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Iron(III)-Promoted Oxidative Coupling of Naphthylamines: Synthetic and Mechanistic Investigations

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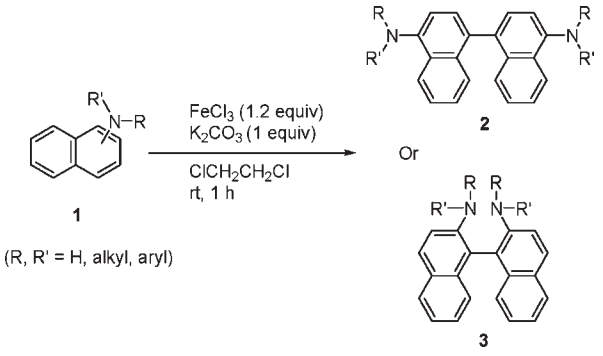
ABSTRACT



A facile route to the synthesis of 1,1′-binaphthyl-4,4′-diamines (naphthidines) and 1,1′-binaphthyl-2,2′-diamines (BINAMs) was developed by the oxidative homocoupling of 1- and 2-naphthylamines, respectively, using $FeCl_3$ as oxidant and K_2CO_3 as base in 1,2-dichloroethane under ambient conditions. A preliminary mechanistic investigation was performed by the ESR spectroscopy and intermediate-trapping technique.

1,1′-Binaphthalene diamines represent a unique class of building blocks in organic synthesis and chemical materials.[1−5] 1,1′-Binaphthyl-4,4′-diamines (naphthidines) are potentially attractive systems for the development of efficient new hole-transport materials;[1] 1,1′-binaphthyl-2,2′-diamines (abbreviated to BINAMs) may constitute chelating or chiral (if enantiomerically resolved) ligands, which have found some synthetic utilities in catalytic reactions[2] and asymmetric synthesis.[3]

However, systematic methods for the preparation of naphthidines and BINAMs have been less studied. Only recently has an efficient procedure for the synthesis of naphthidines been found on the basis of the $TiCl_4$-mediated oxidative coupling of *N*,*N*-disubstituted arylamines.[1,5] In contrast, there has not yet been any general method for the BINAM synthesis until now, and only some sporadic cases appeared in the previous publications. For example, much earlier, Bridger et al.[6]

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(1) Desmarets, C.; Champagne, B.; Walcarius, A.; Bellouard, C.; Omar-Amrani, R.; Ahajji, A.; Fort, Y.; Schneider, R. *J. Org. Chem.* **2006**, *71*, 1351.

(2) For BINAM ligands used in catalytic cross-couplings, see: (a) Prasad, D. J. C.; Naidu, A. B.; Sekar, G. *Tetrahedron Lett.* **2009**, *50*, 1411. (b) Naidu, A. B.; Sekar, G. *Tetrahedron Lett.* **2008**, *49*, 3147. (c) Naidu, A. B.; Raghunath, O. R.; Prasad, D. J. C.; Sekar, G. *Tetrahedron Lett.* **2008**, *49*, 1057. For BINAM-based catalysts used in olefin polymerization, see: (d) Tonzetich, Z. J.; Schrock, R. R. *Polyhedron* **2006**, *25*, 469.

(3) For BINAM-based catalysts or reagents used in asymmetric synthesis, see: (a) Zhou, X.-G.; Yu, X.-Q.; Huang, J.-S.; Li, S.-G.; Li, L.-S.; Che, C.-M. *Chem. Commun.* **1999**, 1789. (b) Vyskočil, Š.; Jaracz, S.; Smrčina, M.; Štícha, M.; Hanuš, V.; Polášek, M.; Kočovský, P. *J. Org. Chem.* **1998**, *63*, 7727. (c) Yamamoto, Y.; Sakamoto, A.; Nishioka, T.; Oda, J.; Fukazawa, Y. *J. Org. Chem.* **1991**, *56*, 1112.

(4) One inspiring example of preparing 7-membered *N*-heterocyclic carbene ligand from 2,2′-diaminobinaphthyl: Scarborough, C. C.; Popp, B. V.; Guzei, I. A.; Stahl, S. S. *J. Organomet. Chem.* **2005**, *690*, 6143.

(5) Periasamy, M.; Jayakumar, K. N.; Bharathl, P. *J. Org. Chem.* **2000**, *65*, 3548.

(6) (a) Bridger, R. F.; Law, D. L.; Bowman, D. F.; Middleton, B. S.; Ingold, K. U. *J. Org. Chem.* **1968**, *33*, 4329. (b) Bridger, R. F. *J. Org. Chem.* **1970**, *35*, 1746.

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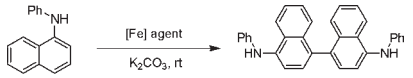
Table 1. Screening of Reaction Conditions for Fe-Mediated Oxidative Coupling of Naphthylamines[a]



1a 2a

run	[Fe] (equiv)	solvent	time (h)	yield[b] (%)
1	$FeCl_3$ (1.2)	toluene	24	45
2	$FeCl_3$ (1.2)	MeCN	24	37
3	$FeCl_3$ (1.2)	MeOH	24	40
4	$FeCl_3$ (1.2)	pyridine	24	22
5	$FeCl_3$ (1.2)	THF	18	65
6	$FeCl_3$ (1.2)	dioxane	24	46
7	$FeCl_3$ (1.2)	CH_2Cl_2	6	73
8	*$FeCl_3$ (1.2)*	*DCE*[c]	*1*	*81*
9	$FeCl_3$ (4)	DCE	0.5	78
10	$FeCl_3$ (0.5)	DCE	16	63
11	$FeCl_3$ (0.1)	DCE	48	20
12	$FeCl_3 \cdot 6H_2O$ (1.2)	DCE	24	62
13	$Fe(acac)_3$ (1.2)	DCE	24	trace
14	FeF_3 (1.2)	DCE	24	trace
15	$Fe(NO_3)_3 \cdot 9H_2O$ (1.2)	DCE	24	58
16	$Fe_2(SO_4)_3 \cdot xH_2O$ (1.2)	DCE	24	21
17	$FeSO_4 \cdot 7H_2O$ (1.2)	DCE	24	0

[a] Conditions: **1a** (1 mmol), K_2CO_3 (1 equiv), solvent (6 mL), room temperature, in air; the proceeding of the reaction was monitored by TLC. [b] Isolated yields. [c] 1,2-Dichloroethane.

described the $KMnO_4$ oxidative dimerization of several *N*-aryl-2-naphthylamines in low yields; 2,2′-diamino-1,1′-binaphthyl was obtained via the thermal rearrangement of 2,2′-hydrazonaphthalene[7] or by the oxidative coupling of 2-aminonaphthalene using Cu,[8a,b] Fe,[8c] and *m*-CPBA,[8d] respectively, as oxidants, and *N*,*N*′-diphenyl-2,2′-diamino-1,1′-binaphthyl was provided in very low yield by an electrochemical oxidation process.[9] In view of the foregoing, it remains desirable to explore new, general methodology for the preparation of naphthidines and BINAMs.

Our recent studies on nickel-catalyzed aromatic aminations made *N*-substituted naphthylamines easily accessible,[10] allowing us to systematically investigate the synthesis of naphthidines and BINAMs on the basis of their oxidative coupling reactions. On the other hand, iron(III) species were considered for utilization in this study because they are the well-known promoters for the oxidative coupling of electron-rich (hetero)arenes and, more importantly, cheap, nontoxic, commercially available, and environmentally benign. Herein we report our findings concerning the $FeCl_3$-mediated dimerization of 1- and 2-naphthylamines.

As a starting point, *N*-phenyl-1-naphthylamine (**1a**) was chosen as a model substrate to screen suitable reaction conditions (Table 1). Some initial experimentation demonstrated that the homocoupling reaction was facilitated by the use of additional bases which consume the H^+ ions produced in the process, and K_2CO_3 (finely ground when used) was the base of choice. The reaction was very sensitive to the nature of solvents used (runs 1−8). Aromatic hydrocarbon (run 1) gave a mediocre yield of the desired product **2a**; polar solvents, such as acetonitrile (run 2), methanol (run 3), and pyridine (run 4), seemed to be poor; ethereal solvents (runs 5 and 6) performed relatively well, and particularly THF (run 6) brought about a good yield of 65%; and chlorinated alkanes (runs 7 and 8) were found to be more suitable solvents for the coupling reaction, among which 1,2-dichloroethane (run 8) was the best. Apparently, the use of excess $FeCl_3$ greatly accelerated the reaction with a comparable high yield (run 9 vs run 8); in contrast, decreasing the amounts of $FeCl_3$ significantly slowed the reaction and reduced the yield (runs 10 and 11). In contrast, hydrated iron(III) chloride produced an adverse effect on the reaction (run 12). For the other iron sources used, $Fe(acac)_3$ (run 13) and FeF_3 (run 14), which contain counteranions that are to dissociate from the central iron ion, almost did not initiate the reaction; $Fe(NO_3)_3 \cdot 9H_2O$ (run 15) and $Fe_2(SO_4)_3 \cdot xH_2O$ (run 16) gave the product in low yields; and no reaction occurred when the iron(II) salt ($FeSO_4 \cdot 7H_2O$) was used (run 17). Finally, the optimized reaction conditions were set as run 8 in Table 1.

With the optimal reaction conditions in hand, an array of 1- and 2-naphthylamine derivatives **1** was used as the substrates in this reaction (Table 2). As can be seen in Table 2, most of the *N*-monoaryl-substituted 1-naphthylamines were excellent substrates, offering a clean conversion of starting materials and high yields of the desired naphthidines (**2a**−**c** and **2e**−**g**). But in the cases of **2d**, **2h**, and **2i**, complete conversions could be achieved via a prolonged reaction time, but some unindentified side reactions occurred apparently, and thus the reduced yields of the coupled products were afforded. In the above-mentioned cases, the substituents on the *N*-aryl imposed remarkable effects on the reaction. Interestingly, the effects depended largely on the site rather than the nature of the substituents. The substituents at the *para* position of *N*-aryl ring, whether electron-donating (**2b** and **2c** vs **2a**) or electron-withdrawing (**2f** and **2g** vs **2a**), promoted the reaction, but the *ortho*- or *meta*-substituents (**2d**, **2e**, **2h**, and **2i** vs **2a**) would be unfavorable for the reaction. Presumably, the reason might be related to the mechanism of this reaction. 1-Naphthylamine with the free amino group afforded a low yield of the dimer product because the reaction was not only slow but also gave large amounts of byproducts (**2j**). *N*-Monoalkyl (**2k**−**m**)

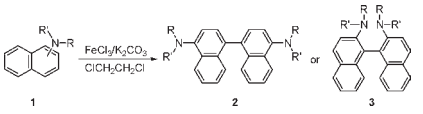
(7) (a) Miyano, S.; Nawa, M.; Mori, A.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2171. (b) Shine, H. J.; Gruzecka, E.; Subotkowski, W.; Brownawel, M.; San Filippo, J., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 3219. (c) Brown, K. J.; Berry, M. S.; Murdoch, J. R. *J. Org. Chem.* **1985**, *50*, 4345.

(8) (a) Smrčina, M.; Lorene, M.; Hanuš, V.; Kočovský, P. *Synlett* **1991**, 231. (b) Smrčina, M.; Lorene, M.; Hanuš, V.; Sedmera, P.; Kočovský, P. *J. Org. Chem.* **1992**, *57*, 1917. (c) Stoddard, J. M.; Nguyen, L.; Mata-Chavez, H.; Nguyen, K. *Chem. Commun.* **2007**, 1240. (d) Wang, K.; Hu, Y.; Wu, M.; Liu, Z.; Su, B.; Yu, A.; Liu, Y.; Wang, Q. *Tetrahedron* **2010**, *66*, 9135.

(9) Hornback, J. M.; Gssage, H. E. *J. Org. Chem.* **1985**, *50*, 541.

(10) (a) Gao, C.-Y.; Yang, L.-M. *J. Org. Chem.* **2008**, *73*, 1624. (b) Huang, J.-H.; Yang, L.-M. *Org. Lett.* **2011**, *13*, 3750.

Table 2. $FeCl_3$-Mediated Oxidative Couplings of 1- and 2-Naphthylamines[a]



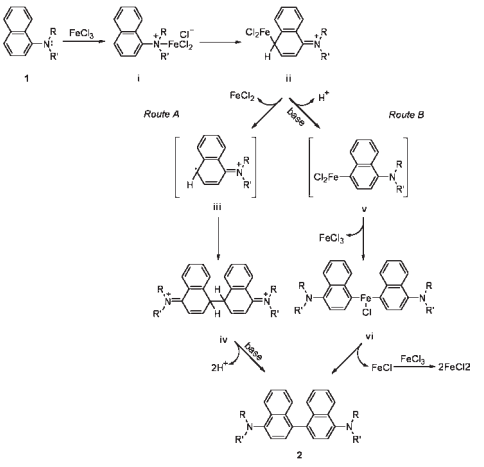
Products **2** and **3**					
2a 81%	**2b** 92%	**2c** 91%	**2d** 63%[b]	**2e** 79%	**2f** 90%
2g 85%	**2h** 52%[b]	**2i** 49%[b]	**2j** 38%[b]	**2k** 75%	**2l** 73%
2m 75%	**2n** 51%[c]	**2o** 76%	**2p** 52%[c]	**2q** 62%[c]	**2r** trace
3a 57%[d]	**3b** 42%[d]	**3c** 86%	**3d** 0%	**3e** 46%	**3f** trace
3g 48%[e]	**3h** trace				

[a] Conditions: 1- or 2-naphthylamine **1** (1 mmol), $FeCl_3$ (1.2 mmol), K_2CO_3 (1 mmol), 1,2-dichloroethane (6 mL), room temperature, 1 h; isolated yields. [b] 6 h. [c] 60 °C, 5 h. [d] 2 mmol of $FeCl_3$, 5 h. [e] 2 mmol of $FeCl_3$, 60 °C, 20 h.

and *N*,*N*-dialkyl (**2n**–**q**) 1-naphthylamines underwent the reaction smoothly with the completely comsumed starting materials, providing the corresponding naphthidines in good or appreciable yields. *N*,*N*-Diphenyl-1-naphthylamine (**2r**) was inert in the reaction, and only the starting material was recovered. The performance of 2-naphthylamine derivatives in this transformation was generally not as successful as the 1-position counterparts, often with slow reaction rate and significant quantities of byproducts (**3a**, **3b**, and **3d**–**h**). *N*-Monoaryl-2-naphthylamines could provide the coupled dimers in mediocre to good yields (**3a**–**c**). In the case of *N*-*p*-anisyl-2-naphthylamine (**3d**), it was found that the starting material was rapidly consumed to furnish a high conversion rate of the unidentified byproduct. *N*,*N*-Diaryl- or *N*-monoalkyl-2-naphthylamines (**3f** and **3h**) did not undergo the reaction with almost quantitative recovery of the starting materials. Under more forced conditions, the reaction of aliphatic secondary cyclic amino 2-naphthalene could go to completion with a mediocre yield (**3g**). In addition, 2-naphthylamine with the free amino group could be homocoupled with a complete conversion rate and an acceptable yield of 46% (**3e**).

Our studies next identify the mechanistic pathway of the reaction. According to previous studies on the metal-mediated oxidative homocouplings of aromatic amines,[1,5,11] the present transformation might be rationalized by the two possible pathways outlined in Scheme 1: one involving radical cation intermediate **III** (route A) and the other naphthyl iron intermediate **V** (route B).

Scheme 1. Proposed Possible Pathways for the $FeCl_3$-Mediated Homocoupling of Naphthylamines



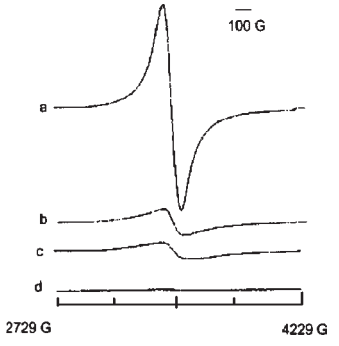


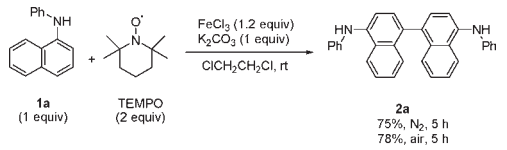
Figure 1. ESR spectra during the $FeCl_3$-mediated oxidative homocoupling of *N*-phenyl-1-naphthylamine. Key: (a) ESR spectrum for a system consisting of $FeCl_3$ (1 mmol) and K_2CO_3 (1 mmol) in 1,2-dichloroethane (6 mL). (b–d) Time-dependent ESR spectra for the system of $FeCl_3$ (1 mmol) and K_2CO_3 (1 mmol) in 1,2-dichloroethane (6 mL) being treated with *N*-phenyl-1-naphthylamine (1 mmol): (b) 5 min later; (c) 15 min later; and (d) 60 min later.

We first monitored the ESR spectra in the course of the oxidative coupling of *N*-phenyl-1-naphthylamine **1a** (Figure 1). The Fe^{3+} species in a 1,2-dichloroethane shows a sharp, strong signal around 3480 G (Figure 1a; relative

(11) Kirchgessner, M.; Sreenath, K.; Gopidas, K. R. *J. Org. Chem.* **2006**, *71*, 9849. (b) Sreenath, K.; Suneesh, C. V.; Kumar, V. K. R.; Gopidas, K. R. *J. Org. Chem.* **2008**, *73*, 3245.

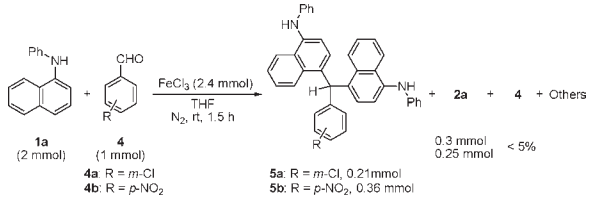
intensity: 100). Followed by the addition of **1a**, the signal decayed rapidly with time up to almost complete disappearance (Figure 1b–d; relative intensity: 13.2, 8.5 and 1.2, respectively, from Figure 1b to c and d), during which time no new signal corresponding to organic radical cations was observed. The ESR spectral facts provided initial evidence against route A in Scheme 1 as the possible mechanism of the present oxidative coupling.

Scheme 2



Then, a control experiment for the oxidative coupling of **1a** was carried out under the standard conditions as described above except with the use of additional radical-trapping agents (Scheme 2). It was found that the addition of a radical inhibitor, 2,2,6,6-tetramethylpiperidinyl-*N*-oxyl (TEMPO), only slowed down the oxidative coupling (roughly and qualitatively evaluated by TLC) but did not lead to an obvious decrease in yields. The results also should rule out the reasonability of the mechanistic pathway (route A) involving radical cation intermediates.

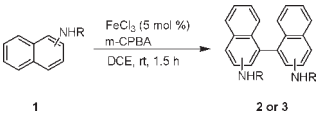
Scheme 3

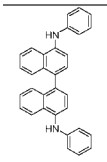
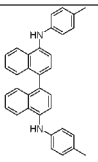
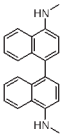
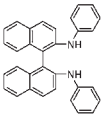
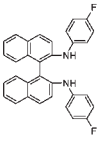


Further, we probed for the possible intermediacy of naphthyl iron by studying a reaction of aldehydes with *N*-phenyl-1-naphthylamine **1a** in THF at room temperature in the presence of $FeCl_3$ (Scheme 3). In the designed reaction, reactant **1a** was consumed, the homocoupled product **2a** was obtained in considerable yields, and larger quantities of other unidentified byproducts were produced. Nevertheless, we indeed separated a class of products, resulting from the reaction between aldehydes and organometallic specie, with appreciable amounts, showing the possibility that organoiron species like the intermediate **V** in Scheme 1 occurred in the reaction. The results implied that the $FeCl_3$-promoted oxidative coupling proceeded more likely via a pathway involving the naphthyl iron intermediate (route B) rather than the free-radical species (route A).

From the standpoint of synthetic studies, it is a necessary task that such a transformation involving the stoichiometric use of metal-based oxidants would be developed into a catalytic process. A preliminary attempt was made to use catalytic amounts of iron(III) chloride associated with other terminal oxidants to achieve efficient oxidative dimerization of naphthylamines. After surveying various terminal oxidants including molecular oxygen, BPO (benzoyl peroxide), DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone), DTBP (di-*tert*-butyl peroxide), and *m*-CPBA (3-chloroperbenzoic acid), we found that 5 mol % of $FeCl_3$ in conjunction with 1 equiv of *m*-CPBA in 1,2-dichloroethane at room temperature served as optimal conditions for the catalytic transformation (see Tables S1, Supporting Information). Table 3 demonstrates that several naphthylamine substrates can undergo $FeCl_3$-catalyzed oxidative homocouplings, providing the desired products in good yields. Work is underway to apply the catalytic coupling reaction in a wider range of naphthylamine substrates.

Table 3. $FeCl_3$-Catalyzed Oxidative Coupling of 1- and 2-Naphthylamine Derivatives[a]



Products **2** and **3**				
				
2a 75%	**2b** 73%	**2k** 62%	**3a** 73%	**3c** 71%

[a] Conditions: 1- or 2-naphthylamine (1 mmol), $FeCl_3$ (5 mol %), *m*-CPBA (1 equiv), DCE (6 mL), room temperature, 1.5 h, in air.

In conclusion, we have developed a simple, benign, and efficient protocol for the preparation of naphthidines and BINAMs by the iron(III)-promoted oxidative coupling of naphtylamine derivatives, and further, a catalytic version of the transformation has been explored. The method is expected to have broad applications in synthetic studies and material synthesis. Additionally, a possible mechanism for this reaction was clarified preliminarily, from which some interesting new subjects of researches would be derived.

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Supporting Information Available. Experimental procedures and characterization data for the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.