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Oxidative addition of *N*-halosuccinimides to palladium(0): the discovery of neutral palladium(II) imidate complexes, which enhance Stille coupling of allylic and benzylic halides

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Abstract—The Stille coupling of organostannanes and organohalides, mediated by air and moisture stable palladium(II) phosphine complexes containing succinimide or phthalimide (imidate) ligands, has been investigated. An efficient synthetic route to several palladium(II) complexes containing succinimide and phthalimide ligands, has been developed. *cis*-Bromobis(triphenylphosphine)(*N*-succinimide)palladium(II) [$(Ph_3P)_2Pd(N\text{-Succ})Br$] is shown to mediate the Stille coupling of allylic and benzylic halides with alkenyl, aryl and allyl stannanes. In competition experiments between 4-nitrobromobenzene and benzyl bromide with a *cis*-stannylvinyl ester, $(Ph_3P)_2Pd(N\text{-Succ})Br$ preferentially cross-couples benzyl bromide, whereas with other commonly employed precatalysts 4-nitrobromobenzene undergoes preferential cross-coupling. Furthermore, preferential reaction of deactivated benzyl bromides over activated benzyl bromides is observed for the first time. The type of halide and presence of a succinimide ligand are essential for effective Stille coupling. The type of phosphine ligand is also shown to alter the catalytic activity of palladium(II) succinimide complexes.

1. Introduction

Great progress has been made in the development of transition metal-catalysed processes for the formation of carbon–carbon bonds.[1] Palladium-catalyzed processes, to date, represent the most frequently applied of these reactions and are increasingly being employed in synthetic routes to complex biological targets and therapeutic agents.[2] The Stille coupling reaction between organohalides and organostannanes, mediated by palladium, has attracted considerable attention and has been used as a 'test-bed' for the development of highly active palladium catalysts.[3,4] The broad utility of the Stille reaction is primarily due to the accessibility of a diverse range of organostannanes, their air and moisture stability and their excellent functional group compatibility, although the toxicity of organotin compounds can present problems. The scope of the Stille reaction has been substantially expanded recently, through state-of-the-art developments in the creation of highly active catalysts that operate under mild conditions.[5] Room temperature protocols for reactions employing organobromides, including hindered derivatives, are now available. Coupling of deactivated substrates such as aryl chlorides, not possible prior to 1998, is facilitated by electron rich bulky two-electron donor ligands such as $t\text{-}Bu_3P$[6] and *N*-heterocyclic carbenes.[7] The importance attached to the use of an activating donor ligand (strong σ-donor) derives from promotion of the oxidative addition process. Steric and electronic properties of ligands also produce pronounced effects, usually by influencing the intrinsic stability/reactivity of the palladium intermediates throughout the catalytic cycle.[8] The use of co-catalysts/additives and variation of the solvent can also be employed to optimize the efficiency of Stille coupling processes.[9]

Halide counterions are also known to play an important role in palladium-mediated cross-coupling processes, as well as in other transition metal-mediated reactions.[10] Pseudohalides (OAc, OTf) can also be influential: for example, in studies by Bedford and co-workers using palladacycles as pre-catalysts, the catalyst activity and lifetime, were dependent on the nature of the pseudohalide.[11] Comprehensive support for the involvement of halide/pseudohalide anions in palladium-catalysed cross-coupling reactions has been elegantly demonstrated by Amatore and Jutand.[12] Thus, in the presence of halides, the existence of an

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alternative catalytic cycle involving tricoordinated anionic complexes such as $L_2Pd(0)Cl^-$ and $L_2Pd(0)OAc^-$ has been demonstrated. Dimeric anionic palladium–halide complexes such as $[Pd_2I_6][Y_2]$, where $Y=DMFH^+$ or Et_3NH^+, have also been detected.[13] In addition, when palladium(II) precursors, for example, $Pd(Ph_3P)_2Cl_2$ or $Pd(OAc)_2$, are employed in coupling reactions, it has been proposed that anionic complexes are active catalysts as well as low-ligated, palladium '$L_nPd(0)$' (L is usually R_3P and $n=1$ or 2). Importantly, the nature of the halide or pseudohalide influences the reactivity of these palladium intermediates. In the absence of halide, the reduced species undergoes rapid reaction to form metallic palladium, which is clearly a limitation. Halide binding serves to stabilize the $L_nPd(0)$ complex. The halide could also stabilize palladium clusters or colloids, which act as a reservoir[14] of active catalytic Pd(0) species (neutral or anionic).

We have been interested in harnessing halide and pseudohalide effects in the design of improved catalysts for Stille coupling, as this is a potentially tunable property that could be exploited in increasing reactivity and substrate scope, but might also produce selective processes. This interest has been driven by our recent finding that succinimide, a pseudohalide, shows intriguing effects in the Stille reaction.[15] At the present time, it has not been established how this ligand exerts its effect, but it is clearly more than just a simple halide mimetic. Mechanistic studies are ongoing but in this paper, the preparation and application of Pd(II) succinimide and phthalimide complexes are discussed.

2. Results

2.1. The initial observation

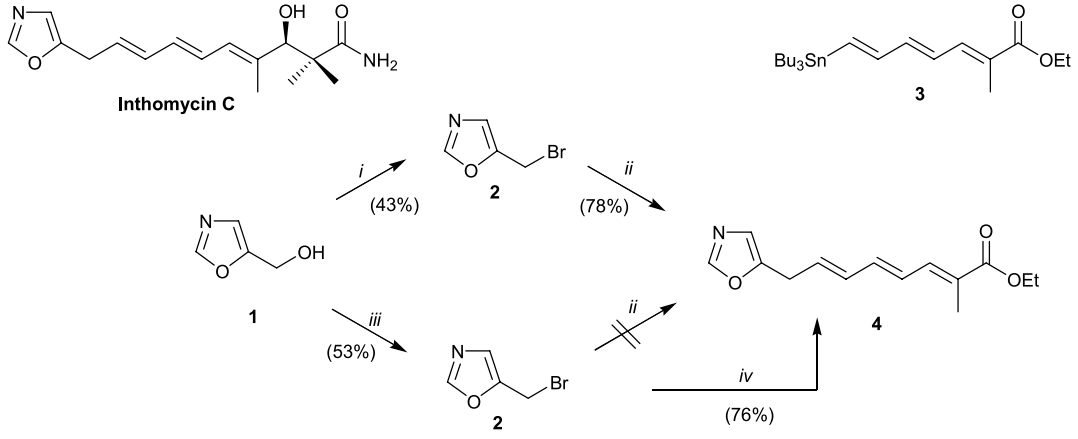
During the course of synthetic studies towards inthomycin C, a Stille coupling of oxazole bromide **2** with *E*,*E*,*E*-triene **3** was investigated (**2**+**3**→**4**, Scheme 1).

Bromide **2** was initially obtained from alcohol **1** using *N*-bromosuccinimide (NBS)/triphenylphosphine.[16] However, it proved to be sensitive to light, temperature, moisture and prolonged chromatography (although at −20 °C in the dark it was largely unchanged after one month); it was therefore semi-purified by passage through a very short silica column. In this form, **2** underwent efficient Stille coupling with organostannane **3** and catalytic $(PPh_3)_4Pd$ to give **4** in 78% yield. As large quantities of **4** were required, the use of CBr_4/Ph_3P[17] was investigated in order to improve the yield of bromide **2**. However, when **2** prepared via this route, was subjected to the Stille reaction as before, no coupling was observed. The reaction was repeated many times without success (purification of solvents/reagents and the use of freshly prepared $(Ph_3P)_4Pd$ did not alter the outcome).

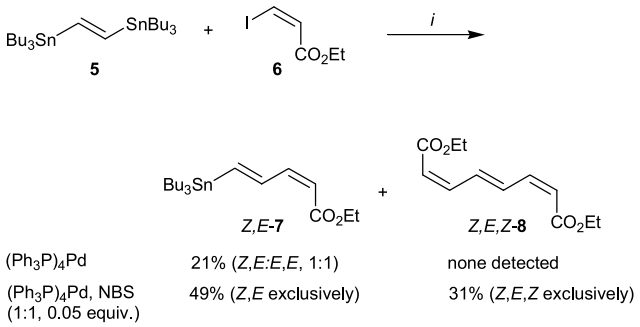
This surprising result led us to compare the two procedures. It seemed likely that traces of an 'impurity' were being carried through undetected with **2**; that is, something remaining from the NBS method could be acting to promote the coupling process or something from the CBr_4 method could be inhibiting coupling. The CBr_4/Ph_3P method produces Ph_3PO and $CHBr_3$, but excess starting reagents could also be present. However, $CHBr_3$ might be expected to enhance the Stille reaction as $CHBr_3$ is known to react with Pd_2dba_3/t-Bu_3P to give a palladium(I) dimer $[Pd_2(\mu\text{-}Br)_2(t\text{-}Bu_3P)_2]$,[18] which is a highly active catalyst for cross-coupling (amination)[19] and an excellent source of mono-ligated palladium(0) 't-Bu_3P-Pd(0)'.

Given that Ph_3P and Ph_3PO are present in both methods, attention was turned to the importance of the NBS. It seemed possible that trace amounts of NBS could be carried through the silica column with **2**, then activating the subsequent Stille coupling in a manner yet to be revealed. Indeed, on closer examination of the ^1H NMR spectrum of **2** used in the successful coupling process, a small singlet was observed at δ 2.7 ($CDCl_3$, 400 MHz), which corresponds to NBS. We therefore repeated the Stille coupling reaction of **2**, formed using the CBr_4 method, with stannane **3** but on this occasion added an equimolar amount of NBS with respect to the $(Ph_3P)_4Pd$. We were delighted to observe that this formerly unsuccessful process, now proceeded to give **4** in 76% yield.

In order to establish that the above observation had some generality, we studied its value in another problematic process investigated during the inthomycin programme (Scheme 2).



Scheme 1. i, Ph_3P, NBS, THF, 25 °C, 1 h; ii, **3** (1.05 equiv), $Pd(Ph_3P)_4$ (0.05 equiv), toluene, reflux, 20 h; iii, Ph_3P, CBr_4, CH_2Cl_2, 0 °C; iv, as for ii with added NBS (0.05 equiv).



Scheme 2. i, Toluene, reflux, 3 h.

Reaction of *E*-bis-1,2-(tributylstannyl)ethene **5**, with ethyl 2-iodo-2*Z*-propenoate **6** using $(Ph_3P)_4Pd$ had been shown to give 11% of the mono-coupled product *Z*,*E*-**7** and 10% of the corresponding *E*,*E*-isomer. Repeating the reaction but with addition of an equimolar amount of NBS with respect to the $(Ph_3P)_4Pd$, resulted in the formation of 49% of *Z*,*E*-**7** and 31% of *Z*,*E*,*Z*-**8**. The stereoselectivity observed in the NBS-modified process was noteworthy, as was the improvement of the overall yield from 21 to 80%.

The results shown in Schemes 1 and 2 indicated that the combination of NBS and $(Ph_3P)_4Pd$ had generated a highly active palladium catalyst. A search of the literature revealed that the oxidative addition of NBS to palladium(0) and platinum(0) precursors to give air and moisture stable complexes *cis*-$(Ph_3P)_2M(N\text{-Succ})Br$ (M=Pd or Pt), had been reported by Serrano and co-workers, although the catalytic properties of these complexes were not studied.[20] We therefore, decided to prepare such complexes and investigate their value in Stille coupling reactions.

2.2. Preparation of Pd(imidate)$(Ph_3P)_2$X complexes (X= halide or imidate; imidate=succinimide or phthalimide)

The published procedure for the preparation of *cis*-$(Ph_3P)_2$-Pd(*N*-Succ)Br **9** utilised Pd_2dba_3 dba (dba=*E*,*E*-dibenzylidene acetone) and NBS in dry CH_2Cl_2 at ambient temperature, followed by addition of 2 equiv of Ph_3P. In our hands **9** was obtained in low yields (~10%) with another palladium complex being isolated as a yellow precipitate in 30–40% yields, whose formation was dependent on a number of variables (vide infra). Recrystallisation of this major product followed by X-ray crystallography (Fig. 1), allowed identification as *trans*-$(Ph_3P)_2PdBr_2$ (^{31}P NMR, 202 MHz, CD_2Cl_2, δ 21.93). Changing to $(Ph_3P)_4Pd$ as the palladium(0) source, resulted in a rapid initial reaction but low conversion, as the additional phosphine removes NBS from the system as the phosphonium salt: addition of excess NBS (~3 equiv) pushes the reaction to completion, but the yield of **9**, although improved, was modest (31%).

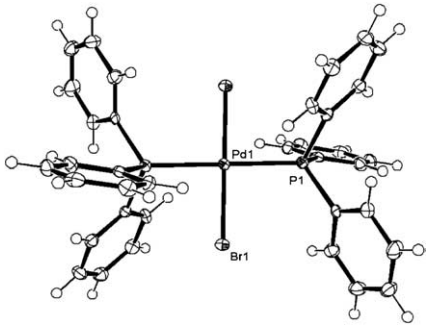
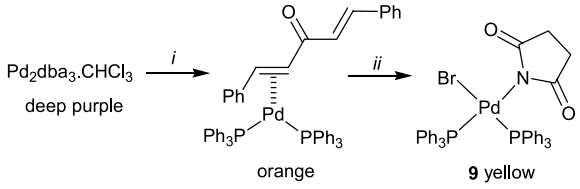


Figure 1. X-ray crystal structure of $(Ph_3P)_2PdBr_2$. Thermal ellipsoids are shown at 50% probability level.

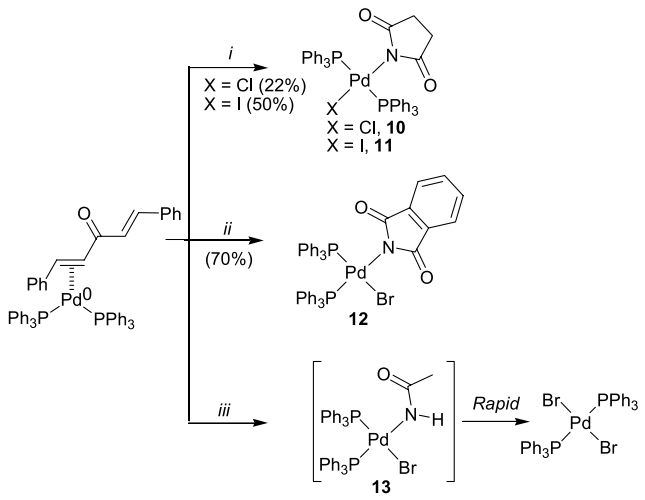
We discovered that improved yields of **9** could be obtained from Pd_2dba_3 dba simply by reversing the order of addition of reagents given in the published procedure.[20] Reaction of Pd_2dba_3 dba (1 equiv) with Ph_3P (4 equiv) in CH_2Cl_2 produced an intense orange colour, which can be attributed to the formation of '$(Ph_3P)_2Pd(0)$-η^2-dba' (Scheme 3).[21] Addition of a solution of NBS in CH_2Cl_2 at 21 °C after 0.15 h caused the reaction mixture to change to a bright yellow colour. The small amount of precipitate, which is *trans*-$(Ph_3P)_2PdBr_2$ is then removed by filtration. Addition of petroleum ether to the resultant filtrate produced a creamy yellow precipitate of **9** in yields, which varied between 20 and 52%. However, switching to $Pd_2dba_3\cdot CHCl_3$ as the palladium source resulted in an improvement to 74% yield. Complex **9** was crystallised from CH_2Cl_2/diethyl ether (1:5, 24 h, −20 °C) to give fine yellow crystals, which were characterised by X-ray diffraction and NMR spectroscopic studies.[15a]



Scheme 3. i, $Pd_2dba_3\cdot CHCl_3$ (0.5 equiv), Ph_3P (2 equiv), CH_2Cl_2, 25 °C, 0.2 h; ii, NBS (1 equiv), 0.2 h.

Related palladium complexes such as $Pd_2dba_3\cdot$solvent; solvent=benzene, toluene or CH_2Cl_2, can also be used to prepare **9**, as can $Pd_2[3,5,3',5'\text{-}(MeO)_4\text{-dba}]_3\cdot CH_2Cl_2$.[22] In this complex, the electron-rich dba dissociates more rapidly from palladium(0) than unsubstituted dba, increasing the relative rate of the oxidative addition process.[23] Using this precursor, a yield of 82% of **9** was attained. It should be noted that small quantities of *trans*-$(Ph_3P)_2PdBr_2$ were obtained if the reaction concentration exceeded 11 mM. Increasing the reaction temperature also leads to increasing amounts of *trans*-$(Ph_3P)_2PdBr_2$ but keeping the reaction temperature in the range 15–21 °C avoids the problem. It is believed that *trans*-$(Ph_3P)_2PdBr_2$ is formed via a bridged halide intermediate species, produced by dimerisation/disproportionation of two molecules of **9**.

We next examined whether other *N*-halo-succinimides, phthalimides and acetamides could used to prepare similar complexes to **9**. Using the optimum procedure for **9**, but employing *N*-chlorosuccinimide (NCS) and *N*-iodosuccinimide (NIS), gave the chloro- **10** and iodo- **11** analogues in ca. 22, and 50% yields, respectively, (Scheme 4). The lower yields are again due to the formation of complexes of the type $(Ph_3P)_2PdX_2$ (X=Cl, I). In fact, it was not possible to isolate **10** in pure form due to this impurity. Complexes **10** and **11** exhibit a *trans*-geometry around the palladium(II)



Scheme 4. Synthesis of other imidato palladium(II) complexes. i, $Pd_2dba_3\cdot CHCl_3$ (0.5 equiv), Ph_3P (2.0 equiv), CH_2Cl_2, 25 °C, 0.2 h, then NBS, NCS or NIS (1 equiv), 0.2 h; ii, as for i, but using NBP (1 equiv); iii, as for i, but using NBA (1 equiv).

centre (based on a singlet signals observed by ^{31}P NMR spectroscopy). On steric grounds, one might predict such a geometry for iodide **11**, but the fact that the NBS reaction gave *cis*-**9**, led us to predict that **10** might be *cis* as well. We presume that for **10** the *trans*-geometry is best rationalised by the relatively strong π-donor nature of chlorine—and with succinimide being a good π-acceptor, the *trans*-effect dominates.

It was not possible to obtain an X-ray crystal structure of chloride **10** but the X-ray structure of **11** was solved, confirming the *trans*-geometry and indicating extensive π-stacking interactions between the phosphorus aryl substituents and the succinimide methylene groups (Fig. 2). This interaction appears to shield both faces of the succinimide ring, but as two signals are observed for the succinimide methylene protons in $CDCl_3$, it would appear that the faces are differentially shielded.

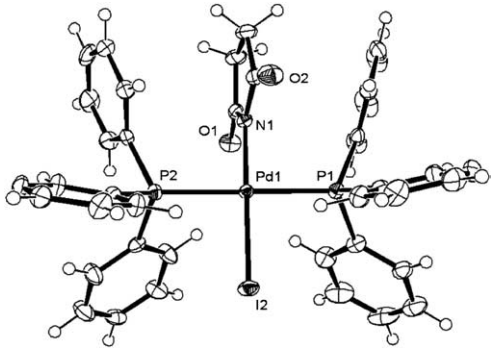
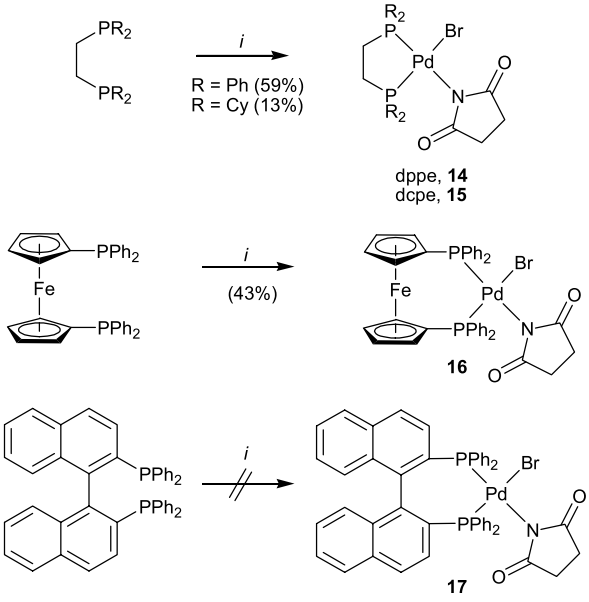


Figure 2. X-ray structure of **11**. Thermal ellipsoids are shown at 50% probability level.

The oxidative addition of *N*-bromophthalimide (NBP) to $Pd_2dba_3\cdot CHCl_3$ proceeded in a similar manner to the reaction with NBS, providing **12** in 70% yield (Scheme 4). The *cis*-geometry was confirmed by two inequivalent phosphorus signals as doublets at δ 24.89 and 33.80. The two-bond phosphorus–phosphorus coupling constant ($^2J_{PP}=8.39$ Hz) is similar to that seen in **9** ($^2J_{PP}=8.49$ Hz). Interestingly, the formation of $(Ph_3P)_2PdBr_2$ is not observed in this reaction. On the other hand, the oxidative addition of *N*-bromoacetamide (NBA) to $Pd_2dba_3\cdot CHCl_3$ to yield **13** was unsuccessful, affording $(Ph_3P)_2PdBr_2$ in 49% yield.

2.3. Preparation of succinimide complexes containing bidentate ligands

Reaction of $Pd_2dba_3\cdot CHCl_3$ with bidentate ligands, followed by oxidative addition with NBS was achieved using 1,2-bis(diphenylphosphino)ethane (dppe), 1,2-bis(dicyclohexylphosphino)ethane (dcpe) and 1,1′-bis(diphenylphosphino)ferrocene (dppf) (Scheme 5). For dppe, **14** was isolated in 59% yield (δ 23.95, br s; and 61.87, br s; ^{31}P NMR, 161.2 MHz, $CDCl_3$), whereas the more electron rich and bulky dcpe ligand gave **15** in a poor 13% yield (δ 88.68, d, $^2J_{PP}=8.39$ Hz; and δ 91.30, d, $^2J_{PP}=8.39$ Hz; ^{31}P NMR, 202 MHz, CD_2Cl_2). The ferrocenyl ligand, dppf, also underwent reaction giving **16** in 43% yield (δ 24.52, br s; and δ 35.10, d, $^2J_{PP}=5.95$ Hz; ^{31}P NMR, 202 MHz, $CDCl_3$). In all three cases the products were formed as the *cis*-isomers. The reaction of (±)-BINAP was also attempted, but the expected complex **17** was not formed (several species were shown to be present by ^{31}P NMR spectroscopy).

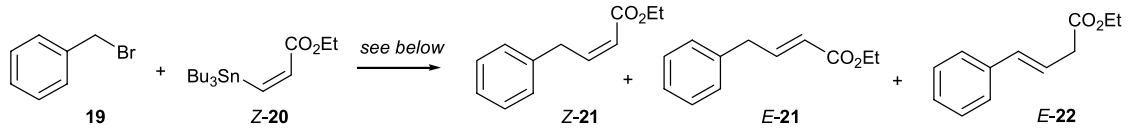


Scheme 5. i, $Pd_2dba_3\cdot CHCl_3$ (0.5 equiv), ligand (1.0 equiv), CH_2Cl_2, 25 °C, 0.2 h, then add NBS (1 equiv), 0.2 h. dppe = 1,2-bis(diphenyl phosphino)ethane, dcpe = 1,2-bis(dicyclohexylphosphino)ethane and dppf = 1,1′-bis(diphenylphosphino)ferrocene.

2.4. Stille coupling of allylic and benzylic substrates

With several palladium(II) imidate complexes in hand, we moved on to study their catalytic properties. The Stille coupling of benzyl bromide **19** with *Z*-organostannane **20** at 60 °C to give *Z*-**2** was used as the benchmark reaction (the reactions proceed significantly slower at temperatures <50 °C). The reactions mediated by our novel palladium imidate catalyst systems and a range of related catalysts/

Table 1. Comparison of various palladium complexes in the benchmark Stille coupling reaction[a]



19 *Z*-**20** *Z*-**21** *E*-**21** *E*-**22**

Entry	Complex	Time/h	Isolated yields/%[b]		
			Z-**21**	*E*-**21**	**22**
1	$(Ph_3P)_4Pd$[c]	18	17	—	—
2	$Pd(OAc)_2$, Ph_3P[d]	18	16	25	5
3	$Pd_2(dba)_3$.dba, Ph_3P[e]	18	13	28	—
4	$(Ph_3P)_2PdBr_2$	18	23	—	—
5	$(Ph_3P)_2Pd(Bn)Br$	18	19	30	5[f]
6	$(Ph_3P)_2Pd(Bn)Cl$	18	66	—	—
7	$(Ph_3P)_4Pd$, NBS[g]	18	83	—	—
8	$(Ph_3P)_4Pd$, NCS[g]	18	61	—	—
9	$(Ph_3P)_4Pd$, NIS[g]	18	33	—	—
10	$Pd_2(dba)_3$.dba, Ph_3P, NBS[g]	18	76	—	—
11	$(Ph_3P)_2Pd$(*N*-succ)Br, **9**	1.5	99	—	—
12	$(Ph_3P)_2Pd$(*N*-succ)I, **11**	18	56	—	—
13	$(Ph_3P)_2Pd$(*N*-phthal)Br,[h] **12**	1.5 (18)	72 (98)	—	—
14	(dppe)Pd(*N*-succ)Br, **14**	18	87	3	—
15	(dcpe)Pd(*N*-succ)Br, **15**	18	43	—	—
16	(dppf)Pd(*N*-succ)Br, **16**	18	64	—	—
17	$(Ph_3P)_2Pd(N\text{-succ})_2$, **23**	48	10	—	—
18	$(Ph_3P)_2Pd(N\text{-phthal})_2$, **24**	48	11	—	—
19	NBS with no added palladium[i]	3	2	—	—

[a] Reaction conditions: benzyl bromide **19** (1 equiv), organostannane *Z*-**20** (1.2 equiv), [Pd] (0.05 equiv), toluene, 60 °C.
[b] Isolated yield after KF work-up and chromatography. Note: A DBU/I_2/Et_2O work-up for this specific reaction results in rapid regio- and stereo-isomerisation (<2 min).
[c] Freshly prepared from $(Ph_3P)_2PdCl_2$, NH_2NH_2 in EtOH at 120 °C.
[d] 3 equiv of Ph_3P were used w.r.t. to Pd.
[e] 2 equiv of Ph_3P were used w.r.t. to Pd.
[f] A mixture of stereoisomers were observed (*E*:*Z*, 1:0.9).
[g] 1 equiv of the *N*-halosuccinimide was added w.r.t. to Pd.
[h] Numbers in brackets are the time after 18 h reaction and the corresponding yield, respectively.
[i] NBS (5 mol%) was added under the reaction conditions described in *a*—but in the absence of palladium (new glassware was employed for this reaction).

precatalysts are summarised in Table 1. The known catalysts/precatalysts $(Ph_3P)_2PdBr_2$, $(Ph_3P)_2Pd(Bn)Br$, $(Ph_3P)_2PdCl_2$ and $(Ph_3P)_4Pd$ are commercially available and $(Ph_3P)_2Pd(Bn)Br$ **18**, was prepared by a reported procedure.[24]

With $(Ph_3P)_4Pd$ alone, a 17% yield of *Z*-**21** was obtained after 24 h (entry 1). Use of a $Pd(OAc)_2/Ph_3P$ combination gave a mixture of the stereoisomers, *Z*-**21** and *E*-**21**, and the regioisomer *E*-**22**, in overall 46% yield (entry 2). Another classic combination is Pd_2dba_3 dba/Ph_3P (entry 3). A mixture of *Z*-**21** and *E*-**21** was obtained in this reaction, which favoured the latter compound, but the overall yield was again modest (41%). The reaction mediated by $(Ph_3P)_2PdBr_2$ gave only a 23% yield of *Z*-**21**, albeit exclusively (entry 4). The neutral oxidative addition intermediate, in Stille couplings mediated by Pd/Ph_3P catalyst systems with benzyl bromide, is $(Ph_3P)_2Pd(Bn)Br$. The use of this complex or $(Ph_3P)_2Pd(Bn)Cl$ in the benchmark reaction gave reasonable yields (entries 5 and 6). However, the former showed poor selectivity, whereas the latter gave *Z*-**21**, exclusively in 66% yield (entry 6).

Having obtained results for comparison, we then examined succinimide-based catalysts. Catalysts formed in situ were examined first (entries 7–10). The addition of NBS to $(Ph_3P)_4Pd$ gave *Z*-**21** as the sole product in an excellent 83% yield (entry 7). Other *N*-halosuccinimides, NCS and NIS, also promoted the reaction, but to a lesser extent (61 and 33%, respectively, entries 8 and 9). The use of the catalyst formed by the addition of NBS to Pd_2dba_3 dba/Ph_3P provided *Z*-**21** exclusively in 76% yield (entry 10).

We then moved on to investigate pre-prepared complexes (entries 11–18). $(Ph_3P)_2Pd$(*N*-succ)Br **9** exhibited the best result by some margin (entry 11). The reaction was complete after 1.5 h and gave a 99% isolated yield of **21** (confirmed by several runs: Lowest yield 92%). The iodo relative, $(Ph_3P)_2Pd$(*N*-succ)I **11** gave a 56% yield, highlighting the importance of the halide (entry 12). It was anticipated that $(Ph_3P)_2Pd$(*N*-phthal)Br **12** would show similar catalytic activity to $(Ph_3P)_2Pd$(*N*-succ)Br **9**, and so it was compared (entry 13). Although the yield was good (72%) after 1.5 h, a reaction time of 18 h was needed for the reaction to reach completion indicating a clear difference between the two imidate ligands.

The bidentate ligand complexes (dppe)Pd(*N*-succ)Br **14**, (dcpe)Pd(*N*-succ)Br **15** and (dppf)Pd(*N*-succ)Br **16** were studied next (entries 14–16); all promoted the reaction but all required longer reaction times than $(Ph_3P)_2Pd$(*N*-succ)Br **9**. For completeness, the $(Ph_3P)_2Pd(N\text{-succ})_2$[15c] **23** and $(Ph_3P)_2Pd(N\text{-phthal})_2$[25] **24** relatives were screened to assess the importance of the halide in the palladium complex (entries 17 and 18). In stark contrast to the other catalysts containing imidate ligands, very poor yields were observed after 48 h (10 and 11% yield, respectively). It is clear that

the presence and nature of the halide are important for the efficacy of this reaction. In the absence of Pd, catalytic NBS (5 mol%), under the same reaction conditions, shows negligible conversion (2% yield, entry 19), confirming the importance of Pd.

It should be noted that when using many of the standard palladium complexes (Table 1, entries 1–6), a precipitate of palladium black is observed whereas with $(Ph_3P)_2Pd$(*N*-succ)Br **9**, the reaction remains yellow (in the absence of air and moisture) at the completion of the coupling process and no precipitate is observed. Also noteworthy is the fact that elevated temperatures can lead to additional isomerisation. For example, coupling using $(Ph_3P)_2Pd$(*N*-succ)Br **9**, which was stereoselective at 60 °C (entry 11), gave isomeric mixtures (*E*:*Z*=80:20) when the reaction was carried out at reflux. We established that this process was mediated by palladium by carrying out control experiments. Thus, pure *Z*-**21** was refluxed in toluene, in the presence and absence of $(Ph_3P)_2Pd$(*N*-succ)Br **9**. In the presence of $(Ph_3P)_2Pd$(*N*-succ)Br after 0.5 h at reflux, *cis–trans* isomerisation was observed by ^1H NMR analysis (*E*:*Z*=35:65) whereas in the absence of palladium, no stereoisomerisation was detected (even after 24 h).

We next carried out experiments to compare coupling reactions of a range of allylic and benzylic substrates using $(Ph_3P)_2Pd$(*N*-succ)Br **9** and other typical catalysts (Table 2). Thus, geranyl bromide **25** underwent coupling with *Z*-stannyl ester *Z*-**20** to give adduct **26** (entry 1). As can be seen, with $(Ph_3P)_2Pd$(*N*-succ)Br **9**- product *E*,*Z*-**26** was obtained in 67% yield, with complete preservation of alkene stereochemistry, whereas the other catalysts gave much lower yields with evidence of product isomerisation.

For the related *E*-stannyl ester *E*-**20** coupling with geranyl bromide **25**, all catalysts gave similar yields, although $(Ph_3P)_2Pd$(*N*-succ)Br **9** was again the catalyst of choice (entry 2). For the coupling between *Z*-**20** and cinnamyl bromide to give *E*,*Z*-**28** (entry 3), the best yield (86%) was again obtained using $(Ph_3P)_2Pd$(*N*-succ)Br **9**. Comparable results were seen in the coupling of *E*-**20** with cinnamyl bromide *E*-**27** (entry 4). Again, complete stereoselectivity was observed in these processes.

The corresponding coupling of benzyl bromide **19** and *E*-**20** was investigated next and predicted to give similar results to the corresponding benchmark study involving benzyl bromide and *Z*-**20** (Table 1), but this turned out not to be the case (entry 5). With all catalysts, the yields were good to excellent (>90% using $(Ph_3P)_2Pd$(Bn)Cl and $(Ph_3P)_2Pd$(*N*-succ)Br **9**). Interestingly, it was noted that the reaction time for the coupling of benzyl bromide **19** and *E*-**20** with $(Ph_3P)_2Pd$(*N*-succ)Br **9** as catalyst was much longer (5 h vs 1.5 h) than that corresponding with *Z*-**20** (Table 2, entry 5 vs Table 1, entry 11). The reaction of phenylstannane **29** with **19** to give **30**, proceeded well with all four catalysts (entry 6).

To assess the substrate scope in benzylic/allylic Stille reactions mediated by $(Ph_3P)_2Pd$(*N*-Succ)Br **9**, several other reactions were studied (Table 3). All but one of the examples gave good yields, with high regio- and stereo-selectivity observed throughout the series. The exception was the reaction of geranyl bromide *E*-**25** with phenylstannane **29**, which give *E*-**37** in only 34% yield after 18 h (entry 4).

Thus, with a range of benzylic (entry 1) and allylic bromides, vinylstannanes **31** and **33**, and phenylstannane **29**, undergo efficient coupling (entries 2,3, 5–7). The reaction of an allylstannane **41** with *E*-cinnamyl bromide *E*-**27**, which is formally an sp^3–sp^3 type of coupling process, also proceeds efficiently (entry 8). Benzyl chloride also underwent efficient coupling reactions (entries 9–10), the reaction with *Z*-**20** at 60 °C giving *Z*-**21** in 81% yield (entry 9). However, 48 h at 60 °C was required for complete consumption of benzyl chloride **43**: Increasing the reaction temperature to 110 °C reduced the reaction time to 18 h (isomerisation is observed if longer reflux times are employed at this temperature). The reaction of *E*-**20**, under the same reactions conditions with elevated temperature, gave *E*-**21** in 68% yield after 18 h (entry 10). A literature survey reveals that few Stille couplings of benzyl chloride have been reported,[4b,15b] and the majority of reactions require harsh conditions or toxic additives, for example, HMPA.

2.5. Stille coupling of aryl substrates

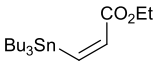
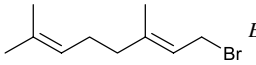
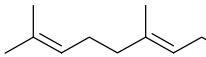
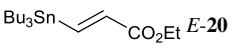
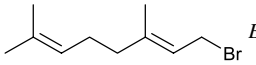
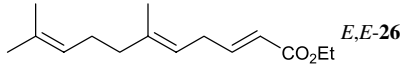
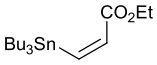
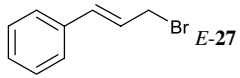
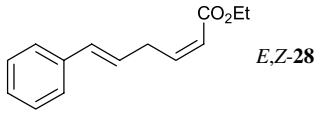
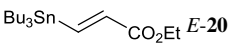
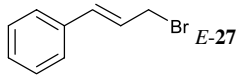
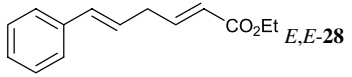
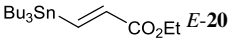
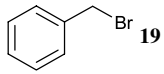
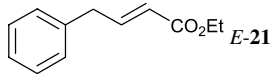
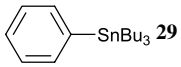
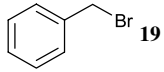
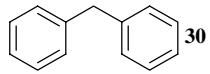
Having established that $(Ph_3P)_2Pd$(*N*-succ)Br **9** is an efficient catalyst for the Stille coupling of allyl and benzylic substrates, coupling reactions with aryl substrates were investigated. 4-Nitrobromobenzene **44** was selected as the model substrate, as it is known to be one of the most active electrophilic substrates for Stille coupling.[5] Tributylvinyltin **33** was chosen as the coupling partner (Scheme 6 and Table 4).

After 5 h at reflux, $(Ph_3P)_4Pd$ gave the coupled product in 65% yield (entry 1). Higher yields were obtained using $(Ph_3P)_2Pd$(Bn)Cl and $(Ph_3P)_2Pd$(Bn)Br (entries 2 and 3, respectively). However, when the reaction was carried out in the presence of the $(Ph_3P)_4Pd$/NBS combination (entry 4), the yield dropped to 35% (after 24 h), showing for the first time that this system could be less active than $(Ph_3P)_4Pd$ alone! $(Ph_3P)_2Pd$(*N*-succ)Br **9** gave an improved yield (66%), but a substantially longer reaction time was required (24 h, entry 5). Thus, for a typical aryl halide Stille coupling, standard catalyst systems are more efficient than both the $(Ph_3P)_4Pd$/NBS combination and $(Ph_3P)_2Pd$(*N*-succ)Br **9**. Similar results were obtained using bromobenzene as the substrate.

2.6. Competition Stille coupling reactions

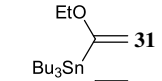
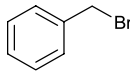
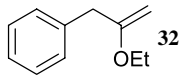
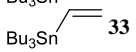
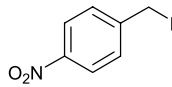
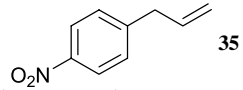
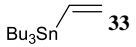
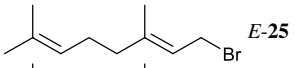
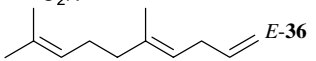
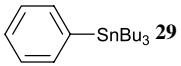
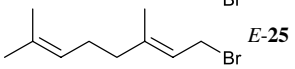
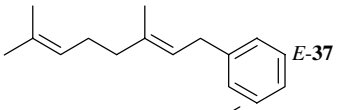
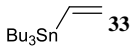
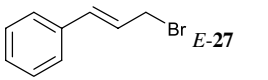
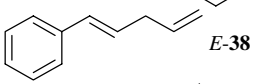
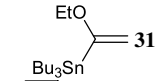
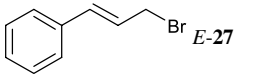
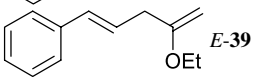
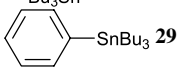
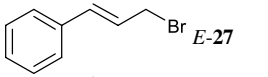
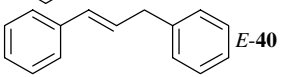
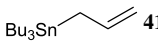
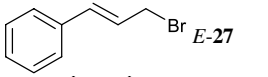
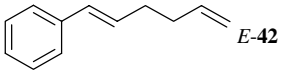
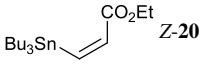
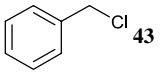
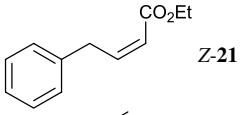
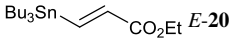
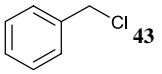
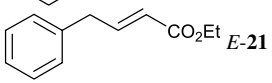
The efficiency of $(Ph_3P)_2Pd$(*N*-succ)Br **9** as a catalyst for allylic/benzylic halide coupling reactions, compared to its low reactivity for the coupling of aryl halides was of some interest. Several competition experiments were therefore devised to evaluate the substrate scope against different palladium catalyst systems. In the first example, bromobenzene **46**, benzyl bromide **19** and *Z*-vinylstannane **20** (in a 1:1:1 ratio) were subjected to the reaction conditions outlined in Scheme 7 and Table 5. Two major products

Table 2. Stille coupling reactions mediated by a range of palladium sources[a]

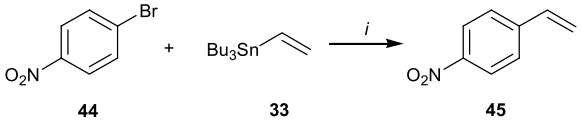
Entry	Organostannane	Organohalide	Catalyst	Time/h	Cross-coupled product	Yield/%[b]
1	 *Z*-**20**	 *E*-**25**	$(Ph_3P)_4Pd$	24	 *E,Z*-**26**	11
			$(Ph_3P)_2Pd(Bn)Br$	24		30[c]
			$(Ph_3P)_2Pd(Bn)Cl$	24		32[c]
			$(Ph_3P)_2Pd$(*N*-succ)Br, **9**	24		67
2	 *E*-**20**	 *E*-**25**	$(Ph_3P)_4Pd$	24	 *E,E*-**26**	51
			$(Ph_3P)_2Pd(Bn)Br$	24		55
			$(Ph_3P)_2Pd(Bn)Cl$	24		49
			$(Ph_3P)_2Pd$(*N*-succ)Br, **9**	24		56
3	 *Z*-**20**	 *E*-**27**	$(Ph_3P)_4Pd$	24	 *E,Z*-**28**	56
			$(Ph_3P)_2Pd(Bn)Br$	20		78
			$(Ph_3P)_2Pd(Bn)Cl$	20		71
			$(Ph_3P)_2Pd$(*N*-succ)Br, **9**	13		86
4	 *E*-**20**	 *E*-**27**	$(Ph_3P)_4Pd$	23	 *E,E*-**28**	56
			$(Ph_3P)_2Pd(Bn)Br$	18		77
			$(Ph_3P)_2Pd(Bn)Cl$	24		58
			$(Ph_3P)_2Pd$(*N*-succ)Br, **9**	13		81
5	 *E*-**20**	 **19**	$(Ph_3P)_4Pd$	24	 *E*-**21**	73
			$(Ph_3P)_2Pd(Bn)Br$	5		97
			$(Ph_3P)_2Pd(Bn)Cl$	24		71
			$(Ph_3P)_2Pd$(*N*-succ)Br, **9**	5		95
6	 **29**	 **19**	$(Ph_3P)_4Pd$	24	 **30**	90
			$(Ph_3P)_2Pd(Bn)Br$	24		97
			$(Ph_3P)_2Pd(Bn)Cl$	24		90
			$(Ph_3P)_2Pd$(*N*-succ)Br, **9**	24		93

[a] Reaction conditions: allylic/benzylic bromide (0.25 mmol), organostannane (0.3 mmol), $C_6H_5CH_3$ (2.5 mL) at 60 °C, under an inert atmosphere of N_2.
[b] Isolated yields after KF work-up and chromatography.
[c] ~1% of the *E*-isomer was detected by ^1H NMR spectroscopy.

Table 3. Products from the Stille coupling of allylic or benzylic substrates with organostannanes, mediated by $(Ph_3P)_2Pd(N\text{-Succ})Br$, **9**[a]

Entry	Organostannane	Organohalide	Coupled product	Yield/%[b]	Reaction time/h
1	 **31**	 **19**	 **32**	84	20
2	 **33**	 **34**	 **35**	67	6
3	 **33**	 *E*-**25**	 *E*-**36**	78	18
4	 **29**	 *E*-**25**	 *E*-**37**	34	18
5	 **33**	 *E*-**27**	 *E*-**38**	92	18
6	 **31**	 *E*-**27**	 *E*-**39**	79	20
7	 **29**	 *E*-**27**	 *E*-**40**	79	18
8	 **41**	 *E*-**27**	 *E*-**42**	70	24
9	 *Z*-**20**	 **43**	 *Z*-**21**	81[c]	48
10	 *E*-**20**	 **43**	 *E*-**21**	68[d]	18

[a] Reaction conditions: allylic/benzylic bromide (0.25 mmol), organostannane (0.3 mmol), $C_6H_5CH_3$ (2.5 mL) at 60 °C, under an inert atmosphere of N_2.
[b] Isolated yields after KF workup and column chromatography.
[c] 79% after 18 h when reaction conducted at 110 °C.
[d] Reaction conducted at 110 °C.



Scheme 6. Stille coupling of 4-nitrobromobenzene **44** with tributylvinyltin **33**. i, [Pd] (0.05 equiv.), toluene, reflux, 6 h (for details, see Table 4).

Table 4. Stille coupling of a vinylstannane with 4-nitrobromobenzene

Entry	Complex	Time/h	Isolated yield/ %
1	$(Ph_3P)_4Pd$	5	65
2	$(Ph_3P)_2Pd(Bn)Cl$	5	80
3	$(Ph_3P)_2Pd(Bn)Br$	5	86
4	$(Ph_3P)_4Pd+NBS$	24	35
5	$(Ph_3P)_2Pd$(*N*-succ)Br **9**	24	66

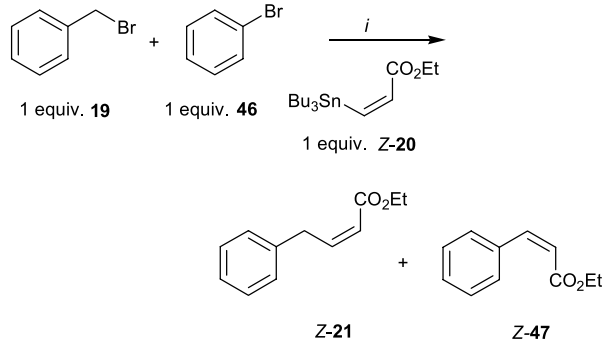
were expected from this reaction, namely *Z*-**21** from benzyl bromide **19**, and *Z*-**47** from bromobenzene **46**.

In the reactions mediated by $(Ph_3P)_4Pd$ and $(Ph_3P)_2PdBr_2$, *Z*-**21** was not detected, the only product isolated being the bromobenzene adduct *Z*-**47**, along with the corresponding *E*-isomer (entries 1 and 2). The use of $(Ph_3P)_2Pd(Bn)Br$ promoted some coupling with benzyl bromide, but again the coupling with bromobenzene **46** predominated (entry 3). A major switch in selectivity was observed when $(Ph_3P)_2$ Pd(*N*-succ)Br was employed as catalyst (entry 4). In this reaction, no aryl coupling was observed, only coupling with benzyl bromide giving *Z*-**21** (86%). The major difference between this catalyst system and $(Ph_3P)_2Pd(Bn)Br$ or $(Ph_3P)_2PdBr_2$ is the presence of the succinimide ligand, as opposed to the benzyl or bromide ligands, respectively. It seemed possible that a bromide salt could influence selectivity. Addition of lithium bromide to the $(Ph_3P)_2Pd$ (*N*-succ)Br coupling competition reaction had a profound effect, causing a large reduction in the selectivity, although *Z*-**21** still predominated (entry 5). The results in Table 5 clearly demonstrate the importance of the succinimide ligand for selectivity (which we will now refer to as the succinimide effect).

The effect of electron-releasing and withdrawing groups in the benzylic coupling partner, relative to benzyl bromide itself, was evaluated in a second competition study with stannane *Z*-**20** (Scheme 8). The outcome from these experiments was once again surprising. 4-Nitrobenzyl bromide **48** was expected to react faster than benzyl bromide **19** but actually the benzyl bromide adduct *Z*-**21** was produced in 36% yield, compared to only 14% of *Z*-**49** (Eq. 1, Scheme 8). In a reaction containing 4-methoxybenzyl bromide **50** and benzyl bromide **19** itself, the product that predominated (*Z*-**51**) was derived from the methoxylated substrate (Eq. 2, Scheme 8). These results exhibit a reversal of the expected reactivity.

In the third competition experiment, the coupling reaction of stannane *Z*-**20** with 4-nitrobromobenzene **40** and 4-nitrobenzyl bromide **36** was compared (Scheme 9).

No selectivity was observed in this reaction, where **51** and **48** reacted equally well to give the cross-coupled products *Z*-**49** and *Z*-**52** in 48% and 49% yield, respectively,



Scheme 7. Competition experiment between aryl and benzylic bromides. i, [Pd] (0.05 equiv), toluene, reflux, 18 h (for details, see Table 5).

Table 5. Competition study between benzyl bromide and bromobenzene

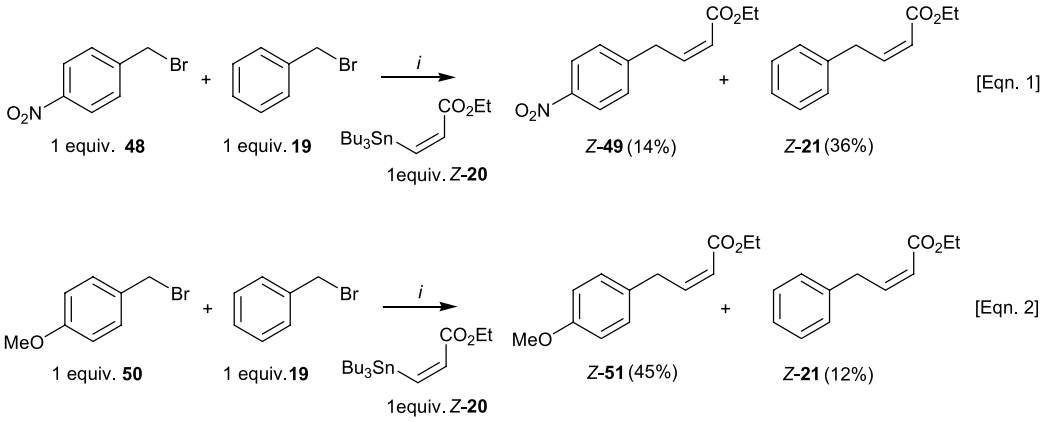
Entry	Complex	Isolated yield/%	
		Z-**21**	*Z*-**47** (*E*-**47**)
1	$(Ph_3P)_4Pd$	0	39 (9)
2	$(Ph_3P)_2PdBr_2$	0	21 (15)
3	$(Ph_3P)_2Pd(Bn)Br$	16	36
4	$(Ph_3P)_2Pd$(*N*-succ)Br	86	0
5	$(Ph_3P)_2Pd$(*N*-succ)Br+LiBr	45	22

indicating that there is essentially no difference in the reactivity of either substrate in coupling reactions mediated by $(Ph_3P)_2Pd$(*N*-Succ)Br **9**. The complete consumption of *Z*-**20** demonstrates the efficiency of these reactions.

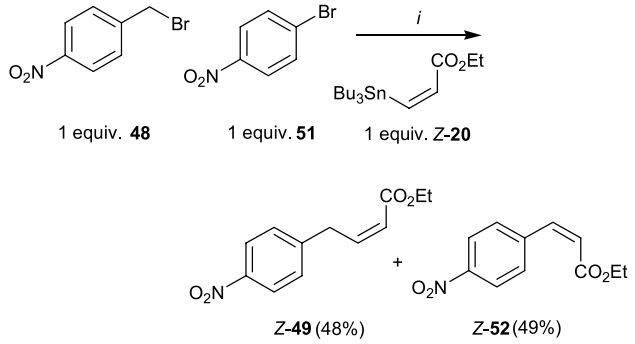
3. Discussion and conclusions

The results above indicate that $(Ph_3P)_2Pd$(*N*-Succ)Br **9** is an effective mediator of Stille coupling reactions involving allylic and benzylic halides. At the present time, we cannot state unambiguously whether $(Ph_3P)_2Pd$(*N*-Succ)Br **9** is a catalyst or precatalyst. A more thorough investigation into the mechanism of Stille coupling reactions mediated by $(Ph_3P)_2Pd$(*N*-Succ)Br is required before a detailed proposal can be made. Important observations have, however, been made in the present study: (1) that in allylic/benzylic Stille processes, increased yields and higher catalytic activity are observed for succinimide-containing palladium complexes, when compared to related palladium(II) complexes containing only Ph_3P as the donor ligand; (2) the increased reactivity of stannnane *Z*-**20** compared to its *E*-isomer in Stille couplings mediated by $(Ph_3P)_2Pd$(*N*-Succ)Br **9**; (3) the preferential Stille coupling of electron-rich benzyl bromides versus electron poor benzyl bromides with stannane *Z*-**20**; (4) the benzylic versus aryl selectivity observed for $(Ph_3P)_2Pd$(*N*-Succ)Br **9** compared to common palladium catalysts/precatalysts.

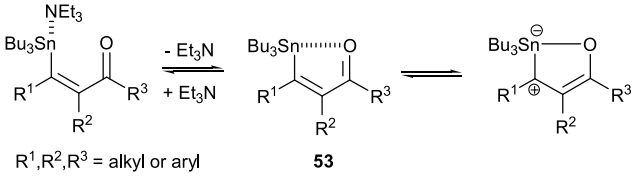
To elaborate on the second point. In reactions mediated by $(Ph_3P)_2Pd$(*N*-Succ)Br **9** the increased reactivity demonstrated by stannane *Z*-**20** over *E*-**20** with respect to benzyl bromide **19** and geranyl bromide *E*-**25** is an intriguing observation. In related studies, Takeda and co-workers showed that β-tributylstannyl-α,β-unsaturated ketones were relatively poor nucleophiles in Stille coupling—coordination of the oxygen lone pair electrons to the Bu_3Sn group



Scheme 8. Competition reactions employing electron-rich and electron-poor benzyl bromides. i, $(Ph_3P)_2Pd(N\text{-succ})Br$ (0.05 equiv), toluene, 60 °C, 18 h.



Scheme 9. Competition between nitro-substituted aryl and benzylic bromide substrates.

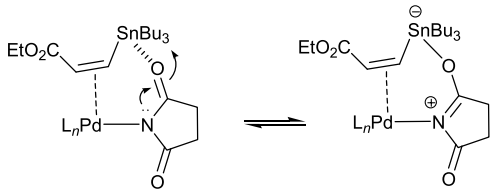


Scheme 10. Activation at tin by Et_3N and deactivation by O→Sn coordination.

deactivating the *cis*-vinyl stannane towards transmetallation (Scheme 10).[26]

In Takeda's study, copper(I) and triethylamine (Et_3N) were required to activate stannane **53** to Stille coupling reactions with benzylic and aryl halides. The former was used to promote the transmetallation step, either by scavenging excess phosphine ligands or by becoming involved in a Sn/Cu pre-transmetallative process (the vinylcuprate is more reactive). It was proposed that the amine donor ligand disrupted O→Sn coordination to give an activated stannane (through Et_3N→Sn coordination). The higher reactivity of stannane *Z*-**20** over *E*-**20** observed in Stille reactions mediated by $(Ph_3P)_2Pd(N\text{-Succ})Br$ **9** is therefore surprising.

Further, analysis of the coupling of *E*-**25** with both *Z*-**20** and *E*-**20** shows a unique trend (entries 1 and 2, Table 2). For *Z*-**20**, deactivation is clearly seen using $(Ph_3P)_4Pd$, $(Ph_3P)_2Pd(Bn)Br$ and $(Ph_3P)_2Pd(Bn)Cl$, whereas a good yield was obtained for $(Ph_3P)_2Pd(N\text{-Succ})Br$ **9**. In contrast to this observation, negligible differences were seen for *E*-**20** with these palladium complexes (entry 2, Table 2; also entries 4 and 5). For *Z*-**20**, there is a possibility that the succinimide ligand is activating tin intramolecularly, as shown in Scheme 11 (intermolecular activation is also possible but seems less likely). It is known that there is significant electron repulsion between the nitrogen lone pair electrons and the d_π electrons of palladium(II).[27] This promotes electron delocalisation onto the carbonyl substituent. η^2-Alkene coordination of *Z*-**20** to the palladium centre facilitates *O*-coordination, and hence activation, from a neighbouring succinimide ligand (a chelation-controlled activation process). We presume that the *trans*-stannane *E*-**20**, does not experience the same activation, possibly due to the incorrect orientation of the Bu_3Sn group (and ester group).



Scheme 11. Activation at tin by the succinimide ligand.

To summarise, the preparation of $(Ph_3P)_2Pd(N\text{-Succ})Br$ **9** and several other novel succinimide and phthalimide-containing palladium complexes, has been described. The complex $(Ph_3P)_2Pd(N\text{-Succ})Br$ **9** has been shown to be an efficient catalyst for the Stille coupling reactions of a range of allylic and benzylic halides with different vinylstannanes. In a number of these reactions, a comparison of the catalytic activities of several different palladium complexes has been carried out. Competition reactions and preliminary mechanistic observations have been reported herein, which indicate the novel selectivity of $(Ph_3P)_2Pd(N\text{-Succ})Br$ **9** and lead to the proposal of a succinimide effect in Stille coupling reactions. Further synthetic studies, as well as mechanistic investigations concerning the oxidation states and geometries of key palladium intermediates (neutral or anionic), possibly involving radicals, in the catalytic cycle, are continuing in our laboratories.

4. Experimental

4.1. General details

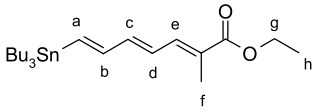
See reference for general experimental information.[15c]

The following routine compounds show comparable characterisation data according to literature precedent: 1, 3-oxazol-5-ylmethanol (**1**),[28] *E*-bis-1,2-tributylstannylethene (*E*-**5**),[29] ethyl 3-iodo-2*Z*-propenoate (*Z*-**6**),[30] ethyl 3-(tributylstannyl)-2*Z*-propenoate (*Z*-**20**), ethyl 3-(tributylstannyl)-2*E*-propenoate (*E*-**20**),[45] ethyl (2*Z*)-4-phenyl-2-butenoate (*Z*-**21**),[31] ethyl (2*E*)-4-phenyl-2-butenoate (*E*-**21**),[32] ethyl (3*E*)-4-phenyl-3-butenoate (*E*-**22**),[33] diphenylmethane (**30**),[34] 2-ethoxy-3-phenylpropene (**31**),[35] 1-allyl-4-nitrobenzene (**35**),[36] (2*E*)-3,7-dimethyl-1-phenyl-2,6-octadiene (*E*-**37**),[37] (1*E*)-1,4-pentadienylbenzene (*E*-**38**),[38] 1,3-diphenylpropene (*E*-**40**),[39] 1*E*-phenyl-1,5-hexadiene (*E*-**42**),[40] 1-nitro-4-vinylbenzene (**45**),[41] ethyl (2*Z*)-3-phenyl-2-propenoate (*Z*-**47**)[42] and ethyl (2*E*)-3-phenyl-2-propenoate (*E*-**47**).[42]

4.1.1. 5-(Bromomethyl)-1,3-oxazole (2). *Method A*.[36] NBS (recrystallised from H_2O) (0.237 g, 1.33 mmol) was added to a solution of **1** (0.12 g, 1.21 mmol) and Ph_3P (0.35 g, 1.33 mmol) in CH_2Cl_2 (4 mL). The reaction was stirred at ambient temperature for 1 h then concentrated in vacuo and passed directly through a short plug of silica using PE–EtOAc (1:1, v:v) as the eluent. This afforded the title compound **2** as a colourless oil (0.058 g, 30%). The compound was extremely unstable, but it may be stored in the freezer at −20 °C. R_f=0.37 (PE–EtOAc, 1:1); R_f=0.26 (CH_2Cl_2); δ_H (270 MHz; $CDCl_3$) 2.85 (1H, br s, OH^d), 4.68 (2H, s, CH_2^c), 7.00 (1H, s, CH^b), 7.85 (1H, s, CH^a) (consistent with data previously reported).[36]

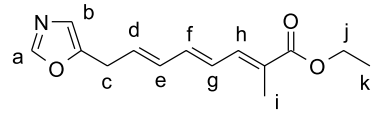
Method B.[43] Carbon tetrabromide (0.68 g, 2.0 mmol) was added to a solution of **1** (0.169 g, 1.7 mmol) and Ph_3P (0.58 g, 2.2 mmol) in CH_2Cl_2 (10 mL) cooled to 0 °C. The reaction was stirred at 0 °C for 1 h, concentrated in vacuo and passed directly through a short plug of silica using PE–EtOAc (1:1, v:v) as the eluent, giving the title compound **2** as a colourless oil (0.148 g, 54%).

4.1.2. Ethyl (2*E*,4*E*,6*E*)-2-methyl-7-(tributylstannyl)-2,4,6-heptatrienoate (*E*,*E*,*E*-3).



TPAP (0.024 g, 0.007 mmol) was added to a cooled mixture (0 °C) of (2*E*,4*E*)-5 (tributylstannyl)-2,4-pentadien-1-ol (0.50 g, 1.34 mmol), powdered 4 Å molecular sieves (0.50 g) and NMO (0.24 g, 2.0 mmol) in CH_2Cl_2 (10 mL). The green solution was stirred for 90 min, then the solvent was removed in vacuo. Subsequent purification by column chromatography using CH_2Cl_2 as the eluent afforded (2*E*,4*E*)-5-(tributylstannyl)-2,4- pentadienal as a pale yellow oil, which was used directly in the following reaction: KHMDS (0.5 M in toluene, 4.0 mL, 2.0 mmol) was added dropwise to a stirred solution of ethyl 2-(diethoxyphosphoryl) propenoate (0.43 mL, 2.0 mmol) in THF (25 mL) at −78 °C. After 15 min, the aldehyde (prepared above) in THF (25 mL) was added. The reaction was stirred at −78 °C for 1 h before addition of saturated aq NH_4Cl (10 mL), whereupon it was warmed to ambient temperature. The resulting mixture was extracted with Et_2O (3×10 mL), the combined organic extracts dried over Na_2SO_4 and the solvent removed in vacuo. Purification by column chromatography using PE–EtOAc–TEA, (97:2:1) afforded the title compound (0.35 g, 58%) as a pale yellow oil. R_f=0.74 (CH_2Cl_2); δ_H (270 MHz, $CDCl_3$) 0.87–0.96 (18H, m, Bu+CH_3^h), 1.25–1.38 (6H, m, Bu), 1.43–1.56 (6H, m, Bu), 1.97 (3H, d, ^4J=1.0 CH_3^f), 4.20 (2H, q, J=7.0 Hz, CH_2^g), 6.37–6.55 (2H, m, CH^{c+d}), superimposed by 6.49 (1H, d, ^3J=11.5 Hz, CH^a), 6.64 (1H, dd, ^3J=11.5, 9.0 Hz, CH^b), 7.21 (1H, d, ^3J=8.5 Hz, CH^e); δ_C (67.9 MHz, $CDCl_3$) 9.7 (CH_2), 12.8 (CH_3), 13.8 (CH_3), 14.4 (CH_3), 27.4 (CH_2), 29.2 (CH_2), 60.6 (CH_2), 126.6 (CH), 127.6 (C), 138.3 (CH), 140.7 (CH), 141.8 (CH), 146.5 (CH), 168.5 (C); ν_{max} (neat, cm^{-1}) 2925, 2854, 1705, 1618, 1454, 1367, 1277, 1232, 1113, 1095, and 1000 cm^{-1}; *m*/*z* (CI), 457 (MH^+, 84%), 399 (58), 308 (100), 167 (35); [HRMS (CI): calcd for $C_{22}H_{41}O_2{}^{116}Sn$, 453.2124. Found: MH^+, 453.2119 (1.0 ppm error)]. Stereochemistry of new double bond confirmed by quantitative NOE measurements (500 MHz): 3.8% NOE observed between CH_3^f and CH^d.

4.1.3. Ethyl (2*E*,4*E*,6*E*)-2-methyl-8-(1,3-oxazole-5-yl)-2,4,6-octatrienoate (*E*,*E*,*E*-4).



$(Ph_3P)_4Pd$ (5.0 mg, 0.05 equiv, 5 mol%) was added to a solution of 3 (0.40 g, 0.79 mmol) and 2 (0.122 g, 0.75 mmol) (synthesised by method A) in dry degassed toluene (5 mL) and heated to reflux in the dark for 20 h. After this time, the reaction was cooled to ambient temperature, then the solvent removed in vacuo. The resulting syrup was purified by column chromatography using PE–EtOAc (1:1) as the eluent. This afforded the title compound as a bright yellow oil (0.152 g, 82%). R_f=0.31 (PE–EtOAc, 1:1, v:v); δ_H (270 MHz, $CDCl_3$) 1.27 (3H, t, ^3J=7.5 Hz, CH_3^k), 1.92 (3H, s, CH_3^i), 3.50 (2H, d, ^3J=7.0 Hz CH_2^c), 4.18 (2H, q, ^3J=7.5 Hz, CH_2^j), 5.89 (1H, dt, ^3J=15.0, 7.0 Hz, CH^d), 6.24 (1H, dd, ^3J=15.0, 11.5 Hz, CH^e), 6.49 (2H, m, CH^{f+g}), 6.79 (1H, s, CH^b), 7.19 (1H, d, ^3J=12.0 Hz, CH^h), 7.78 (1H, s, CH^a); δ_C (67.9 MHz, $CDCl_3$) 12.6 (CH_3), 14.2 (CH_3), 28.8 (CH_2), 60.5 (CH_2), 122.7 (CH), 127.5 (CH), 127.6 (CH), 130.8 (CH), 132.9 (CH), 137.6 (CH), 138.0 (CH), 150.2 (C), 150.4 (C), 168.2 (C); ν_{max} (film) 2956, 2929, 1701, 1614, 1510, 1464, 1367, 1257, 1225, 1103, 991 and 964 cm^{-1}; *m*/*z* (CI), 248 (MH^+, 100%), 234 (10), 174 (7), 82 (6); [HRMS (CI): calcd for $C_{14}H_{18}O_3N$, 248.1287. Found: MH^+, 248.1287 (0.2 ppm error)]. Stereochemistry of new double bond confirmed by a quantitative an NOE experiment 4.5% NOE observed between CH_3^f and CH^e.

4.1.4. Ethyl (2*Z*,4*E*)-5-(tributylstannyl)penta-2,4-dienoate (*Z*,*E*-7) and diethyl octa-2*Z*,4*E*,6*Z*-triendioate (*Z*,*E*,*Z*-8). The palladium catalyst (0.05 equiv, 5 mol%) was added

to a solution of *E*-**5** (1.0 g, 1.65 mmol) and *Z*-**6** (0.36 g, 1.6 mmol) in dry degassed toluene (10 mL). The reaction was heated to reflux for 3 h. The reaction was allowed to cool to ambient temperature, whereupon a saturated aq KF (10 mL) was added. The mixture was stirred vigorously for 1 h, then filtered through Celite®, and the residue rinsed with Et_2O (2×10 mL). The filtrate was washed with saturated aq NaCl and then dried (Na_2SO_4). Subsequent purification by column chromatography, using PE–EtOAc–TEA (97:2:1) as the eluent, afforded the title compounds as pale yellow oils, in yields specified in the text. Data for ethyl (2*Z*,4*E*)-5-(tributylstannyl)penta-2,4-dienoate (*Z*,*E*-**7**): obtained as a yellow oil. R_f=0.60 (PE–EtOAc, 9:1, v:v); δ_H (270 MHz, $CDCl_3$) 0.86–0.98 (15H, m, Bu), 1.24–1.38 (9H, m, CH_2 of Bu and CH_3^f), 1.24–1.38 (6H, m, Bu), 4.20 (2H, q, ^3J=7.0 Hz, CH_2^e), 5.58 (1H, dd, ^3J=11.5 Hz, ^4J=1.0 Hz CH^d), 6.50 (1H, ddd, ^3J=11.5, 10.5 Hz, ^4J=1.0 Hz, CH^c) 6.75 (1H, dd, ^3J=19.0 Hz, ^4J=1.0 Hz, CH^a) 7.81 (1H, ddd, ^3J=19.0, 10.5 Hz, ^4J=1.0 Hz, CH^b); δ_C (67.9 MHz, $CDCl_3$), 9.6 (CH_2), 13.6 (CH_3), 14.3 (CH_3), 27.2 (CH_2), 20.0 (CH_2), 59.9 (CH_2), 115.9 (CH), 142.5 (CH), 146.5 (CH), 147.8 (CH), 166.2 (C); ν_{max} (neat, cm^{-1}) 2958, 1718, 1616, 1550 and 1162; *m*/*z* (CI), 417 (MH^+, 17%), 308 (100); [HRMS (CI): calcd for $C_{19}H_{37}O_2^{116}Sn$, 413.1807. Found: MH^+, 413.1811 (1.1 ppm error)]. Data for diethyl octa-2*Z*,4*E*,6*Z*-triendioate (*Z*,*E*,*Z*-**8**): obtained as a white solid; R_f=0.34 (PE–EtOAc, 9:1, v:v); mp 53.0–53.5 °C; δ_H (270 MHz, $CDCl_3$) 1.30 (3H, t, ^3J=7.5 Hz, CH_3^a), 4.20 (2H, q, ^3J=7.5 Hz, CH_2^b), 5.81 (1H, d, ^3J=11.0 Hz, CH^c), 6.71 (1H, ddd, ^3J=11.0, 10.5,^4J=3.0 Hz, CH^d), 7.76 (1H, dd, ^3J=10.5, 3.0 Hz, CH^e); δ_C (67.9 MHz, $CDCl_3$), 14.2 (CH_3), 60.2 (CH_2), 120.7 (CH), 135.9 (CH), 143.38 (CH), 166.1 (C); ν_{max} (nujol, cm^{-1}) 1718, 1616 and 1165; *m*/*z* (EI) 224 (M^+, 53%), 195 (91), 167 (70), 149 (100); [HRMS (EI): calcd for $C_{12}H_{16}O_4$, 224.1049. Found: M^+, 224.1043 (2.5 ppm error)].

4.1.5. *cis*-Bromobis(triphenylphosphine)(succinimide) palladium(II) (*cis*-9). To a Schlenk tube containing vacuum dried $Pd_2dba_3{\cdot}CHCl_3$ (100 mg, 0.097 mmol) and Ph_3P (101.4 mg, 0.387 mmol) in dry CH_2Cl_2 (7 mL) at 21 °C under N_2, was stirred for 0.2 h, after, which time an orange colour persisted. A solution of recrystallised *N*-bromosuccinimide (34.5 mg, 0.194 mmol) in dry CH_2Cl_2 (2 mL) was added in one portion and the mixture stirred for 0.2 h. If a precipitate is observed, filter off—this is $(Ph_3P)_2PdBr_2$). The resulting yellow solution was concentrated in vacuo to a third of its original volume and petroleum ether added to precipitate the complex. The creamy yellow solid was filtered and washed with small quantities of hexane, which is the title compound (104 mg, 74% yield). A small quantity of *cis*-**9** was recrystallised by slow vapour diffusion of Et_2O in a CH_2Cl_2 solution of the complex (5:1) at 0 °C for 2 days. ν_{max} (CH_2Cl_2, cm^{-1}) 1631 (C=O); δ_H (500 MHz, CD_2Cl_2) 1.59 (2H, dd, $^2J_{HaHa'}$=16.5 Hz, $^3J_{HaHb'}$=4.1 Hz, CH_A and $CH_{A'}$), 2.20 (2H, dd, $^2J_{HbHb'}$=16.5 Hz, $^3J_{HbHa'}$=4.5 Hz, CH_B and $CH_{B'}$), 7.1–7.6 (30H, m, Ph–H); δ_P (202 MHz, CD_2Cl_2) 23.96 (1P, d, $^2J_{PP}$=8.49 Hz, $P1_{(cis)}$) and 32.91 (1P, d, $^2J_{PP}$=8.49 Hz, $P2_{(trans)}$); *m*/*z* (FAB), 810 (MH^+, 4), 710 (29), 629 (17), 339 (100), 263 (Ph_3PH^+, 28), 183 (43), 154 (79). Anal. Calcd for $C_{40}H_{34}BrNO_2P_2Pd{\cdot}½\ CH_2Cl_2$, C, 57.36; H, 4.23; N, 1.63. Found C, 57.49; H, 3.99; N, 1.66.

4.1.6. *trans*-Chlorobis(triphenylphosphine)(succinimide) palladium(II) (*trans*-10). Following a similar procedure to *cis*-**9**. To a Schlenk tube containing vacuum dried $Pd_2dba_3{\cdot}CHCl_3$ (104 mg, 0.1 mmol) and Ph_3P (105 mg, 0.4 mmol) in dry CH_2Cl_2 (8 mL) at 21 °C under N_2, was stirred for 0.2 h, after, which time an orange colour persisted. Then *N*-chlorosuccinimide (NCS) (0.018 g, 0.25 mmol) (recrystallised from H_2O and dried under high vacuum) in CH_2Cl_2 (2 mL), was added in one portion. The solution went pale orange. The mixture was stirred for 0.5 h. The solution was reduced to a third of its original volume in vacuo and then petroleum ether (2 mL) added to precipitate the complex. This gave the title compound as a cream solid (0.033 g, 22%). ν_{max} ($CHCl_3$, cm^{-1}) 1633 (C=O); δ_H (270 MHz, $CDCl_3$, selected data) 1.32 (2H, br s, CH_{2A}), 1.69 (2H, br s, CH_{2B}), 7.26–7.62 (18H, m, Ph–H), 7.70–7.91 (12H, m, Ph–H); δ_P (109.1 MHz, $CDCl_3$) 23.45 (2P, s, P1–P2); *m*/*z* (FAB), 764 (MH^+, 2), 728 (12), 629 (5), 339 (100).

4.1.7. *trans*-Iodobis(triphenylphosphine)(succinimide) palladium(II) (*trans*-11). Following a similar procedure to *cis*-**9**. To a Schlenk tube containing vacuum dried $Pd_2dba_3{\cdot}CHCl_3$ (104 mg, 0.1 mmol) and Ph_3P (105 mg, 0.4 mmol) in dry CH_2Cl_2 (8 mL) at 21 °C under N_2, was stirred for 0.2 h, after, which time an orange colour persisted. Then, *N*-iodosuccinimide (NIS) (0.056 g, 0.25 mmol) in CH_2Cl_2 (2 mL) was added in one portion. The solution went yellow immediately. A small amount of a precipitate (0.028 g) was formed ($(Ph_3P)_2PdI_2$), which was filtered. The solution was reduced to a third of its original volume in vacuo and then petroleum ether (2 mL) added to precipitate the complex. This gave the title compound as a cream solid, which was crystallised from a layered solvent system (CH_2Cl_2/hexane, 1/4, *c* 0.1 M) by slow evaporation in air (0.086 g, 50%). Mp 197–199 °C (decomp.); δ_H (400 MHz, $CDCl_3$) 1.32 (2H, s, CH_{2A}), 1.62 (2H, s, CH_{2B}), 5.30 (1H, s, ½CH_2Cl_2 of recrystallization), 7.37–7.47 (18H, m, Ph–H), 7.78–7.82 (12H, m, Ph–H); δ_P (161 MHz, $CDCl_3$) 21.65 (2P, s, P1–P2); ν_{max} ($CHCl_3$, cm^{-1}) 1631 (C=O); *m*/*z* (FAB), 764 (MH^+, 1), 728 (M–Cl. 16), 665 (8), 629 (58), 495 (50); [HRMS (FAB): 100% rel. abundance, $MH^+C_{40}H_{35}NO_2P_2^{105}PdI$=856.024].

4.1.8. *cis*-Bromobis(triphenylphosphine)(*N*-phthalimide) palladium(II) (*trans*-12). Following a similar procedure to *cis*-**9**. To a Schlenk tube containing vacuum dried $Pd_2dba_3{\cdot}CHCl_3$ (104 mg, 0.1 mmol) and Ph_3P (105 mg, 0.4 mmol) in dry CH_2Cl_2 (8 mL) at 21 °C under N_2, was stirred for 0.2 h, after, which time an orange colour persisted. Then, *N*-bromophthalimide (57 mg, 0.25 mmol) in CH_2Cl_2 (2 mL) was added in one portion. The solution went yellow immediately. The solution was reduced to a third of its original volume in vacuo and then diethyl ether (2 mL) added to precipitate the complex. This gave the title complex as a pale yellow solid (0.120 g, 70%). Mp 199–203 °C (decomp.); (270 MHz, $CDCl_3$) 5.30 (2H, s, CH_2Cl_2 of recrystallization), 7.12–7.42 (27H, m, Ph–H), 7.62–7.86 (7H, m, Ph–H); δ_P (109.1 MHz, $CDCl_3$) 33.80 (1P, d, $^2J_{PP}$=8.39 Hz), 24.89 (1P, $^2J_{PP}$=8.39 Hz); ν_{max} ($CHCl_3$, cm^{-1}) 1651 (C=O), 1628 (C=C); *m*/*z* (FAB), 858 (MH^+, 4%), 776 (21), 711 (25), 629 (15), 332 (100); [HRMS (FAB): 100% rel. abundance, $MH^+C_{44}H_{35}NO_2P_2^{81}BrPd$= 858.036].

4.1.9. *cis*-Bromobis(1,2-bis(diphenylphosphino)ethane) (succinimide)palladium(II) (*cis*-14). Following a similar procedure to *cis*-**9**. To a Schlenk tube containing vacuum dried $Pd_2dba_3 \cdot CHCl_3$ (104 mg, 0.1 mmol) and 1,2-bis(diphenylphosphino)ethane (104 mg, 0.26 mmol) in dry CH_2Cl_2 (8 mL) at 21 °C under N_2, was stirred for 0.2 h, after, which time an orange colour persisted (0.25 h). A solution of recrystallised *N*-bromosuccinimide (46 mg, 0.26 mmol) in dry CH_2Cl_2 (2 mL) was added in one portion. The solution rapidly turned to a yellow colour. The solution was reduced to half of its original volume in vacuo and then petroleum ether (2 mL) added to precipitate the complex. This gave the title compound as a cream solid (209 mg, 59%). δ_H (270 MHz, $CDCl_3$) 2.09–2.16 (4H, br, $2\times CH_2$ dppe backbone), 2.24–2.29 (4H, m, $2\times CH_2$ of succinimide), 5.30 (1H, s, $\frac{1}{2}CH_2Cl_2$ of recrystallization), 7.15–7.68 (30H, m, phenyl groups); δ_P (161.2 MHz, $CDCl_3$) 23.95 (1P, br s), 61.87 (1P, br s) (consistent with data previously reported).[44]

4.1.10. *cis*-Bromobis(1,2-bis(dicyclohexylphosphino) ethane) (succinimide)palladium(II) (*cis*-15). Following a similar procedure to *cis*-**9**. To a Schlenk tube containing vacuum dried $Pd_2dba_3 \cdot CHCl_3$ (41 mg, 39.6 μmol) and 1,2-bis(dicyclohexylphosphino)ethane (34 mg, 793 μmol) in dry CH_2Cl_2 (4 mL) at 21 °C under N_2, was stirred for 0.5 h, after, which time an orange colour persisted. A solution of recrystallised *N*-bromosuccinimide (14 mg, 79.3 μmol) in dry CH_2Cl_2 (1 mL) was added in one portion. The solution rapidly turned a red colour. The solution was reduced to half of its original volume in vacuo and then petroleum ether (2 mL) added to precipitate the complex. This gave the title compound as a pale red solid (7.3 mg, 13%). δ_H (500 MHz, $CDCl_3$) 1.24–1.55 (24H, br, Cy–H), 1.65–1.96 (20H, br, Cy–H), 1.41 (2H, br s, CH_A and $CH_{A'}$), 2.15 (2H, br s, CH_B and $CH_{B'}$), 2.47 (2H, br s, CH_2 dcpe backbone), 2.69 (2H, br s, CH_2 dcpe backbone), 7.41–7.43 (12H, m, Ph–H), 7.64 (8H, m, Ph–H). δ_P (202 MHz, $CDCl_3$) 88.68 (1P, br s), 91.30 (1P, d, $^2J_{PP}=8.39$ Hz) (pure to the limits of detection). *m*/*z* (FAB) 708 (MH^+, 9), 626 (M–Br, 21), 528 (32), 423 (100), 341 (21) (the correct isotopic distribution was observed for the molecular ion of this complex).

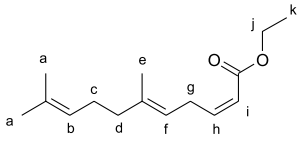
4.1.11. *cis*-Bromobis(1,1′-bis(diphenylphosphino)ferrocene) (succinimide)palladium(II) (*cis*-16). Following a similar procedure to *cis*-**9**. To a Schlenk tube containing vacuum dried $Pd_2dba_3 \cdot CHCl_3$ (60 mg, 58 μmol) and 1,1′-bis(diphenylphosphino)ferrocene (67.5 mg, 0.12 mmol) in dry CH_2Cl_2 (8 mL) at 21 °C under N_2, was stirred for 0.2 h, after, which time an orange colour persisted. A solution of recrystallised *N*-bromosuccinimide (21.6 mg, 0.12 mmol) in dry CH_2Cl_2 (1 mL) was added in one portion. No obvious colour change was observed. The solution was reduced to half of its original volume in vacuo and then petroleum ether (2 mL) added to precipitate an orange complex. This gave the title compound as an orange solid (48 mg, 49%). δ_H (500 MHz, $CDCl_3$) 1.56 (2H, m, CH_A and $CH_{A'}$), 2.22 (2H, m, CH_B and $CH_{B'}$), 3.37 (1H, m, Cp–H), 4.16 (1H, m, Cp–H), 4.60 (1H, m, Cp–H), 5.20 (1H, m, Cp–H), 7.20–8.21 (20H, br. m, Ph–H). δ_P (202 MHz, $CDCl_3$) 24.57 (1P, d, $^2J_{PP}=6.36$ Hz), 35.13 (1P, d, $^2J_{PP}=6.36$ Hz) (pure to the limits of detection). *m*/*z* (FAB) 840 (MH^+, 3), 760 (M–Br, 15), 741 (M–*N*-Succ, 2), 555 (32) (the correct isotopic distribution was observed for the molecular ion of this complex).

4.1.12. *trans*-Bis(triphenylphosphine)palladium(II) (benzyl) bromide (*trans*-18). Prepared by an alternative procedure to that reported.[45] To a Schlenk tube containing vacuum dried $Pd_2dba_3 \cdot CHCl_3$ (100 mg, 0.097 mmol) in dry CH_2Cl_2 (3 mL), under N_2, was added a solution of PPh_3 (101.4 mg, 0.387 mmol) in dry CH_2Cl_2 (2.5 mL). The mixture was stirred for 0.2 h, after, which time an orange colour persisted. A solution of benzyl bromide in CH_2Cl_2 (2 mL) was added in one portion. The mixture turned a yellow colour after a few minutes, although stirring was continued for 0.5 h. The solution was concentrated in vacuo to a third of its original volume and petroleum ether added to precipitate the complex, *trans*-$Pd(Bn)(PPh_3)_2Br$. The yellow solid was filtered and washed with diethyl ether (117 mg, 76%); mp 124–125 °C (decomp.), lit.124–130 °C;[45] δ_H ($CDCl_3$, 300 MHz) 2.73 (2H, br s, CH_2), 7.37–7.70 (35H, m, Ph–H). δ_P ($CDCl_3$, 121 MHz) 23.26 (2P, s, P1–P2). A broad signal at δ 30.43 (s) is also observed.

4.2. General Stille coupling procedure

To a solution of the organohalide (0.25 mmol, 1 equiv) and the organostannane (0.3 mmol, 1.2 equiv) in dry degassed (freeze–pump–thaw cycles) toluene (2.5 mL), was added the palladium catalyst (0.0125 mmol, 0.05 equiv). The mixture was placed under a dry N_2 atmosphere and heated to 60 °C in the dark (flask was covered with domestic foil) for the specified time. All reactions were followed by TLC, GC or GC/MS analysis. On completion, the reaction was cooled to ambient temperature, then saturated aqueous KF (2.5 mL) was added and the mixture stirred vigorously for 1 h. The mixture was filtered through Celite®, and the residue rinsed with Et_2O (2×5 mL), washed with saturated aqueous NaCl (2×2.5 mL) and dried ($MgSO_4$). Concentration in vacuo and subsequent purification by column chromatography (using EtOAc–hexane or PE mixtures) gave the products as oils.

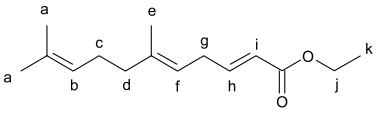
4.2.1. Ethyl (2*Z*,5*E*)-6,10-dimethyl-2,5,9-undecatrienno-ate (*Z*,*Z*-26).



The title compound was obtained as a pale yellow oil. $R_f=0.50$ (PE–EtOAc, 9:1); δ_H (400 MHz, $CDCl_3$) 1.29 (3H, t, $^3J=7.5$ Hz CH_3^k), 1.59 (6H, s, CH_3^a), 1.67 (3H, s CH_3^e), 1.98–2.10 (4H, m, CH_2^{c+d}), 3.36 (2H, dd, $^3J=7.5$, 7.5 Hz, CH_2^g), 4.17 (2H, q, $^3J=7.5$ Hz, CH_2^j), 5.09 (1H, tt, $^3J=6.5$ Hz, $^4J=1.0$ Hz, CH^b), 5.16 (1H, td, $^3J=7.5$ Hz, $^4J=1.0$ Hz, CH^f), 5.74 (1H, dm, $^3J=11.5$ Hz, CH^i), 6.13 (1H, dt, $^3J=11.5$, 7.5 Hz, CH^f); δ_C (100.6 MHz, $CDCl_3$), 14.4 (CH_3), 16.3 (CH_3), 17.8 (CH_3), 25.8 (CH_3), 26.6 (CH_2), 28.2 (CH_2), 39.7 (CH_2), 60.0 (CH_2), 119.0 (CH), 120.6 (CH), 124.2 (CH), 128.7 (CH), 131.6 (C), 137.6 (C), 166.6 (C). ν_{max} (neat, cm^{-1}) 2981, 2938, 1717, 1644, 1450, 1373, 1268,

1182, 1095 and 1032; *m/z* (CI), 254 (MNH_4^+, 26%), 237 (MH^+, 100), 191 (28), 163 (53), 123 (86), 69 (58) 41 (34); [HRMS (CI): calcd for $C_{15}H_{25}O_2$, 237.1855. Found: MH^+, 237.1855 (0.8 ppm error)].

4.2.2. Ethyl (2*Z*,5*E*)-6,10-dimethyl-2,5,9-undecatriennoate (*E*,*E*-26).



The title compound was obtained as a colourless oil. R_f=0.44 (PE–EtOAc, 9:1); δ_H (400 MHz, $CDCl_3$) 1.27 (3H, t, ^3J=7.0 Hz CH_3^k), 1.59 (6H, s, 2×CH_3^a), 1.68 (3H, s, CH_3^e, NB. Isomerisation to cis observed as a singlet at 1.72), 2.00– 2.11 (4H, m, 2×CH_2^{c+d}), 2.88 (2H, app. br. t, dd, ^3J=7.5, 6.0 Hz, CH_2^g), 4.18 (2H, q, ^3J=7.0 Hz, CH_2^j), 5.06 (1H, m, CH^b), 5.13 (1H, br. t, ^3J=7.5 Hz, CH^f), 5.79 (1H, dt, ^3J=15.5 Hz, ^4J=2.0 Hz, CH^i), 6.92 (1H, dt, ^3J=15.5, 6.0 Hz, CH^h); δ_C (100.6 MHz, $CDCl_3$), 14.2 (CH_3), 16.0 (CH_3), 17.6 (CH_3), 25.6 (CH_3), 26.4 (CH_2), 30.6 (CH_2), 39.6 (CH_2), 60.1 (CH_2), 118.9 (CH), 120.9 (CH), 124.0 (CH), 131.6 (C), 138.3 (C), 147.7 (CH), 166.7 (C); ν_{max} (neat, cm^{-1}) 2967, 2926, 1722, 1651, 1448, 1370, 1321, 1266, 1172, 1094 and 1043; *m/z* (CI), 254 (MNH_4^+, 10%), 237 (MH^+, 77), 191 (46), 163 (100), 123 (45); [HRMS (CI): calcd for $C_{15}H_{25}O_2$, 237.1854. Found: MH^+, 237.1849 (2.2 ppm error)].

4.2.3. Ethyl (2*Z*,5*E*)-6-phenyl-2,5-hexadienoate (*E*,*Z*-28).

The title compound was obtained as a colourless yellow oil. R_f=0.36 (PE–EtOAc, 9:1, v:v); δ_H (270 MHz, $CDCl_3$) 1.28 (3H, t, ^3J=7.0 Hz CH_3^g), 3.55 (2H, dd, ^3J=6.5, 7.5 Hz, CH_2^c), 4.17 (2H, q, ^3J=7.0 Hz, CH_2^f), 5.82 (1H, dt, ^3J=11.5 Hz, ^4J=1.5 Hz, CH^e), 6.19 (1H, dt, ^3J=16.0, 6.5 Hz CH^f), 6.25 (1H, dt, ^3J=11.5, 7.5 Hz CH^d), 6.43 (1H, d, ^3J=16.0 Hz, CH^g), 7.14–7.33 (5 H, m, Aryl); δ_C (67.9 MHz, $CDCl_3$), 14.2 (CH_3), 32.3 (CH_2), 59.9 (CH_2), 120.2 (CH), 126.0 (CH), 126.8 (CH), 127.1 (CH), 128.5 (CH), 131.4 (CH), 137.3 (C), 146.8 (CH), 166.3 (C); ν_{max} (film, cm^{-1}) 3028, 2982, 1717, 1642, 1448, 1413, 1199, 1168, 034, 966, 823, 744 and 694; *m/z* (CI), 243 (MNH_4^+, 25%), 217 (MH^+, 100); 188 (12), 169 (16), 143 (22), 125 (12), 112 (7), 106 (12); [HRMS (CI): calcd for $C_{14}H_{17}O_2$, 217.1229. Found: MH^+, 217.1230 (0.5 ppm error)].

4.2.4. Ethyl (2*E*,5*E*)-6-phenyl-2,5-hexadienoate (*E*,*E*-28).

The title compound was obtained as a pale yellow oil. R_f= 0.20 (PE–EtOAc, 9:1); δ_H (400 MHz, $CDCl_3$) 1.18 (3H, t, ^3J=7.0 Hz CH_3), 3.00 (2H, ddd, ^3J=6.5, 6.5 Hz, ^4J=1.5 Hz, CH_2), 4.09 (2H, q, ^3J=7.0 Hz, CH_2), 5.80 (1H, dt, ^3J=15.5 Hz, ^4J=1.5 Hz, CH), 6.08 (1H, dt, ^3J=16.0, 6.5 Hz CH), 6.34 (1H, d, ^3J=16.0 Hz CH), 6.94 (1H, dt, ^3J=15.5, 6.5 Hz, CH), 7.14 (1H, m, aromatic CH), 7.19–7.26 (4H, m, Ph–H); δ_C (100.6 MHz, $CDCl_3$), 14.2 (CH_3), 35.2 (CH_2), 60.2 (CH_2), 122.4 (CH), 125.5 (CH), 126.2 (CH), 127.5 (CH), 128.7 (CH), 132.6 (CH), 137.2 (C), 146.6 (CH), 166.6 (C); ν_{max} (film, cm^{-1}) 3058, 3027, 2982, 2934, 2903, 1719, 1652, 1448, 1367, 1322, 1267, 1201, 1159, 1092, 1042 and 967; *m/z* (CI), 234 (MNH_4^+, 22%), 217 (MH^+, 100); 171 (6), 143 (16), 128 (11), 115 (6); [HRMS (CI): calcd for $C_{14}H_{20}NO_2$, 234.1494. Found: MNH_4^+, 234.1496 (0.7 ppm error)].

4.2.5. (4*E*)-5,9-Dimethyl-1,4,9-decatriene (*E*-36).

The title compound was obtained as a colourless oil. R_f=0.73 (PE–EtOAc, 9:1) on alumina; δ_H (270 MHz, $CDCl_3$) 1.61 (6H, s, CH_3^a), 1.69 (3H, s, CH_3^e), 1.99–2.10 (4H, m, CH_2^{c+d}), 2.75 (2H, app. br. t, dd, ^3J=7.0, 6.5 Hz, CH_2^g), 4.96 (1H, dd, ^3J=15.5 Hz, ^2J=1.0 Hz, $CH_2^{i\ cis}$), 5.01 (1H, dd, ^3J=19.5 Hz, ^4J=1.0 Hz, $CH_2^{i\ trans}$), 5.08– 5.19 (2H, m, CH's$^{f\ and\ b}$), 5.80 (1H, m, CH^h); δ_C (100.6 MHz, $CDCl_3$), 23.4, 25.7, 267 31.9, 32.2, 39.7, 114.0, 114.2, 121.3, 122.3, 124.3, 137.5; *m/z* (EI), 164 [M^+] (2%), 149 (5), 123 (10), 94 (14), 69 (100), 41 (57); [HRMS (EI): calcd for $C_{12}H_{20}$, 164.1565. Found: M^+, 164.1561 (2.2 ppm error)].

4.2.6. Ethoxy-5-phenyl-(1,4*E*)-pentadiene (*E*-39).

The title compound was obtained as a colourless oil. R_f= 0.73 (PE–EtOAc, 9:1) on alumina; δ_H (400 MHz, $CDCl_3$) 1.23 (3H, t, ^3J=7.0 Hz CH_3^f), 2.91 (2H, dd, ^3J=7.0 Hz, CH_2^c), 3.67 (2H, q, ^3J=7.0 Hz, CH_2^e), 3.83 (1H, d, ^3J=2.0 Hz, $CH_2^{d,\ trans}$), 3.84 (1H, d, ^3J=2.0 Hz, $CH_2^{d\ cis}$), 6.19 (1H, dt, ^3J=16.0, 7.0 Hz CH^b), 6.36 (1H, d, ^3J=16.0 Hz, CH^a), 7.10–7.15 (1H, m, CH^3), 7.16– 7.23 (2H, m, CH^1), 7.23–7.30 (2H, m, CH^2); δ_C (100.6 MHz, $CDCl_3$), 14.5 (CH_3), 38.7 (CH_2), 62.9 (CH_2), 81.4 (CH_2), 126.1 (CH), 126.6 (CH), 127.1 (CH), 128.4 (CH), 131.6 (CH), 137.5 (C), 161.7 (C); ν_{max} (film, cm^{-1}) 3028, 2978, 2927, 1653, 1599, 1496, 1448, 1425, 1385, 1294, 1277, 1227, 1192, 1117, 1070, 966, 800, 744 and 692; *m/z* (CI), 189 (MH^+, 100%), 143 (11); [HRMS (CI): calcd for $C_{13}H_{17}O_1$, 189.1279. Found: MH^+, 189.1278 (0.8 ppm error)].

4.2.7. Ethyl (2*Z*)-4-(4-nitrophenyl)-2-butenoate (*Z*-49).

The title compound was obtained as a pale yellow oil. R_f= 0.30 (PE–EtOAc, 9:1); δ_H (400 MHz, $CDCl_3$) 1.30 (3H, t, ^3J=7.0 Hz CH_3), 4.14 (2H, d, ^3J=7.5 Hz, CH_2), 4.21 (2H, q, ^3J=7.0 Hz, CH_2), 5.95 (1H, dd, ^3J=11.5 Hz, ^4J=1.0 Hz, CH), 6.31 (1H, dt, ^3J=11.5, 7.5 Hz, CH), 7.40 (2H, d, ^3J=8.5 Hz CH), 8.17 (2H, d, ^3J=8.5 Hz, CH); δ_C (100.6 MHz, $CDCl_3$), 14.2 (CH_3), 38.4 (CH_2), 60.2 (CH_2), 122.3 (CH), 126.3 (CH), 128.7 (CH), 137.8 (C), 147.2 (CH), 166.5 (C), 171.6 (C); ν_{max} (neat, cm^{-1}) 2957, 2925, 2854, 1716, 1682, 1645, 1600, 1521, 1346, 1206, 1167 and 1037; *m/z* (CI), 253 (MNH_4^+, 53%), 223, (16), 216 (25), 206 (100), 199 (21); [HRMS (CI): calcd for $C_{12}H_{17}O_4N_2$, 253.1188. Found: MNH_4^+, 253.1188 (0.2 ppm error)].

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