Significant Enhancement of the Stille Reaction with a New Combination of Reagents—Copper(I) Iodide with Cesium Fluoride

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Abstract: The combination of copper(I) iodide and cesium fluoride significantly enhances the Stille reaction. After extensive optimisation, a variety of electronically unfavourable and sterically hindered substrates were coupled in very high yields under mild conditions.
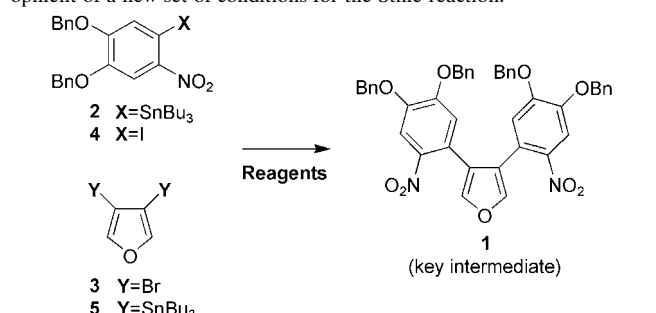
Introduction

Over the last several decades palladium-mediated coupling reactions have proved to be indispensable in organic synthesis. In particular, the Stille coupling[1] of organotin reagents with organic electrophiles has emerged as one of the most popular methods for carbon–carbon bond formation.[2] This is due in large measure to the air- and moisture-stability of the organotin substrates and the compatibility of the process with virtually any functional group.[3]

The reaction process for the Stille coupling is not trivial and often extensive experimentation is required to pinpoint the optimal conditions for a given reaction. We recently encountered a troublesome coupling reaction in our total synthesis of the proposed structure of a natural product isolated from the red beetroot.[4] A systematic investigation to enhance this particular coupling reaction led to the discovery of a new set of conditions for the Stille reaction: copper(I) salts in combination with the fluoride ion. We have previously communicated this work[5] and herein we report the full details of our investigation.

Our initial route to the target compound involved a double Stille coupling in the central carbon–carbon bond formation of the key intermediate **1** (Table 1). Originally attempts were made to couple the aryl stannane **2** with 3,4-dibromofuran (**3**); however, homocoupling of the stannane **2** was the main reaction in all attempts. Homocoupling has often been observed in Stille reactions[6] especially when

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Table 1. Optimisation of the double Stille coupling leading to the development of a new set of conditions for the Stille reaction.

| Entry	Reagents	Conditions		Yield
		Temp [°C]	time [h]	[%][a]
1	**2**, **3**, [Pd(PPh₃)₄], CuBr, THF	50	5	10
2	**4**, **5**, [Pd(PPh₃)₄], CuBr, THF	50	15	30
3	**4**, **5**, [Pd₂(dba)₃], AsPh₃, CuBr, THF	85	15	55
4	**4**, **5**, [Pd(PPh₃)₄], CuI, CsF, DMF	40	2	92

[a] Isolated yield of **1**.

electron-withdrawing substituents are present in conjugation with tin.[7] To overcome this problem we reversed the polarities and hence the functional groups on the coupling partners, which included developing a new efficient synthesis of 3,4-bis(tri-n-butylstannyl)furan (**5**).[8] Couplings of this furan **5** with the required aryl halide **4** gave an improved yield of **1**, but the reaction was slow and was only half complete after 15 h at 85°C. During optimisation of this transformation, we discovered that the combination of CsF and CuI in DMF greatly enhanced this reaction, affording 92% of the desired product **1** after just 2 h at 40°C (Table 1).

Both copper(I) salts[9–14] and fluoride sources[15–19] have been used previously to promote Stille reactions, but until

now there have been no reports of a Stille reaction that employs both reagents at the same time.

The Stille mechanism: The generally accepted mechanism for the Stille reaction[20] involves oxidative addition of Pd^0 into the aryl halide (or triflate) bond, transmetallation of the organotin reagent followed by reductive elimination to form the sp^2–sp^2 bond and regenerate the catalytic Pd^0 species (Scheme 1).
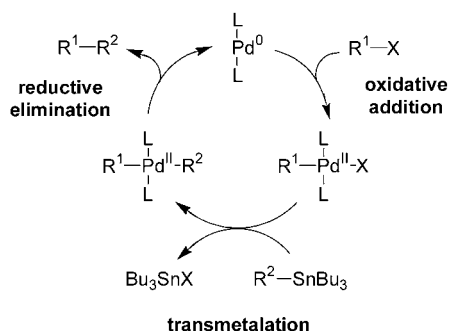

Scheme 1. A simplified outline of the Stille reaction mechanism.

The transmetallation step is generally assumed to be rate-limiting[21] and requires the substitution of a ligand at palladium by R^2.[22] This requirement has promoted attempts to facilitate the removal of a ligand from the palladium(II) species, which has been the main thrust of efforts to enhance the Stille reaction. Much of this effort involves "ligand tailoring", where particular properties of the ligand are proposed to encourage dissociation. The rationalisation for the observed rate increase with $AsPh_3$ as compared to PPh_3 is the lower Pd−As bond enthalpy, which allows $AsPh_3$ to dissociate more easily than PPh_3, enhancing the transmetallation.[22]

Copper(I) in the Stille reaction: The first mention of copper(I) being used in a Stille reaction was by Marino et al., although no emphasis was drawn to it.[9] Subsequently Liebeskind et al. highlighted that CuI, as a co-catalyst to [Pd-$(PPh_3)_2Cl_2$], enhanced Stille couplings of a range of iodides.[10] Mention was made of a preliminary transmetallation from the organostannane to a more reactive organocopper intermediate as a possible mechanistic explanation. It is well known that the Sonogashira[23] coupling of alkynes with aryl and vinyl halides is co-catalysed by copper(I) and it is often presumed that the role of copper(I) is to form a copper acetylide species.[24] However another mechanistic explanation for the role of copper(I) was given by Hobbs et al., who observed that a palladium to copper ratio of 1:2 was the most effective when using [Pd(PPh_3)_4] in Sonagashira couplings.[25] They suggested that copper(I) might facilitate removal of PPh_3 from palladium, resulting in a more reactive catalyst. Liebeskind and Farina et al. later examined the "copper effect" on the Stille reaction more thoroughly and proposed that both mechanistic ex-

planations could be valid, depending on the conditions of the reaction.[13]

With ethereal solvents they suggested that the copper effect could be explained by the "ligand association" mechanism (Scheme 2). In this proposal, the active species is formed by loss of a ligand from the initial palladium(II) species (**A**) that is generated after oxidative addition. The role of copper(I) is to facilitate this loss of ligand by coordination to the excess ligand in solution, which otherwise causes autoretardation of the required ligand loss.
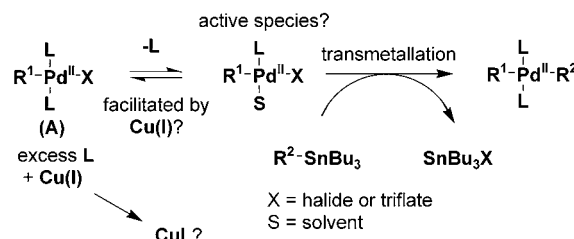
Scheme 2. The "ligand association" mechanistic explanation for the copper effect.

Recently Espinet et al. carried out kinetic studies relating to the above mechanistic proposal.[12, 26] In one report[26] they suggest that the transmetallation does not actually involve a dissociative mechanism as outlined above, but a more "S_N2-type" mechanism with a cyclic associative transition state TS(A) involving the active palladium(II) species PdR^1L_2X, or an open associative transition state TS(B) involving PdR^1L_2Y, depending on the conditions (Figure 1).
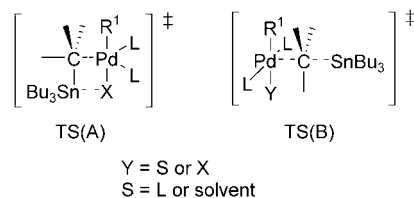

Y = S or X
S = L or solvent

Figure 1. Espinet's proposed associative transition states for transmetallation.

The autoretardation effect of excess ligand (the basis of Liebeskind and Farina's proposed disassociative mechanism in Scheme 2) is still accommodated with Espinet's associative pathways. Another study by Espinet et al. attempted a quantitative evaluation of the "copper effect" in THF.[12] Their report shows that the rate-enhancing effect of CuI is linked to the autoretardation effect caused by the release of two equivalents of ligand when PdL_4 undergoes oxidative addition to afford $PdRL_2X$. They concluded that CuI coordinates to "free" ligand, but does not directly promote the dissociation of ligand from the palladium(II) species. They also pointed out that the effect revealed in their study (con-

ducted in THF) is not the only proposed role of copper salts and that a Sn/Cu transmetallation mechanism may also operate.[10,13]

This Sn/Cu "preliminary transmetallation" mechanism was suggested by Liebeskind and Farina et al. to operate in highly polar solvents and in the absence of strong ligand donors like PPh₃[13] (Scheme 3).
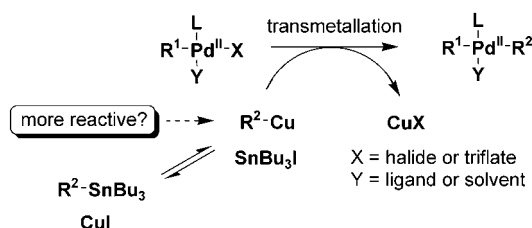
Scheme 3. The "preliminary transmetallation" mechanistic explanation for the copper effect.

Liebeskind and Farina et al. observed that Stille couplings with CuI that were carried out in the highly polar solvent NMP displayed kinetics that was not first-order. This is in contrast to the equivalent reaction performed in dioxane, which showed first-order kinetics. Although this change in kinetics could be attributable to catalyst decomposition, it can also be due to a succession of two transmetallations. This study also included ^{119}Sn NMR experiments, which disclosed that in highly polar solvents such as NMP and DMF, CuI reacts with vinyltributyltin and phenyltributyltin to produce Bu₃SnI and presumably the corresponding organocopper species. Another observation that could support a Sn/Cu transmetallation mechanism is that addition of CuI affects the group transfer selectivity from the organostannane, and that this selectivity occurs during the transmetallation step of the catalytic cycle.[13]

Tin to copper transmetallation has also been suggested in other studies utilising organostannanes in conjunction with copper.[27–30] In particular, couplings of organostannanes with organohalides can be mediated by copper salts alone,[28–30] indicating that a transmetallation from the organostannane to a copper species has taken place. However it remains unclear whether this involves CuX or the copper complex comprising the organohalide–RCuX₂.

Fluoride in the Stille reaction: The use of fluoride in the Stille reaction was first reported by Stille himself in the coupling of vinyl triflates.[15] The observation was made that tetrabutylammonium fluoride (TBAF) enhanced the reaction. More recently fluoride has been used as an additive in the Stille reaction based on the rationale that it could coordinate to the organotin reagent, due to the well-known fluorophilicity of tin,[31] creating a hypervalent organotin species. This hypervalent tin species should then be more nucleophilic, thus facilitating the transmetallation. Preformed hypercoordinate species[16] have also been used in these studies in addition to in situ formation with TBAF.[17] Recently CsF

has been used to enhance the coupling of aryl chlorides[18] and couplings involving alkynes.[19]

Copper(I) and fluoride combined: Our rationale for combining fluoride with copper(I) began with consideration of the possible role of copper(I) in the Stille reaction. As outlined above, one mechanistic model for the acceleration afforded by copper(I) is that copper(I) takes part in a preliminary transmetallation with the organotin reagent, producing a more reactive organocopper intermediate. If this process does take place one could propose that the two organometallic reagents would be in equilibrium—particularly when iodides, bromides or triflates are used. Such an equilibrium would be shifted unfavourably towards the organotin substrate as concentrations of Bu₃SnX increased, retarding the effect of copper(I) on the reaction. In a copper only-catalysed coupling of organostannanes and alkenyl iodides, Liebeskind et al. observed that the reaction rate was initially fast and then slowed considerably as the reaction approached 50% completion.[32] The addition of one equivalent of Bu₃SnCl prevented reaction altogether. These observations are consistent with the proposal of a preliminary transmetallation from tin to copper that is inhibited by increasing concentrations of Bu₃SnX.

If this "preliminary transmetallation" is taking place, we hypothesised that the presence of fluoride might drive the equilibrium towards the more reactive organocopper intermediate by removing the Bu₃SnX by-product from the equilibrium as polymeric Bu₃SnF. Reaction mixtures containing Bu₃SnCl are often purified by treatment with fluoride ion followed by filtration of the insoluble Bu₃SnF that forms.[33] Thus our rationale for using fluoride was not to hypercoordinate with the organotin reagent, but to enhance the copper effect (Scheme 4).
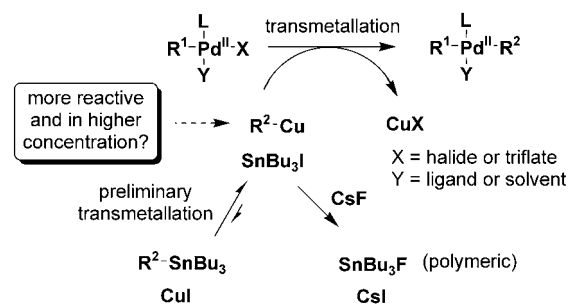

Scheme 4. Rationalisation for combining copper(I) and fluoride in the Stille reaction.

Results and Discussion

To investigate the effect of copper(I) and fluoride on the Stille coupling a test reaction was chosen in which the transmetallation was expected to be rate-limiting. As iodides undergo oxidative addition rapidly,[22] 4-iodotoluene (**8**) was selected as the electrophile. An electron-deficient aryl stannane should undergo transmetallation more slowly,[34] so 4-

(tri-*n*-butylstannyl)nitrobenzene (**7**) was chosen as the nucleophile component. The stannane **7** was synthesised from 4-iodonitrobenzene **6** in 63% yield by treatment with [Pd-(PPh$_3$)$_4$] and Bu$_6$Sn$_2$ in toluene (Scheme 5).[35]
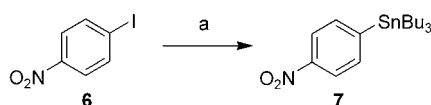
Scheme 5. Preparation of 4-(tri-*n*-butylstannyl)nitrobenzene (**7**): a) [Pd-(PPh$_3$)$_4$], Bu$_6$Sn$_2$, toluene, 120 °C, 48 h, 63%.

With the required stannane **7** in hand, a series of couplings with **8** were carried out to determine the individual effects of CsF and CuI and then the combined effect of both additives (Table 2). Only a very small amount of product

Table 2. Effect of CsF and/or CuI on the coupling of **8** and **7**.

Entry	Reagents[a]	Yield[b] [%]
1	[Pd(PPh$_3$)$_4$]	2
2	[Pd(PPh$_3$)$_4$], CsF	8
3	[Pd(PPh$_3$)$_4$], CuI	46
4	[Pd(PPh$_3$)$_4$], CsF, CuI	98
5	CsF, CuI	0

[a] [Pd(PPh$_3$)$_4$] (10%), CuI (20%), CsF (2.0 equiv). [b] Isolated yields are given and are the average of two repeat experiments. Remaining mass balance is recovered starting materials.

9[36] was isolated after two hours at 40 °C using [Pd(PPh$_3$)$_4$] alone, and most of the starting materials were recovered (Table 2, Entry 1). The addition of CsF increased the yield marginally, with most of the starting materials again being recovered (Table 2, entry 2). When the reaction was carried out with CuI as a co-catalyst a significant increase in yield was observed, and the reaction was almost half complete after two hours (Table 2, entry 3). With both CuI and CsF present, the reaction proceeded to completion in almost quantitative yield (Table 2, entry 4). Cu^I salts have been reported to promote the coupling of stannanes with organic electrophiles,[28,30,37] so to address this possibility the reaction was repeated using CuI, CsF, and in the absence of Pd^0. No product formation was observed demonstrating that CuI is not directly catalysing this reaction (Table 2, entry 5). It is clear that in the presence of palladium, CuI and CsF produce a combined effect that considerably enhances this reaction.

Our working model for combining copper(I) and fluoride outlined in Scheme 4 does provide one possible explanation for the greatly improved reaction outcome, however the effect observed in Table 2 does not necessarily suggest the involvement of the alleged organocopper intermediate. It

may be that copper(I) and fluoride are operating in a different way than that described in our working model, and it may be that the two additives are enhancing the reaction by more than one distinct mechanism. Detailed mechanistic studies will be required to elucidate the precise mechanism for the combination of copper(I) and fluoride in the Stille reaction. Nonetheless the improvement they afford is significant whatever the mechanistic details may be.[38] It is interesting to note that CsF is used as a base in Suzuki coupling reaction,[39] while the palladium-catalysed coupling between cyclic silyl ethers and aryl iodides is promoted by a combination of CsF and CuI.[40]

Optimisation

Solvent: To establish the optimal conditions using copper(I) and fluoride, the effect of different solvents on the coupling of **8** and **7** was initially investigated (Table 3). When the re-

Table 3. Effect of the solvent on the coupling of 4-iodotoluene (**8**) and 4-(tri-*n*-butylstannyl)nitrobenzene (**7**).
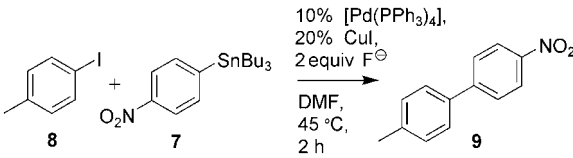
Entry	Solvent	Yield [%][a]
1	toluene	6
2	THF	45
3	dioxane	48
4	NMP	95
5	DMSO	96
6	DMF	98

[a] Yield of isolated product. Remaining mass balance is recovered starting materials.

action was carried out using toluene as the solvent, only a very small amount of product **9** was isolated (Table 3, entry 1). When using either THF (Table 3, entry 2) or dioxane (Table 3, entry 3), the reaction proceeded to almost 50% completion after two hours. Highly polar solvents were by far the most effective, with NMP, DMSO and DMF delivering essentially quantitative yields of the product (Table 3, entries 4, 5 and 6). A possible explanation for these observations is that the solubility of CsF is highest in highly polar solvents. For further optimisation studies DMF was selected as the solvent because of its ease of removal under reduced pressure compared with NMP and DMSO during the work up of the reaction.

Fluoride source: With an optimum solvent found, alternative fluoride sources were considered using the same coupling reaction of **8** and **7** (Table 4). Both LiF (Table 4, entry 1) and NaF (Table 4, entry 2) had basically no effect on the reaction, affording similar yields to the corresponding reaction conducted in the absence of fluoride (see Table 2, entry 3). There was some effect observed with KF (Table 4,

Table 4. Effect of the fluoride source on the coupling of 4-iodotoluene (**8**) and 4-(tri-*n*-butylstannyl)nitrobenzene (**7**).
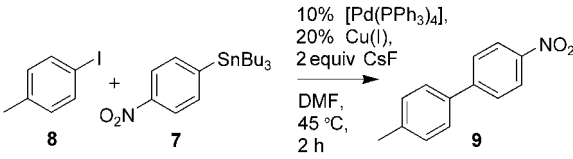

10% [Pd(PPh₃)₄], 20% CuI, 2 equiv F⊖
DMF, 45 °C, 2 h

Entry	Fluoride source	Yield [%][a]
1	LiF	44
2	NaF	46
3	KF	62
4	CsF	98
5	TBAF	98
6	TBAF[b]	96
7	NH₄F	54

[a] Yield of isolated product. Remaining mass balance is recovered starting materials. [b] THF was used as the reaction solvent.

entry 3), but the most effective fluoride sources were CsF and TBAF (Table 4, entries 4 and 5). This trend can perhaps be explained by the availability of fluoride in terms of lattice energies. LiF has the highest lattice energy (LiF 1030 kJ mol^{-1}, NaF 910 kJ mol^{-1}, KF 808 kJ mol^{-1}, CsF 744 kJ mol^{-1}),[41] which would disfavour solubility as compared to CsF, and hence CsF would more easily deliver the fluoride ion. Interestingly, TBAF was equally effective in either DMF or THF (Table 4, entry 6), unlike CsF which is only effective in highly polar solvents (Table 4, entry 4 cf. Table 3). Recently TBAF was shown to be a better fluoride donor than CsF.[42] NH₄F did not significantly enhance the reaction under the conditions examined, which is unfortunate as it is inexpensive (Table 4, entry 7). CsF was chosen as the fluoride source for further optimisation because TBAF comes as a solution in THF which might mean limiting subsequent reaction temperatures to 65 °C.

Copper(I) source: Copper(I) sources were also investigated using the coupling of **8** and **7** (Table 5). There was no significant difference between CuCl, CuBr and CuI (Table 5, entries 1, 2 and 3) on the coupling of **8** and **7** under the conditions examined. Also of note was the observation that increased amounts of CuI did not adversely effect the reaction

Table 5. Effect of the copper(I) source on the coupling of 4-iodotoluene (**8**) and 4-(tri-*n*-butylstannyl)nitrobenzene (**7**).
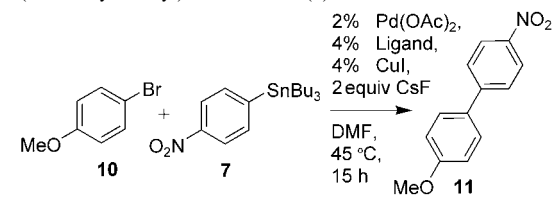

10% [Pd(PPh₃)₄], 20% Cu(I), 2 equiv CsF
DMF, 45 °C, 2 h

Entry	Copper(I) source	Yield [%][a]
1	CuCl	95
2	CuBr	98
3	CuI	98
4[b]	CuI	96

[a] Yield of isolated product. [b] 50% CuI.

(Table 5, entry 4). Liebeskind et al. observed in their study of the ʹcopper effectʹ, that increasing the amount of copper(I) above a copper(I):ligand ratio of 1:2 caused a decrease in yield.[13] The explanation was that too much copper(I) binds up all the ligand causing catalyst decomposition. However their reactions were carried out in THF while ours use DMF, and in their study they pointed out that copper(I) could operate with different mechanisms in THF and DMF. It is possible that catalyst decomposition is more facile in entry 4 than entry 3 (Table 5), in accordance with Liebeskind's proposal, but in this case the effect is not observed because the reaction is very rapid.

Ligand type: To investigate the palladium catalyst with the associated ligands the doubly-deactivated system of 4-bromoanisole **10** and 4-(tri-*n*-butylstannyl)nitrobenzene **7** was employed. We began by examining a variety of different ligands (Table 6). When the coupling of **10** and **7** was carried

Table 6. Effect of the ligand type on the coupling of 4-bromoanisole (**10**) and 4-(tri-*n*-butylstannyl)nitrobenzene (**7**).

2% Pd(OAc)₂, 4% Ligand, 4% CuI, 2 equiv CsF
DMF, 45 °C, 15 h

Entry	Ligand type	Yield [%][a]
1	PPh₃	11
2	AsPh₃	13
3	P(2-furyl)₃	15
4	PCy₃[b]	55
5	P*t*Bu₃	89
6[c]	P*t*Bu₃	49

[a] Yield of isolated product. Remaining mass balance is recovered starting materials. [b] Cy = cyclohexyl. [c] Reaction excluded CuI.

out using Pd(OAc)₂ and PPh₃ as the ligand, only a small amount of the product **11**[43] was isolated after 15 h (Table 6, entry 1). Both AsPh₃ and P(2-furyl)₃ proved to be no more effective than PPh₃ at enhancing the reaction (Table 6, entries 2 and 3). AsPh₃ and P(2-furyl)₃ are believed to enhance Stille couplings by increasing the rate of transmetallation,[22] which could imply that in entries 1, 2 and 3 (Table 6) the rate-limiting step might be oxidative addition rather than transmetallation. With this possibility in mind, electron-rich PCy₃ was investigated as a ligand that might promote oxidative addition by increasing the nucleophilicity of the palladium(0) species. When the reaction was carried out with PCy₃ the yield increased significantly to 55% after 15 h reaction time (Table 6, entry 4). When the electron-rich ligand P*t*Bu₃ was employed the reaction proceeded almost to completion after 15 h (Table 6, entry 5). Without further investigation it is not easy to assert which step of the catalytic cycle is rate-limiting for entry 5 (Table 6). However, when the reaction was repeated in the absence of CuI (Table 6, entry 6) the

yield dropped by almost half, suggesting that CuI is either involved in the rate-limiting step or the exclusion of CuI changes which step is rate-limiting.

As a ligand PtBu$_3$ is clearly effective and has been used before in a variety of palladium-catalysed processes. Koie et al. initially demonstrated the high activity of PtBu$_3$ as a ligand in the palladium-catalysed amination of aryl halides.[44] Since then PtBu$_3$ has been applied in the hydroxylation of aryl halides,[45] α-carbonyl arylation,[46] Suzuki,[47] Negishi,[48] Heck,[49] Sonogashira[50] and Stille couplings.[18] The effectiveness of the ligand might be due to two characteristics. The first is that the ligand is electron-rich and as mentioned above, this property should facilitate the oxidative addition. The second attribute is the steric bulk or cone angle of the ligand, and this property might enhance the transmetallation step of the catalytic cycle. The reasoning behind this suggestion is that the transmetallation step requires substitution of a ligand by the organostannane (or organocopper) reagent, and PtBu$_3$ might disassociate more readily as a result of steric acceleration.

Palladium/ligand ratio: Having established that PtBu$_3$ was the most effective ligand for the coupling of **10** and **7**, the effect of changing the palladium/ligand ratio was examined (Table 7). With a palladium/ligand ratio of 1:1, 53% of the

Table 7. Effect of the Pd:PtBu$_3$ ratio on the coupling of 4-bromoanisole (**10**) and 4-(tri-n-butylstannyl)nitrobenzene (**7**).
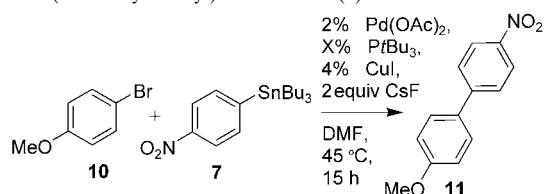
| Entry	Pd/PtBu$_3$ ratio	Yield [%][a]
1	1:1	53
2	1:2	89
3	1:3	90
4	1:4	86

[a] Yield of isolated product. Remaining mass balance is recovered starting materials.

product **11** was isolated after 15 h (Table 7, entry 1), whereas a palladium/ligand ratio of 1:2 gave 89% of **11** (Table 7, entry 2). Increasing the palladium/ligand ratio to 1:3 (Table 7, entry 3), or 1:4 (Table 7, entry 4) virtually did not change the yield of **11**. Other groups who have used PtBu$_3$ in palladium-catalysed processes, report that a palladium/ligand ratio of 1:1 gives the highest rate of reaction,[18,46] however a palladium/ligand ratio of 1:2,[18,50] or 1:4[51] is often used, presumably to provide more stability to the catalyst. In the system we investigated, a palladium/ligand ratio of 1:1 (Table 7, etry 1) might give a higher reaction rate than a ratio of 1:2 (Table 7, etry 2), but a lower yield due to catalyst decomposition. Another explanation could be that

the Pd(OAc)$_2$ is reduced from palladium(II) to the active palladium(0) by PtBu$_3$,[52] resulting in the effective palladium/ligand ratio being decreased to some degree. Thus a palladium/ligand ratio of 1:2 using Pd^{II} might be equivalent to a palladium/ligand ratio of 1:1 using Pd^0. Irrespective of the mechanistic details, a palladium:ligand ratio of 1:2 provided the necessary effect for the coupling of **10** and **7**, and so this ratio was selected for further optimisation.

Palladium source: The final variable considered with the coupling of **10** and **7** was the palladium source (Table 8). The least effective source of palladium investigated was [Pd-

Table 8. Effect of the palladium source on the coupling of 4-bromoanisole (**10**) and 4-(tri-n-butylstannyl)nitrobenzene (**7**).
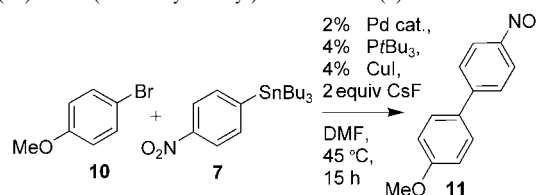
Entry	Palladium source	Yield [%][a]
1	[Pd(MeCN)$_2$Cl$_2$]	56
2	[Pd$_2$(dba)$_3$]	64
3	Pd(OAc)$_2$	89
4	PdCl$_2$	97

[a] Yields are isolated and are the average of two repeat experiments. Remaining mass balance is recovered starting materials.

(MeCN)$_2$Cl$_2$], which resulted in only 56% of the product **11** after 15 h (Table 8, entry 1). [Pd$_2$(dba)$_3$] (dba = dibenzylideneacetone) proved to be slightly better (Table 8, entry 2), but was still not as efficient as Pd(OAc)$_2$ (Table 8, entry 3). The most effective palladium source investigated was PdCl$_2$, which delivered an almost quantitative yield of the product **11** (Table 8, entry 4). One explanation for the results outlined in Table 8 is that the 'preligands' associated with the palladium source will have differing degrees of coordinative ability to palladium, and this could interfere with the formation of the active Pd^0 species.[53] In [Pd$_2$(dba)$_3$] the palladium metal is in the Pd^0 oxidation state, and so the dibenzylideneacetone will invariably have coordinative properties to Pd^0, which could hinder the formation of Pd(PtBu$_3$)$_2$. Studies showed that the species formed from [Pd$_2$(dba)$_3$] and PPh$_3$ is quite different from [Pd(PPh$_3$)$_4$],[54] and Beller et al. recently observed reduced catalytic activity in Suzuki couplings when using ligands such as dba.[51] However there are reports where [Pd$_2$(dba)$_3$] is more efficient than Pd(OAc)$_2$[18] and others where the effectiveness of these two palladium sources is solvent dependant.[55] [Pd(MeCN)$_2$Cl$_2$], Pd(OAc)$_2$ and PdCl$_2$ are all Pd^{II} species rather than Pd^0 species, but they still have coordinating ligands. However PdCl$_2$ contains only the hard Cl$^-$ ion, which would not be expected to have a high binding affinity for the soft Pd^0, and this might allow the most effective formation of Pd(PtBu$_3$)$_2$ in situ under the conditions studied. We emphasise here that the explanation

we provided is highly simplified since the mechanism of Stille coupling reaction has been shown to be very complex.[56]

Having optimised the main variables of the reaction, we established two sets of conditions. For the coupling of aryl iodides and triflates we would employ conditions **A** ([Pd-(PPh₃)₄] (5 %), CuI (10 %), CsF (2 equiv), DMF, 45 °C), and for the less reactive aryl bromides and chlorides we would employ conditions **B** (PdCl₂ (2 %), P*t*Bu₃ (4 %), CuI (4 %), CsF (2 equiv), DMF, 45 °C). These were not the only conditions that could be used however. DMSO and NMP were effective as solvents, CuBr and CuCl both enhanced the reaction and TBAF was as effective as a fluoride source.

Scope

Coupling of iodides: Generally iodides undergo coupling reactions reasonably well, but sometimes if one or both of the coupling partners are sterically hindered or deactivated, they can be reluctant to couple efficiently. Two such examples reported in the literature to be somewhat difficult[57] were attempted using our conditions (Table 9). The vinyl stannane **13** was synthesised by a Sonogashira reaction between aryl iodide **15** and propargyl alcohol,[58] followed by

palladium-catalysed addition of Bu₃SnH to alkyne **20**[59] (Scheme 6).
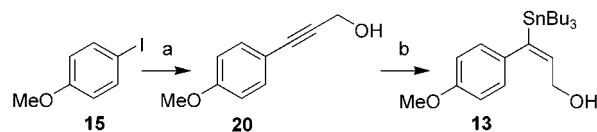
Scheme 6. Synthesis of vinyl stannane **13**: a) propargyl alcohol, [Pd-(PPh₃)₂Cl₂], piperidine, CuI, benzene, RT, 2 h, 92 %; b) Bu₃SnH, [Pd-(PPh₃)₂Cl₂], THF, RT, 20 min, 39 %.

The coupling of hindered iodide **12** and hindered stannane **13** to give **14** has previously been achieved in an optimised yield of only 27 %, and that was after reaction for 15 h at 80 °C.[57] When conducted under our new conditions, this same reaction returned an excellent yield of 92 % (Table 9, entry 1). It is noteworthy that with Cu^I and CsF present, the reaction between **12** and **13** was complete after 8 h at just 45 °C. Similarly, reaction of iodide **15** and stannane **13** afforded **16** in 94 % yield indicating that deactivated iodides can be coupled efficiently with the new conditions. The previously reported best yield of this reaction was a moderate 42 %[57] (Table 9, entry 2). As mentioned in the introduction, 3,4-bis(tri-*n*-butylstannyl)furan **5** reacted with two equivalents of *ortho*-substituted aryl iodide **4** in high yield using our new conditions (Table 9, entry 3). The disubstituted product **1** was obtained exclusively,[4] demonstrating that our conditions can accommodate sterically hindered stannanes in conjunction with sterically hindered iodides. The almost quantitative coupling of 4-iodotoluene **8** with 4-(tri-*n*-butylstannyl)nitrobenzene **7** (used in the initial test reaction) illustrates that reactions employing electronically disfavoured aryl stannanes can also proceed in high yield (Table 9, entry 4). The effect of heterocycles on the coupling of iodides with our conditions was assessed by reaction of 3-iodopyridine (**17**) with 2-(tri-*n*-butylstannyl)thiophene (**18**). Satisfyingly the coupled product **19**[60] was isolated in 99 % yield, displaying that heterocyclic iodides can also undergo coupling efficiently (Table 9, entry 5).
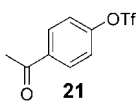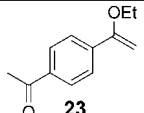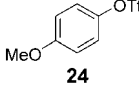
Table 9. Coupling of iodides using conditions **A**.[a]
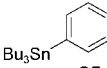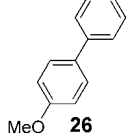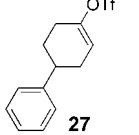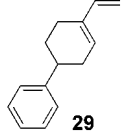
Entry	Halide/Triflate	Stannane	Product	Time [h]	Yield [%][b]
1	**12**	**13**	**14**	8	92
2	**15**	**13**	**16**	8	94
3[c]	**4**	**5**	**1**	2	92
4[d]	**8**	**7**	**9**	2	98
5	**17**	**18**	**19**	1	99

[a] Conditions **A**: [Pd(PPh₃)₄] (5 %), CuI (10 %), CsF (2 equiv), DMF, 45 °C. [a] Yields are isolated and are the average of two repeat experiments. [b] Iodide (2.1 equiv), organostannane (1 equiv), [Pd(PPh₃)₄] (10 %), CuI (20 %), CsF (4 equiv). [c] [Pd(PPh₃)₄] (10 %), CuI (20 %), CsF (2 equiv).

The couplings of iodides could be carried out at room temperature, although the reaction times were longer. For example, when the coupling of **17** with **18** was performed at room temperature the reaction took 2 h to proceed to completion.

Coupling of triflates: Because triflates are readily available from the corresponding phenol or enolate, they have become important coupling partners,[31,61] in synthesis. This easy access to triflates has allowed quick assembly of structures such as conjugated dienes, by coupling vinyl triflates with vinyl stannanes. For the coupling of triflates, [Pd-(PPh$_3$)$_4$] was sufficient using our conditions and the reactions investigated proceeded to completion rapidly (Table 10).

Table 10. Coupling of triflates using conditions **A**.[a]

Entry	Halide/Triflate	Stannane	Product	Time [h]	Yield [%][b]
1	**21**	**22**	**23**	2	95
2	**24**	**25**	**26**	2	91
3	**27**	**28**	**29**	1	98

[a] Conditions **A**: [Pd(PPh$_3$)$_4$] (5%), CuI (10%), CsF (2 equiv), DMF, 45°C. [b] Yields are isolated and are the average of two repeat experiments.
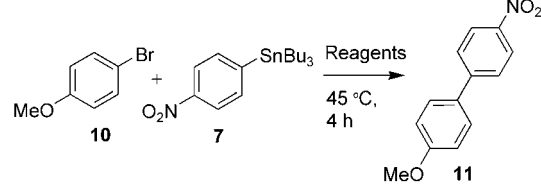
4-Acetophenyl trifluoromethanesulfonate (**21**) reacted rapidly with the vinylstannane **22** to give the coupled product **23**[18b] in 95% yield (Table 10, entry 1). The biaryl coupling carried out between 4-methoxyphenyl trifluoromethanesulfonate (**24**) and phenyltributylstannane (**25**) also proceeded rapidly and gave **26**[62] in high yield, demonstrating that deactivated triflates also respond well to our conditions (Table 10, entry 2). The preparation of 4-phenyl-1-cyclohexen-1-yl triflate (**27**)[63] proceeded from 4-phenyl-1-cyclohexanone (**30**) in 97% yield by treatment with potassium hexamethyldisilazide followed by N-phenyltrifluoromethanesulfonimide (Scheme 7).
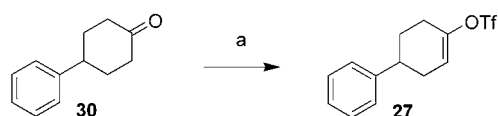
Scheme 7. Preparation of vinyl triflate **27**: a) KHMDS, THF, −78°C, then RT, 1 h, PhN(OTf)$_2$, RT, 2 h, 97%.

Reaction of vinyl triflate **27** with tri-n-butylvinylstannane (**28**) again progressed very quickly under our conditions affording the conjugated diene **29**[64] in almost quantitative yield (Table 10, entry 3). Even when the reaction represented in entry 3 was performed at room temperature it was complete after one hour.

Coupling of bromides: For the coupling of bromides the catalytic system employing PdCl$_2$ and PtBu$_3$ was used (conditions **B**). Recently Fu et al. reported a procedure for the Stille coupling that also makes use of PtBu$_3$.[18] To investigate whether our conditions **B** provide an improvement over the procedure described by Fu et al. for the coupling of bromides, a series of reactions were carried out on the challenging coupling of electron-rich 4-bromoanisole (**10**) and electron-deficient 4-(tri-n-butylstannyl)nitrobenzene (**7**) (Table 11).

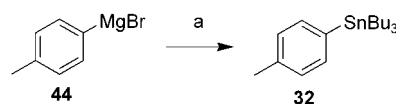Table 11. Evaluating alternative conditions on the coupling of **10** and **7**.

Entry	Reagents[a]	Yield [%][b]
1[c]	PdCl$_2$, PtBu$_3$, CuI, CsF, DMF	92
2	PdCl$_2$, PtBu$_3$, CsF, DMF	29
3[d]	[Pd$_2$(dba)$_3$], PtBu$_3$, CsF, dioxane	16
4	[Pd$_2$(dba)$_3$], PtBu$_3$, CuI, CsF, dioxane	10

[a] PdCl$_2$ (2%) or [Pd$_2$(dba)$_3$] (1%), PtBu$_3$ (4%), CuI (4%), CsF (2.0 equiv). [b] Yields are isolated yields and are the average of two repeat experiments. Remaining mass balance is recovered starting materials. [c] Conditions **B**. [d] Reagent combination reported by Fu et al.[18]

When **10** and **7** were coupled under conditions **B**, a 92% yield of the desired product **11** was isolated after 4 h at 45°C (Table 11, entry 1). To address the question of whether or not CuI is necessary when using PtBu$_3$ under conditions **B**, the coupling of **10** and **7** was repeated without CuI. Only 29% of the coupled product **11** was isolated after the same reaction time, with the remaining starting material being recovered (Table 11, entry 2). This demonstrates that CuI is still necessary to provide the highest yields, even though a coordinatively unsaturated catalytic system is generated under conditions **B**. When the coupling of **10** and **7** was carried out using the reagent combination described by Fu et al.[18] at 45°C for 4 h, a 16% yield of the coupled product **11** was isolated. The reaction had not proceeded to completion during this time and the remaining starting materials were recovered (Table 11, entry 3). Interestingly, the addition of CuI in the same reaction resulted in a slight decrease in the isolated yield (Table 11, entry 4). This particular observation is supported by our optimisation studies where we observed that the synergic effect of CuI and CsF requires highly polar solvents. Our optimisation studies also revealed

that PdCl$_2$ was superior to [Pd$_2$(dba)$_3$] as a palladium source when using DMF as the solvent.

Having established the validity of conditions **B**, a range of bromides were successfully coupled with a variety of stannanes and in all cases investigated the yields were very high (Table 12). 4-(Tri-*n*-butylstannyl)toluene (**32**)[65] was synthesised in 94% yield by reaction of 4-tolylmagnesium bromide (**44**) with tributylstannyl chloride (Scheme 8). Reaction of aryl stannane **32** with bromobenzene (**31**) provided 4-phenyltoluene (**33**)[66] in almost quantitative yield (Table 12, entry 1). The couplings with bromides were carried out overnight for convenience, but the reactions did not necessarily require this extended period. This is evident from the electronically disfavoured coupling of electron-rich bromide **10** and electron-deficient stannane **7**. Overnight the reaction af-

Scheme 8. Preparation of 4-(tri-*n*-butylstannyl)toluene (**32**): a) Bu$_3$SnCl, THF, 30°C, 3 h, 94%.
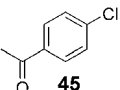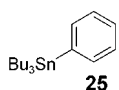
forded a 97% yield of the product **11** (Table 12, entry 2), however it was essentially complete after 4 h (92%) as demonstrated above in Table 11 (entry 1). The successful coupling led to an attempt at an extremely challenging reaction, which is both sterically hindered and electronically disfavoured. Gratifyingly 2,4-dimethoxybromobenzene **34** and 4-(tri-*n*-butylstannyl)nitrobenzene **7** reacted to deliver **35** in high yield, establishing that even highly deactivated bromides will couple with electron-deficient stannanes under our conditions (Table 12, entry 3). Although considerably sterically hindered, di-*ortho*-substituted 9-bromoanthracene (**36**) efficiently underwent reaction with tri-*n*-butylvinylstannane (**28**) affording the product **37**[67] in an excellent yield of 96% (Table 12, entry 4). This is higher than the previously reported yield of 66%,[18] although our reaction was carried out at a higher temperature and for a longer time. In our hands the coupling of **36** and **28** under Fu's conditions ([Pd$_2$-(dba)$_3$], P*t*Bu$_3$, toluene, RT, 3 h) gave 54% of the product **37**, whereas when the reaction was repeated by using our catalytic system under identical conditions (RT, 3 h) a 68% yield of the product **37** was isolated. In both cases the remaining mass balance was largely recovered starting materials. To carry out an example of a biscoupling, (*E*)-1,2-bis(tri-*n*-butylstannyl)ethene (**39**) was prepared by radical addition of tri-*n*-butylstannylhydride to ethynyltri-*n*-butylstannane,[68] then coupled with bromoquinoline **38**.[69] Two quinoline moieties were readily incorporated onto the bis-tin ethene **39** giving a very good yield of the desired disubstituted product **40** (Table 12, entry 5). To investigate the tolerance of heterocyclic bromides under our conditions, 2-bromo-6-methylpyridine (**41**) was subjected to a coupling with phenyltri-*n*-butylstannane (**25**) and satisfyingly reacted smoothly giving 91% of the product **42** (Table 12, entry 6). This yield is significantly higher than the previously reported yield of 61% even though the previous protocol employed higher temperatures (135–140°C) and the more reactive phenyltrimethylstannane.[70] Heterocyclic stannanes were also tolerated well by our conditions, which was demonstrated by the near-quantitative coupling of 2-(tri-*n*-butylstannyl)thiophene (**18**) with 2-bromo-6-methylpyridine (**41**) to give **43**[71] (Table 12, entry 7).

Coupling of chlorides: The coupling of aryl chlorides proved to be significantly more difficult than for aryl bromides, with elevated reaction temperatures required to effect coupling. Aryl chlorides are believed to be poor coupling partners due to the reluctance of Pd^0 to undergo oxidative addition to the strong carbon–chloride bond.[72] The bond dissociation energy for Ph–Cl is 96 kcal mol^{-1}, compared with

Table 12. Coupling of bromides using conditions **B** for 15 h.[a]

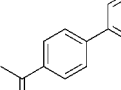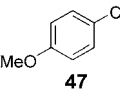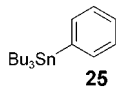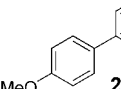| Entry	Halide/Triflate	Stannane	Product	Yield [%][b]
1	**31**	**32**	**33**	98
2	**10**	**7**	**11**	97
3	**34**	**7**	**35**	89
4[c]	**36**	**28**	**37**	96
5[d]	**38**	**39**	**40**	93
6	**41**	**25**	**42**	91
7	**41**	**18**	**43**	98

[a] Conditions **B**: PdCl$_2$ (2%), P*t*Bu$_3$ (4%), CuI (4%), CsF (2 equiv), DMF, 45°C. [b] Isolated yields. [c] Organostannane (1.3 equiv). [d] Bromide (2.1 equiv), organostannane (1 equiv), PdCl$_2$ (4%), P*t*Bu$_3$ (8%), CuI (8%), CsF (4 equiv).

81 kcal mol^{-1} for Ph–Br and 65 kcal mol^{-1} for Ph–I. To evaluate how chlorides would respond to our conditions we carried out couplings with an activated and a deactivated aryl chloride (Table 13).

Table 13. Coupling of chlorides using conditions **B** for 15 h at 100°C.[a]

Entry	Halide/Triflate	Stannane	Product	Yield [%][b]
1	**45**	**25**	**46**	81
2	**47**	**25**	**26**	40–60

[a] Conditions **B**: PdCl$_2$ (2%), PtBu$_3$ (4%), CuI (4%), CsF (2 equiv), DMF. [a] Yields are isolated and are the average of two repeat experiments (entry 2 shows the range). Remaining mass balance is recovered starting materials.

With these substrates it was observed that the electronic effect of the substituents on the aromatic ring of the aryl chloride has considerable influence on the reactivity of the substrate. Reaction of electron-deficient aryl chloride **45** with stannane **25** provided the coupled product **46**[73] in a respectable 81% yield (Table 13, entry 1). The coupling of the electron-rich chloride **47** to stannane **25** proceeded in lower yields, ranging between 40% and 60% (Table 13, entry 2). In both cases, coupling of the aryl chlorides did not proceed to completion even with extended reaction times, suggesting that the catalytic system may be decomposing under the more forcing conditions. Thus our new conditions appear effective for the coupling of electron-deficient aryl chlorides, but less effective when it comes to electron-rich aryl chlorides.[74]

Conclusion

The combination of copper(I) and the fluoride ion has proved to be particularly effective in enhancing the Stille reaction. Mechanistic studies would need to be undertaken to conclusively elucidate the mechanism operating. Optimisation studies revealed that the most effective conditions were Pd cat./CuI/CsF in DMF, with a palladium/ligand ratio of 1:2, a palladium/copper ratio of 1:2 and two equivalents of CsF, although these were not the only conditions that could be used. Highly polar solvents like DMSO and NMP were effective and TBAF appeared similar to CsF as a fluoride source. The most effective palladium catalyst for coupling bromides was PdCl$_2$/PtBu$_3$, but it was not necessary when coupling iodides or triflates, which were effectively coupled with [Pd(PPh$_3$)$_4$]. A range of reactions were then carried out which included sterically hindered and electronically disfavoured coupling partners. In all cases investigated by using iodides, triflates or bromides, the yield of the desired prod-

uct was excellent. Furthermore, our conditions are mild and compatible with a wide variety of functional groups. This combination of copper(I) iodide and cesium fluoride should allow the synthesis of sterically hindered systems and promote electronically disfavoured coupling reactions, expanding the scope of the Stille reaction in synthetic organic chemistry.

Experimental Section

General experimental: Tetrahydrofuran (THF) was distilled over sodium/benzophenone ketyl under nitrogen. PE refers to the fraction of light petroleum ether boiling between 40°C and 60°C, and was distilled before use. Dimethylformamide (DMF), dimethyl sulfoxide (DMSO) and N-methylpyrrolidine (NMP) were distilled from calcium hydride under argon or reduced pressure and stored over 4 Å molecular sieves under argon until used. Toluene was dried over 4 Å molecular sieves under argon. All water used was distilled. Solvents were evaporated at 40°C or below on a Büchi R114 Rotavaporator.

Thin-layer chromatography (TLC) was performed by using Merck aluminium foil backed plates pre-coated with silica gel 60 F$_{254}$ (1.05554). Retention factors (R$_f$) are reported to two decimal places. Column chromatography was performed by using ICN silica 32–63, 60 Å or basic Laporte Actal U.G. alumina.

^{1}H NMR spectra were recorded on a Brüker DPX400 spectrometer at 400 MHz and ^{13}C NMR spectra at 100.6 MHz and are referenced according to IUPAC recommendations, 2001.[75] Proton spectra assignments are supported by ^{1}H–^{1}H COSY where necessary. Carbon spectra assignments are supported by DEPT analysis and ^{1}H–^{13}C correlations where necessary.

Low-resolution mass spectra were recorded by using a TRIO-1 GCMS spectrometer, a Micromass Platform (APCI or ES) Spectrometer, Micromass Autospec spectrometer (CI$^+$) and a micromass ZAB spectrometer (CI$^+$, EI). Only molecular ions (M^+), fragments from molecular ions and other major peaks are reported. High-resolution mass spectra were recorded on a Micromass Autospec spectrometer and are accurate to $\pm$ 5 ppm. Microanalyses were carried out by Elemental Microanalysis Limited, and are quoted to the nearest 0.1%.

Experimental procedures

General procedure for Stille reactions: A mixture of the organohalide (or triflate) (0.840 mmol) and the organotin (0.930 mmol) reagent was dissolved in DMF (2 mL), then caesium fluoride (256 mg, 1.69 mmol) was added. The palladium catalyst and copper(I) iodide (conditions **A**: [Pd(PPh$_3$)$_4$] (5%), CuI (10%); conditions **B**: PdCl$_2$ (2%), PtBu$_3$ (4%), CuI (4%)) were added and the flask was evacuated and refilled with argon five times. The mixture was stirred at 45°C for the required time, then diluted with dichloromethane (DCM) (50 mL) and water (20 mL). After vigorous shaking, the mixture was filtered through Celite with DCM/EtOAc (200 mL, 1:1). The organic layer was separated, dried over Na$_2$SO$_4$/MgSO$_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography.

3-(4′-Methoxyphenyl)-2-propyn-1-ol (20): [Pd(PPh$_3$)$_2$Cl$_2$] (0.300 g, 0.430 mmol) was added to a solution of 4-methoxyiodobenzene **15** (10.0 g, 42.7 mmol), propargyl alcohol (2.70 mL, 46.4 mmol), piperidine (9.30 mL, 93.9 mmol) and copper(I) iodide (80 mg, 0.42 mmol) in benzene (20 mL) under argon. The solution was stirred at room temperature for 2 h then diluted with DCM (100 mL). The solution was washed with water (50 mL), dried over Na$_2$SO$_4$/MgSO$_4$ and the solvent removed under reduced pressure. The residue was purified by column chromatography (DCM/EtOAc, 19:1) to give **20** (6.38 g, 92%) as a white solid.
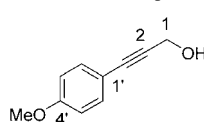
$R_f = 0.26$ (DCM/EtOAc, 19:1); m.p. 62–63 °C; lit. [58] 61–63 °C; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 2.54$ (s, 1H; OH), 3.80 (s, 3H; OCH$_3$), 4.48 (s, 2H; H1), 6.82 (d, $J = 9.0$ Hz, 2H; H3′, 5′), 7.37 ppm (d, $J = 9.0$ Hz, 2H; H2′, 6′); ^{13}C NMR (100.6 MHz, CDCl$_3$): $\delta = 51.5$ (C1), 55.3 (OCH$_3$), 85.5 (C3), 86.0 (C2), 113.9 (C3′, 5′), 114.7 (C4′), 133.2 (C2′, 6′), 159.7 ppm (C1′); IR (KBr): $\tilde{\nu}_{max} = 3258$ (br m, OH str), 2965 (w), 2898 (w), 2838 (w), 2231 (w, CC alkyne str), 1604 (s), 1509 (s), 1441 (m), 1292 (m), 1250 (s), 1174 (m), 1110 (w), 1028 (s), 949 (w), 837 cm^{-1} (s); MS (CI+): m/z (%): 163.2 ([MH]$^+$, 100), 144.8 (46), 133.1 (32), 122.2 (19), 112.1 (13), 95.6 (14); HRMS ([MH]$^+$) requires m/z 163.0759, found: 163.0767.
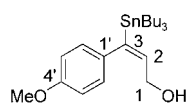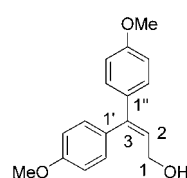
(Z)-3-(4′-Methoxyphenyl)-3-(tri-n-butylstannyl)-2-propyn-1-ol (13):[59] Bu$_3$SnH (3.65 mL, 13.6 mmol) was added slowly to a solution of 3-(4′-methoxyphenyl)-2-propyn-1-ol (**20**; 2.00 g, 12.3 mmol) and [Pd(PPh$_3$)$_2$Cl$_2$] (0.17 g, 0.24 mmol) in THF (20 mL) under argon at room temperature. The dark brown mixture was stirred for 20 min then the solvent was removed under reduced pressure. The residue was purified by column chromatography (DCM/EtOAc, 19:1) to give **13** (2.18 g, 39%) as a pale yellow liquid.

$R_f = 0.41$ (DCM/EtOAc, 19:1); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 0.82$–0.97 (m, 15H; CH$_2$CH$_3$ and SnCH$_2$), 1.28 (sextet, $J_1 = 7.0$ Hz, 6H; CH$_2$CH$_3$), 1.37–1.53 (m, 6H; CH$_2$CH$_2$CH$_3$), 1.61 (br s, 1H; OH), 3.79 (s, 3H; OCH$_3$), 4.13 (t, $J = 5.5$ Hz, 2H; H1), 5.96 (t, $J = 6.0$ Hz, 1H; H2), 6.80–6.88 ppm (m, 4H; Ar CH); ^{13}C NMR (100.6 MHz, CDCl$_3$): $\delta = 10.0$ (SnCH$_2$), 13.6 (CH$_2$CH$_3$), 27.3 (CH$_2$CH$_3$), 28.9 (CH$_2$CH$_2$CH$_3$), 55.2 (OCH$_3$), 60.5 (C1), 113.5 and 136.2 (Ar CH), 136.2 (quat. C), 139.9 (C2), 148.2 and 157.5 ppm (quat. C); IR (thin film): $\tilde{\nu}_{max} = 3322$ (br m, OH str), 2955 (s), 2926 (s), 2871 (s), 2853 (s), 1602 (m), 1505 (s), 1464 (m), 1283 (m), 1244 (s), 1173 (m), 1036 (s), 864 cm^{-1} (m); MS (CI+): m/z (%): 453.3 ([MH]$^+$, (15)) 437.3 (35), 395.3 (92), 381.2 (75), 291.2 (72), 203.2 (37), 163.2 (54), 146.9 (100), 134.8 (33).
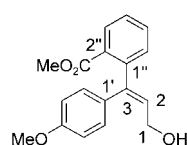
3-(2′-Carboxylic acid methyl ester)-3-(4″-methoxyphenyl)-2-propen-1-ol (14):[57] Methyl 2-iodobenzoate (**12**; 220 mg) and (Z)-3-(4′-methoxyphenyl)-3-(tri-n-butylstannyl)-2-propyn-1-ol (**13**; 422 mg) were coupled by using the general procedure with conditions **A** for 8 h. Column chromatography (DCM/EtOAc, 9:1) gave **14** (231 mg, 92%) as a white solid.

$R_f = 0.20$ (DCM/EtOAc, 9:1); m.p. 89–90 °C; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 3.59$ (s, 3H; OCH$_3$), 3.79 (s, 3H; OCH$_3$), 4.35 (d, $J = 7.0$ Hz, 2H; H1), 5.85 (t, $J = 7.0$ Hz, 1H; H2), 6.82 (d, $J = 8.0$ Hz, 2H; H3″, 5″), 7.04 (d, $J = 7.5$ Hz, 2H; H2″, 6″), 7.32–7.38 (m, 2H; H4′, 6′), 7.43–7.49 (m, 1H; H5′), 7.69 ppm (d, $J = 7.5$ Hz, 1H; H3′); ^{13}C NMR (100.6 MHz, CDCl$_3$): $\delta = 51.9$ and 55.2 (OCH$_3$), 60.3 (C1), 113.1 (C3′, 5′), 127.4 (Ar CH), 128.5 (C2), 129.5 (C3″), 131.0, 131.2 and 131.3 (Ar CH), 131.4, 143.4, 143.8 and 158.9 (quat. C), 168.7 ppm (C=O), (one Ar CH and one quat. C not seen); IR (KBr): $\tilde{\nu}_{max} = 3427$ (br m, OH str), 3007 (m), 2951 (m), 2838 (m), 1721 (s, C=O str), 1608 (s), 1511 (s), 1294 (s), 1250 (s), 1180 (m), 1127 (m), 1084 (m), 1031 (s), 838 (m), 761 cm^{-1} (s); MS (ES+): m/z : ([MH$^+$−H$_2$O]) 280.8 (100%); HRMS ([MH]$^+$) requires m/z 281.1178, found 281.1172.

3,3-Bis(4′-Methoxyphenyl)-2-propen-1-ol (16):[57] 4-Iodoanisole (**15**; 197 mg) and (Z)-3-(4′-methoxyphenyl)-3-(tri-n-butylstannyl)-2-propyn-1-ol (**13**; 422 mg) were coupled by using the general procedure with conditions **A** for 8 h. Column chromatography (DCM/EtOAc, 19:1) gave **16** (213 mg, 94%) as a pale yellow liquid.

$R_f = 0.24$ (DCM/EtOAc, 19:1); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 1.82$ (s, 1H; OH), 3.80 (s, 3H; OCH$_3$), 3.84 (s, 3H; OCH$_3$), 4.21 (d, $J = 7.0$ Hz, 2H; H1), 6.11 (t, $J = 7.0$ Hz, 2H; H2), 6.82 (d, $J = 9.0$ Hz, 2H; H3′ and 5′ or 3″ and 5″), 6.90 (d, $J = 9.0$ Hz, 2H; H3′ and 5′ or 3″ and 5″), 7.09 (d, $J = 9.0$ Hz, 2H; H2′ and 6′ or 2″ and 6″), 7.20 ppm (d, $J = 9.0$ Hz, 2H; H2′ and 6′ or 2″ and 6″); ^{13}C NMR (100.6 MHz, CDCl$_3$): $\delta = 55.2$ (2×OCH$_3$), 60.7 (C1), 113.5 (C3′, 5′), 125.5 (C2), 128.9 and 131.0 (C2′, 6′), 131.6, 134.8, 143.4, 159.0 and 159.2 ppm (quat. C); IR (thin film): $\tilde{\nu}_{max} = 3394$ (br m, OH str), 3004

(m), 2934 (m), 2836 (m), 1607 (s), 1511 (s), 1463 (m), 1287 (m), 1248 (s), 1175 (s), 1033 (s), 835 (s), 756 cm^{-1} (m); MS (ES+): m/z ([MH$^+$−H$_2$O]) 252.8 (100%); HRMS ([MH$^+$−H$_2$O) requires m/z 253.1229, found 253.1234.
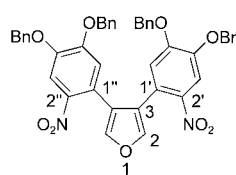
3,4-Bis(3,4-dibenzyloxy-2-nitrophenyl)furan (1): 4,5-Dibenzyloxy-2-nitroiodobenzene (**4**; 406 mg, 0.880 mmol) and 3,4-bis(tri-n-butylstannyl)furan (**5**; 271 mg, 0.420 mmol) were coupled by using the general procedure with conditions **A** [Pd(PPh$_3$)$_4$] (49 mg, 0.042 mmol), CuI (16 mg, 0.084 mmol), CsF (255 mg, 1.68 mmol), DMF (2 mL)] for 2 h. Column chromatography (DCM/PE, 7:3) gave **1** (284 mg, 92%) as a solid yellow foam.

$R_f = 0.44$ (DCM/PE, 7:3); m.p. 55.5–56 °C; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 5.15$, (s, 4H; CH$_2$ of Bn), 5.17 (s, 4H; CH$_2$ of Bn), 6.87 (s, 2H; H6′, 6″), 7.30–7.53 ppm (m, 24H; H2, H5, H3′, H3″, Ar-H of Bn); ^{13}C NMR (100.6 MHz, CDCl$_3$): $\delta = 71.1$ and 71.4 (CH$_2$ of Bn), 110.4 (C3′, 3″), 117.0 (C6′, 6″), 120.8 and 123.7 (quat. C), 127.2, 127.3, 127.4, 127.5, 128.17, 128.24, 128.3, 128.6 and 128.7 (Ar-CH of Bn), 135.7 and 135.9 (ipso-C of Bn), 140.0 (C2, 5), 141.6, 147.9 and 152.3 ppm (quat. C); IR (KBr): $\tilde{\nu}_{max} = 3089$ (w), 3063 (w), 1573 (m), 1519 (s, NO$_2$ str), 1454 (m), 1342 (s, NO$_2$ str), 1280 (s), 1203 (m), 1086 (m), 1023 (m), 868 (m), 738 (m), 696 cm^{-1} (m); MS (ES+): m/z (%): 752.3 ([MNH$_4$]$^+$, 100), 702.2 (33); HRMS ([MNH$_4$]$^+$) requires m/z 752.2608, found 752.2612.
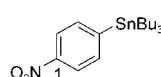
4-(Tri-n-butylstannyl)nitrobenzene (7):[35] A mixture of 4-iodonitrobenzene (**6**; 5.00 g, 20.1 mmol), Bu$_6$Sn$_2$ (15.0 mL, 29.7 mmol) and [Pd(PPh$_3$)$_4$] (1.16 g, 1.00 mmol) in toluene (50 mL) was heated to reflux under argon for 48 h. Saturated aqueous KF solution (50 mL) was added to the cooled mixture and then it was stirred rapidly at room temperature for 1 h. The mixture was filtered through Celite with toluene washings (200 mL), then the organic layer was separated, dried over Na$_2$SO$_4$/MgSO$_4$ and the solvent removed under reduced pressure. The residue was purified by column chromatography (PE/DCM, 9:1) to give **7** (5.21 g, 63%) as a yellow oil.

$R_f = 0.27$ (PE/DCM, 9:1); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 0.90$ (t, $J = 7.5$ Hz, 9H; CH$_3$), 1.04–1.22 (m, 6H; SnCH$_2$), 1.34 (sextet, $J = 7.0$ Hz, 6H; CH$_2$CH$_3$), 1.45–1.62 (m, 6H; CH$_2$CH$_2$CH$_3$), 7.59–7.71 (m, 2H; H3, 5), 8.13 ppm (d, $J = 8.5$ Hz, 2H; H2, 6); ^{13}C NMR (100.6 MHz, CDCl$_3$); $\delta = 9.8$ (SnCH$_2$), 13.6 (CH$_3$), 27.3 (CH$_2$CH$_3$), 29.0 (CH$_2$CH$_2$CH$_3$), 121.9 (C2, 6), 137.0 (C3, 5), 148.1 and 153.3 ppm (quat. C); IR (thin film): $\tilde{\nu}_{max} = 3031$ (w), 2957 (s), 2928 (s), 2871 (s), 2853 (s), 1518 (s, NO$_2$ str), 1347 (s, NO$_2$ str), 850 cm^{-1} (m); MS (CI+): m/z (%): ([MNH$_4$]$^+$) 431.2 (15), 373.2 (18), 356.2 (36), 326.2 (27), 308.2 (29), 291.2 (57), 150.2 (23), 94.2 (100).
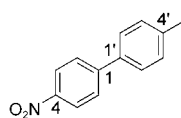
4′-Methyl-4-nitrobiphenyl (9): 4-Iodotoluene **8** (183 mg) and 4-(tri-n-butylstannyl)nitrobenzene **7** (383 mg) were coupled by using the general procedure with 10% [Pd(PPh$_3$)$_4$], 20% CuI and 2 equiv CsF for 2 h at 40 °C. Column chromatography (PE/DCM, 1:1) gave **9** (176 mg, 98%) as a cream solid.

$R_f = 0.41$ (PE/DCM, 1:1); m.p. 135–137 °C; lit. [36] 138–139 °C; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 2.44$ (s, 3H; Ar CH$_3$), 7.32 (d, $J = 8.0$ Hz, 2H; H3′, 5′), 7.53 (d, $J = 8.0$ Hz, 2H; H2′, 6′), 7.71 (d, $J = 9.0$ Hz, 2H; H2, 6), 8.28 ppm (d, $J = 9.0$ Hz, 2H; H3, 5); ^{13}C NMR (100.6 MHz, CDCl$_3$): $\delta = 21.2$ (Ar CH$_3$), 124.1 (C3, 5), 127.2 and 127.4 (C2, 2′, 6, 6′), 129.9 (C3′, 5′), 135.8, 139.1 146.8 and 147.5 ppm (quat. C); IR (KBr): $\tilde{\nu}_{max} = 1594$ (m), 1513 (s, NO$_2$ str), 1484 (m), 1338 (s, NO$_2$ str), 1107 (m), 824 (s), 754 cm^{-1} (m); MS (CI+): m/z (%): 231.2 ([MNH$_4$]$^+$, 20), 213.1 ([MH]$^+$, 100), 183.1 (49), 165.1 (30), 152.1 (41); HRMS ([MH]$^+$) requires m/z 213.0790, found 213.0790.
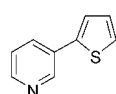
3-Thiophen-2-yl-pyridine (19):[60] 3-Iodopyridine (**17**; 172 mg) and 2-(tri-n-butylstannyl)thiophene (**18**; 347 mg) were coupled by using the general procedure with conditions **A** for 1 h. Column chromatography (PE/diethyl ether, 3:7) gave **19** (134 mg, 99%) as a pale yellow liquid.

$R_f = 0.29$ (PE/diethyl ether, 3:7); ^{1}H NMR (400 MHz, C_6D_6): $\delta = 6.74$ (dd, $J_1 = 4.5$, $J_2 = 8.0$ Hz, 1H; Ar CH), 6.78–6.81 (m, 1H; Ar CH), 6.90–6.92 (m, 1H; Ar CH), 6.98–7.02 (m, 1H; Ar CH), 7.26 (s, 1H; Ar C*H*), 7.45 (dt, $J_1 = 2.0$, $J_2 = 8.0$ Hz, 1H; Ar CH), 8.50 (d, $J = 4.0$ Hz, 1H; H6), 9.10 ppm (s, 1H; H2); ^{13}C NMR (100.6 MHz, C_6D_6): $\delta = 123.7$, 124.5, 126.1 and 128.5 (Ar CH), 130.6 (quat. C), 132.7 (Ar CH), 141.0 (quat. C), 147.6 (C2), 149.1 ppm (C6); IR (thin film): $\tilde{v}_{max} = 3074$ (m), 3030 (m), 1565 (w), 1475 (s), 1433 (m), 1413 (s), 1328 (w), 1264 (w), 1124 (w), 1023 (m), 851 (m), 801 (s), 705 cm^{-1} (s); MS(ES+): m/z (%): 161.6 ([MH]$^+$, 100).
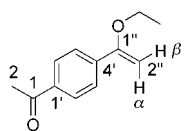
1-[4′-(1″-ethoxyvinyl)phenyl]-ethanone (23):[18b] 4-Acetophenyl trifluoromethanesulfonate (**21**; 225 mg) and vinylstannane **22** (336 mg) were coupled by using the general procedure with conditions **A** for 2 h. Column chromatography (PE/DCM, 3:7) gave **23** (145 mg, 95%) as a colourless liquid.

$R_f = 0.31$ (PE/DCM, 3:7); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 1.44$ (t, $J = 7.0$ Hz, 3H; CH$_2$C*H*$_3$), 2.60 (s, 3H; H2), 3.94 (q, $J = 7.0$ Hz, 2H; C*H*$_2$CH$_3$), 4.32 (d, $J = 3.0$ Hz, 1H; H2″α), 4.77 (d, $J = 3.0$ Hz, 1H; H2″β), 7.12 (d, $J = 8.5$ Hz, 2H; H3′, 5′), 7.92 ppm (d, $J = 8.5$ Hz, 2H; H2′, 6′); ^{13}C NMR (100.6 MHz, CDCl$_3$): $\delta = 14.5$ (CH$_2$*C*H$_3$), 26.6 (C2), 63.5 (*C*H$_2$CH$_3$), 84.3 (C2″), 125.4 (C3′, 5′), 128.2 (C2′, 6′), 136.7, 141.0 and 158.8 (quat. C), 197.7 ppm (C1); IR (thin film): $\tilde{v}_{max} = 2980$ (m), 2931 (m), 1719 (m), 1685 (s, C=O str), 1608 (s), 1406 (m), 1358 (m), 1267 (s), 1130 (m), 1111 (m), 1056 (m), 1016 (m), 958 (m), 847 (m), 808 (m), 770 cm^{-1} (m); MS (GC CI+): m/z(%): 191.1 ([MH]$^+$, 100), 162.1 (18), 148.1 (92), 147.1 (45), 131.1 (7), 70.1 (11); HRMS ([MH]$^+$) requires m/z 191.1072, found 191.1079.
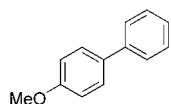
4-Methoxybiphenyl (26): Method A: 4-Methoxyphenyl trifluoromethanesulfonate (**24**; 215 mg) and phenyltri-n-butylstannane (**25**; 341 mg) were coupled by using the general procedure with conditions **A** for 2 h. Column chromatography (PE/DCM, 3:7) gave **26** (142 mg, 91%) as a white solid.

Method B: 4-Chloroanisole (**47**; 120 mg) and tri-n-butylphenylstannane (**25**; 341 mg) were coupled by using the general procedure with conditions **B** at 100°C for 15 h. Column chromatography (PE/DCM, 3:7) gave **26** (62–93 mg, 40–60%) as a white solid.

$R_f = 0.39$ (PE:DCM, 3:7); m.p. 86.5–87°C; lit. [64] 86°C; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 3.90$ (s, 3H; OCH$_3$), 7.04 (d, $J = 9.0$ Hz, 2H; Ar CH), 7.39 (t, $J = 7.5$ Hz, 2H; Ar CH), 7.99 (t, $J = 7.5$ Hz, 2H; Ar CH), 7.58–7.64 ppm (m, 4H; Ar CH); ^{13}C NMR (100.6 MHz, CDCl$_3$): $\delta = 55.4$ (OCH$_3$), 114.3, 126.7, 126.8, 128.2 and 128.8 (Ar CH), 133.8, 140.9 and 159.2 ppm (quat. C); IR (KBr): $\tilde{v}_{max} = 3033$ (w), 3002 (w), 2961 (w), 2836 (w), 1606 (s), 1522 (s), 1488 (s), 1464 (w), 1438 (w), 1288 (m), 1270 (m), 1251 (s), 1201 (s), 1184 (m), 1035 (s), 834 (s), 760 (s), 688 cm^{-1} (s); MS (GC CI+): m/z (%): 184.1 ([MH]$^+$, 100), 169.1 (22), 148.1 (25), 141.1 (22), 115.1 (16); HRMS ([MH]$^+$) requires m/z 184.0888, found 184.0883.
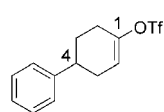
4-Phenyl-1-cyclohexen-1-yl triflate (27):[63] KHMDS in toluene (5.00 mL of a 0.5 M solution, 2.50 mmol) was added slowly to a solution of 4-phenyl-1-cyclohexanone (**30**; 0.400 g, 2.30 mmol) in THF (10 mL) at −78°C under argon. The solution was allowed to warm to room temperature, then it was stirred for 1 h. The reaction mixture was cooled to −78°C and a solution of N-phenyltrifluoromethanesulfonimide (0.940 g, 2.63 mmol) in THF (5 mL) was added by syringe. The reaction mixture was allowed to warm to room temperature, then it was stirred for 2 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography (PE/DCM, 9:1) to give **27** (0.680 g, 97%) as a colourless liquid.

$R_f = 0.24$ (PE/DCM, 9:1); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 1.95$–2.04 (m, 1H), 2.08–2.15 (m, 1H), 2.34–2.64 (m, 4H), 2.85–2.94 (m, 1H), 5.90 (dt, $J_1 = 2.0$, $J_2 = 3.0$ Hz, 1H; H2), 7.20–7.32 (m, 3H; Ar CH), 7.35–7.40 ppm (m, 2H; Ar CH); ^{13}C NMR (100.6 MHz, CDCl$_3$): $\delta = 27.9$ (CH$_2$), 29.7 (CH$_2$), 31.6 (CH$_2$), 38.7 (CH), 118.1 (C2), 118.6 (q, $J_{CF} = 320$ Hz, CF$_3$), 126.7, 126.8 and 128.6 (Ar CH), 144.6 (quat. C), 149.0 ppm (quat. C); IR (thin film): $\tilde{v}_{max} = 3064$ (w), 3031 (w), 2925 (m), 1692 (m), 1495 (m), 1418

(s), 1247 (s), 1209 (s), 1142 (s), 1054 (s), 1026 (s), 894 (s), 861 (s), 760 (m), 700 (s), 617 cm^{-1} (s); MS (GC CI+): m/z (%): 324.1 ([MNH$_4$]$^+$, 4), 190.1 (15), 173.1 (16), 157.1 (7), 104.1 (100); HRMS ([MNH$_4$]$^+$) requires m/z 324.0881, found 324.0865.
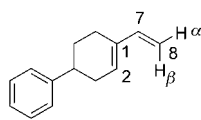
4-Phenyl-1-vinyl-1-cyclohexene (29):[64] 4-Phenyl-1-cyclohexen-1-yl triflate (**27**; 257 mg) and tri-n-butylvinylstannane (**28**; 295 mg) were coupled by using the general procedure with conditions **A** for 1 h. Column chromatography (PE) gave **29** (152 mg, 98%) as a colourless liquid.

$R_f = 0.39$ (PE); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 1.79$–1.91 (m, 1H), 2.06–2.14 (m, 1H), 2.26–2.54 (m, 4H), 2.80–2.91 (m, 1H), 5.01 (d, $J = 11.0$ Hz, 1H; H8α), 5.17 (d, $J = 17.5$ Hz, 1H; H8β), 5.90 (apparent d, $J = 4.5$ Hz, 1H; H2), 6.47 (d, $J_1 = 11.0$, $J_2 = 17.5$ Hz, 1H; H7), 7.20–7.40 ppm (m, 5H; Ar CH); ^{13}C NMR (100.6 MHz, CDCl$_3$): $\delta = 24.4$ (CH$_2$), 29.6 (CH$_2$), 34.0 (CH$_2$), 40.3 (CH), 110.4 (C8), 126.1, 126.9 and 128.4 (Ar CH), 129.1 (C7), 135.9 (quat. C), 139.7 (C2), 146.8 ppm (quat. C); IR (thin film): $\tilde{v}_{max} = 3086$ (m), 3061 (m), 3027 (m), 3002 (m), 2919 (s), 2835 (m), 1644 (m), 1605 (s), 1497 (m), 1453 (m), 989 (m), 894 (s), 829 (m), 760 (s), 699 cm^{-1} (s); MS (GC CI+): m/z (%): 185.1 ([MH]$^+$, 100), 170.1 (42), 104.1 (25); HRMS ([MH]$^+$) requires m/z 185.1330, found 185.1329.
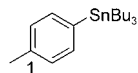
4-(Tri-n-butylstannyl)toluene (32):[65] p-Tolylmagnesium bromide (**44**) in diethyl ether (28.0 mL of a 1.0 M solution, 280 mmol) and Bu$_3$SnCl (5.00 mL, 184 mmol) were stirred in THF (25 mL) at 30°C under argon for 3 h. MeOH (25 mL) was slowly added to the cooled solution, and the mixture was stirred at room temperature for an additional 30 min. The solvent was removed under reduced pressure and the residue was dissolved in DCM (100 mL). The DCM solution was then washed with water (100 mL), dried over Na$_2$SO$_4$/MgSO$_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography (PE) to give **32** (6.60 g, 94%) as a colourless liquid.

$R_f = 0.48$ (PE); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 0.98$ (t, $J = 7.5$ Hz, 9H; CH$_2$C*H*$_3$), 1.04–1.22 (m, 6H; SnC*H*$_2$), 1.42 (sextet, $J = 7.5$ Hz, 6H; C*H*$_2$CH$_3$), 1.53–1.74 (m, 6H; C*H*$_2$CH$_2$CH$_3$), 2.41 (s, 3H; Ar CH$_3$), 7.23 (d, $J = 8.0$ Hz, 2H; H2, 6), 7.45 ppm (d, $J = 8.0$ Hz, 2H; H3, 5); ^{13}C NMR (100.6 MHz, CDCl$_3$): $\delta = 9.6$ (SnCH$_2$), 13.8 (CH$_2$CH$_3$), 21.5 (Ar-CH$_3$), 27.5 (CH$_2$CH$_3$), 29.2 (CH$_2$CH$_2$CH$_3$), 128.9 (C2, 6), 136.5 (C3, 5), 137.7 and 137.9 ppm (quat. C); IR (KBr): $\tilde{v}_{max} = 3061$ (w), 3006 (w), 2957 (s), 2925 (s), 2871 (m), 2854 (m), 1464 (m), 1069 (m), 790 cm^{-1} (m); MS (GC CI+): m/z (%): 342.1 ([M(^{120}Sn)NH$_4$]$^+$−C$_4$H$_{10}$, 22), 325.1 ([M(^{120}Sn)H]$^+$−C$_4$H$_{10}$, 21), 308.1 (100), 291.1 (63); HRMS ([M(^{120}Sn)H]$^+$−C$_4$H$_{10}$) requires m/z 325.0978, found 325.0965.
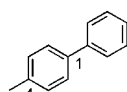
4-Methylbiphenyl (33): Bromobenzene (**31**; 132 mg) and 4-(tri-n-butylstannyl)toluene (**32**; 354 mg) were coupled by using the general procedure with conditions **B** for 15 h. Column chromatography (PE) gave **33** (138 mg, 98%) as a white solid.

$R_f = 0.36$ (PE); m.p. 43–44°C; lit. [66] 44.5–46.5°C; ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 2.50$ (s, 3H; CH$_3$), 7.32–7.37 (m, 2H; Ar CH), 7.40–7.47 (m, 1H; Ar CH), 7.50–7.57 (m, 2H; Ar CH), 7.57–7.62 (m, 2H; Ar CH), 7.67–7.72 ppm (m, 2H; Ar CH); ^{13}C NMR (100.6 MHz, CDCl$_3$): $\delta = 21.2$ (CH$_3$), 127.06, 127.08, 128.80, 128.84 and 129.6 (Ar CH), 137.1, 138.4 and 141.2 ppm (quat. C); IR (KBr): $\tilde{v}_{max} = 3030$ (w), 2915 (w), 1487 (m), 823 (m), 804 (w), 755 (s), 735 (w), 690 cm^{-1} (m); MS (GC CI+): m/z (%): 168.1 ([$M^•$]$^+$, 100), 70.1 (28); HRMS ([$M^•$]$^+$) requires m/z 168.0939, found 168.0943.
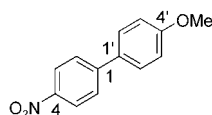
4′-Methoxy-4-nitrobiphenyl (11): 4-Bromoanisole (**10**; 157 mg) and 4-(tri-n-butylstannyl)nitrobenzene (**7**; 383 mg) were coupled by using the general procedure with conditions **B** for 15 h. Column chromatography (PE/DCM, 1:1) gave **11** (187 mg, 97%) as a yellow solid.

$R_f = 0.31$ (PE/DCM, 1:1); m.p. 105–105.5°C; lit. [43] 106–107; ^{1}H NMR (400 MHz, CDCl$_3$):

δ = 3.87 (s, 3H; OCH$_3$), 7.01 (apparent d, J = 9.0 Hz, 2H; H3′, 5′), 7.58 (apparent d, J = 9.0 Hz, 2H; H2′, 6′), 7.67 (apparent d, J = 9.0 Hz, 2H; H2, 6), 8.24 ppm (apparent d, J = 9.0 Hz, 2H; H3, 5); ^{13}C NMR (100.6 MHz, CDCl$_3$): δ = 55.4 (OCH$_3$), 114.6 (C3′, 5′), 124.1 (C3, 5), 127.0 (C2, 6), 128.5 (C2′, 6′), 131.0, 146.5, 147.1 and 160.5 ppm (quat. C); IR (KBr): $\tilde{v}_{max}$ = 2967 (w), 2930 (w), 2835 (w), 1600 (m), 1508 (s, NO$_2$ str), 1343 (s, NO$_2$ str), 1251 (s), 1186 (m), 1107 (w), 1033 (w), 1014 (w), 838 (w), 756 (w), 722 cm^{-1} (w); MS (CI+): m/z (%): 247.1 ([MNH$_4$]$^+$, 60), 229.0 ([M·]$^+$, 51), 214.0 (24), 200.1 (100), 186.1 (50).
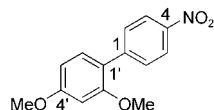
2′,4′-Dimethoxy-4-nitrobiphenyl (35): 2,4-Dimethoxybromobenzene (**34**; 182 mg) and 4-(tri-n-butylstannyl)nitrobenzene (**7**; 383 mg) were coupled by using the general procedure with conditions **B** for 15 h. Column chromatography (PE/DCM, 3:7) gave **35** (194 mg, 89%) as a bright yellow solid.

R_f = 0.38 (PE/DCM, 3:7); m.p. 124–125 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 3.84 (s, 3H; CH$_3$), 3.88 (s, 3H; CH$_3$), 6.57–6.63 (m, 2H; H3′, 5′), 7.28 (d, J = 8.5 Hz, 1H; H6′), 7.67 (apparent d, J = 9.0 Hz, 2H; H2, 6), 8.24 ppm (apparent d, J = 9.0 Hz, 2H; H3, 5); ^{13}C NMR (100.6 MHz, CDCl$_3$): δ = 55.5 and 55.6 (CH$_3$), 99.1 and 105.1 (C3′, 5′), 121.0 (quat. C), 123.2 (C3, 5), 130.0 (C2, 6), 131.3 (C6′), 145.4, 146.2, 157.6 and 161.5 ppm (quat. C); IR (KBr): $\tilde{v}_{max}$ = 2968 (w), 2950 (w), 2841 (w), 1615 (s), 1598 (s), 1576 (s), 1511 (s, NO$_2$ str), 1343 (s, NO$_2$ str), 1311 (s), 1284 (s), 1212 (s), 1166 (s), 1142 (m), 1110 (m), 1050 (m), 1030 (m), 854 (m), 825 (s), 794 (m), 754 (m), 693 cm^{-1} (m); MS (CI+): m/z (%): 277.2 [MNH$_4$]$^+$, 20), 260.2 (100), 244.2 (22), 230.2 (57), 214.2 (12), 198.1 (26), 183.1 (20); HRMS ([MH]$^+$) requires m/z 260.0923, found 260.0930.
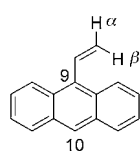
9-Vinylanthracene (37): 9-Bromoanthracene (**36**; 216 mg, 0.840 mmol) and tri-n-butylvinylstannane (**28**; 346 mg, 1.09 mmol) were coupled by using the general procedure with conditions **B** for 15 h. Column chromatography (PE) gave **37** (165 mg, 96%) as a pale yellow solid.

R_f = 0.27 (PE); m.p. 57–60 °C; lit. [67] 60–63 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.68 (d, J = 18.0 Hz, 1H; C=CHβ), 6.06 (d, J = 11.5 Hz, 1H; C=CHα), 7.48–7.60 (m, 5H; Ar CH and C=CH), 8.00–8.08 (m, 2H; Ar CH), 8.35–8.40 (m, 2H; Ar CH), 8.42 ppm (s, 1H; H10); ^{13}C NMR (100.6 MHz, CDCl$_3$): δ = 122.9 (C=CH$_2$), 125.1, 125.4, 126.0, 126.4 and 128.6 (Ar CH), 129.2 and 131.4 (quat. C), 133.6 (C=CH), 133.7 ppm (quat. C); IR (KBr): $\tilde{v}_{max}$ = 3050 (m), 1622 (m), 1442 (m), 1338 (m), 1158 (m), 991 (m), 932 (m), 884 (m), 843 (m), 734 cm^{-1} (s); MS (GC CI+): m/z (%): 205.1 ([MH]$^+$, 100); HRMS ([MH]$^+$) requires m/z 205.1017, found 205.1012.
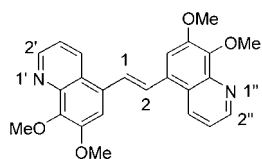
(E)-Bis(7,8-dimethoxyquinol-5-yl)ethene (40): 5-Bromo-7,8-dimethoxyquinoline (**38**)[69] (236 mg, 0.880 mmol) and (E)-1,2-bis(tri-n-butylstannyl)ethene (**39**)[68] (255 mg, 0.420 mmol) were coupled by using the general procedure with conditions **B** [PdCl$_2$ (3 mg, 0.017 mmol), PtBu$_3$ (9 μL, 0.036 mmol), CuI (7 mg, 0.037 mmol), CsF (255 mg, 1.68 mmol), DMF (2 mL)] for 15 h. Column chromatography (DCM/acetone, 1:1) gave **40** (157 mg, 93%) as a yellow solid.

R_f = 0.32 (DCM/acetone, 1:1); m.p. 211–212 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 4.12 (s, 3H; OCH$_3$), 4.18 (s, 3H; OCH$_3$), 7.34 (dd, J_1 = 4.0, J_2 = 8.5 Hz, 2H; H3′, 3″), 7.66 (s, 2H; H1, H2, or H6′, H6″), 7.72 (s, 2H; H1, H2, or H6′, H6″), 8.46 (dd, J_1 = 1.5, J_2 = 8.5, 2H; H4′, 4″), 8.97 (dd, J_1 = 1.5, J_2 = 4.0, 2H; H2′, 2″); ^{13}C NMR (100.6 MHz, CDCl$_3$): δ = 57.1 and 61.9 (OCH$_3$), 113.3 (C1, 2, or C6′, 6″), 119.4 (C3′, 3″), 122.6 (quat. C), 127.8 (C1, 2, or C6′, 6″), 130.8 (quat. C), 132.2 (C4′, 4″), 143.59, 143.64 (quat. C), 150.5 (C2′, 2″), 151.3 ppm (quat. C); IR (KBr): $\tilde{v}_{max}$ = 2999 (w), 2935 (w), 2831 (w), 1594 (s), 1500 (s), 1476 (s), 1334 (s), 1307 (m), 1251 (m), 1165 (m), 1130 (s), 1082 (s), 790 cm^{-1} (m); MS (ES+): m/z (%): 827.1 (51), 425.0 ([MNa]$^+$, 45), 403.0 ([MH]$^+$, 100); HRMS ([MH]$^+$) requires m/z 403.1658, found 403.1653.
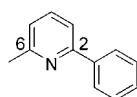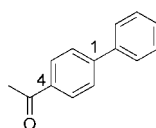
2-Phenyl-6-methylpyridine (42):[70] 2-Bromo-6-methylpyridine (**41**; 144 mg) and phenyltri-n-butylstannane (**25**; 341 mg) were coupled by using the general procedure with conditions **B** for 15 h. Column chromatography (DCM) gave **42** (129 mg, 91%) as a pale yellow liquid.

R_f = 0.27 (DCM); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.65 (s, 3H; CH$_3$), 7.11 (d, J = 7.5 Hz, 1H; Ar CH), 7.38–7.55 (m, 4H; Ar CH), 7.64 (t, J = 7.5 Hz, 1H; Ar CH), 7.98–8.01 ppm (m, 2H; Ar CH); ^{13}C NMR (100.6 MHz, CDCl$_3$): δ = 24.8 (CH$_3$), 117.6, 121.6, 127.0, 128.7 and 136.9 (Ar CH), 139.8, 157.0 and 158.4 ppm (quat. C); IR (thin film): $\tilde{v}_{max}$ = 3061 (w Ar CH str), 2956 (w), 2923 (w), 1591 (s), 1572 (s), 1459 (s), 1160 (w), 1029 (w), 805 (m), 757 (s), 694 cm^{-1} (s); MS (ES+): m/z (%): 169.5 ([MH]$^+$, 100).
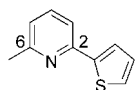
2-(Thiophen-2′-yl)-6-methylpyridine (43):[71] 2-Bromo-6-methylpyridine (**41**; 144 mg) and 2-(tri-n-butylstannyl)thiophene (**18**; 347 mg) were coupled by using the general procedure with conditions **B** for 15 h. Column chromatography (PE/DCM, 1:1) gave **43** (144 mg, 98%) as a pale yellow liquid.

R_f = 0.35 (PE/DCM, 1:1); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.59 (s, 3H; CH$_3$), 7.00 (d, J = 7.5 Hz, 1H; Ar CH), 7.11 (dd, J_1 = 3.5, J_2 = 5.0 Hz, 1H; Ar CH), 7.38 (dd, J_1 = 1.0, J_2 = 5.0 Hz, 1H; Ar CH), 7.45 (d, J = 8.0 Hz, 1H; Ar CH), 7.54 (dd, J_1 = 4.0, J_2 = 7.5 Hz, 1H; Ar CH), 7.58 ppm (d, J_1 = 1.0, J_2 = 3.5 Hz, 1H; Ar CH); ^{13}C NMR (100.6 MHz, CDCl$_3$): δ = 24.6 (CH$_3$), 115.9, 121.5, 124.4, 127.2, 127.9 and 136.8 (Ar CH), 145.2, 151.9 and 158.4 ppm (quat. C); IR (thin film): $\tilde{v}_{max}$ = 3071 (w), 2959 (w), 2922 (w), 1587 (s), 1574 (s), 1532 (m), 1456 (s), 1434 (m), 1290 (w), 1232 (m), 1161 (m), 993 (w), 910 (m), 859 (m), 837 (m), 787 (s), 734 (s), 705 cm^{-1} (s); MS (ES+): m/z (%): 175.6 ([MH]$^+$, 100); HRMS ([MH]$^+$) requires m/z 176.0534, found 176.0539.

4-Acetylbiphenyl (46): 4-Chloroacetophenone (**45**; 130 mg) and phenyltri-n-butylstannane (**25**; 341 mg) were coupled by using the general procedure with conditions **B** at 100 °C for 15 h. Column chromatography (PE/DCM, 1:1) gave **46** (134 mg, 81%) as a white solid.

R_f = 0.17 (PE/DCM, 1:1); m.p. 116–117 °C; lit. [73] 109–110 °C; ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.64 (s, 3H; CH$_3$), 7.42 (t, J = 7.5 Hz, 1H; Ar CH), 7.49 (t, J = 7.5 Hz, 2H; Ar CH), 7.63 (d, J = 7.5 Hz, 2H; Ar CH), 7.69 (d, J = 8.5 Hz, 2H; H2, 6), 8.03 ppm (d, J = 8.5 Hz, 2H; H2, 6); ^{13}C NMR (100.6 MHz, CDCl$_3$): δ = 26.7 (CH$_3$), 127.2, 127.3, 128.3, 128.9 and 129.0 (Ar CH), 135.8, 139.8 and 145.7 (quat. C), 197.7 ppm (C=O); IR (KBr): $\tilde{v}_{max}$ = 3072 (w), 2997 (w), 2916 (w), 1680 (s, C=O str), 1602 (s), 1404 (m), 1358 (m), 1283 (m), 1264 (s), 1208 (m), 1180 (m), 961 (m), 842 (m), 766 (s), 720 (m), 691 (m), 596 cm^{-1} (m); MS (GC CI+): m/z (%): 197.1 [MH]$^+$, 100), 196.1 (48), 181.1 (45), 152.1 (18), 131.1 (26), 87.0 (20), 71.1 (33), 70.1 (72); HRMS ([MH]$^+$) requires m/z 197.0966, found 197.0972; elemental analysis (%) calcd: C 85.68, H 6.16; found: C 85.33, H 6.18.

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