

Palladium-Catalyzed Annulation of Diarylamines with Olefins through C–H Activation: Direct Access to N-Arylindoles**

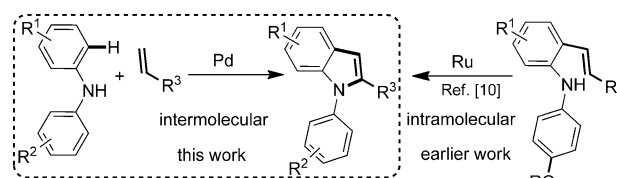
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Abstract: A palladium-catalyzed dehydrogenative coupling between diarylamines and olefins has been discovered for the synthesis of substituted indoles. This intermolecular annulation approach incorporates readily available olefins for the first time and obviates the need of any additional directing group. An *ortho* palladation, olefin coordination, and β -migratory insertion sequence has been proposed for the generation of olefinated intermediate, which is found to produce the expected indole moiety.

Indole is one of the most ubiquitous heterocycles found in nature. Owing to significant biological activities,^[1] indole has become an important component in many pharmaceutical agents.^[2] Consequently, their preparation has been a major area of research for well over a hundred years and innumerable methods,^[3] including Fischer^[4] and Buchwald^[5] indole synthesis have been reported. Recently, transition-metal-catalyzed directing-group-assisted heteroannulation of amines with carbonyl compounds^[6] and alkynes have emerged for their synthesis.^[7]

N-arylindoles are present in many biologically as well as pharmaceutically important compounds.^[8,9] In 2012, the group of Zheng constructed 1,2-disubstituted indoles from styryl anilines by using a ruthenium-based photocatalytic method (Scheme 1).^[10] Unfortunately, this intramolecular reaction does not proceed without an *p*-alkoxyphenyl amine moiety.

In this context, we envisaged that a direct intermolecular oxidative coupling of diaryl amine with abundantly available olefins (Fujiwara–Moritani reaction)^[11] may be utilized for N-arylindole synthesis. Previously, various nitrogen-containing substrates including sulfonyl aniline,^[12a] carbonyl aniline,^[12b,c] aniline,^[12d] and benzyl amine^[12e] were successfully applied as the directing group to enhance the reactivity, selectivity for



Scheme 1. Synthesis of N-arylated indoles involving olefins.

ortho C–H activation, and in a few cases to achieve further heteroannulations.^[12f] Recently, Patureau and co-workers disclosed the dehydrogenative C–N cross-coupling of unprotected secondary anilines through *ortho*-N-carbazolation using a ruthenium catalyst.^[13]

In continuation of our research to utilize widely available olefins for the synthesis of valuable products,^[14] here we disclose a palladium-catalyzed method for the synthesis of 2-substituted N-arylindoles by directly reacting various diarylamines and olefins. Because of the low cost and wide availability of various olefins, such an approach would allow straight-forward synthesis of N-arylindoles. The generality of this strategy is described here by synthesizing an exemplary set of indole compounds (> 40 examples), most of which represent new chemical entities.

Systematic studies revealed that 1,2-disubstituted indole moieties can be synthesized (89% GC yield; 85% isolated) from diphenylamine (1 mmol) and styrene (0.25 mmol) by using Pd(OAc)₂ (10 mol%) and 1,10-phenanthroline (20 mol%), in acetic acid without any additional oxidant.

To explore the substrate scope of this simple system, we reacted different styrenes with diphenylamine under the optimized reaction conditions (Table 1). Along with the expected product, the 1,3-disubstituted indole regioisomer was also formed. Notably, in most of the cases, the ratio of 1,2-diarylated and 1,3-diarylated indole is limited to 99:1.^[15] In a few cases, such as for **3a**, **3c**, **3j**, and **3q**, and increased amount of the 1,3-disubstituted indole product was observed. Styrenes with *ortho/meta/para* substituents reacted with diphenylamine to produce the 1,2-diarylated indole in 41–85% yield (**3a–i** and **3o–q**). Various halides at the *ortho/para* position were well tolerated (**3d–f** and **3o–p**). Styrene with functional groups such as acetoxy, ester, and cyano reacted successfully (**3g–i**). Switching to a substituted diarylamine did not affect the outcome of the reaction and the expected indoles were obtained in preparatively useful yield (**3j–n** and **3r**). A sterically demanding trisubstituted styrene succeeded in producing 1,2-diarylated indole compound (**3s**). Notably, heterocyclic olefins can also be employed to prepare N-arylindoles (**3u** and **3v**). Efforts to incorporate ArNHR

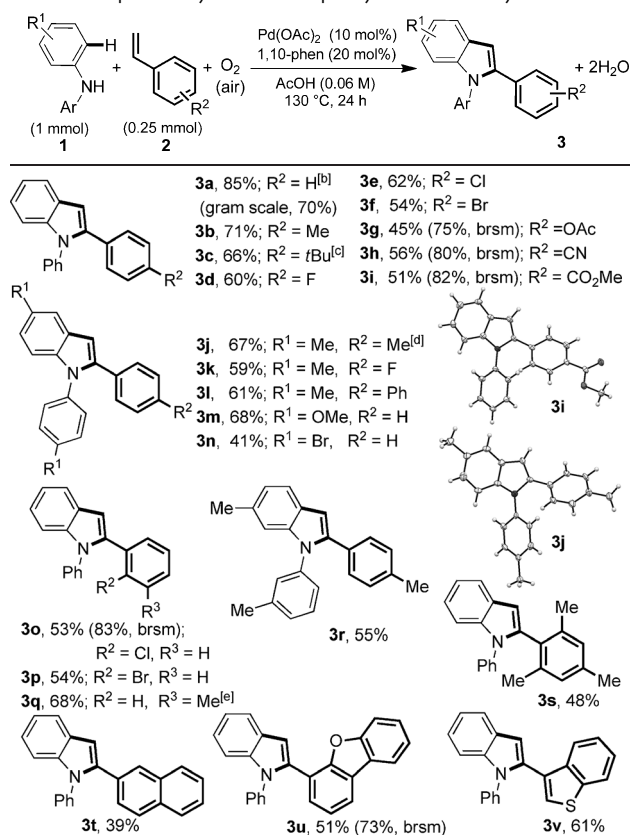
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Table 1: Scope with symmetrical diphenylamines and styrenes.^{[a][18]}



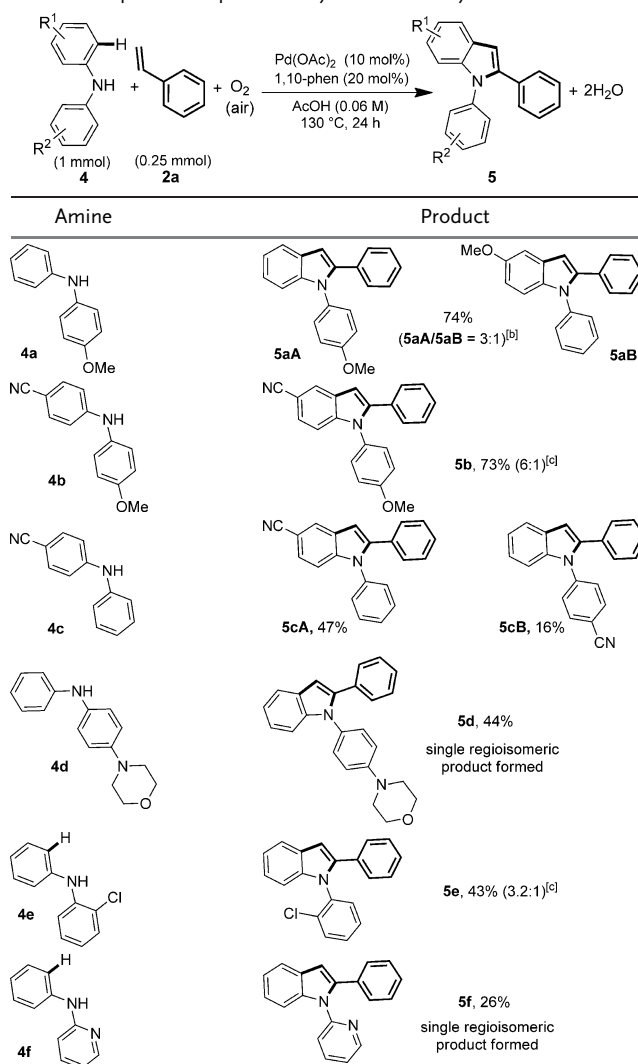
[a] Yield is that of the isolated product and the average of two runs. Ratio of 1,2-diarylated and 1,3-diarylated indole is 99:1.^[15] [b] Ratio is 91:9. [c] Ratio is 3:1. [d] Ratio is 4:1. [e] Ratio is 85:15. brsm = based on recovered starting material.

(R = Me, Et, *i*Pr, Ts, and Ac) in place of ArNH(Ar'), either gave low yields of desired the indole products or formed a mixture of inseparable compounds.

In the case of unsymmetrical diarylamines, there was a preference for cyclization of the electron-deficient aromatic ring with good regioselectivity (Table 2). For example, **4a** and **4b** preferentially cyclized to form the indole in a 3:1 (74%) and 6:1 (73%) ratio, respectively. In the case of 4-(phenylamino)benzonitrile (**4c**), a 47% yield of the isolated major product (**5cA**) was obtained through cyclization of the electron-deficient ring. Following a similar reactivity pattern, a single regioisomer was observed for 4-morpholino-*N*-phenylaniline (**4d**). When *N*-phenylpyridin-2-amine (**4f**) was reacted with styrene, cyclization occurred selectively towards the benzene ring albeit in low yield. Simplicity of the method was further demonstrated by incorporating an *ortho*-chloro-substituted amine (**4e**) as the coupling partner.

After evaluating the scope with styrene derivatives, different unactivated olefins were tested under the optimal reaction conditions (Table 3). Reaction of *cis*- and *trans*-β-methyl styrene (**6a** and **6b**) with diphenylamine provided the same product (**7a**; 53 and 23%, respectively). This difference in the yield may be attributed to the steric hindrance for the nucleophilic attack of the amine. In the case of simple

Table 2: Scope with respect to unsymmetrical diarylamines.^[a]



[a] Yield is that of the isolated product and an average of two runs. **A/B** ratio was determined by GC-MS analysis of the crude reaction mixture. [b] Isolated as an inseparable mixture of two products. [c] Isolated yield of the major isomer.

terminal olefins for example, 1-octene and 1-decene, the desired 2-alkylated indole (**7eA** and **7fA**, respectively) was obtained as the major product along with the 3-methyl isomer (**7eB** and **7fB**). With vinylcyclohexane, 2-cyclohexylindole **7cA** was isolated in 56% yield (**7cA/7cB**, 4:1).

The efficiency of the method was further tested by the heteroannulation of cyclic olefins with diphenylamine to synthesize tricyclic indole derivatives, which are present in many bioactive natural products.^[16] These scaffolds were previously synthesized from heteroannulation of internal alkynes or dienes through intramolecular approaches.^[17] Under the present reaction conditions both cyclic olefins as well as cyclic dienes afforded the desired *N*-phenyl tricyclic indole compounds (Table 4). In spite of the possibility of forming regioisomeric mixtures, only one product was generated exclusively in most of the cases. Regioisomeric 1,5- and 1,3-cyclooctadiene provided the same product **9a** as a result

Table 3: Scope with terminal/internal olefins.^[a]

Olefin	Product

[a] Yield is that of isolated product and an average of two runs. Isolated compounds were characterized by HRMS, 1D (¹H NMR, ¹³C NMR and DEPT) and 2D NMR (HSQC, HMBC, COSY and NOESY) spectroscopy wherever required. [b] Yield of one isolated isomer. The other regioisomer was detected by GC-MS. [c] A/B ratio was determined by GC-MS and was isolated as an inseparable mixture.

of the isomerization of the 1,5-cyclooctadiene under the reaction conditions. In both these cases the product can be obtained in crystalline form and was confirmed by single-crystal X-ray structure.^[15] Cycloheptene and cyclooctene had provided the desired compounds in synthetically useful yield (**9e** and **9f**). In the case of bicyclic olefins, for example, norbornene (**8g–8h**), the corresponding indoline product was obtained because of an unfavorable β-hydride elimination.

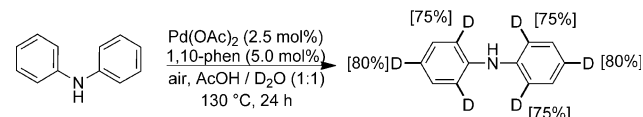
To understand the reaction mechanism, a number of competition experiments between electronically different styrenes and diphenyl amines were carried out. Based on experimental findings, we realized that electron-rich styrene as well as electron-rich diphenylamine was cyclized preferentially over the neutral and electron-deficient analogues.^[15] However, the use of unsymmetrical diarylamines caused the olefin to preferably annulate towards the electron-deficient aromatic ring (Table 2). It is therefore likely that the electron-deficient ring favors the initial *ortho* palladation and the electron-rich phenyl ring supports the sequential N-palladation step.

The observed deuteration (Scheme 2) at the *ortho/para* positions in the absence of an alkene indicated that reversible, electrophilic C–H palladation occurred under the reaction conditions.^[19] However, no *para* C–H olefination of diarylamines was observed in presence of olefins, thus indicating

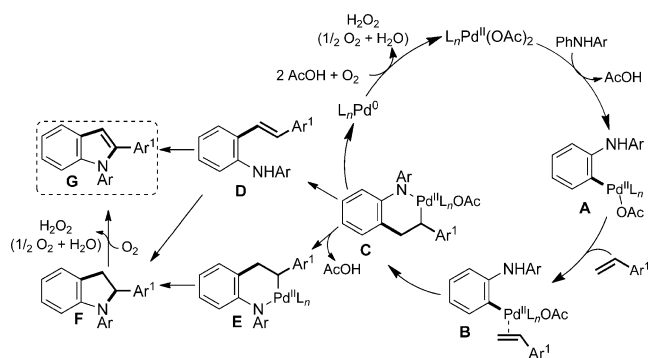
Table 4: Scope with cyclic olefins (mono and dienes).^{[a], [18]}

Olefin	Product

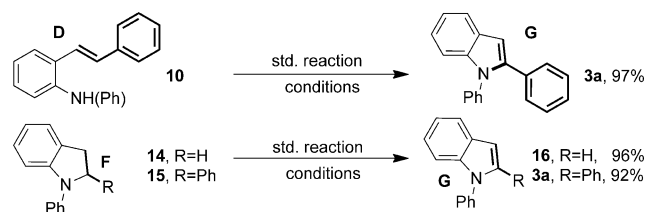
[a] Yield is that of isolated product and an average of two runs. Isolated compounds were characterized by HRMS, 1D (¹H NMR, ¹³C NMR and DEPT), and 2D NMR (HSQC, HMBC, COSY and NOESY) spectroscopy wherever required. [b] Run without Cu(OAc)₂. [c] Two isomers obtained as an inseparable mixture.


Scheme 2. Deuterium-labelling experiments.

that palladium is trapped in the *ortho* position by the nitrogen atom of the diarylamine. This nitrogen-atom-coordinated palladium center is involved in an irreversible step, which might be the alkene insertion leading to the intermediate **C** with a N–Pd bond (Scheme 3). Based on these experiments, *ortho* palladation of the diarylamine was proposed for the generation of the intermediate **A**. Interaction of **A** with olefin will lead to the species **B**. Subsequently β-migratory insertion will form the intermediate **C**, which can undergo β-hydride elimination to provide 2-(*N*-arylated)stilbene (**D**). The final product **G** can be produced via **D** and/or an indoline intermediate **F**. Separate study on these putative intermediates (**D** and **F**) showed that both of them can be converted successfully into the final product **G** (Scheme 4).^[15] Further, in the absence of a stoichiometric oxidant, **F** was generated from **D** under the standard reaction conditions. Therefore, **F** is



Scheme 3. Plausible mechanism.



Scheme 4. Mechanistic study in support of formation of **G**.

an intermediate between **D** and **G**. The palladium(0) formed can be reoxidized to palladium(II) by oxygen (air) possibly via a peroxopalladium(II) complex.^[20]

An alternative mechanism (Wacker-type) involving activation of the alkene by palladium(II), nucleophilic attack of the amine followed by intramolecular C–H activation to produce **F** can also be proposed (Scheme 3).^[15] Detailed studies are planned to gain further insights into the plausible mechanisms.

In summary, a versatile catalytic method for the synthesis of substituted indoles through palladium-catalyzed intermolecular annulation has been disclosed. Widely available olefins and diarylamines are used as coupling partners. Different styrenes with diphenylamine result in 1,2- (major) and 1,3- (minor) diarylated indoles with a ratio of 99:1 in most of the cases. With unsymmetrical diarylamines, cyclization is preferred for the electron-deficient aromatic ring. Cyclic aliphatic olefins, including dienes, afford tricyclic indole compounds. Detailed studies for further understanding of the mechanism and the regioselective synthesis of 3-substituted indoles are currently underway in our laboratory.

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[1] a) A. J. Kochanowska-Karamyan, M. T. Hamann, *Chem. Rev.* **2010**, *110*, 4489–4497; b) L. D. Quin, J. A. Tyrell, *Fundamentals of Heterocyclic Chemistry: Importance in Nature and in the Synthesis of Pharmaceuticals*, Wiley, Hoboken, NJ, **2007**.

[2] a) B. P. Smart, R. C. Oslund, L. A. Walsh, M. H. Gelb, *J. Med. Chem.* **2006**, *49*, 2858–2860; b) A. Dandia, R. Singh, S. Khaturia, C. Merienne, G. Morgant, A. Loupy, *Bioorg. Med. Chem.* **2006**, *14*, 2409–2417; c) S. Petit, Y. Duroc, V. Larue, C. Giglione, C. Léon, C. Soulama, A. Denis, F. Dardel, T. Meinell, I. Artaud, *ChemMedChem* **2009**, *4*, 261–275; d) H. Johansson, T. B. Jorgensen, D. E. Gloriam, H. Brauner-Osborne, D. S. Pedersen, *RSC Adv.* **2013**, *3*, 945–960; e) J. Alvarez-Builla, J. J. Vaquero, J. Barluenga, *Modern Heterocyclic Chemistry*, Vol. 1, Wiley-VCH, Weinheim, **2011**.

[3] For selected examples of indole synthesis, see: a) R. Möhlau, *Ber. Dtsch. Chem. Ges.* **1881**, *14*, 171–175; b) A. Bischler, *Ber. Dtsch. Chem. Ges.* **1892**, *25*, 2860–2879; c) R. C. Larock, E. K. Yum, *J. Am. Chem. Soc.* **1991**, *113*, 6689–6690; d) R. C. Larock, E. K. Yum, M. D. Refvik, *J. Org. Chem.* **1998**, *63*, 7652–7662; e) M. Shen, B. E. Leslie, T. G. Driver, *Angew. Chem. Int. Ed.* **2008**, *47*, 5056–5059; *Angew. Chem.* **2008**, *120*, 5134–5137; f) K. Alex, A. Tillack, N. Schwarz, M. Beller, *Angew. Chem. Int. Ed.* **2008**, *47*, 2304–2307; *Angew. Chem.* **2008**, *120*, 2337–2340; g) O. Leogane, H. Lebel, *Angew. Chem. Int. Ed.* **2008**, *47*, 350–352; *Angew. Chem.* **2008**, *120*, 356–358; h) R. Bernini, G. Fabrizi, A. Sferrazza, S. Cacchi, *Angew. Chem. Int. Ed.* **2009**, *48*, 8078–8081; *Angew. Chem.* **2009**, *121*, 8222–8225; i) Y. Tan, J. F. Hartwig, *J. Am. Chem. Soc.* **2010**, *132*, 3676–3677; j) S. Jana, M. D. Clements, B. K. Sharp, N. Zheng, *Org. Lett.* **2010**, *12*, 3736–3739; k) Z. Shi, F. Glorius, *Angew. Chem. Int. Ed.* **2012**, *51*, 9220–9222; *Angew. Chem.* **2012**, *124*, 9354–9356; l) D. Shan, Y. Gao, Y. Jia, *Angew. Chem. Int. Ed.* **2013**, *52*, 4902–4905; *Angew. Chem.* **2013**, *125*, 5002–5005.

[4] For selected examples of Fischer indole syntheses, see: a) E. Fischer, F. Jourdan, *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 2241–2245; b) E. Fischer, O. Hess, *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 559–568; c) B. Robinson, *Chem. Rev.* **1963**, *63*, 373–401; d) B. Robinson, *Chem. Rev.* **1969**, *69*, 227–250; e) S. Müller, M. J. Webber, B. List, *J. Am. Chem. Soc.* **2011**, *133*, 18534–18537; f) S. Gore, S. Baskaran, B. König, *Org. Lett.* **2012**, *14*, 4568–4571; g) A. Porcheddu, M. G. Mura, L. De Luca, M. Pizzetti, M. Taddei, *Org. Lett.* **2012**, *14*, 6112–6115; h) D. McAusland, S. Seo, D. G. Pintori, J. Finlayson, M. F. Greaney, *Org. Lett.* **2011**, *13*, 3667–3669.

[5] For selected examples of Buchwald indole synthesis, see: a) S. Wagaw, B. H. Yang, S. L. Buchwald, *J. Am. Chem. Soc.* **1998**, *120*, 6621–6622; b) S. Wagaw, B. H. Yang, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 10251–10263; c) J. L. Rutherford, M. P. Rainka, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 15168–15169; d) J. Y. Chae, S. L. Buchwald, *J. Org. Chem.* **2004**, *69*, 3336–3339; e) A. DeAngelis, D.-H. Wang, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2013**, *52*, 3434–3437; *Angew. Chem.* **2013**, *125*, 3518–3521.

[6] Recent examples of indole synthesis through heteroannulation of amines with carbonyl compounds: a) S. Würtz, S. Rakshit, J. J. Neumann, T. Dröge, F. Glorius, *Angew. Chem. Int. Ed.* **2008**, *47*, 7230–7233; *Angew. Chem.* **2008**, *120*, 7340–7343; b) J. J. Neumann, S. Rakshit, T. Dröge, S. Würtz, F. Glorius, *Chem. Eur. J.* **2011**, *17*, 7298–7303; c) Y. Wei, I. Deb, N. Yoshikai, *J. Am. Chem. Soc.* **2012**, *134*, 9098–9101.

[7] For selected recent examples of indole synthesis using alkynes, see: a) D. Zhao, Z. Shi, F. Glorius, *Angew. Chem. Int. Ed.* **2013**, *52*, 12426–12429; *Angew. Chem.* **2013**, *125*, 12652–12656; b) L. Ackermann, A. V. Lygin, *Org. Lett.* **2012**, *14*, 764–767; c) Z. Shi, C. Zhang, S. Li, D. Pan, S. Ding, Y. Cui, N. Jiao, *Angew. Chem. Int. Ed.* **2009**, *48*, 4572–4576; *Angew. Chem.* **2009**, *121*, 4642–4646; d) D. R. Stuart, P. Alsabeh, M. Kuhn, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 18326–18339; e) C. Wang, H. Sun, Y. Fang, Y. Huang, *Angew. Chem. Int. Ed.* **2013**, *52*, 5795–5798; *Angew. Chem.* **2013**, *125*, 5907–5910; f) D. R. Stuart, M.

- Bertrand-Laperle, K. M. N. Burgess, K. Fagnou, *J. Am. Chem. Soc.* **2008**, *130*, 16474–16475.
- [8] For use of N-aryldoles as biologically important scaffolds, see: a) K. Andersen, T. Liljefors, J. Hyttel, J. Perregaard, *J. Med. Chem.* **1996**, *39*, 3723–3738; b) E. Von Angerer, J. Strohmeier, *J. Med. Chem.* **1987**, *30*, 131–136; c) E. J. Glamkowski, J. M. Fortunato, T. C. Spaulding, J. C. Wilker, D. B. Ellis, *J. Med. Chem.* **1985**, *28*, 66–73; d) P. C. Unangst, M. E. Carethers, K. Webster, G. M. Janik, L. J. Robichaud, *J. Med. Chem.* **1984**, *27*, 1629–1633; e) J. Perregaard, J. Arnt, K. P. Boegesoe, J. Hyttel, C. Sanchez, *J. Med. Chem.* **1992**, *35*, 1092–1101.
- [9] For selected examples of N-aryldole synthesis, see: a) J. Barluenga, A. Jimenez-Aquino, F. Aznar, C. Valdes, *J. Am. Chem. Soc.* **2009**, *131*, 4031–4041; b) J. Barluenga, A. Jiménez-Aquino, C. Valdés, F. Aznar, *Angew. Chem. Int. Ed.* **2007**, *46*, 1529–1532; *Angew. Chem.* **2007**, *119*, 1551–1554; c) J. Barluenga, A. Jiménez-Aquino, F. Aznar, C. Valdés, *Chem. Eur. J.* **2010**, *16*, 11707–11711; d) N. Ototake, Y. Morimoto, A. Mokuya, H. Fukaya, Y. Shida, O. Kitagawa, *Chem. Eur. J.* **2010**, *16*, 6752–6755; e) A. Bunesco, C. Piemontesi, Q. Wang, J. Zhu, *Chem. Commun.* **2013**, *49*, 10284–10286; f) L. Ackermann, S. Barfusser, H. K. Potukuchi, *Adv. Synth. Catal.* **2009**, *351*, 1064–1072; g) J. C. Antilla, A. Klapars, S. L. Buchwald, *J. Am. Chem. Soc.* **2002**, *124*, 11684–11688; h) A. Klapars, J. C. Antilla, X. H. Huang, S. L. Buchwald, *J. Am. Chem. Soc.* **2001**, *123*, 7727–7729.
- [10] S. Maity, N. Zheng, *Angew. Chem. Int. Ed.* **2012**, *51*, 9562–9566; *Angew. Chem.* **2012**, *124*, 9700–9704.
- [11] For selected examples on the Fujiwara–Moritani reaction, see: a) S. Moritani, Y. Fujiwara, *Tetrahedron Lett.* **1967**, *8*, 1119–1122; b) Y. Fujiwara, I. Moritani, M. Matsuda, S. Teranishi, *Tetrahedron Lett.* **1968**, *9*, 3863–3865; c) Y. Fujiwara, I. Moritani, S. Danno, R. Asano, S. Teranishi, *J. Am. Chem. Soc.* **1969**, *91*, 7166–7169; d) Y. Fujiwara, I. Moritani, M. Matsuda, S. Teranishi, *Tetrahedron Lett.* **1968**, *9*, 633–636; e) L. Zhou, W. Lu, *Chem. Eur. J.* **2014**, *20*, 634–642.
- [12] a) M. Miura, T. Tsuda, T. Satoh, S. Pivsa-Art, M. Nomura, *J. Org. Chem.* **1998**, *63*, 5211–5215; b) T. Nishikata, B. H. Lipshutz, *Org. Lett.* **2010**, *12*, 1972–1975; c) J.-R. Wang, C.-T. Yang, L. Liu, Q.-X. Guo, *Tetrahedron Lett.* **2007**, *48*, 5449–5453; d) C. S. Yi, S. Y. Yun, *Org. Lett.* **2005**, *7*, 2181–2183; e) G. Cai, Y. Fu, Y. Li, X. Wan, Z. Shi, *J. Am. Chem. Soc.* **2007**, *129*, 7666–7673; f) H. Zhang, E. M. Ferreira, B. M. Stoltz, *Angew. Chem. Int. Ed.* **2004**, *43*, 6144–6148; *Angew. Chem.* **2004**, *116*, 6270–6274.
- [13] M.-L. Louillat, A. Biafora, F. Legros, F. W. Patureau, *Angew. Chem. Int. Ed.* **2014**, *53*, 3505–3509; *Angew. Chem.* **2014**, *126*, 3573–3577.
- [14] a) S. Maity, S. Manna, S. Rana, T. Naveen, A. Mallick, D. Maiti, *J. Am. Chem. Soc.* **2013**, *135*, 3355–3358; b) A. Deb, S. Manna, A. Modak, T. Patra, S. Maity, D. Maiti, *Angew. Chem. Int. Ed.* **2013**, *52*, 9747–9750; *Angew. Chem.* **2013**, *125*, 9929–9932; c) U. Sharma, T. Naveen, A. Maji, S. Manna, D. Maiti, *Angew. Chem. Int. Ed.* **2013**, *52*, 12669–12673; *Angew. Chem.* **2013**, *125*, 12901–12905; d) T. Naveen, S. Maity, U. Sharma, D. Maiti, *J. Org. Chem.* **2013**, *78*, 5949–5954; e) S. Rana, S. Bag, T. Patra, D. Maiti, *Adv. Synth. Catal.* **2014**, *356*, 2453–2458; f) S. Maity, N. Togati, U. Sharma, D. Maiti, *Org. Lett.* **2013**, *15*, 3384–3387.
- [15] See the Supporting Information for a detailed description.
- [16] a) A. Shafiee, A. Ahond, A. M. Bui, Y. Langlois, C. Riche, P. Potier, *Tetrahedron Lett.* **1976**, *17*, 921–924; b) M. Andriantsiferana, R. Besselièvre, C. Riche, H.-P. Husson, *Tetrahedron Lett.* **1977**, *18*, 2587–2590; c) A. R. Carroll, E. Hyde, J. Smith, R. J. Quinn, G. Guymmer, P. I. Forster, *J. Org. Chem.* **2005**, *70*, 1096–1099; d) M. Amat, N. Llor, B. Checa, E. Molins, J. Bosch, *J. Org. Chem.* **2010**, *75*, 178–189.
- [17] D. Shu, W. Song, X. Li, W. Tang, *Angew. Chem. Int. Ed.* **2013**, *52*, 3237–3240; *Angew. Chem.* **2013**, *125*, 3319–3322.
- [18] CCDC 1001842 (**3i**), 1001844 (**3j**), 1001841 (**9a**), and 1001843 (**9f**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
- [19] a) E. M. Simmons, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2012**, *51*, 3066–3072; *Angew. Chem.* **2012**, *124*, 3120–3126; b) M. Gómez-Gallego, M. A. Sierra, *Chem. Rev.* **2011**, *111*, 4857–4963; c) K. B. Wiberg, *Chem. Rev.* **1955**, *55*, 713–743; d) J. J. Gajewski, N. D. Conrad, *J. Am. Chem. Soc.* **1979**, *101*, 6693–6704; e) F. H. Westheimer, *Chem. Rev.* **1961**, *61*, 265–273.
- [20] For the oxidation of Pd⁰ to Pd^{II} by O₂, see: a) D. Wang, Y. Izawa, S. S. Stahl, *J. Am. Chem. Soc.* **2014**, *136*, 9914–9917; b) M. M. Konnick, N. Decharin, B. V. Popp, S. S. Stahl, *Chem. Sci.* **2011**, *2*, 326–330; c) Y. Izawa, D. Pun, S. S. Stahl, *Science* **2011**, *333*, 209–213; d) A. N. Campbell, P. B. White, I. A. Guzei, S. S. Stahl, *J. Am. Chem. Soc.* **2010**, *132*, 15116–15119; e) B. V. Popp, S. S. Stahl, *Chem. Eur. J.* **2009**, *15*, 2915–2933; f) S. S. Stahl, J. L. Thorman, R. C. Nelson, M. A. Kozee, *J. Am. Chem. Soc.* **2001**, *123*, 7188–7189.