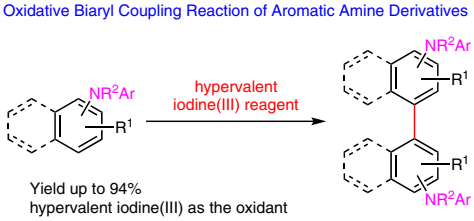
Synlett K. Morimoto et al. Letter

Oxidative Biaryl Coupling of *N*-Aryl Anilines by Using a Hypervalent Iodine(III) Reagent

Koji Morimoto[a,b]
Doichi Koseki[a]
Toshifumi Dohi[a]
Yasuyuki Kita[*b]

[a] Ritsumeikan University College of Pharmaceutical Sciences 1-1-1 Nojihigashi, Kusatsu, Shiga 525-8577, Japan
[b] Ritsumeikan University, Research Organization of Science and Technology, 1-1-1 Nojihigashi, Kusatsu, Shiga 525-8577, Japan
kita@ph.ritsumei.ac.jp

Dedicated to Victor Snieckus in honor of his 80th birthday



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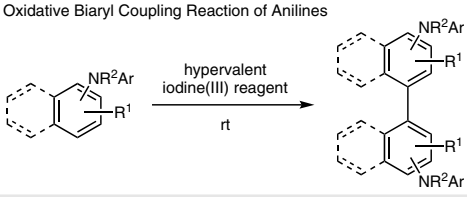
Abstract Biaryl diamines are important building blocks in organic synthesis. Consequently, it is desirable to develop a general and mild synthetic approach to diverse biaryl diamines. Oxidative coupling is an efficient and promising strategy for the synthesis of these targets. We have now developed a direct formation of biaryl diamines by oxidative coupling using a hypervalent iodine(III) reagent.

Key words biaryl diamines, hypervalent iodine, oxidative coupling

The biaryl diamine core is an important motif and a key structural attribute of many bioactive natural products, chiral ligands, and pharmaceuticals.[1] Therefore, the development of efficient synthetic methods for providing biaryl diamines has attracted the attention of researchers in organic chemistry. Among the methods developed, oxidative coupling[2] of anilines is one of the most efficient methods for synthesizing biaryl diamines.[3] One of the advantages of the oxidative strategy is that nonfunctional aniline derivatives are used as green and economic coupling substrates, instead of aryl halides or organometallic derivatives. Recently, various coupling reactions of anilines involving the use of $TiCl_4$,[4] cerium(IV) ammonium nitrate,[5] Cu,[6,7] Fe,[8] or Rh oxidants,[9] or organic 1,8-bis(diphenylmethylium)naphthalenediyl dications[10] have been developed. However, these reactions have problems, such as the need for large excesses of the starting aniline, low-yielding processes, or limited reaction scopes. This is because, when simple biaryl amines are employed in the oxidative couplings, numerous byproducts are often formed alongside the desired products. Here, we report the oxidative coupling of biaryl diamines at ambient temperature by using an environmentally benign hypervalent iodine(III) reagent (Scheme 1).

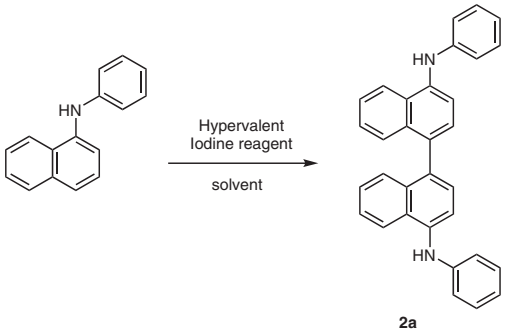


Scheme 1 The metal-free oxidative coupling of aromatic amines by using a hypervalent iodine(III) reagent

The use of hypervalent iodine reagents in oxidative transformations has received significant attention, with consideration of their low toxicity and mild reaction conditions.[11] We recently reported the direct formation of *N*-alkylsulfonyl anilide biaryl compounds by oxidative cross-coupling with a variety of aromatic compounds, especially nonactivated aromatic hydrocarbons.[12]

Initially, we used the reaction of *N*-phenylnaphthalen-1-amine (**1a**) to probe the expected oxidative coupling reaction.[13] We found that when the reaction was performed in the presence of $PhI(OAc)_2$ (PIDA) in CH_2Cl_2 for one hour at room temperature, the coupling product **2a** was obtained through C–C bond formation at the naphthalene ring, albeit in only 13% yield (Table 1, entry 1). Encouraged by this result, we investigated a series of hypervalent iodine(III) reagents. The yield was markedly improved by using $PhI(OCOCF_3)_2$ (PIFA) as the oxidant (entry 2). The use of various solvents [$(F_3C)_2CHOH$ (HFIP), CF_3CH_2OH (TFE), and DCE] was then examined (entries 4, 5, and 8), and DCE proved to be effective for this coupling reaction (entry 8). Moreover, the presence of acids such as AcOH[14] or $BF_3{\cdot}Et_2O$[15] was unsuitable for the reaction (entries 9 and 10). Thus, the optimized reaction conditions were determined as follows: PIFA as the oxidant in DCE at room temperature for three hours.

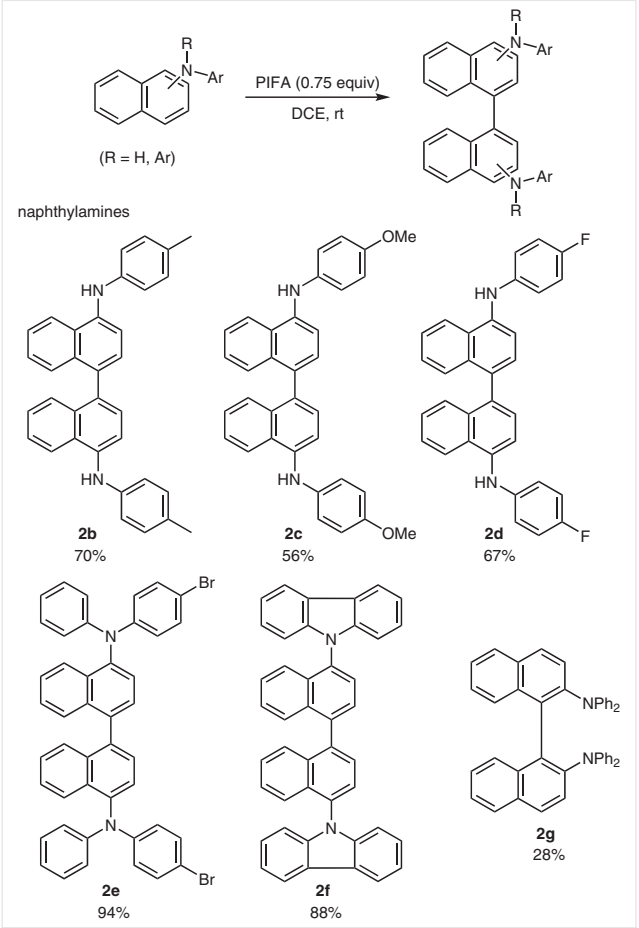
Table 1 Optimization of the Reaction Conditions[a]



2a

Entry	Iodine reagent (equiv)	Solvent	Yield (%)
1	PIDA (1)	CH_2Cl_2	13
2	PIFA (1)	CH_2Cl_2	64
3	PhI(OH)OTs (1)	CH_2Cl_2	49
4	PIFA (1)	TFE	34
5	PIFA (1)	HFIP	25
6	PIFA (1)	CH_2Cl_2	58
7	PIFA (1.5)	CH_2Cl_2	71
8	PIFA (1.5)	DCE	75
9[b]	PIFA (1.5)	DCE	71
10[c]	PIFA (1.5)	DCE	N.D.

[a] Reaction conditions: **1a** (2 equiv.), iodine reagent (1 equiv.), solvent, rt, 3 h.
[b] In the presence of AcOH (2 equiv).
[c] In the presence of $BF_3{\cdot}Et_2O$ (2 equiv).



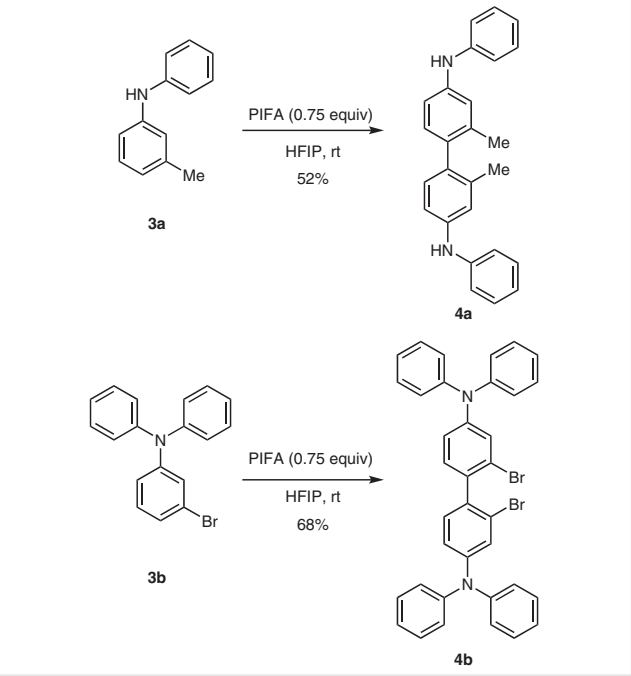
Scheme 2 Scope of substrates

With the optimized reaction conditions in hand (Table 1, entry 8), we next evaluated the scope of various naphthalen-1-amine and -2-amine derivatives (Scheme 2). *N*-Arylnaphthalen-1-amines were smoothly converted into the desired coupling products **2b–d** in moderate to high yields. Substituents in the *para*-position of the *N*-aryl ring, whether the electron-donating (**2b** or **2c**) or electron-withdrawing (**2d**), had no influence for the coupling reaction. The reaction using an *N*,*N*-diphenyl derivative also proceeded to afford dimer **2e** in 94% yield. A carbazole-substituted naphthalen-1-amine gave the corresponding product **2f** in 88% yield. *N*,*N*-Diphenylnaphthalen-1-amine gave the coupling product **2g** in moderate yield. However, naphthalen-1-amine, with a free amino group, afforded a low yield of the dimer product.

To further explore its applicability, we next performed the coupling reaction with various aniline derivatives. However, no coupling products were produced from the anilines, which decomposed under our reaction conditions. Despite this, we optimized the reaction conditions and we were pleased to find that *N*-(3-tolyl)aniline (**3a**) was converted into the desired coupling product **4a** when HFIP was used as a solvent (Scheme 3). The reaction of (3-bromophenyl)diphenylamine (**3b**) similarly afforded the coupling product **4b** in moderate yield (Scheme 3).

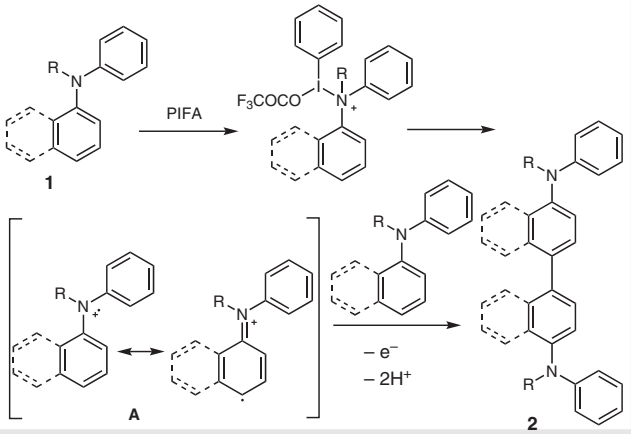
A suggested reaction mechanism for the present iodine-induced oxidative coupling of anilines is shown in Scheme 4. First, the aniline nitrogen coordinates with the iodine(III) reagent to generate the iodine(III) complex **A**;[16,17] this undergoes one-electron oxidation to produce the intermediate radical cation of the aniline **A**. This then reacts with the neutral aniline **1** at the aryl ring to give the coupled product **2** after further one-electron oxidation and deprotonation.

After our synthetic studies, the next necessary task was to improve the oxidative coupling involving a stoichiometric amount of the iodine(III) reagent to a catalytic process. We have already reported a catalytic use of iodine(III) reagents.[18] On the basis of our previous report, we examined the coupling reaction of *N*-phenylnaphthalen-1-amine (**1a**) in the presence of 10 mol % of PhI and one equivalent of *m*CPBA in 1:1 DCE/HFIP at room temperature (Scheme 5).



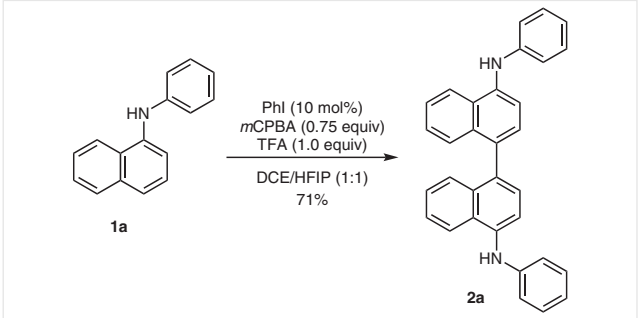
Scheme 3 Scope of aniline derivatives

Amine **1a** was found to undergo an iodine(III)-catalyzed oxidative homocoupling to give the desired dimer **2a** in good yield (71%).



Scheme 4 A suggested reaction mechanism

In summary, we have demonstrated the oxidative biaryl coupling of aniline derivatives by using a hypervalent(III) reagent.[20] The reactions occurred under mild conditions with complete regioselectivity and in good yields. The obtained biaryl diamine derivatives are valuable building blocks, as demonstrated by a series of follow-up reactions. Further studies on the applications of this oxidative coupling protocol are currently under investigation in our laboratory.



Scheme 5 Hypervalent iodine(III) catalyzed oxidative coupling of *N*-phenylnaphthalen-1-amine (**1a**)

Funding Information

This work was partially supported by Grants-in-Aid for Scientific Research (A) from the Japan Society for the Promotion of Science (JSPS), a Grant-in-Aid for Scientific Research on Innovative Areas 'Advanced Molecular Transformation by Organocatalysts' from The Ministry of Education, Culture, Sports, Science and Technology (MEXT), and the Ritsumeikan Global Innovation Research Organization (R-GIRO) project. T.D. acknowledges a Grant-in-Aid for Scientific Research (C) from JSPS and the Asahi Glass Foundation. K.M. also acknowledges support from a Grant-in-Aid for Scientific Research (C) from the JSPS

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(20) **Oxidative Coupling of *N*-Arylnaphthalenamines 1; General Procedure**

PIFA (0.75 equiv.) was added to a stirred solution of the appropriate naphthalenamine **1** (0.30 mmol, 1 equiv) in DCE (3 mL) at r.t., and the mixture was stirred for 30 min. When the reaction was complete, sat. aq $NaHCO_3$ was added to the mixture, and the aqueous phase was extracted with CH_2Cl_2. The extracts were dried (Na_2SO_4) and evaporated to dryness, and the crude residue was purified by column chromatography (silica gel, hexane–EtOAc).

***N,N′*-Diphenyl-(1,1′-binaphthyl)-4,4′-diamine (2a)**[8c]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.04 (s, 2 H), 6.95 (t, *J* = 7.6 Hz, 2 H), 7.11 (dd, *J* = 1.2, 8.8 Hz, 4 H), 7.29–7.35 (m, 6 H), 7.41 (d, *J* = 7.6 Hz, 2 H), 7.46–7.51 (m, 6 H), 8.14 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 115.1, 117.6, 120.6, 121.8, 125.5, 126.1, 127.4, 127.5, 128.3, 129.4, 133.3, 134.1, 138.5, 144.6.

***N,N′*-bis(4-Tolyl)-1,1′-binaphthalene-4,4′-diamine (2b)**[8c]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 6 H), 6.00 (s, 2 H), 7.05 (d, *J* = 8.4 Hz, 4 H), 7.13 (d, *J* = 8.4 Hz, 4 H), 7.30 (t, *J* = 7.6 Hz, 2 H), 7.36–7.37 (m, 4 H), 7.44–7.50 (m, 4 H), 8.11 (d, *J* = 8.8 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7, 113.4, 118.7, 121.5, 125.4, 126.0, 126.9, 127.4, 128.3, 129.9, 130.6, 132.5, 134.1, 139.3, 141.6.

***N,N′*-Bis(4-bromophenyl)-*N,N′*-diphenyl-1,1′-binaphthalene-4,4′-diamine (2e)**

IR (KBr): 3064, 3037, 1582, 1485, 1272, 910, 736 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 6.97 (d, *J* = 8.8 Hz, 4 H), 7.02 (t, *J* = 7.2 Hz, 2 H), 7.15 (d, *J* = 7.6 Hz, 4 H), 7.26–7.34 (m, 10 H), 7.38 (t, *J* = 6.8 Hz, 2 H), 7.42 (d, *J* = 7.6 Hz, 2 H), 7.49 (d, *J* = 8.0 Hz, 2 H), 7.51 (d, *J* = 7.6 Hz, 2 H), 8.02 (d, *J* = 8.0 Hz, 2 H). ^{13}C NMR ($CDCl_3$): δ = 113.8, 122.50, 122.53, 123.0, 124.3, 126.4, 126.5, 126.6, 127.2, 128.5, 129.3, 131.0, 132.1, 134.5, 136.8, 142.9, 147.7, 147.9. MS (MALDI-TOF): *m/z* = 744.12 [M$^+$].

***N,N,N′,N′*-Tetraphenyl-1,1′-binaphthalene-2,2′-diamine (2g)**[19]

^{1}H NMR ($CDCl_3$): δ = 6.44 (d, *J* = 8.1 Hz, 2 H), 6.45–6.58 (m, 12 H), 6.61–6.77 (m, 10 H), 7.12 (td, *J* = 1.2, 7.6 Hz, 2 H), 7.62 (m, 4 H), 7.78 (d, *J* = 8.6 Hz, 2 H). ^{13}C NMR ($CDCl_3$): δ = 121.7, 123.2, 124.4, 125.2, 126.6, 126.7, 127.1, 128.3, 128.7, 131.2, 131.7, 134.0, 144.4, 147.2.

Catalytic Oxidative Coupling of *N*-Phenylnaphthalen-1-amine (1a)

PhI (10 mol%) and TFA (0.2 equiv) were added to a stirred solu-

tion of amine **1a** (1 equiv) in 1:1 DCE/HFIP (0.67 M) at r.t. *m*CPBA (0.75 equiv) was then gradually added, and the mixture was stirred for 3 h under at r.t. When the reaction was complete (TLC), sat. aq $NaHCO_3$ was added to the mixture, and the aqueous phase was extracted with CH_2Cl_2. The extracts were dried (Na_2SO_4) and then evaporated to dryness. The crude residue was purified by column chromatography (silica gel, hexane/EtOAc) to give pure **2a**; yield: 71%.