


# Cationic Palladium Complex-Catalyzed Diastereoselective Tandem Annulation of 2-Iminoarylboronic Acids with Substituted Alkynes: Enantioselective Synthesis of Aminoindene Derivatives by Double Asymmetric Induction

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**Abstract:** The tandem annulation reaction of 2-iminoarylboronic acids and alkynes was developed for the synthesis of aminoindene derivatives catalyzed by cationic palladium complex. In addition, an enantioselective synthesis of aminoindene derivatives from the reaction of substituted (*S*)-2-(*N*-*tert*-butanesulfinylimino)arylboronic acids with a variety of alk-

ynes catalyzed by chiral cationic palladium complex was also achieved by the double asymmetric induction.

**Keywords:** alkynes; aminoindenes; boronic acids; cationic palladium complexes; double asymmetric induction

## Introduction

Indene derivatives are useful compounds serving as building blocks for many functional materials,<sup>[1]</sup> medicines,<sup>[2]</sup> and important intermediates.<sup>[3]</sup> They can also be used as ligands for transition metal complexes.<sup>[4]</sup> There have been many reports on the synthesis of indene derivatives using transition metal-catalyzed reactions.<sup>[5]</sup> However, in sharp contrast to indanol derivatives,<sup>[5f,6]</sup> fewer examples are related to the synthesis of aminoindene derivatives, which are synthetically important targets as a result of their prevalence in natural products, pharmaceuticals, and bioactive molecules.<sup>[7]</sup> Consequently, the asymmetric synthesis of aminoindene derivatives represents an extremely important endeavor in the discovery and preparation of new pharmaceutical agents. Over the past years, Takai and co-workers have developed rhenium-based catalysts for a variety of [3+2]annulations by a tandem sequence to provide aminoindene derivatives.<sup>[8]</sup> Very recently, Zhao and Sun reported an alternative approach of rhodium-catalyzed [3+2]annulation of *N*-unsubstituted aromatic ketimines and internal alkynes based on imine-directed aromatic C–H bond activation.<sup>[9]</sup> Unfortunately, the asymmetric version has not been explored to give the more important chiral aminoindene derivatives.

Transition metal-catalyzed reactions of organometallic reagents with imines provide powerful approaches toward the synthesis of amines.<sup>[10]</sup> Special attention was concentrated to palladium-based catalysts as they provide versatile possibilities for carbon-carbon bond formation.<sup>[11]</sup> Several features of this chemistry make it attractive including the availability and stability of the substrates, the wide functional group tolerance as well as the potential application to asymmetric synthesis.<sup>[12]</sup> Recently, our group has developed a series of addition reactions of arylboronic acids to carbon-heteroatom multiple bonds catalyzed by Pd(II) species.<sup>[10j,13]</sup> In all of these systems, a Pd(II) species was used without the use of any redox system which is indispensable in many Pd(0)-catalyzed reactions. However, the successful examples of targeting 2-iminoarylboronic acids as the substrates are quite limited. Therefore, it is an appealing and challenging project to use these substrates to achieve the synthesis of aminoindene derivatives by successive intramolecular cyclization with simple alkynes in a catalytic way.

Herein we wish to describe an efficient route for the synthesis of aminoindene derivatives based on the cationic palladium complex-catalyzed annulation of 2-iminoarylboronic acids and substituted alkynes. Furthermore, the asymmetric version of the reaction was achieved *via* double asymmetric induction by applying a chiral amine substrate, *N*-*tert*-butanesulfinamide,

under the catalysis of a chiral cationic palladium complex.

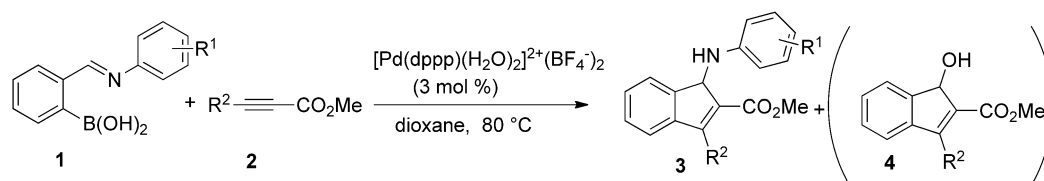
## Results and Discussion

Our investigation was initiated by studying the catalytic reactions between 2-iminophenylboronic acid **1a** and methyl 2-butynoate **2a**. Preliminary studies of the reaction conditions revealed that the main product **3aa** could be obtained in 78% yield, along with the side product **4aa** in 14% yield when complex  $[\text{Pd}(\text{dppp})(\text{H}_2\text{O})_2]^{2+}(\text{BF}_4^-)_2$  was used as the catalyst. Several 2-iminoarylboronic acids and alkynes were investigated under these reaction conditions (Table 1). The substituents on the substrates **1** have no obvious effect on the reaction, giving the aminoindene derivatives in yields from 48 to 80%. While using different substituted alkynes, the reactions proceeded well to afford the products in 60–84% yields (Table 1, entry 1 and entries 8–11). Unfortunately, no reaction occurred when the aryl-substituted alkynes, terminal alkynes, and dialkyl-substituted alkynes were used. It is important to note that these arylimine substrates **1** were susceptible to decomposition and the yields were sharply diminished with the generation of the by-products **4** which were formed by the reaction of 2-formylarylboronic acids (from the hydrolysis of **1**) and the alkynes. The side reaction could not be inhibited completely at the present time.

Subsequently, our attention was turned to the asymmetric version of the reaction (Scheme 1). Initially,  $\text{Pd}^{2+}(\text{CH}_3\text{CN})_4(\text{BF}_4^-)_2$  combined with various chiral ligands was used as the catalysts. (*S,S*)-bdpp and (*R*)-binap were found to be the superior providing the expected products in 69% and 71% *ee*, respectively. In addition, we also studied this asymmetric reaction employing the chiral palladium complexes  $[\text{Pd}[(R)\text{-binap}](\text{H}_2\text{O})_2]^{2+}(\text{TfO}^-)_2$  (**A**) and  $[\text{Pd}[(S,S)\text{-bdpp}](\text{H}_2\text{O})_2]^{2+}(\text{BF}_4^-)_2$  (**B**) as the catalyst, only the catalyst **B** could give the product in 72% *ee*. Disappointedly, the yields of the reactions were very low in all cases together with the generation of trace of by-product **4aa**. It is presumed that the substrate **1a** was prone to hydrolysis and thus made the reaction system complicated.

Considering some limitations associated with the tandem reaction described above, we embarked on modulation of the substrate **1** to circumvent these difficulties. *N*-tert-Butanesulfinylimines, despite their stability, are more electrophilic than typical *N*-alkyl- or arylimines,<sup>[14]</sup> which enables clean and high yield reactions with a very wide range of nucleophiles.<sup>[14,15]</sup> On the other hand, the *N*-tert-butanesulfinyl group is a powerful chiral inducing group in diastereoselective reactions for the synthesis of chiral amine-containing compounds.<sup>[14,16]</sup> Therefore, we put our efforts to optimize the reaction conditions using 2-(*N*-tert-butanesulfinylimino)phenylboronic acid and methyl 2-butynoate as the substrates.

**Table 1.** Cationic palladium-catalyzed tandem annulation reaction of 2-iminoarylboronic acids with substituted alkynes<sup>[a]</sup>



Entry	Imines ( $\text{R}^1$ )	Alkynes ( $\text{R}^2$ )	Yield [%] <sup>[b]</sup>
1	$\text{R}^1 = p\text{-MeO}$ ( <b>1a</b> )	Me ( <b>2a</b> )	<b>3aa</b> (78)
2	$\text{R}^1 = \text{H}$ ( <b>1b</b> )	Me ( <b>2a</b> )	<b>3ba</b> (48)
3	$\text{R}^1 = p\text{-Me}$ ( <b>1c</b> )	Me ( <b>2a</b> )	<b>3ca</b> (78)
4	$\text{R}^1 = p\text{-Cl}$ ( <b>1d</b> )	Me ( <b>2a</b> )	<b>3da</b> (80)
5	$\text{R}^1 = p\text{-Br}$ ( <b>1e</b> )	Me ( <b>2a</b> )	<b>3ea</b> (70)
6	<b>1f</b> <sup>[c]</sup>	Me ( <b>2a</b> )	<b>3fa</b> (70)
7	<b>1g</b> <sup>[d]</sup>	Me ( <b>2a</b> )	<b>3ga</b> (46)
8	<b>1c</b>	<i>n</i> -C <sub>3</sub> H <sub>7</sub> ( <b>2b</b> )	<b>3cb</b> (74)
9	<b>1a</b>	<i>n</i> -C <sub>6</sub> H <sub>13</sub> ( <b>2c</b> )	<b>3ac</b> (84)
10	<b>1a</b>	PhCH <sub>2</sub> CH <sub>2</sub> ( <b>2d</b> )	<b>3ad</b> (74)
11	<b>1a</b>	<b>2e</b> <sup>[e]</sup>	<b>3ae</b> (60)

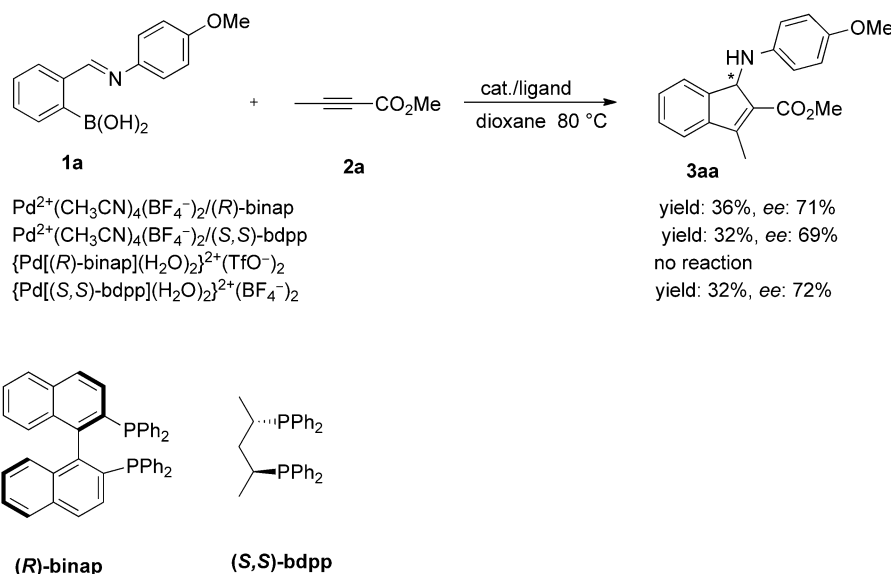
<sup>[a]</sup> All the reactions were carried out with **1** (0.1 mmol) and **2** (0.2 mmol) using dioxane (2 mL) as the solvent.

<sup>[b]</sup> Isolated yield of the pure product after column chromatography.

<sup>[c]</sup> **1f**:  $\text{R}^1 = \text{H}$ , the substituent on N was the  $\beta$ -naphthyl.

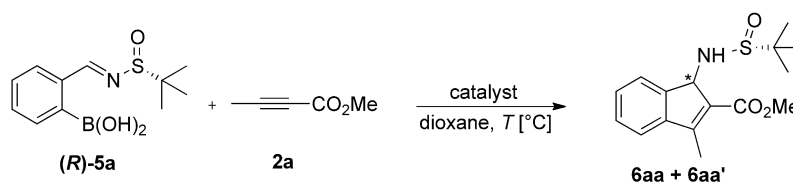
<sup>[d]</sup> **1g**:  $\text{R}^1 = \text{H}$ , the substituent on N was the  $\alpha$ -naphthyl.

<sup>[e]</sup> **2e** is 6-phenylhex-3-yn-2-one.



**Scheme 1.** Screening of the asymmetric reaction conditions of **1a** and **2a** with different ligands and catalysts.

**Table 2.** Optimization of reaction conditions.<sup>[a]</sup>



Entry	Catalyst (3 mol%)	Temperature $T$ [°C]	Time $t$ [h]	Yield [%] <sup>[b]</sup> of <b>6aa + 6aa'</b>
1	$[\text{Pd}(\text{dppp})(\text{H}_2\text{O})_2]^{2+}(\text{BF}_4^-)_2$	80	0.1	75 + 25
2	$[\text{Pd}(\text{dppp})(\text{H}_2\text{O})_2]^{2+}(\text{BF}_4^-)_2$	20	1.5	72 + 28
3 <sup>[c]</sup>	$[\text{Pd}(\text{dppp})(\text{H}_2\text{O})_2]^{2+}(\text{BF}_4^-)_2$	80	0.3	65 + 29
4 <sup>[d]</sup>	$[\text{Pd}(\text{dppp})(\text{H}_2\text{O})_2]^{2+}(\text{BF}_4^-)_2$	80	0.2	68 + 32
5 <sup>[e]</sup>	$[\text{Pd}(\text{dppp})(\text{H}_2\text{O})_2]^{2+}(\text{BF}_4^-)_2$	80	0.5	49 + 16
6	$\{[\text{Pd}(\text{dppp})(\mu\text{-OH})]^{+}\}_2(\text{BF}_4^-)_2$	60	12	72 + 18
7	$[\text{Pd}(\text{dppp})(\text{H}_2\text{O})_2]^{2+}(\text{TfO}^-)_2$	80	10	NR
8	$[\text{Pd}(\text{dppp})(\text{H}_2\text{O})_2]^{2+}(\text{SbF}_6^-)_2$	60	12	65 + 35
9	$[\text{Pd}(\text{bpy})(\text{H}_2\text{O})_2]^{2+}(\text{TfO}^-)_2$	80	24	NR
10	$\{[\text{Pd}(\text{bpy})(\mu\text{-OH})]^{+}\}_2(\text{TfO}^-)_2$	80	24	NR
11 <sup>[f]</sup>	$\text{Pd}^{2+}(\text{CH}_3\text{CN})_4(\text{BF}_4^-)_2/\text{dppp}$	80	0.3	33 + 26

<sup>[a]</sup> All the reactions were carried out with **(R)-5a** (0.1 mmol) and **2a** (0.2 mmol) using dioxane (2 mL) as the solvent.

<sup>[b]</sup> Isolated yield of the pure product after column chromatography.

<sup>[c]</sup> DCE was used as the solvent.

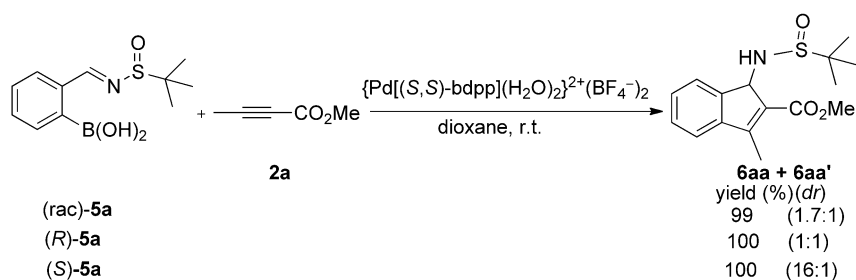
<sup>[d]</sup> THF was used as the solvent.

<sup>[e]</sup> Toluene was used as the solvent.

<sup>[f]</sup> dppp (3.3 mol%) was added.

The reaction proceeded smoothly in nearly quantitative yield within 5 minutes at 80 °C using complex  $[\text{Pd}(\text{dppp})(\text{H}_2\text{O})_2]^{2+}(\text{BF}_4^-)_2$  as the catalyst to generate a 3:1 mixture of products (**6aa** and **6aa'**), which were easily separated by column chromatography (Table 2, entry 1). These products were confirmed to be diastereoisomers by transformation into the corresponding *N*-acetyl derivatives, which were characterized by

<sup>1</sup>H NMR and X-ray crystallography.<sup>[17]</sup> Fortunately, no by-product such as **4aa** was generated in this catalytic annulation reaction using *N*-tert-butanesulfinylimines as the substrates. Lowering the temperature to 20 °C, the reaction was also accomplished in a slightly longer time and this had no marked effect on the diastereoselectivity (Table 2, entry 2). A variety of solvents was tested and dioxane was finally chosen as



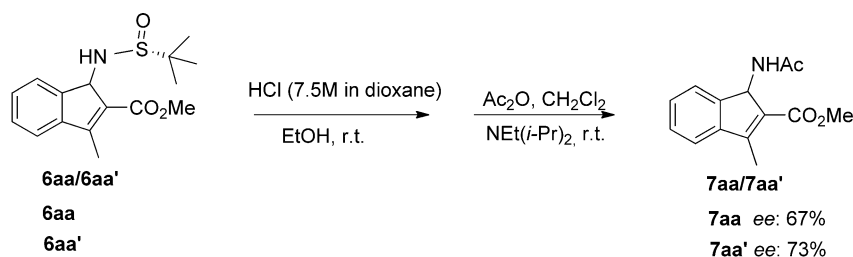
**Scheme 2.** Double asymmetric induction.

the best (Table 2, entry 1 and entries 3–5). Further study of the tandem annulation reaction using other cationic palladium complexes gave promising levels of yield but with unsatisfactory diastereoselectivity (Table 2, entries 6, 8 and 11). The cationic palladium complexes with  $\text{TfO}^-$  as the counter anion could not furnish the tandem annulation reaction (Table 2, entries 7, 9 and 10).

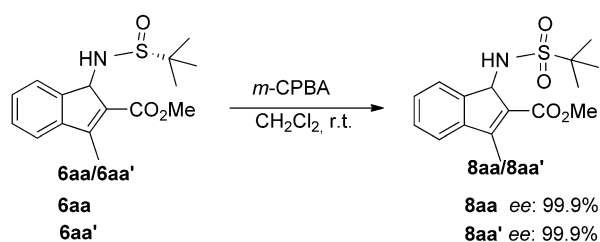
Recently, the double asymmetric induction has been recognized as one of the most useful methodologies in controlling the absolute configuration of the newly created stereogenic centers.<sup>[18]</sup> With these considerations in mind, we started to investigate the influence of the chiral cationic palladium complexes as a catalyst to this reaction, anticipating to enhance the diastereoselectivity. First, the reaction of racemic **5a** with **2a** under the catalysis of  $\{\text{Pd}[(S,S)\text{-bdpp}](\text{H}_2\text{O})_2\}^{2+}(\text{BF}_4^-)_2$  was examined, providing the product in 99% yield along with very low diastereoselectivity ( $dr=1.7:1$ , Scheme 2). To evaluate the matched or mismatched chiral catalyst and chiral substrate combinations, the reactions using both enantiomers of

**5a** with the same chiral catalyst  $\{\text{Pd}[(S,S)\text{-bdpp}](\text{H}_2\text{O})_2\}^{2+}(\text{BF}_4^-)_2$  were carried out. The outcome of the reactions revealed that the chiral cationic palladium complex  $\{\text{Pd}[(S,S)\text{-bdpp}](\text{H}_2\text{O})_2\}^{2+}(\text{BF}_4^-)_2$  is a matched catalyst with (*S*)-**5a**, which could catalyze this reaction in high yield with excellent diastereoselectivity (16:1) (Scheme 2). In sharp contrast, when (*R*)-**5a** was taken with the same chiral catalyst, the reaction proved relatively unsatisfactory in terms of the diastereoselectivity. A high level diastereocontrol was observed with (*S*)-**5a** demonstrated that the diastereoselectivity was highly dependent on the configuration of the substrate and the ligand being incorporated in palladium complex. According to the observed results, it is presumed that the chiral catalyst would interfere with the chiral substrates, resulting in different stereocontrol. In this double asymmetric induction reaction, (*S*)-**5a** and the cationic palladium complex  $\{\text{Pd}[(S,S)\text{-bdpp}](\text{H}_2\text{O})_2\}^{2+}(\text{BF}_4^-)_2$  constituted a matched pair leading to the enhancement of diastereoselectivity.

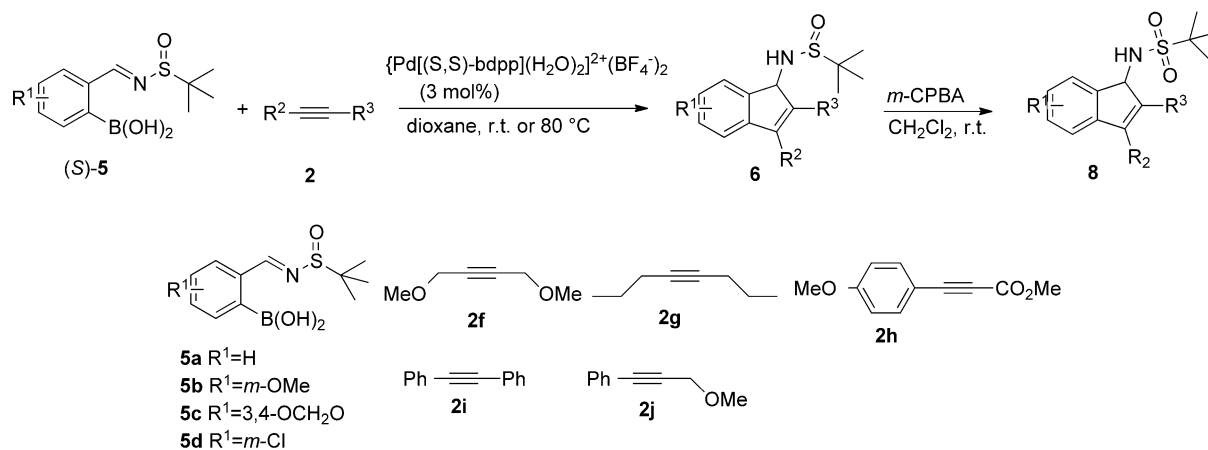
(1) Hydrolysis of the *N*-*tert*-butylsulfinyl group (Method A):



(2) Oxidation of the *N*-*tert*-butylsulfinylamines to *N*-*tert*-butylsulfonylamine (Method B):



**Scheme 3.** Enantioselectivity determination of the *N*-*tert*-butanesulfinylamines.

**Table 3.** Chiral cationic palladium catalyzed diastereoselective tandem annulation reaction.<sup>[a]</sup>

Entry	Yield [%] <sup>[b]</sup>	<b>6</b>	<i>dr</i> <sup>[c]</sup>	Yield [%] <sup>[b]</sup>	<b>8</b>	<i>ee</i> [%] <sup>[d]</sup>
1	<b>6aa</b> (99.9)		16:1	<b>8aa</b> (85)		99.9 (–)
2	<b>6ba</b> (99.9)		99:1	<b>8ba</b> (90)		99.9 (–)
3	<b>6ca</b> (92)		10:1	<b>8ca</b> (68)		99.9 (–)
4	<b>6da</b> (99.7)		– <sup>[e]</sup>	<b>8da</b> (83)		88 (–)
5	<b>6ac</b> (98)		19:1	<b>8ac</b> (77)		99.9 (–)
6	<b>6ad</b> (98)		20:1	<b>8ad</b> (97)		99.9 (–)
7	<b>6ae</b> (94)		18:1	<b>8ae</b> (82)		96 (–)
8	<b>6af</b> (99)		– <sup>[e]</sup>	<b>8af</b> (31)		93 (–)
9 <sup>[f]</sup>	<b>6ag</b> (94)		5:1	<b>7ag</b> (88)		99.9 (–)
10 <sup>[g,h]</sup>	<b>6ah</b> (55)		5:1	–		–
11 <sup>[g]</sup>	<b>6ai</b> (51)		99:1	–		–
12 <sup>[g,i]</sup>	<b>6aj</b> (85)		99:1	–		–

[a] All the reactions were carried out with **5** (0.1 mmol) and **2** (0.2 mmol) using dioxane (2 mL) as the solvent.

[b] Isolated yield of the pure product after column chromatography.

[c] The *dr* value was determined by the ratio of the isolated yields of two diastereoisomers.

[d] The *ee* value was determined by Method B in Scheme 2. The sign of optical rotation is indicated in parentheses.

[e] The mixture of diastereomers could not be isolated but the diastereoselectivity of the product could be determined by measuring the enantiomeric excess of the *N*-Bus-amino derivatives.

[f] The *ee* value was determined by Method A in Scheme 2.

[g] Method A or B was ineffective for the transformation.

[h]  $\text{R}^2 = p\text{-MeOC}_6\text{H}_4$ ,  $\text{R}^3 = \text{CO}_2\text{Me}$ .

[i]  $\text{R}^2 = \text{CH}_2\text{OMe}$ ,  $\text{R}^3 = \text{C}_6\text{H}_5$ .

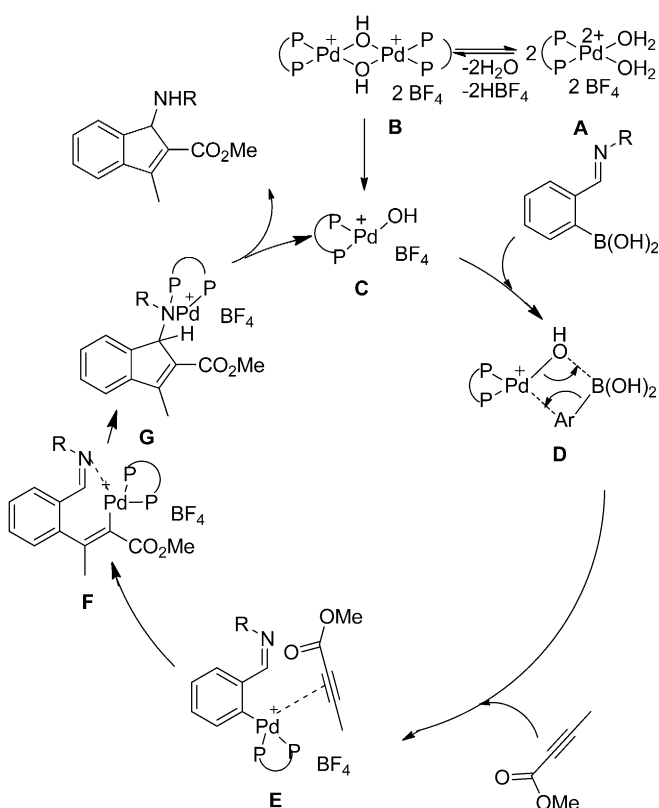
Two methods were used to determine the enantioselectivity of the products **6aa** and **6aa'**. First, the *N*-*tert*-butanesulfinyl group was transformed to get the chiral acetyl amines according to the standard procedure (Scheme 3, Method A).<sup>[19]</sup> When using the diastereomers **6aa** and **6aa'** under the same conditions, the corresponding products were obtained with 67% and 73% *ee*, respectively. From these results, we doubted that a certain racemization might occur in the desulfination and acetylation steps. An alternative method of approaching the chiral amines was tried by oxidizing the *N*-*tert*-butanesulfinyl group to *N*-*tert*-butanesulfonyl (Bus) group by *m*-chloroperbenzoic acid (*m*-CPBA) (Method B).<sup>[20]</sup> High *ee* values of the chiral *N*-Bus-amines were obtained by using this transformation. Thus, Method B was a suitable

method for determining the enantioselectivity of these products.

Following the optimized conditions, we focused on probing the scope of the diastereoselective tandem annulation reaction using **(S)-5** and alkynes **2** as the substrates under the catalysis of the chiral cationic palladium complex  $\{\text{Pd}[(S,S)\text{-bdpp}](\text{H}_2\text{O})_2\}^{2+}(\text{BF}_4^-)_2$ . As depicted in Table 3, the reaction of **(S)-5a** and the methyl 2-butynoate **2a** gave the annulation product **6aa** in quantitative yield with excellent levels of diastereoselectivity and high enantioselectivity (Table 3, entry 1). Reactions conducted with a series of the substituted 2-(*N*-*tert*-butanesulfinylimino)arylboronic acids **5b–5d** occurred in high total yield from 92% to 99.9% with the diastereomeric ratio up to 99:1 (Table 3, entries 2–4). To assess the scope, various

substituted alkynes were also exposed to 2-(*N*-*tert*-butanesulfinylimino)phenylboronic acid **5a** under our disclosed standard conditions. All reactions proceeded smoothly to afford the corresponding aminoindene derivatives **6** in high yields and diastereoselectivity (Table 3, entries 5–9). However, when employing diphenyl-substituted alkyne **2h** and phenyl-substituted alkynate **2i**, the reactions were unlikely to proceed and generated the products in low yields with prolonged times (Table 3, entries 11 and 12). Most of the products could be transferred to the chiral *N*-*tert*-butanesulfonyl group-containing compounds in moderate to high yields with high enantioselectivity by simple oxidation using *m*-CPBA as the oxidant. It should be noted that Method B cannot be used for determining the enantioselectivity of product **6ag** because the double bond here was also easily oxidized, but Method A can be used for it. Meanwhile, neither Method A nor Method B is suitable for the transformation of products **6ah–6aj** which have a phenyl substituent on the double bond (Table 3, entries 10–12). In summary, not only the substituted arylboronic acids but also the substituted alkynes could react successfully to afford the aminoindene derivatives in acceptable yields with good to excellent *dr* and *ee* values.

The proposed reaction mechanism is described in Scheme 4. The palladium complex **A** would dissociate



**Scheme 4.** Proposed mechanism of the tandem reaction.

to generate the Pd hydroxo complex **C**, which is supposed to be the active catalytic species.<sup>[21]</sup> After transmetalation, owing to the vacant coordination site on the cationic palladium complex, intermediate **E** can be produced. Insertion of an alkyne **2a** to the palladium-carbon bond of **E** gives intermediate **F**. The high Lewis acidity of cationic palladium species **F** may activate the imino group by coordination. Intramolecular nucleophilic attack of the formed alkenyl-palladium moiety to a carbon-nitrogen double bond would then produce intermediate **G**. The subsequent protolysis of **G** would afford the product and regenerate the palladium species to complete the catalytic cycle. In the asymmetric version of the annulation reactions, substrates (*S*)-**5** and the catalyst {Pd[(*S,S*)-bdpp]-(H<sub>2</sub>O)<sub>2</sub>}<sup>2+</sup>(BF<sub>4</sub><sup>−</sup>)<sub>2</sub> can constitute a matched pair to give the products with a high diastereomeric ratio. This shows that the reaction would be underway in high diastereoselectivity only in the case where the diastereocontrolling interaction matched well with each other.

## Conclusions

In summary, we have successfully developed a new efficient cationic palladium-catalyzed synthesis of aminoindene derivatives from the reaction of substituted 2-iminoarylboronic acids with a variety of alkynes. The reaction is highly regioselective and many functionalized aminoindene derivatives can be prepared in good yields. Additionally, we have also established the diastereoselective synthesis of chiral aminoindene derivatives involving a double asymmetric induction by the chiral catalyst and chiral substrates.

## Experimental Section

### General

The reactions were monitored by thin-layer chromatography to detect the completion of the reaction. NMR spectra were recorded on a Varian Mercury Vx 300 or Vx 400 spectrometer. Infrared spectra were obtained on a Bio-Rad FTS-185 instrument. Mass spectra were provided on HP 5973 or Agilent 1100 spectrometer. Elemental analyses were carried out on Elementar Vario EL instruments. The optical rotation was measured on a Perkin-Elmer 341 polarimeter and the enantiomeric excesses were determined after separation of the enantiomers by HPLC on Perkin-Elmer (785A, 200 IC Pump) or Waters (515 Pump, 2487: Dual Absorbance Detector) instrument. All solvents were dried and distilled before use according to the standard procedures. All melting points were uncorrected.



### General Procedure for the Synthesis of 2-Iminoarylboronic acids (1a–1h)

The 2-formylboronic acids (6.6 mmol) and the substituted aniline (6.6 mmol) were dissolved in EtOH (35 mL) and toluene (5 mL). The reaction mixture was heated to reflux overnight till the reaction was completed. Then the reaction mixture was cooled to room temperature and the solvent was removed under reduced pressure and the residue was purified by recrystallization to give the desired product **1**.

**Product 1a**: yield: 80%; yellow solid; mp 220–222 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ=8.71 (s, 1H), 7.72 (d, *J*=6.6 Hz, 2H), 7.34–7.25 (m, 5H), 7.16 (d, *J*=6.3 Hz, 1H), 6.80 (d, *J*=8.4 Hz, 2H), 3.75 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ=163.5, 158.9, 139.3, 138.6, 131.9, 131.5, 128.1, 126.3, 123.3, 114.4, 55.4; IR (KBr): ν=2835, 1616, 1506, 1341, 1249, 838 cm<sup>-1</sup>; MS (70 eV, EI): *m/z* (%)=255 (M<sup>+</sup>), 238, 211, 196 (100), 108, 80; HR-MS: *m/z*=255.1066, calcd. for C<sub>14</sub>H<sub>14</sub>BN<sub>3</sub> (M<sup>+</sup>): 255.1067.

### General Procedure for Cationic Palladium-Catalyzed Tandem Reactions of 2-Iminoarylboronic Acids and Alkynes

To a Schlenk tube were added 2-iminophenylboronic acid **1a** (25.5 mg, 0.1 mmol, 1 equiv.), [Pd(dppp)(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup>(BF<sub>4</sub>)<sub>2</sub> (2.2 mg, 3 mol%) and 2-butyne **2a** (19.6 mg, 0.2 mmol, 2 equiv.) and dioxane (2.0 mL) successively. The reaction mixture was stirred at 80 °C for several hours until 2-iminophenylboronic acid had disappeared as monitored by TLC. Then, the mixture was purified by flash column chromatography (pure petroleum ether, then ethyl acetate: petroleum ether=1:7) to obtain the product **3aa** as an oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ=7.53–7.34 (m, 4H), 6.64 (d, *J*=8.1 Hz, 2H), 6.41 (d, *J*=8.1 Hz, 2H), 5.15 (s, 1H), 3.77 (s, 3H), 3.68 (s, 3H), 2.49 (s, 3H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ=165.7, 152.7, 152.3, 145.9, 142.4, 141.1, 131.9, 128.7, 128.1, 123.6, 121.4, 116.5, 114.4, 63.1, 55.5, 51.2, 12.5; IR (neat): ν=3387, 2951, 2835, 1704, 1512, 1242, 1037, 763 cm<sup>-1</sup>; MS (70 eV, EI): *m/z* (%)=309 (M<sup>+</sup>), 277, 250, 155, 122 (100); HR-MS: *m/z*=309.1360, calcd. for C<sub>19</sub>H<sub>19</sub>NO<sub>3</sub> (M<sup>+</sup>): 309.1365.

### General Procedure for the Synthesis of 2-(*N*-*tert*-Butanesulfinyl)iminoarylboronic Acids (5a–5d)

The 2-formylboronic acids (6.6 mmol) and the *N*-*tert*-butanesulfinylamine (6.6 mmol) were dissolved in EtOH (35 mL) and toluene (5 mL). The reaction mixture was heated to reflux overnight till the reaction was completed. Then the reaction mixture was cooled to room temperature, the solvent was removed under the reduced pressure and the residue was purified by recrystallization to give the desired product **5**.

**Product 5a**: yield: 82%; white solid; mp 146–148 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ=9.18 (s, 1H), 8.14–8.11 (m, 1H), 7.96–7.94 (m, 1H), 7.57–7.54 (m, 2H), 7.25 (s, 2H), 1.30 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ=166.9, 136.6, 131.8, 130.7, 130.5, 58.1, 22.4; IR (KBr): ν=3550, 2983, 2963, 2866, 1606, 1581, 1558, 1344, 1039, 765 cm<sup>-1</sup>; MS (ESI): *m/z* (%)=276 (M<sup>+</sup>+Na), 268, 255, 254 (100), 236; anal. calcd. for C<sub>11</sub>H<sub>16</sub>BN<sub>3</sub>S: C 52.19, H 6.37, N 5.53; found: C 52.37, H 6.44, N 5.20; [α]<sub>D</sub><sup>20</sup>: +88.9 (c 1.0800, CHCl<sub>3</sub>).

### Representative Example for Chiral Cationic Palladium-Catalyzed Diastereoselective Tandem Annulation Reaction of Chiral 2-Iminoarylboronic Acids and Alkynes

To a Schlenk tube were added (*S*)-2-(*N*-*tert*-butanesulfinyl-imino)phenylboronic acid **5a** (25.3 mg, 0.1 mmol, 1 equiv.), {Pd[(*S,S*)-bdpp](H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup>(BF<sub>4</sub>)<sub>2</sub> (2.2 mg, 3 mol%), methyl 2-butyne **2a** (19.6 mg, 0.2 mmol, 2 equiv.) and dioxane (2.0 mL) successively. The reaction mixture was stirred at room temperature for 20 minutes until **5a** had disappeared as monitored by TLC. Then, the mixture was purified by flash column chromatography (pure petroleum ether, then ethyl acetate: petroleum ether=1:1) to obtain the product **6aa** as an oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ=7.68–7.66 (m, 1H), 7.45–7.27 (m, 3H), 5.11 (dd, *J*=1.5 and 4.5 Hz, 1H), 3.95 (d, *J*=4.5 Hz, 1H), 3.85 (s, 3H), 2.50 (d, *J*=1.2 Hz, 3H), 1.19 (s, 9H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ=165.6, 152.0, 143.8, 143.2, 132.5, 128.8, 128.6, 124.9, 121.3, 63.0, 55.8, 51.3, 22.5, 12.5; IR (neat): ν=3205, 2952, 2869, 1708, 1618, 1584, 1245, 1061 cm<sup>-1</sup>; MS (70 eV, EI): *m/z* (%)=307 (M<sup>+</sup>), 251, 219, 188, 155 (100), 128, 111, 57; HR-MS: *m/z*=307.1240, calcd. for C<sub>16</sub>H<sub>21</sub>NO<sub>3</sub>S (M<sup>+</sup>): 307.1242; [α]<sub>D</sub><sup>20</sup>: +68.4 (c 1.1000, CHCl<sub>3</sub>).

### Transformation of 6aa and 6aa' to Their Acetyl Derivatives 7aa and 7aa'

To a solution of the *N*-sulfinyl product (**6aa** or **6aa'**) in 2 mL of dry ethanol was added a solution of dry HCl in 1,4-dioxane (7.5 M, 5.0 equiv. based on **6aa** or **6aa'**). The mixture was stirred at room temperature for 3 h and concentrated. The resulting amine hydrochloride was precipitated with diethyl ether. The amine hydrochloride (1.0 equiv.) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (0.1 M) and Hünig's base (6.0 equiv.) was added dropwise. Then, Ac<sub>2</sub>O (3.0 equiv.) was added and the resulting mixture was stirred for 1 h at room temperature. The reaction mixture was quenched with a saturated solution of ammonium chloride and diluted with CH<sub>2</sub>Cl<sub>2</sub>. The resulting mixture was separated, and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> three times. The combined organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was subjected to silica gel chromatography (eluent: EtOAc/petroleum ether) to offer the product **7aa** as a white solid; mp 132–133 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ=7.52–7.50 (m, 1H), 7.42–7.35 (m, 3H), 6.00–5.97 (m, 1H), 5.68 (d, *J*=8.4 Hz, 1H), 3.79 (s, 3H), 2.49 (d, *J*=2.4 Hz, 3H), 2.05 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ=170.3, 165.2, 154.6, 145.2, 142.5, 129.8, 129.2, 128.3, 124.1, 121.3, 55.9, 51.3, 23.3, 12.5; IR (KBr): ν=3270, 3072, 1708, 1643, 1549, 1240, 1199, 1065, 759 cm<sup>-1</sup>; MS (70 eV, EI): *m/z* (%)=245 (M<sup>+</sup>), 227, 213, 202, 170 (100), 143, 115, 43; HR-MS: *m/z*=245.1061, calcd. for C<sub>14</sub>H<sub>15</sub>NO<sub>3</sub> (M<sup>+</sup>): 245.1052.

**Product 7aa'**: white solid, mp 133 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ=7.53–7.50 (m, 1H), 7.42–7.35 (m, 3H), 6.00 (d, *J*=10.4 Hz, 1H), 5.67 (d, *J*=10.4 Hz, 1H), 3.79 (s, 3H), 2.49 (d, *J*=1.6 Hz, 3H), 2.06 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ=170.3, 165.2, 154.6, 145.2, 142.5, 129.8, 129.2, 128.3, 124.1, 121.3, 55.9, 51.3, 23.3, 12.5; IR (KBr) ν=3273, 3070, 1712, 1640, 1544, 1243, 1196, 1061, 754 cm<sup>-1</sup>; MS (70 eV, EI): *m/z* (%)=245 (M<sup>+</sup>), 227, 213, 202, 170 (100), 143,

115, 43; HR-MS:  $m/z$  = 245.1059, calcd. for  $C_{14}H_{15}NO_3$  ( $M^+$ ): 245.1052.

### Methods for *ee* Value Determination of Products 6aa–6af (Method A)

To a round-bottom tube were added the product **6aa** and *m*-CPBA (1.2 equiv.) and  $CH_2Cl_2$  (2.0 mL) successively. The reaction mixture was stirred at room temperature for 5 minutes until substrate disappeared as monitored by TLC. Then, the mixture was purified by flash column chromatography (pure petroleum ether, then ethyl acetate: petroleum ether = 1:7) to obtain the product **8aa** as an oil.  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  = 7.97 (d,  $J$  = 6 Hz, 1H), 7.42–7.39 (m, 3H), 5.37–5.33 (m, 1H), 3.85 (s, 3H), 3.79 (d,  $J$  = 10 Hz, 1H), 2.48 (s, 3H), 1.53 (s, 9H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  = 165.1, 154.3, 145.1, 141.9, 129.6, 129.2, 128.7, 125.6, 121.2, 60.8, 60.6, 51.3, 24.1, 12.6; IR (neat):  $\nu$  = 3295, 3276, 2982, 2945, 1697, 1611, 1433, 1194, 1124, 754  $cm^{-1}$ ; MS (70 eV, EI):  $m/z$  (%) = 323 ( $M^+$ ), 291, 202, 170, 144, 115, 57 (100), 41; HR-MS:  $m/z$  = 323.1193, calcd. for  $C_{16}H_{21}NO_4S$  ( $M^+$ ): 323.1191. The *ee* value was determined by chiral HPLC using a Chiralcel IC column with hexane:2-propanol = 90:10, flow = 0.7 mL/min;  $\lambda$  = 230 nm; *ee*: 99.5%;  $[\alpha]_D^{20}$ : –205.5 (*c* 0.9333,  $CHCl_3$ ).

### Methods for *ee* Value Determination of 6ag (Method B)

To a solution of the *N*-sulfinyl product (**6ag**) in 2 mL of dry ethanol was added a solution of dry HCl in 1,4-dioxane (7.5 M, 5.0 equiv. based on **6ag**). The mixture was stirred at room temperature for 3 h and concentrated. The resulting amine hydrochloride was precipitated with diethyl ether. The amine hydrochloride (1.0 equiv.) was dissolved in  $CH_2Cl_2$  (0.1 M) and Hünig's base (6.0 equiv.) was added dropwise. Then,  $Ac_2O$  (3.0 equiv.) was added and the resulting mixture was stirred for 1 h at room temperature. The reaction mixture was quenched with a saturated solution of ammonium chloride and diluted with  $CH_2Cl_2$ . The resulting mixture was separated, and the aqueous layer was extracted with  $CH_2Cl_2$  three times. The combined organic layer was dried over  $Na_2SO_4$  and concentrated under reduced pressure. The residue was subjected to silica gel chromatography (eluent:  $EtOAc$ /petroleum ether) to isolate the product **7ag** as a white solid; mp 148–150 °C.  $^1H$  NMR (400 MHz,  $CDCl_3$ ):  $\delta$  = 7.37 (d,  $J$  = 7.2 Hz, 1H), 7.28 (t,  $J$  = 8 Hz, 1H), 7.19 (d,  $J$  = 7.6 Hz, 1H), 7.13 (dt,  $J$  = 1.2 and 7.2 Hz, 1H), 5.68 (d,  $J$  = 9.6 Hz, 1H), 5.45 (d,  $J$  = 9.6 Hz, 1H), 2.46–2.15 (m, 4H), 2.04 (s, 3H), 1.65–1.43 (m, 4H), 0.99–0.91 (m, 6H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ):  $\delta$  = 170.5, 144.9, 144.1, 143.2, 138.9, 127.8, 124.8, 123.1, 118.7, 56.6, 27.9, 27.4, 23.3, 22.7, 21.9, 14.3, 14.2; IR (KBr):  $\nu$  = 3288, 2957, 2932, 2870, 1642, 1542, 1371, 745  $cm^{-1}$ ; MS (70 eV, EI):  $m/z$  (%) = 257 ( $M^+$ ), 214, 198 (100), 186, 169, 156, 141, 128, 115, 43; HR-MS:  $m/z$  = 257.1782, calcd. for  $C_{17}H_{23}NO$  ( $M^+$ ): 257.1780. The *ee* value was determined by chiral HPLC using a Chiralcel OD-H (250) column with hexane:2-propanol = 95:5, flow = 0.7 mL/min;  $\lambda$  = 230 nm; *ee*: 99.9%;  $[\alpha]_D^{20}$ : –94.0 (*c* 0.8921,  $CHCl_3$ ).

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