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Tetrahedron 64 (2008) 4268–4274
Tetrahedron
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Air-stable Pd(II) catalysts with cryptand-22 ligand for convenient and efficient Suzuki cross-coupling reactions

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Received 22 November 2007; received in revised form 22 February 2008; accepted 26 February 2008
Available online 29 February 2008

Abstract

Air-stable Pd(II) catalysts with cryptand-22 ligand was easily handled in atm air at room temperature for Suzuki cross-coupling reactions of aryl bromides with arylboronic acids both containing electron-withdrawing and electron-donating groups. Generally, reactions proceeded fast to completion in 2 h to give high product yields. Our $Pd(OAc)_2$/cryptand-22 catalyst is unique, since the reaction solution remained yellow during reaction period and air-stable without formation of Pd black as usually observed for ordinary simple amine ligands.

1. Introduction

The Suzuki cross-coupling reaction has been proved to be one of the most widely used synthetic tools in synthesis of biaryls,[1,2] recurring structural units in many natural products, pharmaceuticals, and advanced materials[3] from aryl halides and boronic acids. Normally suitable ligand is required to stabilize palladium catalyst precursor. Palladium complexes with tertiary phosphine ligands[4] are traditionally employed to activate the catalysts in Suzuki cross-coupling reaction with excellent results. However, phosphine ligands used are sensitive to air oxidation and therefore require air-free condition to maximize the catalytic performance, which causes significant inconvenience in handling and poses some limitations on synthetic applications. Therefore, palladium-catalysts with phosphine-free ligands such as nucleophilic *N*-heterocyclic carbenes,[5] 2-aryl-2-oxazolines,[6] diazabutadienes,[7] thiourea,[8] and *N*,*N*-dimethyl-β-alaninate[9] and ligand-free condition such as $Pd(OAc)_2$/TBAB/PEG-400 system would be desired.[10] Amines are generally used as bases in cross-coupling reactions, which can also serve to stabilize the reactive palladium intermediates.[11] Until recently, only a few papers have been reported to employ simple amines (1°, 2°, and 3°) as ligands in palladium-catalyzed Suzuki cross-coupling reactions.[12] However, Pd catalysts are known to aggregate easily and form Pd black, which may lead to a considerable loss of catalytic activity.[13] To overcome this intrinsic problem of homogeneous Pd catalysis, we explored a new class of Pd catalyst system based on azacrown ether. Although it is well-known that the importance of crown ethers lies in their remarkable ability to complex cations, particularly those in the alkali and alkaline earth metal families,[14] it will be intriguing to investigate the specific binding properties by these macrocycles, which may help to stabilize Pd catalysts while retaining its catalytic reactions. To extend the scope of amines, we plan to evaluate the palladium catalytic systems composed of a series of commercially available azacrown ethers as phosphine-free ligands. The flexible macrocyclic and chelating effect of these N- or O-containing ligands may assist in stabilizing while activating the catalytic species. Herein we report a new homogeneous palladium catalyst system of Pd(II)/diazacrown ether that suppresses the Pd black formation even under 1 atm air. It is air-stable and highly efficient catalyst system for the Suzuki cross-coupling reaction of aryl halides and arylboronic acids.

2. Results and discussion

As illustrated in Table 1, several commercially available azacrown ethers were screened as potential ligands, using a model

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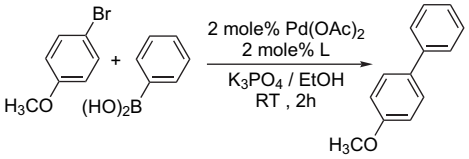
doi:10.1016/j.tet.2008.02.083

Table 1
Screening of ligands[a]



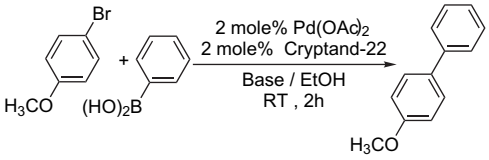
Entry	L	Isolated yield (%)	Pd black formation
1	Aza-12-crown-4 ether	90	−
2	Aza-15-crown-5 ether	88	−
3	Aza-18-crown-6 ether	91	+
4	1,4,10-Trioxa-7,13-diaza-cyclopentadecane	86	−
5	Cryptand-22	93	−
6	4,7,13,16,21,24-Hexaoxa-1,10-diazabicyclo[8.8.8]-hexacosane (2,2,2,-Kryptafix)	91	+
7	Aniline	90	+
8	Diisopropylamine	88	+
9	Dicyclohexylamine	89	+
10	Triethylamine	67	+
11	Pyridine	70	+
12	2,2-Bipyridine	0	−

[a] Reaction conditions: 1.0 mmol of aryl bromide, 1.5 mol of boronic acid, 2.0 mmol of K_3PO_4, 5.0 mL of EtOH.

cross-coupling reaction of 4-bromoanisole and phenylboronic acid in the presence of 2 mol % of $Pd(OAc)_2$, 4 mol % of ligand (entries 1–3) or 2 mol % of ligand (entries 4 and 5), and 2.0 equiv of K_3PO_4 in EtOH in atmospheric air at room temperature for 2 h. Generally, high yields were obtained for the aerobic coupling reactions. Notably, the catalytic reactions proceeded very fast in the yellow solution containing active palladium species, which was stable (entries 1, 2, 4, 5) without formation of Pd black, while Pd black formed significantly within 5 min when simple amines, such as triethylamine, dicyclohexylamine, diisopropylamine, aniline, and pyridine (entries 7–11), were used as ligands. Pd black also formed in 30 min when cryptand-22 and 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo-[8.8.8]-hexacosane (2,2,2,-Kryptafix) were used as ligands (entries 2 and 6). It indicates that azacrown ethers with smaller ring system of 12 or 15 atoms (entries 1 and 2) can stabilize palladium catalyst better than larger ring system of 18 atoms containing only one nitrogen atom (entry 3) or two nitrogen atoms of 3° amine (entry 6). Both bidentate diazacrown ethers, i.e., 1,4,10-trioxa-7,13-diaza-cyclopentadecane (entry 4) and cryptand-22 (entry 5) with either 15 or 18 atoms on the ring were also capable of stabilizing the palladium catalyst through loosely chelating effect. The trend in stabilizing ability on palladium catalyst in situ reflects a trade-off between ring size and coordinating ability. Based on the highest yields and the best air-stability, $Pd(OAc)_2$/cryptand-22 catalyst is unique, since the yellow reaction solution of which remained yellow for at least two weeks. And even on the top of silica-gel column after being chromatographed, the yellow band was air-stable without formation of Pd black. Cryptand-22, a bidentate ligand, is capable of chelating palladium atom adequately, yet not too tightly as to deactivate the catalyst. This is due to the intrinsic flexibility of macrocyclic ring containing four peripheral oxygen atoms assisting as required to protect the palladium atom from aggregation into Pd black. Cryptand-22 is thus the superior ancillary ligand for palladium-catalyzed cross-coupling reactions as compared to simple amines.

Base was required for Suzuki cross-coupling reaction of aryl halides and arylboronic acids, since very low yields were obtained in the absence of base (Table 2). Among the bases screened for their influence on the yields of reaction, use of K_3PO_4 (93%) with mild basicity resulted in the best conversions to the product and was used in all subsequent reactions. A significant cation effect was observed when carbonates (85% for K_2CO_3 vs 10% for Na_2CO_3) and hydroxides (92% for KOH vs 86% for NaOH) were used as bases. Although KOH worked as well, it was not chosen owing to its strong basicity. In many cases, Cs_2CO_3 and KF, usually the best choice of bases, proved to be less effective, leading to only 63 and 64% isolated yields, respectively.

Table 2
Base effect[a]



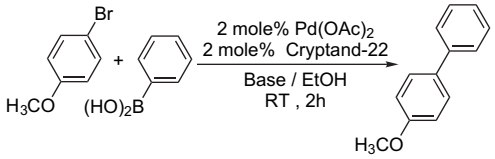
Entry	Base	Yield[b] (%)
1	No base	5
2	Na_2CO_3	10
3	K_2CO_3	85
4	Cs_2CO_3	63
5	K_3PO_4	91/18[c]
6	K_2HPO_4	6.5
7	KF	64
8	KOH	92
9	NaOH	86

[a] Reaction conditions: 1.0 mmol of aryl bromide, 1.5 mmol of boronic acid, 2.0 mmol of base, 5.0 mL of EtOH.
[b] Isolated yield.
[c] K_3PO_4 (0.5 mmol).

Notably, solvents were found to have profound effect on palladium catalytic activity (Table 3). Attempts on optimization with respect to solvent showed that the reaction proceeded best in EtOH (93%), and other protic solvents such as MeOH (77%) and 1-PrOH (87%) produced lower yields than EtOH with the lowest yield for sterically bulky 2-PrOH (34%). All other aprotic nonpolar or polar solvents such as toluene, acetone, dioxane, THF, and DMF proved to be ineffective with no more than 1.3% yields. The optimized conditions thus include EtOH solvent, K_3PO_4 base, cryptand-22, and $Pd(OAc)_2$ catalyst.

The catalytic activities were found not too sensitive to the change in ratios of ligand/Pd (Table 4). Without ligand, cross-coupling reaction gave low yield of 58%. No effect was observed on the reaction yields (91–93%) with ligand/Pd ratios in 0.5–2. The reaction yields started to drop to

Table 3
Solvent effect[a]

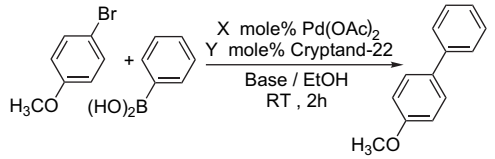


Entry	Solvent	Yield[b] (%)
1	Toluene	1.2
2	Acetone	0.7
3	Dioxane	1
4	DMF	0.6
5	THF	1.3
6	MeOH	77
7	EtOH	91
8	1-PrOH	87
9	2-PrOH	34

[a] Reaction conditions: 1.0 mmol of aryl bromide, 1.5 mmol of boronic acid, 2.0 mmol of K_3PO_4, 5.0 mL of solvent.
[b] Isolated yield.

82% at ratio of 4, and further down to 77% at even higher ratio of 8. The low sensitivity of catalytic activity to the variation of ligand/Pd reflects a weaker binding power of cryptand-22 than ordinary tertiary phosphines. For homogeneous catalytic reactions, it may partly account for the higher catalytic activity of the former than the latter at room temperature. As illustrated in Table 5, the palladium-catalyzed Suzuki coupling reaction with diazacrown ether as ancillary ligand proved exceptionally active. This reaction can tolerate a variety of functionalities including NO_2, CHO, and CN. Generally, the electronic properties of aryl bromides did not influence significantly the ease of the coupling reactions, and reactions proceeded very fast and resulted in high yields in 2 h for both electron-deficient and electron-rich aryl bromides. When reaction time was shortened to 15 min, electron-deficient aryl bromide was found consumed faster than electron-rich aryl bromides (entry 1 vs entry 9). Notably, in contrast to aryl bromides, electronic effect was more pronounced when substituted arylboronic acid was allowed to react with *p*-bromoanisole in 15 min, and reverse electronic effect was observed, where electron-donating arylboronic acid gave higher yields (43%) than that of electron-withdrawing arylboronic acid (30%) (entry 13 vs entry 10), but both produced lower yield than unsubstituted arylboronic acid (68%) (entry 9). In a typical reaction mechanism proposed for Suzuki coupling reaction, arylboronic acid reacts with base to produce borate, an arylboronic acid–base adduct, followed by transmetallation step where aryl group is transferred to palladium. Presumably, a compromise is required on the electronic properties of the acidity of arylboronic acid to form borate species and basicity of which for aryl transmetallation to palladium center. Either electron-withdrawing or electron-donating groups inhibit one of the above two steps. Under the same reaction conditions, similar results were obtained when Na_2PdCl_4 was utilized as Pd source instead of $Pd(OAc)_2$ (Table 6 entries 1–8). When complex **1** was used as Pd source, the reaction yields were 90–95% (Table 6 entries 9–11), and no Pd black was observed. (Cryptand-22)$PdCl_2$, complex **1** a yellow solid, which is stable in the air, was prepared from $Pd(OAc)_2$ and cryptand-22 in ethanol and its structure was fully characterized by ^1H, ^{13}C NMR, elemental analyses, and X-ray crystallography (shown in Fig. 1).

Table 4
Effect of ratios of ligand to Pd[a]



Entry	*X*	*Y*	Yield[b] (%)
1	2	0	58
2	2	1	93
3	2	2	91
4	2	4	92
5	2	8	82
6	2	16	77

[a] Reaction conditions: 1.0 mmol of aryl bromide, 1.5 mmol of boronic acid, 2.0 mmol of K_3PO_4, 5.0 mL of EtOH.
[b] Isolated yield.

3. Conclusion

In conclusion, we have demonstrated that air-stable Pd(II) catalysts with cryptand-22 as ligand were very efficient and conveniently handled in the air at room temperature. Generally, Suzuki cross-coupling reactions of aryl bromides with arylboronic acids both containing electron-withdrawing and electron-donating groups proceeded fast in 2 h to give high yields. Our in situ catalytic system of Pd(II)/cryptand-22 catalyst is unique, since the reaction solution remained yellow and air-stable for at least one month without formation of Pd black as usually observed for ordinary simple amine ligands in several minutes. The utilization of cryptand-22 as the ancillary ligand proved to be effective in stabilizing the reactive palladium intermediates. The isolation of complex **1** may help to understand the reaction mechanism. The reaction proceeded equally well as in situ catalytic system when carried out in the presence of well-defined complex **1**. Studies to delineate the origin of its air-stability and to explore catalyst utility for other reactions are currently in progress.

4. Experimental

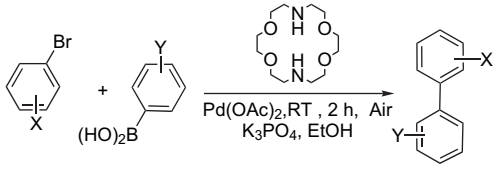
4.1. General remarks

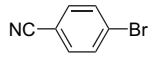
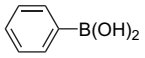
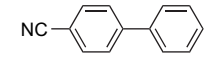
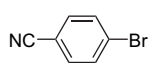
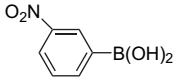
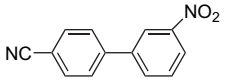
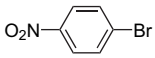
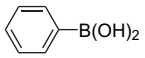
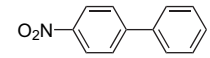
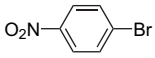
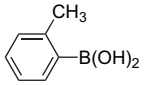
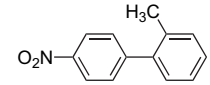
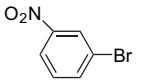
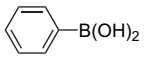
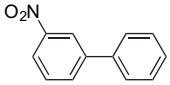
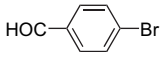
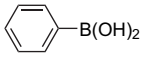
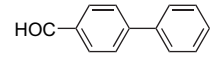
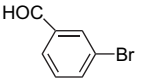
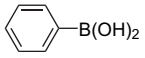
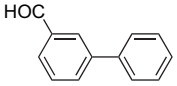
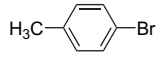
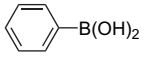
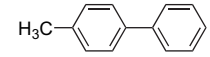
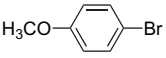
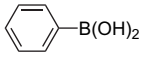
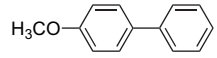
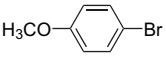
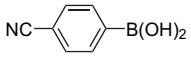
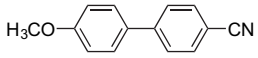
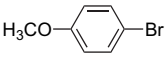
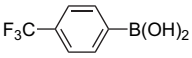
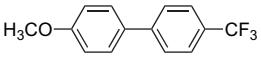
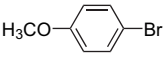
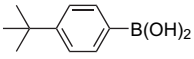
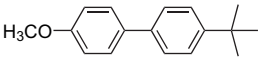
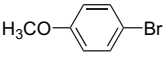
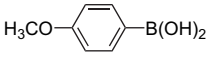
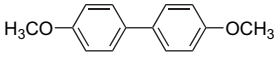
^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker AVA-300 spectrometer with TMS as internal standard. All reagents were used directly as obtained commercially. All products are known.

4.1.1. Typical experimental procedure for the palladium-catalyzed Suzuki cross-coupling reaction

Under an atmosphere of air, a mixture of aryl bromide (1 mmol), arylboronic acid (1.5 mmol), Pd(II) catalyst

Table 5
$Pd(OAc)_2$/cryptand-22-catalyzed cross-coupling of aryl bromides with various arylboronic acids[a]



Entry	Aryl bromide	Boronic Acid	Product	Time[b] (h)	Yield[c] (%)
1				2/0.25	95/75
2				2	90
3				2	92
4				2	83
5				2	90
6				2	86
7				2	90
8				2	93
9				2/0.25	93/68
10				2/0.25	85/30
11				2	84
12				2	89
13				2/0.25	92/43

[a] Reaction conditions: 1.0 mmol of aryl bromide, 1.5 mmol of arylboronic acid, 2.0 mmol of K_3PO_4, 2 mol % of $Pd(OAc)_2$, 2 mol % of cryptand-22, 5.0 ml of EtOH.
[b] Time not optimized.
[c] Isolated yield.

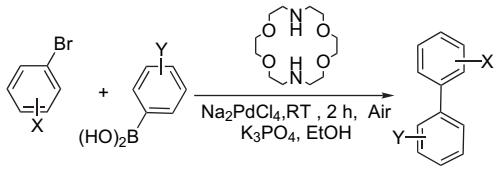
(2 mol %), ligand (2 mol % or as indicated), base (2 mmol), and solvent (5 mL) were added to a 25 mL round-bottom flask and stirred at room temperature for 2 h. After ordinary workup and being evaporated by rotary evaporator, the residue was purified by column chromatography to give the required biphenyl derivative (hexane/ethyl acetate).

4.1.2. Analytical data for biphenyl derivatives (Table 5)

4.1.2.1. Entry 1: 4-phenylbenzonitrile.[15,17] Slightly yellow solid, mp 140–142 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73 (d, J=8.5 Hz, 2H), 7.68 (d, J=8.5 Hz, 2H), 7.59 (t, J=4.5 Hz, 2H), 7.48 (t, J=7.5 Hz, 2H), 7.42–7.49 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.6, 139.1, 132.5, 129.0, 128.6, 127.7, 127.2, 118.9, 110.8.

4.1.2.2. Entry 2: 4-cyano-3′-nitrobiphenyl.[16] Slightly yellow solid, mp 172–173 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.46 (dd, J=1.8, 1.8 Hz, 1H), 8.28 (ddd, J=8.4, 0.9, 1.2 Hz, 1H), 7.92 (ddd, J=7.8, 0.9, 0.9 Hz, 1H), 7.80 (d, J=8.1 Hz, $CDCl_3$), 7.74 (d, J=8.4 Hz, 2H), 7.68 (dd, J=8.1, 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.7, 142.9, 140.7, 133.0, 132.9, 1320.2, 127.8, 123.3, 122.1, 118.4, 112.3.

Table 6
Na_2PdCl_4/cryptand-22-catalyzed cross-coupling of aryl bromides with various arylboronic acids[a]



Entry	Aryl bromide	Boronic Acid	Product	Time[b] (h)	Yield[c] (%)
1	NC–Br	B(OH)$_2$	NC–	2	97
2	O_2N–Br	B(OH)$_2$	O_2N–	2	91
3	HOC–Br	B(OH)$_2$	HOC–	2	89
4	H_3C–Br	B(OH)$_2$	H_3C–	2	95
5	H_3CO–Br	B(OH)$_2$	H_3CO–	2	93
6	H_3CO–Br	NC–B(OH)$_2$	H_3CO–CN	2	94
7	H_3CO–Br	B(OH)$_2$	H_3CO–	2	91
8	H_3CO–Br	H_3CO–B(OH)$_2$	H_3CO–OCH_3	2	93
9	NC–Br	B(OH)$_2$	NC–	2	95[d]
10	HOC–Br	B(OH)$_2$	HOC–	2	90[d]
11	H_3CO–Br	B(OH)$_2$	H_3CO–	2	95[d]

[a] Reaction conditions: 1.0 mmol of aryl bromide, 1.5 mmol of arylboronic acid, 2.0 mmol of K_3PO_4, 2 mol % of Na_2PdCl_4, 2 mol % of cryptand-22, 5.0 ml of EtOH.
[b] Time not optimized.
[c] Isolated yield.
[d] (Cryptand-22)$PdCl_2$ is used.

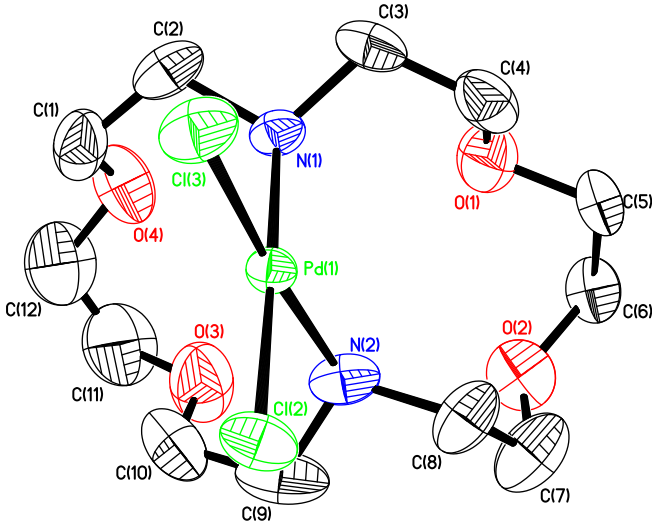


Figure 1. ORTEP drawing of complex **1**. Thermal ellipsoids shown at 30% probability level. Hydrogens are omitted for clarity.

4.1.2.3. Entry 3: 4-nitrobiphenyl.[17–19] White solid, mp 114–115.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.30 (d, J=8.4 Hz, 2H), 7.74 (d, J=8.7 Hz, 2H), 7.62 (dd, J=8.1, 1.5 Hz, 2H), 7.53–7.41 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.6, 147.0, 138.7, 129.1, 128.9, 127.8, 127.4, 124.1.

4.1.2.4. Entry 4: 2′-methyl-4-nitrobiphenyl.[16] White solid, mp 100–102 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.27 (d, J=8.7 Hz, 2H), 7.84 (d, J=8.1 Hz, 2H), 7.31–7.20 (m, 4H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.8, 146.8, 139.6, 135.0, 130.7, 130.1, 129.4, 128.4, 126.1, 123.4, 20.3.

4.1.2.5. Entry 5: 3-nitrobiphenyl.[16] White solid, mp 55–57 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.45 (dd, J=2.1, 1.8 Hz, 1H), 7.19 (dd, J=8.1, 2.1 Hz, 1H), 7.91 (d, J=7.5 Hz, 1H), 7.61 (dd, J=8.1, 8.4 Hz, 3H), 7.52–7.42 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.7, 142.9, 138.6, 133.0, 129.7, 129.1, 128.5, 127.1, 122.02, 121.95.

4.1.2.6. Entry 6: 4-biphenylaldehyde.[15,17] White solid, mp 59–60 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.05 (s, 1H), 7.95 (d, J=8.1 Hz, 2H), 7.75 (d, J=8.1 Hz, 2H), 7.65–7.62 (m, 2H), 7.50–9.39 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.6, 147.0, 138.7, 129.1, 128.9, 127.8, 127.4, 124.1.

4.1.2.7. Entry 7: 3-biphenylaldehyde.[16] ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.08 (s, 1H), 8.10 (s, 1H), 8.49 (dd, J=7.5, 1.8 Hz, 2H), 7.64–7.58 (m, 3H), 7.50–7.37 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.3, 142.1, 139.6, 133.0, 129.4, 128.9, 128.7, 128.1, 127.9, 127.1.

4.1.2.8. Entry 8: 4-methylbiphenyl.[15,18] White solid, mp 44–46 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 (d, J=7.5 Hz, 2H), 7.43 (d, J=8.1 Hz, 2H), 7.35 (dd, J=7.5, 7.8 Hz, 2H), 7.25 (dd, J=7.5, 7.5 Hz, 1H) 7.18 (d, J=8.1 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.1, 138.3, 137.0, 129.4, 128.7, 127.0, 126.9, 21.1.

4.1.2.9. Entry 9: 4-methoxybiphenyl.[17,19] White solid, mp 82–84 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54 (dd, J=7.2, 6.9 Hz, 4H), 7.38 (dd, J=7.5, 7.5 Hz, 2H), 7.30 (dd, J=7.2, 7.2 Hz, 1H), 6.97 (d, J=6.9 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.1, 140.8, 133.7, 128.7, 128.1, 126.7, 126.6, 114.1, 55.3.

4.1.2.10. Entry 10: 4-cyano-4′-methoxybiphenyl.[18,20] White solid, mp 178–180 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.7–7.62 (m, 2H), 7.55–7.52 (m, 2H), 7.02 (t, 2H), 6.9 (t, 2H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.2, 145.2, 132.5, 131.5, 128.3, 127.1, 119.1, 114.5, 110.1, 55.42.

4.1.2.11. Entry 11: 4-trifluoromethyl-4′-methoxybiphenyl.[17,18] White solid, mp 122–124 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67–7.64 (m, 4H), 7.55–7.50 (d, J=8.7 Hz, 2H), 7.0–6.97 (d, J=8.6 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.8, 144.3, 132.2, 128.4, 126.8, 126.2, 125.6, 122.6, 114.4, 55.37.

4.1.2.12. Entry 12: 4-tert-butyl-4′-methoxybiphenyl.[21] White solid, mp 127–128 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.54 (d, J=8.9 Hz, 2H), 7.49 (d, J=8.7 Hz, 2H), 7.43 (d, J=8.7 Hz, 2H), 6.98 (d, J=8.9 Hz, 2H), 3.85 (s, 3H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.9, 149.6, 137.9, 133.6, 128.0, 126.3, 125.6, 114.1, 55.3, 34.5, 31.4.

4.1.2.13. Entry 13: 4,4′-dimethoxybiphenyl.[15,18] White solid, mp 180–182 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49–7.46 (d, J=9.3 Hz, 4H), 6.97–6.94 (d, J=8.7 Hz, 4H), 3.84 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.7, 133.5, 127.7, 114.1, 55.4.

4.1.3. Synthesis of (cryptand-22)$PdCl_2$

Cryptand-22 (118.1 mg, 0.45 mmol) was added into a solution of Na_2PdCl_4 (117.7 mg, 0.4 mmol) in ethanol (30 mL) at room temperature. The mixture was stirred at room temperature for 2.5 h, during which a yellow precipitate appeared. After the reaction mixture was filtered, the yellow precipitate was then dissolved and filtered through a filter paper by DCM. The solvent was removed under reduced pressure. The resulting solid was collected and recrystallized from dichloromethane/diethyl ether to give complex **1** as a yellow-orange solid (1.17 g, yield: 70%). Mp 196–198 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.94–6.92 (m, 2H), 2.82–2.79 (m, 4H), 2.48–2.36 (m, 4H), 1.91–1.66 (m, 30H), 1.29–1.17 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 68.3, 66.1, 52.0. Anal. Calcd for $C_{12}H_{26}N_2O_4Pd$: C, 32.78; H, 5.96; N, 6.37. Found: C, 32.40; H, 6.33; N, 6.34.

4.1.4. Crystal structure data experimental

Structure of complex **1**, (cryptand-22)$PdCl_2$, has been unambiguously identified by X-ray crystallography. Crystals suitable for X-ray structure analysis were grown from DCM/ether. A yellow crystal with dimensions of 0.5×0.5×0.04 mm was mounted on a glass fiber on a Siemens P4 diffractometer equipped with monochromated Mo Kα radiation. Intensity data were collected and reduced by using well-established software package XSCANS.[22] The structure was solved by direct method and was refined using SHELXTL.[23] All non-hydrogen atoms were located from difference maps and refined anisotropically. H-atoms attached on the two N-atoms were found from difference maps and isotropically refined as normal atoms. The rest of the H-atoms were placed at idealized positions. The final residuals of the refinement were $R1$=0.0431, $wR2$=0.0969, and S=1.041. Crystal data in CIF format can be found in the supplementary data.

5. Supplementary data

Crystallographic data for the structure of complex **1** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 665828. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax:+44(0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk.

Acknowledgements

We thank Soochow University for support of this work.

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