Advanced Synthesis & Catalysis

FULL PAPERS

Very Important Publication

DOI: 10.1002/adsc.201500967

Palladium-Catalyzed Divergent Arylation with Triazolopyridines: One-Pot Synthesis of 6-Aryl-2-α-styrylpyridines

Youngtaek Moon,[a,b] Soonhyung Kwon,[a,b] Dahye Kang,[a,b] Honggu Im,[a,b] and Sungwoo Hong[a,b,*]

[a] Department of Chemistry, Korea Advanced Institute of Science and Technology, Daejeon 305-701, Korea
Fax: (+82)-42-350-2810; phone: (+82)-42-350-2811; e-mail: hongorg@kaist.ac.kr
[b] Center for Catalytic Hydrocarbon Functionalization, Institute for Basic Science (IBS), Daejeon 305-701, Korea

Received: October 17, 2015; Revised: November 25, 2015; Published online: January 25, 2016

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201500967.

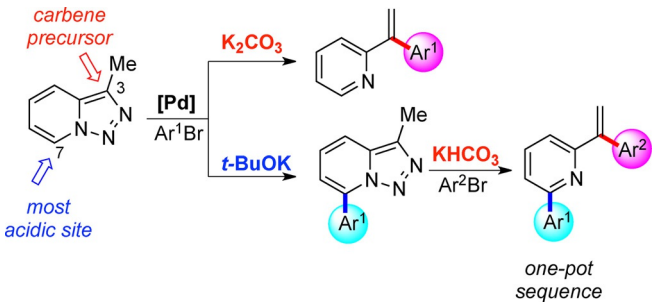
Abstract: We have developed a new strategy for palladium-catalyzed arylation reactions with triazolopyridines, wherein two different chemical transformations (C-3 *vs.* C-7) are observed by differentiating the substrates using different bases. The reactive palladium carbenoids were directly generated from triazolopyridines and underwent denitrogenative arylations with aryl bromides. Intriguingly, when potassium carbonate was replaced with potassium *tert*-butoxide, direct C–H arylation occurred at the most acidic position (C-7). Moreover, two different catalytic arylation events were successfully performed in a one-pot sequence, providing a convenient access to 6-aryl-2-α-styrylpyridines.

Keywords: arylation; carbenes; one-pot reaction; palladium; triazolopyridines

Introduction

The utilization of the 1,2,3-triazole group as a versatile reactive platform for a variety of useful synthetic transformations has been a field of intense research.[1,2] Based on the ability of the triazole moiety to exist in a closed/open form, triazolopyridines can serve as versatile pyridyl carbene precursors for the construction of nitrogen-containing heterocyclic compounds *via* transition metal catalyzed denitrogenative transformations.[3] Important advances have been made with the use of triazolopyridines as precursors of rhodium or copper carbenes to afford valuable pyridine-containing compounds.[4,5] Despite the advances reported thus far, the direct introduction of (hetero)arenes *via* the Pd-catalyzed migratory insertion of an aryl group into triazoles has not been reported previously.

We envisioned that a variety of (hetero)aryl groups could be installed for the synthesis of 2-α-styrylpyridines by trapping the pyridyl carbenes derived from triazolopyridines with a Pd catalyst,[6] if the Lewis basicity of the pyridine nitrogen is attenuated *via* coordination of a Lewis acid to the pyridyl nitrogen atom. We also hypothesized that the reaction site could be switchable to the most acidic position (C-7) in the triazolopyridines *via* a base-assisted deprotonation mechanism; subsequent transfer of an aryl group could then afford C-7 arylated products.[7] Herein, we report a new strategy for the Pd-catalyzed arylation with triazolopyridines, wherein divergent reaction pathways between positions C-3 and C-7 are observed by differentiating substrates using different bases. Moreover, despite the mechanistic dichotomy, two different catalytic arylation events could be successfully linked in a one-pot sequence with a single Pd catalyst to afford valuable 6-aryl-2-α-styrylpyridine compounds (Scheme 1).



Scheme 1. Pd-catalyzed arylation with triazolopyridines.

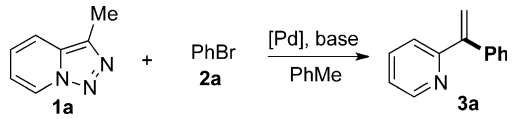
Results and Discussion

First, the feasibility of the denitrogenative arylation of triazolopyridines was tested using the Pd-catalyzed cross-coupling reaction with aryl bromides for the synthesis of 2-α-styrylpyridines (Table 1).[8] After surveying some potential catalytic systems, the use of a catalytic system consisting of $Pd(OAc)_2$, Xphos, and K_2CO_3 was found to initiate the denitrogenative arylation to afford the desired product **3a** but only in an 8% yield (Table 1, entry 2). Thorough ligand screening was conducted and we found that Cy_3P exhibited a much better perfomance (50%, entry 3). No productive reaction was observed with the Rh or Cu catalytic systems, which were employed previously in the denitrogenative transformations of triazolopyridines.[4,5] The base source was also critical for the coupling efficiency, and K_2CO_3 was the most effective for promoting the reactions. Diminished yields were observed, except under reaction conditions that employed toluene as the solvent. Among the Pd sources tested, $(Cy_3P)_2PdCl_2$ (5 mol%) was found to be an optimal catalyst with minimal formation of side products (entry 6). Considering the potential interference of the Lewis basic N-atom of the pyridine moiety with the Pd catalyst,[9] we screened a variety of additives to diminish the Lewis basicity of the pyridine or triazole moiety. During optimization of the reaction conditions, we discovered that $Ni(OAc)_2{\cdot}4H_2O$ (0.1 equiv.) was critical for optimal results (81%, entry 8). Control experiments verified that no reaction occurred without a Pd catalyst, which indicated that Ni-catalyzed coupling was unlikely to be operative (entry 11).

After determining the optimal reaction conditions, we set up a series of experiments to investigate the scope of the triazolopyridines (Table 2). The present methodology was amenable to the presence of a variety of both electron-donating and electron-withdrawing groups, affording the desired products (**3a–l**). In case of the C-7 CF_3-substituted triazolopyridine, the resulting α-styrylpyridine product underwent further the Mizoroki–Heck reaction,[10] leading to 1,2-diphenyl product **3m**.[11] Expanding the scope from the pyridine to the pyrimidyl and pyrazinyl motifs, which are useful for medicinal chemistry, was also possible, leading to the formation of **3o** and **3p**. Substrates bearing ethyl, and phenyl groups at the R^2 position were successfully converted into the *E*-selective adducts (**3q–3s**).

Subsequently, we examined the scope of this new method with respect to the aryl bromides (Table 3). We observed that the coupling of the triazolopyridine worked well with a wide range of aryl bromides bearing electron-neutral, electron-donating, and electron-

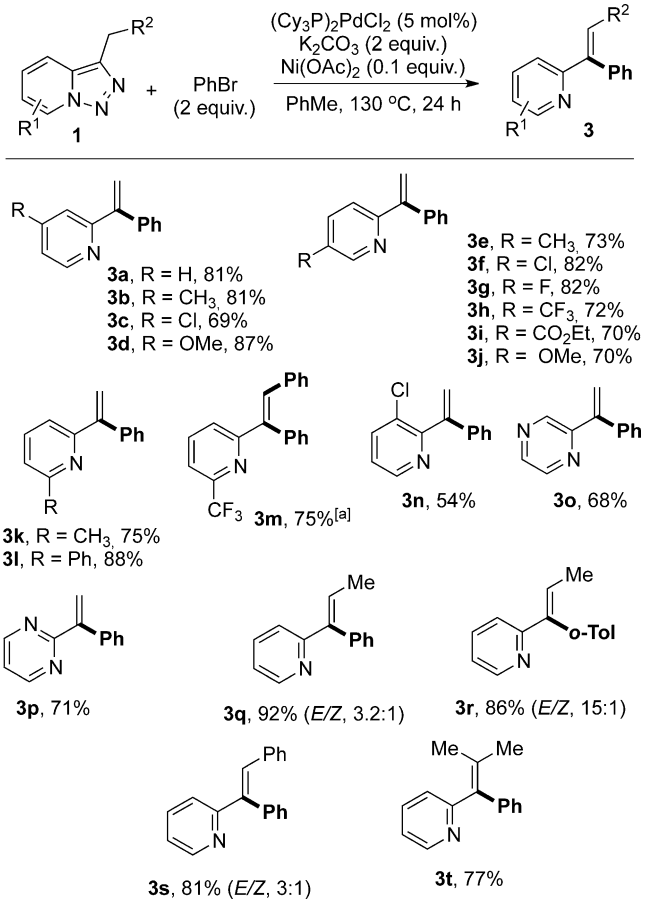
Table 1. Optimization of Pd-catalyzed denitrogenative arylation conditions.[a]



Entry	Pd (5 mol%)	Base (2 equiv.)	Ligand or Additive (0.1 equiv.)	Yield [%]
1	$Pd(OAc)_2$	K_2CO_3	–	–
2	$Pd(OAc)_2$	K_2CO_3	XPhos	8
3	$Pd(OAc)_2$	K_2CO_3	Cy_3P	50
4	$Pd(OAc)_2$	Cs_2CO_3	Cy_3P	6
5	$Pd(TFA)_2$	K_2CO_3	Cy_3P	48
6	$(Cy_3P)_2PdCl_2$	K_2CO_3	–	53
7	$(Cy_3P)_2PdCl_2$	K_2CO_3	$Zn(OAc)_2$	60
8	**$(Cy_3P)_2PdCl_2$**	**K_2CO_3**	**$Ni(OAc)_2{\cdot}4H_2O$**	**81**
9	$(Cy_3P)_2PdCl_2$	K_2CO_3	$Mn(OAc)_2{\cdot}4H_2O$	71
10	$Pd(OAc)_2$	K_2CO_3	Cy_3P/ $Ni(OAc)_2{\cdot}4H_2O$	70
11	–	K_2CO_3	$Ni(OAc)_2{\cdot}4H_2O$	0

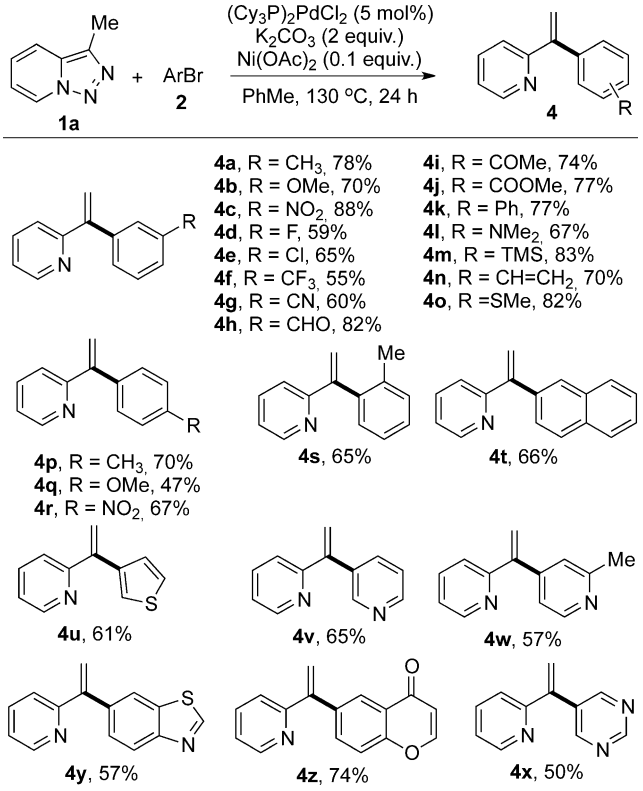
[a] **1a**, (0.1 mmol), **2a** (0.2 mmol), Pd (5 mol%), base (0.2 mmol), and additive (10 mol%) in PhMe (1.5 mL) at 130 °C under N_2 for 24 h; isolated yields. XPhos = 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl, Cy_3P = tricyclohexylphosphine, TFA = trifluoroacetate.

Table 2. Substrate scope of triazolopyridines.



[a] 4 equiv. of PhBr were used.

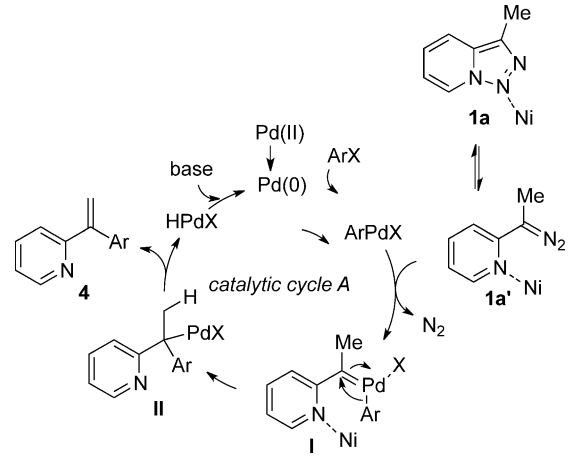
Table 3. Substrate scope of aryl bromides.



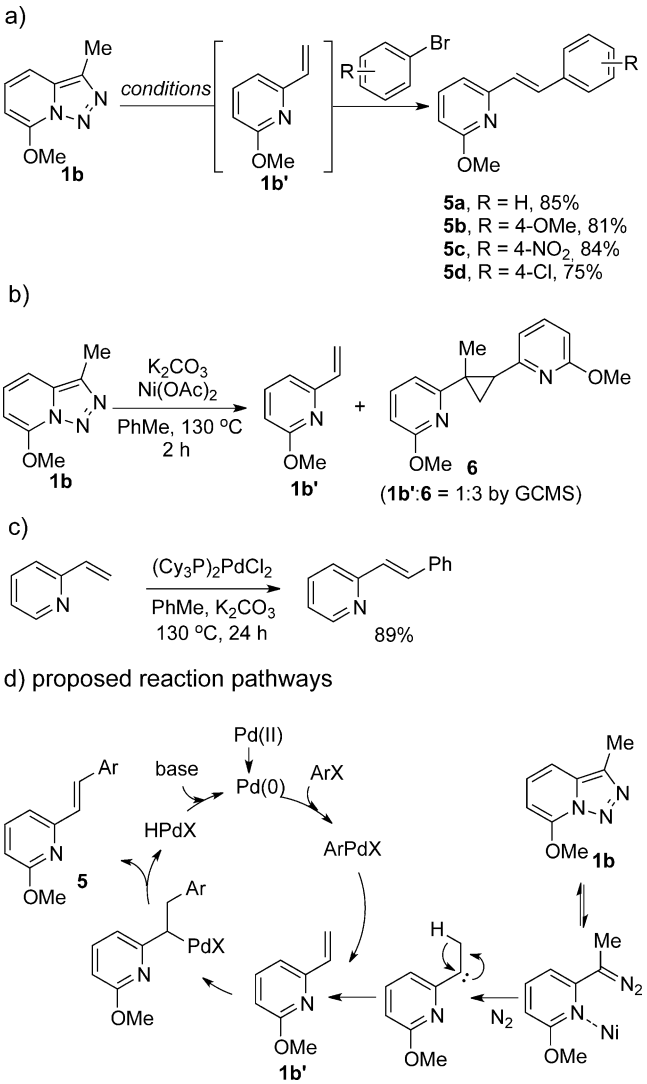
withdrawing groups that are commonly encountered in organic synthesis. The 2-bromonaphthalene substrate was also suitable for this transformation, and the desired product **4t** was obtained in good yield. In view of the frequency of heterocyclic analogs within biologically active molecules, we further investigated heteroaryl substrates and were pleased to observe that this method was further extended using a series of heteroaryl groups, including thiophene (**4u**), pyridines (**4v** and **4w**), pyrimidine (**4x**), benzothiazole (**4y**), and chromone (**4z**).

A plausible mechanism for the Pd-catalyzed denitrogenative arylation of triazolopyridines with aryl bromides is shown in Scheme 2. Oxidative addition initiates the catalytic cycle, generating an organopalladium species. Next, a reactive Pd-carbene complex **I** is formed *via* the reaction of an arylpalladium species with the *in situ*-generated diazo imine **1a′**. Nickel ions may coordinate to the pyridyl nitrogen atom in a diazo form and facilitate Pd-carbene formation. The resulting complex **I** can undergo migratory insertion of the aryl group to give the alkylpalladium species **II**. Subsequent β-hydride elimination provides the desired coupled product **4** and regenerates the Pd(0) catalyst with the aid of the base.

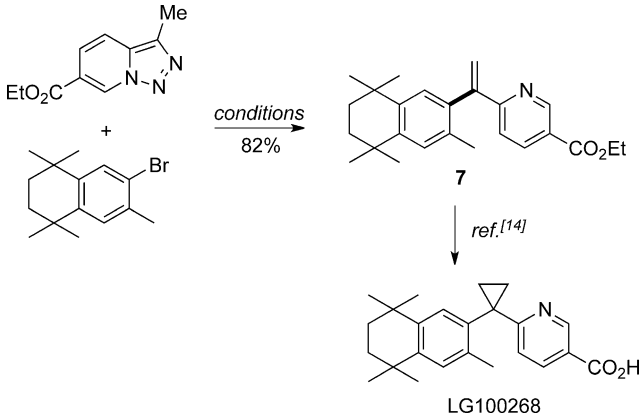
Unexpectedly, the *endo*-olefin products **5a**–**5d** were obtained with the C-7 methoxy-substituted triazolopyridine **1b** (Scheme 3a). A control experiment



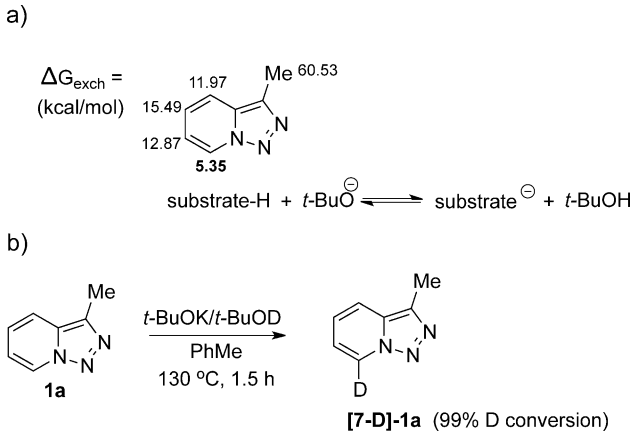
Scheme 2. Plausible mechanism for Pd-catalyzed denitrogenative arylation.



Scheme 3. Reactions of 7-MeO-substituted triazolopyridine with aryl bromides.



Scheme 4. Synthesis of LG100268.



Scheme 5. a) Calculated B3LYP/6-311++G(2df,2p) free energies for the deprotonation of each C–H bonds of substrate. b) H/D exchange experiment.

showed that the mixture of alkene **1b′** and cyclopropyl product **6** could be detected in the absence of Pd and aryl bromide (Scheme 3b). The cyclopropyl product **6** is presumably generated from the reaction of the *in situ* generated carbene with an alkene intermediate. The introduction of a methoxy group at C-7 appears to facilitate the formation of the reactive diazo form,[4a,12] thus spontaneously generating the carbene and alkene intermediates.[13] These observations suggest that the alkene intermediate **1b′**, which is rapidly formed *in situ via* the 1,2-H shift of the carbene intermediate, reacts with the arylpalladium species to afford Heck-type products **5a**–**5d** (Scheme 3d).

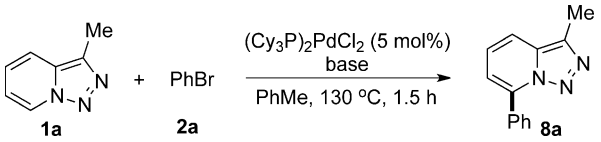
To further showcase the synthetic applicability, this method was employed as a straightforward synthetic route to the selective retinoid X receptor agonist LG100268.[14] Thus, a key intermediate **7** of LG100268 was efficiently prepared (82%), *via* Pd-catalyzed denitrogenative cross-coupling (Scheme 4).

After successfully achieving the Pd-catalyzed denitrogenative arylation, we speculated that the direct C–H arylation of the triazolopyridine could be achieved by taking advantage of the inherent electronic characteristics of this core.[7] Thus, we performed computational studies with density functional theory calculations, showing that the Gibbs free energy for the deprotonation of C-7–H is particularly low (Scheme 5a).[13] Additionally, the H/D exchange experiment revealed that the most acidic site of the triazolopyridines is the C-7 position.

These observations prompted us to explore the feasibility of the installation of an aryl group at the C-7 position in the triazolopyridines *via* the presumed base-assisted deprotonation mechanism. We investigated a possible collection of C–H arylation conditions using the Pd catalytic system and phenyl bromide by evaluating the effect of different bases (Table 4). We found that the C-7 arylated product could be obtained in a 62% yield using KHMDS (entry 3). As predicted, the choice of base had a significant effect on the reactivity, and *t*-BuOK was the most effective for promoting the reactivity (88% yield, entry 4). Interestingly, usage of other bases led to lower yields presumably as a result of competitive ring-opening decomposition.[12] Moreover, no formation of C-3 denitrogenative arylation by-product was observed under the reaction conditions. A diminished conversion rate was observed when the reaction temperature was decreased to 100 or 80 °C (entry 5).

Next, we explored the scope of both triazolopyridine and aryl bromide substrates by conducting direct C-7–H arylation reactions (Table 5). We found that this catalytic system was amenable to a range of functional groups such as alkyl, methoxy, trifluoromethyl, dimethylamino, phenyl, and chloro groups under the optimized conditions, leading to the formation of

Table 4. Discovery and optimization of Pd-catalyzed C-7 arylation.[a]



Entry	Base (2 equiv,)	Temp. [°C]	Time [h]	Yield [%]
1	LiOEt	130	1.5	NR
2	*t*-BuONa	130	1.5	NR
3	KHMDS	130	1.5	62
4	***t*-BuOK**	**130**	**1.5**	**88**
5	*t*-BuOK	80	7	70
6	LiHMDS	130	1.5	NR
7	Cs_2CO_3	130	1.5	72
8	NaH	130	1.5	63
9	K_2CO_3	130	1.5	NR

[a] **1a**, (0.1 mmol), **2a** (0.2 mmol), Pd (5 mol%), base (2 equiv.), in PhMe (1.5 mL) at 130 °C under N_2; isolated yields.

Table 5. Substrate scope for C-7 arylation of triazolopyridine.

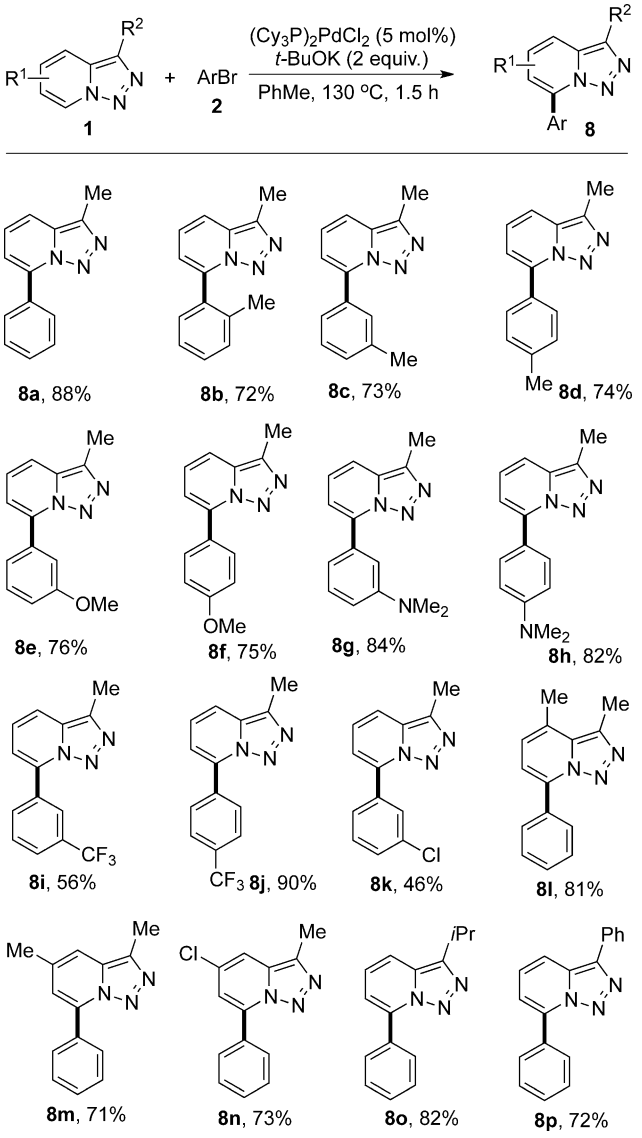
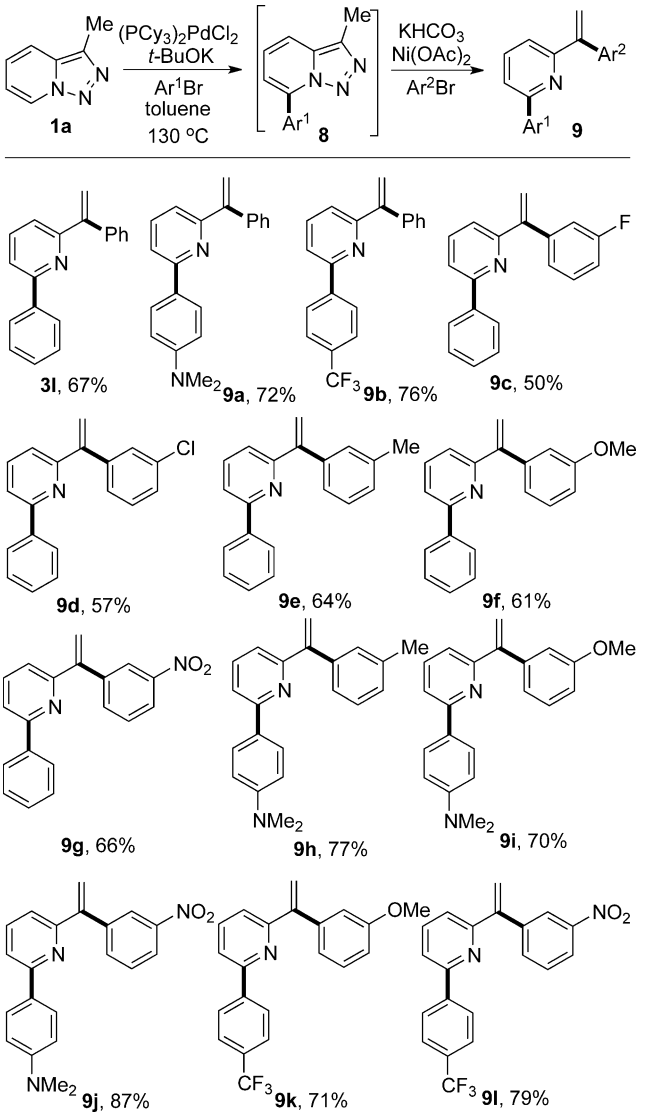


Table 6. One-pot reaction.[a]

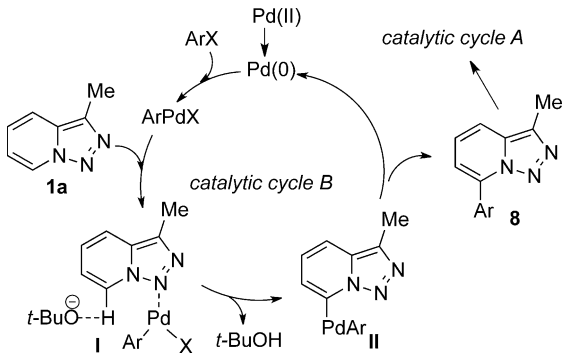


[a] **1a**, (0.1 mmol), Ar^1Br (0.11 mmol), $(Cy_3P)_2PdCl_2$ (10 mol%), and *t*-BuOK (0.2 mmol) in PhMe (1.5 mL) at 130 °C under N_2 for 1.5 h; Ar^2Br (0.2 mmol), $KHCO_3$ (0.2 mmol), and $Ni(OAc)_2{\cdot}4H_2O$ (10 mol%) for 24 h.

a series of C-7 arylated triazolopyridines in good to excellent yields.

We next preliminarily investigated the utility of this approach for the controlled installation of two different aryl groups in a one-pot procedure because the resulting C-7 aryltriazolopyridines are prone to undergo the Pd-catalyzed denitrogenative arylation reaction (e.g., **3l** in Table 2). Indeed, we were delighted to observe that the one-pot catalytic process was facile under slightly modified reaction conditions in which $KHCO_3$ was employed to remove the reactive *tert*-butoxide anion. The second half event operates sequentially *via* the *in situ* generated K_2CO_3 from *t*-BuOK and $KHCO_3$.[15] As demonstrated in Table 6, a series of substrates effectively underwent a one-pot process, in which two different aryl groups are introduced for the construction of diversely functionalized 6-aryl-2-α-styrylpyridines.

A plausible mechanism for the one-pot reaction is shown in Scheme 6. The initial addition of Pd(II) to C-7 would proceed *via* a base-assisted C–H deprotonation–palladation mechanism, leading to the C-7 palladated species **I**. The subsequent reductive elimination of **II** delivered the C-7 arylated triazolopyridine, which was then engaged in the Pd-catalyzed denitrogenative arylation event in the second catalytic cycle.



Scheme 6. Proposed reaction pathways for one-pot catalysis.

Conclusions

In summary, we have developed a new and versatile synthetic strategy for the Pd-catalyzed arylation with triazolopyridines. The synthetic utility of this approach has been verified *via* two different chemical transformations (C-3 *vs.* C-7) from the same set of substrates, which were achieved by differentiating each event using different bases. Moreover, two concurrent arylation events successfully proceeded in the one-pot process with a single Pd catalyst, providing a new straightforward route to 6-aryl-2-α-styrylpyridines of high synthetic utility.

Experimental Section

General Procedure for Synthesis of 2-(1-Phenylvinyl)-pyridine Derivatives

Triazolopyridine (0.1 mmol), aryl bromide (0.2 mmol), $(Cy_3P)_2PdCl_2$ (5 mol%), K_2CO_3 (2 equiv.), and $Ni(OAc)_2{\cdot}4H_2O$ (0.1 equiv.) were combined in anhydrous PhMe (1.5 mL) under nitrogen condition in a sealed tube. The reaction mixture was stirred at 130 °C for 24 h. The mixture was monitored by TLC using EtOAc and *n*-hexane = 1:2 as the mobile phase and stirred until the starting material disappeared. After being cooled to room temperature, the mixture solvent was removed under reduced pressure. The reaction mixture was diluted with CH_2Cl_2 and the residue was extracted with aqueous NH_4Cl (3 × 30 mL). The organic layer was dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography on silica gel to give desired product.

Full characterization data and copies of relevant spectra are provided in the Supporting Information.

General Procedure for 7-Arylation of Triazolopyridine

Triazolopyridine (0.1 mmol), aryl bromide (0.2 mmol), $(Cy_3P)_2PdCl_2$ (5 mol%), and KO-*t*-Bu (2 equiv.) were combined in anhydrous PhMe (1.5 mL) under nitrogen condition in a seal tube. The reaction was stirred at 130 °C for 1.5 h. The mixture was monitored by TLC using EtOAc and *n*-hexane = 1:2 as the mobile phase and stirred until starting material disappeared. After cooled to room temperature, the mixture solvent was removed under reduced pressure. The reaction mixture was diluted with CH_2Cl_2 and the residue was extracted with aqueous NH_4Cl (3 × 30 mL). The organic layer was dried over $MgSO_4$. After removal of solvent, the residue was purified by flash chromatography on silica gel to give desired product.

Full characterization data and copies of relevant spectra are provided in the Supporting Information.

General Procedure for One-Pot Synthesis of 6-Phenyl-2-α-styrylpyridines

Triazolopyridine (0.1 mmol), Ar^1Br (0.11 mmol), $(Cy_3P)_2PdCl_2$ (10 mol%), and KO-*t*-Bu (2 equiv.) were combined in anhydrous PhMe (1.5 mL) under nitrogen n a sealed tube. The reaction mixture was stirred at 130 °C for 1.5 h. The mixture was monitored by TLC using EtOAc and *n*-hexane = 1:2 as the mobile phase and stirred until the starting material disappeared. After being cooled to room temperature, $KHCO_3$ (0.2 mmol), $Ni(OAc)_2{\cdot}4H_2O$ (0.1 equiv.), and Ar^2Br (0.2 mmol) were added. The reaction mixture was stirred at 130 °C for 24 h under nitrogen. The mixture was monitored by TLC using EtOAc and *n*-hexane = 1:5 as the mobile phase and stirred until the intermediate disappeared. After being cooled to room temperature, the mixture solvent was removed under reduced pressure. The reaction mixture was diluted with CH_2Cl_2 and the residue was extracted with aqueous NH_4Cl (3 × 30 mL). The organic layer was dried over $MgSO_4$. After removal of solvent, the residue was purified by flash chromatography on silica gel to give desired product.

Full characterization data and copies of relevant spectra are provided in the Supporting Information.

Acknowledgements

This research was supported financially by the Institute for Basic Science (IBS-R010-G1).

References

[1] For selected recent reviews, see: a) S. R. Chemler, P. H. Fuller, *Chem. Soc. Rev.* **2007**, *36*, 1153; b) M. Schlosser, F. Mongin, *Chem. Soc. Rev.* **2007**, *36*, 1161; c) J. Wencel-Delord, T. Drçge, F. Liu, F. Glorius, *Chem. Soc. Rev.* **2011**, *40*, 4740; d) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068; e) J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem.* **2012**, *124*, 9092; *Angew. Chem. Int. Ed.* **2012**, *51*, 8960; f) J. Wencel-Delord, F. Glorius, *Nat. Chem.* **2013**, *5*, 369.

[2] For selected recent reviews, see: a) A. V. Gulevich, V. Gevorgyan, *Angew. Chem.* **2013**, *125*, 1411; *Angew. Chem. Int. Ed.* **2013**, *52*, 1371; b) H. M. L. Davies, J. S. Alford, *Chem. Soc. Rev.* **2014**, *43*, 5151; c) B. Chattopadhyay, V. Gevorgyan, *Angew. Chem.* **2012**, *124*, 886; *Angew. Chem. Int. Ed.* **2012**, *51*, 862.

[3] For selected examples, see: a) D. J. Lee, H. S. Han, J. Shin, E. J. Yoo, *J. Am. Chem. Soc.* **2014**, *136*, 11606; b) H. J. Jeon, D. J. Jung, J. H. Kim, Y. Kim, J. Bouffard, S. Lee, *J. Org. Chem.* **2014**, *79*, 9865; c) J. E. Spangler, H. M. L. Davies, *J. Am. Chem. Soc.* **2013**, *135*, 6802; d) B. T. Parr, S. A. Green, H. M. L. Davies, *J. Am. Chem. Soc.* **2013**, *135*, 4716; e) M. Zibinsky, V. V. Fokin, *Angew. Chem.* **2013**, *125*, 1547; *Angew. Chem. Int. Ed.* **2013**, *52*, 1507; f) N. Selander, B. T. Worrell, S. Chuprakov, S. Velaparthi, V. V. Fokin, *J. Am. Chem. Soc.* **2012**, *134*, 14670; g) T. Miura, T. Biyajima, T. Fujii, M. Murakami, *J. Am. Chem. Soc.* **2012**, *134*, 194; h) T. Miura, Y. Funakoshi, M. Morimoto, T. Biyajima, M. Murakami, *J. Am. Chem. Soc.* **2012**, *134*, 17440; i) N. Selander, B. T. Worrell, V. V. Fokin, *Angew. Chem.* **2012**, *124*, 13231; *Angew. Chem. Int. Ed.* **2012**, *51*, 13054; j) N. Grimster, L. Zhang, V. V. Fokin, *J. Am. Chem. Soc.* **2010**, *132*, 2510; k) T. Miura, M. Yamauchi, A. Kosaka, M. Murakami, *Angew. Chem.* **2010**, *122*, 5075; *Angew. Chem. Int. Ed.* **2010**, *49*, 4955; l) I. Bae, H. Han, S. Chang, *J. Am. Chem. Soc.* **2005**, *127*, 2038; m) S. H. Cho, E. J. Yoo, I. Bae, S. Chang, *J. Am. Chem. Soc.* **2005**, *127*, 16046.

[4] For selected recent reviews, see: a) I. V. Seregin, V. Gevorgyan, *Chem. Soc. Rev.* **2007**, *36*, 1173; b) A. V. Gulevich, A. S. Dudnik, N. Chernyak, V. Gevorgyan, *Chem. Rev.* **2013**, *113*, 3084.

[5] J. H. Kim, T. Gensch, D. Zhao, L. Stegemann, C. A. Strassert, F. Glorius, *Angew. Chem.* **2015**, *127*, 11126; *Angew. Chem. Int. Ed.* **2015**, *54*, 10957.

[6] For selected examples of Pd-catalyzed arylation reactions with diazo compounds, see: a) J. Barluenga, P. Moriel, C. Valdés, F. Aznar, *Angew. Chem.* **2007**, *119*, 5683; *Angew. Chem. Int. Ed.* **2007**, *46*, 5587; b) C. Peng, Y. Wang, J. Wang, *J. Am. Chem. Soc.* **2008**, *130*, 1566; c) J. Barluenga, M. Escribano, F. Aznar, C. Valdés, *Angew. Chem.* **2010**, *122*, 7008; *Angew. Chem. Int. Ed.* **2010**, *49*, 6856; d) X. Zhao, J. Jing, K. Lu, Y. Zhang, J. Wang, *Chem. Commun.* **2010**, *46*, 1724; e) Y.-T. Tsoi, Z. Zhou, A. S. C. Chan, W.-Y. Yu, *Org. Lett.* **2010**, *12*, 4506.

[7] a) R. B. Bedford, S. J. Durrant, M. Montgomery, *Angew. Chem.* **2015**, *127*, 8911; *Angew. Chem. Int. Ed.* **2015**, *54*, 8787; b) Y. Boutadla, D. L. Davis, S. A. Macgregor, A. I. Poblador-Bahamonde, *Dalton Trans.* **2009**, 5820; c) S. Liu, J. Sawicki, T. G. Driver, *Org. Lett.* **2012**, *14*, 3744.

[8] See the Supporting Information for more details. Note that the transformation was not successful when ArCl was used as an arylating reagent.

[9] a) H. A. Malik, B. L. H. Taylor, J. R. Kerrigan, J. E. Grob, K. N. Houk, J. Du Bois, L. G. Hamanna, A. W. Patterson, *Chem. Sci.* **2014**, *5*, 2352; b) Y.-J. Liu, H. Xu, W.-J. Kong, M. Shang, H.-X. Dai, J.-Q. Yu, *Nature* **2014**, *515*, 389.

[10] a) T. Mizoroki, K. Mori, A. Ozaki, *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581; b) R. F. Heck, J. P. Nolley Jr, *J. Org. Chem.* **1972**, *37*, 2320.

[11] S. Oi, K. Sakai, Y. Inoue, *Org. Lett.* **2005**, *7*, 4009.

[12] B. Abarca, R. Ballesteros, F. Mojarred, G. Jones, D. J. Mouat, *J. Chem. Soc. Perkin Trans. 1* **1987**, 1865.

[13] For details of the computational studies, see the Supporting Information.

[14] a) D. S. Lala, R. Mukherjee, I. G. Schulman, S. S. C. Koch, L. J. Dardashti, A. M. Nadzan, G. E. Croston, R. M. Evans, R. A. Heyman, *Nature* **1996**, *383*, 450; b) H. Yoshida, Y. Takemoto, K. Takaki, *Chem. Commun.* **2014**, *50*, 8299.

[15] Removal of the reactive *tert*-butoxide anion was crucial for the Pd-catalyzed denitrogenative arylation reaction and the addition of K_2CO_3 was not effective for a one-pot procedure.

