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Development of Second Generation Gold-Supported Palladium Material with Low-Leaching and Recyclable Characteristics in Aromatic Amination

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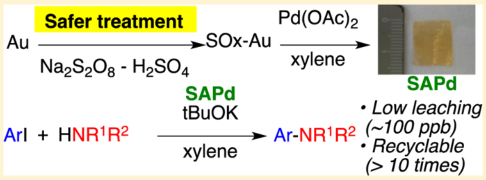
S *Supporting Information*



ABSTRACT: An improved process for the preparation of sulfur-modified gold-supported palladium material [SAPd, second generation] is presented. The developed preparation method is safer and generates less heat (aqueous $Na_2S_2O_8$ and H_2SO_4) for sulfur fixation on a gold surface, and it is superior to the previous method of preparing SAPd (first generation), which requires the use of the more heat-generating and dangerous piranha solution (concentrated H_2SO_4 and 35% H_2O_2) in the sulfur fixation step. This safer and improved preparation method is particularly important for the mass production of SAPd (second generation) for which the catalytic activity was examined in ligand-free Buchwald–Hartwig cross-coupling reactions. The catalytic activities were the same between the first and second generation SAPds in aromatic aminations, but the lower palladium leaching properties and safer preparative method of second generation SAPd are a significant improvement over the first generation SAPd.

■ INTRODUCTION

Catalyst immobilization is an important strategy in advanced organic synthesis in both academia and industrial laboratories.[1] The chemical and pharmaceutical industries currently have a strong preference for immobilized catalysts, because their low leaching properties decrease the possibility of contamination and the catalysts can be recovered and reused.[2] Moreover, the recovery and reuse of the immobilized catalysts simplify the workup, separation, and isolation of the product.

Considerable efforts are focused on methods to immobilize Pd catalysts on supports such as activated carbon, hybrid organic–inorganic solids, various silica materials, and polymers.[3] In our continuous efforts to develop a low-leaching immobilized Pd catalyst, we recently discovered the sulfur-modified Au-supported Pd material [SAPd (first generation)], an immobilized Pd catalyst for both carbon–carbon and carbon–nitrogen bond-forming reactions (Scheme 1).[4]

Because of its low Pd-leaching and highly recyclable characteristics, there is a high demand for SAPd (first generation) in mass production and industrially relevant processes. Because of safety issues and reproducibility, however, the previously reported procedure for the preparation of the first generation SAPd is not feasible for mass production, 25 sheets of SAPd. Herein we describe a new, more efficient and safer preparative method for SAPd (second generation), which is useful for mass production. The catalytic activities of the first and second generation SAPds in the ligand-free Buchwald–Hartwig cross-coupling reaction were compared in detail.

In our previous preparation of first generation SAPd,[4] the first step involved the fixation of sulfur on a gold surface by piranha treatment (Scheme 1). We prepared the piranha solution in situ by mixing concentrated H_2SO_4 and 35% H_2O_2 (3:1). When 35% H_2O_2 was added dropwise to the concentrated H_2SO_4, heat was vigorously generated and difficult to control, sometimes requiring specific safety equipment and extremely careful handling. Moreover, the preparative method of the first generation SAPd was difficult to reproduce.[5] To overcome these problems of safety and reproducibility, we aimed to develop an alternative and facile method for second generation SAPd preparation.

■ RESULTS AND DISCUSSION

Because of the safety issues, several chemical experiments were performed by changing the ratio of concentrated H_2SO_4 and 35% H_2O_2 for sulfur fixation on the gold surface, but the uncontrollable heat generation and poor reproducibility of SAPd could not be overcome. Therefore, to avoid the use of H_2O_2, we applied an alternative method for sulfur fixation on a gold surface (Table 1), first by using aqueous $K_2S_2O_8$ with

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Scheme 1. Preparation of SAPd (First Generation) and Its Use in Pd Couplings

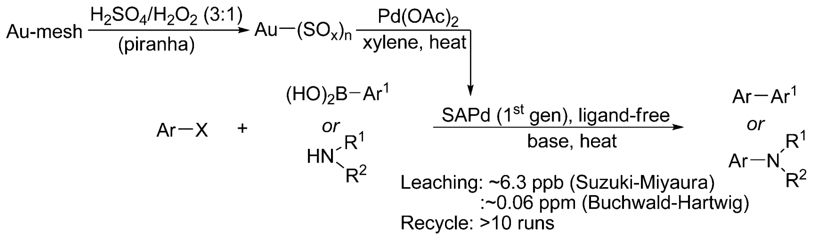
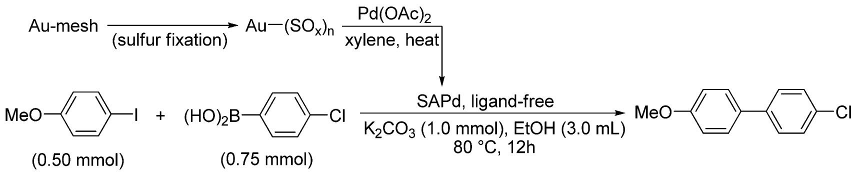


Table 1. Comparisons between the Preparative Methods of the First and Second Generation SAPds and Their Catalytic Activities in the Suzuki–Miyaura Reaction



entry	sulfur fixation method for SAPd	biaryl yield (%)[a]									
		1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th
1[b]	35% H_2O_2 + H_2SO_4	96	97	98	96	93	97	95	97	96	92
2	$K_2S_2O_8$ (aq) + H_2SO_4	89	90	87	88	95	88	85	91	89	90
3	$(NH_4)_2S_2O_8$(aq) + H_2SO_4	94	93	91	97	99	90	96	95	91	90
4	$Na_2S_2O_8$ (aq) + H_2SO_4	>99	>99	>99	>99	>99	>99	99	98	97	>99

[a]The HPLC yield. [b]The result obtained using first generation SAPd.[4a]

Scheme 2. Aromatic Amination of Bromobenzene 1a with Morpholine 2a

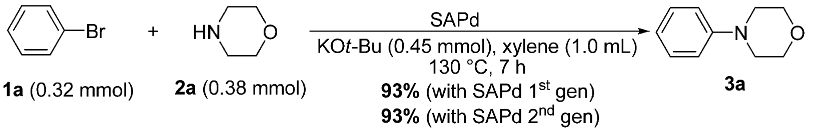
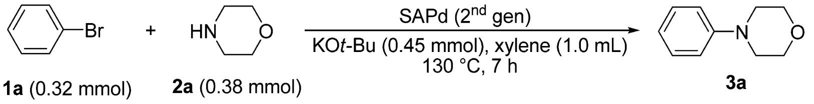


Table 2. The Second Generation SAPd Was Used Repeatedly for 10 Cycles



3a yield (%)[a,b]										
1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	mean yield (%)
93 (93)	92 (93)	93 (92)	92 (93)	91 (92)	93 (92)	92 (92)	91 (92)	91 (91)	93 (91)	**92 (92)**

[a]The HPLC yield. [b]The yield in parentheses was produced using the first generation SAPd.[4c]

H_2SO_4.[6] Although this method led to better control of the heat generation, the poor reproducibility of SAPd continued (entry 2). We next considered the use of ammonium or sodium peroxodisulfate with H_2SO_4. The heat generation and reproducibility problems were overcome, but the use of the SAPd prepared by the $(NH_4)_2S_2O_8$ and H_2SO_4 method resulted in a lower yield of the Suzuki–Miyaura product (entry 3) compared with the first generation SAPd (entry 1).

The high reproducibility of the second generation SAPd prepared by the safer $Na_2S_2O_8$ and H_2SO_4 method for sulfur fixation on a gold surface (entry 4) solved the above-mentioned problems and allowed for safe mass scale production.

Catalytic Activities of Second Generation SAPd in the Buchwald–Hartwig Reaction. Because the Buchwald–Hartwig reaction is more challenging than the Suzuki–Miyaura reaction under ligand-free conditions, we applied the second generation SAPd to the Buchwald–Hartwig reaction to compare the catalytic activities of the first and second generation SAPds in detail. First, we applied the second generation SAPd to the ligand-free Buchwald–Hartwig reaction under standard conditions with bromobenzene **1a** and morpholine **2a** to yield the coupling product of arylamine (**3a**).[4c] Thus, when **1a** (0.32 mmol) was treated with **2a** (0.38 mmol) in the presence of KO*t*-Bu (0.45 mmol) in xylene (1.0 mL) at 130 °C, the yield of product **3a** was 93% (Scheme 2). This initial result indicated that the second generation SAPd had the same chemical nature as the first generation SAPd.

Recyclability Test. After the initial screening, we carefully examined the surface of the catalyst and observed no damage, so we next aimed to utilize the second generation SAPd repeatedly for 10 cycles. By following the same conditions as shown in Scheme 2, we recycled the second generation SAPd for 10 cycles using bromobenzene **1a** and morpholine **2a**, and the reaction proceeded smoothly with a similar chemical yield

(Table 2). We then compared the chemical yields of the synthesis of **3a** mediated by the two generations of SAPd and found that the mean yields were both equivalent and excellent.[4c]

Kinetic Studies/Filtration Test. To identify the actual catalytic species of the second generation SAPd catalyst, we performed kinetic studies/filtration tests and compared the time conversion plots of the following three reactions (A, B, and C). These investigations were performed to confirm whether the leached Pd-species possessed catalytic activity for the aromatic amination (Figure 1). Reaction A was performed by maintaining the conditions shown in Scheme 2, and the reaction proceeded efficiently to give the coupled product **3a** in 93% yield after 7 h. Reactions B and C were also performed under the same conditions with one exception, the second generation SAPd was removed from the mixture after 2 h and after 30 min from the starting of the reaction, respectively. Reaction B yielded 91% of product **3a** after 11 h, whereas, in reaction C, only 10% of product **3a** was detected after 12 h. Thus, it is likely that active Pd species are indeed released from the second generation SAPd and that some time is required for the release of the active Pd-species from the second generation SAPd, similar to the first generation SAPd.

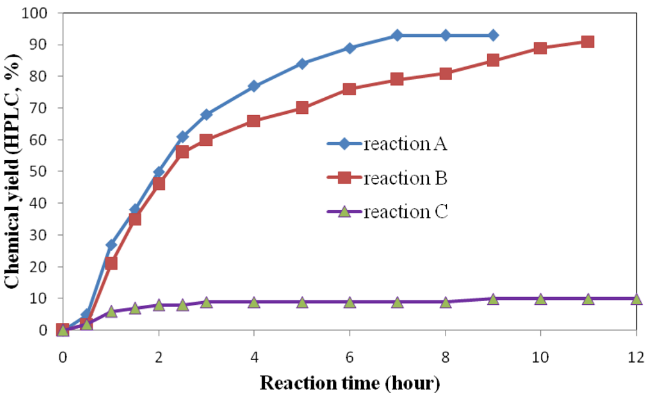


Figure 1. Filtration test for the coupling of **1a** and **2a**.

Measurement of the Pd Amount in Second Generation SAPd and in the Reaction Mixture. We measured the amount of immobilized Pd in the second generation SAPd and also the leached Pd in the reaction mixture by inductively coupled plasma mass spectroscopy. The measurement of immobilized Pd in the second generation SAPd was performed before and after applying the tenth cycle of reactions. Table 3 shows the amount of the immobilized Pd in the second generation SAPd before and after the reactions.[7] The amount of released Pd after cooling in each cycle was extremely low [108−405 ng (0.1−0.4 ppm) for a 0.32 mmol scale reaction] and the amount of Pd was far lower than the US government-required value of residual metal in product streams.[8] Comparison of the leaching properties of the two generations of SAPds revealed that the second generation SAPd released less active Pd in the reaction mixture (less than 0.4 ppm) than the first generation SAPd (less than 0.6 ppm). Although the amount of leached Pd in each cycle was lower than that when using first generation SAPd,[4c] the Buchwald−Hartwig amination reaction proceeded efficiently from the first to tenth cycle in ligand-free conditions.

X-ray Absorbtion Fine Structure (XAFS) Measurement. In order to obtain information on the actual active

Table 3. Amount of Pd in the Reaction Mixture of 1a with 2a[a] and in Second Generation SAPd Itself

amount of leached-Pd (ng) in the reaction mixture[b,c,d]											immobilized Pd on second generation SAPd itself (μg)[c]	
1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	total	before use	after use
405 ± 127	123 ± 60	121 ± 28	168 ± 31	219 ± 88	208 ± 82	188 ± 91	186 ± 131	210 ± 120	108 ± 38	1936 ± 796	57 ± 16 = 0.16 mol %	65 ± 23 = 0.19 mol %
(0.4)	(0.1)	(0.1)	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)	(0.1)			
(0.6)	(0.4)	(0.06)	(0.2)	(0.2)	(0.4)	(0.3)	(0.2)	(0.3)	(0.3)			

[a] Reaction conditions: **1a** (0.32 mmol), **2a** (1.2 equiv), KO*t*-Bu (1.4 equiv), xylene (1.0 mL), 130 °C, 7 h. [b] The entire reaction mixture was acidified and subjected directly to inductively coupled plasma mass spectroscopy measurement. [c] The standard deviation was calculated from four sets of samples. [d] Numbers in parentheses above and below the dashed line indicate the amount of leached Pd in ppm from the second generation and first generation SAPds,[4c] respectively.[9]

species in first and second generations SAPds, we measured the XAFS. Figure 2 shows the Pd K-edge X-ray absorption near edge structure (XANES) spectra of standard materials (Pd foil, PdO, $PdSO_4$, PdS, $Pd(PPh_3)_4$) and SAPds, both first and second generations. The Pd K-edge XANES spectra of the both SAPds are the same and are analogous to that of the Pd foil. These results indicate that the Pd species of SAPds, both first and second generations, are the same.

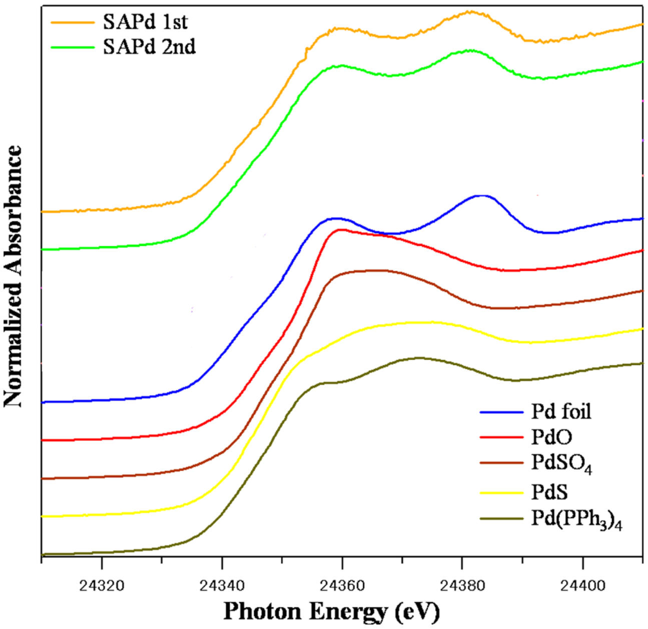


Figure 2. Pd K-edge XANES spectra: first generation SAPd and second generation SAPd.

Scope and Limitations. To generalize the second generation SAPd-catalyzed aromatic aminations, we first used bromobenzene **1a** as a substrate with a variety of secondary amines, and the catalytic activity of the second generation SAPd in all reactions was examined by performing the reactions from the first to tenth cycles (Table 4). Thus, when **1a** was reacted with cyclic amines, i.e., morpholine **2a**, 1,4-dioxa-8-azaspiro[4.5]decane **2b**, and piperidine **2c**, the mean yields of coupled products **3a**, **3b**, and **3c** were 92, 91, and 96%, respectively (entries 1−3). The acyclic secondary amine, dibutylamine **2d**, and an aromatic secondary amine, *N*-methylaniline **2e**, with **1a** yielded the corresponding products **3d** and **3e** in 97 and 92% mean yield, respectively (entries 4 and 5). We then investigated the reaction of **1a** with primary amines, such as benzylamine **2f** and cyclohexylamine **2g**, in which the corresponding monoarylated products **3f** and **3g** were obtained in mean yields of 88 and 91%, respectively (entries 6 and 7). We then explored the coupling reactions using a variety of aryl bromides with **2a**. Thus, when 4-bromoanisole **1b**, having an electron-donating methoxy group, was treated with **2a**, the corresponding product **3h** was obtained in a mean yield of 92% (entry 8). 4-Bromobenzonitrile **1c**, with an electron-withdrawing cyano group, also coupled successfully with **2a**, and the mean yield of the product **3i** was 88% (entry 9). In the reaction of a fused aryl bromide, 2-bromonaphthalene **1d** and **2a**, the coupled product **3j** was obtained in 91% mean yield (entry 10). The aryl tribromide 1,3,5-tribromobenzene **1e** underwent the coupling reaction with **2a** to give the triaminated product **3k** in mean yield of 85% (entry 11).

Aminations of Chlorobenzene. We next examined ligand-free cross-coupling of the less reactive chlorobenzene **4** using the second generation SAPd repeatedly for 10 cycles (Table 5). When **4** was treated with **2a** or **2b**, the corresponding coupling products **3a** and **3b** were successfully obtained after 12 h in mean yields of 88 and 92%, respectively (entries 1 and 2).

■ CONCLUSIONS

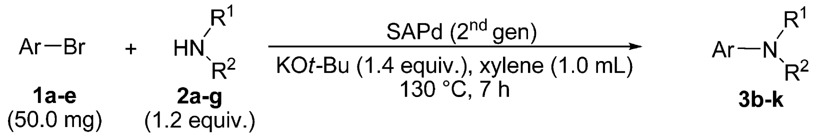
We developed a new and safer heat generation-controllable preparative method of sulfur-modified Au-supported Pd material, second generation SAPd, whose catalytic activity was examined in ligand-free Buchwald−Hartwig cross-coupling reactions. Although we observed no differences in the catalytic activities between the first and second generation SAPds in the Buchwald−Hartwig cross-coupling reactions, the second generation SAPd leached lower amounts of the active Pd species (less than 0.4 ppm for a 0.32 mmol scale reaction) in the reaction mixtures than the first generation SAPd (less than 0.6 ppm for a 0.32 mmol scale reaction). Because of the low leaching, the second generation SAPd could also be recycled for more than the 10 cycles without loss of catalytic activity. As this preparative method is safer than that of the first generation SAPd, the second generation SAPd-mediated catalytic reactions are very efficient. Efforts to elucidate the details of the active catalytic species and chemical properties of the second generation SAPd and its applications to other ligand-free organic transformations are in progress.

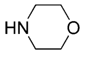
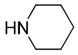
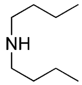
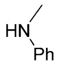
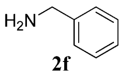
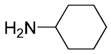
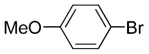
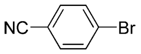
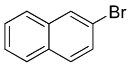
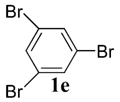
■ EXPERIMENTAL SECTION

Preparation of Second Generation Sulfur-Modified Au-Supported Pd Material. $Na_2S_2O_8$ (4.0 g) was added in small portions to ice-cooled 98% H_2SO_4 (4.7 g) with continuous stirring, and then crushed ice (13.0 g) and water (4.0 g) were added to the solution while the temperature was maintained below 15 °C.[6] When all the salt dissolved to a homogeneous solution at room temperature, the Au (100 mesh-14 × 12 mm^2, 100.7 mg) was placed in the solution (3.0 mL) for 5 min and washed first with H_2O (3.0 mL × 10) and then with EtOH (3.0 mL × 6). The resulting Au-mesh was placed in a round-bottom flask and dried for 10 min under reduced pressure (ca. 6 mmHg). The resulting sulfur-modified Au was placed in a solution of $Pd(OAc)_2$ (5.3 mg, 0.023 mmol) in xylene (3.0 mL) and stirred for 12 h at 100 °C under an Ar atmosphere. The mesh was then rinsed with xylene (3.0 mL × 50) and, after vacuum drying, placed in xylene (3.0 mL) and heated for 12 h at 135 °C. Finally, it was rinsed with xylene (3.0 mL × 50) and dried under a vacuum for 10 min to give the second generation SAPd (100.8 mg, immobilized Pd: 57 ± 16 μg), and only this second generation SAPd was used for the present research. This alternative new method is applicable to large scale second generation SAPd preparation.

Typical Experimental Procedure of Buchwald−Hartwig Coupling Reaction Using Arylbromide Catalyzed by the Second Generation SAPd, Table 4, Entry 1. A mixture of bromobenzene (**1a**, 50.0 mg, 0.32 mmol), morpholine (**2a**, 33.3 mg, 0.38 mmol), and KO*t*-Bu (50.3 mg, 0.45 mmol) in xylene (1.0 mL) was heated in the presence of the second generation SAPd in a glovebox for 7 h at 130 °C. The reaction mixture was cooled to room temperature, and the second generation SAPd (immobilized Pd: 57 ± 16 μg = 0.16 mol %) was recovered from the cold reaction mixture and washed several times with xylene. The reaction mixture was poured into water (5.0 mL), and the organic layer was extracted with AcOEt (3 × 10 mL). The combined organic extracts were washed with brine (3 × 10 mL) and dried over Na_2SO_4. Concentration at reduced pressure gave a yellowish oil, which was chromatographed on silica gel

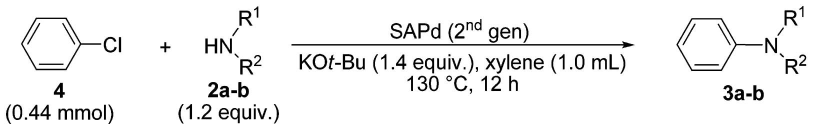
Table 4. Aromatic Aminations of Various Aryl Bromides with a Variety of Amines Using the Second Generation SAPd

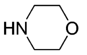
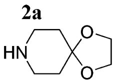


Entry	Ar—Br	$\mathrm{HNR^1R^2}$	Yields (%)[a]										Average yields (%)
			1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	
1[b]	Ph—Br **1a**	 **2a**	93 (93)	92 (92)	93 (92)	92 (93)	91 (92)	93 (92)	92 (92)	91 (92)	91 (91)	93 (91)	**92** **(92)**
2	**1a**	 **2b**	91 (93)	92 (92)	92 (92)	91 (94)	91 (92)	91 (93)	91 (92)	90 (91)	90 (92)	92 (92)	**91** **(92)**
3	**1a**	 **2c**	97 (97)	97 (97)	96 (97)	96 (95)	96 (96)	96 (96)	95 (95)	96 (96)	95 (96)	96 (95)	**96** **(96)**
4	**1a**	 **2d**	99 (98)	97 (97)	98 (99)	97 (97)	97 (97)	96 (96)	96 (96)	97 (96)	96 (96)	96 (96)	**97** **(97)**
5	**1a**	 **2e**	93 (93)	93 (91)	92 (92)	92 (93)	92 (92)	92 (92)	91 (91)	91 (92)	91 (92)	91 (91)	**92** **(92)**
6[c]	**1a**	 **2f**	88 (89)	89 (89)	88 (88)	89 (89)	88 (88)	88 (89)	89 (88)	89 (88)	88 (88)	88 (88)	**88** **(88)**
7[c]	**1a**	 **2g**	92 (92)	92 (92)	92 (92)	89 (92)	89 (89)	92 (88)	89 (92)	88 (92)	92 (89)	92 (91)	**91** **(91)**
8	 **1b**	**2a**	91 (92)	92 (92)	92 (91)	92 (92)	92 (91)	92 (92)	91 (91)	91 (91)	91 (92)	91 (90)	**92** **(91)**
9	 **1c**	**2a**	88 (89)	89 (88)	89 (89)	88 (88)	89 (88)	88 (87)	89 (89)	88 (88)	88 (88)	87 (87)	**88** **(88)**
10	 **1d**	**2a**	91 (89)	91 (91)	90 (91)	91 (90)	91 (90)	90 (90)	90 (90)	90 (90)	91 (90)	90 (90)	**91** **(90)**
11[d]	 **1e**	**2a**	86 (86)	86 (87)	85 (97)	85 (88)	85 (87)	85 (87)	85 (87)	85 (86)	85 (87)	85 (87)	**85** **(87)**

[a] Isolated yields and the yields in parentheses were obtained with first generation SAPd. [b] Results shown in Table 2. [c] Monoarylated product was isolated. [d] 3.6 equiv of amine and 4.0 equiv of KO*t*-Bu were used to give the corresponding triaminated product. When carried out 1.2 equiv of morpholine and 1.4 equiv of KO*t*-Bu, only 30% of triaminated product was yielded with 54% of starting material tribromobenzene.

Table 5. Aromatic Aminations of Chlorobenzene 4 with Amines, 2a and 2b Using SAPd (Second Generation)



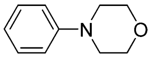
Entry	$\mathrm{HNR^1R^2}$	Yields (%)[a]										Average yields (%)
		1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	
1	 **2a**	88 (89)	89 (89)	88 (89)	89 (88)	89 (88)	89 (89)	88 (89)	87 (88)	87 (88)	88 (87)	**88** **(88)**
2	 **2b**	94 (94)	94 (94)	92 (94)	92 (92)	92 (93)	92 (93)	92 (92)	91 (92)	91 (91)	91 (91)	**92** **(93)**

[a] Isolated yields and the yields in parentheses were obtained with the first generation SAPd.

with hexane–AcOEt (90:10 v/v) as the eluent to give the 4-phenylmorpholine (**3a**, 47.1 mg, 93%) as a white solid. The recovered second generation SAPd catalyst was again subjected to the above reaction condition for a second cycle, and this procedure was repeated for a total of 10 cycles.

Typical Experimental Procedure of Buchwald–Hartwig Coupling Reaction Using Chlorobenzene Catalyzed by the Second Generation SAPd, Table 5, Entry 1. A mixture of chlorobenzene (**4**, 50.0 mg, 0.44 mmol), morpholine (**2a**, 46.0 mg, 0.53 mmol), and KO*t*-Bu (69.0 mg, 0.62 mmol) in xylene (1.0 mL) was heated in the presence of second generation SAPd in a glovebox for 12 h at 130 °C. The reaction mixture was cooled to room temperature, and the second generation SAPd (immobilized Pd: 57 ± 16 μg = 0.12 mol %) was recovered from the cold reaction mixture and washed several times with xylene. The reaction mixture was poured into water (5.0 mL), and the organic layer was extracted with AcOEt (3 × 10 mL). The combined organic extracts were washed with brine (3 × 10 mL) and dried over Na_2SO_4. Concentration at reduced pressure gave a yellowish oil, which was chromatographed on silica gel with hexane–AcOEt (90:10 v/v) as the eluent to give the 4-phenylmorpholine (**3a**, 63.8 mg, 88%) as a white solid. The recovered second generation SAPd catalyst was again subjected to the above reaction condition for a second cycle, and this procedure was repeated for a total of 10 cycles.

4-Phenylmorpholine (3a).[10,11]

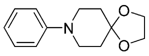


From arylbromide method. Average yield: 92%.

From arylchloride method. Average yield: 88%.

White solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28–7.23 (2H, m), 6.90–6.85 (3H, m), 3.82 (4H, t, *J* = 4.6 Hz), 3.11 (4H, t, *J* = 4.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.1, 129.0, 119.8, 115.5, 66.7, 49.1; LRMS (EI) *m*/*z* 163 (100%, M^+).

8-Phenyl-1,4-dioxa-8-azaspiro[4.5]decane (3b).[12]

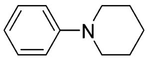


From arylbromide method: By following the same procedure described for **3a**, amine **3b** was prepared from bromobenzene (**1a**) and 1,4-dioxa-8-azaspiro[4.5]decane (**2b**). Average yield: 91%.

From arylchloride method: By following the same procedure described for **3a**, amine **3b** was prepared from chlorobenzene (**1h**) and 1,4-dioxa-8-azaspiro[4.5]decane (**2b**). Average yield: 92%.

Yellowish oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.20 (2H, m), 6.9 (2H, d, *J* = 8.7 Hz), 6.83–6.79 (1H, dd, *J* = 7.4 and 7.4 Hz), 3.9 (4H, s), 3.80 (4H, t, *J* = 5.5 Hz), 1.82 (4H, t, *J* = 5.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 128.9, 119.3, 116.4, 107.0, 64.1, 47.6, 34.4; LRMS (EI) *m*/*z* 219 (55%, M+).

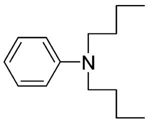
1-Phenylpiperidine (3c).[13]



By following the same procedure described for **3a**, amine **3c** was prepared from bromobenzene (**1a**) and piperidine (**2c**). Average yield: 96%.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.23 (2H, m), 6.94 (2H, d, *J* = 7.8 Hz), 6.82 (1H, dd, *J* = 7.3 and 7.3 Hz), 3.15 (4H, t, *J* = 5.0 Hz), 1.74–1.68 (4H, m), 1.60–1.54 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 128.9, 119.1, 116.4, 50.5, 25.8, 24.2; LRMS (EI) *m*/*z* 116 (100%, M+).

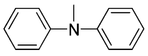
N,*N*-Dibutylaniline (3d).[13]



By following the same procedure described for **3a**, amine **3d** was prepared from bromobenzene (**1a**) and *n*-dibutylamine (**2d**). Average yield: 97%.

Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22–7.17 (2H, m), 6.65–6.60 (3H, m), 3.25 (4H, t, *J* = 7.4 Hz), 1.60–1.52 (4H, m), 1.40–1.30 (4H, m), 0.95 (6H, t, *J* = 7.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 129.1, 115.0, 111.6, 50.7, 29.3, 20.3, 14.0; LRMS (EI) *m*/*z* 205 (70%, M+).

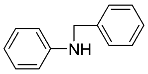
N-Methyl-*N*-phenylaniline (3e).[14]



By following the same procedure described for **3a**, amine **3e** was prepared from bromobenzene (**1a**) and *N*-methylaniline (**2e**). Average yield: 92%.

Yellowish oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (4H, dd, *J* = 7.8 and 7.8 Hz), 7.02 (4H, d, *J* = 7.8 Hz), 6.95 (2H, d, *J* = 7.3 Hz), 3.32 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 129.1, 121.2, 120.3, 40.1; LRMS (EI) *m*/*z* 183 (100%, M+).

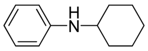
N-Benzylaniline (3f).[15]



By following the same procedure described for **3a**, amine **3f** was prepared from bromobenzene (**1a**) and benzylamine (**2f**). Average yield: 88%.

Yellowish oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38–7.32 (4H, m), 7.26 (1H, dd, *J* = 7.5 and 7.5 Hz), 7.19–7.15 (2H, m), 6.71 (1H, dd, *J* = 7.3 and 7.3 Hz), 6.63 (2H, d, *J* = 6.4 Hz), 4.32 (2H, s), 4.02 (1H, brs); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 139.4, 129.2, 128.6, 127.4, 127.1, 117.5, 112.7, 48.2; LRMS (EI) *m*/*z* 183 (100%, M+).

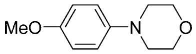
N-Cyclohexylaniline (3g).[16]



By following the same procedure described for **3a**, amine **3g** was prepared from bromobenzene (**1a**) and cyclohexylamine (**2g**). Average yield: 91%.

Yellowish oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (2H, dd, *J* = 7.8 and 7.8 Hz), 7.65 (1H, dd, *J* = 7.8 and 7.8 Hz), 6.59 (2H, d, *J* = 7.3 Hz), 3.51 (1H, br s), 3.27–3.23 (1H, m), 2.07–2.05 (2H, m), 1.78–1.74 (2H, m), 1.67–1.64 (1H, m), 1.41–1.32 (2H, m), 1.26–1.11(3H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.3, 129.1, 116.7, 113.0, 51.5, 33.3, 25.8, 24.9; LRMS (EI) *m*/*z* 175 (50%, M+).

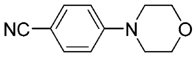
4-(4-Methoxyphenyl)morpholine (3h).[17]



By following the same procedure described for **3a**, amine **3h** was prepared from 4-bromoanisole (**1b**) and morpholine (**2a**). Average yield: 92%.

White solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90–6.84 (4H, m), 3.86 (4H, t, *J* = 4.8 Hz), 3.77 (3H, s), 3.05 (4H, t, *J* = 4.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.9, 145.6, 117.8, 114.4, 67.0, 55.5, 50.8; LRMS (EI) *m*/*z* 193 (60%, M+).

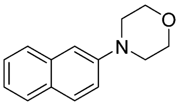
4-Morpholinobenzonitrile (3i).[17]



By following the same procedure described for **3a**, amine **3i** was prepared from 4-bromobenzonitrile (**1c**) and morpholine (**2a**). Average yield: 88%.

Yellowish solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (2H, d, *J* = 8.7 Hz), 6.87 (2H, d, *J* = 8.6 Hz), 3.85 (4H, t, *J* = 4.6 Hz), 3.28 (4H, t, *J* = 4.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.4, 133.4, 119.8, 114.0, 100.8, 66.4, 47.2; LRMS (EI) *m*/*z* 188 (60%, M+).

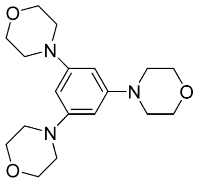
4-(Naphthalen-2-yl)morpholine (3j).[18]



By following the same procedure described for **3a**, amine **3j** was prepared from 2-bromonaphthalene (**1d**) and morpholine (**2a**). Average yield: 91%.

White solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74−7.69 (3H, m), 7.41 (1H, dd, J = 7.5 and 7.5 Hz), 7.31−7.27 (1H, m), 7.26−7.24 (1H, m), 7.11 (1H, d, J = 6.0 Hz), 3.91 (4H, t, J = 4.6 Hz), 3.25 (4H, t, J = 4.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.0, 134.5, 128.8, 128.6, 127.4, 126.7, 126.3, 123.5, 118.8, 110.0, 66.9, 49.7; LRMS (EI) m/z 213 (80%, M+).

1,3,5-Trimorpholinobenzene (3k).[19]



By following the same procedure described for **3a**, amine **3k** was prepared from 1,3,5-tribromobenzene (**1e**) and morpholine (**2a**). Average yield: 85%.

Yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.07 (3H, s), 3.85 (12H, t, J = 5.2 Hz), 3.13 (12H, t, J = 5.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.1, 97.2, 66.9, 49.9; LRMS (EI) m/z 333 (100%, M+).

Large Scale Second Generation SAPd Preparation. $Na_2S_2O_8$ (24.0 g) was added in small portions to ice-cooled 98% H_2SO_4 (28.2 g) with continuous stirring, and then crushed ice (78.0 g) and water (24.0 g) were added to solution while keeping the temperature below 20 °C. The Au-mesh case containing 25 sheets of Au mesh was dipped into the solution for 5 min. The Au-mesh case was washed first with water while stirring 5 times for 3 min and then 3 times by ethanol while stirring for 3 min. The resulting Au-mesh case was then dried under reduced pressure. The resulting sulfur-modified Au-mesh case was placed in a solution of $Pd(OAc)_2$ (156 mg, 0.69 mmol) in xylene (90.0 mL), and the solution stirred for 12 h at 100 °C under an Ar atmosphere. The case was washed 5 times for 5 min with xylene while stirring, and after vacuum drying, the case was placed in xylene and heated for 12 h at 135 °C. Finally, the case was washed 3 times for 5 min with xylene and dried under a vacuum for 10 min to give 25 sheets of second generation sulfur-modified Au-supported Pd material.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectral data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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