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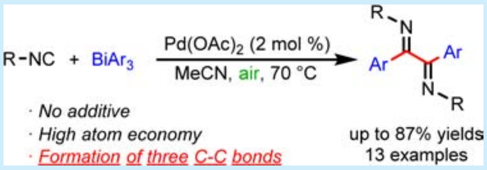
Palladium-Catalyzed Synthesis of α-Diimines from Triarylbismuthines and Isocyanides

Yohsuke Kobiki, Shin-ichi Kawaguchi, and Akiya Ogawa*

Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University, 1-1 Gakuen-cho, Nakaku, Sakai, Osaka 599-8531, Japan

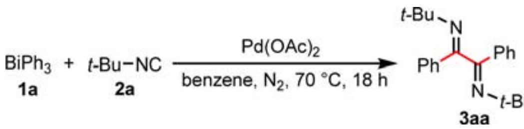
Supporting Information

ABSTRACT: In this study, we report a highly selective coupling reaction between triarylbismuthines and isocyanides using palladium diacetate as the catalyst, affording α-diimines, with the formation of three C−C bonds. Among several aryl sources ($Ar-YL_n$: Y = B, Sn, Pb, Sb, Bi, I), only triarylbismuthines successfully undergo coupling with isocyanides to selectively afford α-diimines. The coupling reaction exhibits the advantages of high atom economy and convenient operation, with no need for any additive.



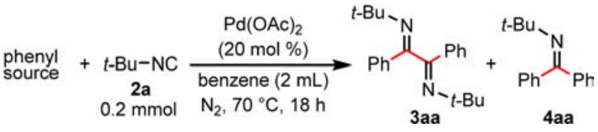
Organic isocyanides have been reported to be attractive sources of carbon and nitrogen for use in organic synthesis,[1] and a number of imine derivatives and N-containing heterocycles have been synthesized using isocyanides as starting materials. For these transformations in particular, transition-metal-catalyzed reactions of isocyanides are useful tools.[2] However, only a few examples of the double insertion of isocyanides in the presence of catalysts have been reported,[3,4] because generally isocyanides are easily oligomerized in the presence of transition-metal compounds.[5]

On the other hand, triarylbismuthines ($BiAr_3$) have been used as an effective, environmentally friendly aryl source for some arylation reactions[6] because of their low toxicity[7] and low bond-dissociation energy of the Bi−C bond.[8] In particular, the latter property allows for transmetalation between $BiAr_3$ and transition-metal complexes, affording the M−Ar bond in situ.[9] As isocyanides can smoothly insert into the Pd−C bond, imine derivatives can be obtained by the reaction of $BiAr_3$ with isocyanides in the presence of a palladium catalyst. Interestingly, the reaction between triphenylbismuthine (**1a**) and *tert*-butyl isocyanide (**2a**) in the presence of palladium(II) acetate selectively afforded α-diimine **3aa**, which consists of two imine moieties and two phenyl groups (eq 1). In this synthesis of α-diimines, three carbon−carbon bonds are successfully formed simultaneously. α-Diimines are known to be typical π-acceptor ligands;[10] their metal complexes have been used in several catalytic reactions.[11] Thus, we believed that the above reaction is an effective synthetic route to α-diimines and investigated the proposed method in detail.



(1)

Table 1. Reaction of Phenyl Sources with Isocyanide 2a[a]



entry	phenyl source	yield of **3aa**[b]	yield of **4aa**[b]
1	$BiPh_3$ (**1a**, 0.2 mmol)	90%	9%
2	$PhB(OH)_2$ (**5a**, 0.6 mmol)	3%	trace
3	PhBpin (**5b**, 0.6 mmol)	4%	trace
4	PhI (**6**, 0.2 mmol)	ND	ND
5[c]	$SbPh_3$ (**7**, 0.2 mmol)	18%	0%
6[c]	$SnPh_4$ (**8**, 0.2 mmol)	15%	ND
7	$PbPh_4$ (**9**, 0.2 mmol)	28%	72%
8	$PbPh_4$ (**9**, 0.1 mmol)	19%	65%

[a] Bpin = boronic acid pinacol ester. [b] Determined by ^1H NMR. ND = not detected. [c] A complex mixture was also formed.

First, we investigated the synthesis of α-diimines by using different aryl sources (Table 1). The use of phenylboronic acid (**5a**) and its pinacol ester **5b** afforded α-diimine **3aa** in low yield (entries 2 and 3, respectively), while phenyl iodide (**6**) did not afford **3aa** (entry 4). Under the reaction conditions, triphenylstibine (**7**) and tetraphenylstannane (**8**) afforded complex mixtures (entries 5 and 6, respectively). On the other hand, tetraphenylplumbane (**9**), an organometallic compound containing lead, which is located in the same period as bismuth, afforded α-diimine **3aa** and imine **4aa** in good yields (entries 7 and 8, respectively). However, the selectivity of products between **3aa** and **4aa** was insufficient. $BiAr_3$ were found to be the most suitable organometallic compounds for the synthesis of α-diimines in terms of the selectivity of **3aa**, as well as toxicity.

Next, we optimized the reaction conditions of the synthesis of α-diimines using $BiAr_3$ (Table 2). The reactions between **2a** (0.4 mmol) and **1a** (1/3 equiv) were conducted in the presence of $Pd(OAc)_2$ (5 mol %) under N_2 (entry 1). α-Diimine **3aa** was

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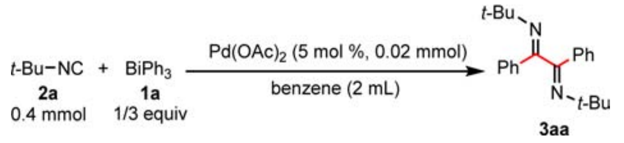
Table 2. Optimization of Reaction Conditions



entry	reaction condition	yield[a]
1	18 h, 70 °C, under N_2	24%
2	18 h, 70 °C, under air	85%
3	18 h, 70 °C, under O_2	41%
4	18 h, RT, under air	62%
5	4 h, 70 °C, under air	93%
6	2 h, 70 °C, under air	85%
7	4 h, 70 °C, under dry air[b]	88%
8	4 h, 70 °C, under air, H_2O (2 equiv)	87%
9[c]	4 h, 90 °C, under air	80%
10[d]	4 h, 70 °C, under air	>99% (80%)

[a] Determined by ^{1}H NMR (isolated yield is indicated within parentheses). [b] Air was dried by passing through P_2O_5. [c] Instead of benzene, toluene was used as the solvent. [d] Instead of benzene, MeCN was used as the solvent.

obtained as the major product with high selectivity, albeit in low yield (24%), along with minor amounts of **4aa** (4%). After the reaction, the residual bismuth precipitated as metallic bismuth. Surprisingly, the yield of **3aa** dramatically improved under air (entry 2). In entry 2, **10aa** (Figure 1, right), not **4aa**, was obtained in 8% yield as the byproduct. Moreover, when the reaction was conducted under O_2, the yields of both **4aa** and **10aa** increased (ca. 10% yield, entry 3). When the reaction was conducted at room temperature, **3aa** was obtained in moderate yield (entry 4). On the other hand, when the reaction was conducted at 70 °C, it was completed in a shorter time (4 and 2 h) (entries 5 and 6, respectively). As the reactions were conducted under air, the effect of moisture (water) on the reaction was investigated (entries 7 and 8): regardless of the presence or absence of water, the reaction afforded **3aa** in a similar yield. The effect of temperature on the reaction was also investigated, and the yield of **3aa** slightly decreased at higher temperature (entry 9). By employing the conditions listed in entry 5, the optimization of the palladium catalyst and solvent was carried out (see the Supporting Information). From the optimization results, palladium acetate and MeCN were found to be the most suitable catalyst and solvent, respectively, and **3aa** was obtained with excellent yield and selectivity (entry 10).

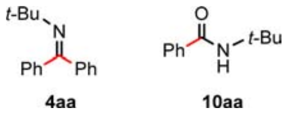
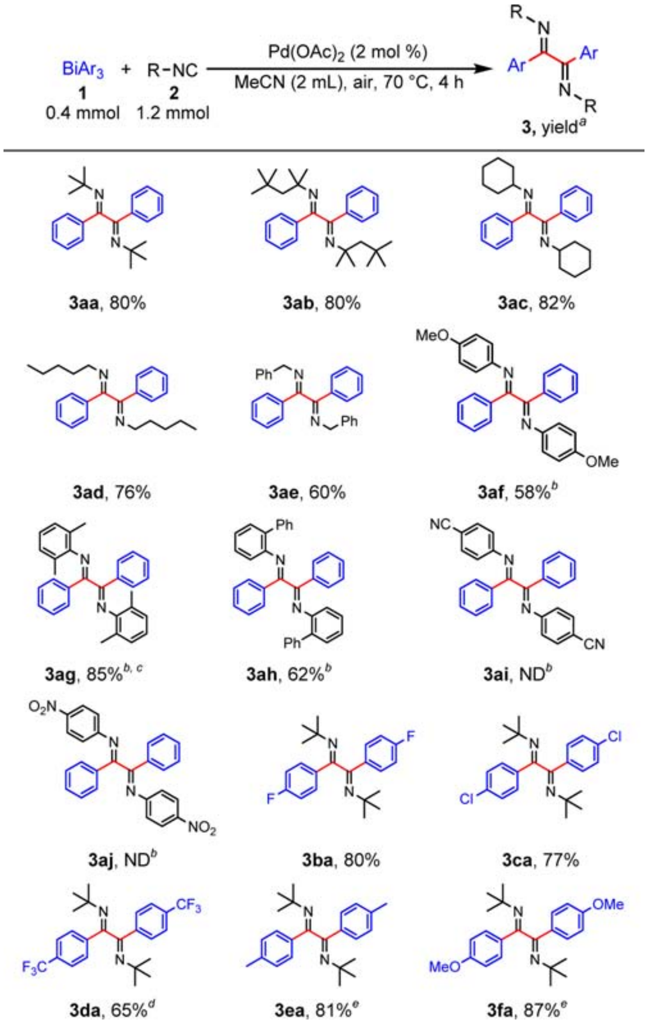


Figure 1. Byproducts in the synthetic reaction of **3aa**.

Scheme 1. Pd-Catalyzed Synthesis of α-Diimines



[a] Isolated yield. [b] Reaction conditions: **2** (0.4 mmol) and $Pd(OAc)_2$ (5 mol %) were used. Yield was calculated on the basis of the amount of **2**. [c] Obtained as mixtures of geometric isomers. [d] The reaction was conducted in toluene (2 mL) at 100 °C. [e] The reaction was conducted in benzene (2 mL).

Using the optimized conditions, we next investigated the scope of isocyanides and bismuthines (Scheme 1). Primary, secondary, and tertiary aliphatic isocyanides were applied to the palladium-catalyzed synthesis of α-diimines, and the corresponding *N*-alkylated α-diimines (**3aa**−**3ae**) were obtained in good yields. Electron-rich aromatic isocyanides such as **2f** and **2g** smoothly afforded the corresponding α-diimines. On the other hand, electron-deficient aromatic isocyanides such as **2i** and **2j** did not form imines. Moreover, $BiAr_3$ containing halogen substituents at the para position could also be used in this reaction under the optimized conditions, and the corresponding halogenated diimines **3ba** and **3ca** were obtained in high yield. The electron density of the aryl rings on bismuth strongly affected the accessibility of α-diimine **3**. For instance, when electron-deficient bismuthine such as **1d** was used, high temperature was required for the completion of the reaction, affording **3da** in moderate yield. On the other hand, electron-rich bismuthines such as **1e** and **1f** smoothly afforded the corresponding α-diimines **3ea** and **3fa**, respectively.

Before gaining insight into the possible mechanistic pathway to α-diimines from $BiAr_3$ and isocyanides, related studies are mentioned below. Organobismuth compounds have been reported to smoothly undergo transmetalation with transition metals.[9] Boschi has reported the formation of a phenylimidoyl (Ph−C(=NPh)−) ligand on palladium by the reaction between phenyl derivatives of heavy metals, such as triphenylbismuthine, and a palladium(II)-phenylisocyanide complex.[12] The ligand was probably formed by the transmetalation of triphenylbismuthine with the palladium complex, followed by the insertion of isocyanide into the Pd−C bond. Moreover, Amii has reported that α-diimines were obtained from the palladium complex bearing one arylimidoyl ligand by heating[13] and indicated that the reaction was accomplished by the intermolecular ligand exchange of the palladium complexes.

With these precedent studies, a plausible reaction pathway is proposed (Figure 2). First, a reaction between palladium(II) diacetate and isocyanide afforded a palladium(II)-isocyanide complex **A** in situ. Second, complex **A** reacts with BiAr$_3$, affording complex **B** bearing a Pd−Ar bond. Third, complex **B** is smoothly converted to arylimidoyl complex **C** by insertion of isocyanides into the Pd−Ar bond. Next, ligand exchange occur between two arylimidoyl complexes (**C**), followed by disproportionation to afford complex **A** and complex **D** bearing two arylimidoyl ligands.[14] Finally, the desired product **3** is obtained by the reductive elimination of complex **D**. The palladium(0) complex **E** is reoxidized by molecular oxygen and bismuth acetate.[15] In this reaction, residual bismuth is precipitated as metallic bismuth and a small amount of an insoluble white solid.

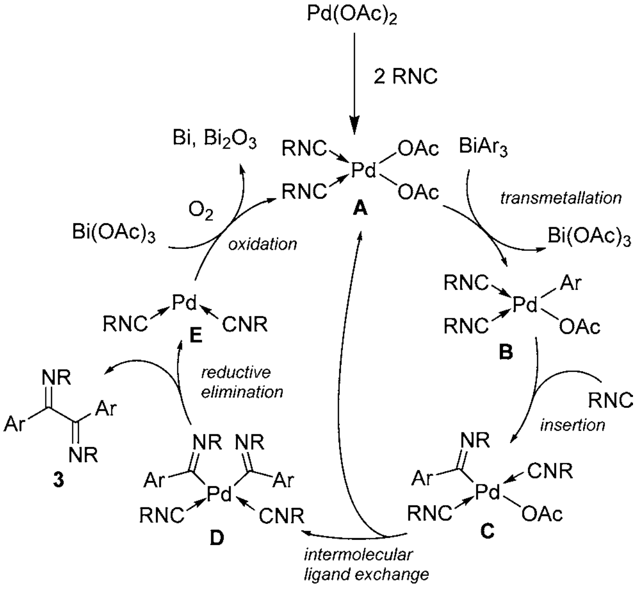


Figure 2. A plausible reaction pathway.

To confirm the formation of intermediate **C**, the reactions between **1a** and **2a** were conducted in the presence of palladium complex **11** (Figure 3). The palladium complex **11**, which was synthesized by Amii's method,[13] has a structure similar to that of complex **C** in Figure 2. Diimine **3aa** was obtained in only 13% yield. However, by the addition of potassium acetate to this reaction, the reaction smoothly proceeded, affording **3aa** in high yield. These results indicated that complex **11** acts as a precatalyst for the reactions between **1a** and **2a**, acetate is essential for the smooth progress of this reaction, and complex **C** plays a significant role in the synthesis of α-diimines. In addition, acetate anions can back onto Pd atom from Bi(OAc)$_3$.

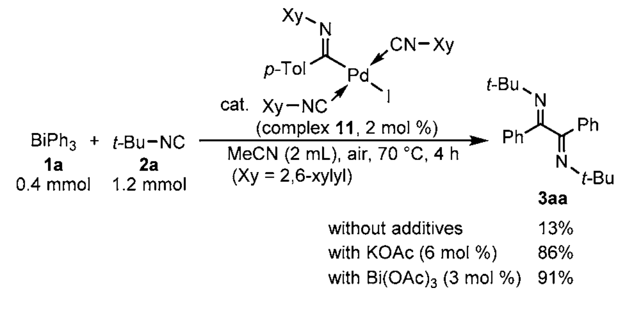


Figure 3. Reactions in the presence of complex **11**.

In conclusion, we developed a novel synthetic route to α-diimines starting from triarylbismuthines and isocyanides using palladium diacetate as the catalyst. This reaction affords symmetrical α-diimines under air without the use of additives via the formation of three carbon−carbon bonds. Of note, α-diimines are formed only when triarylbismuthines were used as organometallic reagents. The details of the reaction mechanism are currently under way.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures, spectroscopic data of all new compounds, and copies of ^{1}H and ^{13}C NMR spectra. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b01566.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: ogawa@chem.osakafu-u.ac.jp.

Notes

The authors declare no competing financial interest.

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