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Novel bisamide palladium(II) pincer complexes: effective catalysts in α-arylation of ketones

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Abstract Three benzenedicarboxamide ligands (L) were designed and synthesized, and each was used to prepare a palladium(II) complex Pd(L)Br and Pd(L)(OAc). These NCN pincer complexes were used to catalyze the α-arylations of a variety of ketones with aryl chlorides or bromides in various solvents, and moderate-to-excellent yields were obtained (up to 95%). Further research showed that unactivated and sterically hindered aryl halides and ketones are also suitable substrates for the synthesis of α-arylation.

Introduction

The α-aryl carbonyl functionality is an important component of many natural products, pharmaceutical candidates, synthetic intermediates, and precursors of emissive polymers [1–3]. The first practical reports [4] of palladium mediated α-arylation of carbonyl compounds appeared independently in 1997 by Buchwald [5], Miura [6] and Hartwig [7]. Research focusing on palladium compounds [8–11] and their use in catalytic of α-arylation of ketones has increased rapidly over the past decades, and several Pd complexes derived from bulky and electron-rich alkylphosphine ligands are reported to be effective catalysts for the α-arylation [12]. However, alkylphosphine ligands have many practical drawbacks, such as high cost, air and moisture sensitivity, and pollution, which have been recognized as a considerable limitation. As an alternative, the design of electron-rich, bulky ligands has addressed many challenges in this field, allowing the coupling of highly unactivated coupling partners under mild conditions and using low catalyst dosage [13–15].

Pincer palladium(II) complexes have found wide applications in catalytic organic transformations such as stannylation of allylic or propargylic substrates, allylation of aldehydes or imines, Michael additions, aldol reactions, and particularly a variety of cross-coupling reactions [16–20]. Pincer complexes [21–26], which appear to combine in one molecule the advantages of palladacycles and a modulation of catalyst properties by ligands, have proved to be highly active in a number of C–C bond-forming reactions [27–30]. Connell and coworkers [31] have firstly reported an efficient catalytic system using new NCN-Pd pincer complexes for selective α-arylation of ketones. However, the syntheses of NCN pincer ligands involve multistep procedures and air-sensitive substances, making the synthesis atmosphere relatively rigorous. To the best of our knowledge, the use of pincer-type palladacycles in α-arylation of ketones has been investigated scarcely so far. Inspired by their work, we were attracted to explore a method with less synthesis procedures and develop new routes to design the pincer ligands.

In this context, we reported novel structure of the NCN-Pd complexes using easily accessible 3-aminopyrazole or benzenamine as part of the pincer ligands directly. The molecular nature of this structure makes it easy to modify the catalytic activity in organic reactions by selecting suitable metal center or ligands. The preparation of the NCN-Pd catalysts (Fig. 1) is straightforward, and the complexes have been stored in air at room temperature for several months without decomposition. In addition, these catalysts exhibit efficacy in the α-arylation of various

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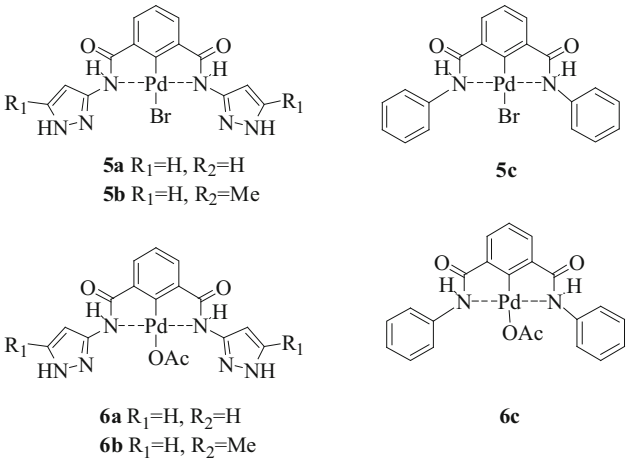


Fig. 1 NCN-Pd pincer complexes

substrates and the reaction protocol is mild, and functional group tolerant.

Experimental

Materials and methods

All solvents were purified by the standard methods. Ketones and aryl halides reported in this manuscript were obtained from commercial sources of reagent grade and used without further purification.

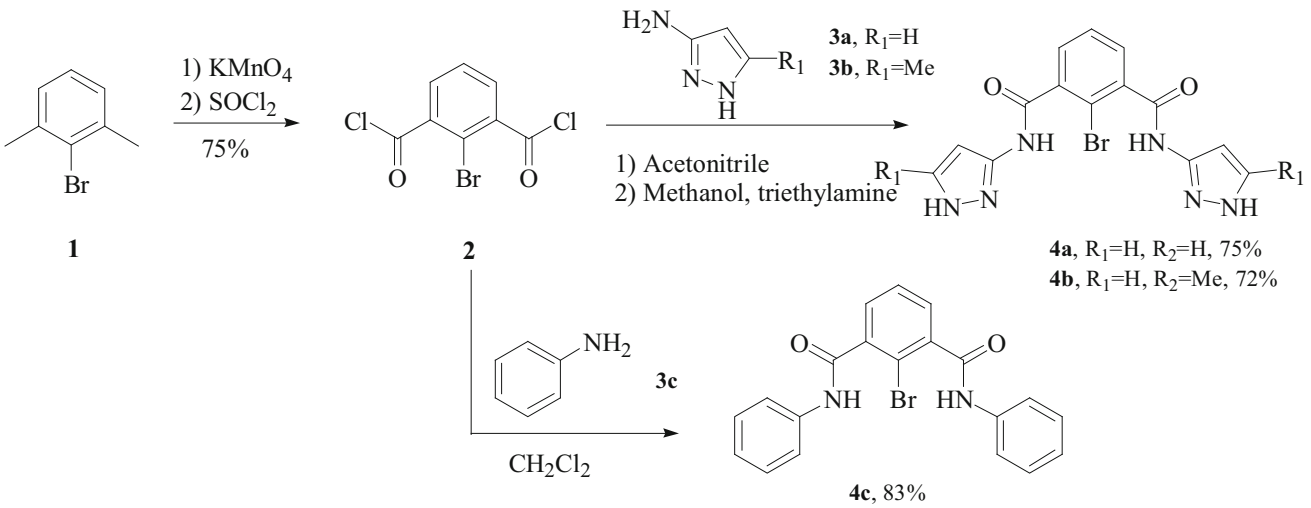
All the products were fully characterized by elemental analysis, HRMS, and ^{1}H NMR spectroscopy. ^{1}H NMR spectra were recorded on a Bruker DRX 500 spectrometer. ^{13}C NMR spectra were recorded at 75 MHz and referenced to the solvent resonance. High-resolution mass spectra were measured on a Waters Q-Tof Micro spectrometer. Elemental analysis was recorded on an Elementar Vario EL III. Melting points were determined using a Buchi M565 melting point apparatus.

Synthetic procedure for ketone α-arylations reaction

An oven-dried, resealable Schlenk tube containing a stir bar was charged with aryl halide (1.0 mmol), ketone (1.1 mmol), potassium tert-butoxide (1.5 mmol), and 1.0 mol % catalyst. Acetonitrile (10 mL) was sequentially added and the tube was backfilled with nitrogen, and the mixture was stirred in an oil bath at reflux temperature for the time specified. After the reaction was completed, the solvent was removed on a rotary evaporator and the mixture was purified by chromatography on silica gel. The pure product was obtained, and the yield was calculated based on ArX.

Synthetic procedure for the free ligand

The synthetic procedure for the free ligand is illustrated in Scheme 1. Compounds **2** were prepared following the procedures reported previously [32]. In a typical experiment, a mixture of 2-bromo-m-xylene (4.0 mL, 30.0 mmol) and distilled water (80 mL) was charged into a 150-mL round-bottom flask, and $KMnO_4$ (51.0 g, 320 mmol) was added at room temperature. The mixture was heated at reflux temperature for 24 h and filtrated through a pad of Celite, and the filtrate was concentrated to 1/3 of its initial volume. The resulting concentrate was acidified with concentrated HCl and then evaporated under reduced pressure to give crude 2-bromoisophthalic acid which contains KCl and used directly in the next reaction.



Scheme 1 Synthetic procedure for ligands

Stoichiometric ratio of 2-bromoisophthalic acid and benzene (64 mL) was placed in a 100-mL flask immersed in an ice-water bath. $SOCl_2$ (9 mL, 100 mmol) was added dropwise, and the mixture was refluxed for 5 h and evaporated under reduced pressure to remove excess $SOCl_2$. The solid product was dissolved in benzene, and then the resultant suspension was filtered and concentrated to give a pale yellow solid in 75% yield. ^{1}H NMR (500 MHz, $CDCl_3$): 8.01 (d, 2H), 7.61 (t, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 139.1, 134.5, 127.9, 117.3.

Synthesis of N^1,N^3-bis(1H-pyrazol-3-yl)-1,3-benzenedicarboxamide (4a)

To a solution of 2-bromo-1,3-benzenedicarbonyl dichloride **2** (1.41 g, 5.0 mmol) in dried acetonitrile (10 mL) was slowly added a solution of 1H-pyrazol-3-amine (0.91 g, 11.0 mmol) in acetonitrile (10 mL). After it was refluxed overnight under nitrogen atmosphere, the precipitate so obtained was filtered off and dried in vacuum. The solid was dissolved in methanol, excess triethylamine was added, the mixture was stirred at room temperature overnight, and white solid compound was obtained, filtered off, washed with cold water, and dried. Yield: 1.41 g (75%). ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C, TMS): 12.29 (s, 2H, pzNH), 10.66 (s, 2H, amide NH), 8.11 (m, 2H, aromatic H), 7.69–7.65 (d, J = 5.6 Hz, 2H, pz H), 7.61 (m, 1H, aromatic H), 6.68 (d, J = 6.6 Hz, 2H, pz H); ^{13}C NMR (75 MHz, DMSO-d_6, 25 °C, TMS):165.1, 145.3, 139.1, 134.4, 132.6, 131.6, 128.8, 95.6. Anal. Calc. for $C_{14}H_{11}O_2N_6Br$: C, 44.82, H, 2.96, N, 22.40; Found: C, 44.80, H, 2.95, N, 22.39.

Synthesis of N^1,N^3-bis(5-methyl-1H-pyrazol-3-yl)-1,3-benzenedicarboxamide (4b)

To a solution of 2-bromo-1,3-benzenedicarbonyl dichloride **2** (1.41 g, 5.0 mmol) in dried acetonitrile (10 mL) was slowly added a solution of 5- methyl-1H-pyrazol-3-amine (1.07 g, 11.0 mmol) in acetonitrile (10 mL). After it was refluxed overnight under nitrogen atmosphere, the precipitate so obtained was filtered off and dried in vacuum. The solid was dissolved in methanol, excess triethylamine was added, the mixture was stirred at room temperature overnight, and white solid compound was obtained, filtered off, washed with cold water, and dried. Yield: 1.45 g (72%). ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C, TMS): 12.43 (s, 2H, pzNH), 10.68 (s, 2H, amide NH), 8.09 (m, 2H, aromatic H), 7.59 (m, 1H, aromatic H), 6.47 (d, 2H, J = 5.6 Hz, pz H), 2.78 (s, 6H, methyl H); ^{13}C NMR (75 MHz, DMSO-d_6, 25 °C, TMS):165.5, 149.6, 139.4, 135.1, 132.2, 129.4, 127.6, 97.1, 13.6. Anal. Calc. for $C_{16}H_{15}O_2N_6Br$: C, 47.66, H, 3.75, N, 20.84; Found: C, 47.80, H, 3.69, N, 20.89.

Synthesis of N^1,N^3-diphenyl-1,3-benzenedicarboxamide (4c)

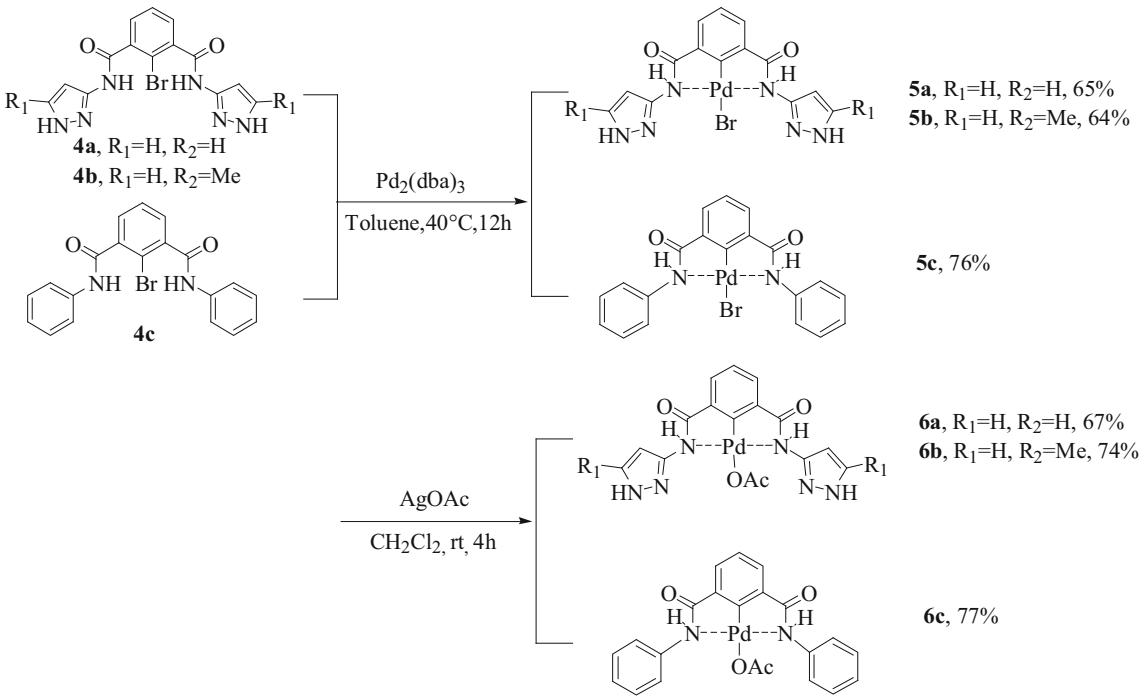
Compounds **4c** were prepared following the procedures reported previously [33]. To a solution of benzenamine (1.02 g, 11.0 mmol) in CH_2Cl_2 (20 mL) was added dropwise a solution of 2-bromo-1, 3-benzenedicarbonyl dichloride **2** (1.41 g, 5.0 mmol) in CH_2Cl_2 (20 mL) at 0 °C. After it was warmed to room temperature and stirred overnight, the mixture was washed with 10% aqueous NaOH (2 × 20 mL), water (2 × 20 mL), and 10% HCl (2 × 20 mL). The organic layer was washed with water, dried with anhydrous Na_2SO_4, and concentrated to afford a white solid. Yield: 1.63 g (83%). ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C, TMS): 10.54 (s, 2H, amide NH), 7.72 (d, J = 7.6 Hz, 2H, aromatic H), 7.64–7.56 (m, 4H, aromatic H), 7.28–7.25 (m, 4H, aromatic H), 7.10 (t, J = 7.6 Hz, 3H, aromatic H); ^{13}C NMR (75 MHz, DMSO-d_6, 25 °C, TMS):167.6, 140.6, 139.4, 128.5, 128.2, 127.6, 127.0, 125.7, 120.5. Anal. Calc. for $C_{20}H_{15}O_2N_2Br$: C, 60.78, H, 3.83, N, 20.22; Found: C, 60.80, H, 3.85, N, 20.39.

Typical procedure for (NCN)PdBr pincer complexes

The synthetic procedure for (NCN)PdBr pincer complexes is illustrated in Scheme 2. A Schlenk flask equipped with a magnetic bar was loaded with **4a–4c** (1 equiv), anhydrous toluene (30 mL), $Pd_2(dba)_3$ (1.1 equiv) and sealed with a screw cap. The mixture was stirred at 40 °C overnight. The reaction mixture was filtered through silica eluting with toluene and washed with ethyl acetate to give a yellow solution, and the solvent was removed under reduced pressure to give **5a–5c**.

Synthesis of 5a

A Schlenk flask equipped with a magnetic bar was loaded with **4a** (56.3 mg, 0.15 mmol), anhydrous toluene (30 mL), $Pd_2(dba)_3$ (72.7 mg, 0.16 mmol) and sealed with a screw cap. The mixture was stirred at 40 °C overnight. The reaction mixture was filtered through silica eluting with toluene and washed with ethyl acetate to give a yellow solution, and the solvent was removed under reduced pressure to give **5a** as a yellow solid. Yield: 47.0 mg (65%). ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C. TMS): 12.48 (s, 2H, pzNH), 10.81 (s, 2H, amide NH), 8.07 (m, 2H, aromatic H), 7.71–7.75 (d, J = 5.6 Hz, 2H, pz H), 7.61 (m, 1H, aromatic H), 6.83 (d, J = 4.3 Hz, 2H, pz H); ^{13}C NMR (75 MHz, DMSO-d_6, 25 °C, TMS):170.4, 159.9, 145.6, 136.6, 134.5, 133.5, 131.0, 96.5. Anal. Calc. for $C_{14}H_{11}O_2N_6PdBr$: C, 34.91, H, 2.30, N, 17.45; Found: C, 34.93, H, 2.30, N, 17.45. HRMS (positive ESI) Calc. for $C_{14}H_{12}O_2N_6PdBr$ (MH^+): 482.5143; found: 482.5264.



Scheme 2 Synthetic procedure for NCN pincer Pd(II) complexes

Synthesis of 5b

A Schlenk flask equipped with a magnetic bar was loaded with **4b** (60.5 mg, 0.15 mmol), anhydrous toluene (30 mL), $Pd_2(dba)_3$ (72.7 mg, 0.16 mmol) and sealed with a screw cap. The mixture was stirred at 40 °C overnight. The reaction mixture was filtered through silica eluting with toluene and washed with ethyl acetate to give a yellow solution, and the solvent was removed under reduced pressure to give **5b** as a yellow solid. Yield: 49.2 mg (64%). ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C, TMS): 12.22(s, 2H, pzNH), 10.46 (s, 2H, amide NH), 8.07 (m, 2H, aromatic H), 7.59 (m, 1H, aromatic H), 6.60 (d, J = 4.3 Hz, 2H, pz H), 2.83 (s, 6H, methyl H); ^{13}C NMR (75 MHz, DMSO-d_6, 25 °C, TMS):171.4, 161.4, 146.2, 138.1, 135.1, 132.2, 131.3, 98.1, 15.1. Anal. Calc. for $C_{16}H_{15}O_2N_6PdBr$: C, 37.71, H, 2.97, N, 16.49; Found: C, 37.73, H, 2.90, N, 16.45. HRMS (positive ESI) Calc. for $C_{16}H_{16}O_2N_6PdBr$ (MH^+): 510.5523; found: 510.5782.

Synthesis of 5c

A Schlenk flask equipped with a magnetic bar was loaded with **4c** (59.3 mg, 0.15 mmol), anhydrous toluene (30 mL), $Pd_2(dba)_3$ (72.7 mg, 0.16 mmol) and sealed with a screw cap. The mixture was stirred at 40 °C overnight. The reaction mixture was filtered through silica eluting with toluene and washed with ethyl acetate to give a yellow solution, and the solvent was removed under reduced pressure to give **5c** as a pale yellow solid. Yield: 57.2 mg (76%). ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C, TMS): 10.33 (s, 2H, amide NH), 8.07 (m, 2H, aromatic H), 7.78 (d, J = 5.6 Hz, 4H, aromatic H), 7.55 (m, 1H, aromatic H), 7.25–7.29 (m, 4H, aromatic H), 7.12 (m, 2H aromatic H); ^{13}C NMR (75 MHz, DMSO-d_6, 25 °C, TMS):179.2, 152.5, 147.5, 132.2, 131.3, 129.5, 128.5, 127.9, 124.5. Anal. Calc. for $C_{20}H_{15}O_2N_2PdBr$ (501.67 g/mol): C, 47.88, H, 3.01, N, 5.58; Found: C, 47.83, H, 3.30, N, 5.45. HRMS (positive ESI) Calc. for $C_{20}H_{16}O_2N_2PdBr$ (MH^+): 502.3472; found: 502.3114.

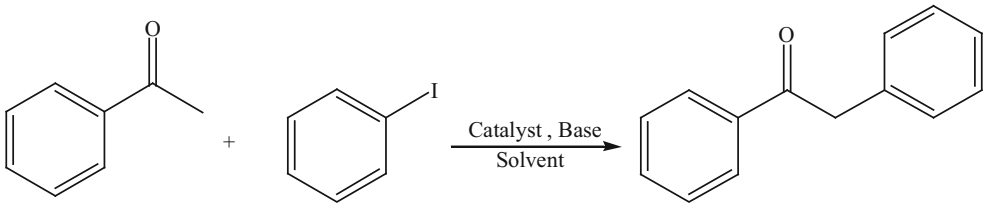
Typical Procedure for (NCN)PdOAc Pincer Complexes

A mixture of **5a–5c** (1 equiv) and AgOAc (1.2 equiv) was stirred in dry dichloromethane for 4 h at room temperature under nitrogen in the dark. After the reaction was completed (monitored by TLC), the mixture was filtered through Celite eluting with dichloromethane, and the solvent was removed under reduced pressure to give the brown product **6a–6c**.

Synthesis of 6a

A mixture of **5a** (144.5 mg, 0.30 mmol) and AgOAc (60.1 mg, 0.36 mmol) was stirred in dry dichloromethane for 4 h at room temperature under nitrogen in the dark. After the reaction was completed (monitored by TLC), the

Table 1 Screening of the optimal condition for α-arylation[a]



Entry	Cat	Base	Solvent	*T* (°C)	Yield[b](%)
1	**5a**	KO^{t}Bu	Toluene	Reflux	47
2	**5b**	KO^{t}Bu	Toluene	Reflux	46
3	**5c**	KO^{t}Bu	Toluene	Reflux	35
4	**6a**	KO^{t}Bu	Toluene	Reflux	59
5	**6b**	KO^{t}Bu	Toluene	Reflux	52
6	**6c**	KO^{t}Bu	Toluene	Reflux	30
7	**6a**	KO^{t}Bu	Acetonitrile	Reflux	95
8	**6a**	KO^{t}Bu	DMF	140	10
9	**6a**	KO^{t}Bu	THF	Reflux	10
10	**6a**	KO^{t}Bu	CH_3OH	Reflux	6
11	**6a**	NaO^{t}Bu	Acetonitrile	Reflux	72
12	**6a**	K_2CO_3	Acetonitrile	Reflux	Trace
13	**6a**	KOAc	Acetonitrile	Reflux	Trace
14	**6a**	K_3PO_4	Acetonitrile	Reflux	3
15	**6a**	Cs_2CO_3	Acetonitrile	Reflux	Trace

[a] Reaction conditions: iodobenzene (1.0 mmol), acetophenone (1.1 mmol), catalyst (1.0 mol %), base (1.5 mmol), solvent (10 mL), reaction time: 2 h

[b] Isolated yields

mixture was filtered through Celite eluting with dichloromethane, and the solvent was removed under reduced pressure to give the brown product **6a**. Yield: 92.8 mg (67%). ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C, TMS): 12.33 (s, 2H, pzNH), 10.67 (s, 2H, amide NH), 8.09 (m, 2H, aromatic H), 7.65–7.67 (d, J = 6.3 Hz, 2H, pz H), 7.61 (m, 1H, aromatic H), 6.83 (d, J = 8.6 Hz, 2H, pz H), 2.08 (s, 3H, acetate H); ^{13}C NMR (75 MHz, DMSO-d_6, 25 °C, TMS):176.1, 157.6, 144.3, 135.7, 134.4, 133.2, 130.4, 94.3, 23.2. Anal. Calc. for $C_{16}H_{14}O_4N_6Pd$: C, 41.71, H, 3.06, N, 18.24; Found: C, 41.70, H, 3.07, N, 18.25. HRMS (positive ESI) Calc. for $C_{16}H_{15}O_4N_6Pd$ (MH^+): 461.0145; found: 461.0255.

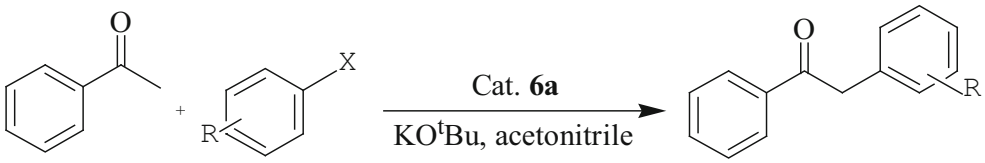
Synthesis of 6b

A mixture of **5b** (152.9 mg, 0.30 mmol) and AgOAc (60.1 mg, 0.36 mmol) was stirred in dry dichloromethane for 4 h at room temperature under nitrogen in the dark. After the reaction was completed (monitored by TLC), the mixture was filtered through Celite eluting with dichloromethane, and the solvent was removed under reduced pressure to give the brown product **6b**. Yield: 109.0 mg (74%). ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C, TMS): 12.26 (s, 2H, pzNH), 10.50 (s, 2H, amide NH), 8.09 (m, 2H, aromatic H), 7.59 (m, 1H, aromatic H), 6.64 (d, J = 5.6 Hz, 2H, pz H), 2.86 (s, 6H, methyl H), 2.08 (s, 3H, acetate H); ^{13}C NMR (75 MHz, DMSO-d_6, 25 °C, TMS):176.1, 169.2, 159.3, 145.0, 137.0, 134.7, 131.0, 130.1, 97.8, 23.2, 14.8. Anal. Calc. for $C_{18}H_{18}O_4N_6Pd$: C, 44.23, H, 3.71, N, 17.19; Found: C, 44.30, H, 3.67, N, 17.25. HRMS (positive ESI) Calc. for $C_{18}H_{19}O_4N_6Pd$ (MH^+): 489.4421; found: 489.4996.

Synthesis of 6c

A mixture of **5c** (150.5 mg, 0.30 mmol) and AgOAc (60.1 mg, 0.36 mmol) was stirred in dry dichloromethane for 4 h at room temperature under nitrogen in the dark. After the reaction was completed (monitored by TLC), the mixture was filtered through Celite eluting with dichloromethane, and the solvent was removed under reduced pressure to give the yellow product **6c**. Yield: 110.6 mg (77%). ^{1}H NMR (500 MHz, DMSO-d_6, 25 °C, TMS): 10.43 (s, 2H, amide NH), 8.09 (m, 2H, aromatic H), 7.80–7.65 (m, 5H, aromatic H), 7.29–7.27 (m, 4H, aromatic H), 7.12 (m, 2H, aromatic H), 2.08 (s, 3H, acetate H); ^{13}C NMR (75 MHz, DMSO-d_6, 25 °C, TMS):177.6, 176.1,

Table 2 α-Arylation of ketones with aryl halides[a]



Entry	*R*	*X*	Product	Time (h)	Yield[b](%)
1	H	I	**7a**	2	95
2	H	Br	**7a**	2	89
3	H	Cl	**7a**	2	87
4	4-Me	Br	**7b**	2	91
5	2-Me	Br	**7c**	2	89
6	1,3-dimethyl	Br	**7d**	2	76
7	4-MeO	Br	**7e**	2	93
8	4-MeO	Cl	**7e**	2	90
9	3-Bromopyridine	Br	**7f**	2	10
				24	22
10	3-Chloropyridine	Cl	**7f**	2	Trace
				24	Trace
11	4-NO_2	Br	**7 g**	2	20
				24	32
12	4-NO_2	Cl	**7 g**	2	Trace
				24	Trace

[a] Reaction conditions: aryl halide (1.0 mmol), aromatic ketones (1.1 mmol), catalyst (1.0 mol %), base (1.5 mmol), solvent (10 mL), 82 °C

[b] Isolated yields

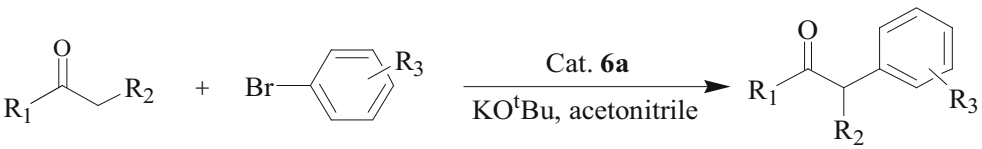
151.5, 146.6, 131.3, 131.0, 128.8, 128.2, 127.6, 124.8, 23.2. Anal. Calc. for $C_{22}H_{18}O_4N_2Pd$: C, 54.96, H, 3.77, N, 5.83; Found: C, 54.90, H, 3.67, N, 5.85. HRMS (positive ESI) Calc. for $C_{22}H_{19}O_4N_2Pd$ (MH^+): 481.9144; found: 481.9236.

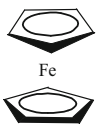
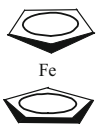
Results and discussion

The complexes **5a–5c** and **6a–6c** were examined as catalysts for α-arylation reactions, and the reaction of acetophenone with iodobenzene was taken as a model reaction to screen the optimal catalysts, reaction conditions including temperature and bases (Table 1). Toluene was initially taken as the solvent for its excellent dissolving capacity; however, the yields were unsatisfactory with the highest yield 59% (entries 1–6), which was much lower compared with the previous studies. To our delight, when acetonitrile was utilized, it led to the highest conversion among other solvents (entries 6–10) and the yields were increased remarkably to 95% (entry 7). The influence of the bases was also studied (Table 1, entries 11–15), and it was obvious that KO^{t}Bu (potassium tert-butoxide) could give the best results.

With this optimized system in hand, we screened a number of aryl halides to probe the scope of this new methodology on one hand (Table 2), and by reacting bromobenzene and several aryl halides with various ketones on the other (Table 3). As shown in Table 2, we found that the reaction was drastically influenced by electronic effects from the aryl halides, and moderate-to-excellent yields were obtained when the electron-rich aryl halides were employed (entries 1–8), especially aryl iodides showed a slightly better result than bromine and chlorine analogues. As for the electron-deficient aryl halides, such catalytic system was suitable for limited substrates. For example, the reaction of 3-bromopyridine with acetophenone could give a yield of 22% after refluxing for 24 h in acetonitrile, while trace amounts of α-arylation products were obtained for 3-chloropyridine even going into an overtime for 24 h (entries 9 and 10). Aryl halides with strong electron-withdrawing groups like –NO_2 would prejudice against the process of reaction (entries 11 and 12). Notably, the use of an electron-poor aryl halide analogue required longer reaction time to afford a low yield of the desired product. To our delight, the **6a** catalyst system is also applicative for coupling sterically hindered aryl bromide with acetophenone (Table 2, entry 6), in order to gain further insight into

Table 3 α-Arylation of aryl halides with sterically hindered ketones[a]



Entry	R_1	R_2	R_3	Product	Time (h)	Yield[b](%)
1[c]	Ph	CH_3	H	**7h**	2	90
2	Ph	CH_3	H	**7h**	2	86
3[d]	Ph	CH_3	H	**7h**	2	85
4	4- Me-Ph	H	H	**7i**	2	83
5	2- Me-Ph	H	H	**7j**	2	77
6	4-O Me-Ph	H	H	**7k**	2	88
7	4-O$(CH_3)_2$-Ph	H	H	**7l**	2	59
8	4-F-Ph	H	H	**7m**	2	90
9[d]	Ph	CH_3	3-Chloropyridine	**7n[1]**	2	Trace
					24	Trace
10	Ph	CH_3	3-Bromopyridine	**7n[2]**	2	Trace
					24	19
11	Ph	CH_3	2-OMe	**7o**	2	91
12	4-OMe-Ph	H	4-Me	**7p**	2	92
13	4-OMe-Ph	H	1,3-dimethyl	**7q**	2	72
14	Ph	H	1,3-dimethyl	**7d**	2	74
15		H	H	**7r**	2	78
16		H	2-Me	**7 s**	2	64
17	2-Me-Ph	H	1,3-dimethyl	**7t**	2	77
18	1-Naphthyl-	H	2-Me	**7u**	2	78

[a] Reaction conditions: aryl halide (1.0 mmol), aromatic ketones (1.1 mmol), catalyst (1.0 mol %), base (1.5 mmol), solvent (10 mL), 82 °C

[b] Isolated yields

[c] Iodobenzene

[d] Chlorine analogue

the reaction, further experiments were carried out, and the results are illustrated in Table 3.

The scope of the α-arylation was investigated by varying the aromatic ketones under the same conditions. As shown in Table 3, good yields were also obtained in the case of propiophenone (entries 1–3), which is similar to the results for acetophenone. Using bromobenzene, α-arylated products could be generated from both electron-rich (entries 2 and 4–7) and electron-poor (entry 8) acetophenone derivatives in satisfactory yields. However, the reaction of propiophenone with 3-chloropyridine afforded negligible products under the optimized conditions even giving an extension of reaction time (entry 9). This required us to obtain 1-phenyl-2-(3-pyridinyl)-1-propanone selectively from the bromine derivatives (entry 10). Following the same procedure, we could see that aryl halides with electron-donating groups tend to result in higher yields (entries 11, 12). It was noteworthy that the coupling of hindered aryl halides and ketones, such as 2-bromo-1, 3-dimethylbenzene, 1-ferrocenylethanone, 1′-acetonaphthone, could give the desired products in good yields (entries 13–18), which shows that the steric hindrances have few deleterious effects on these reactions. This proved that sterically hindered aryl bromides were suitable substrates under the optimized conditions and could undergo α-arylation with electron-rich, electron-

neutral, electron-deficient, or sterically hindered ketones in satisfactory yields.

Conclusions

In conclusion, we have synthesized a series of novel, effective NCN-Pd complexes for the α-arylation of various ketones with aryl chlorides and bromides in satisfactory yields under mild reaction conditions. These novel structure catalysts allow for modification of catalytic activity by selecting suitable metal center or ligands. This method provides new routes for the design of pincer ligands. The results of application experiments show that these catalysts exhibit efficacy in the α-arylation of various substrates, including unactivated and sterically hindered aryl chlorides or bromides.

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