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Full Paper

Exploring the Catalytic Reactivity of Nickel Phosphine–Phosphite Complexes

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In this study, we present an investigation into various nickel phosphite and phosphite–phosphine complexes for use in the Mizoroki–Heck and Suzuki–Miyaura cross-coupling reactions and the ammonia arylation reaction. In these coupling reactions, it was discovered that the $Ni[P(OEt)_3]_4$, $(dppf)Ni[P(OPh)_3]_2$, and $(binap)Ni[P(OPh)_3]_2$ catalysts were the most effective. In addition, an optimisation process for these catalytic systems as well as functional group compatibility are discussed.

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Introduction

Nickel phosphite complexes have had an interesting history throughout diverse fields of chemistry. Perhaps most importantly, zero-valent nickel phosphite complexes were used as part of a seminal investigation into the effect of cone angles in phosphorus ligand exchange equilibria by the group of Tolman in the 1970s.[1] In their organometallic study, the steric effects of ligand cone angles along with the equilibrium ligand dissociation, K_d, from a tetrakis(aryl phosphite)complex to tris(aryl phosphite)complex were measured and were used as guiding principles in this field.[2] As catalysts, nickel phosphites were originally used in hydrocyanation reactions in industry.[3,4] Later, this work was developed through the use of interesting ligands such as diphosphite **1**[5] (Fig. 1) being explored in combination with various Ni^0 precatalysts. An asymmetric hydrocyanation has also been reported with nickel catalysts derived from [1,1′-binaphthalene]-2,2′-diol (binol) phosphite ligands,[6,7] along with bidentate phosphinite ligands derived from glucose.[8] Related to these early investigations, the phosphine–phosphite ligands **2** (including SchmalzPhos) have been used in combination with $Ni(cod)_2$ (cod = cycloocta-1,5-diene) as a catalytic system for the hydrocyanation of styrene (Fig. 1).[9,10] The chiral phosphine–phosphite-substituted α,α,α,α-tetraaryl-1,3-dioxolane-4,5-dimethanol (taddol) ligands and derivatives, as well as other chiral phosphoramidite ligands, have also been applied in combination with a nickel precatalyst to a range of modern synthetic transformations including asymmetric hydroalkynylation.[11]

The studies that stimulated our interest in this field was the brief investigation specifically using simple homoleptic nickel

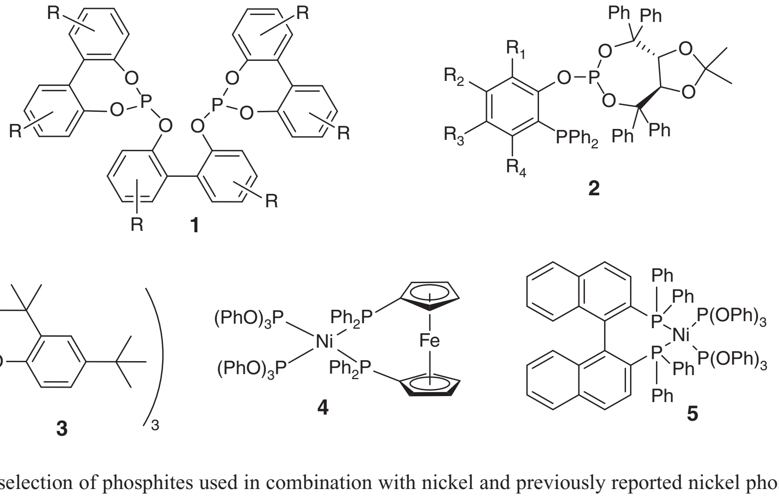
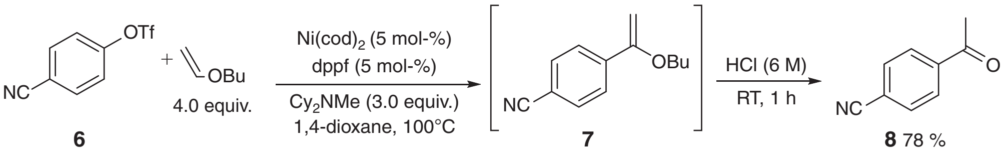


Fig. 1. A selection of phosphites used in combination with nickel and previously reported nickel phosphite complexes.



Scheme 1. Nickel-catalysed Mizoroki–Heck reaction of aryl triflates **6** with butyl vinyl ether by Skrydstrup and coworkers.[19]

phosphite complexes $Ni[P(OPh)_3]_4$ and $Ni[P(OEt)_3]_4$ in the Heck cross-coupling reactions of aryl bromides and iodides.[12] Furthermore, the latter complex has been used in C–S coupling reactions between allylic acetates and thiols.[13] The sterically hindered *t*-butyl-substituted phosphites **3** also have been used in combination with $Ni(OAc)_2{\cdot}4H_2O$ for amino carbonylation reactions with DMF.[14]

We recently reported the synthesis of $(dppf)Ni[P(OPh)_3]_2$ **4** (dppf = 1,1′- bis(diphenylphosphanyl) ferrocene) (Fig. 1), and explored its utility as a catalyst, along with other nickel phosphites, in a series of C–N cross-coupling reactions.[15] Following this work, we also reported the crystal structure of the interesting, coordinatively unsaturated tris(tri-*o*-tolyl phosphite)nickel Ni[P(O-*o*-Tol)$_3$]$_3$ complex.[16] Later, we prepared the complex, $(binap)Ni[P(OPh)_3]_2$ **5** (binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl), and reported its compatibility with the Buchwald–Hartwig coupling of normally inactive primary alkyl amines.[17]

Following these successful studies in carbon nitrogen cross-coupling reactions, we wanted to explore the reactivity of various nickel phosphites in a series of other interesting cross-coupling reactions. For these studies, we chose the commonly used Mizoroki–Heck and Suzuki–Miyaura reactions, and the more recently reported ammonia arylation reaction.

Results and Discussion

The Mizoroki–Heck Cross-Coupling Reaction

Given simple nickel phosphite tetrakis complexes $Ni[P(OPh)_3]_4$ and $Ni[P(OEt)_3]_4$ had been briefly explored in Mizoroki–Heck cross-coupling reactions with electron-deficient olefins, other less traditional cross-coupling reactions systems were sought. Nickel catalysts have been used in Heck cross-couplings by several groups.[18–23] In a recent report by Skrydstrup and coworkers,[19] it was shown that aryl triflates (**6**) can be coupled with the electron-rich olefin, butyl vinyl ether, using the air-sensitive catalyst $Ni(cod)_2$ in combination with the chelating ligand dppf. Under the reported conditions, the reaction occurred regioselectively to give hydrolytically unstable 1,1-disubstitued olefins, like compound **7**. These reactive Mizoroki–Heck cross-coupling products were subsequently hydrolysed to the corresponding ketones **8** in good to high yields. Given this success, we examined a similar process with an air-stable nickel phosphite complex. For this purpose, $Ni[P(OPh)_3]_4$ and $Ni[P(OEt)_3]_4$ were prepared using known procedures starting with $NiCl_2$ or $Ni(NO_3)_2$,[24] and an initial evaluation of their catalytic activities was conducted.

A series of reaction conditions for the model transformation between aryl triflate **6** and butyl vinyl ether were explored. The yield of the desired ketone **8** was determined by gas chromatography (GC) using dodecane as an internal standard, and reactions having a good conversion were subjected to further workup and isolation. To our delight, simply replacing the air-sensitive $Ni(cod)_2$ with air-stable $Ni[P(OPh)_3]_4$ and otherwise identical reaction conditions to those shown in Scheme 1 gave a very similar yield (70 %, Table 1, entry 2) compared with the benchmark reaction (78 %, entry 1). Replacing the dppf ligand with a ligand containing a smaller bite angle, ethane-1,2-diylbis(diphenylphosphane) (dppe) had a slightly deleterious effect on the yield (60 %, entry 3).[25] The combination of dppf with the triethylphosphite complex, $Ni[P(OEt)_3]_4$, resulted in a poor conversion to **8** (7 %, entry 4). Surprisingly, when $Ni[P(OEt)_3]_4$ was combined with dppe, the yield increased dramatically to 79 % (entry 5).

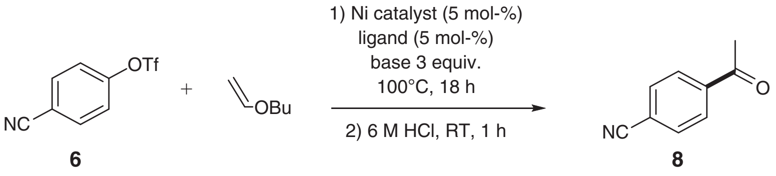
Next, the role of the base was explored in this reaction. The reaction did not proceed when triethylamine was used (entry 6), whereas Hünig's base, *N*,*N*-diisopropylethylamine (DIPEA), gave the desired product **8** in a high yield (81 %, entry 7). Unfortunately, only trace amounts of product were formed when K_2CO_3 was used as the base (entry 8). The yield was slightly enhanced by changing the solvent from 1,4-dioxane to toluene (83 %, entry 9). No reaction occurred in the absence of phosphines (entry 10), or if diphosphines with large bite angles, such as 1,5-bis(diphenylphosphino)pentane (dppPent) or 4,5-bis (diphenylphosphino)-9,9-dimethylxanthene (Xantphos), were employed (entries 11 and 12). Using the monodentate ligand triphenylphosphine was also ineffective (entry 13). A reaction with 4-chlorobenzonitrile was carried out to compare the leaving group ability of Cl versus OTf (entry 14); unfortunately, this reaction was also unsuccessful.

It was found that the product yield is dramatically diminished with reduced reaction times. No product was detected by GC at the 1- and 2-h time points (Table 2, entries 1 and 2). The desired product **8** started to form after 4 h (entry 3), but it was evident that extended reaction times are necessary for high conversions (entry 5). Gratifyingly, it was also found that both the amount of alkene and Cy_2NMe (Cy = cyclohexyl) could be greatly reduced without significantly affecting the yield (entries 5–7). The reaction was still high-yielding when the catalyst loading and the amount of dppe were lowered to 2 mol-% (85 %, entry 8), a significant point in this methodology study. Unfortunately, the reaction did not proceed when the temperature was reduced to 60 or 80°C (entry 9). Additionally, the ratio of $Ni[P(OEt)_3]_4$ to dppe ligand appeared to be crucial, as the yield dropped significantly (51 %) when the amount of diphosphine was doubled (entry 10) and the reaction yield was greatly diminished when the catalyst loading was dropped to 1 mol-% (36 %, entry 11). Extended reaction times at 1 mol-% catalyst loading surprisingly led to even less product **8** (6 %, entry 12), possibly indicating decomposition of the intermediately formed 1,1-disubstituted alkene. As expected, no product was formed in the absence of any catalyst (entry 13).

With the optimised conditions in hand (Table 2, entry 8), a range of substrates was explored. All aryl triflates **9** in this section were synthesised by treating the corresponding phenols with triflic anhydride according to literature procedures.[26,27]

The optimised conditions were successful, however, only on a limited number of substrates (Table 3). When exploring a variety of aryl groups, it was discovered the naphthyl ketones **10a** and **10b** could be obtained in moderate (56 %) to good yields

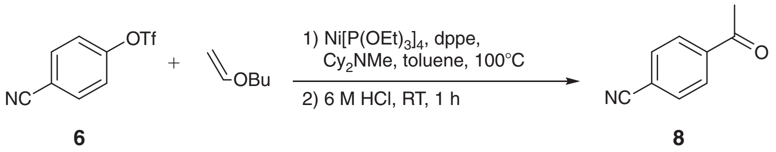
Table 1. Optimisation of the Heck reaction between triflate 6 and butyl vinyl ether[A]



Entry	Catalyst [5 mol-%]	Ligand [5 mol-%]	Base [equiv.]	Solvent	Yield [%][B]
1	$Ni(cod)_2$	dppf	Cy_2NMe (3)	1,4-Dioxane	(78)[C]
2	$Ni[P(OPh)_3]_4$	dppf	Cy_2NMe (3)	1,4-Dioxane	75 (70)
3	$Ni[P(OPh)_3]_4$	dppe	Cy_2NMe (3)	1,4-Dioxane	60
4	$Ni[P(OEt)_3]_4$	dppf	Cy_2NMe (3)	1,4-Dioxane	7
5	$Ni[P(OEt)_3]_4$	dppe	Cy_2NMe (3)	1,4-Dioxane	79 (79)
6	$Ni[P(OEt)_3]_4$	dppe	Et_3N (3)	1,4-Dioxane	0
7	$Ni[P(OEt)_3]_4$	dppe	DIPEA (3)	1,4-Dioxane	89 (81)
8	$Ni[P(OEt)_3]_4$	dppe	K_2CO_3 (3)	1,4-Dioxane	<1
9	$Ni[P(OEt)_3]_4$	dppe	Cy_2NMe (3)	Toluene	>99 (83)
10	$Ni[P(OEt)_3]_4$	No ligand	Cy_2NMe (3)	Toluene	0
11	$Ni[P(OEt)_3]_4$	dppPent	Cy_2NMe (3)	Toluene	0
12	$Ni[P(OEt)_3]_4$	Xantphos	Cy_2NMe (3)	Toluene	0
13	$Ni[P(OEt)_3]_4$	PPh_3	Cy_2NMe (3)	Toluene	0
14[D]	$Ni[P(OEt)_3]_4$	dppe	Cy_2NMe (3)	Toluene	(7)

[A] All reactions were conducted on a 0.50-mmol scale using 4.0 equiv. of butyl vinyl ether.
[B] GC yield using dodecane as an internal standard. Isolated yields are indicted in brackets.
[C] Benchmark reaction from work by Skrydstrup et al.[19]
[D] The reaction was conducted using the aryl chloride and the conversion was 7 % as determined by GC.

Table 2. Role of the ratio of reagents and reaction time in the coupling of 6 with butyl vinyl ether[A]



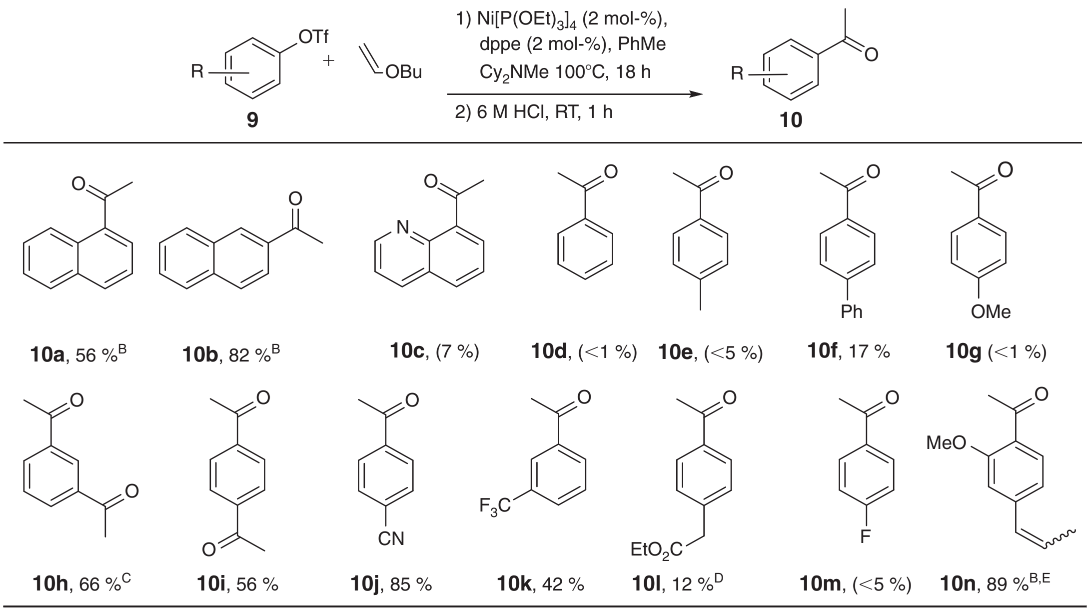
Entry	$Ni[P(OEt)_3]_4$ [mol-%]	DPPE [mol-%]	Cy_2NMe [equiv.]	Alkene	Time	Yield [%][B]
1	5	5	3.0.	4.0	1 h	0
2	5	5	3.0.	4.0	2 h	0
3	5	5	3.0	4.0	4 h	6
4	5	5	3.0	4.0	6 h	36
5	5	5	3.0	1.5	18 h	95 (76)
6	5	5	1.0	4.0	18 h	>99 (84)
7	5	5	1.0	1.5	18 h	80
8	**2**	**2**	**1.0**	**1.5**	**18 h**	**>99 (85)**
9	2[C]	2	1.0	1.5	18 h	0
10	2	4	1.0	1.5	18 h	51
11	1	1	1.0	1.5	18 h	38
12	1	1	1.0	1.5	4 d	6
13	–	2	1.0 e	1.5	18 h	0

[A] All reactions were conducted on a 0.50-mmol scale.
[B] GC yield using dodecane as an internal standard. Isolated yields are indicted in brackets.
[C] Reaction was conducted at both 60 and 80°C.

(82 %) respectively. The *N*-heterocyclic substrate was unreactive, giving quinoline derivative **10c** in only poor yields. Neutral or electron-rich substrates bearing alkyl groups, ethers, and amides were unreactive, or the corresponding ketones (**10d**, **10e** and **10f**) were obtained in very low yields. Longer reactions times did not result in an increased yield in any case. Interestingly, the reaction conditions where $Ni(cod)_2$ was simply replaced with $Ni[P(OPh)_3]_4$ (cf. Table 1, entry 2) worked well in some instances where the optimised conditions with $Ni[P(OEt)_3]_4$ (cf. Table 1, entry 8) had failed.

Reactions with substrates bearing an electron-withdrawing substituent were only moderately or modestly yielding under standard conditions. For example, the diketones **10h** and **10i** were isolated in reasonable yields (66 and 56 %), whereas the 3-(trifluoromethyl)acetophenone (**10k**) (42 %) was lower-yielding. In all cases, a large amount of the corresponding aryl

Table 3. Scope of the aryl triflate coupling partners 9[A]



10a, 56 %[B]
10b, 82 %[B]
10c, (7 %)
10d, (<1 %)
10e, (<5 %)
10f, 17 %
10g (<1 %)
10h, 66 %[C]
10i, 56 %
10j, 85 %
10k, 42 %
10l, 12 %[D]
10m, (<5 %)
10n, 89 %[B,E]

[A] All reactions were conducted on a 0.40–1.00-mmol scale using 1.5 equiv. of butyl vinyl ether unless noted otherwise. Isolated yields are indicated unless in brackets (GC).

[B] Reaction conducted with $Ni[P(OPh)_3]_4$ (5 mol-%) and DPPF (5 mol-%) in 1,4-dioxane, 4.0 equiv., 3.0 equiv. Cy_2NMe.

[C] No improvement in yield after extending the reaction time to 3 days.

[D] NMR yield.

[E] Isomerisation to conjugated olefin (10 : 6 *E* : *Z*).

triflate **9** was left in the reaction mixture. Unlike its trifluoromethyl counterpart, 4-fluoroacetophenone (**10m**) was obtained in a poor yield (<5 %). When the isoeugenol derivative was used with the $Ni[P(OPh)_3]_4$/dppf catalyst system, cross-coupling was high-yielding. However, and similarly to the report by the group of Skrydstrup,[19] the terminal olefin isomerised to the conjugated olefin product **10n** (89 % yield) during the course of the reaction.

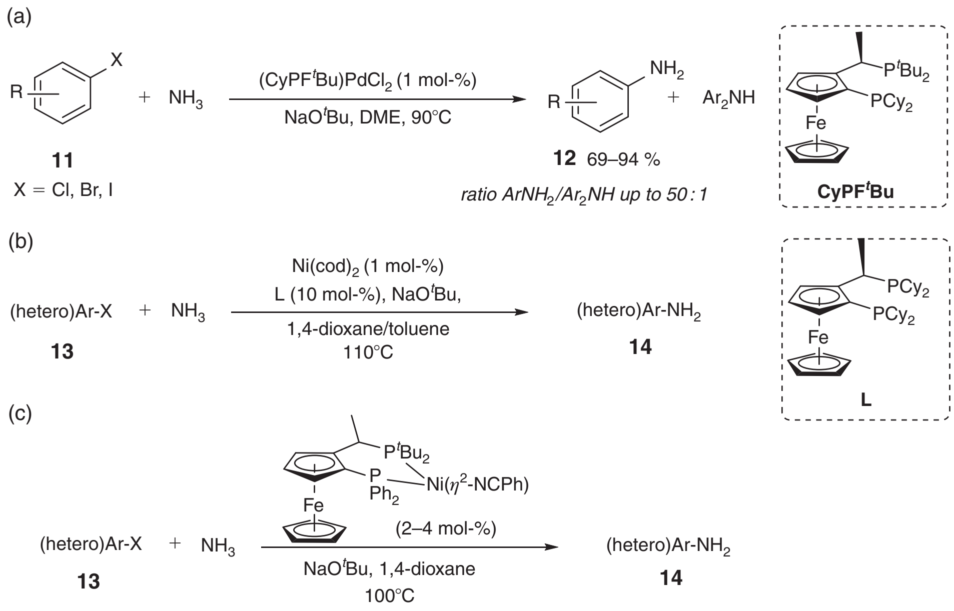
Notwithstanding the limited substrate scope of the air-stable nickel(0) phosphites $Ni[P(OPh)_3]_4$ and $Ni[P(OEt)_3]_4$, it was shown that it is possible to replace the air-sensitive $Ni(cod)_2$ as a catalyst in cross-coupling reactions. Further investigation and optimisation of the catalytic system are necessary to make the use of nickel phosphites a viable method for Heck cross-coupling reactions on a wider range of substrates.

The Ammonia Arylation Reaction

Following the promising results for a diverse range of amine-based C–N coupling reactions in our previous studies,[17] the focus was turned to direct ammonia coupling using an ammonia solution. Reactions with ammonia in metal-catalysed processes are very challenging owing to several factors. First, catalysts are often poisoned, as transition metals readily form very stable Werner ammine complexes with ammonia; second, the aniline product is often more reactive than ammonia itself and, therefore, the reaction results in undesired diarylamine products. The first example of a selective direct C–N coupling of ammonia was achieved by the Hartwig group in 2006 via palladium catalysis (Scheme 2a).[28] In their study, the chiral ferrocenyldiphosphine ligand CyPF^{t}Bu (Josiphos ligands) was used. The arylation of ammonia had been further reported by several groups using palladium and with copper, albeit at higher catalytic loadings.[28–40] In the field of nickel chemistry, the Iranpoor group has recently used a trichlorotriazine reagent for the activation of phenols in a nickel-catalysed ammonia arylation reaction.[41] During our investigations into the scope of this reaction and the preparation of this manuscript, two reports of nickel-catalysed ammonia arylation reactions with aryl halides were published, using ammonia solution, ammonia gas or ammonium salts as their nitrogen sources. The group of Stradiotto utilised a $Ni(cod)_2$ and a Josiphos catalytic system,[42] which was then independently reported by the Hartwig group (Scheme 2b and Scheme 2c respectively).[43] The latter publication also included a small study using a conveniently air-stable (Josiphos)Ni(η^2-NC-Ph) precatalyst.

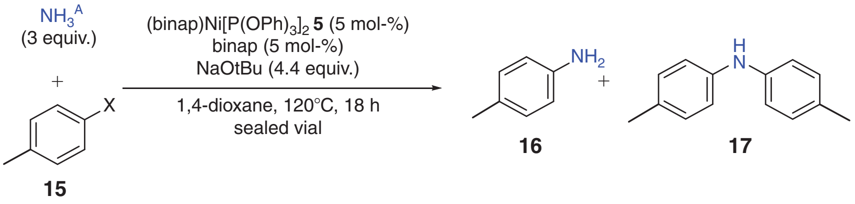
Optimisation of the Ammonia Arylation Reaction

Our investigations into the reaction with *p*-chlorotoluene (**15**) and the air-stable catalyst (binap)$Ni[P(OPh)_3]_2$ (**5**)[17] were initially unsuccessful at fairly low temperatures (40 or 80°C), using a 0.5 M 1,4-dioxane ammonia solution as the ammonia source (Table 4, entries 1–3). The dioxane solution was chosen owing to its practicality and commercial availability. In each case of this methodological study, the reaction was monitored by GC-mass spectrometry (MS). Conducting the reaction in a sealed vial, and increasing the temperature to 100 or 120°C with the addition of binap allowed the desired aniline **16** to form. Unfortunately, the biarylation product **17**, resulting from the aniline **16** competing with ammonia, also formed in the process. This scenario was originally observed in many of the earlier ammonia arylation reactions reported with palladium.[34,44,45] Drastically increasing the amount of base (4.4 equivalents)



Scheme 2. (a) The first palladium-catalysed selective ammonia arylation; and (b, c) two later nickel-catalysed ammonia arylation reactions.[28] DME = dimethoxyethane.

Table 4. Optimisation of the ammonia arylation reaction of *p*-chlorotoluene 15



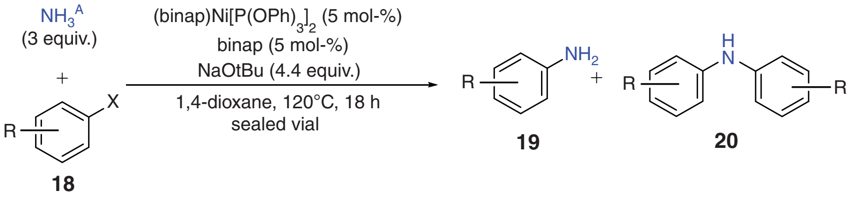
Entry	Catalyst and additional ligand	Base	Temperature [°C)]	GC yield [%]^C	Ratio **16** : **17**
1	(binap)Ni[P(OPh)$_3$]$_2$ (5 mol-%)	NaO^{t}Bu (1.4 equiv.)	40^B	0	–
2	(binap)Ni[P(OPh)$_3$]$_2$ (5 mol-%)	NaO^{t}Bu (1.4 equiv.)	80^B	0	–
3	(binap)Ni[P(OPh)$_3$]$_2$ (5 mol-%) + binap (5 mol-%)	NaO^{t}Bu (1.4 equiv.)	80^B	3	2 : 1
4	(binap)Ni[P(OPh)$_3$]$_2$ (5 mol-%) + binap (5 mol-%)	NaO^{t}Bu (1.4 equiv.)	100	37	1 : 1
5	(binap)Ni[P(OPh)$_3$]$_2$ (5 mol-%) + binap (5 mol-%)	NaO^{t}Bu (1.4 equiv.)	120	59	1 : 1.8
6	(binap)Ni[P(OPh)$_3$]$_2$ (5 mol-%) + binap (5 mol-%)	NaO^{t}Bu (4.4 equiv.)	120	99	1.2 : 1
7	(binap)Ni[P(OPh)$_3$]$_2$ (5 mol-%) + binap (5 mol-%)^D	NaO^{t}Bu (4.4 equiv.)	120	61	1 : 1
8	(binap)Ni[P(OPh)$_3$]$_2$ (10 mol-%) + binap (10 mol-%)	NaO^{t}Bu (1.4 equiv.)	100	42^E	1 : 2.2
9	Ni(cod)$_2$ (5 mol-%), BINAP (10 mol-%)	NaO^{t}Bu (1.4 equiv.)	100	16	1 : 1.3
10	Ni[P(O-*o*-Tol)$_3$]$_3$(5 mol-%) + binap (10 mol-%)	NaO^{t}Bu (1.4 equiv.)	100	11	1.2 : 1
11	(binap)Ni[P(OPh)$_3$]$_2$(5 mol-%) + binap (5 mol-%)	K$_3$PO$_4$ (2.0 equiv.)	120	0	–

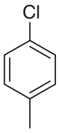
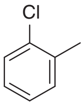
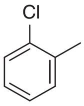
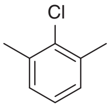
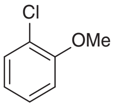
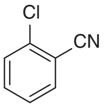
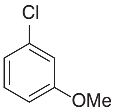
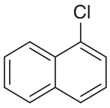
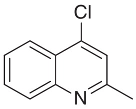
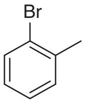
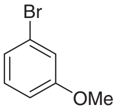
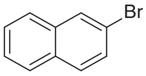
[A] 0.5 M solution in 1,4-dioxane.
[B] Unsealed tube.
[C] All reactions were monitored by GC and conversions are indicated.
[D] 2-h reaction.
[E] 31 % homocoupled product.

greatly improved the yield to 99 % along with a 1.2 : 1 ratio of mono- to diarylation product (**16** : **17**) (entry 6). At this stage, we are unable to determine the role of the additional base in this reaction. A reduced reaction time did not improve the mono- to diarylation product ratio (entry 7), suggesting that at these temperatures, the aniline **16** has a much greater coupling reactivity than ammonia. A higher catalytic loading was less successful in both overall yield and ratio of **16** to **17** (Table 4, entry 8). In a further example, a reaction using Ni(cod)$_2$ and (±)-binap did produce the desired product **16**, but only in a low overall yield of 16 % (entry 9). Use of the coordinatively unsaturated nickel(0) complex Ni[P(O-*o*-Tol)$_3$]$_3$, for which we recently determined the crystal structure,[16] proved similarly ineffective (entry 10). Changing the base to a commonly used inorganic base for cross-couplings, K$_3$PO$_4$, was also unsuccessful (entry 11).

Using our most efficacious conditions for the ammonia arylation (Table 4, entry 6), we sought to explore the reaction scope (Table 5). In this study, and as discovered by other groups investigating this type of reaction, the functional group

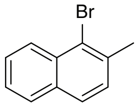
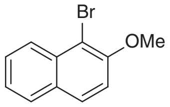
Table 5. Scope of the aryl halide coupling partner (0.50-mmol scale)



Entry	Substrate	Yield,[B] $ArNH_2$ [%] compound	Ratio[C] $ArNH_2/Ar_2NH$
1		(51) **16**	1.1 : 1
2		66, **19a**	2.2 : 1
3		50[D], **19a**	1.2 : 1
4		(<10), **19b**	1 : 0
5		70, **19c**	2.3 : 1
6		(<10), **19d**	1 : 0
7		(20), **19e**	1 : 3.4
8		68, **19f**	2.3 : 1
9		46, **19g**	n.d.
10		66, **19h**	6 : 1
11		(16), **19i**	1 : 1.2[E]
12		50, **19j**	1 : 0[F]

(*Continued*)

Table 5. (Continued)

Entry	Substrate	Yield,[B] $ArNH_2$ [%] compound	Ratio[C] $ArNH_2/Ar_2NH$
13		93, **19k**	1 : 0[G]
14		72, **19l**	1 : 0[H]

[A] 0.5 M solution in 1,4-dioxane.
[B] Yields are isolated yields unless in brackets (GC).
[C] Determined by GC.
[D] $(NH_4)_2SO_4$ (1.5 equiv.).
[E] ~14 % dehalogenation.
[F] ~46 % dehalogenation.
[G] >10 % dehalogenation.
[H] ~30 % dehalogenation.
n.d, not determined.

compatibility is not as extensive compared with other C–N cross-coupling reactions. Additionally, as also found by other research groups in this field,[44] fused ring systems, *N*-heterocyclic halides, and *ortho*-substituted aryl halides were more compatible under these conditions than simple sterically unhindered aryl halides. The reaction using *p*-chlorotoluene (Table 5, entry 1) provided *p*-toluidine (**16**) in 51 % GC yield. As expected, having the methyl group closer to the oxidative addition site (or C–Cl bond) in *o*-tolyl chloride improved the ratio in favour of the monoarylation product **19a** (entry 2). The equivalent reaction with ammonium sulfate, a convenient and cheap ammonia surrogate, also proceeded moderately in 50 % yield (entry 3).[46] Reactions testing the tolerance of *ortho*-substitution (entries 3–6) inferred that using a substrate containing an electron-donating group such as OMe was advantageous whereas the electron-withdrawing CN group had the opposite effect. Having an electron-donating group in the *meta*-position (entry 7) resulted in a higher proportion of the diaryl compound **20** being formed. This scenario occurs possibly through a loss of the steric influence when compared with the corresponding *ortho*-derived equivalent. Similarly to the earlier primary alkyl amine investigation (Table 3), both the coupling of naphthyl chloride and chloroquinoline provided good yields of the corresponding aminonaphthalene **19f** and aminoquinoline **19g** (entries 8 and 9).

A series of five aryl bromides were also reacted under the same conditions (entries 10 to 14, producing compounds **19h**–**19l**). The yield of the simple aryl bromides, entries 10 and 11, and reactions were comparable with the corresponding aryl chlorides, entries 2 and 7. In this same series, reactions of the brominated naphthalene substrates were very successful, with only the monoarylation product being isolated in good to excellent yields (entries 12–14). In some instances, however, a significant amount of the dehalogenated product was also formed (see Table 5 footnote).

Suzuki–Miyaura Cross-Coupling Reactions

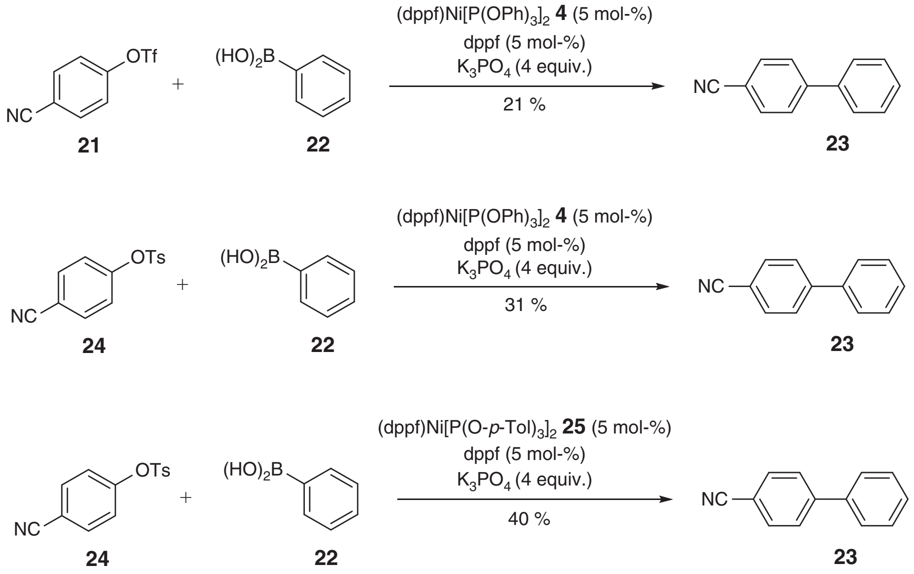
As part of our investigations into the viability of the nickel phosphite–phosphine systems discussed, we have begun a preliminary investigation into their reactivity in Suzuki cross-coupling reactions. Nickel catalysts have been applied in the Suzuki–Miyaura cross-coupling reaction for several years, often as a replacement for the palladium variant.[18,47] Some of these investigations have provided a plethora of new C–O-based and uncommon electrophilic moieties that can be used in substrates under nickel-catalysed reaction conditions.[48–54] In particular, the ability of organonickel complexes to oxidatively add into Ar–O bonds including both aryl triflates and tosylates has been well documented.[18,55–60] Furthermore, the cost-effectiveness and diversity provided by the availability of phenols are another attractive feature of these substrates.

In our trial, we examined the potential of the previously described catalyst (dppf)Ni[P(OPh)$_3$]$_2$ (**4**), which was able to initiate a simple reaction between the cyanophenyl triflate **21** and the phenylboronic acid **22** (Scheme 3). Under the same reaction conditions, the tosylate substrate **24** underwent a more efficient reaction to afford 31 % of the biaryl compound **23**. In a final reaction, the catalyst was changed to its *p*-tolyl derivative, (dppf)Ni[P(O-*p*-Tol)$_3$]$_2$ **25**, which also had a positive effect on the reaction, resulting in a 40 % yield. In this small group of reactions, we have determined that there is potential for further methodological studies of nickel phosphite catalysts for the Suzuki cross-coupling reaction.

In conclusion, we have shown that nickel phosphites and nickel phosphite–phosphine complexes be used in a range of diverse cross-coupling reactions. In the Heck cross-coupling, a series of reactions with the simple Ni[P(OEt)$_3$]$_4$ was successful; however, a catalyst compatible with a larger number of functional groups is still being sought. In the ammonia arylation reaction, simple aryl chlorides were most successful in combination with the (binap)Ni[P(OPh)$_3$]$_2$ (**5**) catalyst system. Although this system was not fully selective for the monosubstituted product in all cases, this catalyst offers an air-stable and more economical alternative to those reported previously. Finally, a short investigation into the Suzuki cross-coupling reaction with (dppf)Ni[P(OPh)$_3$]$_2$ (**4**) was explored, which is intended to lead to further investigations of other nickel phosphite–phosphine complexes.

Experimental

Starting materials and reagents were available from Sigma–Aldrich, Alfa Aesar, TCI or Strem chemicals and used as received unless stated otherwise. Amines were distilled under



Scheme 3. Suzuki reactions with aryl triflates and tosylates using (dppf)Ni[P(OPh)$_3$]$_2$ **4** and (dppf)Ni[P(O-*p*-Tol)$_3$]$_2$ **25**.

argon before use. NaO^{t}Bu was stored in an argon-filled glovebox and removed immediately before use. Ni[P(OPh)$_3$]$_4$, Ni[P(O-*m*-Tol)$_3$]$_4$ and Ni[P(O-*p*-Tol)$_3$]$_4$ were prepared from Ni(NO$_3$)$_2$·6H$_2$O according to a procedure by Levison et al.[24] (dppf)Ni[P(OPh)$_3$]$_2$,[15] (binap)Ni[P(OPh)$_3$]$_2$,[17] and Ni[P(O-*o*-Tol)$_3$]$_3$[16] were prepared as reported previously. NH$_3$ in 1,4-dioxane (Aldrich) was transferred into a Rotaflo® flask and stored in a glovebox. All reactions were performed under argon unless stated otherwise. All solvents used in reactions were anhydrous. Anhydrous solvents were distilled over the appropriate drying agent or acquired from a Pure Solv 5-Mid Solvent Purification System (Innovative Technology Inc.). Hexanes and EtOAc for column chromatography were distilled before use.

^{1}H, ^{13}C, ^{31}P, and ^{19}F nuclear magnetic resonance (NMR) spectra were acquired on a Varian 300, Varian 400, Bruker AV500 or Bruker AV600 spectrometer and all signals (δ) are reported in parts per million (ppm). Chemical shifts in ^{1}H and ^{13}C spectra were referenced to the residual (partially) undeuterated solvent according to Fulmer et al.[61] ^{31}P spectra were referenced to external H$_3$PO$_4$ (0.00 ppm), and ^{19}F spectra to C$_6$F$_6$ (164.9 ppm). Mass spectra were recorded on a Waters LCT Premier XE instrument, Waters GCT Premier coupled to an Agilent GC 7890A GC (equipped with an Agilent DB-5MS column; 30 m, 0.25 mm × df (film thickness) = 0.25 µm, serial no. US9562423) with an Agilent 7683B series Injector or a Shimadzu GC-MS QP2010 (equipped with a Stabilwax Crossbond Carbowax-PEG column; 30 m, 0.25 mm × df = 0.1 µm, serial no. 703411). GC conversions were determined from the crude reaction mixture by dividing the area of the product peak by the total area of product and starting material peak. GC yields were determined by use of an internal standard (dodecane). Infrared spectra were acquired on a PerkinElmer Spectrum One spectrometer equipped with an attenuated total reflection (ATR) diamond at 2-cm^{-1} resolution. Melting points were recorded on a Reichart heated-stage microscope. The reported retention factors (R_f) were acquired via thin-layer chromatography (TLC) performed on Merck silica gel 60 F$_{254}$ precoated aluminium sheets. Column chromatography was performed using silica gel 60 (0.04–0.063 mesh) supplied by Silicycle.

General Procedure for Heck Coupling Reactions

A flame-dried Schlenk tube was charged sequentially with the corresponding aryl triflate, nickel catalyst (Ni[P(OPh)$_3$]$_4$ or Ni[P(OEt)$_3$]$_4$), diphosphine ligand (dppf or dppe), and Cy$_2$NMe. The mixture was dissolved in toluene or 1,4-dioxane (~6 mL mmol^{-1}), followed by the addition of butyl vinyl ether. The reaction vessel was sealed, and stirred at 100°C for 18 h in a preheated oil bath. For the hydrolysis step, the reaction mixture was allowed to cool to room temperature (RT), and then treated with 6 M HCl (~6 mL mmol^{-1}). The mixture was stirred vigorously at RT for 1 h. After dilution with Et$_2$O (10 mL), the organic layer was separated and fused onto silica gel. Purification by flash column chromatography on silica gave the desired ketone products.

1-Acetylnaphthalene (**10a**)

Following the general procedure, using 1-naphthyl triflate (118 mg, 0.430 mmol, 1.00 equiv.), Ni[P(OPh)$_3$]$_4$ (29.0 mg, 0.022 mmol, 5 mol-%), dppf (12 mg, 0.022 mmol, 5 mol-%), Cy$_2$NMe (276 µL, 1.29 mmol, 3.00 equiv.), butyl vinyl ether (222 µL, 1.72 mmol, 4.00 equiv.), and 1,4-dioxane (3 mL), the desired ketone **10a** was obtained after hydrolysis and purification by flash column chromatography (hexanes/EtOAc 100 : 0 → 90 : 10) as a colourless oil (40 mg, 0.24 mmol, 56 %). The spectral data were in accordance with those reported in the literature.[19] R_f 0.43 (hexanes/EtOAc 90 : 10). δ_H (CDCl$_3$, 300 MHz) 8.76 (1H, d, *J* 8.4, Ar–H), 8.03–7.84 (3H, m, 3 × Ar–H), 7.66–7.45 (3H, m, 3 × Ar–H), 2.75 (3H, s, CH$_3$).

2-Acetylnaphthalene (**10b**)

Following the general procedure (21 h), using 2-naphthyl triflate (138 mg, 0.500 mmol, 1.00 equiv.), Ni[P(OPh)$_3$]$_4$ (33.0 mg, 0.025 mmol, 5 mol-%), DPPF (14 mg, 0.025 mmol, 5 mol-%), Cy$_2$NMe (320 µL, 1.50 mmol, 3.00 equiv.), butyl vinyl ether (250 µL, 2.00 mmol, 4.00 equiv.), and 1,4-dioxane (3 mL), the desired ketone **10b** was obtained after hydrolysis and purification by flash column chromatography (hexanes/Et_2O 98 : 2) as a colourless oil (69 mg, 0.41 mmol, 82 %). The spectral data were in accordance with those reported in the literature.[19] R_f 0.14 (hexanes/EtOAc 98 : 2). δ_H ($CDCl_3$, 400 MHz) 8.41 (1H, s, Ar–H), 7.99 (1H, d, *J* 8.6, Ar–H), 7.91 (1H, d, *J* 8.1, Ar–H), 7.85–7.80 (2H, m, 2 × Ar–H), 7.58–7.48 (2H, m, 2 × Ar–H), 2.67 (3H, s, CH_3).

4′-Phenylacetophenone (**10f**)

Following the general procedure, using 4-(1,1′-biphenyl) triflate (309 mg, 1.02 mmol, 1.00 equiv.), $Ni[P(OEt)_3]_4$ (15.0 mg, 0.020 mmol, 2 mol-%), DPPE (8.0 mg, 0.020 mmol, 2 mol-%), Cy_2NMe (216 µL, 1.02 mmol, 1.00 equiv.), butyl vinyl ether (196 µL, 1.53 mmol, 1.50 equiv.), and toluene (6 mL), the desired ketone **10f** was obtained after hydrolysis and purification by flash column chromatography (hexanes/EtOAc 95 : 5) as a white solid (33 mg, 0.17 mmol, 17 %). The spectral data were in accordance with those reported in the literature.[62] R_f 0.28 (hexanes/EtOAc 90 : 10). δ_H ($CDCl_3$, 300 MHz) 8.04 (2H, d, *J* 8.4, 2 × Ar–H), 7.69 (2H, d, *J* 8.4, 2 × Ar–H), 7.67–7.59 (2H, m, 2 × Ar–H), 7.54–7.36 (3H, m, 3 × Ar–H), 2.64 (3H, s, CH_3).

1,3-Diacetylbenzene (**10h**)

Following the general procedure, using 3-acetylphenyl triflate (274 mg, 1.02 mmol, 1.00 equiv.), $Ni[P(OEt)_3]_4$ (14.0 mg, 0.020 mmol, 2 mol-%), DPPE (8.0 mg, 0.020 mmol, 2 mol-%), Cy_2NMe (217 µL, 1.02 mmol, 1.00 equiv.), butyl vinyl ether (198 µL, 1.53 mmol, 1.50 equiv.), and toluene (6 mL), the desired ketone **10h** was obtained after hydrolysis and purification by flash column chromatography (hexanes/EtOAc 90 : 10 → 80 : 20) as a colourless oil (109 mg, 0.670 mmol, 66 %). The spectral data were in accordance with those reported in the literature.[63] R_f 0.12 (hexanes/EtOAc 90 : 10). δ_H ($CDCl_3$, 300 MHz) 8.52 (1H, t, *J* 1.8, Ar–H), 8.15 (2H, dd, *J* 7.8, 1.8, 2 × Ar–H), 7.58 (1H, t, *J* 7.8, Ar–H), 2.66 (6H, s, 2 × CH_3).

1,4-Diacetylbenzene (**10i**)

Following the general procedure, using 4-acetylphenyl triflate (256 mg, 0.95 mmol, 1.00 equiv.), $Ni[P(OEt)_3]_4$ (13.0 mg, 0.019 mmol, 2 mol-%), DPPE (7.0 mg, 0.019 mmol, 2 mol-%), Cy_2NMe (202 µL, 0.95 mmol, 1.00 equiv.), butyl vinyl ether (184 µL, 1.43 mmol, 1.50 equiv.), and toluene (6 mL), the desired ketone **10i** was obtained after hydrolysis and purification by flash column chromatography (hexanes/EtOAc 80 : 20) as a pale-yellow solid (87 mg, 0.54 mmol, 56 %). The spectral data were in accordance with those reported in the literature.[63] R_f 0.40 (hexanes/EtOAc 70 : 30). δ_H ($CDCl_3$, 300 MHz,) 8.03 (4H, s, 4 × Ar–H), 2.65 (6H, s, 2 × CH_3).

4-Acetylbenzonitrile (**10j**)

Following the general procedure, using 4-cyanophenyl triflate (115 mg, 0.460 mmol, 1.00 equiv.), $Ni[P(OEt)_3]_4$ (7.0 mg, 0.0092 mmol, 2 mol-%), DPPE (4.0 mg, 0.0092 mmol, 2 mol-%), Cy_2NMe (98 µL, 0.46 mmol, 1.00 equiv.), butyl vinyl ether (89 µL, 0.69 mmol, 1.50 equiv.), and toluene (3 mL), the desired ketone **10j** was obtained after hydrolysis and purification by flash column chromatography (hexanes/EtOAc 100 : 0 → 90 : 10) as a tan solid (57 mg, 0.39 mmol, 85 %). The spectral data were in accordance with those reported in the literature.[19] R_f 0.26 (hexanes/EtOAc 90 : 10). δ_H ($CDCl_3$, 400 MHz) 8.04 (2H, d, *J* 8.5, 2 × Ar–H), 7.78 (2H, d, *J* 8.5, 2 × Ar–H), 2.64 (3H, s, CH_3).

4′-(Trifluoromethyl)acetophenone (**10k**)

Following the general procedure (22 h), using 3-(trifluoromethyl) phenyl triflate (285 mg, 0.970 mmol, 1.00 equiv.), $Ni[P(OEt)_3]_4$ (14.0 mg, 0.019 mmol, 2 mol-%), dppe (8.0 mg, 0.019 mmol, 2 mol-%), Cy_2NMe (206 µL, 0.970 mmol, 1.00 equiv.), butyl vinyl ether (188 µL, 1.46 mmol, 1.50 equiv.), and toluene (6 mL), the desired ketone **10k** was obtained after hydrolysis and purification by flash column chromatography (hexanes/EtOAc 95 : 5) as a colourless oil (77 mg, 0.41 mmol, 42 %). The spectral data were in accordance with those reported in the literature.[19] R_f 0.24 (hexanes/EtOAc 95 : 5). δ_H ($CDCl_3$, 300 MHz) 8.21 (1H, s, Ar–H), 8.14 (1H, d, *J* 7.8, Ar–H), 7.82 (1H, d, *J* 7.8, Ar–H), 7.62 (1H, 't', *J* 7.8, Ar–H), 2.65 (3H, s, CH_3). δ_F ($CDCl_3$, 282 MHz) −63.2.

(E/Z)-1-(2-Methoxy-4-(prop-1-en-1-yl)phenyl)ethanone (**10n**)

Following the general procedure (20 h), using 4-allyl-2-methoxyphenyl triflate (109 mg, 0.380 mmol, 1.00 equiv.), $Ni[P(OPh)_3]_4$ (25.0 mg, 0.019 mmol, 5 mol-%), DPPF (11 mg, 0.019 mmol, 5 mol-%), Cy_2NMe (250 µL, 1.14 mmol, 3.00 equiv.), butyl vinyl ether (213 µL, 1.52 mmol, 4.00 equiv.), and 1,4-dioxane (3 mL), the *title compound* **10n** was obtained after hydrolysis and purification by flash column chromatography (hexanes/EtOAc 98 : 2 → 96 : 4) as a colourless oil (10 : 6 *E/Z* mixture, 65 mg, 0.34 mmol, 89 %). The spectral data were in accordance with those reported in the literature.[19] R_f 0.13 (hexanes/EtOAc 98 : 2). *Major isomer (E):* δ_H ($CDCl_3$, 400 MHz) 7.73 (1H, d, *J* 8.1, Ar–H), 6.99 (1H, dd, *J* 8.1, 1.3, Ar–H), 6.90 (1H, s, Ar–H), 6.48–6.32 (2H, m, $HC{=}CHCH_3$), 3.94 (3H, s, OMe), 2.62 (3H, s, C(O)Me), 1.93 (3H, d, *J* 5.0 Hz, $HC{=}CHCH_3$). *Minor isomer (Z):* δ_H ($CDCl_3$, 400 MHz) 7.76 (1H, d, *J* 8.0, Ar–H), 6.96 (1H, d, *J* 8.0, Ar–H), 6.88 (1H, s, Ar–H), 6.47–6.33 (1H, m, $HC{=}CHCH_3$), 5.97–5.87 (1H, m, $HC{=}CHCH_3$), 3.94 (3H, s, OMe), 2.63 (3H, s, C(O)Me), 1.95 (3H, dd, *J* 7.0, 2.1, $HC{=}CHCH_3$).

General Procedure for Ammonia Arylation

An oven-dried vial (35 × 12 mm) equipped with a PTFE-sealed screw cap was loaded with a magnetic stirrer bar, ((±)-binap) $Ni[P(OPh)_3]_2{\cdot}2PhCH_3$ (**9**) (39 mg, 25 µmol, 5 mol-%), (±)-binap (15 mg, 25 µmol, 5 mol-%), and the corresponding aryl halide (0.50 mmol, 1.0 equiv.). The vial was then transferred into an argon-filled glovebox, where NaO^tBu (216 mg, 2.20 mmol, 4.40 equiv.) and NH_3 (0.5 M in 1,4-dioxane, 3.0 mL, 1.5 mmol, 3.0 equiv.) were added. The reaction vial was capped, removed from the glovebox, and placed into a preheated oil bath at 120°C to stir for 18 h. On cooling, the reaction mixture was diluted with Et_2O (15 mL), and washed with 1 M NaOH (10 mL) and H_2O (2 × 10 mL). The organic layer was fused onto silica and purified via flash column chromatography (EtOAc/hexanes or EtOAc/MeOH) to give the corresponding aniline.

o-Toluidine (**19a**)

Following the general procedure using 2-chlorotoluene (60 µL, 0.50 mmol), the desired compound **19a** was obtained after purification via flash column chromatography (hexanes/EtOAc 90 : 10) as a light-brown liquid (34 mg, 0.32 mmol, 64 %). The spectral data were in accordance with those reported in the literature.[32] R_f 0.20 (hexanes/EtOAc 90 : 10). δ_H ($CDCl_3$, 500 MHz) 7.08–7.02 (2H, m, 2 × Ar–H), 6.75–6.67 (2H, m, 2 × Ar–H), 3.48 (2H, br s, NH_2), 2.18 (3H, s, CH_3). δ_C ($CDCl_3$, 125 MHz) 144.6 (Ar–C), 130.6 (Ar–CH), 127.1 (Ar–CH), 122.5 (Ar–C), 118.8 (Ar–CH), 115.1 (Ar–CH), 17.5 (CH_3).

o-*Anisidine (**19c**)*

Following the general procedure using 2-chloroanisole (63 μL, 0.50 mmol), the desired compound **19c** was obtained after purification via flash column chromatography (hexanes/EtOAc 90 : 10) as a dark-orange liquid (43 mg, 0.35 mmol, 70 %). The spectral data were in accordance with those reported in the literature.[33] R_f 0.19 (hexanes/EtOAc 90 : 10). δ_H ($CDCl_3$, 300 MHz) 6.85–6.70 (4H, m, 4 × Ar–H), 3.86 (3H, s, OMe), 3.77 (2H, br s, NH_2). δ_C ($CDCl_3$, 75 MHz) 147.4 (Ar–C), 136.2 (Ar–C), 121.2 (Ar–CH), 118.6 (Ar–CH), 115.1 (Ar–CH), 110.5 (Ar–CH), 55.5 (OMe).

*1-Naphthylamine (**19f**)*

Following the general procedure using 1-chloronaphthalene (68 μL, 0.50 mmol), the desired compound **19f** was obtained after purification via flash column chromatography (hexanes/EtOAc 90 : 10) as a light-brown oil (49 mg, 0.34 mmol, 68 %). The spectral data were in accordance with those reported in the literature.[32] R_f 0.17 (hexanes/EtOAc 90 : 10). δ_H ($CDCl_3$, 500 MHz) 7.88–7.82 (2H, m, 2 × Ar–H), 7.53–7.46 (2H, m, 2 × Ar–H), 7.39–7.31 (2H, m, 2 × Ar–H), 6.80 (1H, dd, *J* 7.0, 1.3, Ar–H), 4.15 (2H, br s, NH_2). δ_C ($CDCl_3$, 125 MHz) 142.2 (Ar–C), 134.5 (Ar–C), 128.6 (Ar–CH), 126.4 (Ar–CH), 125.9 (Ar–CH), 124.9 (Ar–CH), 123.7 (Ar–C), 120.9 (Ar–CH), 119.0 (Ar–CH), 109.8 (Ar–CH).

*2-Methylquinolin-4-amine (**19g**)*

Following the general procedure using 4-chloroquinaldine (100 μL, 0.500 mmol), the desired compound **19g** was obtained after purification via flash column chromatography (EtOAc/MeOH 90 : 10) as an orange solid (36 mg, 0.23 mmol, 46 %). The spectral data were in accordance with those reported in the literature.[32] R_f 0.23 (EtOAc/MeOH 90 : 10). δ_H ($CDCl_3$, 500 MHz) 8.06 (1H, d, *J* 8.4, Ar–H), 7.96 (1H, d, *J* 8.4, Ar–H), 7.72 (1H, 't', *J* 7.7, Ar–H), 7.50 (1H, 't', *J* 7.7, Ar–H), 7.08 (1H, s, Ar–H), 2.66 (3H, s, CH_3), 2.07 (2H, br s, NH_2). δ_C ($CDCl_3$, 125 MHz) 159.6 (Ar–C), 149.2 (Ar–C), 145.8 (Ar–C), 130.1 (Ar–CH), 129.5 (Ar–C), 125.6 (Ar–CH), 120.5 (Ar–CH), 120.1 (Ar–CH), 109.0 (Ar–CH), 25.7 (CH_3).

*2-Naphthylamine (**19j**)*

Following the general procedure using 2-bromonaphthalene (104 mg, 0.500 mmol), the desired compound **19j** was obtained after purification via flash column chromatography (hexanes/EtOAc 90 : 10) as a brown solid (36 mg, 0.25 mmol, 50 %). The spectral data were in accordance with those reported in the literature.[40] R_f 0.12 (hexanes/EtOAc 90 : 10). δ_H ($CDCl_3$, 500 MHz) 7.72 (1H, d, *J* 8.1, Ar–H), 7.68 (1H, d, *J* 8.6, Ar–H), 7.61 (1H, d, *J* 8.3, Ar–H), 7.39 (1H, ddd, *J* 8.1, 6.9, 1.2, Ar–H), 7.25 (1H, ddd, *J* 8.1, 6.9, 1.2, Ar–H), 6.99 (1H, d, *J* 2.0, Ar–H), 6.95 (1H, dd, *J* 8.6, 2.3, Ar–H), 3.81 (2H, br s, NH_2). δ_C ($CDCl_3$, 125 MHz) 144.2 (Ar–C), 135.0 (Ar–C), 129.3 (Ar–CH), 128.1 (Ar–C), 127.8 (Ar–C), 126.4 (Ar–CH), 125.9 (Ar–CH), 122.6 (Ar–CH), 118.4 (Ar–CH), 108.7 (Ar–CH).

*2-Methylnaphthalen-1-amine (**19k**)*

Following the general procedure using 1-bromo-2-methylnaphthalene (84 μL mg, 0.50 mmol), the desired compound **19k** was obtained after purification via flash column chromatography (hexanes/EtOAc 90 : 10) as a dark orange oil (73 mg, 0.46 mmol, 93 %). The spectral data were in accordance with those reported in the literature.[64] R_f 0.20 (hexanes/EtOAc 90 : 10). δ_H ($CDCl_3$, 500 MHz) 7.85–7.80 (2H, m, 2 × Ar–H), 7.50–7.43 (2H, m, 2 × Ar–H), 7.33 (1H, d, *J* 8.3, Ar–H), 7.28 (1H, d, *J* 8.3, Ar–H), 4.11 (2H, br s, NH_2), 2.38 (3H, s, CH_3). δ_C ($CDCl_3$, 125 MHz) 139.0 (Ar–C), 133.2 (Ar–C), 129.4 (Ar–CH), 128.6 (Ar–CH), 124.92 (Ar–CH), 124.87 (Ar–CH), 123.4 (Ar–C), 120.3 (Ar–CH), 118.3 (Ar–CH), 116.3 (Ar–CH), 17.8 (CH_3).

*2-Methoxynaphthalen-1-amine (**19l**)*

Following the general procedure using 1-bromo-2-methoxynaphthalene (119 mg, 0.500 mmol), the desired compound **19l** was obtained after purification via flash column chromatography (hexanes/EtOAc 90 : 10) as a dark-orange oil (62 mg, 0.36 mmol, 72 %). The spectral data were in accordance with those reported in the literature.[65] R_f 0.22 (hexanes/EtOAc 90 : 10). δ_H ($CDCl_3$, 500 MHz) 7.80–7.77 (2H, m, 2 × Ar–H), 7.46–7.42 (1H, m, Ar–H), 7.38–7.33 (2H, m, 2 × Ar–H), 7.26 (1H, d, *J* 8.8, Ar–H), 4.23 (2H, br s, NH_2), 3.98 (3H, s, OMe). δ_C ($CDCl_3$, 125 MHz) 142.6 (Ar–C), 129.6 (Ar–C), 129.5 (Ar–C), 128.5 (Ar–CH), 125.1 (Ar–CH), 124.0 (Ar–C), 123.7 (Ar–CH), 120.4 (Ar–CH), 118.5 (Ar–CH), 113.7 (Ar–CH), 56.8 (OMe).

*4-Phenyl Benzonitrile **23***

Method A

4-Trifluoromethanesulfonylbenzonitrile **21** (126 mg, 0.500 mmol), phenylboronic acid **22** (106.8 mg, 0.6 mmol), (dppf)Ni[P(OPh)$_3$]$_2$ (30.6 mg, 0.0250 mmol), DPPF (13.9 mg, 0.0250 mmol), and potassium phosphate (424 mg, 2.00 mmol) were dissolved in 1,4-dioxane (3 mL) and stirred in a sealed vessel at 100°C under nitrogen for 16 h. The reaction was cooled to RT and water was added (3 mL). The aqueous layer was extracted with dichloromethane (3 × 5 mL) and the combined organic layers were washed with water (2 × 5 mL) and dried with $MgSO_4$. After filtration, the solvent was removed under reduced pressure to give a yellow-brown oil, which was subjected to column chromatography (hexanes/EtOAc 100 : 0 → 97 : 3) to afford a yellow solid, which was then stirred with H_2O_2 (3 mL of a 30 % w/w aqueous solution) for 30 min. The mixture was extracted with ethyl acetate (2 × 3 mL), dried over $MgSO_4$, and filtered through a plug of silica to afford 4-phenyl benzonitrile **23** as a white solid (18.4 mg, 21 %). The spectral data were in accordance with those reported in the literature.[66] δ_H ($CDCl_3$, 500 MHz) 7.68 (2H, d, *J* 8.5, Ar–H), 7.72 (2H, d, *J* 8.0, Ar–H), 7.59 (2H, d, *J* 7.5, Ar–H), 7.48 (2H, dd, *J* 7.5,7, Ar–H), 7.42 (1H, d, *J* 7.5,7, Ar–H). δ_C ($CDCl_3$, 125 MHz): 145.7, 139.2, 132.6, 128.7, 127.8, 127.3, 119.0, 110.9.

Method B

4-Tosylbenzonitrile **24** (137 mg, 0.500 mmol), phenylboronic acid **22** (107 mg, 0.600 mmol), (dppf)Ni[P(OPh)$_3$]$_2$ (30.6 mg, 0.0250 mmol), DPPF (13.9 mg, 0.0250 mmol), and potassium phosphate (424 mg, 2.00 mmol) were dissolved in 1,4-dioxane (3 mL) and stirred in a sealed vessel at 100°C under nitrogen for 16 h. The reaction was cooled to RT and water

(3 mL) was added. The aqueous layer was extracted with dichloromethane (3 × 5 mL) and the combined organic layers were washed with water (2 × 5 mL) and dried with $MgSO_4$. After filtration, the solvent was removed under reduced pressure to give a yellow-brown oil, which was subjected to column chromatography (hexanes/EtOAc 100 : 0 → 97 : 3) to afford a yellow solid, which was then stirred with H_2O_2 (3 mL of a 30 % w/w aqueous solution) for 30 min. The mixture was extracted with ethyl acetate (2 × 3 mL), dried over $MgSO_4$, and filtered through a plug of silica to afford 4-phenyl benzonitrile **23** as a white solid (27.6 mg, 31 %).

Method C

4-Tosylbenzonitrile **24** (137 mg, 0.5 mmol), phenylboronic acid (107 mg, 0.600 mmol), (dppf)Ni[P(O-*p*-Tol)$_3$]$_2$ **25** (30.6 mg, 0.0250 mmol), DPPF (13.9 mg, 0.0250 mmol), and potassium phosphate (424.3 mg, 2 mmol) were dissolved in 1,4-dioxane (3 mL) and stirred in a sealed vessel at 100°C under nitrogen for 16 h. The reaction was cooled to RT and water was added (3 mL). The aqueous layer was extracted with dichloromethane (3 × 5 mL) and the combined organic layers were washed with water (2 × 5 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure to give a yellow-brown oil, which was subjected to column chromatography (hexanes/EtOAc 100 : 0 → 97 : 3) to afford a yellow solid, which was then stirred with H_2O_2 (3 mL of a 30 % w/w aqueous solution) for 30 min. The mixture was extracted with ethyl acetate (2 × 3 mL), dried over $MgSO_4$, and filtered through a plug of silica to afford 4-phenyl benzonitrile **23** as a white solid (35.9 mg, 40 %).

*[1,1′-Bis(diphenylphosphino)ferrocene]bis[tri(*para*-tolyl) phosphite]nickel(0)* **25**

Ni[P(O-*p*-Tol)$_3$]$_4$ (400 mg, 0.27 mmol) and DPPF (300 mg, 0.540 mmol) were placed into a flame-dried Schlenk flask and dried under high vacuum for 10 min. Toluene (6 mL) was added and the resulting orange solution was stirred at reflux for 2 h. The mixture was cooled to RT and the solvent was removed completely under high vacuum (cold trap). The remaining oily residue was triturated with *n*-hexane (4 mL), and the precipitate was collected by vacuum filtration under air. The filter cake was washed with hexanes (10 mL) to afford the desired nickel complex as a yellow powder (202 mg, 0.150 mmol, 57 %). δ_H (CD_2Cl_2, 600 MHz) 7.34–6.99 (20H, m, 4 × Ph–H), 6.74 (12H, br s, *p*-Tol–H), 6.47 (12H, br s, *p*-Tol–H), 4.12 (4H, br s, cp–H), 3.96 (4H, br s, cp–H), 2.21 (18H, br s, 6 × CH_3). δ_C (CD_2Cl_2, 150 MHz): 151.2 (6 × Ar–C), 134.6 (6 × Ar–C and Ar–CH), 132.3 (6 × Ar–C/Ar–CH), 129.4 (12 × Ar–CH), 128.3 (6 × Ar–C/Ar–CH), 127.4 (6 × Ar–CH), 121.7 (12 × Ar–CH), 74.6 (cp), 70.9 (cp), 20.7 (6 × CH_3). δ_P (CD_2Cl_2, 243 MHz) 128.6 (t, *J* 31.9), 23.6 (t, *J* 31.9). ν_{max}/cm^{-1} 3056, 1607, 1584, 1502, 1477, 1430, 1231, 1202, 1164, 1088, 1025, 883, 814, 793, 744, 694, 677, 627, 568.

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