylboronic acids investigated, confirming that the erosion of the double bond geometry in the coupling procedure originates from a geometric instability in the substrate (Table 5, entries 2 and 3).

X-ray diffraction structures of **32a**, **32b** (Figure 3), and **33a** (see Supporting Information) were obtained to ensure the double bond configuration and to confirm our stereochemical assignments for the first coupling reactions on *gem*-dibromoalkene precursor **10** with arylboronic acids **17**, **18**, and **21** (Table 2). Indeed, the comparison of these X-ray crystal structures with the $^1H$ and $^{19}F$ NMR spectra of the corresponding compounds have allowed us to unequivocally establish the spectral signatures of the 4-substituted groups of compounds prepared in this study for the *syn* and *anti* positions with relation to the ester functionality.

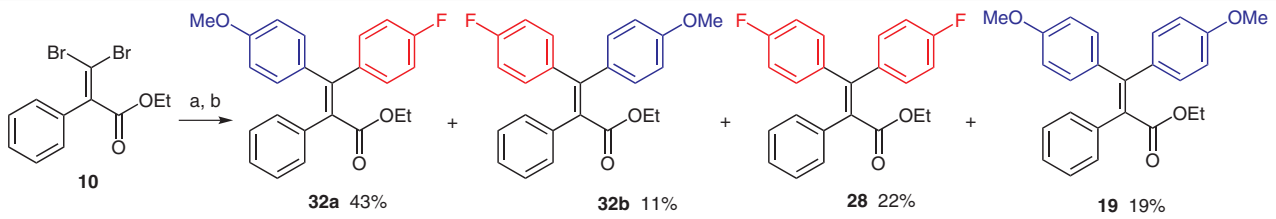
Separate syntheses of both diastereomers of **32a**/**32b** and **33a**/**33b** (Table 5, entries 2, 3 and 3, 4) illustrated the usefulness of our method to selectively prepare two diastereomeric compounds by varying the order of the boronic acids involved in the two consecutive SMC reactions.

We were able to prepare 2.3.3-triarylacrylic acid esters with all the possible substitution patterns (Class **A** to **E**) with control over the stereochemistry of the desired product. Even if the yields of the analogues with the 4-methoxyphenyl group in a *syn* relationship with the ester are lowered by isomerization during the second SMC, these compounds can be easily accessed because all pairs of diastereomers are separable by conventional flash chromatography.

As previously mentioned, the use of the $PdCl_2(PPh_3)_2$/TFP catalytic system for the first and second single SMC reactions may work with a sequential one-pot procedure to prepare 2,3,3-triarylacrylic acid esters. We attempted to prepare compound **32a** by this procedure, starting from *gem*-dibromoalkene precursor **10**.

This one-pot experiment (Scheme 6) gave the desired compound **32a** as the main product (43%). Minor isomer **32b** (11%) was also isolated from the crude reaction mixture, as were double SMC products **19** and **28** (19% and 22% respectively).

Even if this procedure leads to a more complex purification step for the desired product, it surely represents a more straightforward route to 2,3,3-triarylacrylic acid ester




**Scheme 6** Synthesis of **32a** from **10** by a one-pot procedure. *Reagents and conditions*: (a) **21** (1.1 equiv), $PdCl_2(PPh_3)_2$ (5 mol%), TFP (30 mol%), 2 M $K_2CO_3$, DME, 85 °C, 24 h; (b) addition of **17** (1.5 equiv), 85 °C, 24 h.

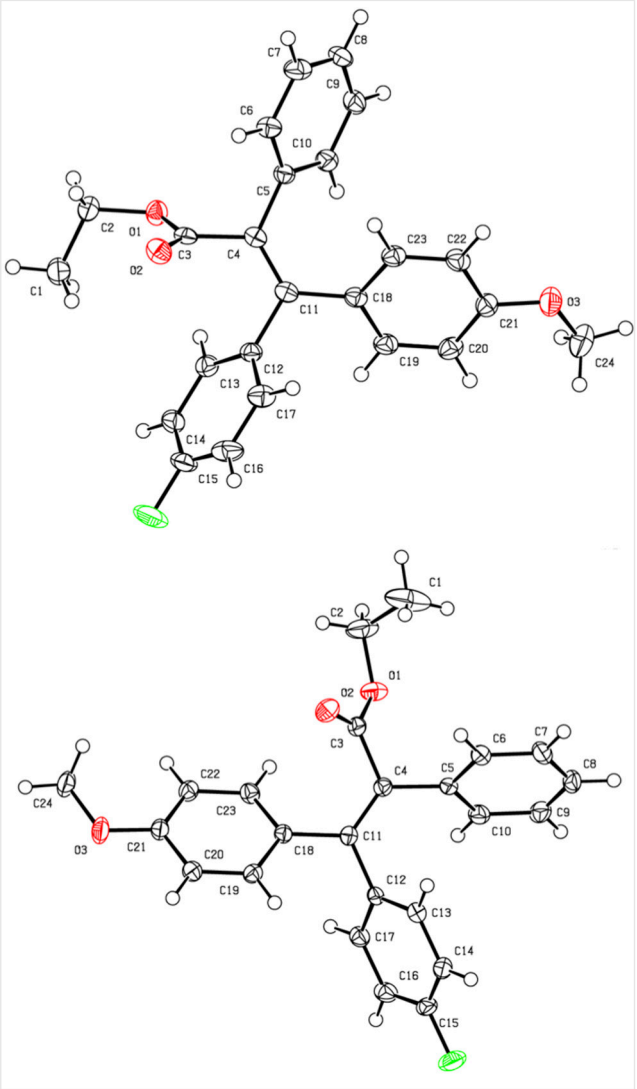



**Figure 3** X-ray diffraction structures of compounds **32a** (up) and **32b** (down)

**32a**. For this preliminary experiment, the yield obtained for product **32a** is slightly lower (43% vs. 52%) compared with the overall yield of the stepwise synthesis (Table 2, entry 2 and Table 5, entry 1). Though optimization work is needed to fully adapt this synthetic approach to one-pot conditions, this procedure represents a promising extension of our method for the rapid and selective preparation of complex highly substituted 1,2,2-triarylethene compounds.

In summary, we have developed an efficient approach for the selective preparation of 2,3,3-triarylacrylic acid esters, by the installation of aryl groups on a *gem*-dibromoalkene compound using SMC reactions. Various analogues can be obtained from a single precursor. We have demonstrated the versatility of the synthetic strategy by preparing 2,3,3-triarylacrylic acid esters covering the entire range of substitution patterns on the alkene, according to the nature of the aryl groups. We determined efficient conditions to prepare 2,3,3-triarylacrylic acid esters with one or two different aryl groups (Classes **A** and **B**) by double SMC reactions. We varied the conditions to favor the single coupling reaction and good diastereoselectivity in the formation of (*E*)-1,2-diaryl-2-bromoethene products, then used these in a subsequent single SMC reaction to provide 2,3,3-triarylacrylic acid esters with two (Classes **C** and **D**) or three (Class **E**) different aryl groups.

Preliminary results showed that the two SMC reactions can be performed sequentially in one pot. In most cases, the 1,2,2-triarylethene compounds in this study were efficiently prepared with complete regio- and stereocontrol, except for the candidates with a 4-methoxyphenyl group in a *syn* relationship with the ester, for which the stereochemistry was compromised by isomerization. More detailed mechanistic studies and optimization of the catalytic system are underway, especially concerning these isomerizable cases.

The ester functionality present on the 2,3,3-triarylacrylic acid esters prepared by our method is an interesting functional group as its transformation could lead to a variety of other 1,2,2-triarylethene moieties. We are currently also exploring the use of other *gem*-dibromoalkene precursors to extend the methodology developed to other types of complex 1,2,2-triarylethene compounds.

Unless otherwise indicated, all starting materials were purchased from commercial sources (Sigma-Aldrich and VWR) and used without further purification. The reagents and the solvents were dried and purified before use by the usual procedures and kept under argon. All reagents were assembled under an inert atmosphere. $^{1}H$ and $^{13}C$ NMR spectra were recorded on an Agilent DD2 500 MHz, a Varian 400 MHz, or a Bruker 300 MHz spectrometer. Melting points were taken using a Standford Research Systems OptiMelt MPA 100 instrument. Mass spectra were obtained on an Agilent 6210 LC Time of Flight Mass Spectrometer in direct injection mode. IR spectra were taken on a Bomem MB-Series Arid-Zone spectrophotometer (NaCl windows) or a Thermo Nicolet 380 (ATR, ZnSe).

### Preparation of Functionalized α-Keto Ester Compounds

#### Ethyl 4-Hydroxy-3-methoxymandelate (4)[4]

4-Hydroxy-3-methoxymandelic acid (**3**, 0.500 g, 2.52 mmol) was dissolved in MeOH/$H_2O$ (10:1, 5 mL) and then treated with 20% aq $Cs_2CO_3$ to adjust the pH to 7. After removal of the solvent, DMF (6 mL) was added to the dry residue. After 5 min, EtBr (226 µL, 3.02 mmol) was added and the mixture was stirred for 96 h or until completion was shown by TLC (EtOAc/hexanes 50:50). 1 M HCl was then added and the ester was extracted with $CH_2Cl_2$ (3 ×) The combined organic layers were washed with brine, dried ($Na_2SO_4$), and concentrated in vacuo to give an oil that was purified by flash chromatography (EtOAc/hexanes 50:50, $R_f$ 0.27) to yield **4** (0.438 g, 77%) as a white solid; mp 76–79 °C.

IR (NaCl): 3436, 1731, 1516, 1274, 1206, 1152, 1031 $cm^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 6.94–6.88 (m, 3 H), 5.75 (br, 1 H), 5.08 (s, 1 H), 4.30–4.23 (m, 1 H), 4.22–4.15 (m, 1 H), 3.88 (s, 3 H), 1.24 (t, *J* = 7.4 Hz, 3 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 145.8, 130.4, 119.9, 114.4, 108.8, 72.7, 62.2, 55.9, 14.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{14}NaO_5$: 249.0733; found: 249.0739.

### Ethyl 4-(Benzyloxy)-3-methoxymandelate (5)[4]

Ethyl 4-hydroxy-3-methoxymandelate (**4**, 1.00 g, 4.42 mmol) was dissolved in anhyd acetone (15 mL) in an oven-dried three-neck flask under argon. $K_2CO_3$ (1.038 g, 7.51 mmol) was added. After 5 min, BnBr (0.90 mL, 7.51 mmol) was added and the mixture was refluxed for 20 h or until completion was shown by TLC (EtOAc/hexanes 50:50). The mixture was allowed to warm up to r.t., poured into sat. $K_2CO_3$ and extracted with EtOAc (3 ×). The combined organic layers were washed with brine, dried ($MgSO_4$), concentrated in vacuo, and purified by flash chromatography (EtOAc/hexanes 50:50, $R_f$ 0.45) to yield **5** (1.168 g, 84%) as a white solid; mp 118–121 °C.

IR (NaCl): 3467, 1735, 1513, 1263, 1225, 1206, 1156, 1139, 1031 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.28 (m, 5 H), 6.97 (s, 1 H), 6.98–6.85 (m, 2 H), 5.16 (s, 2 H), 5.10 (s, 1 H), 4.30–4.23 (m, 1 H), 4.22–4.15 (m, 1 H), 3.90 (s, 3 H), 1.24 (t, *J* = 7.2 Hz, 3 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 173.8, 149.7, 148.3, 137.0, 131.5, 128.6, 127.9, 127.3, 119.1, 113.7, 110.0, 72.7, 71.0, 62.2, 56.0, 14.1.

HRMS (ESI): *m*/*z* [2 M + Na]$^+$ calcd for $C_{36}H_{40}O_{10}Na$: 655.2514; found: 655.2531.

### Benzyl 4-(Benzyloxy)-3-methoxymandelate (6)

At r.t., 4-hydroxy-3-methoxymandelic acid (**3**, 1.00 g, 5.05 mmol) was dissolved in anhyd acetone (15 mL) in an oven-dried three-neck flask under argon. $K_2CO_3$ (2.09 g, 15.1 mmol) was added. After 5 min, BnBr (1.80 mL, 15.14 mmol) was added and the mixture was refluxed for 72 h. The mixture was allowed to cooled to r.t., poured into sat. $K_2CO_3$ and extracted with EtOAc (3 ×). The combined organic layers were washed with brine, dried ($MgSO_4$), concentrated in vacuo, and purified by flash chromatography (EtOAc/hexanes 50:50, $R_f$ 0.40) to yield **6** (1.03 g, 54%) as a white solid; mp 76–78 °C.

IR (NaCl): 3465, 1737, 1513, 1454, 1263, 1226, 1139, 742, 697 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.30 (m, 8 H), 7.24–7.20 (m, 2 H), 6.93–6.85 (m, 3 H), 5.20 (d, *J* = 6.1 Hz, 2 H), 5.17 (d, *J* = 2.1 Hz, 3 H), 3.90 (s, 3 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 173.6, 149.8, 148.3, 137.0, 135.1, 131.2, 128.6, 128.5, 128.0, 127.9, 127.3, 119.2, 113.8, 109.9, 72.7, 71.0, 67.6, 55.9.

HRMS (ESI): *m*/*z* [M – $H_2O$ + H]$^+$ calcd for $C_{23}H_{21}O_4$: 361.1434; found: 361.1465.

### Benzyl [4-(Benzyloxy)-3-methoxyphenyl](oxo)acetate (7)

At r.t., **6** (0.854 g, 2.26 mmol) was dissolved in anhyd $CH_2Cl_2$ (100 mL) in an oven-dried three-neck flask under argon. The flask was cooled to 0 °C and Dess–Martin periodinane (1.92 g, 4.51 mmol) was added. The mixture was stirred at 0 °C until completion was observed by TLC (EtOAc/hexanes 50:50). The solution was then diluted with $CH_2Cl_2$ and a solution 10% $Na_2S_2O_3$ in sat. $NaHCO_3$ (100 mL) was added. The mixture was stirred for 15 min and the organic layer was separated, dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by column chromatography (silica gel, EtOAc/hexanes 20:80, $R_f$ 0.45) to yield **7** (0.802 g, 94%) as yellow needles; mp 57–62 °C.

IR (NaCl): 1735, 1673, 1593, 1512, 1283, 1259, 1167, 1141, 1018, 744, 697 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 7.54–7.50 (m, 2 H), 7.47–7.31 (m, 10 H), 6.91 (d, *J* = 6.9 Hz, 1 H), 5.41 (s, 2 H), 5.25 (s, 2 H), 3.88 (s, 3 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 184.7, 164.0, 154.1, 149.8, 135.8, 134.7, 128.7, 128.3, 127.2, 125.8, 125.7, 112.2, 111.2, 70.9, 67.6, 56.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{21}O_5$: 377.1384; found: 317.1378.

### Ethyl [4-(Benzyloxy)-3-methoxyphenyl](oxo)acetate (8)[4]

At r.t., **5** (1.15 g, 3.64 mmol) was dissolved in anhyd $CH_2Cl_2$ (160 mL) in an oven-dried three-neck flask under argon. The flask was cooled to 0 °C and Dess–Martin periodinane (3.08 g, 7.27 mmol) was added. The mixture was stirred at 0 °C until completion was observed by TLC (EtOAc/hexanes 20:80). The solution was then diluted with $CH_2Cl_2$ and a solution of 10% $Na_2S_2O_3$ in sat. $NaHCO_3$ (100 mL) was added. The mixture was stirred for 15 min and the organic layer was separated, dried ($MgSO_4$), and concentrated in vacuo. The crude product (yellowish solid) was purified by column chromatography (silica gel, EtOAc/hexanes 20:80, $R_f$ 0.37) to yield **8** (1.142 g, quantitative yield) as a white solid; mp 71–73 °C.

IR (NaCl): 1733, 1673, 1593, 1513, 1284, 1259, 1193, 1170, 1143, 1021 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 7.59–7.55 (m, 2 H), 7.45–7.31 (m, 5 H), 6.93 (d, *J* = 8.5 Hz, 1 H), 5.25 (s, 2 H), 4.43 (q, *J* = 7.3 Hz, 2 H), 3.95 (s, 3 H), 1.41 (t, *J* = 7.1 Hz, 3 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 164.2, 154.1, 149.8, 135.9, 128.8, 128.3, 127.2, 126.0, 125.8, 112.2, 111.1, 70.9, 62.2, 56.1, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{19}O_5$: 315.1227; found: 315.1234.

### Ethyl 3,3-Dibromo-2-phenylpropenoate (10); General Procedure for the Preparation of *gem*-Dibromoalkenes

$PPh_3$ (3.28 g, 12.5 mmol) was dissolved in anhyd $CH_2Cl_2$ (3 mL) in an oven-dried three-neck flask under argon. The mixture was cooled to 0 °C and $CBr_4$ (2.07 g, 6.25 mmol) in solution in anhyd $CH_2Cl_2$ (2 mL) was added dropwise. The mixture was stirred at 0 °C for 30 min and a solution of ethyl mandelate (**9**, 0.559 g, 3.12 mmol) in anhyd $CH_2Cl_2$ (1.5 mL) was added dropwise. The mixture was allowed to warm to r.t. and stirred for 12 h or until completion was observed by TLC ($Et_2O$/hexanes 10:90). Pentane (50 mL) was added to the mixture, which was stirred for 30 min. After filtration, the solvent was evaporated in vacuo and the crude product was purified by column chromatography (silica gel, $Et_2O$/hexanes 10:90, $R_f$ 0.43) yielding **10**[19b] (0.880 g, 85%) as a colorless oil.

IR (ATR, ZnSe): 1722, 1284, 1199, 1037, 1021, 794, 693 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.38 (m, 5 H), 4.27 (q, *J* = 7.2 Hz, 2 H), 1.31 (t, *J* = 7.2 Hz, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 165.9, 141.6, 135.7, 129.0, 128.6, 128.2, 95.4, 62.3, 14.0.

HRMS (ESI): *m*/*z* [M]$^+$ calcd for $C_{11}H_{10}O_2Br$: 334.9056; found: 334.9091.

**Benzyl 2-[4-(Benzyloxy)-3-methoxyphenyl]-3,3-dibromopropenoate (11)**

White solid (0.978 g, 91%) obtained upon purification by column chromatography (silica gel, $Et_2O$/hexanes 20:80, $R_f$ 0.28); mp 73–76 °C.

IR (NaCl): 3033, 1729, 1511, 1455, 1246, 1190, 1167, 1141, 1023, 736, 697 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.46–7.33 (m, 10 H), 6.93–6.89 (m, 3 H), 5.25 (s, 2 H), 5.18 (s, 2 H), 3.84 (s, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 166.0, 149.3, 148.8, 140.9, 136.7, 134.9, 128.6, 128.2, 128.0, 127.3, 121.0, 113.3, 111.6, 95.1, 67.9, 56.0.

HRMS (ESI): *m*/*z* $[M + NH_4]^+$ calcd for $C_{24}H_{24}Br_2NO_4$: 548.0048; found: 548.0040.

**Ethyl 2-[4-(Benzyloxy)-3-methoxyphenyl]-3,3-dibromopropenoate (12)**[4]

White solid (1.47 g, 91%) obtained upon purification by column chromatography (silica gel, $Et_2O$/hexanes 20:80, $R_f$ 0.25); mp 71–74 °C.

IR (NaCl): 1726, 1510, 1247, 1193, 1170, 1141, 1026, 734 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.47–7.30 (m, 5 H), 6.90–6.88 (m, 3 H), 5.17 (s, 2 H), 4.29 (q, *J* = 7.2 Hz, 2 H), 3.90 (s, 3 H), 1.33 (t, *J* = 6.5 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 166.2, 149.3, 148.8, 141.3, 136.7, 128.6, 128.3, 128.0, 127.3, 120.9, 113.3, 111.7, 94.3, 70.9, 62.3, 56.1, 14.0.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{19}Br_2O_4$: 470.9625; found: 470.9617.

**Ethyl 2,3,3-Triphenylacrylate (15); General Procedure for Double Suzuki–Miyaura Coupling with the $Pd_2(dba)_3$/SPhos Catalytic System**

Ethyl 3,3-dibromo-2-phenylpropenoate (**10**, 0.150 g, 0.45 mmol), phenylboronic acid (**13**, 0.165 g, 1.35 mmol), $Pd_2(dba)_3$ (0.034 g, 0.036 mmol), SPhos (0.030 g, 0.072 mmol), and $K_3PO_4$ (0.477 g, 2.25 mmol) were poured into an oven-dried three-neck flask under argon. Three vacuum/argon purges were performed and freshly distilled toluene (10 mL) was added. The mixture was refluxed for 24 h and then allowed to cool to r.t. and filtered on a Celite pad. The filtrate was concentrated in vacuo and the crude product was purified by column chromatography (silica gel, $Et_2O$/hexanes 20:80, $R_f$ 0.40) to yield **15** (0.128 g, 87%) as a white solid; mp 117–121 °C.

IR (NaCl): 1709, 1494, 1444, 1326, 1302, 1266, 1220, 1152, 1044, 1027 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.36–7.28 (m, 5 H), 7.21–7.12 (m, 8 H), 7.05–7.02 (m, 2 H), 4.05 (q, *J* = 7.2 Hz, 2 H), 0.99 (t, *J* = 7.3 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 170.5, 146.0, 142.5, 140.6, 137.0, 133.8, 130.9, 129.9, 129.2, 128.2, 128.1, 127.9, 127.7, 127.4, 61.0, 13.7.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{21}O_2$: 329.15361; found: 329.15517.

**Benzyl 2,3,3-Tris[4-(benzyloxy)-3-methoxyphenyl]propenoate (16)**

Orange solid (1.18 g, 84%) obtained upon purification by column chromatography (silica gel, $Et_2O$/hexanes 70:30, $R_f$ 0.13); mp 46–55 °C.

IR (NaCl): 1714, 1599, 1511, 1237, 1168, 1140, 1025, 735, 697 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.45–7.24 (m, 20 H), 6.78–6.45 (m, 9 H), 5.14 (s, 2 H), 5.12 (s, 2 H), 5.10 (s, 2 H), 4.98 (s, 2 H), 3.73 (s, 3 H), 3.51 (s, 3 H), 3.48 (s, 3 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 171.0, 149.2, 149.1, 148.6, 148.4, 147.8, 145.3, 137.0, 136.9, 135.6, 133.7, 131.5, 131.2, 124.0, 123.2, 122.2, 122.1, 115.0, 113.8, 113.0, 112.9, 70.9, 70.8, 67.0, 55.7.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{52}H_{47}O_8$: 799.3265; found: 799.3416.

**Ethyl 2,3,3-Tris(4-benzyloxy-3-methoxyphenyl)propenoate (2)**[4]

Orange solid (1.18 g, 85%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 40:60, $R_f$ 0.29); mp (decomp).

IR (NaCl): 1711, 1511, 1463, 1454, 1262, 1236, 1139, 1129, 1027, 735 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.48–7.30 (m, 15 H), 6.86–6.52 (m, 9 H), 5.19 (s, 2 H), 5.13 (s, 2 H), 5.11 (s, 2 H), 4.04 (q, *J* = 7.1 Hz, 2 H), 3.82 (s, 3 H), 3.56 (s, 3 H), 3.50 (s, 3 H), 0.99 (t, *J* = 7.2 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 171.2, 149.1, 148.2, 147.8, 147.4, 144.8, 137.0, 136.9, 135.7, 133.7, 131.9, 131.1, 128.6, 127.9, 127.3, 124.0, 122.1, 115.0, 113.9, 113.5, 113.2, 113.0, 70.8, 61.0, 56.0, 55.7, 13.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{47}H_{45}O_8$: 731.3109; found: 731.3126.

**Ethyl 3,3-Bis(4-methoxyphenyl)-2-phenylpropenoate (19)**

Yellowish solid (0.354 g, 86%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 5:95, $R_f$ 0.12); mp 117–121 °C.

IR (NaCl): 1713, 1606, 1510, 1249, 1217, 1174, 834 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.24–7.12 (m, 7 H), 6.96–6.92 (m, 2 H), 6.89–6.85 (m, 2 H), 6.69–6.64 (m, 2 H), 4.07 (q, *J* = 7.1 Hz, 2 H), 3.83 (s, 3 H), 3.74 (s, 3 H), 1.04 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR ($CDCl_3$, 100 MHz,): δ = 171.0, 159.6, 159.1, 145.7, 138.3, 135.3, 133.1, 132.5, 131.9, 130.7, 130.0, 130.6, 128.3, 127.1, 113.5, 113.1, 60.9, 55.3, 55.1, 13.9.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{25}O_4$: 389.1747; found: 389.1742.

**Ethyl 2-Phenyl 3,3-bis[4-(trifluoromethyl)phenyl]propenoate (20)**

White solid (0.392 g, 70%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 5:95, $R_f$ 0.35); mp 126–128 °C.

IR (NaCl): 1721, 1324, 1219, 1167, 1127, 1112, 1068 $cm^{-1}$.

$^1H$ NMR ($CDCl_3$, 400 MHz,): δ = 7.63–7.59 (m, 2 H), 7.42–7.37 (m, 4 H), 7.24–7.21 (m, 3 H), 7.13–7.08 (m, 4 H), 4.05 (q, *J* = 7.1 Hz, 2 H), 0.99 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 169.4, 145.2, 143.5, 142.49, 136.5, 136.2, 131.0, 129.6, 129.5, 128.5, 128.2, 125.3, 125.0, 122.6, 61.4, 13.6.

$^{19}F$ NMR (376 MHz, $CDCl_3$): δ = –62.68 (s, 3 F), –62.75 (s, 3 F).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{19}F_6O_2$: 465.1284; found: 465.1298.

**Ethyl 3,3-Bis(4-benzyloxy-3-methoxyphenyl)-2-phenylpropenoate (27)**

Obtained while attempting to perform single coupling with the $Pd_2(dba)_3$/SPhos catalytic system (Table 1, entry 2); only 1.1 equiv of arylboronic acid used for the coupling procedure. Orange solid (0.098 g, 27%) obtained upon purification by column chromatography (silica gel, $Et_2O$/hexanes 20:80 to >30:70); $R_f$ 0.14 ($Et_2O$/hexanes 30:70); mp 136–140 °C.

IR (ATR, ZnSe): 1712, 1508, 1230, 1203, 1181, 1126, 1036, 1001, 748, 698 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.50–7.45 (m, 2 H), 7.43–7.29 (m, 8 H), 7.25–7.12 (m, 5 H), 6.87–6.82 (m, 3 H), 6.70 (d, *J* = 8.3 Hz, 1 H), 6.55 (d, *J* = 2.1 Hz, 2 H), 5.19 (s, 2 H), 5.09 (s, 2 H), 4.04 (q, *J* = 7.1 Hz, 2 H), 3.82 (s, 3 H), 3.46 (s, 3 H), 0.99 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 171.0, 149.1, 148.4, 148.2, 147.9, 145.8, 138.3, 137.0, 136.9, 136.0, 133.3, 132.1, 129.8, 128.6, 128.5, 128.3, 127.9, 127.4, 127.3, 127.2, 124.2, 122.1, 115.1, 113.1, 113.0, 112.7, 70.8, 60.9, 56.0, 55.6, 13.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{39}H_{37}O_6$: 601.2585; found: 601.2706.

**Ethyl 3,3-Bis(4-fluorophenyl)-2-phenylpropenoate (28)**

Obtained while attempting to perform single coupling with the $Pd_2(dba)_3$/SPhos catalytic system (Table 1, entry 3); only 1.1 equiv of arylboronic acid used for the coupling procedure. White solid (0.090 g, 41%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 5:95 to >10:90); $R_f$ 0.37 (EtOAc/hexanes 10:90); mp 118–120 °C.

IR (NaCl): 1718, 1601, 1507, 1221, 1158 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.25–7.19 (m, 2 H), 7.18–7.14 (m, 3 H), 7.09–7.04 (m, 2 H), 7.02–6.96 (m, 2 H), 6.95–6.89 (m, 2 H), 6.81–6.76 (m, 2 H), 4.02 (q, *J* = 7.1 Hz, 2 H), 0.99 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 170.1, 163.6, 163.1, 161.6, 161.1, 143.5, 138.1, 137.2, 136.2, 134.1, 132.6, 130.9, 130.8, 129.7, 128.3, 127.6, 115.3, 115.1, 115.0, 114.9, 61.0, 13.7.

$^{19}F$ NMR (470 MHz, $CDCl_3$): δ = –113.23 to –113.33 (m, 2 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{19}F_2O_2$: 365.1348; found: 365.1349.

**Ethyl (*E*)-3-Bromo-3-(4-methoxyphenyl)-2-phenylpropenoate (24a); General Procedure for Single Suzuki–Miyaura Coupling with the $PdCl_2(PPh_3)_2$/TFP Catalytic System**

Ethyl 3,3-dibromo-2-phenylpropenoate (**10**, 1.00 g, 2.99 mmol) and 4-methoxyphenylboronic acid (**17**, 0.500 g, 3.29 mmol) were poured into an oven-dried three-neck flask under argon. Three vacuum/argon purges were performed, then anhyd DME (15 mL) and 2 M $K_2CO_3$ (3.89 mL, 7.77 mmol) were added at r.t. After 10 min, $PdCl_2(PPh_3)_2$ (0.105 g, 0.150 mmol) and TFP (0.208 g, 0.897 mmol) were added and the mixture was heated to 85 °C. After approx. 20 h the mixture was allowed to cool to r.t. and diluted with $CH_2Cl_2$. 1 M HCl was then added and the ester was extracted with $CH_2Cl_2$ (3 ×) The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by flash chromatography (EtOAc/hexanes 3:97 to >10:90) to yield **24a** (0.631 g, 39%) as a white solid; $R_f$ 0.37 (EtOAc/hexanes 10:90); mp 81–85 °C.

IR (NaCl): 1718, 1604, 1509, 1295, 1253, 1192, 1174, 1026, 833 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.51–7.42 (m, 6 H), 7.41–7.37 (m, 1 H), 6.91 (d, *J* = 8.8 Hz, 2 H), 4.00 (q, *J* = 7.1 Hz, 2 H), 3.85 (s, 3 H), 0.98 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 167.1, 160.3, 137.7, 136.2, 132.7, 130.7, 130.0, 128.8, 128.3, 113.6, 61.4, 55.4, 13.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{18}BrO_3$: 363.0415; found: 363.0406.

Single crystals of **24a** were recrystallized (hexanes) (see Supporting Information for checkCIF file); CCDC 1410092.[27]

**Ethyl (*Z*)-3-Bromo-3-(4-methoxyphenyl)-2-phenylpropenoate (24b)**

White solid (0.105 g, 6%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 3:97 to> 10:90); $R_f$ 0.43 (EtOAc/hexanes 10:90); mp 54–59 °C.

IR (NaCl): 1727, 1604, 1508, 1296, 1251, 1172, 1083 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.21–7.16 (m, 5 H), 7.16–7.11 (m, 2 H), 6.72–6.68 (m, 2 H), 4.35 (q, *J* = 7.1 Hz, 2 H), 3.75 (s, 3 H), 1.36 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 166.7, 137.3, 137.2, 136.4, 136.3, 130.5, 130.4, 129.3, 128.7, 128.6, 128.4, 115.4, 115.2, 61.6, 13.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{18}BrO_3$: 363.0415; found: 363.0361.

**Ethyl (*E*/*Z*)-3-Bromo-3-(4-fluorophenyl)-2-phenylpropenoate (23a/b)**

White solid (0.667 g, 64%, *E*/*Z* 5.4:1) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 3:97 to >10:90); $R_f$ (EtOAc/hexanes 3:97) 0.25.

**Ethyl (*E*)-3-Bromo-3-(4-fluorophenyl)-2-phenylpropenoate (23a)**

Early fractions were put aside during column chromatography (*E*/*Z* 96:4) for subsequent reactions and characterization of **23a**; mp 62–67 °C.

IR (NaCl): 2983, 1714, 1597, 1506, 1289, 1268, 1235, 1189, 837 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.51–7.38 (m, 7 H), 7.07 (m, 2 H), 3.97 (q, *J* = 7.1 Hz, 2 H), 0.95 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 166.7, 137.3, 137.2, 136.4, 136.3, 130.5, 130.4, 129.3, 128.7, 128.6, 128.4, 115.4, 115.2, 61.6, 13.6.

$^{19}F$ NMR (470 MHz, $CDCl_3$): δ = –111.22 to –111.28 (m, 2 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{15}OBrFO_2$: 349.0234; found: 349.0279.

**Ethyl (*Z*)-3-Bromo-3-(4-fluorophenyl)-2-phenylpropenoate (23b)**

Compound **23b** could not be characterized because no fraction isolated during chromatography contained the (*Z*)-product as the major isomer. The following spectral signatures (ethyl group and fluorine atom) for **23b** were found in the mixed *E*/*Z* fractions containing the most (*Z*) isomer (*E*/*Z* 78:22).

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 4.37 (q, *J* = 7.1 Hz, 2 H), 1.38 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 61.9, 13.7.

$^{19}F$ NMR (470 MHz, $CDCl_3$): δ = –111.29 to –111.36 (m, 1 F).

**Ethyl (*E*)-3-Bromo-2-phenyl-3-[4-(trifluoromethyl)phenyl]propenoate (25a)**

White solid (0.651 g, 54%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 3:97 to >10:90); $R_f$ 0.36 (EtOAc/hexanes 3:97); mp 66–71 °C.

IR (NaCl): 2985, 1719, 1327, 1265, 1193, 1166, 1114, 1068, 837 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.67–7.59 (m, 4 H), 7.51–7.38 (m, 5 H), 3.96 (q, *J* = 7.1 Hz, 2 H), 0.90 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 166.3, 143.8, 138.2, 136.9, 128.8, 128.7, 128.4, 125.3, 61.7, 13.5.

$^{19}F$ NMR (376 MHz, $CDCl_3$): δ = –62.80 (s, 3 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{15}BrF_3O_2$: 401.0183; found: 401.0209.

**Ethyl (*Z*)-3-Bromo-2-phenyl-3-[4-(trifluoromethyl)phenyl]propenoate (25b)**

Compound **25b** could not be isolated as pure isomer during chromatography, thus compromising its complete characterization. The following spectral signatures (ethyl group and fluorine atoms) and properties for **25b** were found in the mixed *E*/*Z* fractions containing the most (*Z*) isomer (*E*/*Z* 1:1); $R_f$ 0.3 (EtOAc/hexanes 3:97).

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 4.38 (q, *J* = 7.1 Hz, 2 H), 1.38 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 62.1, 14.1.

$^{19}F$ NMR (376 MHz, $CDCl_3$): δ = –62.85 (s, 3 F).

**Ethyl (*E*/*Z*)-3-Bromo-2,3-diphenylpropenoate (26a/b)**

White solid (0.602 g, 60%, *E*/*Z* 6.5:1) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 3:97 to >10:90); $R_f$ (EtOAc/hexanes 3:97) 0.24.

**Ethyl (*E*)-3-Bromo-2,3-diphenylpropenoate (26a)**

Early fractions were put aside during column chromatography (*E*/*Z* 92:8) for subsequent reactions and characterization of **26a**; mp 55–60 °C.

IR (NaCl): 1722, 1445, 1286, 1267, 1234, 1191, 1040 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.52–7.49 (m, 4 H), 7.46–7.35 (m, 6 H), 3.95 (q, *J* = 7.1 Hz, 2 H), 0.89 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 166.9, 140.3, 137.4, 136.9, 130.7, 129.2, 128.8, 128.5, 128.4, 128.2, 61.5, 13.5.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{16}BrO_2$: 333.0309; found: 333.0251.

**Ethyl (*Z*)-3-Bromo-2,3-diphenylpropenoate (26b)**

Compound **26b** could not be characterized because no fraction isolated during chromatography contained the (*Z*)-product as the major isomer. The following spectral signatures (ethyl group) for **26b** were found in the mixed *E*/*Z* fractions containing the most (*Z*) isomer (*E*/*Z* 83:17).

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 4.38 (q, *J* = 7.1 Hz, 2 H), 1.40 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 62.0, 14.1.

**Ethyl (*Z*)-3-(4-Fluorophenyl)-2,3-diphenylpropenoate (29a); General Procedure for Second Suzuki–Miyaura Coupling with the $PdCl_2(PPh_3)_2$/TFP Catalytic System**

Ethyl (*E*/*Z*)-3-bromo-3-(4-fluorophenyl)-2-phenylpropenoate (**23a**/**b** 96:4, 0.075 g, 0.215 mmol) and phenylboronic acid (**13**, 0.053 g, 0.430 mmol) were poured into an oven-dried three-neck flask under argon. Three vacuum/argon purges were performed, then anhyd DME (3 mL) and 2 M $K_2CO_3$ (0.280 mL, 0.559 mmol) were added at r.t. After 10 min, $PdCl_2(PPh_3)_2$ (0.008 g, 0.011 mmol) and tri(2-furyl)phosphine (TFP) (0.015 g, 0.065 mmol) were added and the mixture was heated to 85 °C. After approx. 24 h, the mixture was allowed to cool to r.t. and diluted with $CH_2Cl_2$. 1 M HCl was then added and the ester was extracted with $CH_2Cl_2$ (3 ×). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by flash chromatography (EtOAc/hexanes 2:98 to >10:90) to yield **29a** (0.063 g, 85%) as a white solid; $R_f$ 0.32 (EtOAc/hexanes 4:96); mp 130–132 °C.

IR (ATR, ZnSe): 1709, 1505, 1219, 1156, 1023, 873, 843, 773, 756, 696 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.29–7.23 (m, 2 H), 7.21–7.08 (m, 8 H), 7.06–6.95 (m, 4 H), 4.06 (q, *J* = 7.1 Hz, 2 H), 1.03 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 170.4, 163.8, 161.3, 144.7, 140.3, 138.4, 137.3, 134.0, 131.0, 130.8, 129.8, 128.2, 127.9, 127.8, 127.5, 115.2, 115.0, 61.0, 29.7, 13.8.

$^{19}F$ NMR (376 MHz, $CDCl_3$): δ = –111.55 to –111.63 (m, 1 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{20}FO_2$: 347.1442; found: 347.1462.

**Ethyl (*E*)-3-(4-Fluorophenyl)-2,3-diphenylpropenoate (29b)**

Pinkish solid (0.071 g, 91%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 2:98 to >10:90); $R_f$ 0.23 (EtOAc/hexanes 4:96); mp 110–114 °C.

IR (NaCl): 1712, 1601, 1505, 1219, 1158, 1044, 1026, 837 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.38–7.33 (m, 3 H), 7.32–7.28 (m, 2 H), 7.25–7.18 (m, 3 H), 7.17–7.12 (m, 2 H), 7.02–6.98 (m, 2 H), 6.86–6.81 (m, 2 H), 4.05 (q, *J* = 7.1 Hz, 2 H), 0.98 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 170.3, 163.1, 161.1, 144.9, 142.3, 137.4, 136.5, 133.9, 132.8, 132.7, 129.8, 129.1, 128.3, 128.2, 127.5, 114.8, 61.0, 13.7.

$^{19}F$ NMR (470 MHz, $CDCl_3$): δ = –113.50 to –113.58 (m, 1 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{20}FO_2$: 347.1442; found: 347.1423.

**Ethyl (*Z*)-3-(4-Methoxyphenyl)-2,3-diphenylpropenoate (30a)**

Yellowish solid (0.054 g, 36%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 5:95, $R_f$ 0.18); mp 102–106 °C.

IR (NaCl): 1714, 1245, 1216, 1038, 1025, 775, 721, 696 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.25–7.08 (m, 10 H), 7.05–7.00 (m, 2 H), 6.89–6.84 (m, 2 H), 4.08 (q, *J* = 7.1 Hz, 2 H), 3.83 (s, 3 H), 1.05 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 170.9, 159.6, 145.7, 140.8, 137.8, 134.9, 132.9, 131.0, 130.5, 129.9, 129.6, 128.1, 127.8, 127.6, 127.2, 120.6, 115.3, 113.5, 60.9, 55.3, 13.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{23}O_3$: 359.1642; found: 359.1644.

**Ethyl (*E*)-3-(4-Methoxyphenyl)-2,3-diphenylpropenoate (30b)**

Brownish solid (0.067 g, 86%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 5:95, $R_f$ 0.24); mp 114–118 °C.

IR (NaCl): 1716, 1606, 1509, 1249, 1217, 1151, 1042, 831 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.38–7.29 (m, 5 H), 7.25–7.14 (m, 5 H), 6.98–6.90 (m, 2 H), 6.71–6.64 (m, 2 H), 4.03 (q, *J* = 7.1 Hz, 2 H), 3.75 (s, 3 H), 0.97 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 170.8, 159.1, 146.0, 142.9, 138.0, 132.9, 132.7, 132.4, 129.9, 129.3, 128.3, 128.1, 128.0, 127.2, 113.2, 60.9, 55.1, 13.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{23}O_3$: 359.1642; found: 359.1656.

**Ethyl (*Z*)-2,3-Diphenyl-3-[4-(trifluoromethyl)phenyl]propenoate (31a)**

White solid (0.067 g, 84%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 4:96, $R_f$ 0.46); mp 128–132 °C.

IR (NaCl): 1718, 1325, 1219, 1160, 1127, 1110, 1066 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 8.0 Hz, 2 H), 7.40 (d, *J* = 8.0 Hz, 2 H), 7.23–7.08 (m, 8 H), 7.00–6.94 (m, 2 H), 4.03 (q, *J* = 7.1 Hz, 2 H), 0.97 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 169.9, 146.1, 144.4, 139.8, 136.9, 135.0, 130.8, 129.8, 129.5, 128.8, 128.3, 128.0, 127.8, 126.3, 125.1, 61.2, 13.6.

$^{19}F$ NMR (376 MHz, $CDCl_3$): δ = –62.55 (s, 3 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{20}O_2F_3$: 397.1410; found: 397.1427.

**Ethyl (*E*)-2,3-Diphenyl-3-[4-(trifluoromethyl)phenyl]propenoate (31b)**

White solid (0.070 g, 92%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 4:96, $R_f$ 0.26); mp 115–118 °C.

IR (NaCl): 2925, 1719, 1324, 1218, 1166, 1125, 1067, 1043, 1021, 723, 701 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.43–7.39 (m, 2 H), 7.38–7.35 (m, 3 H), 7.31–7.28 (m, 2 H), 7.24–7.21 (m, 3 H), 7.17–7.13 (m, 4 H), 4.07 (q, *J* = 7.1 Hz, 2 H), 1.00 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 170.0, 144.3, 144.1, 141.6, 136.8, 135.3, 131.2, 129.7, 129.1, 128.4, 128.3, 127.9, 124.8, 122.9, 77.3, 61.1, 13.7.

$^{19}F$ NMR (376 MHz, $CDCl_3$): δ = –62.62 (s, 3 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{20}F_3O_2$: 397.1410; found: 397.1415.

**Ethyl (*Z*)-3-(4-Fluorophenyl)-3-(4-methoxyphenyl)-2-phenylpropenoate (32a)**

Brownish solid (0.078 g, 96%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 4:96, $R_f$ 0.23); mp 100–106 °C.

IR (ATR, ZnSe): 1710, 1509, 1251, 1213, 1145, 1037, 1024, 830, 764, 730, 702 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.30–7.25 (m, 2 H), 7.22–7.18 (m, 3 H), 7.15–7.12 (m, 2 H), 7.06–7.01 (m, 2 H), 6.92–6.89 (m, 2 H), 6.69–6.65 (m, 2 H), 4.05 (q, *J* = 7.1 Hz, 2 H), 3.75 (s, 3 H), 1.02 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 170.6, 163.6, 161.6, 159.2, 144.7, 138.8, 137.8, 132.4, 131.0, 130.0, 128.3, 127.3, 115.2, 115.0, 113.3, 60.9, 55.1, 13.8.

$^{19}F$ NMR (470 MHz, $CDCl_3$): δ = –113.61 to –113.70 (m, 1 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{22}FO_3$: 377.1547; found: 377.1479.

Single crystals of **32a** were recrystallized (hexanes) (see Supporting Information for checkCIF file); CCDC 1410093.[27]

**Ethyl (*E*)-3-(4-Fluorophenyl)-3-(4-methoxyphenyl)-2-phenylpropenoate (32b)**

Yellowish solid (0.061 g, 39%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 4:96, $R_f$ 0.16); mp 100–104 °C.

IR (ATR, ZnSe): 1719, 1504, 1252, 1207, 1174, 1159, 1142, 1031, 838, 801, 770, 703 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ = 7.23–7.17 (m, 5 H), 7.12–7.08 (m, 2 H), 7.01–6.96 (m, 2 H), 6.89–6.80 (m, 4 H), 4.08 (q, *J* = 7.1 Hz, 2 H), 3.83 (s, 3 H), 1.05 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ = 170.7, 163.1, 161.1, 159.7, 144.6, 137.6, 136.8, 134.6, 133.0, 132.9, 132.8, 130.5, 129.8, 128.3, 127.4, 114.9, 114.8, 113.6, 61.0, 55.3, 13.9.

$^{19}F$ NMR (470 MHz, $CDCl_3$): δ = –113.65 to –113.73 (m, 1 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{22}FO_3$: 377.1547; found: 377.1480.

Single crystals of **32b** were recrystallized (hexanes) (see Supporting Information for checkCIF file); CCDC 1410094.[27]

**Ethyl (*Z*)-3-(4-Methoxyphenyl)-2-phenyl-3-[4-(trifluoromethyl)phenyl]propenoate (33a)**

White solid (0.034, 38%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 4:96, $R_f$ 0.17); mp 70–72 °C.

IR (NaCl): 1718, 1607, 1510, 1324, 1250, 1218, 1166, 1125, 1110, 1067, 1028, 874 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 8.0 Hz, 2 H), 7.21–7.17 (m, 5 H), 7.16–7.12 (m, 2 H), 7.11–7.07 (m, 2 H), 6.87 (d, *J* = 8.8 Hz, 2 H), 4.09 (q, *J* = 7.1 Hz, 2 H), 3.83 (s, 3 H), 1.06 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 170.3, 159.8, 144.6, 143.7, 137.0, 134.3, 134.0, 131.3, 130.5, 129.7, 128.4, 127.7, 124.7, 113.7, 61.1, 55.3, 13.9.

$^{19}F$ NMR (376 MHz, $CDCl_3$): δ = –62.61 (s, 3 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{22}F_3O_3$: 427.1516; found: 427.1529.

Single crystals of **33a** were recrystallized (hexanes) (see Supporting Information for checkCIF file); CCDC 1410095.[27]

**Ethyl (*E*)-3-(4-Methoxyphenyl)-2-phenyl-3-[4-(trifluoromethyl)phenyl]propenoate (33b)**

Brownish solid (0.079 g, 99%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 4:96, $R_f$ 0.25); mp 114–118 °C.

IR (NaCl): 1717, 1606, 1509, 1325, 1250, 1217, 1165, 1125, 1066, 1040, 832 $cm^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.1 Hz, 2 H), 7.44 (d, *J* = 8.0 Hz, 2 H), 7.28–7.15 (m, 5 H), 6.91 (d, *J* = 8.8 Hz, 2 H), 6.69 (d, *J* = 8.8 Hz, 2 H), 4.04 (q, *J* = 7.1 Hz, 2 H), 3.75 (s, 3 H), 0.97 (t, *J* = 7.1 Hz, 3 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 170.2, 159.3, 146.5, 144.4, 137.4, 133.9, 132.3, 132.1, 129.9, 129.6, 128.4, 127.6, 125.1, 113.4, 61.0, 55.1, 13.6.

$^{19}$F NMR (376 MHz, $CDCl_3$): δ = –62.49 (s, 3 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{22}F_3O_3$: 427.1516; found: 427.1525.

### Ethyl (*E*)-3-(4-Benzyloxy-3-methoxyphenyl)-3-(4-fluorophenyl)-2-phenylpropenoate (34a)

Brownish solid (0.315 g, 74%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 15:85, $R_f$ 0.32); mp 110–114 °C.

IR (ATR, ZnSe): 1713, 1505, 1250, 1221, 1206, 1182, 1131, 1039, 1023, 852, 748, 730, 698 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.31 (m, 4 H), 7.35–7.16 (m, 6 H), 7.18–7.11 (m, 2 H), 7.03 (t, *J* = 8.7 Hz, 2 H), 6.69 (d, *J* = 8.3 Hz, 1 H), 6.54–6.42 (m, 2 H), 5.08 (s, 2 H), 4.05 (q, *J* = 7.1 Hz, 2 H), 3.45 (s, 3 H), 1.02 (t, *J* = 7.1 Hz, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 170.6, 163.9, 161.4, 148.5, 148.0, 145.0, 138.5, 138.0, 136.8, 133.1, 133.0, 131.1, 131.0, 129.7, 128.5, 128.4, 127.9, 127.4, 127.3, 124.0, 115.2, 115.0, 114.9, 112.8, 70.8, 61.0, 55.6, 13.8.

$^{19}$F NMR (470 MHz, $CDCl_3$): δ = –113.43 to –113.55 (m, 1 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{28}FO_4$: 483.1966; found: 483.1953.

### Ethyl (*Z*)-3-(4-Benzyloxy-3-methoxyphenyl)-3-(4-fluorophenyl)-2-phenylpropenoate (34b)

White solid (0.017 g, 4%) obtained upon purification by column chromatography (silica gel, EtOAc/hexanes 15:85, $R_f$ 0.24); mp 144–147 °C.

IR (ATR, ZnSe): 1720, 1508, 1204, 1143, 1134, 1024, 1004, 820, 748, 697 cm$^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 1.6 Hz, 2 H), 7.40–7.36 (m, 2 H), 7.34–7.29 (m, 1 H), 7.22–7.17 (m, 3 H), 7.09 (m, 2 H), 6.99 (m, 2 H), 6.87–6.76 (m, 5 H), 5.18 (s, 2 H), 4.04 (q, *J* = 7.1 Hz, 2 H), 3.81 (s, 3 H), 0.99 (t, *J* = 7.1 Hz, 3 H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ = 170.7, 163.1, 161.1, 149.2, 148.3, 144.5, 137.5, 136.9, 136.4, 135.3, 133.2, 132.8, 129.8, 128.6, 128.3, 127.9, 127.4, 127.3, 122.0, 115.0, 114.8, 113.2, 112.8, 70.8, 61.0, 56.0, 13.9.

$^{19}$F NMR (470 MHz, $CDCl_3$): δ = –113.50 to –113.58 (m, 1 F).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{28}FO_4$: 483.1966; found: 483.1979.

### One-Pot Preparation of 2,3,3-Triarylacrylic Acid Ester 32a from *gem*-Dibromoalkene Precursor 10

Ethyl 3,3-dibromo-2-phenylpropenoate (**10**, 0.300 g, 0.898 mmol) and 4-fluorophenylboronic acid (**21**, 0.126 g, 0.898 mmol) were poured into an oven-dried three-neck flask under argon. Three vacuum/argon purges were performed, then anhyd DME (10 mL) and 2 M $K_2CO_3$ (1.16 mL, 2.33 mmol) were added at r.t. After 10 min, $PdCl_2(PPh_3)_2$ (0.032 g, 0.045 mmol) and TFP (0.063 g, 0.269 mmol) were added and the mixture was heated to 85 °C. After 20 h, 4-methoxyphenylboronic acid (**17**, 0.205 g, 1.347 mmol) was added and the mixture was stirred for an extra 24 h before the mixture was allowed to cool to r.t. and diluted with $CH_2Cl_2$. 1 M HCl was then added and the ester was extracted with $CH_2Cl_2$ (3 ×). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by flash chromatography (EtOAc/hexanes 10:90) to yield **32a** (0.144 g, 43%).

## Acknowledgment

The authors thank Charles Racine-Berthiaume and Pierre-Alexandre Paquet Côté for bringing new insights to the project, and Dr. Wenhua BI for X-ray crystallography experiments. This work was supported by the NSERC of Canada, the FQRNT of Quebec, PROTEO and Université Laval. SC is also indebted to NSERC of Canada and PROTEO for post-graduate scholarships and for a travel award.

## Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1560419.

## References

(1) (a) Doni, E.; Zhou, S.; Murphy, J. A. *Molecules* **2015**, *20*, 1755; http://www.mdpi.com/journal/molecules. (b) Takeda, Y.; Shimizu, M.; Hiyama, T. *Angew. Chem. Int. Ed.* **2007**, *46*, 8659. (c) Uddin, M. J.; Rao, P. N. P.; McDonald, R.; Knaus, E. E. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 439. (d) Liu, X. Y.; Shimizu, M.; Hiyama, T. *Angew. Chem. Int. Ed.* **2004**, *43*, 879. (e) Hellwinkel, D.; Goke, K.; Karle, R. *Synthesis* **1994**, 973.

(2) (a) Shoda, T.; Okuhira, K.; Kato, M.; Demizu, Y.; Inoue, H.; Naito, M.; Kurihara, M. *Bioorg. Med. Chem.* **2014**, *24*, 87. (b) Ganapathy, D.; Sekar, G. *Org. Lett.* **2014**, *16*, 3856. (c) Christodoulou, M. S.; Fokialakis, N.; Passarella, D.; Garcia-Argaez, A. N.; Gia, O. M.; Pongratz, I.; Dalla Via, L.; Haroutounian, S. A. *Bioorg. Med. Chem.* **2013**, *21*, 4120. (d) Abdellatif, K. R. A.; Belal, A.; Omar, H. A. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 4960. (e) Matsumoto, K.; Shindo, M. *Adv. Synth. Catal.* **2012**, *354*, 642. (f) Shiina, I.; Sano, Y.; Nakata, K.; Suzuki, M.; Yokoyama, T.; Sasaki, A.; Orikasa, T.; Miyamoto, T.; Ikekita, M.; Nagahara, Y.; Hasome, Y. *Bioorg. Med. Chem.* **2007**, *15*, 7599. (g) Jordan, V. C. *Nat. Rev. Drug Discovery* **2003**, *2*, 205. (h) Itami, K.; Kamei, T.; Yoshida, J. *J. Am. Chem. Soc.* **2003**, *125*, 14670.

(3) (a) Nagata, T.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2014**, *79*, 8960. (b) Zhu, Y.; Sun, P.; Yang, H. L.; Lu, L. H.; Yan, H.; Creus, M.; Mao, J. C. *Eur. J. Org. Chem.* **2012**, 4831. (c) Itami, K.; Tonogaki, K.; Nokami, T.; Ohashi, Y.; Yoshida, J. *Angew. Chem. Int. Ed.* **2006**, *45*, 2404. (d) Itami, K.; Ohashi, Y.; Yoshida, J. *J. Org. Chem.* **2005**, *70*, 2778.

(4) Cardinal, S.; Voyer, N. *Tetrahedron Lett.* **2013**, *54*, 5178.

(5) Strategies involving the uncatalyzed double addition of an organometallic compound on an alkyne: (a) Zhou, C.; Larock, R. C. *J. Org. Chem.* **2006**, *71*, 3184. (b) Shimizu, K.; Takimoto, M.; Mori, M.; Sato, Y. *Synlett* **2006**, 3182. (c) Zhou, C.; Larock, R. C. *Org. Lett.* **2005**, *7*, 259. (d) Takahashi, T.; Xi, C.; Ura, Y.; Nakajima, K. *J. Am. Chem. Soc.* **2000**, *122*, 3228. (e) Oda, H.; Morishita, M.; Fugami, K.; Sano, H.; Kosugi, M. *Chem. Lett.* **1996**, *25*, 811. (f) Ossor, H.; Pfeffer, M. *J. Chem. Soc., Chem. Commun.* **1985**, 1540.

(6) Examples involving the palladium-catalalyzed coupling of an internal alkyne with an aryl iodide and an arylboronic acid: (a) Scanlan, T. S.; Iijima, T. US 8236987, **2012**. (b) Jiang, H.-F.; Xu, Q.-X.; Wang, A. Z. *J. Supercrit. Fluids* **2009**, *49*, 377. (c) Zhou, C.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 3765. (d) Zhou, C.; Emrich, D. E.; Larock, R. C. *Org. Lett.* **2003**, *5*, 1579.

(7) Miscellaneous methods starting from different starting materials: (a) Nagao, K.; Ohmiya, H.; Sawamura, M. *Org. Lett.* **2015**, *17*, 1304. (b) Zhu, D.; Wu, Y.; Wu, B.; Luo, B.; Ganesan, A.; Wu, F.-H.; Pi, R.; Huang, P.; Wen, S. *Org. Lett.* **2014**, *16*, 2350. (c) Oliva-Madrid, M.-J.; García-López, J.-A.; Saura-Llamas, I.; Bautista, D.; Vicente, J. *Organometallics* **2014**, *33*, 19. (d) Zhou, L.; Zhang, W.; Jiang, H. *Sci. China, Ser. B: Chem.* **2008**, *51*, 241. (e) Nakatsuji, H.; Ashida, Y.; Hori, H.; Sato, Y.; Honda, A.; Taira, M.; Tanabe, Y. *Org. Biomol. Chem.* **2015**, *13*, 8205. (f) Banert, K.; Hagedorn, M.; Pester, T.; Siebert, N.; Staude, C.; Tchernook, I.; Rathmann, K.; Hollóczki, O.; Friedrich, J. *Chem. Eur. J.* **2015**, *21*, 14911.

(8) Flynn, A. B.; Ogilvie, W. W. *Chem. Rev.* **2007**, *107*, 4698.

(9) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *13*, 3769.

(10) Selected examples in medicinal chemistry: (a) Novoa, A.; Pellegrini-Moise, N.; Bourg, S.; Thoret, S.; Dubois, J.; Aubert, G.; Cresteil, T.; Chapleur, Y. *Eur. J. Med. Chem.* **2011**, *46*, 3570. (b) Koh, M.; Park, S. B. *Mol. Diversity* **2011**, *15*, 69. (c) Bauer, A.; Miller, M. W.; Vice, S. F.; McCombie, S. W. *Synlett* **2001**, 254.

(11) Selected examples in material science: (a) Zeng, Z. B.; Sung, Y. M.; Bao, N. N.; Tan, D.; Lee, R.; Zafra, J. L.; Lee, B. S.; Ishida, M.; Ding, J.; Navarrete, J. T. L.; Li, Y.; Zeng, W. D.; Kim, D.; Huang, K. W.; Webster, R. D.; Casado, J.; Wu, J. S. *J. Am. Chem. Soc.* **2012**, *134*, 14513. (b) Pola, S.; Kuo, C. H.; Peng, W. T.; Islam, M. M.; Chao, I.; Tao, Y. T. *Chem. Mater.* **2012**, *24*, 2566. (c) Loo, Y. L.; Hiszpanski, A. M.; Kim, B.; Wei, S. J.; Chiu, C. Y.; Steigerwald, M. L.; Nuckolls, C. *Org. Lett.* **2010**, *12*, 4840. (d) Ramana, C. V.; Reddy, B. K. K.; Reddy, C. N.; Gonnade, R. G.; Gurjar, M. K. *Synlett* **2007**, 127. (e) Bures, F.; Schweizer, W. B.; May, J. C.; Boudon, C.; Gisselbrecht, J. P.; Gross, M.; Biaggio, I.; Diederich, F. *Chem. Eur. J.* **2007**, *13*, 5378.

(12) (a) Kotek, V.; Dvořáková, H.; Tobrman, T. *Org. Lett.* **2015**, *17*, 608. (b) Gu, S.; Xu, H.; Zhang, N.; Chen, W. *Chem. Asian. J.* **2010**, *5*, 1677.

(13) Li, Y. H.; Zhao, X. M.; Lu, L. *J. Fluorine Chem.* **2004**, *125*, 1821.

(14) (a) Chelucci, G.; Capitta, F.; Baldino, S.; Pinna, G. A. *Tetrahedron Lett.* **2007**, *48*, 6514. (b) Molander, G. A.; Yokoyama, Y. *J. Org. Chem.* **2006**, *71*, 2493. (c) Shen, W. *Synlett* **2000**, 737. (d) Roush, W. R.; Brown, B. B.; Drozda, S. E. *Tetrahedron Lett.* **1988**, *29*, 3541.

(15) Shimizu, M.; Takeda, Y.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **2011**, *84*, 1339.

(16) (a) Jiao, J.; Hyodo, K.; Hu, H.; Nakajima, K.; Nishihara, Y. *J. Org. Chem.* **2014**, *79*, 285. (b) Shimizu, M.; Nakamaki, C.; Shimono, K.; Schelper, M.; Kurahashi, T.; Hiyama, T. *J. Am. Chem. Soc.* **2005**, *127*, 12506.

(17) Desai, N. B.; McKelvie, N.; Ramirez, F. *J. Am. Chem. Soc.* **1962**, *84*, 1745.

(18) Preparation of compound **2** as well as synthesis of precursors **8** and **12** has been previously reported by our group.[4] They are presented in this paper to show the complete current scope of this synthetic strategy.

(19) (a) Morken, P. A.; Bachand, P. C.; Swenson, D. C.; Burton, D. J. *J. Am. Chem. Soc.* **1993**, *115*, 5430. (b) Vu, V. A.; Marek, I.; Knochel, P. *Synthesis* **2003**, 1797.

(20) Boudreault, P. L.; Cardinal, S.; Voyer, N. *Synlett* **2010**, 2449.

(21) (a) Walker, S. D.; Barder, T. E.; Martinelli, J. R.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2004**, *43*, 1871. (b) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685.

(22) Ritchie, C. D.; Sager, W. F. *Prog. Phys. Org. Chem.* **1964**, *2*, 323.

(23) (a) de Vaal, P.; Dedieu, A. *J. Organomet. Chem.* **1994**, *478*, 121. (b) Amatore, C.; Bensalem, S.; Ghalem, S.; Jutand, A. *J. Organomet. Chem.* **2004**, *689*, 4642.

(24) (a) Krijnen, E. S.; Zuilhof, H.; Lodder, G. *J. Org. Chem.* **1994**, *59*, 8139. (b) Rossi, R.; Bellina, F.; Carpita, A.; Mazzarella, F. *Tetrahedron* **1996**, *52*, 4095. (c) Shi, J.-c.; Zeng, X.; Negishi, E.-i. *Org. Lett.* **2003**, *5*, 1825. (d) Simard-Mercier, J.; Jiang, J. L.; Ho, M. L.; Flynn, A. B.; Ogilvie, W. W. *J. Org. Chem.* **2008**, *73*, 5899.

(25) Zeng, X.; Hu, Q.; Qian, M.; Negishi, E.-i. *J. Am. Chem. Soc.* **2003**, *125*, 13636.

(26) For the synthesis of 2,3,3-triarylacrylic acid esters of Class **D** from *trans vic*-dibromoalkenes see: Zhou et al. 2008 (ref. 7d).

(27) CCDC 1410092, CCDC 1410093, CCDC 1410094, and CCDC 1410095 contain the supplementary crystallographic data for **24a**, **32a**, **32b**, and **33a**, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.