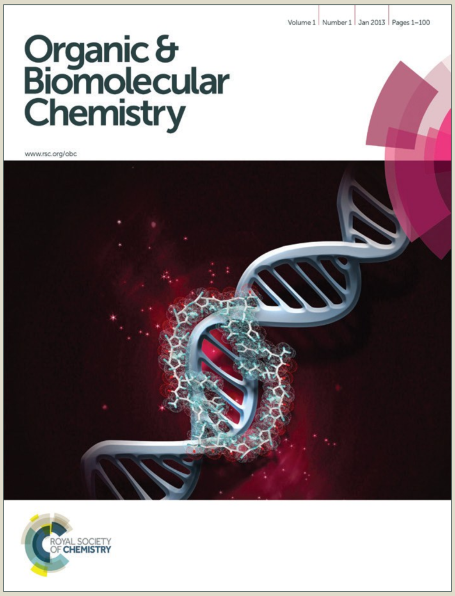

Volume 1 | Number 1 | Jan 2013 | Pages 1–100
Organic & Biomolecular Chemistry
www.rsc.org/obc
ROYAL SOCIETY OF CHEMISTRY

Journal Name RSCPublishing

COMMUNICATION

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2015,
Accepted 00th January 2015

DOI: 10.1039/x0xx00000x

www.rsc.org/

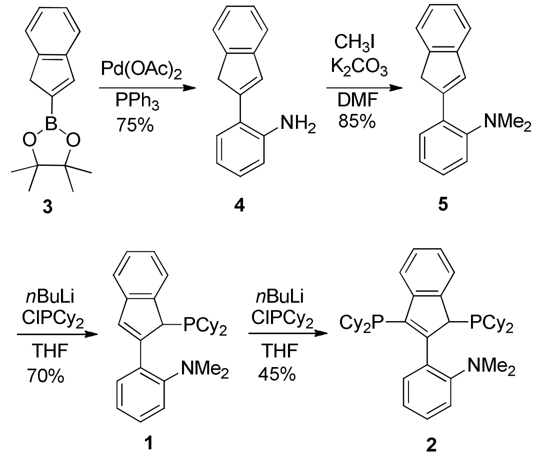
Pd-Indenyl-diphosphine: An Effective Catalyst for the Preparation of Triarylamines†

Meng-Qi Yan,[a] Jia Yuan,[b] Yun-Xiao Pi,[a] Jin-Hua Liang,[a] Yan Liu,[c] Qing-Guo Wu, [a] Xue Luo, [a] Sheng-Hua Liu, [a] Jian Chen, [a] Xiao-Lei Zhu,*[a] and Guang-Ao Yu*[a]

A new Buchwald-type diphosphine ligand has been developed for applications in Pd-catalyzed amination reactions towards the preparation of triarylamines. The catalyst can be used to perform the amination of a diverse array of aryl and heteroaryl chlorides. This diphosphine ligand can be changed into an anionic ligand in situ. The advantages and importance of this catalyst system outline herein make it a valuable contribution to applications in Pd-catalyzed amination reactions with aryl chlorides.

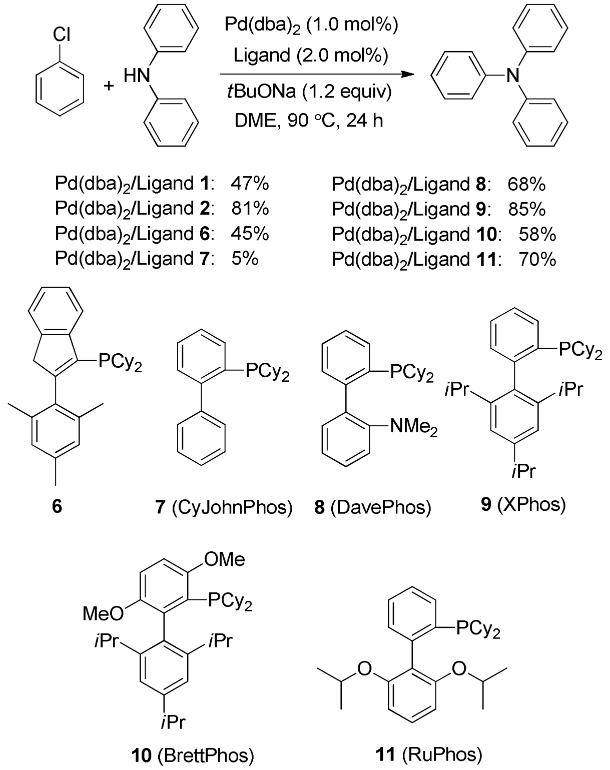
The ligand structure defines the steric and electronic properties of the palladium catalyst and therefore plays a crucial role in the efficiency of the Buchwald–Hartwig cross-coupling reaction. The biaryl dialkyl monophosphine ligands developed by Buchwald and co-workers, such as Brettphos, RuPhos, and JohnPhos have demonstrated a broad substrate scope in the Buchwald–Hartwig cross-coupling reaction.[1] However, the development of anionic phosphine ligands for cross-coupling reactions have rarely been explored.[2] Herein, we report a class of novel aryl substituted indenyl monophosphine ligands and diphosphine ligands, which can react with base and generate anionic phosphine ligands in situ;[3] the electron-donor ability of the indenyl anion may increase the electron density at the phosphorus atom and improve the activity of the catalytic system. We expect that these unique structural and electronic properties of **1** and **2** would afford excellent reactivity and substrate scope towards the synthesis of triarylamines via a Buchwald–Hartwig coupling reaction and would be complementary to those known catalytic systems.

The synthesis of **1** was accomplished in three steps from indenyl boronic ester **3** (Scheme 1), which could be prepared on a kilogram scale from 2-bromoindene. The palladium-catalyzed Suzuki–Miyaura coupling of **3** with 2-bromoaniline provided **4** in 73 % yield. Methylation of **4** with methyl iodide afforded **5** in 85 % yield. The straightforward deprotonation of **5** using *n*BuLi and trapping the resulting lithiated intermediate with dicyclohexyl phosphine chloride Cy_2PCl afforded the monophosphine ligand **1** in 70 % yield. The monophosphine ligand **1** was deprotonated using *n*BuLi and reacted with dicyclohexyl phosphine chloride to obtain the bidentate phosphine **2** in 45 % yield. **2** could also be obtained in one-pot from **5** in 30 % total yield. Ligands **1** and **2** were found to be air-sensitive. Therefore, treatment of the reaction mixtures with BH_3 led to their corresponding air-stable phosphine•BH_3 complexes.[4]



Scheme 1. Syntheses of Phosphine Ligands 1 and 2

Ligands **1** and **2** were applied in the palladium-catalyzed Buchwald–Hartwig coupling reaction of diphenyl amine with aryl chloride. The cross-coupling reaction between diphenyl amine and chlorobenzene was chosen as the model system (Scheme 2). Besides ligands **1** and **2**, various structural monophosphine ligands were also examined for comparison. The reactions were carried out at 90 °C in DME for 24 h with $Pd(dba)_2$ as the catalyst precursor. Whereas low conversions were generally observed in this challenging cross-coupling reaction with ligands such as (2-mesityl-1*H*-inden-3-yl) dicyclohexylphosphine (**6**), CyJohnPhos (**7**), DavePhos (**8**), BrettPhos (**10**) and RuPhos (**11**), it is gratifying to report that ligand **2** and XPhos (**9**) provided a rapid conversion and excellent yields (81 % and 85 %, respectively). Since ligand **1**, **2**, and **8** possess the same lower aryl ring, their dramatic difference in reactivity clearly demonstrates the influence of the steric and electronic properties of the upper ring on their reactivity. We hypothesized that the bulky sterically hindered and relatively electron-rich nature of **2** compared to DavePhos (**8**) facilitates the key transmetallation step of this reaction.[5]



Scheme 2. Ligand Screening for Buchwald-Hartwig Coupling of Chlorobenzene and Diphenylamine

Deprotonation of indene by base has been well-documented. We believe that the reaction of **1** and **2** with *t*BuONa in DME can generate the anionic ligand in situ, and the strong electron-donor ability of the indene anion may increase the electron density at phosphorus and improve the reaction rate as a result. To provide support for this finding, we undertook a series of ^{31}P NMR studies. When two equivalents of *t*BuONa was added to a solution of ligand **1** in DME, a red solution was formed immediately, the resonance for the ligand (δ = -15.65 ppm) disappeared, and another new signal appeared (δ = -19.65 ppm), corresponding to anionic phosphine ligand. Whereas, when two equivalents of *t*BuONa was added to a solution of ligand **2** in DME, a black-red solution was formed immediately, the two resonances for the ligand (δ = 9.19 ppm and δ = -20.18 ppm) disappeared, and another new signal appeared (δ = -15.79 ppm) corresponding to the anionic diphosphine ligand (See Supporting Information).

Many researchers have proved that the Pd-arene interaction is very important in Pd-catalyzed cross-coupling reactions. Despite numerous attempts employing various conditions, we have not been able to obtain structural information on the **1**(anion)/**2**(anion)-Pd oxidative addition complex using X-ray crystallography. Thus, we turned to DFT calculations in order to gather insight into the structural framework of the oxidative addition complexes based upon **1**(anion)-Pd(Ph)Cl, **2**(anion)-Pd(Ph)Cl, and **8**-Pd(Ph)Cl. The starting structure of **8**-Pd(Ph)Cl was obtained from Buchwald et al.[6] In this case, we located two possible complexes by performing ground-state energy optimization on the oxidative addition product of **1**-Pd and chlorobenzene (Figure 1). Complex **2** (anion)-Pd(Ph)Cl possesses two Pd-arene interactions with the non-phosphine-containing ring of the ligand: Pd-C (2.85 Å) and Pd-N (2.61 Å). On the contrary, complex **1**(anion)-Pd(Ph)Cl only possesses Pd-C (2.83 Å) and/or Pd-N (3.33 Å) interactions with the non-phosphine-containing ring of the ligand and complex **8**-Pd(Ph)Cl only shows a Pd-N (2.59 Å) interaction with the non-phosphine-containing ring of the ligand. The larger the distance between Pd-arene, the lower the catalyst rate. Therefore, **2** took on the largest catalyst rate (81%) compared to **1** (47%) and **8** (68%). We believe that the ability of anionic **2** to stabilize the Pd(II) center of the oxidative addition complex through labile Pd-C and Pd-N interactions was mainly responsible for the effectiveness of **2** as a supporting ligand in Pd-catalyzed cross-coupling reactions.

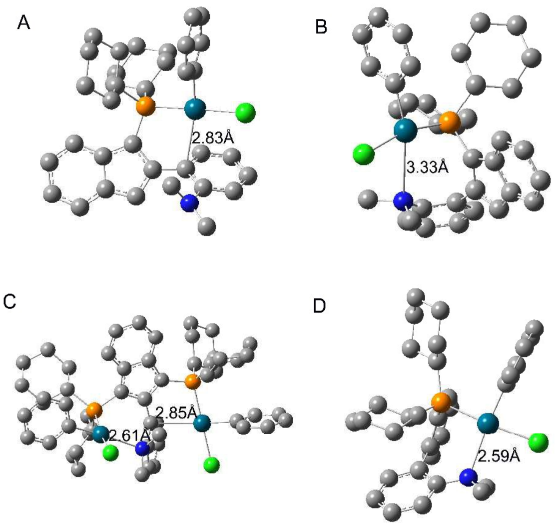
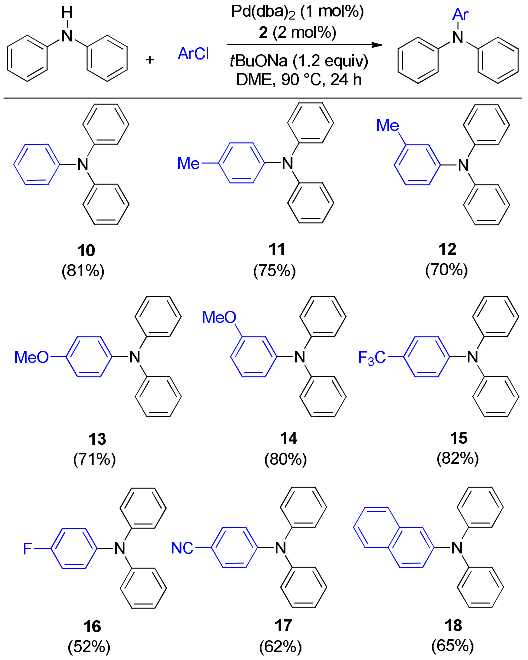


Figure 1 . The Optimized Oxidation Addition Complexes Composed of 1-Pd(Ph)Cl (A, B), 2-Pd(Ph)Cl (C), and 8-Pd(Ph)Cl (D)

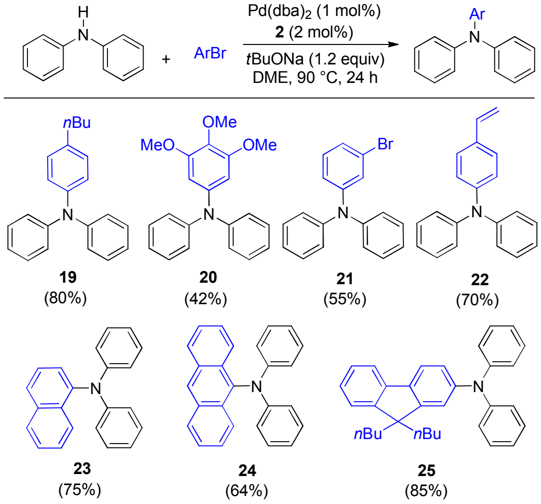
The high effectiveness of ligand **2** observed in the coupling reaction between chlorobenzene and diphenyl amine encouraged us to study the substrate scope in the Buchwald–Hartwig coupling reaction of substituted aryl chlorides and the results summarized in Scheme 3. In most cases, different aryl chlorides reacted with diphenyl amine leading to their corresponding products in good yield. For example, the reaction of chlorobenzene with diphenyl amine gave rise to the corresponding tertiary amine in 81 % yield (**10**), coupling reactions of aryl chlorides bearing electron-donating substituents such as –Me and –OMe at the *para* and *meta* positions with diphenyl amine went smoothly, providing moderate to high yields of the expected products (70 %–80 % yield) (**11**, **12**, **13**, **14**). The reaction of aryl chlorides bearing electron-withdrawing groups such as –CF$_3$ and –F at the *para* position also permit the coupling reaction with diphenyl amine, giving the required products in moderate to good yields (**15**, **16**). Moreover, the base-sensitive –CN group was tolerated using our catalytic system and the corresponding triarylamine (**17**) was obtained in 62 % yield. In addition, 2-chloronaphthalene underwent the desired coupling reaction with diphenylamine, giving the triarylamine product in 65 % yield (**18**).



Scheme 3. Synthesis of Triarylamines from Chlorides and Diphenyl amine

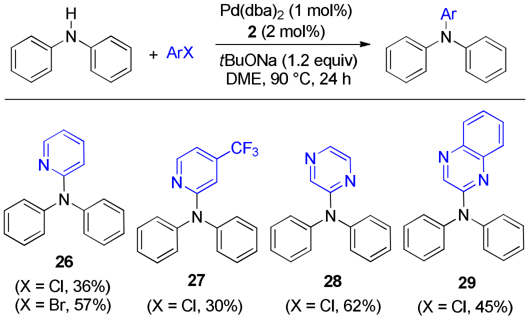
To further demonstrate the general applicability of our catalyst system, we studied the Buchwald–Hartwig amination reaction with substituted aryl bromides (Scheme 4). We adopted the optimized reaction conditions to the amination of various aryl bromides with diphenylamine. 1-Bromo-4-butylbenzene, 1-bromo-3, 4, 5-trimethoxybenzene, 1, 3-dibromobenzene and 4-bromostyrene could be aminated smoothly to give the triarylamine products in satisfactory yields (Scheme 4, **19**, **20**, **21**, **22**). In addition, sterically hindered aryl bromides underwent smooth transformations under the standard conditions to give the desired products in moderate yield (**23**, **24**). Furthermore, the reaction of 2-bromo-9, 9-dibutylfluorene with diphenylamine gave the triarylamine product in excellent yield (**25**).

Heterocyclic triarylamine compounds are of particular interest to materials science. The application of heterocyclic compounds in cross-coupling reactions still remains a synthetic challenge, because the ligating ability of the heteroatoms present can lead to catalyst deactivation.[7] In addition, the electronic properties at certain positions in the heterocycle used can be unfavorable for the elementary reactions required in these catalytic processes.[8] To the best of our knowledge, only a few heterocyclic triarylamines have been reported.[9] We have examined the use of our catalytic system in the coupling reaction for a range of heteroaryl halides (Scheme 5). For example, 2-chloropyridine and 2-bromopyridine underwent the desired coupling reaction with diphenylamine to afford the corresponding products in moderate yield (**26**). Unfortunately, 4-trifluoromethyl-2-chloropyridine coupled with diphenylamine to give the triaryl amine in a low 30 % yield (**27**). However, in the case of 2-chloropyrazine and 2-chloroquinoxaline, the coupling reaction gave the desired products in moderate yield (**28**, **29**).



Scheme 4. Synthesis of Triarylamines from Bromides and Diphenyl amine

In summary, we have developed a novel class of Buchwald-type bidentate phosphine ligand for the Buchwald–Hartwig coupling reaction incorporating an indenyl diphosphine framework. Ligand **2**, which could be changed into an anionic phosphine ligand upon reaction with *t*BuONa in situ, has provided different steric and electronic properties in contrast to the biaryl ligands reported by Buchwald and co-workers, which have shown special applications towards the preparation of triaryl amines. Ligand **2** has demonstrated its catalytic ability for the Buchwald–Hartwig coupling reaction with a broad substrate scope, which includes sterically congested aryl halides, compounds possessing a variety of functional groups, and heteroaryl halides.



Scheme 5. Synthesis of Heterocyclic Triarylamine From Aryl halides and Diphenyl Amine

Acknowledgements

The authors would like to thank the National Natural Science Foundation of China (Nos. 21472060, 21072071 and 21272088), self-determined research funds of CCNU from the colleges' basic research and operation of MOE (Nos. CCNU15KFY001, CCNU15A02012).

Notes and references

[a]*Key Laboratory of Pesticide & Chemical Biology, Ministry of Education, Central China Normal University, Wuhan 430079, China. E-Mail: yuguang@mail.ccnu.edu.cn*
[b]*State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, China*
[c]*State Key Laboratory of Catalysis, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, China*
Electronic supplementary information (ESI) available: For ESI see DOI: 10.1039/b000000x

1 (a) D. S. Surry and S. L. Buchwald, *Chem. Sci.*, 2011, **2**, 27; (b) D. Maiti, B. P. Fors, J. L. Henderson, Y. Nakamura and S. L. Buchwald, *Chem. Sci.*, 2011, **2**, 57; (c) N. C. Bruno, M. T. Tudge and S. L. Buchwald, *Chem. Sci*., 2013, **4**, 916; (d) T. Noël, J. R. Naber, R. L. Hartman, J. P. McMullen, K. F. Jensen and S. L. Buchwald, *Chem. Sci.*, 2011, **2**, 287.

2 J. Zhang, A. Bellomo, N. Trongsiriwat, T. Jia, P. J. Carroll, S. D. Dreher, M. T. Tudge, H. Yin, J. R. Robinson, E. J. Schelter and P. J. Walsh, *J. Am. Chem. Soc.*, 2014, **136**, 6276.

3 L. Chen, G.-A. Yu, F. Li, X. Zhu, B. Zhang, R. Guo, X. Li, Q. Yang, S. Jin, C. Liu and S.-H. Liu, *J. Organomet. Chem.*, 2010, **695**, 1768.

4 G. C. Lloyd-Jones and N. P. Taylor, *Chem. Eur. J.*, 2015, **21**, 5423.

5 (a) K. L. Billingsley and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2008, **47**, 4695; (b) R. Ghosh, N. N. Adarsh and A. Sarkar, *J. Org. Chem.*, 2010, **75**, 5320; (c) A. Thakur, K. Zhang and J. Louie, *Chem. Commun.*, 2012, **48**, 203; (d) K. L. Billingsley, K. W. Anderson and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2006, **45**, 3484; (e) T. Noël and A. J. Musacchio, *Org. Lett.*, 2011, **13**, 5180; (f) N. Kudo, M. Perseghini and G. C. Fu, *Angew. Chem., Int. Ed.*, 2006, **45**, 1282.

6 X.-Q. Shen, G. O. Jones, D. A. Watson, B. Bhayana and S. L. Buchwald, *J. Am. Chem. Soc.*, 2010, **132**, 11278.

7 (a) J. Hankache, M. Niemi, H. Lemmetyinen and O. S. Wenger, *J. Phys. Chem. A*, 2012, **116**, 8159; (b) J. Hankache and O. S. Wenger, *Chem. Commun*., 2011, **47**, 10145; (c) J. Hankache, M. Niemi, H. Lemmetyinen and O. S. Wenger, *Inorg. Chem.*, 2012, **51**, 6333; (d) J. Hankache and O. S. Wenger, *Chem. Eur. J.*, 2012, **18**, 6443.

8 (a) M. Su, N. Hoshiya and S. L. Buchwald, *Org. Lett.*, 2014, **16**, 832; (b) I. P. Beletskaya and A. V. Cheprakov, *Organometallics*, 2012, **31**, 7753; (c) Q. Shen and J. F. Hartwig, *J. Am. Chem. Soc.*, 2007, **129**, 7734.

9 (a) D. S. Surry and S. L. Buchwald, *J. Am. Chem. Soc.*, 2007, **129**, 10354; (b) K. H. Hoi, J. A. Coggan and M. G. Organ, *Chem. Eur. J.*, 2013, **19**, 843; (c) C. Bolm, J.-C. Frison, J. L. Paih, C. Moessner and G. Raabe, *J. Organomet. Chem.*, 2004, **689**, 3767.

10 X. Hao, J. Yuan, G.-A. Yu, M.-Q. Qiu, N.-F. She, Y. Sun, C. Zhao, S.-L. Mao, J. Yin and S.-H. Liu, *J. Organomet. Chem.*, 2012, **706-707**, 99.