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Neopentylphosphines as effective ligands in palladium-catalyzed cross-couplings of aryl bromides and chlorides

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Abstract

The use of neopentylphosphine ligands in the palladium-catalyzed Suzuki, Sonogashira, Heck, and Hartwig–Buchwald couplings of aryl bromides and chlorides are reported. Di-*tert*-butylneopentylphosphine (DTBNpP) provided highly active catalysts for the coupling of aryl bromides at mild temperatures. Trineopentylphosphine, an air-stable trialkylphosphine, gave inactive catalysts at room temperature, but showed good activity in the H–B amination of aryl chlorides at elevated temperatures.

1. Introduction

Palladium-catalyzed cross-coupling reactions are one of the cornerstones of modern synthetic methodology. Despite their widespread use in academic[1] and industrial syntheses,[2] there remains active interest in identifying new catalyst systems that offer improved activity and stability. Significant advances have been made in the development of 'ligand-free' catalyst systems, but these catalysts typically require high reaction temperatures and more reactive aryl bromide or iodide substrates.[3,4] In addition, although many of these systems are successful for the Suzuki coupling, only a few examples of the use of ligand free catalyst systems in the more challenging Heck,[5–7] Sonogashira,[8,9] and Hartwig–Buchwald (H–B) couplings of aryl bromides have been reported. These examples generally require high temperatures (>120 °C). Ligand supported catalyst systems are typically required for these more challenging reactions, particularly when using less reactive substrates under mild conditions.

While the design of ligands for Pd-catalyzed coupling reactions remains somewhat a trial-and-error enterprise, certain general concepts have become clear over the past decade. Ligands that promote reactions of aryl bromides (<50 °C) and aryl chlorides (<110 °C) under mild conditions are typically sterically demanding and strong σ donors. Examples of these types of ligands include sterically demanding trialkylphosphines,[10–18] dialkylarylphosphines,[19–26] bicyclic triaminophosphines,[27,28] and *N*-heterocyclic carbenes.[29–37] The effectiveness of these ligands can be rationalized by considering the key steps in the generic catalytic cycle (Scheme 1). The large steric bulk of these ligands promotes ligand dissociation from the coordinatively saturated PdL_2 resting state to form the highly reactive PdL active species. Sterically demanding ligands can also promote reductive elimination and migratory insertion in cases where these are rate limiting steps. Electron rich ligands are thought to promote the oxidative addition step with less reactive substrates, such as aryl chlorides.

On the basis of these trends, we have become interested in applying neopentylphosphines as ligands in cross-coupling reactions. The neopentyl substituent is more sterically demanding than the *tert*-butyl group, yet it is less electron donating. Given the importance of ligand size in coupling reactions,

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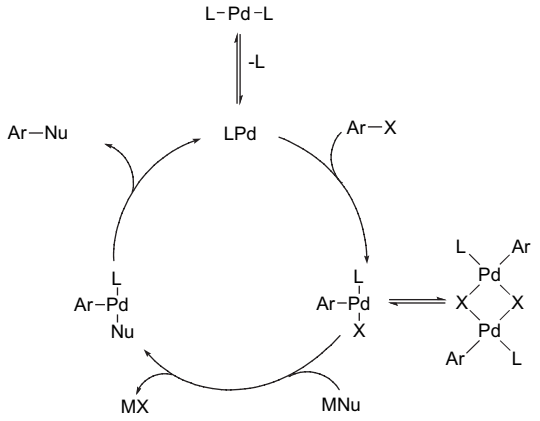


Scheme 1.

introduction of neopentyl substituents may lead to more effective ligands. Despite the large number of ligands that have been studied in palladium-catalyzed cross-coupling reactions, neopentylphosphines have received limited attention.[38,39] We have previously reported the use of di-*tert*-butylneopentylphosphine (DTBNpP, Fig. 1) and other analogous neopentylphosphines in the H—B coupling of aryl bromides and chlorides.[18] DTBNpP was found to give catalysts with better activity than those derived from tri-*tert*-butylphosphine (TTBP) for the amination of aryl bromides, but the DTBNpP-derived catalysts were less effective in couplings of aryl chlorides. DTBNpP and TNpP gave less active catalysts for the amination of aryl bromides.

We now report the use of neopentylphosphines in Suzuki, Heck, Sonogashira, and H—B coupling of aryl bromides and chlorides. DTBNpP has been found to be an effective ligand for the coupling of aryl bromides in each of these reactions. Surprisingly, the more sterically demanding and less electron donating TNpP ligand gave catalysts with good activity in the H—B amination of aryl chlorides. We also report the use of a new ligand, di-*tert*-butyl-(3-methoxy-2,2-dimethylpropyl)phosphine (DTBMONpP), which is a methoxy-substituted analog of DTBNpP. This ligand offers some potential advantages over DTBNpP. The oxygen of DTBMONpP provides a point of attachment for the addition of solubility control elements, such as hydrophilic groups. In addition, DTBMONpP is expected to be less expensive to produce than DTBNpP, since the 3-chloro-2,2-dimethylpropanol precursor is approximately an order of magnitude less expensive than 3-chloro-2,2-dimethylpropane.[40] DTBMONpP has been found to be

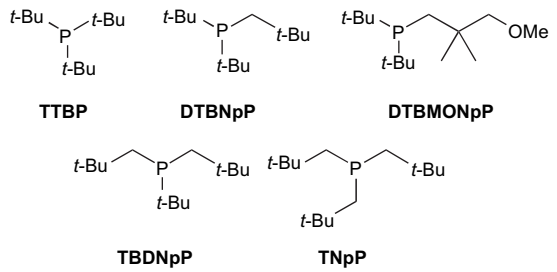


Figure 1.

a suitable substitute for DTBNpP for the Sonogashira, Heck, and H—B couplings, but not in the Suzuki coupling.

2. Results and discussion

2.1. Ligand properties

Ligand steric and electronic properties have been shown to play important roles in the ability to correlate and predict catalyst activity in a variety of systems. We have previously reported experimentally and computationally derived steric and electronic properties for a variety of phosphines and correlated this data with catalyst activity in cross-coupling reactions.[18,41,42] Solid cone angle values were calculated for DTBMONpP to allow it to be compared with the other neopentylphosphines (Table 1). The cone angle of DTBMONpP (194°) was calculated to be smaller than the value calculated for DTBNpP by 4° and is identical to the value calculated for TTBP. The smaller cone angle for DTBMONpP compared to DTBNpP is consistent with the slightly larger B3LYP BDE for Pd(DTBMONpP) as compared to the DTBNpP complex.

The relative electronic parameters of DTBMONpP and the other neopentylphosphines were also compared (Table 1). Experimentally determined electronic parameters were obtained from the CO stretching frequency of *trans*-$RhL_2(CO)Cl$ complexes.[43] The CO stretching frequencies of the DTBNpP and DTBMONpP complexes were identical, which suggest that these two ligands have the same electron donating ability. In contrast, the calculated electronic parameters for the ligands and their palladium complexes showed some electronic differences. The HOMO energy level of DTBMONpP is predicted to be at lower energy than that of DTBNpP, which would suggest that DTBNpP is a stronger electron donor. The same trend is observed for the palladium complexes of DTBMONpP and DTBNpP, although the difference is smaller. We note that the HOMO on the free phosphine is the P lone pair, whereas the HOMO on the PdL complex is on the Pd. The HOMO of a Pd atom is predicted to be −5.52 eV and complexation with the ligand increases the HOMO energy in most cases by about 1 eV. Thus, complexation with the ligand makes the palladium center a stronger electron donor. We have previously noted a good correlation between the increasing HOMO energy levels for the PdL complex and increased catalyst activity.[18,41,42] Interaction of the ligand with the Pd makes the highest occupied orbital in the ligand less accessible by about 1 eV. The GAP defined as HOMO−LUMO energy difference is large in the ligand, ∼7 eV except for PPh_3, where it is just greater than 5 eV. The gap for the palladium atom is predicted to be 2.51 eV. The GAP values for the PdL complexes are intermediate between those of the free ligand and the free Pd atom.

Many trialkylphosphines, such as tri-*tert*-butylphosphine, are classified as pyrophoric in pure form and rapidly oxidize in solution. This air-sensitivity makes them inconvenient to handle. Conversion to the air-stable phosphonium salts can overcome this problem, however,[45] DTBNpP, like TTBP, is highly air-sensitive. After exposure of DTBNpP to air for

Table 1
Steric and electronic parameters of phosphine ligands

Ligand	Cone angle[a] (°)	ν_{CO}[b] (cm^{-1})	BDE_{Pd-P}[c] (kcal/mol)	R_{Pd-H}[d] (Å)	Free ligand			Pd^0L complex			
					q(P)[e]	HOMO[f] (eV)	GAP[g] (eV)	q(P)[e]	HOMO[f] Pd (eV)	HOMO[h] P_{LP} (eV)	GAP[g] (eV)
TTBP	194	1921[i]	37.3	2.69	0.34	−5.66	7.20	0.47	−4.51	−8.07	3.33
DTBNpP	198	1939	35.8	2.41	0.36	−5.74	7.03	0.53	−4.50	−8.08	3.27
DTBMONpP	194	1939	36.2	2.47	0.34	−5.84	7.18	0.51	−4.63	−8.10	3.32
TBDNpP	210	1946	35.2	2.32	0.36	−5.85	7.01	0.55	−4.52	−8.20	3.24
TNpP	227	1950	33.7	2.38	0.36	−5.86	7.04	0.57	−4.46	−8.20	3.16
$(i\text{-}Pr)_3P$	182	1946[j]	38.7	2.93	0.36	−5.87	7.04	0.54	−4.64	−8.22	3.47
$(n\text{-}Bu_3)P$	177	1953[j]	39.2	3.06	0.40	−5.99	7.31	0.60	−4.66	−8.39	3.48
Ph_3P	173	1978[j]	37.1	3.07	0.35	−5.98	5.13	0.47	−4.91	−6.96	3.42

[a] Cone angle values determined from LDFT-optimized LPd(0) structures using the STERIC program.
[b] Carbonyl stretching frequency measured in solution of in situ prepared *trans*-$(L)_2Rh(CO)Cl$ complex.
[c] Calculated at the DFT level with the B3LYP exchange-correlation functional at the LDA optimized geometries.
[d] Closest non-bonded Pd–H distances.
[e] Calculated charge on the phosphorus atom.
[f] HOMO energy at the B3LYP level.
[g] GAP=HOMO–LUMO energy difference.
[h] Energy of P lone pair orbital.
[i] Estimated using the reported value for $Ni(TTBP)(CO)_3$[44] and the correlation reported by Vastag et al.[43]
[j] Literature values.[43]

3 h, 75% of the DTBNpP had been oxidized as determined by ^1H NMR spectroscopy (Fig. 2). After 6 h, nearly 90% of the DTBNpP had been oxidized, while no DTBNpP was present after exposure to air for 30 h. TBDNpP showed a similar, although slower, rate of decomposition upon exposure to air. After 3 h, only 56% of the phosphine remained, while 28% remained after 30 h. In contrast, TNpP is quite stable in air, both as a solid and in solution. A pure sample of TNpP was exposed to air for 9 days, after which the percentage of TNpP in the sample had remained essentially unchanged (97 to 96.7%). A solution of TNpP in toluene (10 wt %) also showed no evidence of oxidation after exposure to air for 24 h. This degree of air stability is unusual for a simple trialkylphosphine. The air stability of TNpP compared with DTBNpP may be explained in part by the lower electron donating ability of TNpP as determined both by the measured ν_{CO} values and the calculated HOMO energies for these two ligands. TBDNpP has similar calculated electronic parameters to TNpP, yet is also much less air-stable. Thus electronic properties do not appear to be the sole explanation. Steric shielding of the lone pair in TNpP, which has a much larger cone angle than TBDNpP, may also contribute to the stability of TNpP.

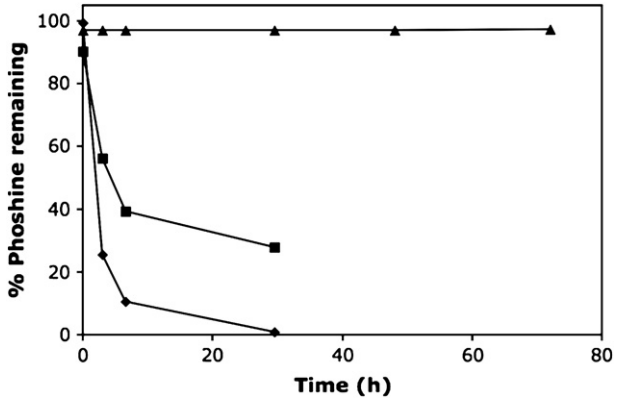


Figure 2. Decomposition of trialkylphosphines in air as determined by ^1H NMR spectroscopy; DTBNpP (diamond), TBDNpP (square), TNpP (triangle).

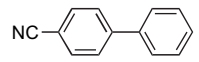
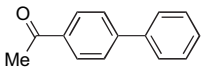
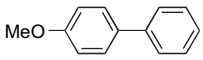
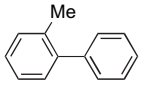
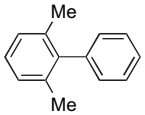
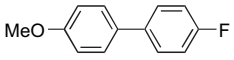
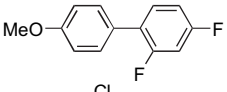
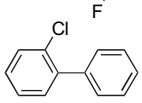
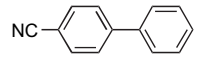
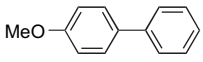
2.2. Application in palladium-catalyzed coupling reactions

We have previously reported that DTBNpP in combination with $Pd_2(dba)_3$ gave a highly efficient catalyst for the amination of aryl bromides under mild conditions.[18] In direct comparisons, DTBNpP gave a more active catalyst than TTBP. DTBNpP gave active catalysts for the coupling of aryl chlorides at elevated temperatures, although higher temperatures and/or catalysts loadings were required than had been reported with TTBP. TBDNpP gave a lower activity catalyst for the amination of aryl bromides than DTBNpP, whereas catalysts derived from TNpP were ineffective.

2.2.1. Suzuki coupling of aryl halides

Catalysts derived from DTBNpP, TBDNpP, and TNpP all gave effective catalysts for the Suzuki coupling of aryl bromides in the presence of sodium carbonate in a 1:1 mixture of THF/water (Table 2). DTNpP- and TBDNpP-derived catalysts gave high yields for Suzuki coupling reactions at room temperature, even with an electron rich aryl bromide (**1c**). 2-Bromotoluene (**1d**) gave good yields at room temperature as well, but 2-bromo-*m*-xylene (**1e**) gave no product, even at elevated temperatures. The catalyst derived from TNpP gave a good yield at room temperature with an activated aryl bromide (**1a**), but gave no reaction with non-activated or unactivated aryl bromides at room temperature. At 80 °C, TNpP/$Pd_2(dba)_3$ did give good yields for the coupling of **1c** and **1d**. The catalyst derived from DTBMONpP was not active for the Suzuki coupling of aryl bromides, despite having similar structural and electronic properties to those of DTBNpP.

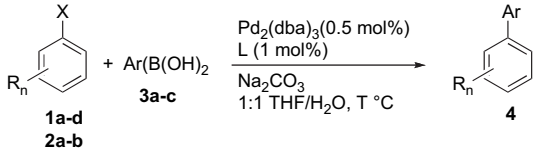
Table 2
Suzuki coupling of aryl halides using neopentylphosphines

Entry	1/2	3	4	Ligand	T (°C)	Yield[a] (%)
1	**1a**	**3a**		DTBNpP	23	94
				TBDNpP	23	94
				TNpP	23	84
2	**1b**	**3a**		DTBNpP	23	91
				TBDNpP	23	98
3	**1c**	**3a**		DTBNpP	23	99
				TBDNpP	23	99
				TNpP	80	85
4	**1d**	**3a**		DTBNpP	23	95
				TBDNpP	23	93
				TNpP	80	99
5	**1e**	**3a**		DTBNpP	23	0
				DTBNpP	100	0
6	**1c**	**3b**		DTBNpP	23	80
7	**1c**	**3c**		DTBNpP	23	95
8	**1f**	**3a**		TNpP	23	97
9	**2a**	**3a**		TBDNpP	23	73
				TBDNpP	23	99
				TNpP	23	99
10	**2b**	**3a**		DTBNpP	100	40
				TBDNpP	100	78
				TNpP	100	80

[a] Average isolated yield of two trials agreeing within 5%.

Based on the performance in other coupling reactions (vide infra), this result is surprising. We do note that the HOMO of the PdL complex is calculated to be at lower energy for DTBMONpP as compared to DTBNpP, but it is unclear if this difference is responsible for the failure of this ligand in the Suzuki coupling.

Catalysts derived from the neopentylphosphine ligands showed modest activity toward aryl chlorides. Good yields of coupled products were obtained in the coupling of an activated aryl chloride (**2a**) with phenylboronic acid using all three ligands, although the catalyst derived from DTBNpP gave a lower isolated yield than the catalysts employing TBDNpP or TNpP. Higher temperatures were required with a deactivated aryl chloride (**2b**). Again, the catalyst derived from DTBNpP gave a lower yield than those derived from TBDNpP or TNpP. These results are surprising, since TBDNpP and TNpP are less electron donating than DTBNpP, which would suggest that they should give less effective catalysts for the coupling of aryl chlorides. Coupling of aryl chlorides would be expected to be promoted by a more electron rich ligand if oxidative addition is the rate limiting step.



1: X = Br
1a: R = 4-CN
1b: R = 4-Ac
1c: 4-OMe
1d: 2-Me
1e: 2,6-Me_2
1f: 2-Cl

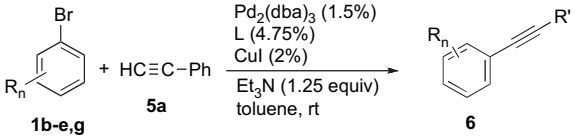
3a: Ar = Ph
3b: Ar = 4-FC_6H_4
3c: Ar = 2,4-$F_2C_6H_3$

2: X = Cl
2a: R = CN
2b: R = OMe

2.2.2. Sonogashira coupling of aryl bromides

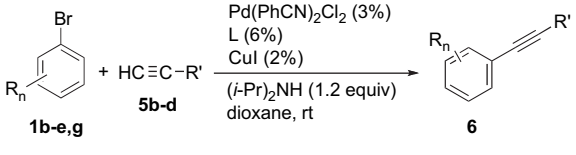
The neopentylphosphines were screened for their ability to promote the Sonogashira coupling of 4-bromotoluene (**1g**) and phenylacetylene (**5a**) using $Pd_2(dba)_3$ (2 mol % Pd, 2:1 L/Pd), CuI (2 mol %), and triethylamine in toluene. The catalyst derived from DTBNpP gave complete conversion to product in 4 h (Fig. 3). The TBDNpP-derived catalyst showed comparable activity to the DTBNpP system after 1 h, but gave little conversion after that time. No conversion was observed with the TNpP-derived catalyst.

Based on the success of the DTBNpP/$Pd_2(dba)_3$ system, couplings of aryl bromides with phenylacetylene were carried out (Table 3). Similar yields were obtained with activated (**1b**) and deactivated aryl bromides (**1c**). The DTBMONpP/$Pd_2(dba)_3$ catalyst system also gave good yields in these reactions. In most cases, the yields were nearly identical for DTBNpP and DTBMONpP. Good yields were also obtained with a moderately sterically hindered aryl bromide (**1d**). No conversion to product occurred in attempts to couple 2-bromo-*m*-xylene (**1e**) and phenylacetylene at 80 °C using the catalysts derived from DTBNpP or DTBMONpP, however.



1b: R = 4-Ac
1c: R = 4-OMe
1d: R = 2-Me
1e: R = 2,6-Me_2
1g: R = 4-Me

Attempts to extend the scope of the reaction to alkyl-substituted alkynes gave slow conversion rates and modest yields. Further optimization showed that the catalyst derived from $Pd(PhCN)_2Cl_2$ was more effective than that derived from $Pd_2(dba)_3$ and that diisopropylamine was the optimal base.[46] The DTBNpP- and DTBMONpP-derived catalysts gave similar yields for most combinations of substrates (Table 4). The catalyst derived from DTBMONpP gave measurably lower yields in the coupling of 4-bromoanisole with 1-hexyne and TMS/acetylene than did the DTBNpP system, however. The catalysts derived from DTBNpP and DTBMONpP were inactive for the Sonogashira coupling of aryl chlorides even at high temperature (100 °C, 3 mol % Pd).



1b: R = 4-Ac
1c: R = 4-OMe
1d: R = 2-Me
1e: R = 2,6-Me_2
1g: R = 4-Me

5b: R = C_4H_9
5c: R = TMS
5d: R = $-CH_2CH_2OH$

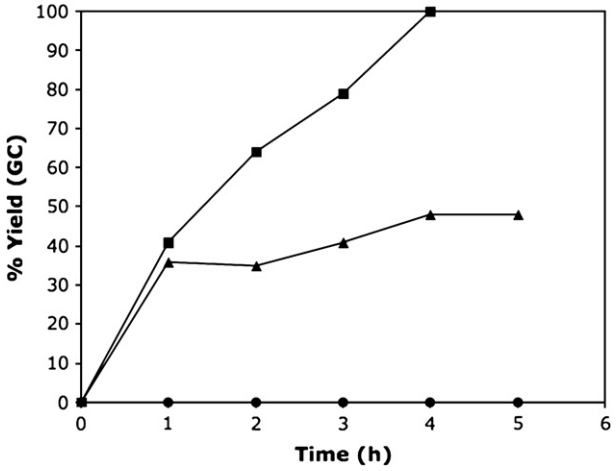
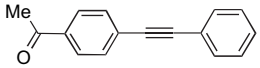
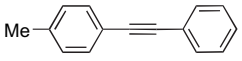
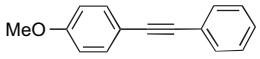
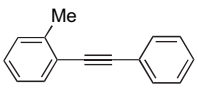
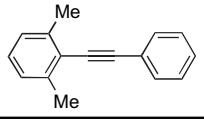


Figure 3. Coupling of 4-bromotoluene with phenylacetylene $Pd_2(dba)_3$ (1 mol %), ligand (4 mol %), CuI (2 mol %), and trimethylamine; DTBNpP (square), TBDNpP (triangle), TNpP (circle).

2.2.3. Heck coupling of aryl bromides

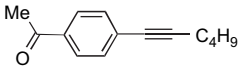
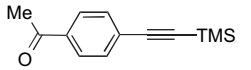
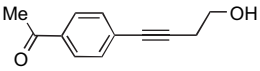
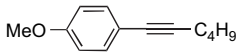
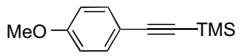
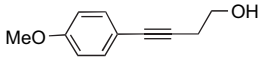
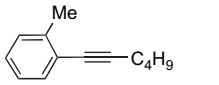
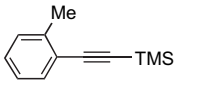
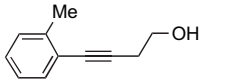
The Heck coupling of aryl bromides using the DTBNpP and DTBMONpP catalyst systems required higher reaction temperatures than the Suzuki or Sonogashira coupling. Electron-deficient and non-activated aryl bromides gave good yields when coupled with styrene at 80 °C (Table 5). 4-Bromoanisole (**1c**) required a higher reaction temperature (100 °C) to give complete conversion to product, although the more electron rich 4-bromo-*N*,*N*-dimethylaniline (**1h**) gave complete conversion to product at 80 °C. Aryl halides with *ortho*-substituents were unreactive toward styrene using these catalyst systems. TBDNpP and TNpP gave modestly active catalysts for the coupling of **1c** with styrene at 100 °C. The isolated yields decreased with increasing numbers of neopentyl substituents.

Table 3
Sonogashira coupling of aryl bromides with phenylacetylene

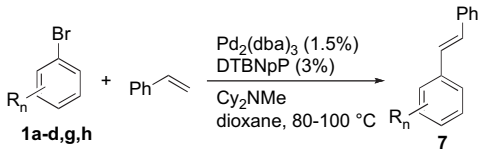
Entry	1	6	Ligand	Yield[a] (%)
1	**1a**		DTBNpP DTBMONpP	85 97
2	**1g**		DTBMONpP	99
3	**1c**		DTBNpP DTBMONpP	95 98
4	**1d**		DTBNpP DTBMONpP	93 97
5	**1e**		DTBNpP DTBMONpP	0[b] 0[b]

[a] Average isolated yield of two trials agreeing within 5%.
[b] Reaction carried out at 80 °C.

Table 4
Sonogashira coupling of aryl bromides with aliphatic alkynes

Entry	1	5	6	Ligand	Yield[a] (%)
1	**1a**	**5b**		DTBNpP	95
2	**1a**	**5c**		DTBNpP	97
3	**1a**	**5d**		DTBNpP	93
4	**1c**	**5b**		DTBNpP DTBMONpP	92 79
5	**1c**	**5c**		DTBNpP DTBMONpP	97 66
6	**1c**	**5d**		DTBNpP DTBMONpP	90 99
7	**1d**	**5b**		DTBNpP DTBMONpP	87 85
8	**1d**	**5c**		DTBNpP DTBMONpP	81 91
9	**1d**	**5d**		DTBNpP DTBMONpP	86 77

[a] Average isolated yield of two trials agreeing within 5%.

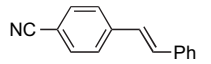
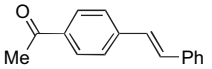
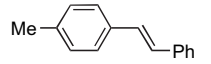
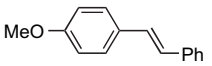
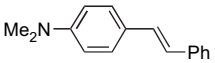
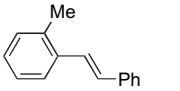


1a: R = 4-CN
1b: R = 4-Ac
1c: R = 4-OMe
1d: R = 2-Me
1g: R = 4-Me
1h: R = 4-NMe_2

2.2.4. H–B coupling of aryl bromides

In our previous report, we found that DTBNpP in combination with palladium sources gave a catalyst for the coupling of aryl bromides with amines that gave similar or higher activity to the catalyst derived from TTBP.[18] These reactions could be carried out at room temperature, with the exception of the coupling of secondary alkyl amines, which required a reaction temperature of 50 °C in order to go to completion within a few hours. Catalysts derived from TBDNpP and TNpP were ineffective in these reactions.

Table 5
Heck coupling of aryl bromides using neopentylphosphines

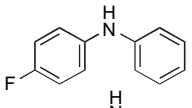
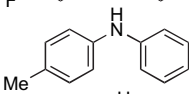
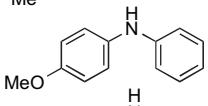
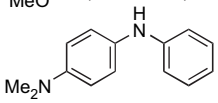
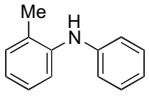
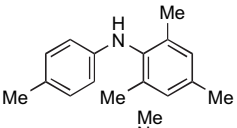
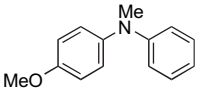
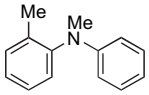
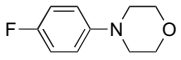
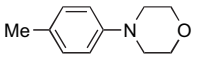
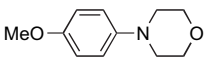
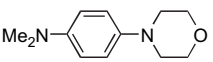
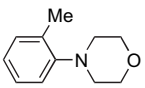
Entry	1	7	Ligand	Yield[a] (%)
1	**1a**		DTBNpP DTBMONpP	64 79
2	**1b**		DTBNpP DTBMONpP	86 84
3	**1g**		DTBNpP DTBMONpP	75 75
4	**1c**		DTBNpP DTBMONpP TBDNpP TNpP	76[b] 83[b] 67[b] 36[b]
5	**1h**		DTBNpP DTBMONpP	89 67
6	**1d**		DTBNpP DTBMONpP	0 0

[a] Average isolated yield of two trials agreeing within 5%.
[b] Reaction carried out at 100 °C.

In order to determine what effect, if any, the methoxy substituent would have on catalyst activity in the H–B amination, we have repeated a number of the amination reactions previously reported with DTBNpP (Table 6). The catalyst derived from DTBMONpP and $Pd_2(dba)_3$ gave similar yields to that derived from DTBNpP, although there were some noticeable differences in the optimal conditions required by these catalysts. In the DTBNpP system, coupling of aryl bromides and aniline could be accomplished at room temperature. In contrast, the DTBMONpP-derived catalyst gave very slow conversion at room temperature, although the reactions could be completed within a few hours at 50 °C. The opposite situation was found with morpholine. In the case of DTBNpP, the reactions were carried out at 50 °C in order to give complete conversion within a few hours. In contrast, the DTBMONpP-derived catalyst gave good activity for these coupling reactions at room temperature. Similar yields (within 10%) were obtained in reactions using DTBMONpP and DTBNpP for a variety of aryl bromide and amine substrates. The one exception to this trend was in the coupling of a sterically hindered aniline derivative (**2b**). The yield obtained with this substrate was 30% higher when using the DTBMONpP-derived catalyst system compared to the catalyst derived from DTBNpP. It is possible that the slightly smaller size of DTBMONpP compared to DTBNpP allowed the arylations of **8b** to proceed more efficiently. In contrast, the catalyst derived from DTBNpP gave higher yields than the DTBMONpP catalyst system in the arylations of *N*-methylaniline (**8c**).

We had previously shown that the DTBNpP/Pd catalyst system gave modest yields for the amination of aryl chlorides at elevated temperatures. Based on the unexpected effectiveness of TNpP in the Suzuki coupling of aryl chlorides, we compared the activity of the TNpP catalyst system with those of DTBNpP and DTBMONpP. At 75 °C (Fig. 4), the DTBNpP and DTBMONpP catalyst systems gave about 50% conversion

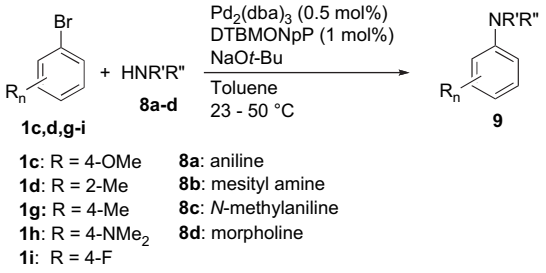
Table 6
H–B amination of aryl bromides catalyzed by DTBMONpP/Pd

Entry	1	8	9	*T* (°C)	Yield[a] (%)
1	**1i**	**8a**		50	90 (84)[b]
2	**1g**	**8a**		50	95 (86)[b]
3	**1c**	**8a**		50	89 (92)[b]
4	**1h**	**8a**		50	92 (78)[b]
5	**1d**	**8a**		50	84 (79)[b]
6	**1g**	**8b**		23	97 (60)
7	**1c**	**8c**		23	73 (89)
8	**1d**	**8c**		23	73 (90)
9	**1i**	**8d**		23	85
10	**1g**	**8d**		23	83 (89)[c]
11	**1c**	**8d**		23	90 (97)[c]
12	**1h**	**8d**		23	95 (89)[c]
13	**1d**	**8d**		23	96 (93)[c]

[a] Average isolated yield of two trials agreeing within 5%. Values in parentheses are yields obtained using DTBNpP.[18]
[b] DTBNpP reaction carried out at room temperature.
[c] DTBNpP reaction carried out at 50 °C using $Pd(OAc)_2$.

after 30 min, but showed only slow conversion after this time. The TNpP catalyst showed no activity over the first 30 min, after which it gave a small amount of product. When the comparison was repeated at 100 °C (Fig. 5), both the DTBNpP and DTBMONpP systems gave complete conversion after 1 h, although the DTBNpP system reached completion slightly sooner. The TNpP system again showed an induction period and a slower overall rate of conversion than the other two ligands. After 75 min, the TNpP reaction had reached about 75% conversion with the catalyst continuing to show good activity.

It is interesting to note that the TNpP/$Pd_2(dba)_3$ catalyst shows little to no activity in the coupling of aryl bromides at room temperature. At 100 °C, this catalyst shows good activity



for the coupling of aryl chlorides, however. The observation of an induction period with the TNpP/$Pd_2(dba)_3$ catalyst systems suggests that formation of the catalytically active species involves a step that is slow even at 80 °C. The complete absence of activity at room temperature using TNpP may indicate that the active catalyst cannot be formed with TNpP as the ligand at this temperature. In the DTBNpP/$Pd_2(dba)_3$ systems, formation of the active species occurs rapidly at room temperature, as an induction period has not been seen with this catalyst system.[18] Given the very large cone angle for TNpP, it is tempting to suggest that the induction period is due to the slow formation of $Pd(TNpP)_2$ from $Pd_2(dba)_3$. Initial studies of the complexation of DTBNpP, TBDNpP, and TNpP with $Pd_2(dba)_3$ have shown that the ligand substitution occurs at approximately the same rate with all three ligands. Another possible explanation would be that $Pd(TNpP)_2$ does not readily undergo ligand dissociation to form the active Pd(TNpP) species (Scheme 1). This hypothesis is inconsistent with the fact that TNpP has a lower calculated BDE than DTBNpP, however; if the BDEs for the PdL_2 complex track those for the PdL complex. It is also possible that the induction period represents the conversion of the $Pd(TNpP)_2$ species into an as yet unidentified active species, rather than the Pd(TNpP) expected based on the mechanism in Scheme 1.

Based on the promising results at 100 °C, we carried out preparative scale couplings of two challenging aryl chloride substrates, 4-chloroanisole and 2-chloroanisole, with aniline, *N*-methylaniline, and morpholine using DTBMONpP and

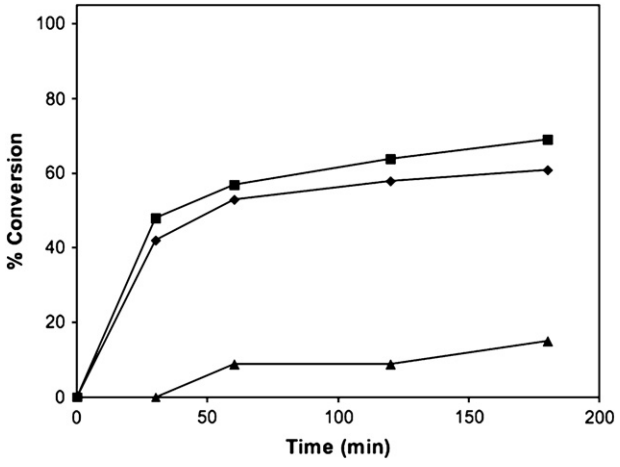


Figure 4. Reaction profile in the coupling of 4-chloroanisole with aniline at 75 °C using $Pd_2(dba)_3$ (0.5 mol %), ligand (1 mol %); DTBNpP (square), DTBMONpP (diamond), TNpP (triangle).

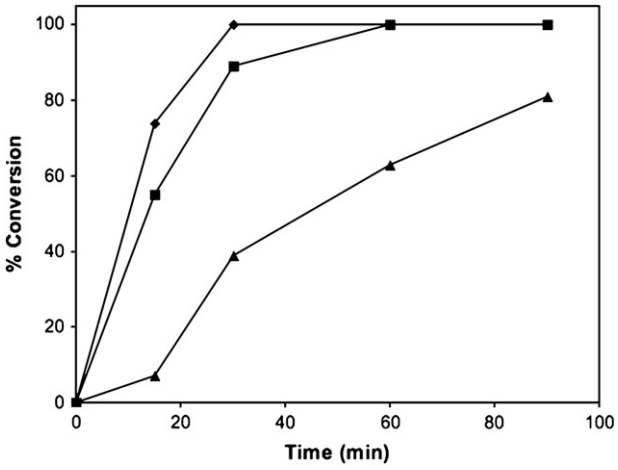
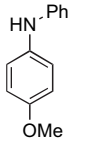
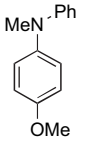
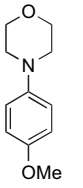
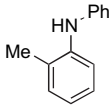
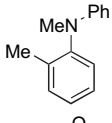
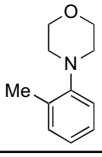


Figure 5. Reaction profile in the coupling of 4-chloroanisole with aniline at 100 °C using $Pd_2(dba)_3$ (0.5 mol %), ligand (1 mol %); DTBNpP (square), DTBMONpP (diamond), TNpP (triangle).

TNpP (Table 7). The catalyst derived from DTBMONpP was found to be effective for the coupling of aryl chlorides and amines. In the amination of 4-chloroanisole, the DTBMONpP catalyst gave similar or better efficiency than

Table 7
H–B amination of aryl chlorides using neopentylphosphines

Entry	2	8	9	% Pd	*T* (°C)	Ligand	Yield[a] (%)
1	**2b**	**2a**		1	140	DTBNpP	89[b]
				1	110	DTBMONpP	94
				1	110	TNpP	70
2	**2b**	**2d**		5	100	DTBNpP	99[b]
				4	120	DTBMONpP	78
				4	120	TNpP	92
3	**2b**	**2e**		5	80	DTBNpP	79[b]
				2	120	DTBMONpP	97
				2	120	TNpP	90
4	**2c**	**2a**		1	120	DTBNpP	95[b]
				1	110	DTBMONpP	94
				1	110	TNpP	87
5	**2c**	**2d**		1	120	DTBNpP	89
				2	120	DTBMONpP	89
				2	120	TNpP	63
6	**2c**	**2e**		1	120	DTBNpP	90
				2	120	DTBMONpP	98
				2	120	TNpP	90

[a] Average isolated yield of two trials agreeing within 5%.
[b] Previously published results.[18]

the DTBNpP catalyst. In the coupling of 4-chloroanisole with aniline, the DTBNpP catalyst system showed little activity below 140 °C, while excellent yields were obtained at 110 °C with the DTBMONpP catalyst. In the case of morpholine, the DTBMONpP catalyst gave the best yield using 2 mol % Pd at 120 °C, while the DTBNpP system required 5 mol % Pd, although at lower temperature (80 °C). In the case of DTBNpP, lower catalyst loadings were ineffective even if the reaction temperature was raised to 120 °C. DTBMONpP also gave effective catalysts for the coupling 2-chlorotoluene with **8a–c** under similar conditions to those used for 4-chloroanisole.

As suggested by the comparative rate studies, TNpP gave an effective catalyst for the amination of aryl chlorides at elevated temperatures. Although Figure 5 shows that the TNpP-derived catalyst is less active than the DTBNpP-derived catalyst, comparable yields were obtained in most cases when the reactions were allowed to proceed for several hours. The TNpP-derived catalyst gave significantly lower yields than the DTBNpP and DTBMONpP systems in two cases: the coupling of 4-chloroanisole and aniline, and the coupling of 2-chlorotoluene and *N*-methylaniline. In the coupling of 4-chloroanisole and *N*-methylaniline, the TNpP-derived catalyst gave a measurably higher yield than the DTBMONpP-derived catalyst.

In summary, DTBNpP provides effective catalysts for the Suzuki, Sonogashira, Hartwig–Buchwald, and Heck couplings of aryl bromides. With the exception of the Heck coupling, the reactions can be carried out at room temperature. The TBDNpP and TNpP ligands give less active catalysts for couplings of aryl bromides at room temperature than DTBNpP, with the exception of the Suzuki coupling. The lower activity of catalysts derived from these ligands is likely due to a combination of the larger size and the decreased electron donating ability of TBDNpP and TNpP. While we have previously seen a good correlation between larger cone angle and increased catalyst activity,[41,42] catalyst activity appears to drop off at cone angles larger than 205°.[18] The decrease in catalyst effectiveness with very large ligands may be due to a decrease in catalyst activity due to steric congestion, or may reflect decreased catalyst stability resulting in shorter catalyst lifetimes. Further studies of the role of ligand sterics on catalyst activity and lifetime are ongoing. The disparity in activity between DTBNp and TNpP disappears at elevated temperatures. Thus at 100 °C, TNpP provides a catalyst with comparable activity the DTBNpP-derived catalyst for the H–B amination of aryl chlorides. Although the TNpP-derived catalyst is less general than the DTBNpP system, the air stability of TNpP may make it an attractive ligand in some applications.

3. Experimental

3.1. General experimental details

DTBNpP, TBDNpP, and TNpP were obtained from FMC Lithium as 10 wt % solutions in toluene. DTBMONpP was provided by FMC Lithium in pure form. DTBMONpP and the ligand solutions were stored in a dry box under nitrogen. Toluene was distilled from molten sodium and then degassed under vacuum prior to use. THF was distilled from a sodium/benzophenone ketyl and degassed under vacuum prior to use. Deionized water used as a reaction solvent was deoxygenated by sparging with nitrogen gas for at least 15 min prior to use. All other reagents were obtained from commercial sources and were used as received.

3.2. Computational determination of ligand properties

Geometries of Pd^0L complexes were optimized at the LDFT level with the polarized double-ζ DZVP2 basis set on all atoms except Pd.[47] We used the Stuttgart relativistic pseudopotential and the associated basis set for Pd[48] with 28 electrons in the core of the ECP. The basis set for Pd was contracted to [6s5p3d]. The LDFT calculations were done with the potential fit of Vosko, Wilk and Nusair for the correlation functional[49] and the exchange functional of Slater.[50] The calculations were done with the program Gaussian 03[51] on Cray XD-1 and Silicon Graphics Altix computers at the Alabama Supercomputing Center. The bond dissociation energies ($BDE=E_{Pd}+E_L-E_{PdL}$) were calculated at the LDA geometries with the B3LYP exchange-correlation functional[52,53] and above basis set. Cone angle values for TPPTS, TXPTS, and TMAPTS were calculated from the LDA optimized geometries for the Pd^0(phosphine) complexes by using the STERIC program and the volumetric parameters for the atoms therein with the Pd atom set at the origin.[54,55]

3.3. General procedure for the Suzuki coupling of aryl bromides

In a dry box, a 1 dram vial was charged with $Pd_2(dba)_3$ (0.005 mmol, 4.58 mg), ligand (0.01 mmol), arylboronic acid (1.1 mmol), Na_2CO_3 (1.1 mmol, 116.0 mg), aryl halide (1 mmol), and THF (1 mL). The vial was then removed from the dry box and charged with deoxygenated water (1 mL). The reaction mixture was stirred at room temperature until judged complete by GC. Reactions carried out at elevated temperatures were stirred in an oil bath preheated to the desired temperature. Ethyl acetate (25 mL) was added to the reaction mixture, which was then washed with 2×25 mL portions of brine. The organic layer was dried over $MgSO_4$ and the solvent removed under reduced pressure. The crude products were purified using flash chromatography through a short plug of silica gel using a gradient mixture of hexanes and ethyl acetate (100:0–85:15 hexane/EtOAc) as the eluent. All products were spectroscopically pure and consistent with previously reported spectra.

3.3.1. 4-Cyanobiphenyl (Table 2, entries 1 and 9)[20]

4-Bromobenzonitrile (1.00 mmol, 181 mg) and phenylboronic acid (1.30 mmol, 161 mg) were coupled under the general procedure. The product was isolated as a cream-colored solid (DTBNpP: 94%, 174 mg; TBDNpP: 94%, 174 mg; TNpP: 84%, 155 mg). ^1H NMR (500 MHz, $CDCl_3$): δ 7.72 (d,

J=8.2 Hz, 2H), 7.68 (d, J=8.2 Hz, 2H), 7.58 (t, J=6.5 Hz, 2H), 7.47 (t, J=6.5 Hz, 2H), 7.41 (t, J=7.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 145.7, 139.2, 132.6, 129.1, 128.7, 127.7, 127.2, 118.9, 110.9. Mp: 83–84 °C (lit. Mp: 86–87 °C).

Alternatively, 4-chlorobenzonitrile (1.00 mmol, 138 mg) was coupled with phenylboronic acid (1.30 mmol, 161 mg) to give the product in 73% yield (190 mg) using DTBNpP, 99% yield (192 mg) using TBDNpP, and 99% yield (203 mg) using TNpP.

3.3.2. 4′-Phenylacetophenone (Table 2, entry 2)[56]

4-Bromoacetophenone (1.00 mmol 199 mg) and phenylboronic acid (1.30 mmol, 161 mg) were coupled under the general procedure. The product was isolated as a white solid (DTBNpP: 91%, 186 mg; TBDNpP: 98%, 192 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.02 (d, J=8.4 Hz, 2H), 7.67 (d, J=8.5 Hz, 2H), 7.61 (d, J=7.2 Hz, 2H), 7.46 (t, J=6.9 Hz, 2H), 7.39 (t, J=7.2 Hz, 1H), 2.62 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.6, 145.7, 139.8, 135.8, 128.8, 128.7, 128.1, 127.2, 127.1, 26.7. Mp: 116–118 °C (lit. Mp: 120–121 °C).

3.3.3. 4-Methoxybiphenyl (Table 2, entries 3 and 10)[57]

4-Bromoanisole (1 mmol, 125 μL) and phenylboronic acid (1.30 mmol, 161 mg) were coupled under the general procedure. The product was isolated as a white solid (DTBNpP: 99%, 183 mg; TBDNpP: 94%, 174 mg; TNpP: 85%, 156 mg at 80 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (d, J=7.2 Hz, 2H), 7.52 (d, J=8.8 Hz, 2H), 7.40 (t, J=10.9 Hz, 1H), 7.29 (t, J=7.5 Hz, 2H), 6.97 (d, J=8.8 Hz, 2H), 3.83 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 159.1, 140.9, 133.8, 128.8, 128.2, 126.8, 126.7, 114.2, 55.4.

Alternative, 4-chloroanisole (1.0 mmol 122 μL) and phenylboronic acid (1.30 mmol, 161 mg) were coupled under the general procedure, but at 100 °C using dioxane in place of toluene (DTBNpP: 40% (GC); TBDNpP: 78%, 154 mg; TNpP: 80%, 156 mg).

3.3.4. 2-Methylbiphenyl (Table 2, entry 4).[58]

2-Bromotoluene (1.0 mmol, 120 μL) and phenylboronic acid (1.30 mmol, 161 mg) were coupled under the general procedure. The product was isolated as a translucent liquid (DTBNpP: 95%, 161 mg; TBDNpP: 93%, 158 mg; TNpP: 99%, 166 mg at 80 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (m, 2H), 7.44 (m, 3H), 7.37 (m, 4H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 142.1, 135.4, 130.5, 130.0, 128.8, 128.2, 127.4, 127.3, 126.8, 125.9, 20.6.

3.3.5. 4′-Fluoro-4-methoxybiphenyl (Table 2, entry 6)[59]

4-Fluorophenylboronic acid (1.10 mmol, 154 mg) and 4-bromoanisole (1 mmol, 125 μL) were coupled under the general procedure using DTBNpP. The product was isolated in 80% yield as a tan solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (m, 2H), 7.43 (d, J=8.8 Hz, 2H), 7.09 (t, J=8.5 Hz, 2H), 6.96 (d, J=8.8 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 162.1 (d, 246 Hz), 159.1, 137.0, 132.7, 128.2 (d, J=7.3 Hz), 128.0, 115.5 (d, J=21.0 Hz), 114.3, 55.4. Mp: 86–87 °C (lit. Mp 84–86 °C).

3.3.6. 2,4-Difluoro-4′-methoxybiphenyl (Table 2, entry 7)[60]

2,4-Difluorophenylboronic acid (1.10 mmol, 174 mg) and 4-bromoanisole (1 mmol, 125 μL) were coupled under the general procedure using DTBNpP. The product was isolated in a 95% yield as a white solid (220.0 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44 (dd, J=1.87, 7.04 Hz, 2H), 7.38 (m, 1H), 6.98 (d, J=8.9 Hz, 2H), 6.92 (m, 1H), 6.89 (m, 1H), 3.85 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 161.8 (dd, J=11.9, 247.4 Hz), 160.8 (dd, J=11.9, 237.4 Hz), 159.2, 131.1 (dd, J=5.49 Hz), 129.9 (d, J=2.7), 127.3 (d, J=1.8,), 125.0 (dd, J=3.7, 13.7 Hz), 114.0, 111.4 (dd, J=3.67, 21.1 Hz), 104.3 (dd, J=25.7 Hz), 55.2.

3.3.7. 2-Chlorobiphenyl (Table 2, entry 8)[61]

Phenylboronic acid (1.30 mmol, 160 mg) and 2-bromochlorobenzene (1 mmol, 122 μL) were coupled under the general procedure using TNpP. The product was isolated in 97% yield as a low-melting, tan solid. GC/MS: 188 (100%), 190 (33%). ^{1}H NMR (360 MHz, $CDCl_3$): δ 7.46 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 140.6, 139.5, 132.6, 131.5, 130.0, 129.5, 128.6, 128.1, 1277, 126.9.

3.4. General procedure for the Sonogashira coupling of aryl halides with phenylacetylene

In a dry box, $Pd_2(dba)_3$ (0.012 mmol, 11.0 mg), CuI (0.016 mmol, 3.1 mg), DTBNpP (0.038 mmol, 84.8 μL of a 10 wt % solution) or DTBMONpP (0.03 mmol, 8.7 μL), and toluene (1 mL) were combined in a septa topped vial. The reaction mixture was removed from the dry box and the aryl halide (0.8 mmol), alkyne (1.0 mmol), and triethylamine (1.00 mmol, 135 μL) were added via syringe. The mixture was stirred at room temperature for several hours and monitored by TLC or GC. Upon completion, the product was purified by flash chromatography using a mixture of ethyl acetate and hexanes as the eluent. All products were spectroscopically pure and consistent with previous reported spectra.

3.4.1. 4′-(Phenylethynyl)acetophenone (Table 3, entry 1)[62]

The above procedure was carried out using 4-bromoacetophenone (0.80 mmol, 159 μL) and phenylacetylene (0.96 mmol, 105 μL). The crude product mixture was purified by column chromatography (2:98 EtOAc/hexanes) to afford the product as a gray solid (DTBNpP: 149 mg, 83%; DTBMONpP: 170 mg, 97%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, J=8.5 Hz, 2H), 7.63 (d, J=8.5 Hz, 2H), 7.57 (m, 2H), 7.39 (m, 3H), 2.63 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 197.3, 136.2, 121.8, 121.7, 128.8, 128.5, 128.3, 128.2, 122.7, 92.7, 88.6, 26.6. Mp: 94–96 °C (lit. Mp: 95–97 °C).

3.4.2. 4-(Phenylethynl)toluene (Table 3, entry 2)[63]

The above procedure was carried out using 4-bromotoluene (0.90 mmol, 115 μL) and phenylacetylene (0.96 mmol, 105 μL). The mixture was purified by column chromatography

(1:99 EtOAc/hexanes) to afford the product as a yellow solid (DTBNpP: 153 mg, 99%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (d, J=8.2 Hz, 2H), 7.43 (d, J=8.2 Hz, 2H), 7.33 (m, 3H), 7.16 (d, J=8.2 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 138.4, 131.6, 131.5, 129.1, 128.3, 128.0, 123.5, 120.2, 88.7, 89.6, 21.5. Mp: 69–70 °C (lit. Mp: 72–73 °C).

3.4.3. 4-(Phenylethynl)anisole (Table 3, entry 3)[63]

The above procedure was carried out using 4-bromoanisole (0.80 mmol, 100 μL) and phenylacetylene (0.96 mmol, 105 μL). The crude product mixture was purified by column chromatography (2:98 EtOAc/hexanes) to afford the product as a yellow solid (DTBNpP: 159 mg, 95%; DTBMONpP: 164 mg, 98%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (d, J=7.9 Hz, 2H), 7.47 (d, J=9.1 Hz, 2H), 7.3 (m, 3H), 6.88 (d, J=8.8 Hz, 2H), 3.83 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 159.7, 133.1, 131.5, 128.3, 127.9, 123.6, 115.4, 114.0, 89.4, 88.1, 55.3. Mp: 54–56 °C (lit. Mp: 56–58 °C).

3.4.4. 2-(Phenylethynyl)toluene (Table 3, entry 4)[63]

The above procedure was carried out using 2-bromotoluene (0.80 mmol, 96.1 μL) and phenylacetylene (0.96 mmol, 105 μL). The crude product mixture was purified by column chromatography (1:99 EtOAc/hexanes) to afford the product as a clear oil (DTBNpP: 142 mg, 93%; DTBMONpP: 97%, 147 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53 (d, J=6.6 Hz, 2H), 7.49 (d, J=7.6 Hz, 1H), 7.32 (m, 3H), 7.22 (d, J=4.4 Hz, 2H), 7.16 (m, 1H), 2.51 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 140.3, 131.9, 131.6, 129.6, 128.44, 128.40, 128.3, 125.7, 123.7, 123.1, 93.5, 88.5, 20.8.

3.5. General procedure for the Sonogashira coupling of aryl bromides and aliphatic alkynes

In a dry box, $Pd(PhCN)_2Cl_2$ (0.03 mmol, 11.5 mg), CuI (0.02 mmol, 3.81 mg), DTBNpP (0.06 mmol, 132 μL of a 10 wt % solution) or DTBMONpP (0.06 mmol, 16.2 μL), and dioxane (1.0 mL) were combined in a septa topped vial. The reaction mixture was removed from the dry box and the aryl halide (1.0 mmol), alkyne (1.2 mmol), and diisopropylamine (1.20 mmol, 170 μL) were added via syringe. The mixture was stirred at room temperature for several hours and monitored by TLC or GC. Upon completion, the product was purified by flash chromatography using a mixture of ethyl acetate and hexanes as the eluent.

3.5.1. 4′-(1-Hexyn-1-yl)acetophenone (Table 4, entry 1)[64]

The above procedure was carried out using 4-bromoacetophenone (1.00 mmol, 199 mg) and 1-hexyne (1.20 mmol, 135 μL). The crude product mixture was purified by column chromatography (1:99 EtOAc/hexanes) to afford the product as an oil (204 mg, 95%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86 (d, J=8.9 Hz, 2H), 7.45 (d, J=8.6 Hz, 2H), 2.58 (s, 3H), 2.43 (t, J=7.0 Hz, 2H), 1.61 (qn, J=7.0 Hz, 2H), 1.47 (sx, J=8.2, 2H), 0.95 (t, J=7.3, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 197.0, 135.5, 131.4, 129.0, 128.0, 94.1, 79.9, 30.5, 26.3, 21.8, 19.0, 13.4.

3.5.2. 4′-(Trimethylsilylethynyl)acetophenone (Table 4, entry 2)[65]

The above procedure was carried out using 4-bromoacetophenone (1.00 mmol, 199 mg) and TMS/acetylene (1.20 mmol, 170 μL). The mixture was purified by column chromatography (1:99 EtOAc/hexanes) to afford the product as an oil (185 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87, (d, J=8.5 Hz, 2H), 7.52 (d, J=8.2 Hz, 2H), 2.58 (s, 3H), 0.26 (s, 9H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 197.3, 136.4, 132.1, 128.1, 128.0, 104.0, 98.1, 26.6, −0.18 (3C).

3.5.3. 4-(4-Acetylphenyl)-3-butyn-1-ol (Table 4, entry 3)[66]

The above procedure was carried out using 4-bromoacetophenone (1.0 mmol, 199 mg) and 3-butyn-1-ol (1.2 mmol, 91 μL). The mixture was purified by column chromatography (1:99 EtOAc/hexanes) to afford the product as a yellow solid (174 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87 (d, J=8.5 Hz, 2H), 7.47 (d, J=8.5 Hz, 2H), 3.84 (t, J=6.3 Hz, 2H), 2.72 (t, J=6.3 Hz, 2H), 2.58 (s, 3H), 1.95 (br s, 1H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 197.4, 136.0, 131.8, 128.4, 128.2, 90.2, 81.8, 61.0, 26.6, 23.9. Mp: 68–70 °C (lit. Mp: 65–66 °C).

3.5.4. 1-(4-Methoxyphenyl)hex-1-yne (Table 4, entry 4)[64]

The above procedure was carried out using 4-bromoanisole (1.00 mmol, 125 μL) and 1-hexyne (1.20 mmol, 135 μL). The crude product mixture was purified by column chromatography (1:99 EtOAc/hexanes) to afford the product as an oil (DTBNpP: 185 mg, 92%; DTBMONpP: 158 mg, 79%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (d, J=8.8 Hz, 2H), 6.81 (d, J=9.1 Hz, 2H), 3.79 (s, 3H), 2.39 (t, J=6.9 Hz, 2H), 1.58 (qn, J=6.9 Hz, 2H), 1.47 (sx, J=7.2 Hz, 2H), 0.94 (t, J=7.6, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 159.0, 132.8, 116.3, 113.8, 88.7, 80.2, 55.2, 31.0, 22.0, 19.2, 13.7.

3.5.5. 2-(4-Methoxyphenyl)ethynyltrimethylsilane (Table 4, entry 5)[67]

The above procedure was carried out using 4-bromoanisole (1.00 mmol, 125 μL) and TMS/acetylene (1.2 mmol, 170 μL). The crude product mixture was purified by column chromatography (1:3:96 EtOAc/NEt_3/hexanes) to afford the product as an oil (DTBNpP: 197 mg, 97%; DTBMONpP: 134 mg, 66%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 (d, J=8.8 Hz, 2H), 6.81 (d, J=8.8 Hz, 2H), 3.80 (s, 3H), 0.24 (s, 9H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 159.7, 133.4, 115.3, 113.8, 105.2, 92.4, 55.2, 0.04 (3C).

3.5.6. 4-(4-Methoxyphenyl)-3-butyn-1-ol (Table 4, entry 6)[68]

The above procedure was carried out using 4-bromoanisole (1.00 mmol, 125.2 μL) and 3-butyn-1-ol (1.20 mmol, 91 μL). The crude product mixture was purified by column chromatography (5:95 EtOAc/hexanes) to afford the product as a yellow solid (DTBNpP: 159 mg, 90%; DTBMONpP: 175 mg, 99%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, *J*=7.6 Hz, 2H), 7.50 (d, *J*=8.2 Hz, 2H), 3.86, (t, *J*=5.4 Hz, 2H), 2.75 (t, *J*=6.3 Hz, 2H), 2.61 (s, 3H), 1.90 (s, 1H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 159.3, 133.0, 115.5, 113.9, 84.7, 82.3, 61.2, 55.3, 23.8. Mp: 59–61 °C (lit. Mp: 61 °C).

3.5.7. 1-(2-Methylphenyl)hex-1-yne (Table 4, entry 7)[69]

The above procedure was carried out using 2-bromotoluene (1.0 mmol, 120 μL) and 1-hexyne (1.2 mmol, 135 μL). The mixture was purified by column chromatography (hexanes) to afford the product as a yellow oil (DTBNpP: 149 mg, 87%; DTBMONpP: 146 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45 (d, *J*=7.2 Hz, 1H), 7.25 (m, 2H), 7.19 (m, 1H), 2.55 (t, *J*=6.9 Hz, 2H), 2.51 (s, 3H), 1.71 (qn, *J*=8.2, 2H), 1.49 (sx, *J*=7.2, 2H), 1.06 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 139.9, 131.8, 129.3, 127.4, 125.4, 123.9, 94.4, 79.5, 31.0, 22.0, 20.7, 19.3, 13.7.

3.5.8. Trimethyl-(2-methylphenyl)ethynylsilane (Table 4, entry 8)

The above procedure was carried out using 2-bromotoluene (1.00 mmol, 120 μL) and TMS/acetylene (1.20 mmol, 170 μL). The crude product mixture was purified by column chromatography (3:97 NEt_3/hexanes) and dried using a vacuum line to afford the product as an oil (DTBNpP: 152 mg, 81%; DTBMONpP: 171 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50 (d, *J*=7.6 Hz, 1H), 7.26 (m, 2H), 7.18 (t, *J*=6.94 Hz, 1H), 2.52 (s, 3H), 0.34 (s, 9H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 140.6, 132.1, 129.4, 128.5, 125.4, 122.9, 104.0, 98.2, 20.6, 0.09 (3C). HRMS (EI): Calculated for $C_{10}H_{16}Si$ 188.1021; found 188.1017.

3.5.9. 4-(2-Methylphenyl)-3-butyn-1-ol (Table 4, entry 9)[5]

The above procedure was carried out using 2-bromotoluene (1.00 mmol, 120 μL) and 3-butyn-1-ol (1.20 mmol, 91 μL). The mixture was purified by column chromatography (hexanes) to afford the product as a yellow oil (DTBNpP: 138 mg, 86%; DTBMONpP: 123 mg, 77%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 (d, *J*=7.6 Hz, 1H), 7.18 (m, 2H), 7.12 (m, 1H), 3.83, (br s, 2H), 2.73 (t, *J*=6.3 Hz, 2H), 2.42 (s, 3H), 2.02 (br s, 1H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 140.0, 131.9, 129.4, 127.9, 125.5, 123.1, 90.2, 81.4, 61.3, 24.0, 20.7.

3.6. General procedure for the Heck coupling of aryl bromides with styrene

In a dry box, $Pd_2(dba)_3$ (0.03 mmol, 13.8 mg), DTBNpP (0.03 mmol, 70.0 μL of a 10 wt % solution) or DTBMONpP (0.03 mmol, 7.41 mg), and dioxane (0.8 mL) were combined in a septa top vial. The reaction mixture was removed from the dry box and the aryl halide (0.8 mmol), styrene (1.10 mmol, 108.6 mg), and dicyclohexylmethylamine (1.03 mmol, 200.6 mg) were added via syringe. The mixture was placed in a preheated oil bath at 80 °C and stirred for several hours until judged complete by TLC or GC. Upon completion, the product was purified by column chromatography (5:95 EtOAc/hexanes). All products were spectroscopically pure and consistent with previous reported spectra.

3.6.1. E-4-Cyanostilbene (Table 5. entry 1)[70]

The above procedure was carried out using 4-bromobenzonitrile (0.80 mmol, 146 mg) to afford the product as a white solid (DTBNpP: 106 mg, 64%; DTBMONpP: 129 mg, 79%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (d, *J*=8.2 Hz, 2H), 7.58 (d, *J*=8.3 Hz, 2H), 7.53 (d, *J*=7.4 Hz, 2H), 7.39 (t, *J*=7.6 Hz, 2H), 7.32 (t, *J*=7.2 Hz, 1H), 7.22 (d, *J*=16.4 Hz, 1H), 7.09 (d, *J*=16.3, 1H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 141.9, 136.3, 132.5, 132.4, 128.9, 128.7, 126.9, 126.8, 126.7, 119.0, 110.6. Mp: 112–114 °C (lit. Mp: 114–116 °C).

3.6.2. E-4-Acetylstilbene (Table 5, entry 2)[70]

The above procedure was carried out using 4-bromoacetophenone (0.8 mmol, 159 mg) to afford the product as a yellow solid (DTBNpP: 153 mg, 86%; DTBMONpP: 149 mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, *J*=8.1 Hz, 2H), 7.58 (d, *J*=8.2 Hz, 2H), 7.54 (d, *J*=6.8 Hz, 2H), 7.39 (t, *J*=7.6, 2H), 7.30 (t, *J*=7.5 Hz, 1H), 7.23 (d, *J*=16.4 Hz, 1H), 7.13 (d, *J*=16.4 Hz, 1H), 2.61 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 197.5, 142.0, 136.7, 136.0, 131.5, 128.9, 128.8, 128.3, 127.5, 126.8, 126.5, 26.6. Mp: 137–138 °C (lit. Mp: 139–141 °C).

3.6.3. E-4-Methylstilbene (Table 5, entry 3)[70]

The above procedure was carried out using 4-bromotoluene (0.8 mmol, 138 mg) to afford the product as a yellowish solid (DTBNpP: 131.4 mg, 75%; DTBMONpP: 131.0 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54 (d, *J*=6.8 Hz, 2H), 7.45 (d, *J*=8.1 Hz, 2H), 7.39 (t, *J*=7.6 Hz, 2H), 7.28 (t, *J*=7.4, 1H), 7.20 (d, *J*=7.6 Hz, 2H), 7.13 (d, *J*=16.4 Hz, 1H), 7.09 (d, *J*=16.4 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 137.5, 137.4, 134.5, 129.3, 128.6, 128.6, 127.7, 127.4, 126.4, 126.3, 21.2. Mp: 112–114 °C (lit. Mp: 117–119 °C).

3.6.4. E-4-Methoxystilbene (Table 5, entry 3)[70]

The above procedure was carried out using 4-bromoanisole (0.8 mmol, 150 mg) and a reaction temperature of 100 °C to afford the product as a whittish solid (DTBNpP: 139 mg, 76%; DTBMONpP: 152 mg, 83%; TBDNpP: 122 mg, 67%; TNpP: 65 mg, 36%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.50–7.45 (m, 4H), 7.35 (t, *J*=7.8 Hz, 2H), 7.24 (t, *J*=7.4 Hz, 1H), 7.07 (d, *J*=16.3 Hz, 1H), 6.97 (d, *J*=16.3 Hz, 1H), 6.90 (d, *J*=8.9 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 159.3, 137.7, 130.2, 128.6, 128.2, 127.7, 127.2, 126.6, 126.3, 114.1, 55.3. Mp: 125–126 °C (lit. Mp: 131–132 °C).

3.6.5. E-4-(N,N-Dimethylamino)stilbene (Table 3, entry 5)[70]

The above procedure was carried out using 4-bromo-*N*,*N*-dimethylaniline (0.80 mmol, 160 mg) to afford the product as a peach-colored solid (DTBNpP: 152 mg, 89%; DTBMONpP: 119 mg, 67%). ^{1}H NMR (500 MHz, CDCl3): δ 7.48 (d, *J*=6.9 Hz, 2H), 7.42 (d, *J*=8.6 Hz, 2H), 7.33 (t,

J=7.7 Hz, 2H), 7.21 (t, J=7.3, 1H), 7.06 (d, J=16.4 Hz, 1H), 6.92 (d, J=16.5 Hz, 1H), 6.72 (d, J=8.8, 2H), 2.99 (s, 6H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 150.1, 138.2, 128.8, 128.6, 127.6, 126.7, 126.0, 125.8, 124.4, 112.5, 40.5 (2C). Mp: 130 °C (lit. Mp: 144–146 °C).

3.7. General procedure for Hartwig–Buchwald amination of aryl bromides

Under an inert atmosphere of nitrogen gas in a glove box, a 1 dram vial with a flea stir bar and a septa screw top was charged with $Pd_2(dba)_3$ (0.005 mmol, 4.6 mg), sodium *tert*-butoxide (1.00 mmol, 96.1 mg), DTBMONpP (0.01 mmol, 2.7 μL), and dry toluene (2 mL). The vial was then removed from the glove box and the amine (1.0 mmol) and aryl bromide (0.8 mmol) were added via a glass micro-syringe. The reaction was allowed to stir at room temperature unless otherwise noted. All reactions were monitored by GC until judged complete. Upon completion, the crude product was purified by column chromatography eluting with a 95:5 mixture of hexanes and ethyl acetate.

3.7.1. N-(4-Fluorophenyl)aniline (Table 6, entry 1)[71]

Aniline (91 μL, 1.0 mmol) and 1-bromo-4-fluoro-benzene (86.1 μL, 0.8 mmol) were coupled using the procedure above at 50 °C to give a yellow oil (132 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23 (t, J=7.3 Hz, 2H), 7.02 (m, 2H), 6.96 (m, 4H), 6.89 (t, J=7.3 Hz, 1H), 5.54 (s, 1H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 158.0 (d, J_{C-F}=240.1 Hz), 144.0, 139.0, 129.4, 120.6, 120.58, 116.8, 115.9 (d, J_{C-F}=23.0 Hz).

3.7.2. N-Phenyl-p-toluidine (Table 6, entry 2)[72]

Aniline (91 μL, 1.0 mmol) and 4-bromotoluene (100 μL, 0.78 mmol), were coupled using the general procedure above, but at 50 °C to afford the product as pale yellow crystals (120.5 mg, 95%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.23 (t, J=7.3 Hz, 2H), 7.08 (d, J=8.8 Hz, 2H), 7.01 (m, 4H), 6.87 (t, J=7.3 Hz, 1H), 5.59 (s, 1H), 1.53 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 144.0, 140.3, 130.9, 129.9, 129.3, 120.3, 118.9, 116.9, 20.7. Mp: 85–87 °C (lit. Mp: 87–88 °C).

3.7.3. N-Phenyl-p-anisidine (Table 6, entry 3)[73]

Aniline (91 μL, 1.00 mmol) and 4-bromoanisole (98 μL, 0.80 mmol) were coupled using the general procedure, but at 50 °C, to give a pale yellow crystalline product (140 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.20 (t, J=7.5 Hz, 2H), 7.06 (d, J=8.8 Hz, 2H), 6.90 (d, J=8.5 Hz, 2H), 6.85 (d, J=8.8 Hz, 2H), 6.82 (t, J=7.3 Hz, 1H), 5.47 (s, 1H), 3.79 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 155.3, 145.2, 135.7, 129.3, 122.2, 119.6, 115.7, 114.7, 55.6. Mp: 99–101 °C (lit. Mp: 102–103 °C).

3.7.4. N,N-Dimethyl-N′-phenylbenzene-1,4-diamine (Table 6, entry 4).[74]

Aniline (91 μL, 1.00 mmol) and (4-bromo-phenyl)-dimethyl-amine (157 mg, 0.8 mmol) were coupled under the general procedure, but at 50 °C, to afford yellow crystals (152 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.18 (t, J=7.8 Hz, 2H), 7.06 (d, J=8.8 Hz, 2H), 6.85 (d, J=7.8 Hz, 2H), 6.78 (t, J=7.3 Hz, 1H), 6.74 (d, J=8.8 Hz, 2H), 5.41 (s, 1H), 2.92 (s, 6H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 147.3, 132.4, 129.2, 123.3, 118.8, 115.0, 114.9, 114.0, 41.2. Mp: 123–125 °C (lit. Mp: 115 °C).

3.7.5. N-Phenyl-o-toluidine (Table 6, entry 5)[75]

Aniline (91 μL, 1.0 mmol) and 2-bromotoluene (94 μL, 0.8 mmol) were coupled under the standard conditions to yield the product as a yellow oil (121 mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24 (m, 3H), 7.19 (d, J=7.6 Hz, 1H), 7.13 (t, J=7.7 Hz, 1H), 6.94 (m, 3H), 6.89 (t, J=7.4 Hz, 1H), 5.34 (br s, 1H), 2.24 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 144.0, 141.3, 131.0, 129.4, 128.4, 126.8, 122.1, 120.5, 118.9, 117.5, 17.9.

3.7.6. N-(4-Methylphenyl)-2,4,6-trimethylaniline (Table 6, entry 6)[76]

2,4,6-Trimethylaniline (140 μL, 1.00 mmol) and 4-bromotoluene (100 μL, 0.80 mmol) were coupled under the standard conditions to give a yellow oil (171 mg, 97%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.95 (d, J=7.88 Hz, 2H), 6.93 (3, 2H), 6.41 (d, J=8.51 Hz, 2H), 5.00 (br s, 1H), 2.30 (s, 3H), 2.24 (s, 3H), 2.17 (s, 6H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 144.3, 136.0, 135.6, 135.1, 129.7, 129.2, 127.1, 113.5, 20.9, 20.4, 18.2.

3.7.7. N-Methyl-N-phenyl-p-anisidine (Table 6, entry 7)[75]

N-Methylaniline (109 μL, 1.00 mmol) and 4-bromoanisole (98 μL, 0.80 mmol) were coupled under the standard conditions to give the product as a yellow oil (155 mg, 73%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.18 (t, J=7.8 Hz, 2H), 7.08 (d, J=8.9 Hz, 2H), 6.88 (d, J=8.8 Hz, 2H), 6.77 (t, J=7.9 Hz, 3H), 3.79 (s, 3H), 3.24 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 156.3, 149.8, 142.3, 129.0, 126.2, 118.4, 115.8, 114.8, 55.5, 40.5.

3.7.8. N-Methyl-N-phenyl-o-toluidine (Table 6, entry 8)[26]

N-Methylaniline (109 μL, 1.00 mmol) was reacted with 2-bromotoluene (98 μL, 0.8 mmol) according to the general procedure to give the product as a yellow oil (143.1 mg, 73%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (d, J=7.2 Hz, 1H), 7.22 (d, J=7.6 Hz, 1H), 7.16 (m, 4H), 6.70 (t, J=7.2 Hz, 1H), 6.53 (d, J=8.0 Hz, 2H), 3.21 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 149.2, 136.9, 146.9, 131.5, 129.1, 128.4, 127.6, 126.5, 116.9, 112.9, 39.1, 17.9.

3.7.9. 4-(4-Fluorophenyl)morpholine (Table 6, entry 9)[77]

Morpholine (87 μL, 1.0 mmol) with 1-bromo-4-fluorobenzene (86 μL, 0.8 mmol) were coupled using the coupled using the general procedure above to give the product as pale yellow crystals (121 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.98 (t, J=8.4 Hz, 2H), 6.88 (m, 2H), 3.86 (t, J=4.8 Hz, 4H), 3.08 (t, J=4.8 Hz, 4H). ^{13}C NMR (90.6 MHz, $CDCl_3$):

δ 157.0 (d, *J*=239 Hz), 147.9 (d, *J*=2.8 Hz), 117.5 (d, *J*=7.3 Hz), 115.7 (d, *J*=22.0 Hz), 66.9, 50.3. Mp: 52–54 °C.

3.7.10. 4-(4-Methylphenyl)morpholine (Table 6, entry 10)[75]

Morpholine (87 μL, 1.0 mmol) and 4-bromotoluene (100 μL, 0.80 mmol) were coupled under the general procedure to give the product as a pale yellow crystalline solid (115 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.12 (d, *J*=8.6 Hz, 2H), 6.86 (d, *J*=7.9 Hz, 2H), 3.89 (t, *J*=4.6 Hz, 4H), 3.13 (t, *J*=4.8 Hz, 4H), 2.30 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 149.2, 129.7, 129.6, 116.1, 67.0, 49.9, 20.4. Mp: 45–46 °C (lit. Mp: 49–50 °C).

3.7.11. 4-(4-Methoxyphenyl)morpholine (Table 6, entry 11)[75]

Morpholine (87 μL, 1.0 mmol) and 4-bromoanisole (98 μL, 0.8 mmol) were coupled using the general procedure above to give the product as pale yellow crystals (136 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.87 (m, 4H), 3.86 (t, *J*=4.8 Hz, 4H), 3.77 (s, 3H), 3.06 (t, *J*=4.8 Hz, 4H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 154.0, 145.7, 117.8, 114.5, 67.1, 55.6, 50.8. Mp: 70–71 °C (lit. Mp: 71 °C).

3.7.12. 4-(4-*N*,*N*-Dimethylaminophenyl)morpholine (Table 6, entry 12)[78]

Morpholine (87 μL, 1.0 mmol) was reacted with 4-bromo-*N*,*N*-dimethylaniline (157 mg, 0.8 mmol) using the general procedure above to give the product as yellowish crystals (153 mg, 95%). ^{1}H NMR (360 MHz, $CDCl_3$): δ 6.89 (d, *J*=9.1 Hz, 2H), 6.75 (d, *J*=9.1, 2H), 3.86 (t, *J*=4.7 Hz, 4H), 3.04 (t, *J*=4.8 Hz, 4H), 2.88 (s, 6H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 145.9, 143.2, 118.0, 114.5, 67.1, 51.1, 41.5. Mp: 115–117 °C (lit. Mp: 117–120 °C).

3.7.13. 4-(2-Methylphenyl)morpholine (Table 6, entry 13)[75]

Morpholine (87.1 μL, 1.0 mmol) and 2-bromotoluene (94.3 μL, 0.8 mmol) were coupled using the general procedure to give the product as a pale yellow oil (133 mg, 96%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17 (t, *J*=7.3 Hz, 2H), 7.01 (m, 2H), 3.84 (t, *J*=4.5 Hz, 4H), 2.90 (t, *J*=4.5 Hz, 4H), 2.31 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 150.3, 131.6, 130.1, 125.6, 122.4, 117.9, 66.4, 51.2, 16.8.

3.8. General procedure for the H–B coupling of amines with aryl chlorides

In a dry box, $Pd_2(dba)_3$ (0.005–0.025 mmol, 4.6–23 mg), DTBNpP (0.01 mmol 23 μL), DTBMONpP (0.01–0.04 mmol, 2.7–10.8 μL) or TNpP (0.01–0.04 mmol, 22.9–91.6 μL of a 10 wt % solution), and sodium *tert*-butoxide (1.00 mmol, 96.1 mg) were combined in a round bottom flask with toluene (1.0 mL) and a stir bar. After placing a rubber septa on the flask, the reaction mixture was removed from the dry box. The amine (1.0 mmol) and the aryl halide (0.8 mmol) were added by syringe. The mixture was placed in a preheated oil bath at 80–140 °C and stirred until judged complete by GC. Upon completion, the crude product was purified by column chromatography eluting with a 95:5 mixture of hexanes and ethyl acetate.

3.8.1. *N*-Phenyl-*p*-anisidine (Table 7, entry 1)[73]

The above procedure was carried out using $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol), DTBMONpP (0.01 mmol, 2.7 μL) or TNpP (0.01 mmol, 23 μL), 4-chloroanisole (0.80 mmol, 98.0 μL), and aniline (1.0 mmol, 93.1 mg) at 110 °C to afford the product as a gray solid (DTBMONpP: 94%, 149 mg; TNpP: 112 mg, 70%). ^{1}H NMR (500 MHz, DMSO): δ 7.21 (t, *J*=7.4 Hz, 2H), 7.08 (d, *J*=8.8 Hz, 2H), 6.91 (d, *J*=7.6, 2H), 6.86 (m, 3H), 5.49 (br s, 1H), 3.81 (s, 3H). ^{13}C NMR (90.6 MHz, DMSO): δ 155.3, 145.2, 135.8, 129.3, 122.2, 119.6, 115.7, 114.7, 55.6. Mp: 97–99 °C (lit. Mp: 102–103 °C).

3.8.2. *N*-Methyl-*N*-phenyl-*p*-anisidine (Table 7, entry 2)[75]

The above procedure was carried out using $Pd_2(dba)_3$ (18.3 mg, 0.02 mmol), DTBMONpP (0.02 mmol, 5.43 μL) or TNpP (0.02 mmol, 45.8 μL), 4-chloroanisole (0.80 mmol, 98.0 μL), and *N*-methylaniline (0.9 mmol, 98 μL) at 120 °C to afford the product as an orange oil (DTBMONpP: 133 mg, 78%; TNpP: 157 mg, 92%). ^{1}H NMR (500 MHz, DMSO): δ 7.18 (t, *J*=6.9 Hz, 2H), 7.08 (d, *J*=9.1 Hz, 2H), 6.88 (d, *J*=8.8 Hz, 2H), 6.78 (d, *J*=8.5 Hz, 3H), 3.80 (s, 3H), 3.25 (s, 3H). ^{13}C NMR (90.6 MHz, DMSO): δ 156.3, 149.8, 142.2, 128.9, 126.2, 118.4, 115.8, 114.8, 55.5, 40.5.

3.8.3. 4-(4-Methoxyphenyl)morpholine (Table 7, entry 3)[75]

The above procedure was carried out using $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), DTBMONpP (0.02 mmol, 5.43 μL of a 10 wt % solution) or TNpP (0.02 mmol, 45.8 μL of a 10 wt % solution), 4-chloroanisole (0.80 mmol, 98.0 μL), and morpholine (1.0 mmol, 87 μL) were coupled under the standard conditions at 120 °C. The product was isolated as a lavender solid (DTBMONpP: 149 mg, 97%; TNpP 138 mg, 90%). ^{1}H NMR (500 MHz, DMSO): δ 6.89 (m, 4H), 3.88 (m, 4H), 3.80 (s, 3H), 3.08 (m, 4H). ^{13}C NMR (90.6 MHz, DMSO): δ 154.0, 145.6, 117.8, 114.6, 67.0, 55.6, 50.9. Mp: 68–70 °C (lit. Mp: 71 °C).

3.8.4. *N*-Phenyl-*o*-toluidine (Table 7, entry 4)[75]

The above procedure was carried out using $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol), DTBMONpP (0.01 mmol, 2.7 μL) or TNpP (0.01 mmol, 23 μL), 2-chlorotoluene (0.77 mmol, 94 μL), and aniline (1.00 mmol, 93.1 mg) at 110 °C to give the product as a yellow oil (DTBMONpP: 138 mg, 94%; TNpP: 129 mg, 87%). ^{1}H NMR (500 MHz, DMSO): δ 7.30 (t, *J*=8.04 Hz, 3H), 7.25 (d, *J*=7.25 Hz, 1H), 7.19 (t, *J*=7.57 Hz, 1H), 6.98 (m, 4H), 5.42 (br s, 1H), 2.31 (s, 3H). ^{13}C NMR (90.6 MHz, DMSO): δ 144.0, 141.2, 131.0, 129.3, 128.4, 126.8, 122.0, 120.5, 118.9, 117.5, 17.9.

3.8.5. *N*-Methyl-*N*-phenyl-*o*-toluidine (Table 7, entry 5)[26]

2-Chlorotoluene (0.77 mmol, 94.0 μL) and *N*-methylaniline (0.9 mmol, 98 μL) were coupled using $Pd_2(dba)_3$ (9.2 mg, 0.01 mmol) and DTBMONpP (0.02 mmol, 5.43 μL) or TNpP

(0.02 mmol, 45.8 μL of a 10 wt % solution) under the procedure above to give the product as an orange oil (DTBNpP: 140 mg, 89%; DTBMONpP: 125 mg, 84%; TNpP: 95 mg, 63%). ^{1}H NMR (500 MHz, DMSO): δ 7.31 (m, 6H), 6.82 (t, J=7.7 Hz, 1H), 6.65 (d, J=8.5 Hz, 2H), 3.33 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (90.6 MHz, DMSO): δ 149.2, 146.9, 136.9, 131.5, 129.0, 128.4, 127.6, 126.5, 116.9, 112.9, 39.1, 17.9.

Alternatively, *N*-methyl-*N*-phenyl-*o*-toluidine was prepared as above, but using $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol) and DTBNpP (0.01 mmol, 23.3 μL) as the catalyst precursor at 120 °C to give the product as an orange oil (140 mg, 89%).

3.8.6. 4-(2-Methylphenyl)morpholine (Table 7, entry 6)[75]

The above procedure was carried out using 2-chlorotoluene (0.77 mmol, 94.0 μL) and morpholine (1.0 mmol, 87 μL) with $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), DTBMONpP (0.02 mmol, 5.43 μL) or TNpP (0.02 mmol, 45.8 μL of a 10 wt % solution) at 120 °C to give the product as a yellow oil (DTBMONpP: 133 mg, 89%; TNpP: 121 mg, 90%). ^{1}H NMR (500 MHz, DMSO): δ 7.23 (m, 2H), 7.06 (m, 2H), 3.89 (m, 4H), 2.95 (m, 4H), 2.37 (s, 3H). ^{13}C NMR (90.6 MHz, DMSO): δ 151.3, 132.7, 131.2, 126.7, 123.5, 119.0, 67.5, 52.3, 17.9.

Alternatively, 4-(2-methylphenyl)morpholine was prepared as above, but using $Pd(OAc)_2$ (0.01 mmol, 2.2 mg) and DTBNpP (0.01 mmol, 23.3 μL of a 10 wt % solution) as the catalyst precursor. The reaction yielded the above product (129 mg, 91%) as a yellow oil.

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