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A General Palladium-Phosphine Complex for Exploring Aryl Tosylates in *N*-arylation of Amines: Scope and Limitation

Pui Ying Choy,[†] Kin Ho Chung,[†] Qingjing Yang, Chau Ming So,* Raymond Wai-Yin Sun and Fuk Yee Kwong*

Abstract: The scope and limitation of mono-selective *N*-arylation of various amines using aryl or heteroaryl tosylates are presented. Air-stable and easily accessible $Pd(OAc)_2$/CM-phos catalyst system was found capable to deal with a wide range of aryl tosylate substrates as well as amine nucleophiles, including primary and secondary cyclic/acyclic aliphatic amines, and anilines. *N*H-bearing heterocycles such as indole, carbazole, pyrrole, 10-phenothiazine and 10-phenoxazine were shown to be feasible coupling partners under this catalytic system. The described reaction conditions tolerate a wide range of functional groups and allow an array of aromatic amines as well as unsymmetrical amine products to be easily accessed from the various pattern of phenolic derivatives. Interestingly, this catalyst system even offers opportunity for reaction to be performed under water medium. We also reported the intermolecular coupling of optically active α-central chiral amines with aryl tosylates without the erosion of enantiomeric purity.

Introduction

It has been well-documented that arylamine-containing compounds are important basic building blocks of many natural products and biologically active molecules.[1] The development of efficient catalytic methods for diversely accessing these valuable products is thus significantly desirable. Traditional nucleophilic substitution,[2] addition to benzyne,[3] electrophilic nitration[4] and reductive amination[5] are commonly used synthetic routes to achieve $C_{(sp2)}$–N bonds. Metal-assisted (-catalyzed) $C_{(sp2)}$–N bond-forming reaction was first reported by Ullmann over a century using copper as the promotor.[6] In the last two decades, many transition metals have been shown to efficiently promote the coupling between aryl halides and amines.[7] Among them, palladium-catalyzed amination of aryl halides, in which it was reported by Migita using tin-mediated protocol,[8] and significantly expanded and extraordinary improved by Buchwald and Hartwig (a tin-free protocol, and later named as Buchwald-Hartwig amination),[9,10] is one of the most well-adopted synthetic tools in frontier organic syntheses. Key to success of this transformation has been illustrated regarding the use of appropriately-tuned ancillary ligands, which allow more challenging substrates to be applicable in this aromatic C–N bond-construction process.[11]

In addition to aryl(alkenyl) halides, tremendous effort has been made to expand the choice of electrophiles as the complementary coupling partners. Arene electrophiles coming from phenolic raw materials are indeed sustainable.[12] In fact, aryl sulfonates are alternative electrophiles which receive increasing popularity in the $C_{(sp2)}$–N bond-forming reactions.[13] Among them, aryl tosylates are of particularly attractive due to their ease of preparation (easily accessible from the corresponding phenol), ease of purification (simply by crystallization in most cases), more stable towards hydrolysis and lower cost (as compared to triflate). Nevertheless, their inherently low activity toward oxidative addition limited their genuine application in cross-coupling reactions. In fact, this difficulty can be addressed by modifying the ligand structure. The first Pd-catalyzed amination of aryl tosylates was reported by Hartwig in 1998 using Pd-DB*t*PF as the catalyst.[14] After this discovery, some other supporting ligands were reported to facilitate this reaction, for instance, XPhos,[15] JosiPhos-type ligands,[16] DPPF,[17] Mor-DalPhos,[18] MOP-type phosphine,[19] Pd/NHC precatalyst[20] and graphene-oxide supported $PdCl_2$ catalyst.[21]

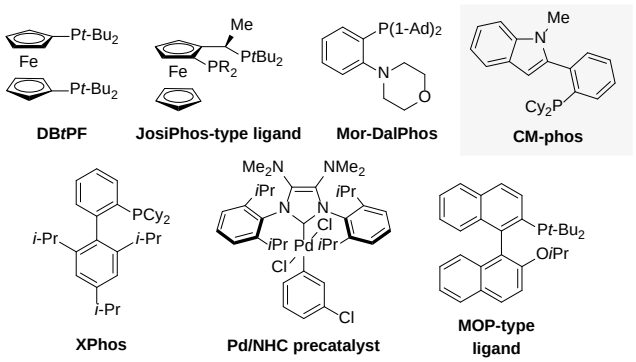

Figure 1. Selected ligand examples used in Pd-catalyzed amination of aryl tosylates (present work, CM-phos)

Although progress has been made, it is still highly desirable to develop a general catalyst system for this C–N bond-forming process, in particular it can handle across various

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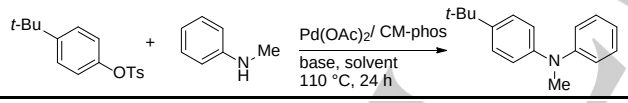
nature of nitrogen nucleophiles (e.g. primary/secondary aliphatic amine, cyclic/acyclic amine, aryl(heteroaryl) amine, *N*H-heterocycle and etc.) without significant change of reaction conditions. In continuing our research program on developing ligand system for tackling challenging coupling reactions,[22] we herein report the full scope of using Pd/CM-phos complex for coupling of aryl(heteroaryl) tosylates across a wide range of aromatic amines, aliphatic amines, heterocyclic amines, and α-chiral amines. Particularly noteworthy is that this catalyst system allowed the C–N bond-forming reaction to be proceeded even in aqueous medium without diminishing the product yields.

Results and Discussion

To probe the best reaction conditions, we carried out an array of experiments with different reaction parameters using electronically neutral 4-(*tert*-butyl)phenyl tosylate and *N*-methylaniline as model substrates (Table 1). Initial base screening revealed that K_3PO_4 was the best base of choice (Table 1, entries 1-5). Strong base NaO*t*-Bu is often employed in amination reaction, however, in this reaction, majority of phenolic side product was detected due to the competitive alkaline hydrolysis of aryl tosylate (Table 1, entry 2). Previous reports showed that alcoholic solvent gave superior effect in amination of aryl sulfonates probably due to the better solubility of the substrates and faster oxidative addition in polar solvent.[23] Therefore, we aimed to evaluate the efficacy of several common alcoholic solvents including *tert*-butanol, *iso*-propanol, and *tert*-amyl alcohol. Surprisingly, only *tert*-butanol afforded the desired product while other alcoholic solvents were found inferior (Table 1, entries 1, 8, and 9). Other polar solvents were tested and DMF was proven to be an ideal alternative solvent for achieving the desired coupling product (Table 1, entry 6).

Table 1. Initial screening of Pd-catalyzed *N*-arylation of amine with aryl tosylate[a]



entry	base	solvent	%yield[b]
1	K_2CO_3	*t*-BuOH	84
2	NaO*t*-Bu	*t*-BuOH	0
3	K_3PO_4	*t*-BuOH	96
4	Cs_2CO_3	*t*-BuOH	14
5	Na_2CO_3	*t*-BuOH	39
6	K_3PO_4	DMF	95
7	K_3PO_4	dioxane	41
8	K_3PO_4	*i*-PrOH	0
9	K_3PO_4	*t*-AmOH	0
10[c]	K_3PO_4	*t*-BuOH	0

[a] Reaction conditions: ArOTs (1.0 mmol), amine (1.5 mmol), base (2.5 mmol), $Pd(OAc)_2$ (0.5 mol%), CM-phos (2.0 mol%), Pd/L = 1:4, $PhB(OH)_2$ (0.04 mmol), solvent (3.0 mL) were stirred for 24 h at 110 °C under nitrogen. [b] Calibrated GC yields were reported using dodecane as the internal standard. [c] In the absence of CM-phos ligand.

Exploration of Substrate Scopes

With the optimized reaction conditions in hand, we first explored the substrate scope with respect to arylamines and functionalized aryl tosylates (Table 2). The coupling of unactivated aryl tosylate with *N*-methylaniline proceeded smoothly and the catalyst loading of even 0.2 mol% Pd was reached (Table 2, entry 1). Arene electrophiles bearing functional group substituents (e.g. ester-, keto-, cyano-group) were feasible coupling partners (Table 2, entries 2, 3, 7-9). Deactivated electron-rich aryl tosylate was successfully coupled with aniline (Table 2, entry 9). Examples of heteroaryl tosylates, for instance 2-methylbenzo[*d*]thiazol-5-yl tosylate and quinolin-6-yl tosylate gave the corresponding products in 80% and 94% yields, respectively (Table 2, entries 4, 5). The coupling of sterically hindered 2,6-dimethylanilines with aryl tosylates also proceeded well to afford the target products in good yields (Table 2, entries 10-12).

Table 2. Palladium-catalyzed *N*-arylation of arylamines with aryl/heteroaryl tosylates[a]

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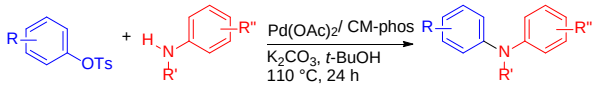
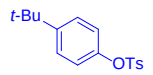
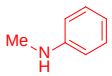
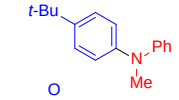
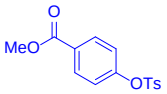
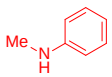
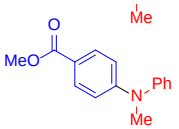
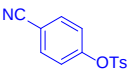
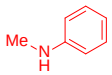
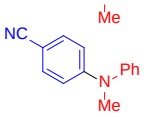
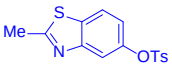
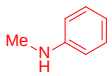
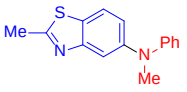
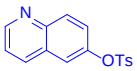
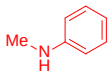
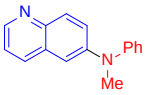
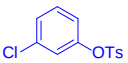
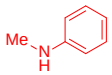
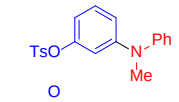
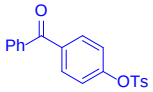
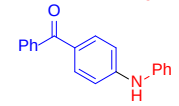
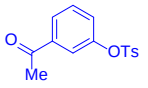
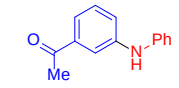
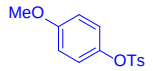
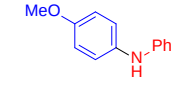
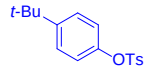
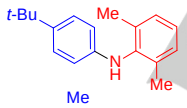
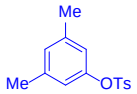
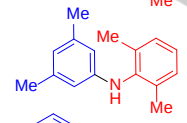
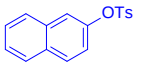
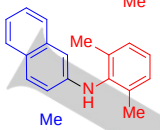
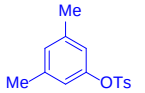
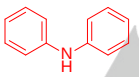
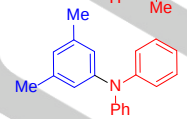


entry	ArOTs	Amine	product	[Pd]	%yield[b]
1[c]				0.2	90
2				0.5	90
3				0.5	87
4				2.0	80
5				1.0	94
6[c,d]				1.0	75
7				0.5	92
8				1.0	75
9				1.0	77
10[c]				2.0	89
11				0.5	83
12				0.5	77
13[d]				2.0	67

[a] Reaction conditions: ArOTs (1.0 mmol), amine (1.5 mmol), K_2CO_3 (2.5 mmol), $Pd(OAc)_2$ (as indicated), Pd/CM-phos = 1:4, $PhB(OH)_2$ (0.04 mmol), *t*-BuOH (3.0 mL) were stirred for 24 h at 110 °C under nitrogen. Reaction times were not optimized for each substrate. [b] Isolated yields. [c] K_3PO_4 was used as base. [d] ArOTs (1.5 mmol), amine (1.0 mmol) were used.

To further evaluate the Pd/CM-phos catalytic system, we next turned our attention to investigate the scope of primary aliphatic amines, secondary cyclic, and acyclic aliphatic amines (Table 3). Morpholine was used as the secondary amine model for coupling with various electrophilic partners. Notably, excellent yield was obtained even the catalyst loading down to 0.05 mol% Pd was employed (Table 3, entry 2).

Table 3. Palladium-catalyzed *N*-arylation of secondary aliphatic amines with aryl/alkenyl tosylates[a]

entry	ArOTs	Amine	product	[Pd]	%yield[b]
1				0.25	96
2[c]				0.05	90
3[d]				0.5	83
4[d]				0.5	95
5				1.0	84
6				1.0	75
7[e,f]				2.0	66
8[d]				1.0	66
9				0.5	88
10				1.0	91
11				1.0	80
12[e]				2.0	79
13[e]				2.0	62
14[e]				2.0	74
15[e]				2.0	87
16[e]				2.0	91
17[e]				1.0	84

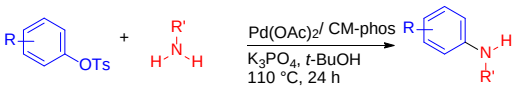
[a] Reaction conditions: ArOTs (1.0 mmol), secondary amine (1.5 mmol), K_3PO_4 (2.5 mmol), $Pd(OAc)_2$ (as indicated), Pd/CM-phos = 1:4, $PhB(OH)_2$ (0.04 mmol), *t*-BuOH (3.0 mL) were stirred for 24 h at 110 °C under nitrogen.

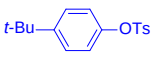
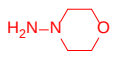
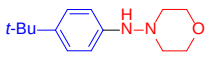
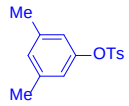
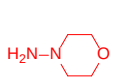
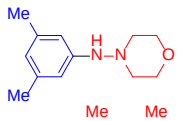
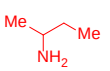
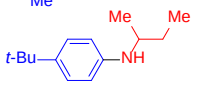
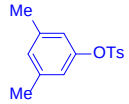
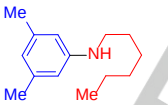
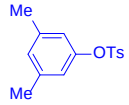
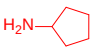
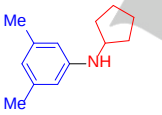
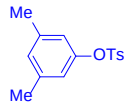
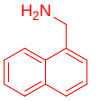
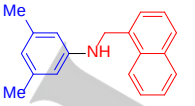
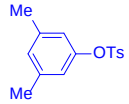
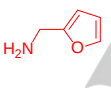
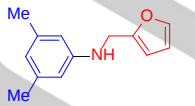
10.1002/asia.201800575

Reaction times were not optimized for each substrate. [b] Isolated yields. [c] The reaction was run for 40 hours. [d] K_2CO_3 was used as base. [e] DMF was used as solvent. [f] Reaction temperature was 120 °C.

Ester-, keto-substituted aryl tosylates provided the desired product in good yields (83-95%) (Table 3, entries 3 and 4). Alkenyl tosylate 1-methyl-2-oxo-1,2-dihydroquinolin-4-yl tosylate also served as an applicable coupling partner (Table 3, entry 8). With the excellent results obtained, we next investigated the amination of aryl tosylates with other alkyl amines. Secondary cyclic amines including pyrrolidine, and 1-methylpiperazine also provided the corresponding products in good-to-excellent yields (Table 3, entries 9-11). Acyclic secondary amines were also found to be suitable coupling partners (Table 3, entries 13-17).

Table 4. Palladium-catalyzed monoarylation of primary aliphatic amines with aryl tosylates[a]

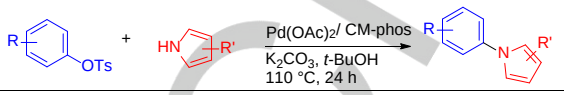


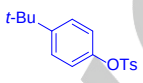
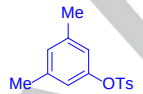
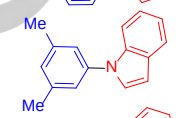
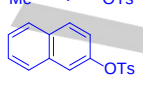
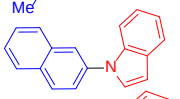
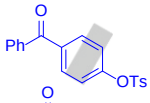
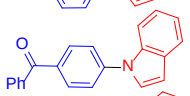
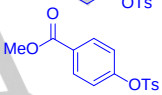
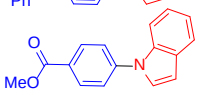
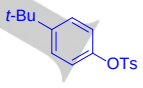
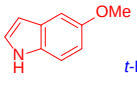
entry	ArOTs	Amine	product	[Pd]	%yield[b]
1				1.0	73
2				1.0	75
3[c]				2.0	91
4				2.0	79
5[c]				2.0	70
6[c]				2.0	91
7[c]				2.0	82

[a] Reaction conditions: ArOTs (1.0 mmol), primary amine (1.5 mmol), K_3PO_4 (2.5 mmol), $Pd(OAc)_2$ (as indicated), Pd/CM-phos = 1:4, $PhB(OH)_2$ (0.04 mmol), *t*-BuOH (3.0 mL) were stirred for 24 h at 110 °C under nitrogen. Reaction times were not optimized for each substrate. [b] Isolated yields. [c] DMF was used as solvent.

Primary aliphatic amines underwent the *N*-arylation transformation smoothly and essentially only mono-*N*-arylated products were afforded (Table 4). *N*-Aminomorpholine reacted with aryl tosylates in the presence of 1.0 mol% Pd catalyst to give secondary amines without noticeable formation of diarylated tertiary amines (Table 4, entries 1-2). Sterically hindered α-branched primary amine provided the desired coupling products in good-to-excellent yields (Table 4, entries 3 and 5). Heterocyclic-moiety containing primary aliphatic amine, e.g. furfurylamine, reacted smoothly to afford the coupling product (Table 4, entry 7).

Table 5. Palladium-catalyzed *N*-arylation of various *N*H-heterocycles with aryl tosylates[a]



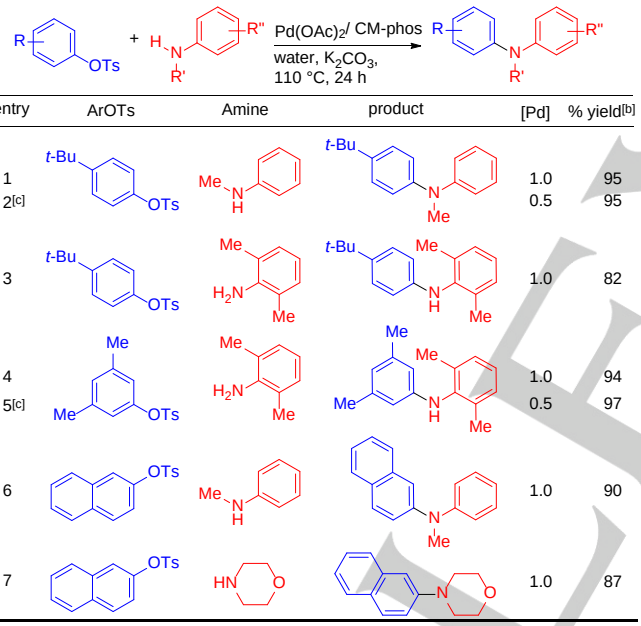
entry	ArOTs	Amine	product	[Pd]	%yield[b]
1				0.5	97
2				0.25	99
3				0.5	90
4				0.5	93
5				0.5	72
6				0.5	91
7				0.5	90
8				0.5	88
9				0.5	78
10				1.0	77
11[c]				1.0	96
12[d]				1.0	87
13				1.0	84

[a] Reaction conditions: ArOTs (1.0 mmol), *N*H-heterocycle (1.5 mmol), K_2CO_3 (2.5 mmol), $Pd(OAc)_2$ (as indicated), Pd/CM-phos = 1:4, $PhB(OH)_2$

(0.04 mmol), *t*-BuOH (3.0 mL) were stirred for 24 h at 110 °C under nitrogen. Reaction times were not optimized for each substrate. [b] Isolated yields. [c] ArOTs (1.5 mmol), amine (1.0 mmol) were used. [d] Cs_2CO_3 was used as base.

Nitrogen-containing heterocycles are important constituents of pharmaceutically active compounds and hence versatile method for diversely modifying these skeletons are of high interest.[24] We came across the coupling reaction between *N*H-heterocyclic compounds and aryl tosylates (Table 5). Indole core with different substituents were investigated. Excellent product yields were obtained even the catalyst loading was down to 0.25-0.5 mol% of Pd (Table 5, entries 1-8). Other *N*H-heterocylces such as pyrrole, 1,2,3,4-tetrahydrocyclopenta[*b*]indole, carbazole, 10-phenothiazine and 10-phenoxazine were also found to be applicable (Table 5, entries 9-13). Weakly nucleophilic and/or more steric bulky *N*H-heterocycles required slightly higher catalyst loading in this coupling reaction (from 0.5 mol% Pd to 1.0 mol% Pd).

Table 6. Palladium-catalyzed *N*-arylation of amines with aryl tosylates under aqueous medium or solvent-free conditions[a]

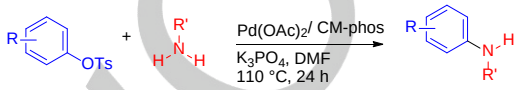


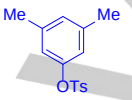
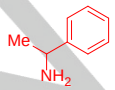
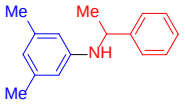
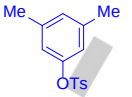
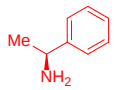
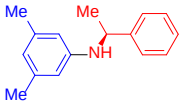
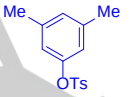
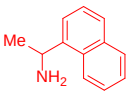
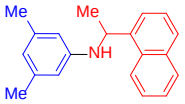
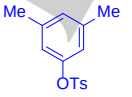
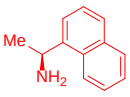
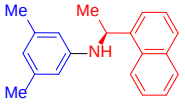
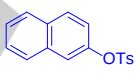
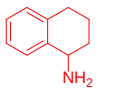
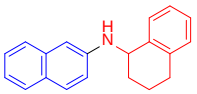
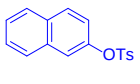
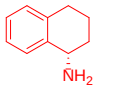
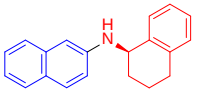
entry	ArOTs	Amine	product	[Pd]	% yield[b]
1				1.0	95
2[c]				0.5	95
3				1.0	82
4				1.0	94
5[c]				0.5	97
6				1.0	90
7				1.0	87

[a] Reaction conditions: ArOTs (1.0 mmol), amine (2.0 mmol), K_2CO_3 (2.5 mmol), $Pd(OAc)_2$ (as indicated), Pd/CM-phos = 1:4, $PhB(OH)_2$ (0.04 mmol), water (3.0 mL) were stirred for 24 h at 110 °C under nitrogen. Reaction times were not optimized for each substrate. [b] Isolated yields. [c] Amine (5.0 mmol) was used and no solvent was added.

Organic solvents are often employed in various cross-coupling reactions. Yet, it would be of great interest if more environmentally benign solvents can be used to replace common organic solvents. In view of the attractiveness of using water as solvent, we embarked to perform this reaction in aqueous medium. To our delight, by using the weak base K_2CO_3, no alkaline hydrolysis of aryl tosylates was observed under these aqueous conditions (Table 6). Sterically hindered amines were able to afford the desired product in excellent yields (Table 6, entries 1-5). Particularly noteworthy is that the Pd/CM-phos system retained to be effective even in solvent-free environment. No detrimental effects were found when the catalyst loading was down to 0.5 mol% of Pd (Table 6, entries 2 and 5). A comparison between the aqueous system and solvent-free conditions revealed that the solventless system required slightly lower catalyst loading (Table 6, entries 1 *vs* 2, and 4 *vs* 5).

Table 7. Palladium-catalyzed *N*-arylation of α-chiral amines with aryl tosylates[a]



entry	ArOTs	Amine	product	% yield[b]	% ee[c]
1				78	
2[d]				72	97 (*S*)
3				91	
4				85	99 (*S*)
5				71	
6				70	97 (*R*)

[a] Reaction conditions: ArOTs (1.0 mmol), chiral amine (1.5 mmol), K_3PO_4 (2.5 mmol), $Pd(OAc)_2$ (2.0 mol%), Pd/CM-phos = 1:4, $PhB(OH)_2$ (0.04 mmol), DMF (3.0 mL) were stirred for 24 h at 110 °C under nitrogen. Reaction times were not optimized for each substrate. [b] Isolated yields. [c] Determined by HPLC analysis using Daicel Chiralcel OD-H column. [d] 5.0 mmol of amine was used.

Amine having proximal central chiral carbon(s) are often found sub-skeleton in various bioactive compounds, such as topoisomerase II inhibitor GL331,[25] and 4β-*N*-amino-4-desoxypodophylotoxin congeners (antitumor antibiotics).[26] In fact, the challenge of C–N coupling between α-central chiral amine and electrophile is to keep the product enantioselectivity.[27] The possible β-elimination of the Pd-N-C*H*R_2 intermediate, and subsequent re-insertion of flipped $C_{(sp2)}$-imine moiety would ruin the enantiomeric purity of the final product. To our delight, under our monophosphine/Pd system, no racemization of the products was observed (Table 7). (*S*)-1-Phenylethanamine (98% *ee*) (Table 7, entry 2), (*S*)-1-(naphthalen-1-yl)ethanamine (99% *ee*) (Table 7, entry 4) and (*R*)-1,2,3,4-tetrahydronaphthalen-1-amine (98% *ee*) (Table 7,

entry 6) were examined and the product enantioselectivities were retained under this catalyst system.

Conclusions

In conclusion, we reported a Pd/CM-phos catalyst system that promote the cross-coupling between *N*-nucleophiles and aryl tosylates for the first time. This system broadly allowed the C–N bond coupling to be proceeded across different nature of amines, e.g. arylamines, primary and secondary aliphatic amines, cyclic and acyclic amines, *N*-heterocycles and α-central chiral amines. It is of note that particular catalyst loading can be as low as 0.05 mol% Pd. Interestingly, no erosion of product enantiopurity was observed when α-chiral amine was subjected to this coupling reaction under the Pd/CM-phos catalytic system. While most reported aryl sulfonate coupling procedures required organic solvents (to minimize undesirable alkaline hydrolysis), we here also showed the feasibility of using water as the solvent medium without detrimental effects. We believe this general catalyst system would be of interest to organic and pharmaceutical chemists working on phenol-related (sulfonate-protected phenol) areas, as the inherently inert feature of the tosyloxy group could serve as the protecting group in the early stage of synthetic route and ultimately allow post-functionalization *via* cross-coupling strategy.

Experimental Section

General considerations

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All the reactions were performed in Rotaflo®(England) resealable screw-cap tube (approx. 20 mL volume) in the presence of Teflon coated magnetic stirrer bar (4 mm × 10 mm). Dioxane was freshly distilled over sodium under nitrogen. *N,N*-Dimethylformamide (DMF) was distilled from calcium hydride under reduced pressure. *t*-Butanol was first distilled over sodium and stored with calcium hydride under nitrogen.[28] CM-phos ligand was developed by Kwong group and prepared according to literature.[29] Thin layer chromatography was performed on precoated silica gel 60 F254 plates. Silica gel (230-400 mesh) was used for column chromatography. ^{1}H NMR spectra were recorded on a 400 MHz or 500 MHz spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with TMS (δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were recorded on a 100 MHz or 125 MHz spectrometer and the spectra were referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). Coupling constants (*J*) were reported in Hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a Mass Spectrometer. High-resolution mass spectra (HRMS) were obtained on an ESI-QToF mass spectrometer which the ionization method is electrospray ionization (ESI) and the mass analyzer is a quadrupole time-of-flight mass analyzer. HPLC analyses were performed on a HP 1100 instrument using Chiralcel® OD-H columns (0.46 cm diameter x 25 cm long).

General procedures for palladium-catalyzed N-arylation of amines with aryl tosylates:

$Pd(OAc)_2$ (2.0 mol%, 0.02 mmol) and CM-phos (8.0 mol%, 0.08 mmol) in freshly distilled dichloromethane (2 ml, 1.0 mol% Pd per 1 ml stock solution) were initially prepared with continuously stirring at room temperature for 5 min. A Schlenk tube was charged with a Teflon-coated magnetic stir bar (4 mm x 10 mm) and was evacuated and backfilled with nitrogen (3 cycles). The corresponding volume of stock solution was added by syringe to the tube (indicated in Tables 2-6). Et_3N (0.4 equiv.) was introduced to the tube for precomplexation. The palladium complex solution was then stirred and warmed using a hair drier for 1 to 2 minutes until the solvent started boiling. The solvent was removed under reduced pressure. Aryl tosylates (1.0 mmol), phenylboronic acid (0.04 mmol, 0.04 equiv.) and K_2CO_3 or K_3PO_4 (2.5 mmol, 2.5 equiv.) were loaded into the tube, which was again evacuated and flushed with nitrogen for three times. Amines (1.5 mmol, 1.5 equiv.) and *t*-BuOH or DMF (3.0 mL if solvent is used) were then added with continuous stirring at room temperature for 3-4 minutes. The tube was resealed and then placed into a preheated oil bath (110 °C) and stirred for 24 hours. After completion of reaction, the reaction tube was allowed to reach room temperature and quenched with water and diluted with ethyl acetate. The organic layer was separated and the aqueous layer was washed with ethyl acetate. The organic layers were combined and concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

4-(*tert*-Butyl)-*N*-methyl-*N*-phenylaniline (Table 2, Entry 1; Table 6, Entry 1 and 2)[22b]

Hexane: DCM = 20:1, R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.55 (s, 9H), 3.49 (s, 3H), 7.10 (t, *J*=7.3 Hz, 1H), 7.18-7.25 (m, 4H), 7.43-7.47 (m, 2H), 7.52-7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.4, 34.1, 40.1, 118.9, 120.2, 121.2, 126.0, 129.0, 144.6, 146.3, 149.1.

Methyl 4-(*N*-methyl(*N*-phenyl)amino)benzoate (Table 2, Entry 2)[30]

Hexane: DCM = 20:1, R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.55 (s, 9H), 3.49 (s, 3H), 7.10 (t, *J*=7.3 Hz, 1H), 7.18-7.25 (m, 4H), 7.43-7.47 (m, 2H), 7.52-7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.4, 34.1, 40.1, 118.9, 120.2, 121.2, 126.0, 129.0, 144.6, 146.3, 149.1.

4-(*N*-Methyl(*N*-phenyl)amino)benzonitrile (Table 2, Entry 3)[22b]

Hexane: EA = 4:1, R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.32 (s, 3H), 6.70 (d, *J*=9.0 Hz, 2H), 7.17-7.19 (m, 2H), 7.22-7.26 (m, 1H), 7.34-7.43 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.7, 98.7, 113.4, 119.9, 125.8, 126.0, 129.7, 132.7, 146.3, 151.5.

***N*,2-Dimethyl-*N*-phenylbenzo[*d*]thiazol-5-amine (Table 2, Entry 4)**[31]

Hexane: EA = 20:1, R_f = 0.16; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.28 (s, 3H), 3.35 (s, 3H), 6.96-7.07 (m, 4H), 7.26-7.30 (m, 2H), 7.57-7.65 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7, 40.2, 112.7, 118.7, 120.3, 121.0, 121.3, 127.7, 128.9, 147.5, 148.7, 154.4, 167.2.

***N*-Methyl-*N*-phenylquinolin-6-amine (Table 2, Entry 5)**[32]

Hexane: EA = 9:1, R_f = 0.16; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.32 (s, 3H), 7.05-7.06 (m, 2H), 7.10-7.12 (m, 2H), 7.18-7.20 (m, 1H), 7.27-7.35 (m, 3H), 7.85-7.90 (m, 2H), 8.65-8.66 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.2, 110.6, 121.0, 123.0, 123.2, 123.4, 129.2, 129.4, 134.0, 143.6, 146.5, 147.1, 148.1.

3-(Methyl(phenyl)amino)phenyl 4-methylbenzenesulfonate (Table 2, Entry 6)[33]

Hexane: EA = 3:7, R_f = 0.3; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.44 (s, 3H), 3.26 (s, 3H), 6.80-6.87 (m, 4H), 7.03-7.07 (m, 3H), 7.29-7.32 (m, 4H), 7.75 (d, *J*=8.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 40.0, 118.3, 122.2, 122.6, 128.2, 129.2, 129.5, 132.2, 142.3, 145.0, 147.5, 148.1.

Phenyl(4-(phenylamino)phenyl)methanone (Table 2, Entry 7)[34]

Hexane: EA = 4:1, R_f = 0.33; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.55 (bs, 1H), 7.02-7.10 (m, 3H), 7.21 (d, *J*=7.7 Hz, 2H), 7.34 (t, *J*=7.7 Hz, 2H), 7.47 (t, *J*=7.5 Hz, 1H), 7.54-7.56 (m, 1H), 7.78 (t, *J*=7.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 114.2, 120.6, 123.1, 128.0, 128.2, 129.4, 129.5, 131.5, 132.6, 138.6, 140.6, 148.3, 195.2.

1-(3-(Phenylamino)phenyl)ethanone (Table 2, Entry 8)[35]

Hexane: EA = 9:1, assist with high vacuum, R_f = 0.2; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.58 (s, 3H), 6.24 (bs, 1H), 7.00 (t, *J*=7.3 Hz, 1H), 7.13 (d, *J*=7.6 Hz, 2H), 7.30-7.35 (m, 4H) 7.48 (d, *J*=7.2 Hz, 1H), 7.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.5, 116.2, 118.1, 120.3, 121.3, 121.4, 129.2, 138.0, 142.2, 143.7, 198.4.

4-Methoxy-*N*-phenylaniline (Table 2, Entry 9)[36]

Hexane: EA = 9:1, R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.87 (s, 3H), 5.56 (bs, 1H), 6.91-7.00 (m, 5H), 7.15 (d, *J*=8.8 Hz, 2H), 7.29-7.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 114.5, 115.5, 119.4, 122.0, 129.2, 135.6, 145.0, 155.1.

***N*-(4-(*tert*-Butyl)phenyl)-2,6-dimethylaniline (Table 2, Entry 10; Table 6, Entry 3)**[22b]

Hexane: EA = 20:1, R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.53 (s, 9H), 2.44 (s, 6H), 5.27 (bs,1H), 6.69 (d, *J*=8.5 Hz, 2H), 7.29-7.35 (m, 3H), 7.41 (d, *J*=8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 31.5, 33.8, 113.3, 125.3, 125.8, 128.4, 135.4, 138.7, 140.8, 143.6.

***N*-(3,5-Dimethylphenyl)-2,6-dimethylaniline (Table 2, Entry 11; Table 6, Entry 4 and 5)**[22b]

Hexane: EA = 20:1, R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.53 (s, 12H), 5.3 (bs, 1H), 6.46 (s, 2H), 6.74 (s, 1H), 7.39-7.45 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.2, 21.3, 111.2, 120.1, 125.4, 128.3, 135.7, 138.3, 138.6, 146.1.

***N*-(2,6-Dimethylphenyl)naphthalen-2-amine (Table 2, Entry 12)**[34]

Hexane: EA = 20:1, R_f = 0.16; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.43 (s, 6H), 5.42 (bs, 1H), 6.76 (d, *J*=1.8 Hz, 1H), 7.10 (q, *J*=6.6 Hz, 1H), 7.33-7.41 (m, 4H), 7.50 (m, 1H), 7.68 (d, *J*=8.2 Hz, 1H), 7.86 (t, *J*=9.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.3, 106.0, 117.4, 122.2, 125.9, 125.9, 126.2, 127.6, 127.8, 128.6, 129.1, 134.9, 136.0, 137.9, 143.9.

3,5-Dimethyl-*N*,*N*-diphenylaniline (Table 2, Entry 13)[36]

Hexane, R_f = 0.4; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.27 (s, 6H), 6.73 (s, 1H), 6.78 (s, 2H), 7.04 (t, *J*=7.5 Hz, 2H), 7.14 (d, *J*=1.0 Hz, 4H), 7.29 (t, *J*=2.0 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3, 122.3, 122.4, 124.0, 124.8, 129.1, 138.8, 147.7, 148.0.

4-(4-*tert*-Butylphenyl)morpholine (Table 3, Entry 1 and 2)[22b]

Hexane: EA = 9:1, R_f = 0.3; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.41 (s, 9H), 3.21 (t, *J*=4.8 Hz, 4H), 3.93 (t, *J*=4.7 Hz, 4H), 6.96 (d, *J*=8.8 Hz, 2H), 7.41 (d, *J*=8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 33.8, 49.4, 66.8, 115.2, 125.8, 142.5, 148.8.

4-Morpholinobenzoic acid methyl ester (Table 3, Entry 3)[37]

Hexane: EA = 9:1, R_f = 0.13; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.23 (t, *J*=4.8 Hz, 4H), 3.80 (t, *J*=4.8 Hz, 4H) 3.83 (s, 3H), 6.81 (d, *J*=8.9 Hz, 2H), 7.90 (d, *J*=8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.4, 51.5, 66.4, 113.2, 120.0, 131.0, 154.0, 166.8.

(4-Morpholinophenyl)(phenyl)methanone (Table 3, Entry 4)[34]

Hexane: EA = 9:1, R_f = 0.1; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.25 (t, *J*=4.8 Hz, 4H), 3.79 (t, *J*=4.8 Hz, 4H), 6.84 (d, *J*=8.9 Hz, 2H), 7.41 (t, *J*=7.4 Hz, 2H), 7.48-7.50 (m, 1H), 7.69-7.71 (m, 2H), 7.76 (d, *J*=8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.1, 66.2, 112.8, 127.3, 127.8, 129.3, 131.3, 132.1, 138.4, 153.7, 194.8.

4-(Benzo[*d*][1,3]dioxol-5-yl)morpholine (Table 3, Entry 5)[38]

Hexane: EA = 4:1, R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.03 (t, *J*=4.8 Hz, 4H), 3.84 (t, *J*=4.8 Hz, 4H), 5.90 (s, 2H), 6.34-6.37 (dd, *J*=2.4, 8.4 Hz, 1H), 6.55 (d, *J*=2.4 Hz, 1H), 6.72 (d, *J*=8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.0, 66.9, 99.5, 100.9, 108.2, 108.6, 141.7, 147.3, 148.3.

4-(Naphthalen-1-yl)morpholine (Table 3, Entry 6)[38]

Hexane: EA = 20:1, R_f = 4.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.15 (t, *J*=4.4 Hz, 4H), 4.02 (t, *J*=4.4 Hz, 4H), 7.12 (d, *J*=7.6 Hz, 1H), 7.45 (t, *J*=8.0 Hz, 1H), 7.50-7.55 (m, 2H), 7.61 (d, *J*=8.0 Hz, 1H); 7.86-7.89 (m, 1H), 8.25 (d, *J*=9.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 53.5, 67.5, 114.7, 123.4, 123.8, 125.5, 125.9, 128.5, 128.8, 134.8, 149.4.

4-(2,5-Dimethylphenyl)morpholine (Table 3, Entry 7)[39]

Hexane: EA = 20:1, R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (t, *J*=7.6 Hz, 6H), 3.2.95 (t, *J*=4.4Hz, 4H), 3.90 (t, *J*=4.4 Hz, 4H), 6.87 (s, 1H), 6.89 (s, 1H), 7.14 (d, *J*=7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.4, 21.2, 52.3, 67.5, 119.7, 124.0, 129.3, 131.0, 136.2, 151.1.

1-Methyl-4-morpholinoquinolin-2(1*H*)-one (Table 3, Entry 8)

Hexane: EA = 1:2, R_f = 0.3; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.13 (t, *J*=4.4 Hz, 4H), 3.69 (s, 3H), 3.95 (t, *J*=4.4 Hz, 4H), 6.22 (s, 1H), 7.23 (t, *J*=8.0 Hz, 1H), 7.38 (d, *J*=8.4 Hz, 1H), 7.54-7.58 (m, 1H), 7.81 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.1, 52.2, 66.7, 106.6, 114.8, 117.4, 121.4, 124.9, 130.5, 140.5, 157.9, 163.2; HRMS: calcd. for $C_{14}H_{16}N_2O_2$: 245.1285, found 245.128.

1-(4-(*tert*-Butyl)phenyl)pyrrolidine (Table 3, Entry 9)[22b]

Hexane: EA = 1:4, R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.58 (s, 9H), 2.19-2.23 (m, 4H), 3.50- 3.53 (m, 4H), 6.79 (d, *J*=8.7 Hz, 2H), 7.52-7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.4, 31.5, 33.6, 47.5, 111.2, 125.7, 137.7, 145.8.

1-(Naphthalen-2-yl)pyrrolidine (Table 3, Entry 10)[22b]

Hexane: DCM = 1:4, R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.08-2.11 (m, 4H), 3.44-3.47 (m, 4H), 6.83 (m, 1H), 7.04-7.07 (m, 1H), 7.22-7.26 (m, 1H), 7.41-7.45 (m, 1H), 7.71-7.78 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

25.4, 47.7, 104.6, 115.6, 120.1, 125.7, 126.1, 126.2, 127.5, 128.7, 135.2, 145.8.

1-(3,5-Dimethylphenyl)-4-methylpiperazine (Table 3, Entry 11)[36]

Acetone: EA = 1:4, R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 6H), 2.38 (s, 3H), 2.60 (t, *J*=4.8 Hz, 4H), 3.23 (t, *J*=4.8 Hz, 4H), 6.56 (s, 1H), 6.61 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 46.1, 49.2, 55.2, 114.0, 121.7, 138.6, 151.4.

4-(*tert*-Butyl)-*N*-cyclohexyl-*N*-methylaniline (Table 3, Entry 12)

Hexane: EA = 20:1, R_f = 0.7;^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20-1.23 (m, 1H), 1.39 (s, 9H), 1.42-1.57 (m, 4H), 1.79 (d, *J*=13.0 Hz, 1H), 1.90 (t, *J*=16.4 Hz, 4H), 2.85 (s, 3H), 3.59-3.66 (m, 1H), 6.82 (d, *J*=8.8 Hz, 2H), 7.34-7.36 (dd, *J*=1.9, 6.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 26.1, 30.0, 31.1, 31.4, 33.6, 58.1, 112.8, 125.7, 138.7, 147.8; HRMS: calcd. for $C_{17}H_{28}N^+$: 246.2222, found 246.2223.

4-(*tert*-Butyl)-*N*,*N*-dihexylaniline (Table 3, Entry 13)

Hexane: EA = 20:1, R_f = 0.7; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11 (t, *J*=5.8 Hz, 6H), 1.50 (d, *J*=9.9 Hz, 21H), 1.78 (s, 4H), 3.43 (t, *J*=7.6 Hz, 4H), 6.79 (d, *J*=8.6 Hz, 2H), 7.42 (d, *J*=8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.7, 26.9, 27.3, 31.5, 31.7, 33.5, 51.1, 111.3, 125.8, 137.5, 145.9; HRMS: calcd. for $C_{22}H_{40}N^+$: 318.3161, found 318.3154.

4-(*tert*-Butyl)-*N*,*N*-dihexylaniline (Table 3, Entry 14)[40]

Hexane: EA = 20:1, R_f = 0.7; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.09 (t, *J*=7.2 Hz, 6H), 1.43 (s, 9H), 1.46-1.54 (m, 4H), 1.67-1.74 (m, 4H), 3.38 (t, *J*=7.6 Hz, 4H), 6.74 (d, *J*=8.4 Hz, 2H), 7.36 (d, *J*=8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 20.5, 29.6, 31.7, 33.7, 51.0, 111.5, 126.0, 137.8, 146.1.

***N*-Benzyl-4-(*tert*-butyl)-*N*-methylaniline (Table 3, Entry 15)**[40]

Hexane: EA = 1:20, R_f = 0.7; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.67 (s, 9H), 3.29 (s, 3H), 4.80 (s, 2H), 7.06 (d, *J*=8.7 Hz, 2H), 7.58-7.62 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.5, 33.6, 38.3, 56.8, 112.1, 125.8, 126.7, 128.4, 139.0, 139.2, 147.5.

***N*-Benzyl-*N*-ethyl-3,5-dimethylaniline (Table 3, Entry 16)**

Hexane: EA = 1:20, R_f = 0.7, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.35 (t, *J*=7.2 Hz, 3H), 2.41 (s, 6H), 3.57-3.62 (q, *J*=6.8, 7.2 Hz, 2H), 4.66 (s, 2H), 6.54 (s, 3H), 7.37-7.49 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.2, 21.9, 44.9, 53.9, 110.2, 118.4, 126.8, 128.6, 138.9, 139.6, 148.9; HRMS: calcd. for $C_{17}H_{21}N$: 240.1747, found 240.1751.

***N*,*N*-Dibenzyl-4-(*tert*-butyl)aniline (Table 3, Entry 17)**[22b]

Hexane: EA = 4:1, R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ1.57 (s, 9H), 4.89 (s, 4H), 6.99 (d, *J*=8.9 Hz, 2H), 7.46-7.59 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.5, 33.6, 54.2, 112.1, 125.9, 126.6, 126.7, 128.5, 138.8, 139.1, 146.9.

***N*-(4-(*tert*-Butyl)phenyl)morpholin-4-amine (Table 4, Entry 1)**[41]

Hexane: EA = 9:1, R_f = 0.2; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (s, 9H), 2.78 (s, 4H), 3.84 (t, *J*=4.8 Hz, 4H), 4.35 (bs, 1H), 6.90 (d, *J*=8.4 Hz, 2H), 7.27 (d, *J*=8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.5, 34.0, 56.5, 67.0, 113.5, 125.9, 142.6, 144.6.

***N*-(3,5-Dimethylphenyl)morpholin-4-amine (Table 4, Entry 2)**[41]

Hexane: EA = 1:7, R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (s, 6H), 2.78 (s, 4H), 3.86 (t, *J*=4.8 Hz, 4H), 3.52 (s, 1H), 6.60 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 56.5, 67.0, 111.6, 121.7, 138.9, 147.1.

***N*-(*sec*-Butyl)-4-(*tert*-butyl)aniline (Table 4, Entry 3)**[42]

Hexane: EA = 9:1, R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.04 (t, *J*=7.6 Hz, 3H), 1.24 (d, *J*=6.4 Hz, 3H), 1.37 (s, 9H), 1.51-1.58 (m, 1H), 1.65-1.72 (m, 1H), 3.43-3.48 (m, 1H), 6.63 (t, *J*=6.8 Hz, 2H), 7.27 (t, *J*=6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.4, 20.4, 29.8, 31.6, 33.8, 50.0, 112.8, 126.0, 139.5, 145.4.

***N*-Hexyl-3,5-dimethylaniline (Table 4, Entry 4)**[42]

Hexane: EA = 9:1, R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.01 (t, *J*=6.8 Hz, 3H), 1.41-1.51 (m, 6H), 1.66-1.72 (m, 2H), 2.32-2.37 (m, 6H), 3.16 (d, *J*=6.8 Hz, 2H), 3.19 (bs, 1H), 6.34 (s, 2H), 6.46 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 21.5, 22.7, 26.9, 29.7, 31.7, 44.1, 110.7, 118.8, 119.1, 138.8, 148.7.

***N*-Cyclopentyl-3,5-dimethylaniline (Table 4, Entry 5)**[43]

Hexane: EA = 20:1, R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.48-1.56 (m, 2H), 1.64-1.83 (m, 4H), 2.04-2.12 (m, 2H), 2.31 (s, 6H), 3.81-3.88 (m, 1H), 6.32 (s, 2H), 6.42 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 24.1, 33.7, 54.7, 111.2, 119.0, 138.8, 148.1.

3,5-Dimethyl-*N*-(naphthalen-1-ylmethyl)aniline (Table 4, Entry 6)[44]

Hexane: EA = 20:1, R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.39 (s, 6H), 4.80 (s, 2H), 6.44 (s, 2H), 6.57 (s, 1H), 7.54 (t, *J*=7.2 Hz, 1H), 7.62-7.65 (m, 3H), 7.91 (d, *J*=8.0 Hz, 1H), 8.00-8.02 (m, 1H), 8.17-8.20 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 46.5, 110.8, 119.7, 123.8, 125.7, 125.9, 126.1, 126.4, 128.2, 128.8, 131.7, 134.0, 134.7, 139.1, 148.5.

***N*-(Furan-2-ylmethyl)-3,5-dimethylaniline (Table 4, Entry 7)**[45]

Hexane: EA = 20:1, R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.28 (s, 6H), 4.33 (s, 2H), 6.26 (d, *J*=3.2 Hz, 1H), 6.36 (s, 3H), 6.45 (s, 1H), 7.40 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 41.6, 106.9, 110.3, 111.2, 120.1, 138.9, 141.8, 147.6, 152.9.

1-(4-(*tert*-Butyl)phenyl)-1*H*-indole (Table 5, Entry 1)[22b]

Hexane: EA = 20:1, R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.57 (s, 9H), 6.86 (d, *J*=3.1 Hz, 1H), 7.36-7.42 (m, 2H), 7.48 (d, *J*=3.2 Hz, 1H), 7.59 (d, *J*=8.5 Hz, 2H), 7.68 (d, *J*=8.5 Hz, 2H), 7.77 (d, *J*=8.0 Hz, 1H), 7.89 (d, *J*=7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.4, 34.5, 103.2, 110.6, 120.2, 121.0, 122.2, 123.9, 126.4, 128.0, 129.2, 135.9, 137.2, 149.3.

1-(3,5-Dimethylphenyl)-1*H*-indole (Table 5, Entry 2)[46]

Hexane: EA = 20:1, R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.65 (s, 6H), 6.95-6.96 (m, 1H), 7.24 (s, 1H), 7.39 (s, 2H), 7.46-7.56 (m, 3H), 7.90 (d, *J*=8.0 Hz, 1H), 8.00 (d, *J*=7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 103.1, 110.6, 120.1, 121.0, 121.9, 122.1, 127.9, 128.0, 129.2, 135.8, 139.2, 139.6.

1-(Naphthalen-2-yl)-1*H*-indole (Table 5, Entry 3)[22b]

Hexane: EA = 9:1, R_f = 0.3; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05 (d, *J*=3.1 Hz, 1H), 7.56-7.58 (m, 2H), 7.67-7.65 (m, 1H), 7.75-7.77 (m, 2H), 7.86 (m, 1H), 8.04 (m, 1H), 8.09-8.13 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 103.8, 110.5, 120.4, 121.1, 121.6, 122.4, 122.9, 125.8, 126.7, 127.5, 127.7, 128.0, 129.4, 131.6, 133.6, 135.9, 137.0.

(4-(1*H*-Indol-1-yl)phenyl)(phenyl)methanone (Table 5, Entry 4)[22b]

Hexane: DCM = 7:3, R_f = 0.15; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.80 (d, *J*=3.2 Hz, 1H), 7.29-7.34 (m, 2H), 7.42 (d, *J*=3.2 Hz, 1H), 7.54-7.66 (m, 5H), 7.74-7.79 (m, 2H), 7.92 (d, *J*=7.2 Hz, 2H), 8.01 (d, *J*=8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 104.8, 110.4, 120.8, 121.2, 122.7, 127.2, 128.1, 129.6, 129.7, 131.6, 132.2, 134.5, 135.1, 137.3, 143.0, 195.0.

Methyl 4-(1*H*-indol-1-yl)benzoate (Table 5, Entry 5)[22b]

Hexane: EA = 9:1, R_f = 0.3; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.01 (s, 3H), 6.78 (d, *J*=3.0 Hz, 1H), 7.27-7.37 (m, 3H), 7.57 (d, *J*=8.5 Hz, 2H), 7.69 (d, *J*=7.8 Hz, 1H), 7.78 (d, *J*=7.8 Hz, 1H), 8.22 (d, *J*=8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 51.9, 104.7, 110.3, 120.7, 121.1, 122.6, 122.8, 127.1, 127.2, 129.6, 130.9, 135.1, 143.3, 166.0

1-(4-(*tert*-Butyl)phenyl)-5-methoxy-1*H*-indole (Table 5, Entry 6)

Hexane: EA = 9:1, R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.57 (s, 9H), 4.03 (s, 3H), 6.79 (d, *J*=3.1 Hz, 1H), 7.10 (q, *J*=6.5 Hz, 1H), 7.36 (d, *J*=2.4 Hz, 1H), 7.45 (d, *J*=3.2 Hz, 1H), 7.54-7.56 (m, 2H), 7.64-7.68 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 34.4, 55.6, 102.5, 102.9, 111.3, 112.3, 123.4, 126.3, 128.2, 129.7, 131.0, 137.2, 149.0, 154.4; HRMS: calcd. for $C_{19}H_{22}NO^+$: 280.1701, found 280.1698.

1-(3,5-Dimethylphenyl)-5-methyl-1*H*-indole (Table 5, Entry 7)[22b]

Hexane: DCM = 20:1, R_f = 0.3; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.70 (s, 6H), 2.85 (s, 3H), 6.93 (d, *J*=3.1 Hz, 1H), 7.27 (s, 1H), 7.39-7.44 (m, 3H), 7.58 (d, *J*=3.2 Hz, 1H), 7.38-7.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 21.3, 102.7, 110.3, 120.7, 121.7, 123.7, 127.7, 127.8, 129.2, 129.6, 134.1, 139.1, 139.8.

1-(3,5-Dimethylphenyl)-5-fluoro-1*H*-indole (Table 5, Entry 8)

Hexane: DCM = 9:1, R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.54 (s, 6H), 6.75 (d, *J*=3.0 Hz, 1H), 7.12-7.14 (m, 2H), 7.22 (s, 2H), 7.44 (d, *J*=3.2 Hz, 1H), 7.48-7.51 (m, 1H), 7.61-7.62 (m, 1H); 13C NMR (100 MHz, $CDCl_3$) δ 21.2, 102.9, 103.0, 105.5, 105.7, 110.2, 110.4, 111.3, 111.3, 121.8, 128.2, 129.4, 129.5, 129.6, 132.4, 139.3, 156.8, 159.2; HRMS: calcd. for $C_{16}H_{15}NF^+$: 240.1189, found 240.1192.

1-(4-(*tert*-Butyl)phenyl)-1*H*-pyrrole (Table 5, Entry 9)[22b]

Hexane: EA = 20:1, R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.55 (s, 9H), 6.56 (s, 2H), 7.27 (s, 2H), 7.50 (d, *J*=8.7 Hz, 2H), 7.62 (d, *J*=8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 34.3, 110.1, 119.2, 120.0, 126.2, 138.2, 148.4.

4-(3,5-Dimethylphenyl)-1,2,3,4-tetrahydrocyclopenta[*b*]indole (Table 5, Entry 10)[22b]

Hexane: DCM = 9:1, R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.58 (s, 6H), 2.72-2.77 (m, 2H), 3.07-3.14 (m, 4H), 7.16 (s, 1H), 7.27 (s, 2H), 7.32-7.34 (m, 2H), 7.66-7.72 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 24.5, 26.2, 28.3, 110.9, 118.5, 119.9, 120.0, 120.6, 122.4, 124.9, 127.8, 138.8, 139.0, 140.9, 145.6.

9-(4-(*tert*-Butyl)phenyl)-9*H*-carbazole (Table 5, Entry 11)[22b]

Hexane: DCM = 9:1, R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.60 (s, 9H), 7.45 (t, *J*=7.3 Hz, 2H), 7.54-7.64 (m, 6H), 7.74 (d, *J*=8.4 Hz, 2H), 8.33 (d, *J*=7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.4, 34.7, 109.8, 119.7, 120.2, 123.2, 125.8, 126.5, 126.6, 134.9, 140.9, 150.3.

10-(3,5-Dimethylphenyl)-10*H*-phenothiazine (Table 5, Entry 12)

Hexane: EA = 9:1, R_f = 0.8; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.47 (s, 6H), 6.32-6.34 (dd, *J*=1.2, 6.8 Hz, 2H), 6.84-6.93 (m, 4H), 7.06-7.08 (dd, *J*=1.6, 5.6 Hz, 2H), 7.09 (s, 2H), 7.18 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 116.0, 119.9, 122.3, 126.6, 126.8, 128.3, 129.9, 140.6, 140.7, 144.3; HRMS: calcd. for $C_{20}H_{17}NS^+$: 303.1076, found 303.1067.

10-(3,5-Dimethylphenyl)-10*H*-phenothiazine (Table 5, Entry 13)

Hexane, R_f = 0.7; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.42 (s, 6H), 5.99 (s, 2H), 6.63-6.72 (m, 6H), 6.99 (s, 2H), 7.14 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.29, 113.3, 115.3, 121.0, 123.2, 128.0, 130.1, 134.5, 138.8, 140.8, 143.9; HRMS: calcd. for $C_{20}H_{17}NO$: 287.1305, found 287.1309.

***N*-Methyl-*N*-phenylnaphthalen-2-amine (Table 6, Entry 6)**[22b]

Hexane: DCM = 20:1, R_f = 0.26; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.61 (s, 3H), 7.26 (m, 1H), 7.35 (d, *J*=8.0 Hz, 2H), 7.48-7.58 (m, 5H), 7.65 (m, 1H), 7.88-7.95 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.4, 114.5, 121.3, 121.7, 121.8, 123.6, 126.2, 126.6, 127.4, 128.5, 129.0, 129.2, 134.6, 146.5, 148.9.

4-(Naphthalen-2-yl)morpholine (Table 6, Entry 7)[38]

Hexane: EA = 9:1, R_f = 0.23; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24 (t, *J*=4.8 Hz, 4H), 3.94 (t, *J*=4.7 Hz, 4H), 7.18 (d, *J*=2.0 Hz, 1H), 7.28 (q, *J*=6.7 Hz, 1H), 7.46-7.48 (m, 1H), 7.55-7.59 (m, 1H), 7.82-7.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.2, 66.5, 109.6, 118.5, 123.2, 126.0, 126.5, 127.2, 128.3, 128.4, 134.3, 148.8.

3,5-Dimethyl-*N*-(1-phenylethyl)aniline (Table 7, Entry 1 and 2)[46,47]

Hexane: EA = 20:1, R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.60 (d, *J*=6.4 Hz, 3H), 2.29 (d, *J*= 10.8 Hz, 6H), 4.57-4.62 (q, *J*=6.8 Hz, 1H), 6.29 (s, 2H), 6.44 (s, 1H), 7.33 (t, *J*=7.2 Hz, 1H), 7.41-7.49 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 24.9, 53.4, 111.3, 119.4, 125.9, 126.8, 128.6, 138.8, 145.5, 147.4. Enantiomeric excess was determined by HPLC analysis (UV) on Chiralcel OD-H column using hexane/*i*-PrOH (98/2) as eluent (0.5 mL/min). Retention time of the enantiomers: 10.6 min, 12.3 min, 97% *ee.*

3,5-Dimethyl-*N*-(1-phenylethyl)aniline (Table 7, Entry 3 and 4)

Hexane: EA = 20:1, R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.82 (s, 3H), 2.36 (s, 6H), 4.18 (bs, 1H), 5.48 (d, *J*=6.4 Hz, 1H), 6.37 (s, 2H), 6.55 (s, 1H), 7.58 (d, *J*=7.2 Hz, 1H), 7.61-7.77 (m, 2H), 7.84 (d, *J*=6.8 Hz, 1H), 7.92 (d, *J*=7.2 Hz, 1H), 8.07 (d, *J*=7.2 Hz, 1H), 8.36 (d, *J*=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 23.2, 49.1, 110.9, 119.2, 122.2, 122.7, 125.2, 125.7, 125.9, 127.3, 128.9, 130.7, 134.0, 138.6, 140.0, 147.1; HRMS: calcd. for $C_{20}H_{22}N^+$: 276.1752, found 276.1758. Enantiomeric excess was determined by HPLC analysis (UV) on Chiralcel OD-H column using hexane/*i*-PrOH (98/2) as eluent (0.7 mL/min). Retention time of the enantiomers: 10.0 min, 11.5 min, 99% *ee.*

_N_-(1,2,3,4-Tetrahydronaphthalen-1-yl)naphthalen-2-amine (Table 7, Entry 5 and 6)

Hexane: EA = 20:1, R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.92-2.07 (m, 2H), 2.12-2.20 (m, 2H), 2.87-3.01 (m, 2H), 4.15 (s, 1H), 4.89 (t, *J*=4.8 Hz, 1H), 6.95-6.98 (dd, *J*=2.4, 8.8 Hz, 1H), 7.05 (s, 1H), 7.26-7.36 (m, 4H), 7.49 (t, *J*=8.0 Hz, 1H), 7.54 (d, *J*=7.6 Hz, 1H), 7.74 (d, *J*=8.8 Hz, 2H), 7.80 (d, *J*=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4, 28.5, 29.2, 51.0, 104.2, 117.9, 121.7, 125.7, 126.1, 126.3, 127.1, 127.3, 127.5, 129.0, 129.2, 135.2, 137.5, 138.0, 145.0; HRMS: calcd. for $C_{20}H_{19}N$: 274.1590, found 274.1593. Enantiomeric excess was determined by HPLC analysis (UV) on Chiralcel OD-H column using hexane/*i*-PrOH (90/10) as eluent (0.9 mL/min). Retention time of the enantiomers: 7.9 min, 9.7 min, 97% *ee*.

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Conflict of interest

The authors declare no conflict of interest.

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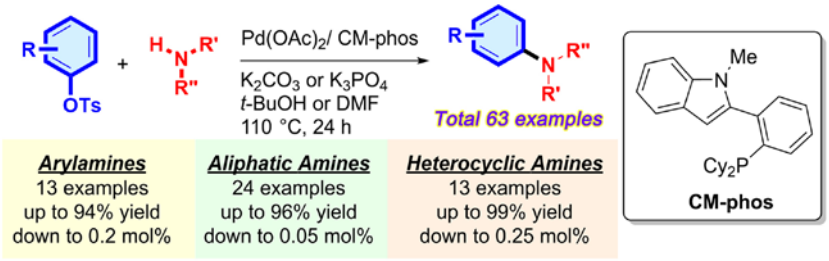

A general Pd/CM-phos catalyst system is presented for broad scope of amination of aryl tosylates. Various nature of *N*-nucleophiles are applicable substrates and the reactions can even be performed under water medium or at a particular catalyst loading as low as 0.05 mol% Pd.

Pui Ying Choy, Kin Ho Chung, Qingjing Yang, Chau Ming So, Raymond Wai-Yin Sun and Fuk Yee Kwong**

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A General Palladium-Phosphine Complex for Exploring Aryl Tosylates in *N*-arylation of Amines: Scope and Limitation