P(*t*-Bu)$_3$: A Versatile and Efficient Ligand in Homogeneous Catalysis

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Abstract: Changing substituents on phosphorus ligands can cause marked changes in the behaviour of the free ligands and of their transition metal complexes. In this review, we will describe the synthesis and the application of P(*t*-Bu)$_3$, an efficient ligand in numerous homogeneous catalytic systems and rationalise its singular behaviour.

Keywords: Tri-*tert*-Butyl Phosphine (P(*t*-Bu)$_3$), Palladium, Catalysis, Amination, Cross Coupling.

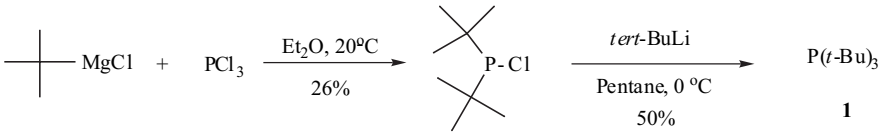
I. INTRODUCTION

It has long been recognised that changing substituents on phosphorus ligands can cause marked changes in the behaviour of the free ligands and of their transition metal complexes. Recently, it has appeared in this area that P(*t*-Bu)$_3$ (tri-*tert*-butyl phosphine) may have a singular behaviour since numerous reactions can be only performed using this ligand. In this review, we will describe the application of P(*t*-Bu)$_3$ as an efficient ligand in homogeneous catalysis and rationalise its particular properties.

II. SYNTHESIS AND PROPERTIES OF TRI-*TERT*-BUTYL PHOSPHINE

P(*t*-Bu)$_3$ **1** was readily accessible by addition of *tert*-Butyl Grignard reagent on PCl_3 followed by subsequent addition of one equivalent of *tert*-Butyl Lithium in 13% overall yield (Scheme **1**) [1].

Even if this synthesis was performed in 1967, the X-ray structure analysis has only been realised in 1995 by Bruckmann *et al.* [2]. Although the *tert*-Butyl groups are crystallographically independent, they are arranged in a pseudosymmetric way generated by a three-fold rotation axis passing through the phosphorus atom. Corresponding angles show no significant differences, but five of the six tetrahedral angles at every tertiary carbon atom are significantly different. The C-P-C angles are widered to 107.1 (1), 107.4 (1) and 107.8 (1) by steric effects and the cone angle is 176º (+/- 2º) and differs slightly from the value of 182º(+/- 2º) given by Tolman [3, 4]. Another interesting property was that the pK_a of P(*t*-Bu)$_3$ has been evaluated around 11.4. Thus, P(*t*-Bu)$_3$ appeared to be one of the most basic phosphine leading to a particular behaviour as ligand in numerous catalysed reactions [5].



Scheme 1.

III. PALLADIUM-CATALYSED AMINATION

Various triarylamines can be readily prepared in excellent yields by palladium-catalysed cross-coupling reaction of aryl halides and diarylamines. In 1998, Yamamoto *et al.* found that the palladium-catalysed amination reaction of bromobenzene with *N*-(3-methylphenyl)aniline in the presence of NaOtBu and a catalytic combination of Pd(OAc)$_2$/phosphine led to the synthesis of *N*-(3-methylphenyl)diphenylamine in varying chemical yields (Table **1**) [6].

On the other hand, it is noteworthy that a catalyst generated from a sterically small phosphine P(*n*-Bu)$_3$ did not provide any products whereas the use of a sterically hindered P(*t*-Bu)$_3$ ligand afforded the triarylamine in 99% yield. Due to its electron-donating property, ligand P(*t*-Bu)$_3$ influences the reactivity of the catalyst in the determined reductive elimination step from a palladium amide complex in the catalytic cycle [7]. Thus, the amination reaction of polybrominated aromatic compounds with the combination catalyst of Pd(OAc)$_2$ and P(*t*-Bu)$_3$ proceeds in excellent isolated yields up to 91% (Table **2**).

The same group has reported the use of the Pd(OAc)$_2$/P(*t*-Bu)$_3$ combination for the synthesis of *N*-aryl and *N*-heteroarylpiperazines from aryl halides and unprotected piperazine with turnover numbers up to 6400 (mol product/mol palladium) in numerous cases. Selected examples are illustrated in Table **3** [8].

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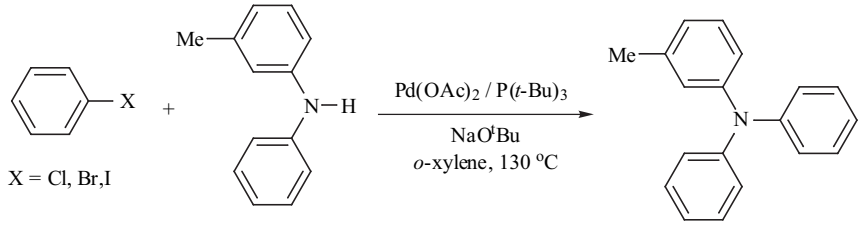
Since 1999, Hartwig *et al.* have extensively developed the Pd catalysed amination reaction of aryl halides in the presence of inexpensive and air-stable alkali metal hydroxide bases and Pd $[P(t\text{-}Bu)_3]_2$ as catalysts. On the basis of the previous cited articles, conditions can be found for the amination of aryl bromides with arylamines and with secondary alkylamines at room temperature using commercially available ligand $P(t\text{-}Bu)_3$ **1**. Moreover, this ligand allows for similar amination to be conducted with unactivated aryl chlorides at room temperature. Thus,

Table 1. Reactivity of Aryl Halides in the Synthesis of *N*-(3-methylphenyl)diphenylamine

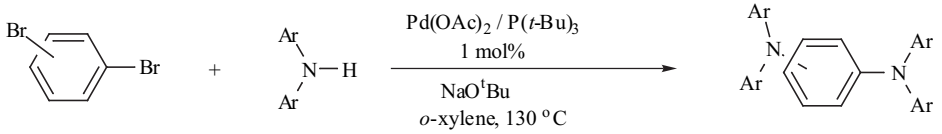


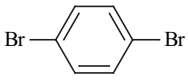
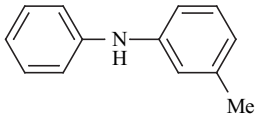
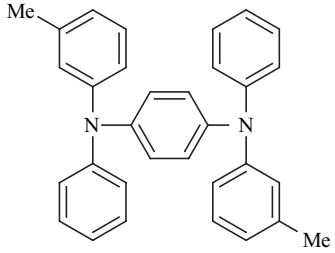
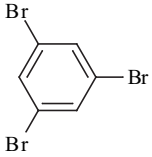
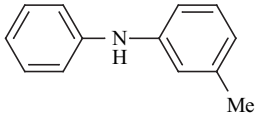
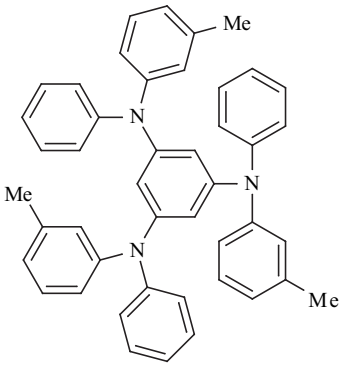
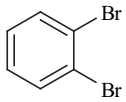
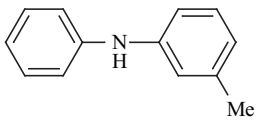
Entry	Aryl halide	Yield (%)
1	Chlorobenzene	58
2	Bromobenzene	99
3	Iodobenzene	98

Aryl halide / N-(3-methylphenyl)aniline / NaOtBu = 1:1:1.2

$Pd(OAc)_2$ 0.025 mol%, $P(t\text{-}Bu)_3$ / Pd = 4:1

Table 2. Synthesis of Various Triarylamines from Aryl Polyhalides and Diarylamines



Entry	Aryl polybromide	Diarylamine	Product	Yield (%)
1				80
2				77
3			-	No reaction

(Table 2)contd.....

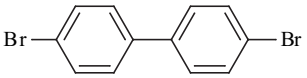
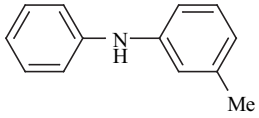
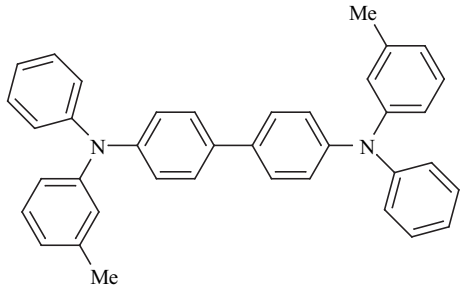
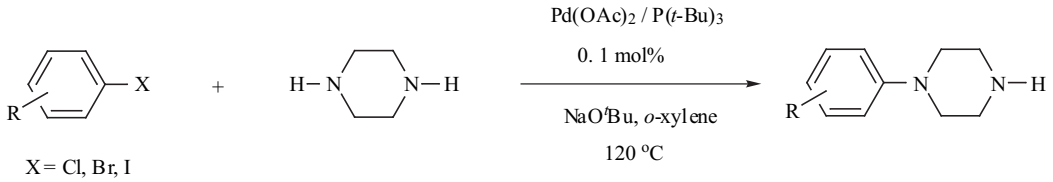
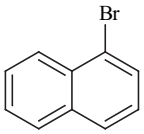
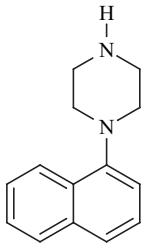
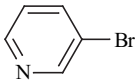
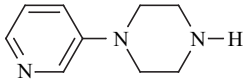
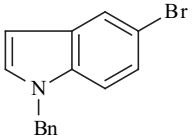
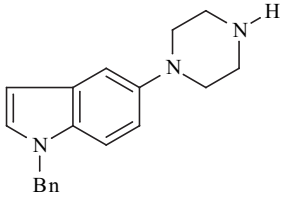
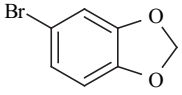
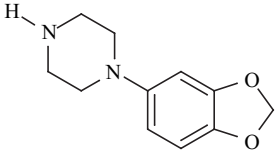
Entry	Aryl polybromide	Diarylamine	Product	Yield (%)
4				91

Table 3. Synthesis of *N*-heteroarylpiperazines

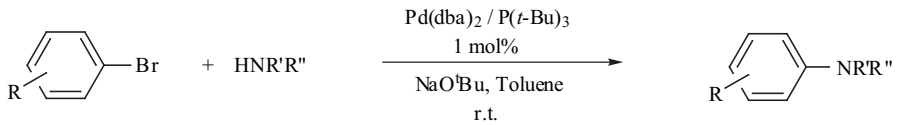


Entry	Aryl halide	Aryl piperazine	Yield (%)
1			84
2			76
3			89
4			85

amination of aryl bromides with arylamines and secondary alkylamines is summarised in Table **4** [9].

Finally, the use of aryl chlorides rather than bromides or iodides has been actively pursued because of the low cost of these reagents. The optimised conditions for aromatic amination allow for the formation of dialkylanilines, diarylamines or triarylamines from aryl chlorides at 70ºC with 1-5 mol% catalyst in yields that are similar to those observed at room temperature with bromides (Table **5**) [9].

Table 4. Room Temperature Reactions of Aryl Bromides with Amines Catalysed by Pd(0)/P(*t*-Bu)$_3$



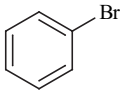
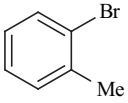
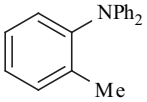
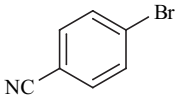
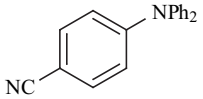
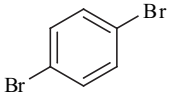
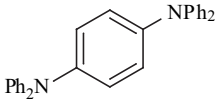
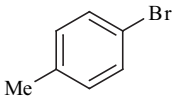
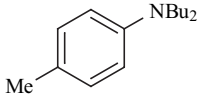
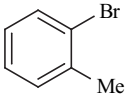
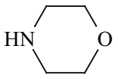
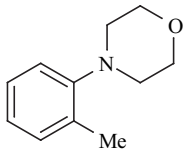
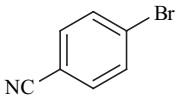
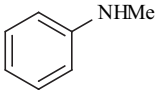
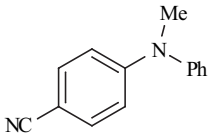
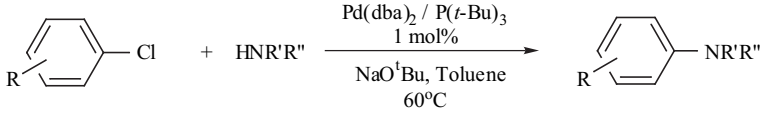
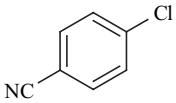
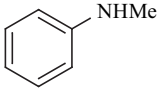
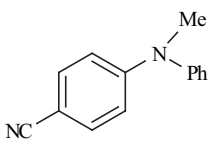
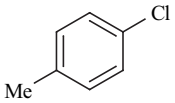
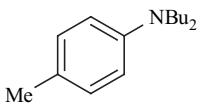
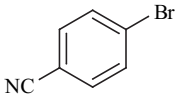
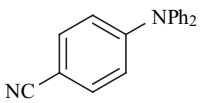
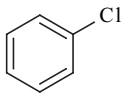
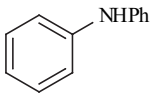
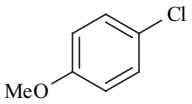
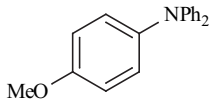
Entry	Aryl bromide	Amine	Product	Yield (%)
1		Ph_2NH	Ph_3N	91
2		Ph_2NH		97
3		Ph_2NH		97
4		Ph_2NH		85
5		$NHBu_2$		90
6				96
7				95

Table 5. Reactions of Aryl Chlorides with Amines Catalysed by Pd(0)/P(*t*-Bu)$_3$



Entry	Aryl chloride	Amine	Product	Yield (%)
1				90
2		Bu_2NH		86
3		Ph_2NH		82

(Table 5)contd.....

Entry	Aryl chloride	Amine	Product	Yield (%)
4		$PhNH_2$		75
5		$HNPh_2$		97

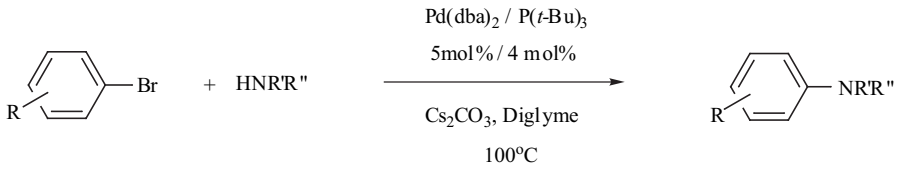
The scope of this reaction has been extended to the C-N bond formation between indole or pyrrole and unhindered aryl halides, either activated or unactivated occurring at 100ºC after 12 hours and using Cs_2CO_3 as crucial base, rather than NaO-*t*-Bu (Table **6**) [9].

Formation of Boc-protected anilines from aryl halides has been also investigated with chemical yields varying from 59 to 86% depending on the nature of the considered aryl halides (Table **7**) [9].

Alcazar-Roman *et al.* have provided that the catalytic reaction of aryl chlorides with amine and alkoxide base occurs by two concurrent mechanisms. One of these mechanisms involves direct participation of the base in the oxidative addition step. This pathway (path A) dominates when a highly active catalyst containing a 1:1 ratio of P(*t*-Bu)$_3$ and palladium is used (Scheme **2**) [10].

As an extension of this work, a simple palladium-catalysed method to convert aryl halides to the parent

Table 6. Reactions of Aryl Halides with Azoles Catalysed by Pd(0)/P(*t*-Bu)$_3$



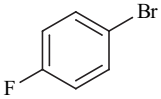
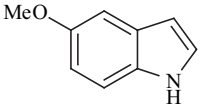
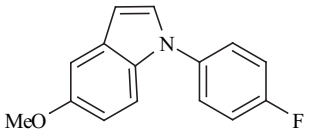
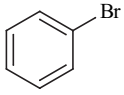
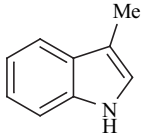
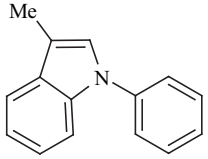
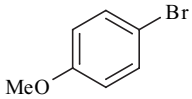
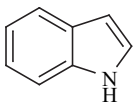
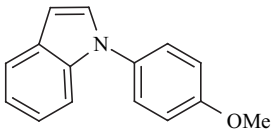
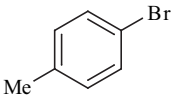
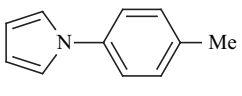
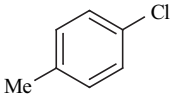
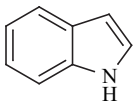
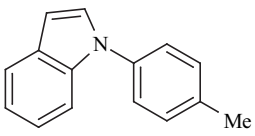
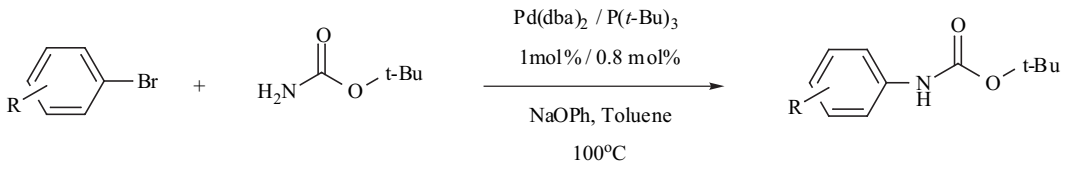
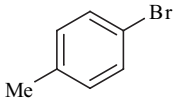
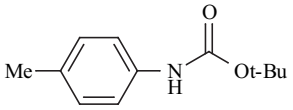
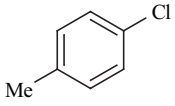
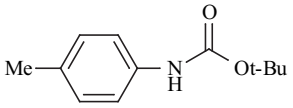
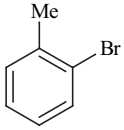
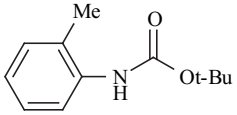
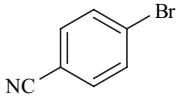
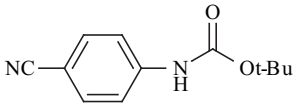
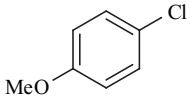
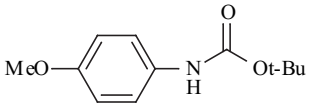
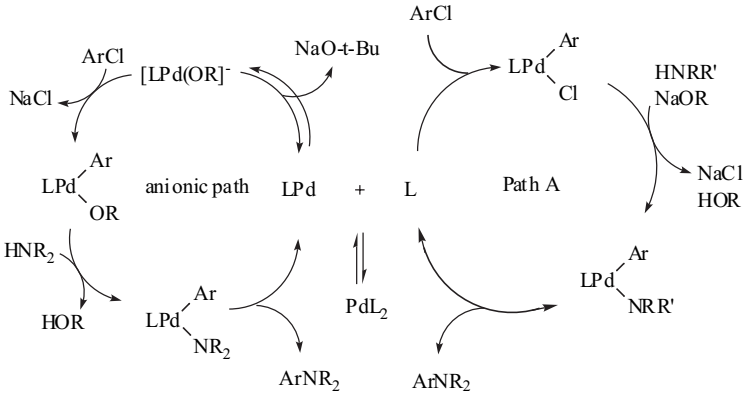
Entry	Aryl halide	Azole	Product	Yield (%)
1				72
2				88
3				83
4				77
5				64

Table 7. Reactions of Aryl Halides with *tert*-Butyl Carbamates Catalysed by Pd(0)/P(*t*-Bu)$_3$



Entry	Aryl halide	Product	Yield (%)
1			80
2			59
3			86
4			83
5			62

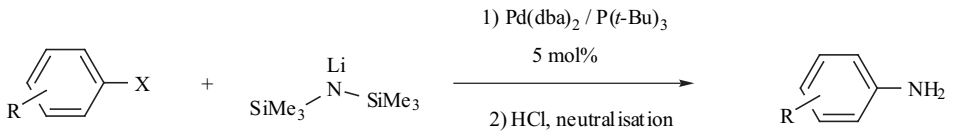


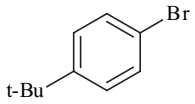
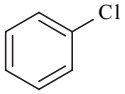
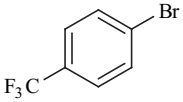
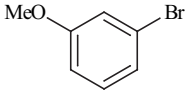
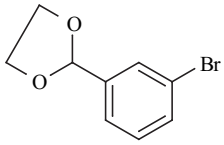
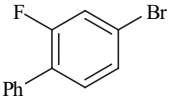
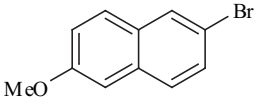
Scheme 2.

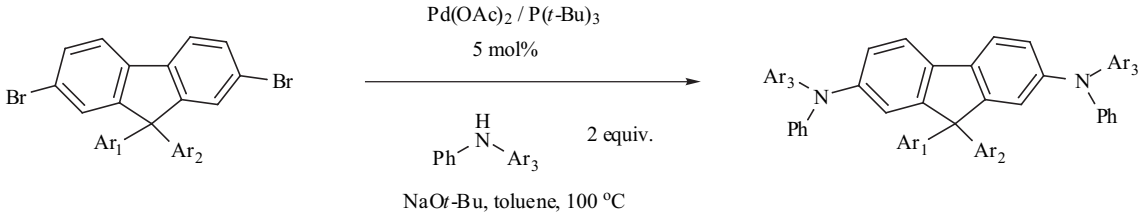
anilines using lithium bis(trimethylsilyl)amide has been reported by Lee *et al.* The reaction is catalysed by Pd(dba)$_2$ and P(*t*-Bu)$_3$ and can be run with as little as 0.2 mol% of catalyst. The reaction is faster than competing generation of benzyne intermediates and, therefore, provides the aniline products in chemical yields varying from 65 to 99% (Table **8**) [11].

In 2001, Wong *et al.* have investigated this reaction for the synthesis of a novel class of triarylamines with high glassy state stability, which are suitable as hole-transporting materials in organic light-emitting devices. The reactions of the 9,9-diaryl-2,7-dibromofluorene derivatives with different diarylamines were carried out in the presence of a catalytic amount of Pd(OAc)$_2$ and P(*t*-Bu)$_3$ in toluene at 100ºC with NaO*t*-Bu as the base (Scheme **3**) [12].

Table 8. Aromatic C-N Coupling of Lithium *bis*(trimethylsilyl)amide at Low Loading of Pd(0)/P(*t*-Bu)3 (1:1)



Entry	Substrate	Cat loading	Time	Yield (%)
1		0.2%	12h	89
2		0.5%	18h	90
3		0.5%	18h	65
4		0.2%	12h	91
5		1%	14h	99
6		1%	18h	86
7		0.2%	16h	95

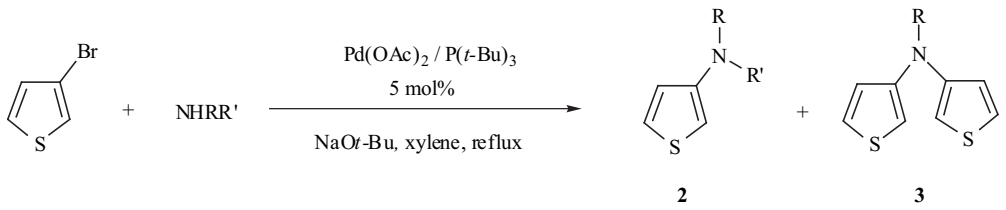


Scheme 3.

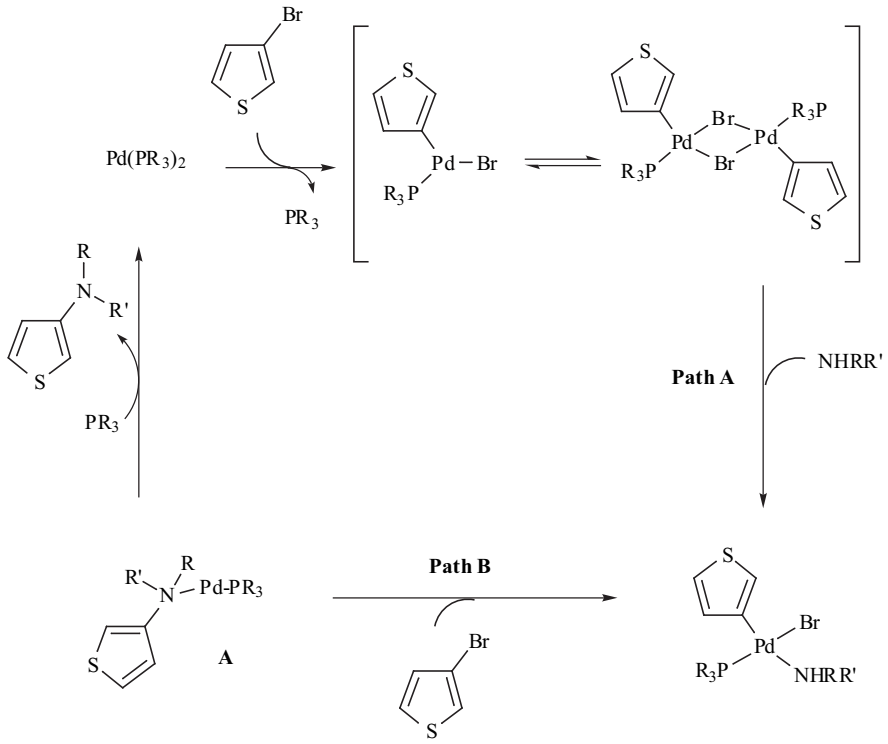
In this case, after column chromatography purification, the isolated yields for the products were good to excellent varying from 69 to 96%.

In another area of interest, functionalised thiophenes have appeared to be useful precursors for natural products and pharmaceuticals but few routes of synthesis have been envisioned and are limited to the production of primary 2-aminothiophenes containing electron-withdrawing groups in the 3-position. Thus, application of the $Pd(OAc)_2$ and P(*t*-Bu)$_3$ catalyst system to the amination of 3-bromothiophene successfully produced the desired 3-(*N*-alkyl)- and 3-(*N*,*N*-dialkyl)-aminothiophenes as shown in Table **9** [13].

Table 9. Pd-Catalysed Amination of 3-Bromothiophene



Entry	Amine	Yield of 2 (%)	Yield of 3 (%)
1	$NH_2C_6H_{13}$	37	20
2	$NH_2C_8H_{17}$	36	29
3	$NH_2C_{10}H_{21}$	44	44
4	$NH_2C(CH_3)_3$	54	19
5	$NH(C_6H_{13})_2$	24	-
6	*p*-$NH_2ArC_6H_{13}$	75	18



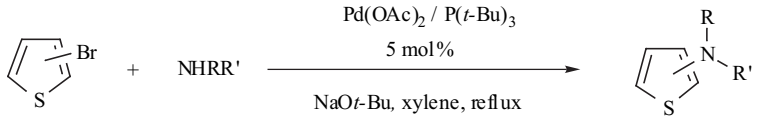
Scheme 4.

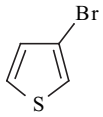
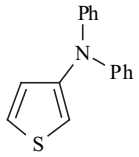
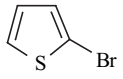
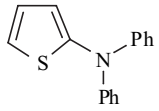
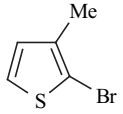
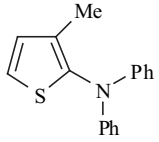
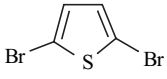
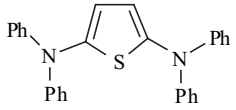
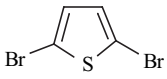
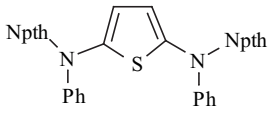
On the basis of these experimental results, a catalytic cycle based on the previous mechanistic studies of haloaryl aminations has been postulated (Scheme **4**).

The lower yields resulting from the use of akylamines is at least partially due to a β-elimination pathway that competes with the desired reductive elimination step (i.e. formation of complex **A**). Variations in the ratio of bromothiophene to amine used had only minor effects on the distribution of secondary to tertiary products. For this reason, it is believed that the aminothiophene product must remain coordinated to the palladium centre after reductive elimination. Formation of the tertiary diarylation product would then be controlled by competition between bromothiophene oxidative addition (path B) and product displacement rather than the competitive binding of different amines.

Watanabe *et al.* have also investigated the synthesis of novel (bis)(diarylamino)thiophenes *via* Pd-catalysed reaction of bromo- and dibromothiophenes with diarylamines leading to the expected compounds in chemical yields varying from 36 to 81% (Table **10**) [14].

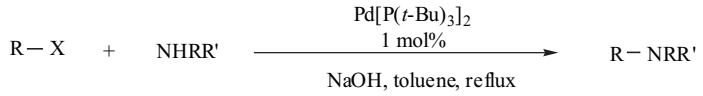
Table 10. Pd-Catalysed Synthesis of Bis(diarylamino)thiophenes

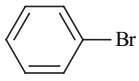
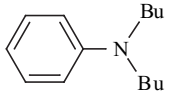
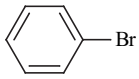
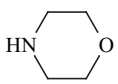
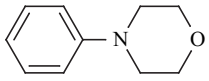
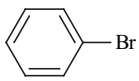
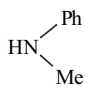
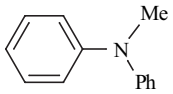


Entry	Substrate	Diarylamine	Product	Yield (%)
1		Ph_2NH		69
2		Ph_2NH		36
3		Ph_2NH		58
4		Ph_2NH		57
5		(Ph)(Npth)NH		56

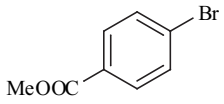
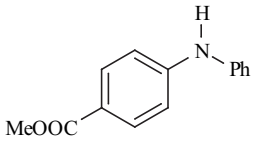
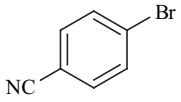
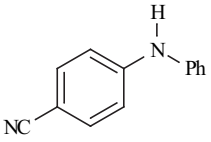
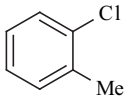
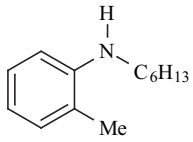
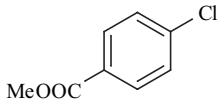
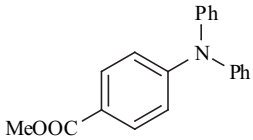
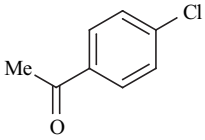
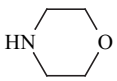
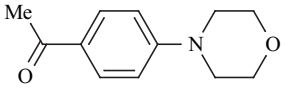
In 2002, Kuwano *et al.* have reported the amination of aryl halides in the presence of inexpensive and air-stable metal hydroxide bases and Pd $[P(t\text{-}Bu)_3]_2$ as catalyst giving arylamines in high yields. The reactions were conducted with a catalytic amount of cetyltrimethylammonium bromide as phase transfer agent and either aqueous hydroxide or solid hydroxide in the presence of water (Table **11**) [15].

Table 11. Amination of Aryl Halides in the Presence of Aqueous NaOH or Aqueous KOH



Entry	Aryl halide	Amine	Product	Yield (%)
1		$HNBu_2$		92
2				95
3				94

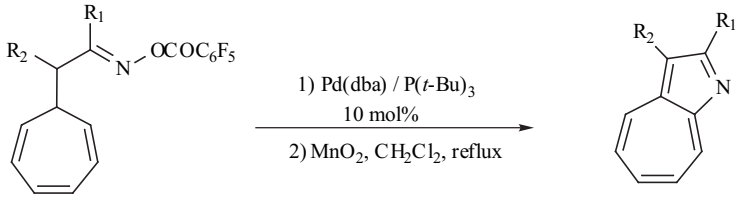
(Table 11)contd.....

Entry	Aryl halide	Amine	Product	Yield (%)
4		H_2NPh		92
5		H_2NPh		70
6		C_6H_{13}		91
7		$HNPh_2$		97
8				86

Although azaazulene derivatives have received much interest for several decades due to their physical properties as aza-nonbenzenoid aromatics and pharmacological activities, few preparative methods have been known. Thus, Kitamura *et al.* have recently apply the amino-Heck reaction to the synthesis of 1-azaazulenes from cycloheptatrienylmethyl ketone oximes (Table **12**) [16].

On the other hand, vinylation of various azoles (pyrrole, indole, carbazole and their derivatives) and phenothiazine with vinyl bromides catalysed by palladium-P(*t*-Bu)$_3$ complexes has been achieved leading to the expected N-vinylazoles compounds in 30-99% yield. It has been also noticed that this reaction with *cis*- and *trans*-β-bromostyrenes is stereospecific giving the respective products with full retention of configuration (Table **13**) [17].

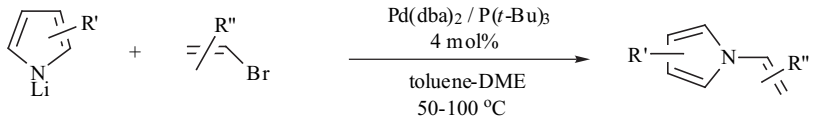
Table 12. Synthesis of Azaazulene 5 from Oxime 4 by Amino-Heck Reaction

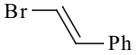
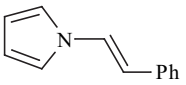
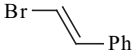
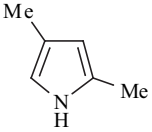
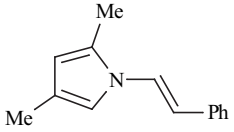
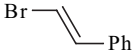
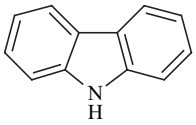
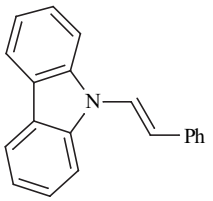
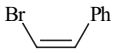
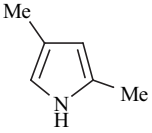
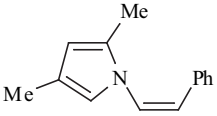
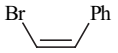
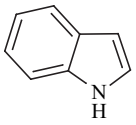
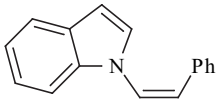
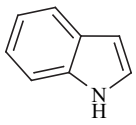
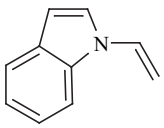
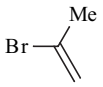
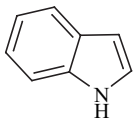
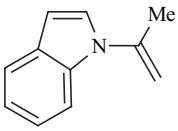


4 **5**

Entry	R_1	R_2	Yield (%)
1	Ph	H	78
2	*tert*-Bu	H	84
3	*i*-Pr	H	62
4	Me	H	27
5	Ph	Me	52
6	Ph	Ph	55

Table 13. Catalytic Vinylation of Azoles and Phenothiazine



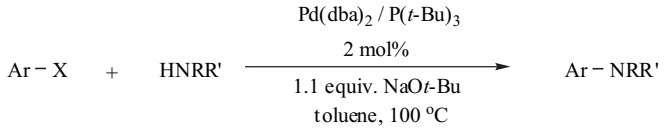
Entry	Vinyl bromide	Azole	Product	Yield (%)
1				30
2				91
3				75
4				96
5				99
6				61
7				58

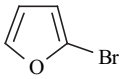
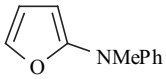
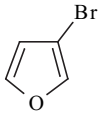
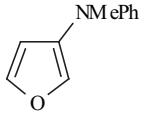
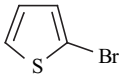
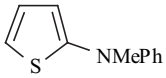
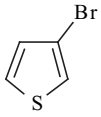
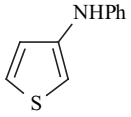
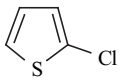
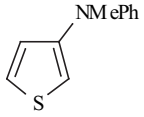
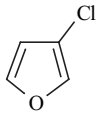
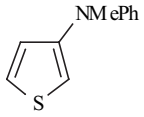
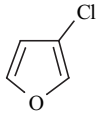
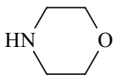
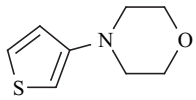
Because *N*-vinylazoles are widely used as building blocks for photosensitive and photoelectronic polymers and composites, the Pd-catalysed vinylation of azoles is an appealing method, suitable for industrial application. It can be a good alternative to the direct hydroamination of acetylene, since the latter method can lead to a formation of explosive byproducts in industrial equipment.

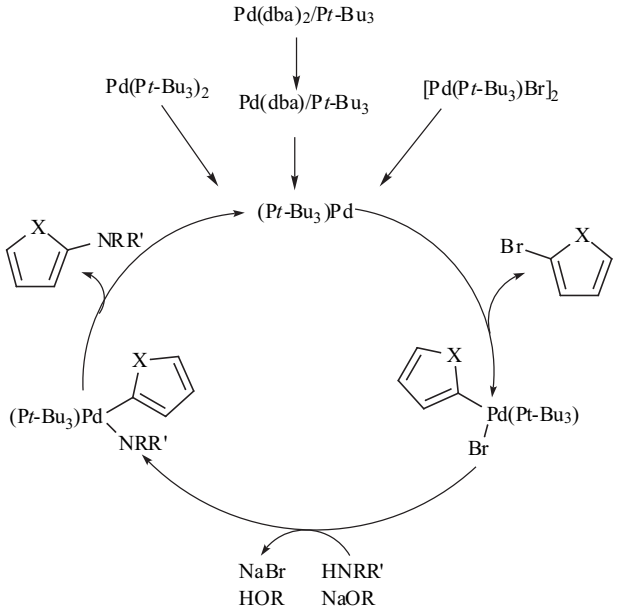
Recently, detailed studies have been conducted by Hooper *et al*. to determine the activity of Pd catalysts for the amination of five membered heterocyclic and to determine the factors that control the scope of this reaction. Pd-catalysed aminations of the electron-rich furanyl, thiophenyl and indolyl halides and of the related 2-halogenated thiazoles, benzimidazole and benzoxazole have been shown to occur with a subset of amines (Table **14**) [18].

The studies reported by Hooper *et al.* suggest that efficient generation of the $Pd(P(t\text{-}Bu)_3)$ intermediate is crucial to observe amination with less reactive substrates, such as bromothiophenes and bromofurans. It is clear that $Pd(P(t\text{-}Bu)_3)_2$ cannot initiate most of the couplings of the heteroaryl bromides and Hartwig suggests that unfavourable thermodynamics for ligand dissociation and oxidative

Table 14. Amination of Heteroaryl Halides with $Pd(dba)_2/P(t\text{-}Bu)_3$



Entry	Aryl halide	Amine	Product	Yield (%)
1		HNMePh		56
2		HNMePh		85
3		HNMePh		82
4		H_2NPh		88
5		HNMePh		49
6		HNMePh		50
7				41

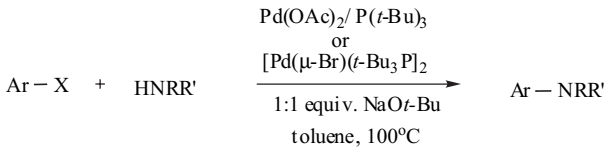


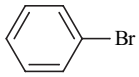
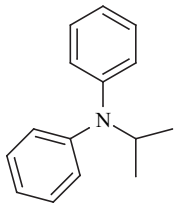
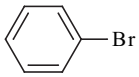
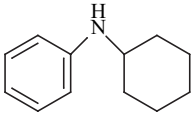
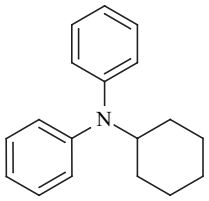
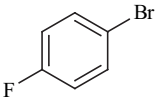
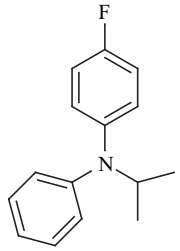
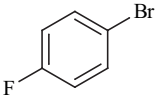
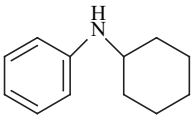
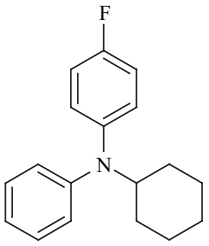
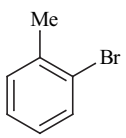
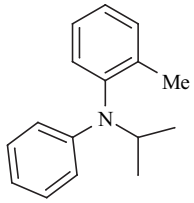
Scheme 5.

addition to $Pd(P(t\text{-}Bu)_3)_2$ makes the addition unfavourable enough to prevent formation of the amido complex. Instead, mixing of $Pd(dba)_2$ and $P(t\text{-}Bu)_3$ may feed the system higher concentrations of $Pd(P(t\text{-}Bu)_3)(dba)$ and $Pd/P(t\text{-}Bu)_3$ then would be generated from full equilibration of $Pd(dba)_2$ and $Pd/P(t\text{-}Bu)_3$ or from dissociation of ligand from $Pd(P(t\text{-}Bu)_3)_2$. Consistent with the assertion that a 1:1 stoichiometry of ligand and metal is present in the active catalyst, the palladium(I) dimer $[Pd(Br)(P(t\text{-}Bu)_3)]_2$ serves as one of the most active precatalysts (Scheme **5**) [18].

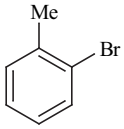
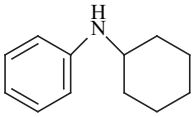
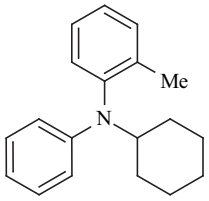
Recently, an efficient Pd-catalysed amination of aromatic bromides with hindered N-alkylsubstituted anilines has been described either using the combination of $Pd(OAc)_2$ and $P(t\text{-}Bu)_3$ or a Pd(I)tri-*tert*-butylphosphine bromide dimer $[Pd(\mu\text{-}Br)(t\text{-}Bu_3P)]_2$ a commercially available and easily handled catalyst (Table **15**) [19].

Table 15. Pd-Catalysed Amination with Hindered Anilines



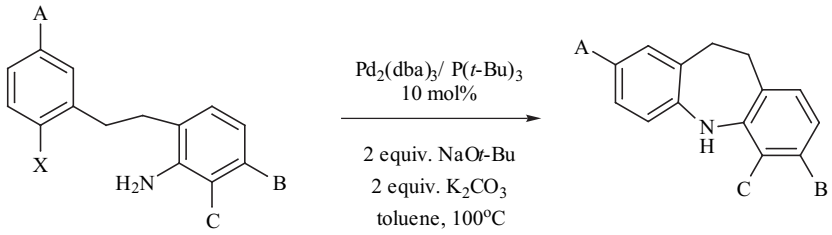
Entry	Aryl halide	Amine	Product	Yield (%)
1		HN(*i*-Pr)Ph		85
2				86
3		HN(*i*-Pr)Ph		68
4				71
5		HN(*i*-Pr)Ph		25

(Table 15)contd.....

Entry	Aryl halide	Amine	Product	Yield (%)
6				52

In 2003, Margolis *et al.* have disclosed an alternative synthesis of hetero benzazepine ring systems. The key step in the synthesis exploits recent advances in Pd catalysis to form oxazepine and thiazepine ring systems. Overall the best conditions for this reaction were $Pd_2(dba)_3$ as a palladium source, P(*t*-Bu)$_3$ as the ligand, NaO*t*-Bu alone or with K_2CO_3 in toluene. This reaction worked on a variety of substrates as shown in Table **16** [20].

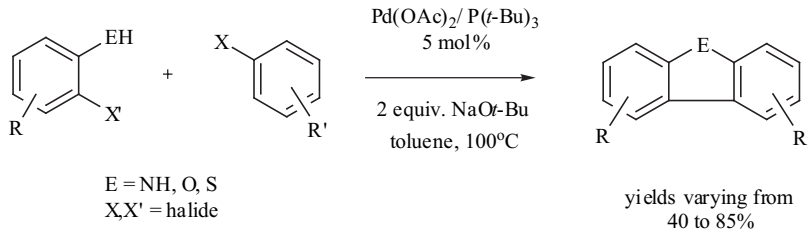
Table 16. Intramolecular Pd-Catalysed Amination



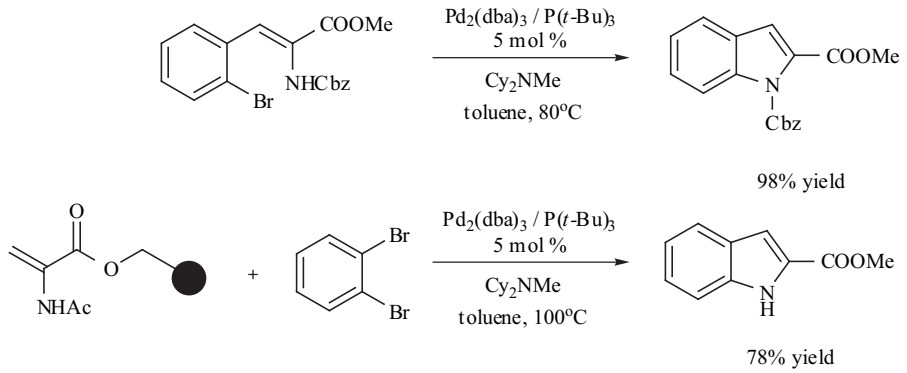
Entry	A group	B group	C group	Yield (%)
1	H	H	H	67
2	H	CF_3	H	70
3	H	H	Me	65
4	F	H	H	93
5	OMe	H	H	69

Bedford *et al.* have investigated the synthesis of carbazoles by a sequential double coupling of 2-chloroanilines with arylbromides catalysed by a Pd complex generated from palladium acetate and 1.25-1.4 equivalents of P(*t*-Bu)$_3$ using NaO*t*-Bu as base in toluene. Scheme 6 illustrates this reaction yielding the carbazole products in yields varying from 40 to 85% [21].

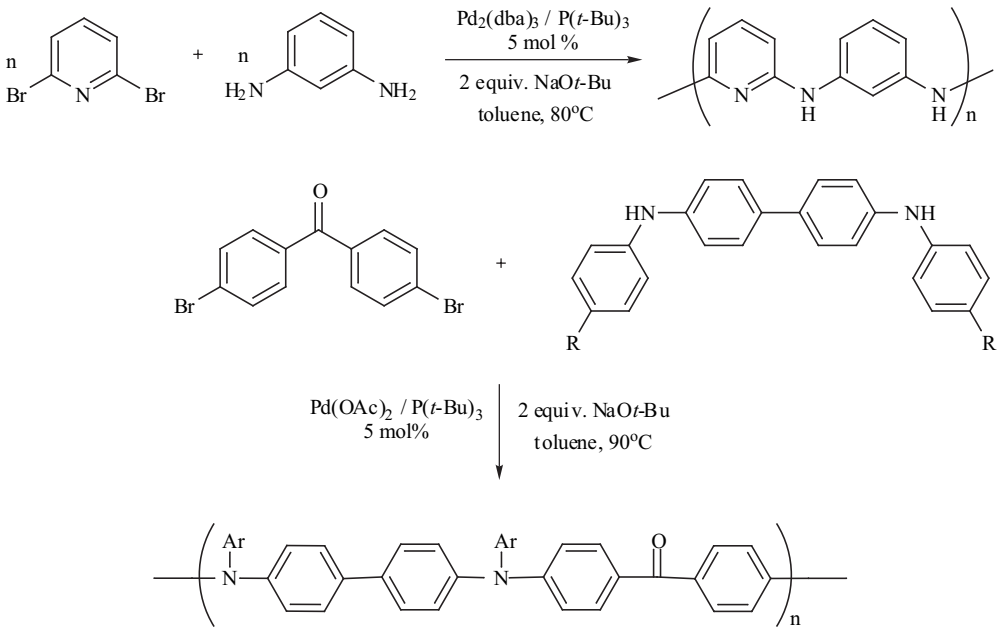
As already mentioned, an intramolecular version of the amination reaction has permitted to synthesise a wide variety of nitrogen-containing heterocyclic compounds. As an extension of this reaction, intramolecular Pd-catalysed *N*-arylation of immobilised dehydrohalophenylalaninate was found to proceed smoothly to form indolecarboxylates. The method was successfully combined with the Heck reaction to perform one pot indole synthesis *via* Pd-catalysed tandem C,N-arylation reactions (Scheme **7**) [22, 23].



Scheme 6.



Scheme 7.



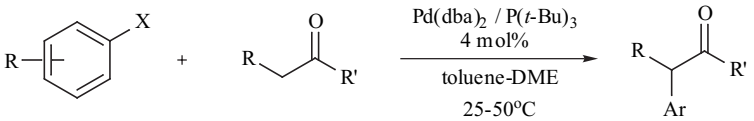
Scheme 8.

Since the discovery in 1985 that doped polyaniline is capable of conducting electricity in the metallic regime, researches have been focused on the methods of synthesis of such polymers. Goodson and Kanbara have examined utility of the Pd-catalysed amination in the polycondensation of aryl dibromides with secondary diamines to afford poly(arylenediamine)s and triarylamine polymers (Scheme **8**) [24, 25].

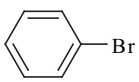
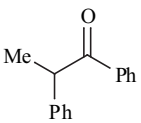
Pd-Catalysed Arylation of Ketones and Malonates

Introduction of an sp3 carbon side-chain into an aromatic ring is one of the most important processes in organic synthesis. In 1999, Kawatsura *et al.* reported for the first time a remarkably catalytic palladium active system for α-arylation of ketones and malonates using P(*t*-Bu)$_3$ as sterically hindered ligand. Thus, this catalytic system gave exceptionally fast rates and high turnover numbers for these reactions (Table **17**) [26].

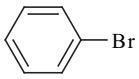
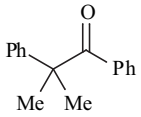
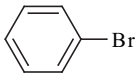
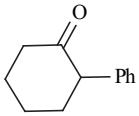
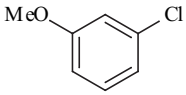
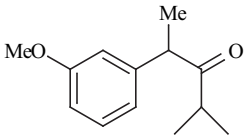
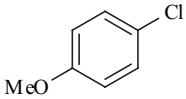
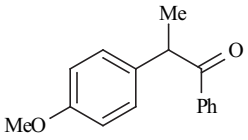
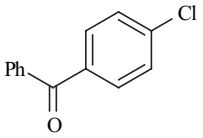
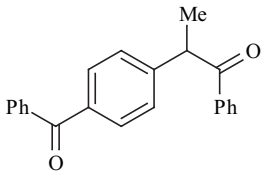
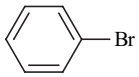
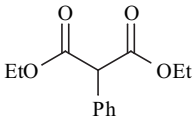
Table 17. Pd-Catalysed Reactions of Ketones and Malonates with ArBr and ArCl



R,R' = alkyl, aryl
X = Br, Cl

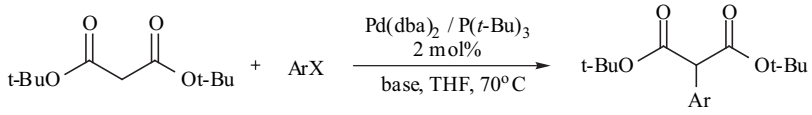
Entry	Aryl halide	Product	Yield (%)
1			97

(Table 17)contd.....

Entry	Aryl halide	Product	Yield (%)
2			96
3			73
4			69
5			91
6			95
7			80

Turnover numbers of 20000 were observed in many cases. Moreover, activation of chloroarenes under mild conditions does not require chelation as one might expect from previous palladium chemistry with chloroarenes. The

Table 18. Arylation of Di-*tert*-Butylmalonate



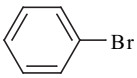
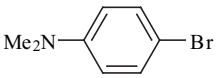
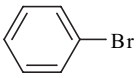
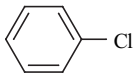
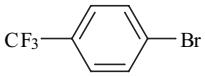
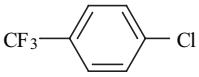
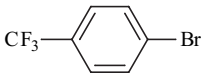
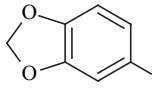
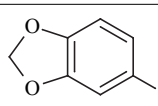
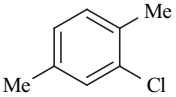
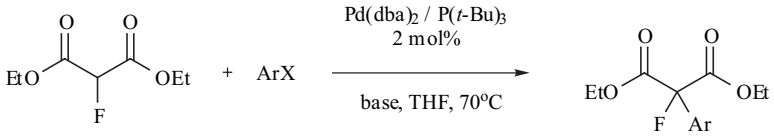
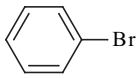
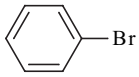
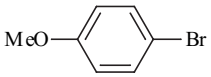
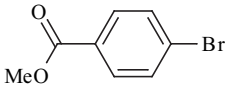
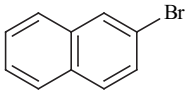
Entry	Aryl halide	Base, Yield (%)	Entry	Aryl halide	Base, Yield (%)
1		NaH, 89	6		NaH, 90
2		K_3PO_4, 91	7		NaH, 88
3		NaH, 88	8		NaH, 86
4		K_3PO_4, 90	9		NaH, 87
5		NaH, 87	10		NaH, 90

Table 19. Palladium-Catalysed Arylation of Diethyl Fluoromalonate



Entry	Aryl halide	Base, Yield (%)
1		NaH, 84
2		K_3PO_4, 88
3		NaH, 88
4		NaH, 89
5		NaH, 79

results of reaction between di-*tert*-butyl malonate and diethyl 2-fluoromalonate are presented in Tables **18** and **19** [27].

In all cases the conversions are excellent and it is noteworthy that both K_3PO_4 and NaH were suitable bases, although reactions containing K_3PO_4 as base required substantially longer times for complete generation of the coupled product.

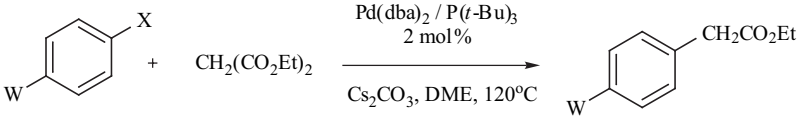
Recently, One-pot conversion of aryl halides into aryl acetates was achieved by Kondo *et al.* by the Pd-catalysed arylation of malonate accompanying dealkoxycarboxylation of aryl malonates using Cs_2CO_3 as a base (Table **20**) [28].

Pd-Catalysed Arylation of Esters

A catalytic amount of $Pd(dba)_2$ ligated by P(*t*-Bu)$_3$ ligand mediated the coupling of aryl halides and ester enolates to produce α-aryl esters in high yields at room temperature. The reaction was highly tolerant of functionalities and substitution patterns on the aryl halide as underlined in Tables **21** and **22** [29].

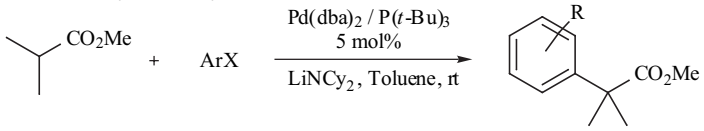
In the same area, Lee *et al.* have reported a Pd-catalysed arylation of esters and protected amino acids. In this case, excellent results have been obtained using 2 mol% of a $Pd(dba)_2$/P(*t*-Bu)$_3$ catalyst system with chemical yields up to 80% in numerous cases (Scheme **9**) [30].

Table 20. Palladium-Catalysed Conversion of Aryl Halides into Aryl Acetates



Entry	W	Yield (%)
1	H	87
2	OMe	70
3	COOEt	61
4	H	78
5	H	75

Table 21. Scope of the Arylation of Methyl Isobutyrate



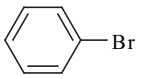
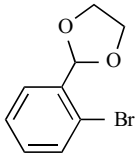
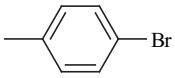
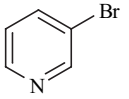
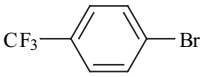
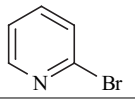
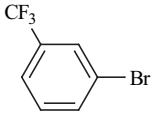
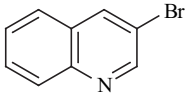
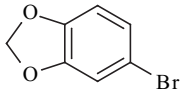
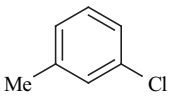
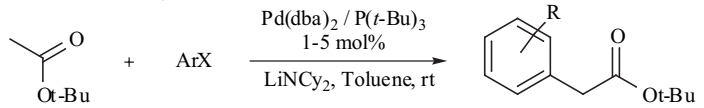
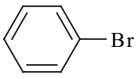
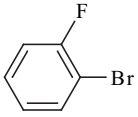
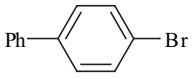
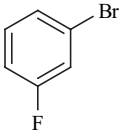
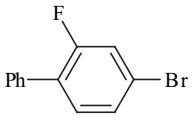
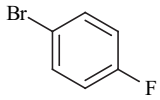
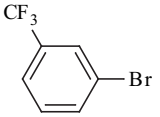
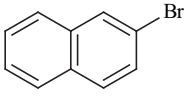
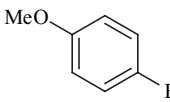
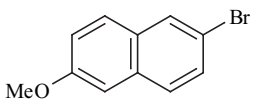
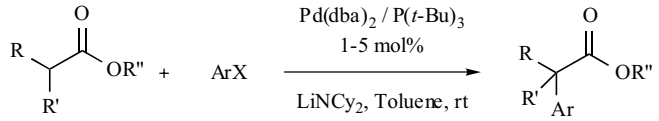
Entry	Aryl halide	Yield (%)	Entry	Aryl halide	Yield (%)
1		87	6		77
2		90	7		80
3		86	8		94
4		89	9		70
5		95	10		71

Table 22. Arylation of the Enolate of *tert*-Butyl Acetate



Entry	Aryl halide	Yield (%)	Entry	Aryl halide	Yield (%)
1		92	6		88
2		96	7		95
3		93	8		95
4		85	9		93
5		95	10		96

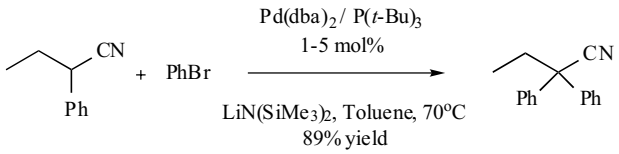


Scheme 9.

Pd-Catalysed Arylation of Ethylcyanoacetate and Nitriles

α-aryl cyanoacetates are useful intermediates in the preparation of amino alcohols, β-amino acids and arylacetic acids. Previous methods for the direct coupling of cyanoacetates with aryl halides used stoichiometric amounts or high catalyst loadings of copper and required iodide substrates and high temperatures [31, 32]. In 2001, Stauffer *et al.* reported a mild arylation of cyanoesters displaying broad reaction scope and permitting to construct materials with highly hindered quaternary carbons (Table **23**) [33].

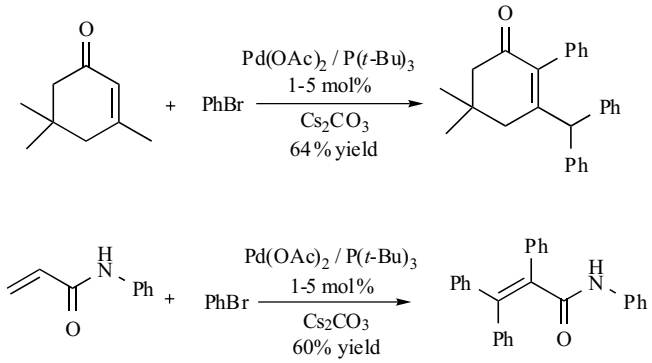
As an extension of this study, the Pd-catalysed arylation of nitriles has been investigated by Culkin *et al.* as illustrated in Scheme **10** [34].



Scheme 10.

Pd-Catalysed Arylation of Carbonyl Compounds

The Pd-catalysed direct arylation of carbonyl compounds using aryl halides has been recently developed by Satoh *et al.* Thus, a convenient method using P(*t*-Bu)$_3$ as ligand of a palladium source led to the formation of desired compounds in high chemical yields (Scheme **11**) [35, 36].

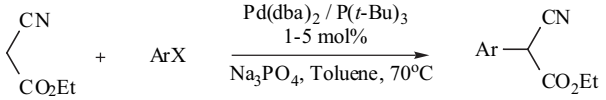


Scheme 11.

Pd-Catalysed Heck Reactions

Since its discovery in the early 1970's, the Pd-catalysed arylation of olefins has been applied to a diverse array of fields, ranging from natural products synthesis, to materials science to bioorganic chemistry [37, 38]. In 1999, Littke *et al.* have established that certain Pd-catalysed coupling

Table 23. Pd-Catalysed Arylation of Ethyl Cyanoacetate



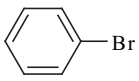
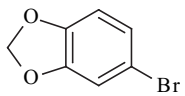
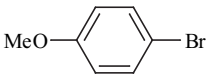
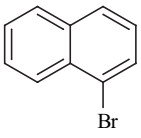
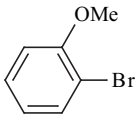
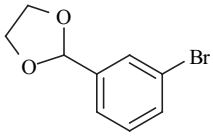
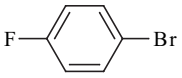
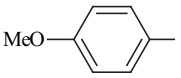
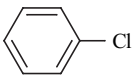
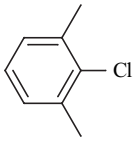
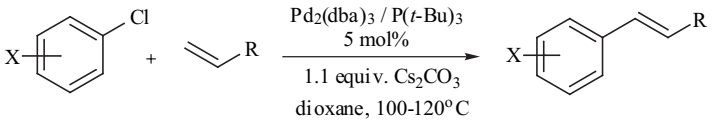
Entry	Aryl halide	Yield (%)	Entry	Aryl halide	Base, Yield (%)
1		87	6		84
2		89	7		83
3		83	8		81
4		91	9		90
5		86	10		87

Table 24. Scope of the $Pd_2(dba)_3/P(t\text{-}Bu)_3$-Catalysed Heck Coupling of Aryl Chlorides



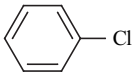
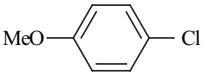
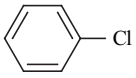
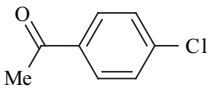
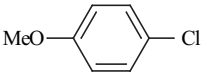
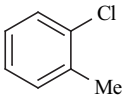
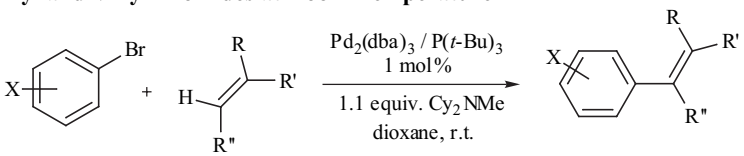
Entry	Aryl halide	R	Yield (%)
1		CO_2Me	76
2		CO_2Me	82
3		Ph	83
4		Ph	74
5		Ph	84
6		Ph	70

Table 25. Heck Coupling of Aryl and Vinyl Bromides at Room Temperature



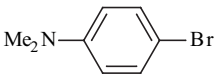
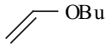
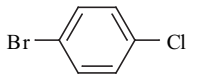
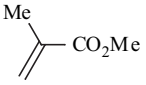
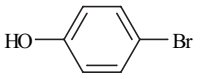
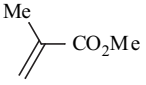
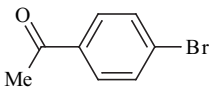
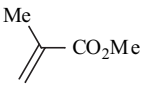
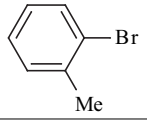
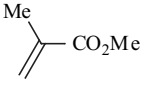
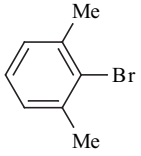
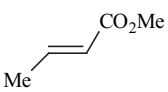
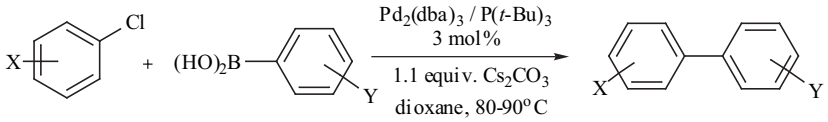
Entry	Aryl halide	Olefin	Yield (%)
1			97
2			70
3			77
4			74
5			86
6			83

Table 26. Scope of the $Pd_2(dba)_3/P(t\text{-}Bu)_3/Cs_2CO_3$-Catalysed Suzuki Coupling of Aryl Chlorides

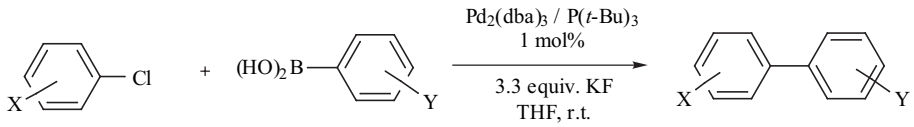


Entry	X	Y	Yield (%)
1	4-Me	H	87
2	4-MeCO	H	91
3	4-MeO	H	89
4	4-NH_2	H	92
5	4-Me	4-CF_3	86
6	4-Me	4-OMe	82

reactions of aryl chlorides can be accomplished quite efficiently in the presence of sterically hindered, electron rich phosphines (such as $P(t\text{-}Bu)_3$). Thus, $Pd/P(t\text{-}Bu)_3$ serves as an exceptionally mild and versatile catalyst for Heck reactions of aryl chlorides (Table **24**) [39].

The choice of the base has a crucial effect on the outcome of the reaction and Cs_2CO_3 appears to be the base of choice in terms of chemical yield performing the reaction at 100ºC in dioxane. As an extension of this work, Littke *et al.* have reported in 2001 that the replacement of Cs_2CO_3 with Cy_2NMe improved the reaction permitting the room temperature coupling of a wide array of aryl bromides with a broad spectrum of olefins. Thus, in all cases the expected compounds were obtained in high chemical yields varying from 64 to 97% (Table **25**) [40].

Table 27. Suzuki Cross-Coupling of Activated Aryl Chlorides at Room Temperature



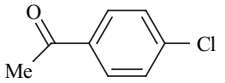
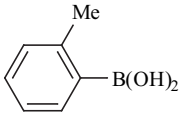
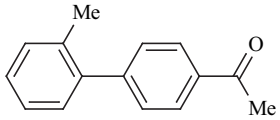
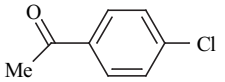
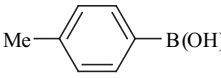
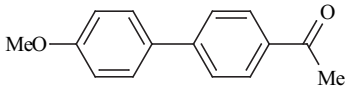
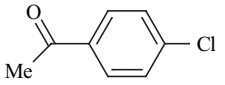
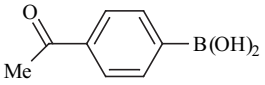
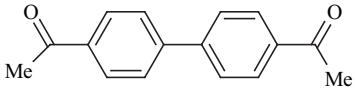
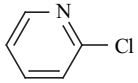
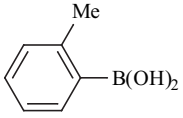
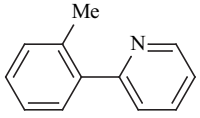
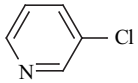
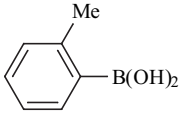
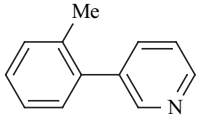
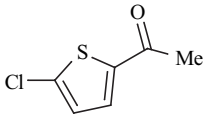
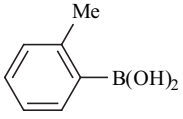
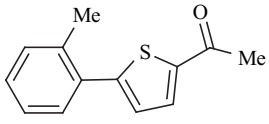
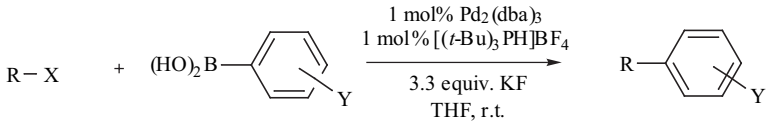
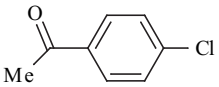
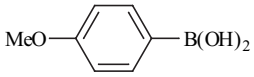
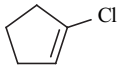
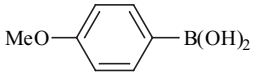
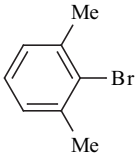
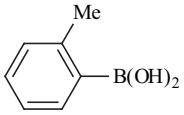
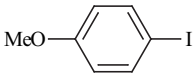
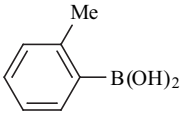
Entry	Aryl Chloride	Boronic acid	Product	Yield (%)
1				99
2				93
3				84
4				97
5				97
6				99

Table 28. Suzuki Cross-Coupling Using $[(t\text{-Bu})_3PH]BF_4$



Entry	Aryl Chloride	Boronic acid	Yield (%)
1			90
2			82
3			93
4			98

Pd-Catalysed Suzuki Cross-Coupling of Arylboronic Acids with Aryl Halides

The Pd-catalysed Suzuki cross coupling of aryl halides and aryl triflates with arylboronic acids to form biaryls has emerged as an extremely powerful tool in organic syntheses. In 1998, Littke *et al.* discovered that $Pd_2(dba)_3/P(t\text{-Bu})_3$ catalyses the Suzuki cross coupling of a wide array of aryl chlorides and arylboronic acids with Cs_2CO_3 or CsF as the base in dioxane at 80-90ºC (Table **26**) [41].

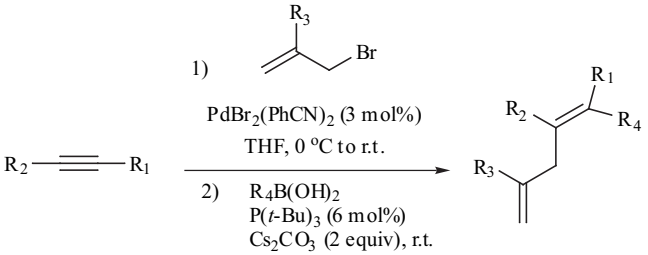
Since then, Littke *et al.* have investigated the replacement of CsF by less expensive KF and found that Suzuki reactions are even more rapid in the presence of KF and that the reaction may occur in THF at room temperature in high chemical yields (Table **27**) [42].

Because most Pd-catalysed coupling reactions that employ $P(t\text{-Bu})_3$ as a ligand also require Bronsted-base additives, Netherton *et al.* envisioned that simply substituting the $P(t\text{-Bu})_3$ in the original $Pd_2(dba)_3/P(t\text{-Bu})_3$ protocols with $[(t\text{-Bu})_3PH]BF_4$ would lead to comparable results. The data in Table **28** establish that air stable $[(t\text{-Bu})_3PH]BF_4$ is indeed a suitable substitute for air sensitive $P(t\text{-Bu})_3$ in Suzuki cross coupling reactions. Thus, Fu *et al.* have obtained comparable (within 5%) isolated yields for cross coupling reactions of aryl and vinyl halides under mild conditions [43].

It is noteworthy that the phosphonium salt may also be used instead of the free phosphine in Heck and Stille coupling of aryl halides without any loss in terms of chemical yields.

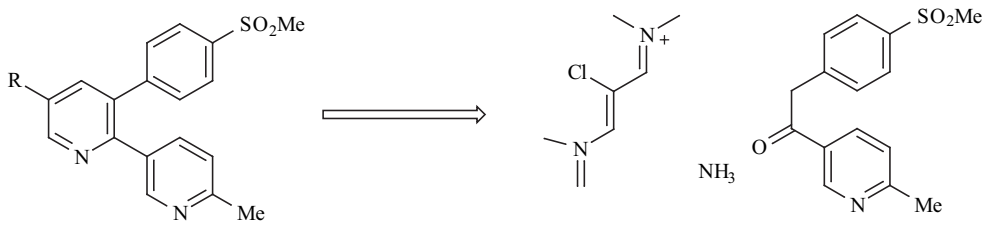
In 2002, Thadani *et al.* have reported the development of a stereospecific haloallylation/Suzuki cross-coupling of a wide range of alkynes and boronic acids in which the same palladium catalyst promotes both reactions (Table **29**) [44].

Table 29. One-Pot Tandem Bromoallylation/Suzuki Cross-Coupling of Alkynes at r.t



Entry	R_1	R_2	R_3	R_4	Yield (%)
1	H	CO_2Me	H	4-$MeOC_6H_4$	83
2	CH_2OTBS	H	H	3-Me(O)CC_6H_4	86
3	$C(Me)_2OH$	H	H	4-$MeOC_6H_4$	81
4	Ph	H	Me	4-$MeOC_6H_4$	83
5	Ph	H	H	(*E*)-PhCH=CH	86
6	*n*-Pr	*n*-Pr	Me	*N*-tosyl-3-indoyl	83

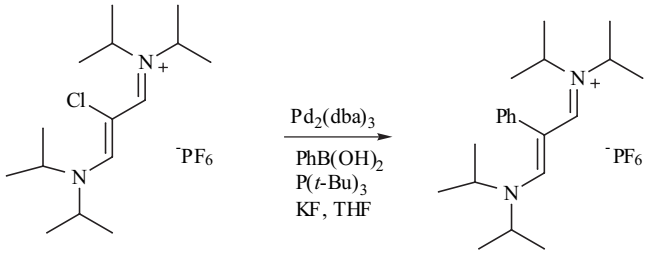
In all cases, excellent chemical yields have been observed up to 86%. Recently, several groups have investigated the Fu conditions in specific reactions employing a Suzuki cross coupling step. Thus, Etoricoxib **6** has been identified by Merck as a very potent and specific COS-2 inhibition [45, 46]. This group has described how **6** can be assembled by the construction of the central pyridine ring from the readily accessible ketone **8**, the vinamidinium species **7** and ammonia (Scheme **12**) [47].



Etoricoxib **6** **7** **8**

Scheme 12.

Boronic acids, esters and borinic anhydrides are partners in Suzuki-Miyaura cross coupling reactions with a variety of β-chlorovinamidinium salts to give the desired β-arylvinamidinium salts in up to 70% yield (Scheme **13**).



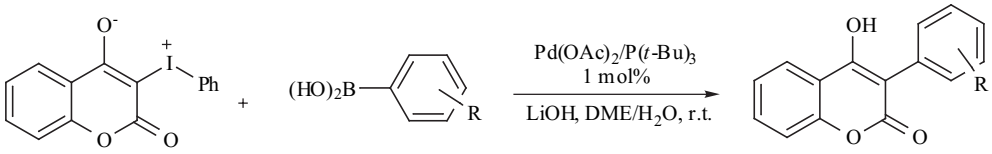
70% yield

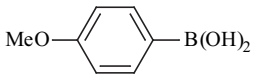
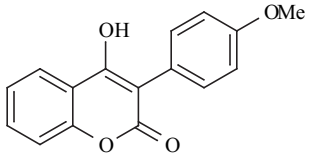
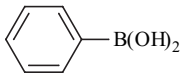
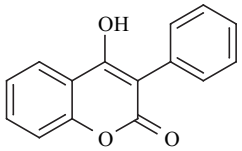
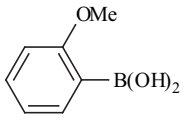
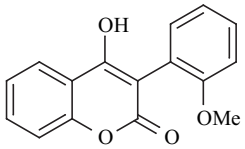
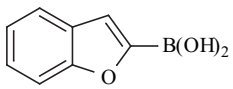
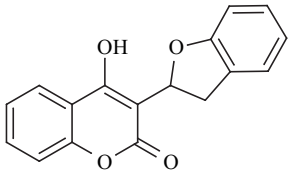
Scheme 13.

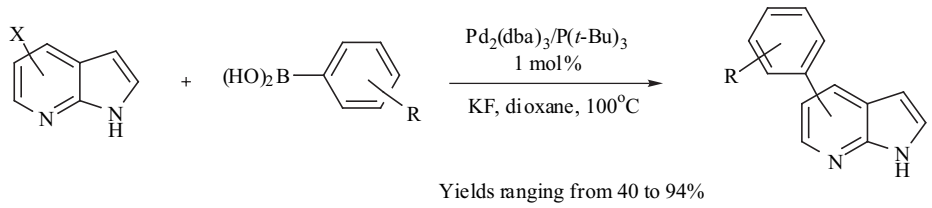
On the other hand, a palladium catalysed coupling reaction of phenyliodonium zwitterions with aryl boronic acids has been developed by Zhu *et al.* to generate 3-arylcoumarins that would not be otherwise easily synthesised *via* alternative methods (Table **30**) [48].

Recently, the synthesis of 4- and 6-substituted-7-azaindoles through Pd-catalysed coupling reactions of the corresponding halosubstituted-7-azaindoles has been described by Allegretti *et al.* in excellent yields varying from 40 to 94% (Scheme **14**) [49].

Table 30. Pd-Catalysed Cross-Coupling of Phenyl-Iodonium Zwitterion with Aryl Boronic Acids



Entry	Boronic acid	Product	Yield (%)
1			92
2			72
3			82
4			80

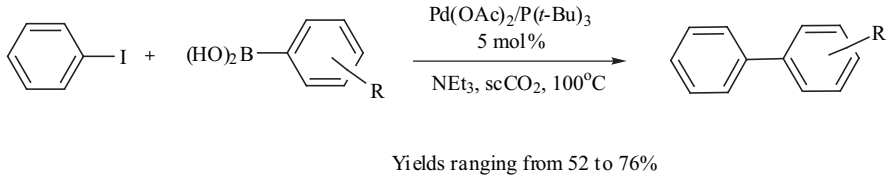


Scheme 14.

The synthesis of organic molecules in the absence of volatile organic solvents remains an important industrial goal and the use of alternative reaction media in synthetic chemistry has attracted widespread attention. Thus, Suzuki reactions proceed in good yield in supercritical carbon dioxide in the presence of palladium acetate and tri-*tert*-butylphosphine with both free and polymer-tethered substrates (Scheme **15**) [50].

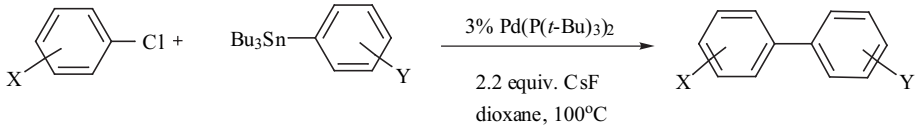
Pd-Catalysed Stille Reaction

Stille cross-coupling has proved to be an especially popular tool for synthetic organic chemists due in part to the air and moisture stability of organotin reagents, as well as the excellent functional group compatibility of the process. In 2002, Littke *et al.* found that Pd/P(*t*-Bu)$_3$ combination serves as an unusually reactive catalyst for Stille reactions of aryl chlorides and bromides, providing solutions to a



Scheme 15.

Table 31. Stille Cross-Coupling of Aryl Chlorides by Pd(P(*t*-Bu)$_3$)$_2$



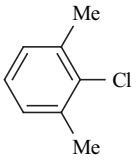
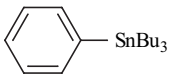
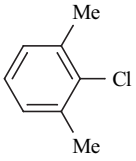
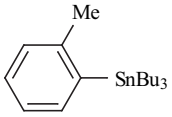
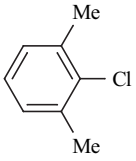
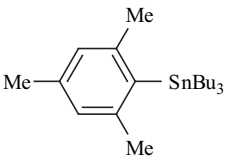
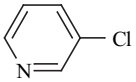
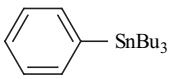
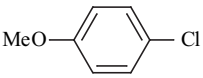
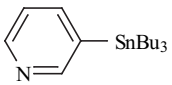
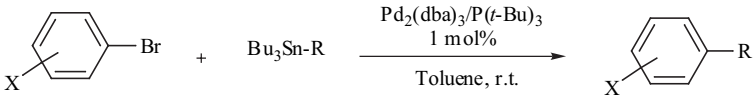
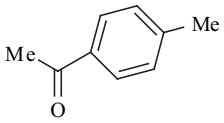
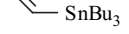
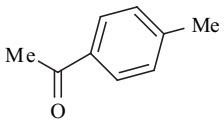
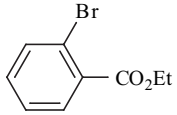
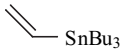
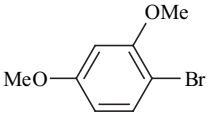
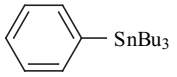
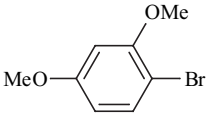
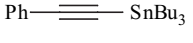
Entry	Aryl chloride	Bu_3Sn-R	Yield (%)
1			94
2			96
3			89
4			76
5			47

Table 32. Room Temperature Stille Cross-Coupling of Aryl Bromides



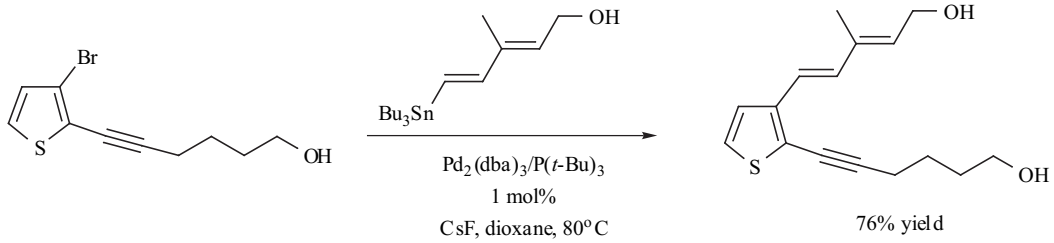
Entry	Aryl bromide	Bu_3Sn-R	Yield (%)
1			88
2			97
3			92
4			97
5			83

number of long standing challenges. Thus, in the case of the development of a general method for Stille reactions of aryl chlorides, it has been demonstrated the transfer of a wide array of groups from the organotin reagent and the synthesis of very hindered biaryls (Table **31**) [51].

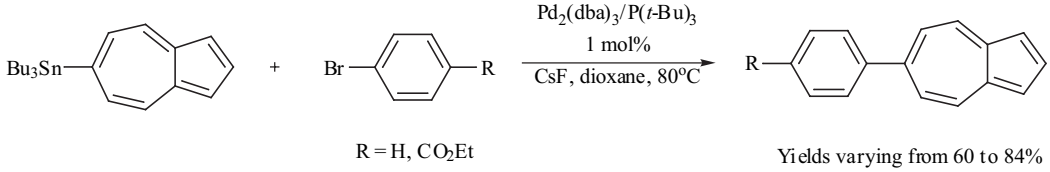
Moreover, Littke *et al.* have determined that Pd/P(*t*-Bu)$_3$ effects the room temperature cross-coupling of a wide variety of aryl bromides with a broad range of organotin reagents. As illustrated in Table 32 in the presence of 1mol% Pd, Stille couplings proceed in very good yield at room temperature [52].

This methodology has been successfully applied by de Pereira *et al.* in the synthesis of 2,3-disubstituted thiophene derivatives performing the reaction in dioxane at 80ºC. In this case, the expected products have been obtained in chemical yield of up to 76% (Scheme **16**) [53].

On the other hand, organometallic reagents derived from azulenes, *i.e.*, 6-(tri-n-butylstannyl)azulene and its 1,3-diethoxycarbonyl derivatives have been prepared by Pd(0) catalysed stannylation of 6-bromoazulenes with bis(tri-*n*-butyltin) and applied in the Stille cross-coupling reaction with aryl and acyl halides to afford 6-aryl and 6-acyl derivatives in good yields (Scheme **17**) [54].

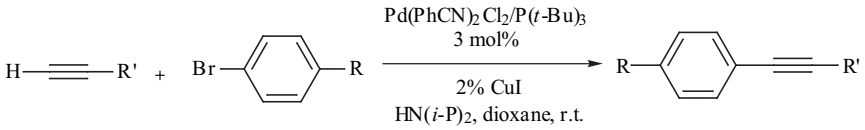


Scheme 16.



Scheme 17.

Table 33. Room Temperature Sonogashira Couplings Catalysed by $Pd(PhCN)_2Cl_2/P(t\text{-}Bu)_3$



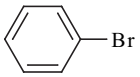
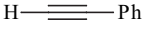
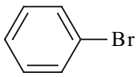
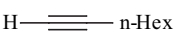
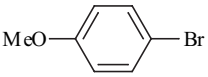
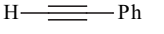
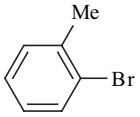
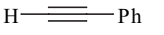
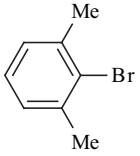
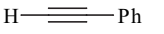
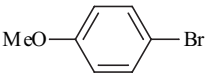
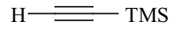
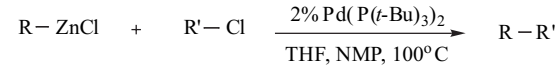
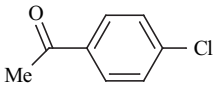
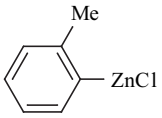
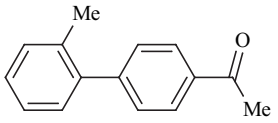
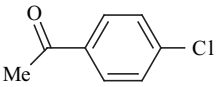
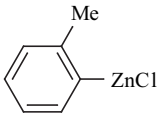
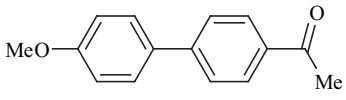
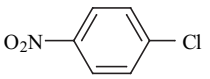
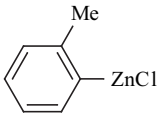
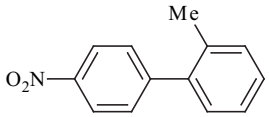
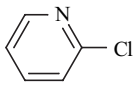
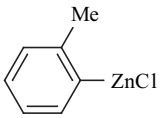
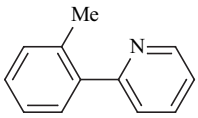
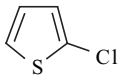
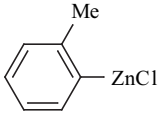
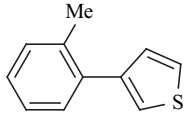
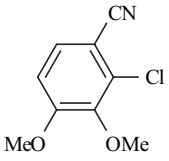
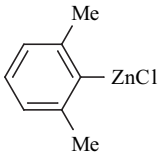
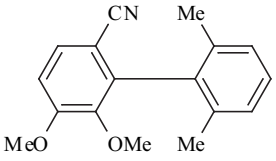
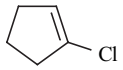
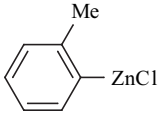
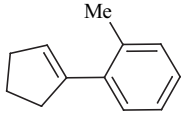
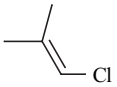
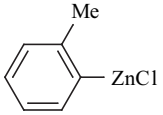
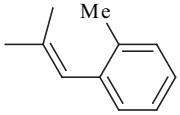
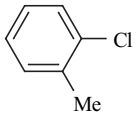
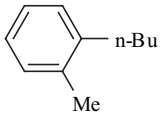
Entry	Aryl bromide	Alkyne	Yield (%)
1			94
2			70
3			94
4			94
5			63
6			90

Table 34. Pd-Catalysed Negishi Cross-Coupling of Aryl and Vinyl Chlorides



Entry	R'-Cl	R-ZnCl	Product	Yield (%)
1				50
2				97
3				92
4				92

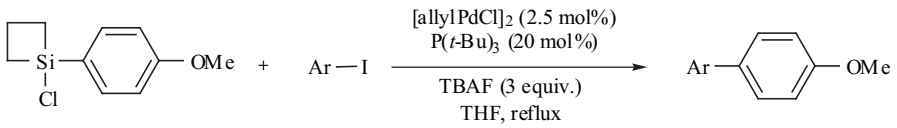
(Table 34)contd.....

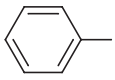
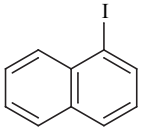
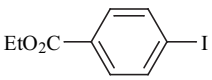
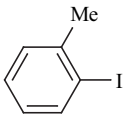
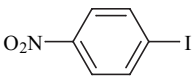
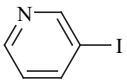
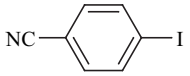
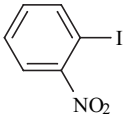
Entry	R'-Cl	R-ZnCl	Product	Yield (%)
5				97
6				76
7				94
8				87
9		ClZn-*n*Bu		83

Pd-Catalysed Sonogashira Reaction

The Sonogashira coupling reaction of terminal acetylenes with aryl and vinyl halides provides a powerful method for synthesising conjugated alkynes, an important class of molecules that have found application in diverse areas ranging from natural product chemistry to materials science. Thus, in 2000 Hundertmark *et al.* have found that $Pd(PhCN)_2Cl_2/P(t\text{-}Bu)_3$ serves as an efficient and a versatile

Table 35. Cross Coupling of Selected Aryl Iodides



Entry	Aryl iodide	Yield (%)	Entry	Aryl iodide	Yield (%)
1		91	5		85
2		83	6		89
3		75	7		71
4		81	8		84

catalyst for room temperature Sonogashira reactions of aryl bromides in high chemical yields (Table **33**) [55].

Pd-Catalysed Negishi Reaction

The Pd-catalysed cross coupling of aryl and vinyl halides/triflates with organozinc reagents represents a powerful method for generating aromatic compounds such as styrene derivatives and biaryls. Recently, Dai *et al.* reported that with a single protocol, commercially available Pd(P(*t*-Bu)$_3$)$_2$ can effect the Negishi cross-coupling of a wide range of aryl and vinyl chlorides with aryl- and alkylzinc reagents. The processes tolerates nitro groups, and it efficiently generates strically-hindered biaryls. In addition, a high turnover number (>3000) can be achieved (Table **34**) [56].

MISCELLANEOUS

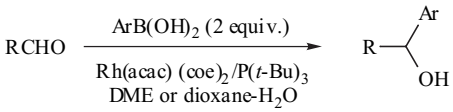
Synthesis of Unsymmetrical Biaryls from Arylsilacyclobutanes

The biaryl subunit is a commonly found motif in biologically active molecules. Thus, aryl(fluoro)silacyclobutanes and aryl(chloro)silacyclobutanes have been found to undergo cross-coupling reactions with aryl iodides. Thus, with P(*t*-Bu)$_3$ a wide range of electronically and structurally diverse unsymmetrical biaryls have been prepared in good to excellent yields (Table **35**) [57].

Rhodium-Catalysed Addition of Arylboronic Acids to Aldehydes

In 2000, Ueda *et al.* described a large accelerating effect of P(*t*-Bu)$_3$ in the rhodium-catalysed addition of arylboronic acids to aldehydes affording the expected alcohols in high chemical yield as outlined in Table **36** [58, 59].

Table 36. Addition of Arylboronic Acids to Aldehydes

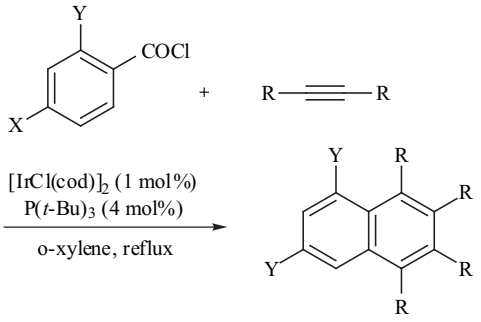


Entry	$ArB(OH)_2$	RCHO	Yield (%)
1	$PhB(OH)_2$	3-$O_2NC_6H_4CHO$	94
2	$PhB(OH)_2$	4-$O_2NC_6H_4CHO$	94
3	$PhB(OH)_2$	4-NCC_6H_4CHO	94
4	$PhB(OH)_2$	4-BrC_6H_4CHO	97
5	4-$MeOC_6H_4B(OH)_2$	4-$MeOC_6H_4CHO$	91
6	2-$MeC_6H_4B(OH)_2$	4-$MeOC_6H_4CHO$	99
7	2,4,6-$Me_3C_6H_2B(OH)_2$	4-$F_3CC_6H_4CHO$	trace
8	$PhB(OH)_2$	$C_5H_{11}CHO$	35

Iridium-Catalysed Reaction of Aroyl Chlorides with Internal Alkynes

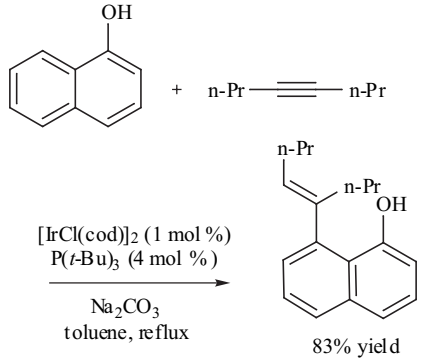
Yasukawa *et al.* have developed a new, useful method for aromatic homologation with two aliphatic alkynes molecules using an iridium catalyst, giving condensed aromatics with substantial solubilities. The reaction proceeds efficiently without causing β-elimination and excessive insertion of alkyne. The tolerance of C-halogen bonds under the iridium catalysis enables various catalytic derivatisations of the products (Table **37**) [60].

Table 37. Preparation of Naphthalenes by the Reaction of Aroyl Chlorides with Internal Alkynes



Entry	Chloride, X, Y	Alkyne	Yield (%)
1	Me, H	*n*-Pr	91
2	*t*-Bu, H	*n*-Pr	96
3	OMe, H	*n*-Pr	50
4	H, OMe	*n*-Pr	35
5	Cl, H	*n*-Pr	67
6	Br, H	*n*-Pr	69
7	H, H	*n*-Bu	79
8	H, H	Ph	70

This methodology has been successfully applied to the regioselective reaction of 1-naphthols with alkynes at the *peri*-position to afford the corresponding 8-substituted 1-naphthol derivatives as illustrated in Scheme **18** [61].



Scheme 18.

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