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Aerobic Oxidative Homocoupling of Aryl Amines Using Heterogeneous Rhodium Catalysts

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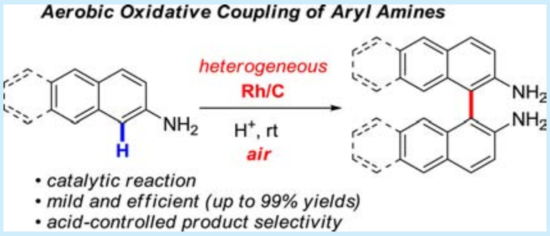
Supporting Information

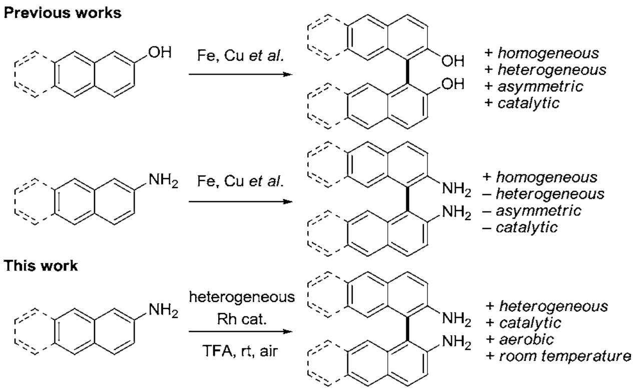
ABSTRACT: The first heterogeneous catalyzed oxidative coupling of aryl amines is reported. Aryl amines were dimerized at room temperature under air using a heterogeneous Rh/C catalyst in the presence of acids. By choosing a suitable acidic solvent, biaryl compounds and carbazoles were selectively prepared in good yields. This reaction is operationally simple and provides an efficient synthetic methodology for the preparation of biaryl diamines via oxidative C−H activation.



Biaryl compounds are privileged structural motifs employed in organic chemistry, natural product chemistry, and material sciences such as organic light-emitting diodes (OLED), organic solar cells, and organic photoconductors.[1] Particularly, axial chiral biaryl compounds, including BINAP and BINOL, are known as the most successful ligands in asymmetric catalysis, affording a wide range of catalytic enantioselective transformations.[2] Recently, 1,1′-binaphthyl-2,2′-diamine (BINAM) and its derivatives have also been developed as effective chiral ligands/catalysts with high enantioselectivity.[3] However, in contrast to the wide use of BINAP derivatives, reports on asymmetric syntheses using BINAM derivatives as a chiral ligand are limited, probably because of the relatively expensive and limited number of reliable synthetic methodologies.[4] Thus, the development of novel and powerful synthetic strategies of 1,1′-biaryl-2,2′-diamines is strongly needed.

Oxidative coupling of aryl amines is a simple and direct method for the preparation of 1,1′-biaryl-2,2′-diamines. Typically, the Suzuki−Miyaura reaction and other related cross-coupling reactions are often used for the aryl−aryl bond formation of biaryls. However, these methods require prefunctionalization of both coupling components.[5] Recently, the direct C−C bond formation between two aromatic C−H bonds using C−H activation methodology has gained significant attention.[6] Thus, the oxidative coupling of arenes is desirable from the viewpoint of improved atom economy. The oxidative coupling of naphthols and phenols using homo- and heterogeneous metals has been well studied (Scheme 1).[7−10] Additionally, numerous applications in the development of asymmetric reactions,[11,12] heterogeneous catalysis,[13] and total synthesis of natural products have been developed. However, the oxidative coupling of aryl amines remains largely unexplored,[14,15] and synthetic processes for the preparation of 1,1′-biaryl-2,2′-diamines using heterogeneous metal catalysts are particularly limited.[16] Because aryl amines are easily oxidized, generating many side products, this type of oxidative reaction is usually uncontrollable. Here, we report the oxidative coupling of aryl amines under air using a heterogeneous Rh/C catalyst to produce 1,1′-biaryl-2,2′-diamines in high yields.

Scheme 1. Oxidative Coupling of Aryl Amines



During the course of preparation of aminoanthracene derivatives, we accidentally isolated a small amount of dimer **2** in the presence of a heterogeneous rhodium catalyst in an acidic solvent under air conditions (Scheme 2). We anticipated that, upon protonation of aryl amines under acidic conditions, the resulting ammonium salts may prevent side reactions induced by *N*-oxidation and undergo the desired coupling to yield the dimer. Although the use of HCl (aq.) did not induce any coupling reactions, the use of methanesulfonic acid (MsOH) resulted in a trace amount of coupling product **2a** (Table 1, entries 1 and 2). Following these results, various

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Scheme 2. Aerobic Oxidative Coupling of Aryl Amine

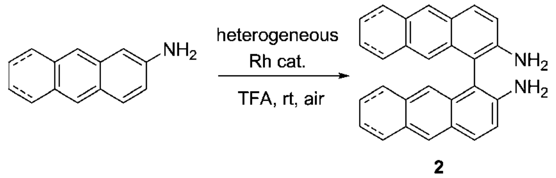
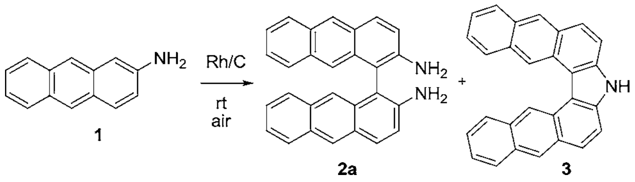


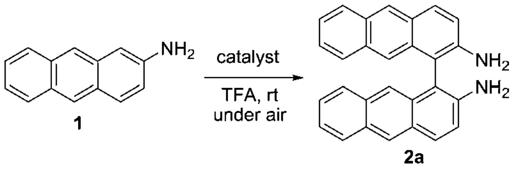
Table 1. Effect of Solvent[a]



				yield (%)	
entry	solvent	pK_a	time	2a	3
1	12 M HCl	−8.0	27 h	no reaction	
2	MsOH	−2.6	26 h	low yield	
3	TFA	−0.2	45 min	90	2
4	CCl_3CO_2H	0.6	12 h	76	0
5	CF_2HCO_2H	1.2	4 h	60	14
6	AcOH	4.8	34 h	51	36
7	HFIP	9.3	6 h	0	76
8	CF_3CH_2OH	12.4	25 h	12	15
9	EtOH	15.5	24 h	15	6
10	THF	–	26 h	no reaction	
11	CH_2Cl_2	–	26 h	no reaction	

[a] Reaction conditions: aryl amine (**1**, 0.25−0.50 mmol), 5% Rh/C (5 mol %), room temperature under air.

Table 2. Effect of Metal Catalysts[a]



entry	catalyst	mol %	time	yield (%)
1	Rh/C	2	2 h	99
2[b]	Rh/C	2	40 min	94
3[c]	Rh/C	2	2 h	13
4[b,e]	Rh/C	2	1 h	94
5[b]	Rh/C	0.25	6 h	79
6	Rh/Al_2O_3	5	3.5 h	80
7	$RhCl(PPh_3)_3$	15	20 h	messy
8	$RhCl_3$	100	22 h	no reaction
9[d]	Rh_2O_3	5	34 h	10
10	Ru/C	5	24 h	77
11	Ru/Al_2O_3	10	48 h	56
12	Pd/C	5	18 h	81
13	Pt/C	5	20 min	messy
14	PtO_2	5	7.5 h	84

[a] Reaction conditions: aryl amine (**1**, 0.25−0.50 mmol), TFA, room temperature under air. [b] Under O_2. [c] Under argon. [d] Conducted at rt to 70 °C. [e] 2.6 mmol scale.

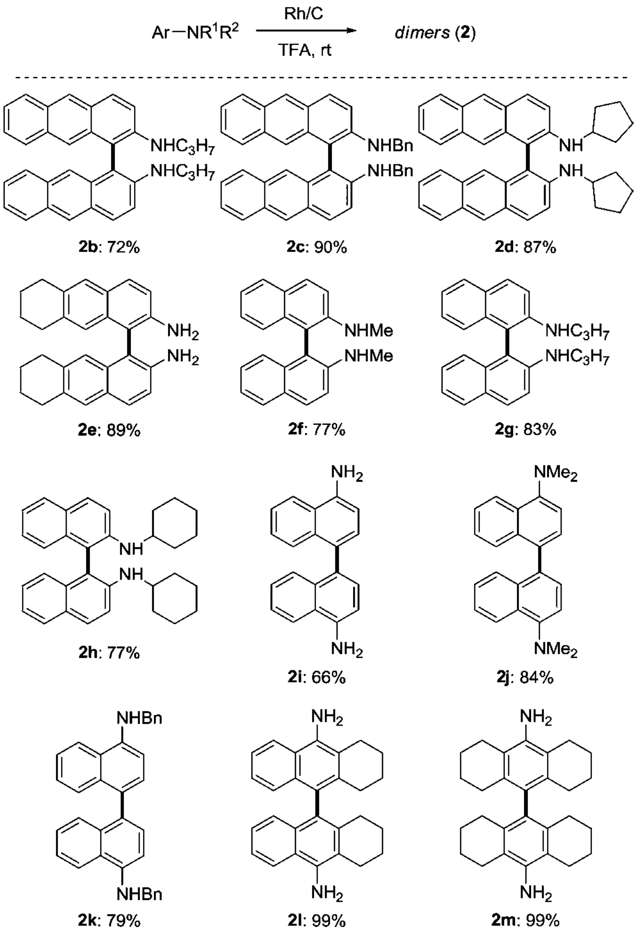
acidic solvents were examined. As observed, the reaction was very sensitive to the pK_a values of the solvents used. Trifluoroacetic acid (TFA) was the best solvent for obtaining dimer **2a** in high yields, and a small amount of carbazole **3** was also generated (entry 3). In the absence of Rh/C in TFA under air, the reaction did not proceed even after heating to 70 °C overnight. The use of trichloroacetic acid afforded dimer **2a** in good yields (entry 4). The reaction in either difluoroacetic acid or acetic acid, the acidities of which are weaker than that of TFA, afforded a reduced yield of **2a**, and carbazole **3** was obtained in 14% and 36% yields, respectively (entries 5 and 6). Interestingly, the reaction in hexafluoroisopropanol (HFIP) resulted in the exclusive formation of carbazole **3** in 76% yield, whereas both trifluoroethanol and ethanol were unsuitable solvents under these conditions (entries 7−9).[17] The other aprotic solvents, such as THF and CH_2Cl_2, did not afford the coupling products (entries 10 and 11). This indicates that the acidic properties of solvents not only accelerate the reaction but also control the product selectivity.

We then examined various catalysts for the coupling reaction (Table 2). Though the amount of the Rh/C catalyst was reduced to 2 mol %, **2a** was obtained in quantitative yield (entry 1). Under 1 atm of oxygen, the reaction proceeded faster and was complete within 40 min to give **2a** in 94% yield (entry 2). In contrast, under an argon atmosphere, only a trace amount of **2a** was obtained (entry 3). Thus, this indicates that molecular oxygen plays an important role in this rhodium-catalyzed oxidative coupling as a terminal oxidant. The fluorinated solvents are also expected to accelerate oxidation because of the high solubility of oxygen.[18] The coupling reaction could be carried out on a large scale and with a lower catalyst loading to provide excellent yields of **2a**, indicating both the scalability and reliability of the protocol (entries 4 and 5). Besides Rh/C, the use of Rh/Al_2O_3 afforded dimer **2a** in high yields despite the slightly longer reaction time (entry 6). Other rhodium-based catalysts were also examined. However, results were not satisfactory (entries 7−9). Because the heterogeneous rhodium-based catalysts gave superior results, various other heterogeneous catalysts were investigated. The use of Ru/C, Ru/Al_2O_3, Pd/C, and PtO_2 afforded good product yields, and the use of Pt/C afforded complex mixtures (entries 10−14).

Subsequently, we examined the effect of substrates under the established optimal conditions (Scheme 3). Using *N*-mono-substituted 2-aminoanthracene, dimer **2b**−**2d** were obtained in good yields. The reaction using a 2-aminonaphthalene derivative also proceeded smoothly to afford dimer **2e** in 89% yield. Likewise, *N*-substituted substrates possessing both primary and secondary alkyl groups led to dimer **2f**−**2h** in good yields. Interestingly, 1-aminonaphthalene and its derivatives underwent C−C bond formation at the 4-position, generating **2i**−**2l** in 66−99% yields. The reaction using a *N,N*-dimethyl derivative also proceeded to afford dimer **2j** in 84% yield. The octahydroanthracene derivative, which is not a fused aromatic compound, also dimerized to afford the corresponding product **2m** in quantitative yield. Thus, the anthracene derivatives as well as naphthalene and aniline derivatives underwent oxidative coupling to afford the corresponding dimers in good yields. As described above, this catalytic coupling reaction is highly versatile.

To gain insights into the reaction mechanism, the electron spin resonance (ESR) spectrum of the reaction mixture using **1** and 5 mol % Rh/Al_2O_3 under air was measured at rt.[19] A broad signal at *g* 2.0021 was observed, whereas the signal was not observed in the absence of either TFA or Rh/Al_2O_3. The ESR results indicate that the radical species are generated in the

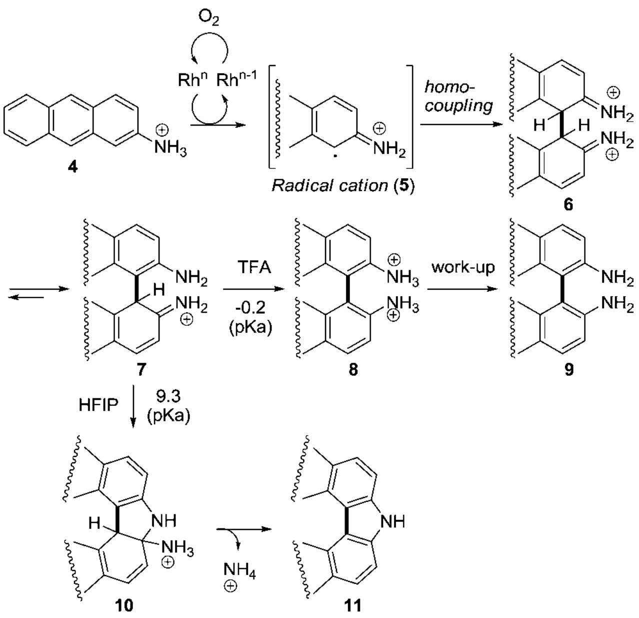
Scheme 3. Scope of Substrates[a]



[a]Reaction conditions: aryl amine (0.18−1.0 mmol), 5% Rh/C (5 mol %), TFA, room temperature under air.

reaction mixture.[20] Accordingly, the proposed mechanism is shown in Scheme 4. First, a one-electron transfer from the ammonium salt **4** to the rhodium catalyst occurs to give the radical cation intermediate **5** and reduced rhodium. The radical cation **5** dimerizes to give the diiminium salt **6**,[21] which tautomerizes to afford the coupled product **9** after workup. Molecular oxygen oxidizes the reduced catalyst to regenerate the active rhodium metal. Unlike the TFA system, in the presence of HFIP, the carbazole **3** is preferably produced. Because the reaction using dimer **2a** and 5 mol % Rh/C in HFIP did not occur,[22] carbazole **3** is not generated from diamine **9**. In contrast, the diiminium salt **6** is rapidly converted into diammonium **8** in TFA. In the presence of HFIP, owing to the higher pK_a value, cyclization proceeds to give **10** via amino iminium intermediate **7**. Finally, elimination of ammonium results in carbazole **11**. However, other route mechanisms involving aryl rhodium species cannot be ignored.[23]

Scheme 4. Proposed Mechanism



In conclusion, we developed the heterogeneous rhodium-catalyzed oxidative homocoupling reaction of aryl amines to prepare biaryl compounds. We demonstrate that the acidic solvent has a strong influence on the yield and selectivity of the products. By choosing a suitable acidic solvent, biaryl compounds and carbazole can be selectively prepared in good yields. The current synthetic strategies for aryl−aryl bond formation provide greener alternatives to previously reported methods and involve heterogeneous catalysts, fewer steps, and milder conditions. Further studies on the synthetic applications and mechanistic details are underway.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details and spectroscopic data. 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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(19) See the Supporting Information for details.

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(21) For the oxidative dimerization of 2-naphthol, several mechanisms such as radical−radical and radical−anion coupling have been proposed; see refs 11e and 13g.

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