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Synthesis of Benzidine Derivatives via $FeCl_3 \cdot 6H_2O$-Promoted Oxidative Coupling of Anilines

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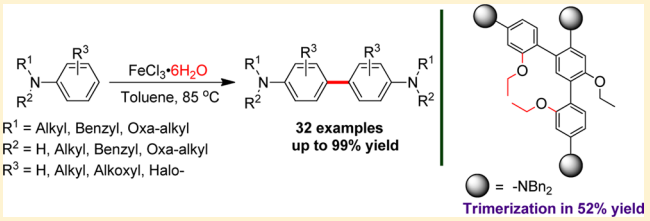
Supporting Information

ABSTRACT: Under open-flask conditions in the presence of commercially available $FeCl_3 \cdot 6H_2O$, N,N-disubstituted anilines can be converted into diversely functionalized benzidines with yields of up to 99%. Oxidative coupling was extended to N-monosubstituted anilines, and the method was applied to the efficient preparation of 6,6′-biquinoline. Mechanistic investigations have also been performed to explain the observed reactivities.



INTRODUCTION

The development of efficient synthetic methodologies to prepare structurally diverse benzidine derivatives has received increasing attention in recent years due to its applicability in a wide variety of domains. For instance, the derivatives have found applications as building blocks to construct functionalized heterocycles.[1] The chemical and physical properties of benzidine-based compounds have enabled their use in the manufacture of azodyes[2] and in cell biology as staining reagents.[3] Furthermore, they are important units for the implementation of molecular machines[4] and construction of functionalized organic materials.[5,6]

The synthesis of benzidines is based on two major synthetic strategies: (1) rearrangement of hydrazobenzenes and (2) direct self-coupling of anilines. Generally, the rearrangement of hydrazobenzenes suffers from low yields because of the formation of byproducts.[7] In an important contribution to the field, Cho et al. disclosed that aryl hydrazides with substituent(s) at the *ortho* or *meta* position could suppress the formation of byproducts.[8] However, access is limited to *ortho*- and *meta*-substituted benzidines, which lowers the synthetic appeal of this transformation. Besides rearrangement of hydrazobenzenes, oxidative coupling of arylamines represents a straightforward approach to prepare functionalized benzidines. Metal salt oxidants such as $TiCl_4$, cerium(IV) ammonium nitrate (CAN), $CuBr/H_2O_2$, and $Cu(ClO_4)_2$ were employed for this reaction.[9] Organic oxidants could also be used; to this aim, 1,8-bis(diphenylmethylium)naphthalenediyl dications were synthesized by Ichikawa et al., and they were successfully applied to the self-coupling of N,N-disubstituted anilines.[10] The combination of anhydrous $FeCl_3$ and oxygen was also employed to investigate the transformation of *N,N*-dimethylaniline, which tended to form *N*-methylaniline and 4,4′-methylenebis(*N,N*-dimethylaniline) through an iminum cation intermediate.[11] Utilizing anhydrous $FeCl_3/K_2CO_3$, coupling products of naphthylamines were obtained through a possible naphthyl iron intermediate reported by Yang's group.[12] Although extensive efforts have been devoted to devise more general and higher-yielding transformations, the preparation of diversely functionalized benzidines remains an important synthetic challenge. We report here the successful implementation of an oxidative coupling of N,N-disubstituted and N-monosubstituted anilines to prepare benzidines using $FeCl_3 \cdot 6H_2O$ as an efficient oxidant. In the past decade, the interest in synthetic methodologies based on iron has undergone explosive growth due to the easy accessibility, favorable safety profile, and low cost of iron derivatives.[13]

RESULTS AND DISCUSSION

Oxidative coupling of *N,N*-dimethylaniline **1a** under air in toluene at 85 °C was used as a model reaction to optimize the conditions (Table 1). A set of different iron sources was investigated, and iron(III) chloride gave the best results (entries 1−6). The reaction of **1a** in the presence of 2.5 equiv of anhydrous $FeCl_3$ gave rise to a mixture of benzidine **2a** and 4,4′-methylenebis(*N,N*-dimethylaniline) **3a** with 28% and 24% yields, respectively (entry 4). The formation of **3a** has already been observed under similar reaction conditions through oxidation of the methyl groups in **1a**.[11] Interestingly, the use of $FeCl_3 \cdot 6H_2O$ suppressed the formation of **3a**; under these conditions, benzidine **2a** was obtained with an 88% yield (entry 5). The difference between $FeCl_3 \cdot 6H_2O$ and $FeCl_3$ prompted us to investigate the effect of water in the system. When 15.0 equiv of water was added to anhydrous $FeCl_3$, the coupling reaction proceeded smoothly, and **2a** was obtained with an 80% yield (entry 6). Subsequently, the amount of $FeCl_3 \cdot 6H_2O$ was investigated. Addition of 1.0 equiv of $FeCl_3 \cdot 6H_2O$ led to formation of product **2a** with a very low yield of 2% along with byproduct **3a** as the major product, whereas a large excess of

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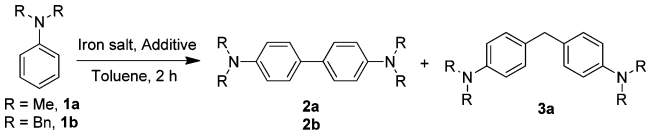
Table 1. Initial Screening Results[a]



entry	1	iron salt/additive (equiv)	T (°C)	yield (%)[b]
1	**1a**	$FeCl_2·4H_2O$ (2.5)	85	4
2	**1a**	$Fe_2(SO_4)_3$ (2.5)	85	*c*
3	**1a**	$Fe(NO_3)_3·9H_2O$ (2.5)	85	*c*
4	**1a**	$FeCl_3$ (2.5)	85	28 (24)[d]
5	**1a**	$FeCl_3·6H_2O$ (2.5)	85	88
6	**1a**	$FeCl_3$ (2.5)/H_2O (15.0)	85	80
7	**1a**	$FeCl_3·6H_2O$ (1.0)	85	2 (33)[d]
8	**1a**	$FeCl_3·6H_2O$ (4.0)	85	83
9	**1a**	$FeCl_3·6H_2O$ (10.0)	85	67
10	**1a**	$FeCl_3·6H_2O$ (2.5)	60	50
11	**1a**	$FeCl_3·6H_2O$ (2.5)	120	83
12	**1a**	$FeCl_3·6H_2O$ (2.5)/Et_3N (1.0)	85	0 (68)[d]
13	**1a**	$FeCl_3·6H_2O$ (2.5)/K_2CO_3 (1.0)	85	23 (45)[d]
14	**1b**	$FeCl_3·6H_2O$ (2.5)	85	96[e]
15	**1b**	$FeCl_3$ (2.5)	85	42
16	**1b**	$FeCl_3·6H_2O$ (2.5)/K_2CO_3 (1.0)	85	36

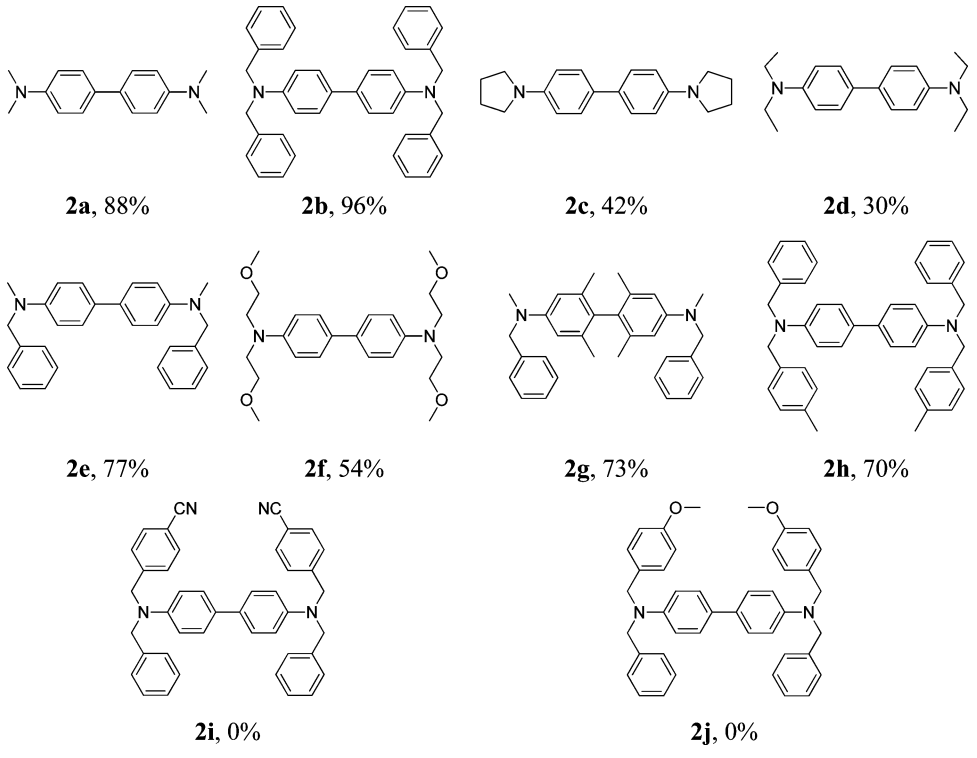
[a]Reaction conditions: anilines (0.4 mmol), iron sources, and additives (specified amounts) in 2.0 mL of toluene for 2 h. [b]Isolated yields. [c]No product. [d]Yield of 4,4′-methylenebis(*N*,*N*-dimethylaniline) **3a** presented in parentheses. [e]Yield of 91% was obtained in distilled toluene under N_2.

$FeCl_3·6H_2O$ gave rise selectively to **2a** in unimproved yields (entries 7−9). After the temperature had been screened, oxidative coupling of **2a** at 85 °C using 2.5 equiv of $FeCl_3·6H_2O$ turned out to be the best reaction condition (entries 5, 10, and 11). In an iron(III)-promoted oxidative coupling of naphthylamines, Yang et al. reported that the reaction was facilitated by the addition of a base.[12] Addition of Et_3N or K_2CO_3 to the system was investigated in the self-coupling of **2a** (entries 12 and 13). Dimerization of anilines in the presence of Et_3N gave only the byproduct **3a** with a 68% yield, whereas the use of K_2CO_3 furnished a mixture of **2a** and **3a** in a ratio of about 1:2. Formation of **3a** is supposed to proceed through oxidation of the methyl groups; as a result, we envisioned that the use of *N*,*N*-dibenzylaniline would lead selectively to the corresponding benzidine. The reaction of **1b** in the presence of $FeCl_3·6H_2O$ gave self-coupling product **2b** with an excellent yield of 96% (entry 14). It is worthwhile to note that the reaction of **1b** in the presence of anhydrous $FeCl_3$ or $FeCl_3·6H_2O/K_2CO_3$ afforded only compound **2b** in a diminished yield, whereas **3a** was the major compound for the self-coupling of **1a** under indentical conditions (entries 15 and 16).

With the optimal reaction conditions in hand ($FeCl_3·6H_2O$, toluene, 85 °C, 2 h), the reaction scope was investigated focusing on the influence of nitrogen substitution on the reaction (Table 2). Oxidative coupling of 1-phenylpyrrolidine and *N*,*N*-diethylaniline afforded **2c** and **2d** in moderate yields, whereas *N*-benzyl-*N*-methylanilines underwent self-coupling in good yields. Oxa-alkyl-substituted aniline gave the coupling product **2f** with a yield of 54%. The substitution pattern of the benzyl group showed a dramatic influence on the reactivity. The methyl substituent was well tolerated in the formation of **2h** with a 70% yield, whereas starting materials were recovered with methoxy- and cyano-containing substrates.

Among all the nitrogen protecting groups tested, the benzyl group gave the best result. In addition, the benzyl group can be easily introduced and requires mild conditions (H_2, Pd/C) to

Table 2. Influence of the Nitrogen Protecting Group[a]



[a]Reaction conditions: anilines (0.4 mmol), $FeCl_3·6H_2O$ (1.0 mmol), toluene (2.0 mL), 85 °C, 2 h; isolated yields.

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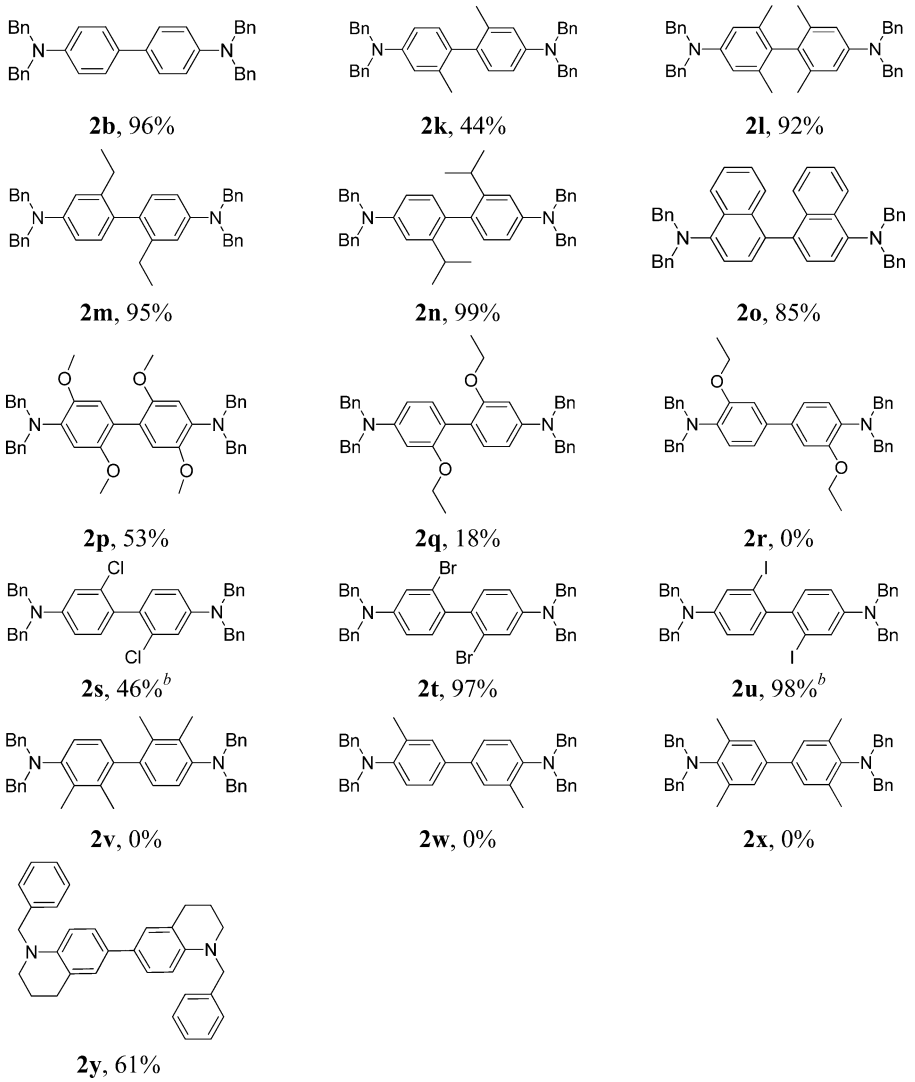
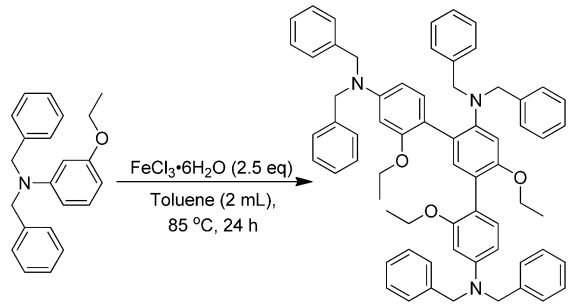
Table 3. Self-Coupling Reactions of Functionalized *N,N*-Dibenzylanilines[a]



[a]Reaction conditions: anilines (0.4 mmol), $FeCl_3 \cdot 6H_2O$ (1.0 mmol), toluene (2.0 mL), 85 °C, 2 h; isolated yields. [b]In 8 h.

be cleaved. As a result, the benzyl moiety was selected as a nitrogen-protecting group to explore the influence of the aromatic substitution pattern of anilines (Table 3). The oxidative coupling of anilines bearing *meta*-alkyl substitutents gave the corresponding benzidines **2k−n** with moderate to good yields. Naphthylamine is a suitable substrate, and self-coupling product **2o** was obtained with an 85% yield. Electron-donating groups such as methoxy and ethoxy impinge on the reaction outcome. Whereas **2p** was obtained with a 53% yield, benzidine **2q** was obtained with an 18% yield along with the trimer product **2z** with a 29% yield. Extending the reaction time of **1q** to 24 h gave rise to trimer **2z** with an improved yield of 52%, and only a trace of benzidine **2q** was observed (Scheme 1). The reaction also worked well when using halogenated anilines. *N,N*-Dibenzyl-3-bromoaniline and *N,N*-dibenzyl-3-iodoaniline gave the corresponding products **2t** and **2u** with excellent yields of 97% and 98%, respectively. However, the coupling reactions did not proceed with *N,N*-dibenzylanilines containing fluoro, nitro, or acetyl groups at the *meta* position, and only the starting materials were recovered. 1-Benzyl-1,2,3,4-tetrahydroquinoline was effectively transformed into **2y** with a 61% yield, and we were pleased to get crystals suitable

Scheme 1. Trimerization of *N,N*-Dibenzyl-3-ethoxyaniline (1q)



1q **2z**, 52%

for X-ray analysis. Anilines bearing only *ortho* substitution(s) proved to be unreactive in oxidative coupling reactions (**2r**, **2v−x**).

The lack of reactivities in the self-coupling of **2r** and **2v−x** might be explained by steric repulsions between the *ortho* methyl or alkoxyl group(s) of the benzene ring and the benzyl

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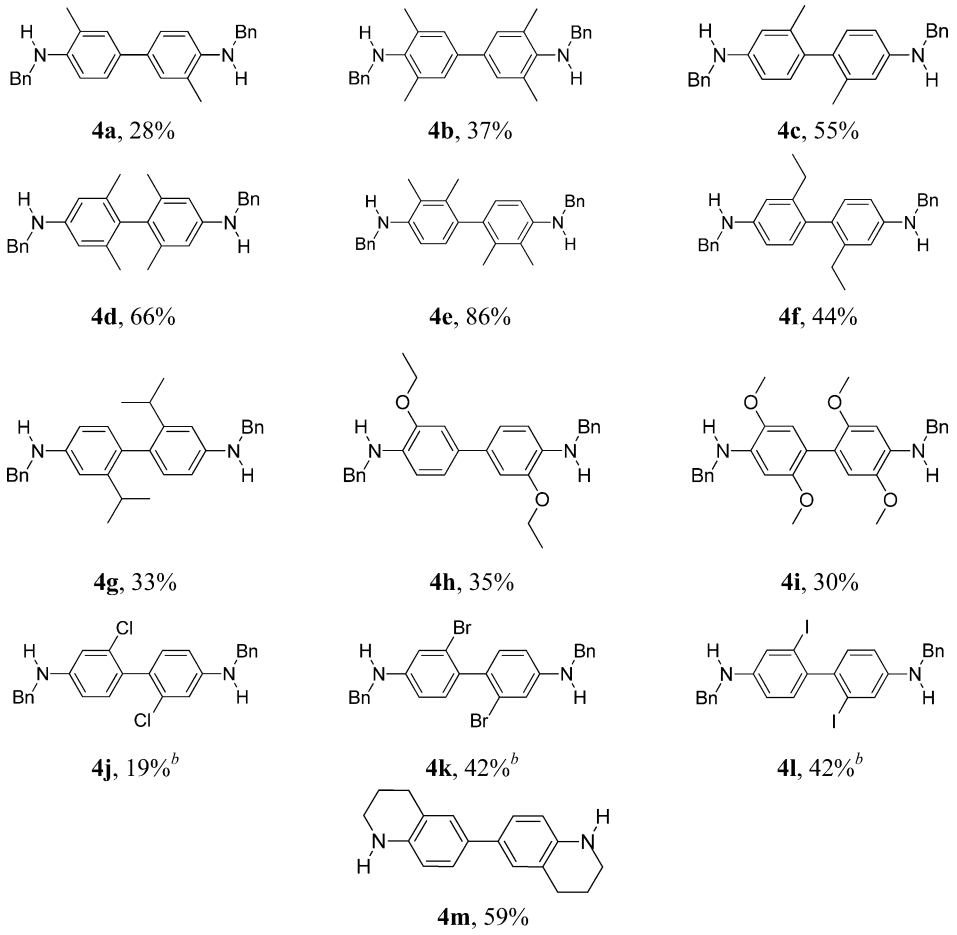
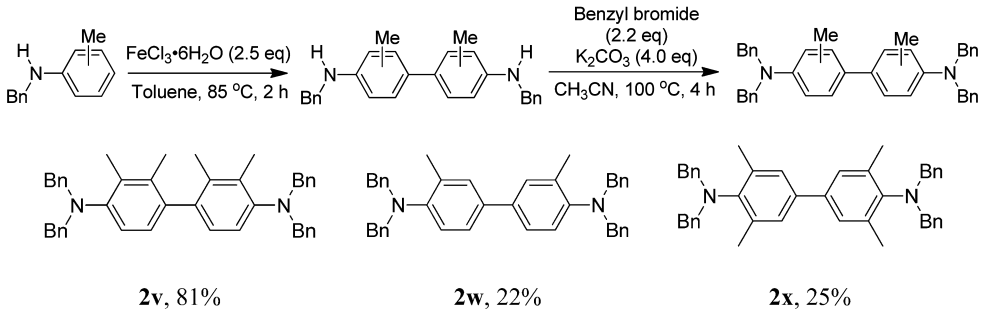
Table 4. Self-Coupling Reactions of Functionalized *N*-Benzylanilines[a]



[a]Reaction conditions: anilines (0.4 mmol), $FeCl_3 \cdot 6H_2O$ (1.0 mmol), toluene (2.0 mL), 85 °C, 2 h; isolated yields. [b]In 8 h.

Scheme 2. Synthesis of *o*-Methyl-Substituted Benzidines



groups borne by the nitrogen. As a result, the rotations of aromatic carbon−nitrogen bonds break the coplanar p−π conjugation, and this decreases the ability of anilines to be oxidized. In this context, we surmised that oxidative coupling of *N*-benzylanilines should be facilitated with lower steric shielding around the nitrogen. Unlike *N*,*N*-dibenzylanilines, *N*-monobenzylanilines underwent self-coupling to provide the corresponding benzidines (Table 4). Alkyl substitutions at the *ortho* or *meta* position of the aromatic ring were tolerated, and they provided the desired products with 28−86% yields (**4a**−**g**). It is worthwhile to note that benzidine **4b** can be readily transformed through a simple debenzylation step into 3,3′,5,5′-tetramethylbenzidine (TMB), an important and *safe* staining agent.[3] *ortho*-Alkoxy-substituted anilines generated the corresponding self-coupling products **4h** and **4i** with moderate yields. Halo substitutions at the *meta* position of the mother benzene ring could afford coupling products **4j**−**l**, whereas the coupling reaction did not proceed using anilines bearing *ortho* halo substitutions. Commercially available 1,2,3,4-tetrahydroquinoline gave benzidine **4m** directly with a 59% yield.

In order to prepare *ortho*-substituted *N*,*N*-dibenzylaninlines **2v**−**x**, we investigated the synthetic route, which was composed of two steps: (1) self-coupling of *ortho*-methyl-substituted *N*-benzylanilines under optimized conditions and (2) N-benzylation with benzyl bromide (Scheme 2). Following this strategy, benzidines **2v**−**x** were obtained in moderate to good overall yields over the two steps. In addition, the oxidative coupling of *N*-benzylaniline was applied to the preparation of

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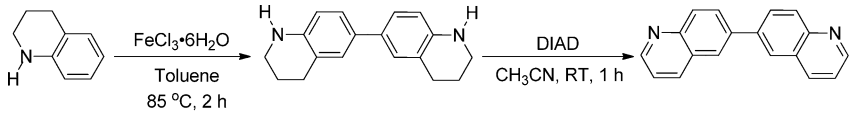
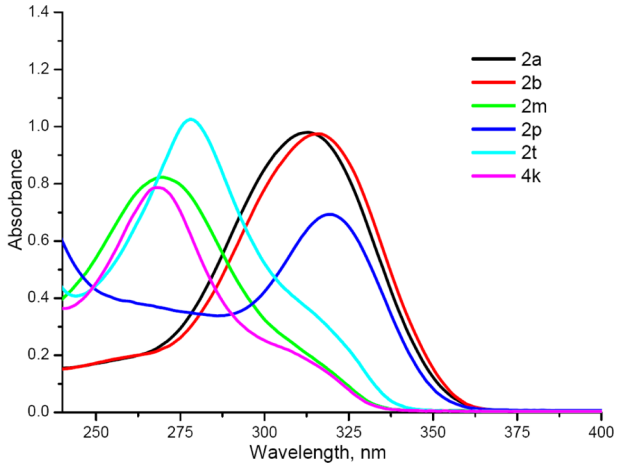
Scheme 3. Synthesis of 6,6′-Biquinoline



4m, 59% **5**, 61%

6,6′-bisquinoline **5**, which was found to be a potential photoactive material (Scheme 3).[14] Benzidine **4m** was obtained through oxidative coupling of the corresponding aniline and underwent diisopropyl azodicarboxylate (DIAD)-mediated dehydrogenation to afford **5** with a 61% yield.[15]

Analysis of ultraviolet−visible (UV−vis) spectroscopy on selected coupling products (**2a**, **2b**, **2m**, **2p**, **2t**, and **4k**) is shown in Figure 1. Compared to that of the dimethyl



compound	λ_{max}, nm	ϵ, M^{-1} cm^{-1} (log ϵ)
2a	313	39200 (4.59)
2b	316	39000 (4.59)
2m	269	32920 (4.51)
2p	319	27720 (4.44)
2t	278	41040 (4.61)
4k	268	31480 (4.50)

Figure 1. UV−vis spectra of **2a**, **2b**, **2m**, **2p**, **2t**, and **4k** (2.5×10^{-5} M) in dichloromethane.

substituent **2a** (λ_{max} = 313 nm), the wavelengths of maximum absorption (λ_{max}) for *N*,*N*,*N*′,*N*′-tetrabenzylic substituent **2b** and *N*,*N*,*N*′,*N*′-tetrabenzylic 2,5-methoxyl substituent **2p** red-shift to 316 and 319 nm, respectively, which indicates that π electrons in **2b** and **2p** are more easily excited to a higher antibonding molecular orbital. Different substitutions on anilines lead to larger blueshifts of the wavelengths of maximum absorption from 313 nm. *N*,*N*,*N*′,*N*′-Tetrabenzylic bromo substituent **2t**, *N*,*N*′-dibenzylic bromo substituent **4k**, and *N*,*N*,*N*′,*N*′-tetrabenzylic ethyl substitution **2m** give the wavelengths of maximum absorption at 278, 268, and 269 nm, respectively, which shows that substitutions on the benzene ring have a stronger impact on the energy gap between the HOMO and the LUMO.

In an effort to glean insights into the mechanism, the self-coupling of **1b** was investigated by mass spectrometry in an attempt to trap iron intermediates. Under the optimal conditions, iron intermediates were not detected during the course of the reaction, and only aniline **1b** and product **2b** were observed. A control experiment for the $FeCl_3 \cdot 6H_2O$-promoted oxidative coupling of *N*,*N*-dibenzylaniline **1b** in the presence of the radical scavenger 2,2,6,6-tetramethylpiperidinyloxy (TEMPO) was performed; under these conditions, the reaction was blocked, contrary to Yang's report,[12] and benzidine **2b** could not be detected by LC−MS. On the basis of these results, a possible radical mechanism for the oxidative self-coupling reaction was proposed (Figure 2). Aniline **1a** first coordinates

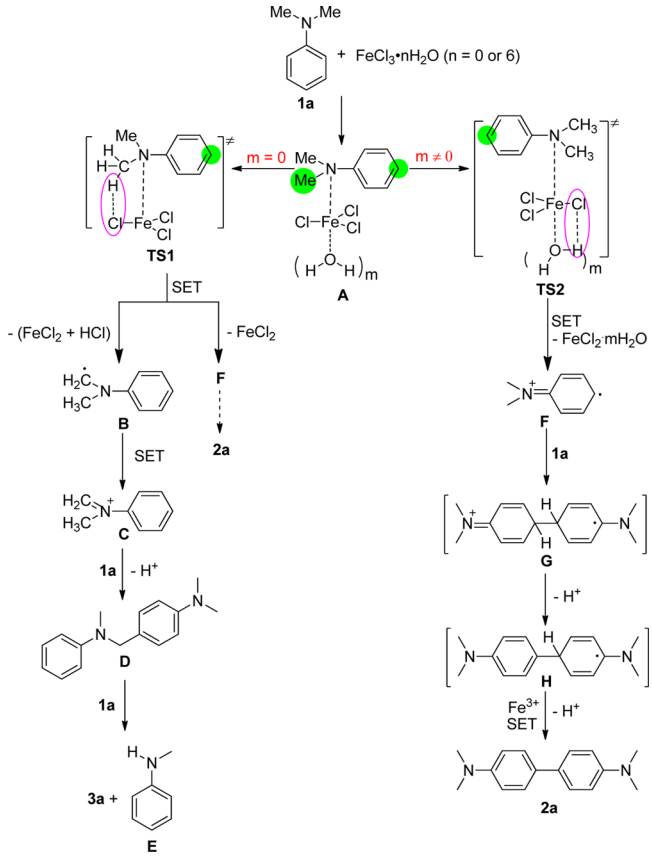


Figure 2. Proposed mechanism.

with Fe^{3+} to generate iron(III) complex **A**, in which a methyl group on nitrogen and the *para* position on aniline are both activated. With anhydrous $FeCl_3$, radicals **B** and **F** are formed from the active transition state **TS1** and give rise to benzidine **2a** and 4,4′-methylenebis(*N*,*N*-dimethylaniline) **3a**, respectively (Table 1, entry 4). It is worthwhile to note that an effective hydrogen bond interaction between the chlorine anion and one hydrogen of the methyl group leads to formation of only **3a**. The existence of crystal water decreases the basicity of the chlorine anion through a hydrogen bonding interaction with water and suppresses Cl^--assisted deprotonation of the methyl group to form **3a**.[11] Thus, the *para* position on the aniline is relatively more reactive than the methyl group. When hydrated

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$FeCl_2$ is released from transition state **TS2**, a free radical cation **F** is formed via a SET process. Free radical cation **F** reacts with aniline **1a** to generate the coupling free radical cation **G**. Followed by deprotonation and another SET deprotonation process, the self-coupling product **2a** is produced. The addition of an extra base such as Et_3N and K_2CO_3 favors the formation of **3a**, which lends further credence to the hypothesis that Cl absorbs hydrogen (Table 1, entries 12 and 13).

CONCLUSIONS

In summary, we have developed a novel and effective self-coupling transformation for the preparation of diversely functionalized benzidine derivatives from *N*,*N*-dialkylanilines and *N*-monoalkylanilines utilizing commercially available $FeCl_3·6H_2O$ as an oxidant. This methodology was applied to the preparations of valuable, safe staining precursors and 6,6′-biquinoline. The trimerization product is obtained by one-step synthesis, which possesses a potential application in the new ligand design of metal complex catalysis. From our performances, a radical mechanism has been suggested to account for the formation of benzidines.

EXPERIMENTAL SECTION

General Information. NMR spectra were recorded on a 500 spectrometer (500 MHz for ^1H, 125 MHz for ^{13}C) with deuterated chloroform ($CDCl_3$) as a solvent at 20−25 °C. ^1H NMR spectra were reported in parts per million using TMS (δ = 0.00 ppm) as an internal standard. ^{13}C NMR spectra were reported in parts per million using solvent $CDCl_3$ (δ = 77.2 ppm) as an internal standard. High-resolution mass spectra (HRMS) were obtained with a Q-TOF MS spectrometer. UV−visible spectroscopy experiments were performed with CH_2Cl_2 as solvent at ambient temperature. Unless otherwise specified, all reagents were purchased from commercial suppliers and used as received, and all experiments were conducted in the atmosphere. Column chromatography and thin layer chromatography (TLC), which was used to monitor the reactions, were performed on silica gel.

General Procedure for the Oxidative Self-Coupling Reactions. *N*,*N*-Dimethylaniline **1a** (48.4 mg, 0.4 mmol) at room temperature was added to a stirred mixture of $FeCl_3·6H_2O$ (270.3 mg, 1.0 mmol) and 2.0 mL of toluene. The reaction mixture was stirred at 85 °C for 2 h in the atmosphere. After it was cooled to room temperature, the reaction mixture was quenched by aqueous ammonia solution (mass fraction: 25−28%, 10 mL) and extracted with dichloromethane (10 mL per time) until no product was observed in the extract, as monitored by TLC. The combined extract was washed with water (10 mL × 3) followed by saturated NaCl solution (10 mL × 1). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give crude product, which was chromatographed on a silica gel column using 1:80 (v/v) EtOAc−petroleum ether solution as eluent to afford isolated product **2a**.

Procedure for LC−MS Experiments. *N*,*N*-Dibenzylaniline (109.3 mg, 0.4 mmol) at room temperature was added to a stirred mixture of $FeCl_3·6H_2O$ (270.3 mg, 1.0 mmol) and 2.0 mL of toluene. The reaction mixture was stirred at 85 °C for 40 or 120 min in the atmosphere. After it was cooled to room temperature, the reaction mixture was concentrated under reduced pressure to give a dark red solid. The solid was dissolved in acetonitrile for LC−MS analysis, the results of which demonstrated that only the starting material **1b** and coupling product **2b** were detected after 40 min, and only coupling product **2b** was observed after 120 min. See Supporting Information for LC−MS spectra.

Procedure for Control Experiment Utilizing 2,2,6,6-Tetramethylpiperidin-1-oxyl (TEMPO). *N*,*N*-Dibenzylaniline **1b** (109.3 mg, 0.4 mmol) and 2,2,6,6-tetramethylpiperidin-1-oxyl (125.0 mg, 0.8 mmol) were added successively at room temperature to a stirred mixture of $FeCl_3·6H_2O$ (270.3 mg, 1 mmol) and 2.0 mL of toluene. The reaction mixture was stirred at 85 °C for 2 h in the atmosphere. After it was cooled to room temperature, the reaction mixture was quenched by aqueous ammonia solution (mass fraction: 25−28%, 10 mL). After extraction, no desired coupling product **2b** was found by TLC and LC−MS, which indicated that the self-coupling of *N*,*N*-dibenzylaniline was prohibited by TEMPO. Therefore, the self-coupling reaction might proceed via a radical pathway.

***N*,*N*,*N*′,*N*′-Tetramethyl-[1,1′-biphenyl]-4,4′-diamine (2a)[9a]:** white solid; yield 88%, 42.3 mg; mp 190−192 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, J = 9.0 Hz, 4H), 6.80 (d, J = 8.5 Hz, 4H), 2.97 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.4, 130.0, 127.1, 113.2, 41.0; HRMS (ESI) calcd for $C_{16}H_{21}N_2$ $(M + H)^+$ 241.1705, found 241.1704.

***N*,*N*,*N*′,*N*′-Tetrabenzyl-[1,1′-biphenyl]-4,4′-diamine (2b):** white solid; yield 96%, 104.6 mg; mp 196−197 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34−7.31 (m, 12H), 7.27−7.23 (m, 12H), 6.75 (d, J = 9.0 Hz, 4H), 4.66 (s, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9, 138.8, 129.9, 128.8, 127.2, 127.0, 126.8, 112.9, 54.4; HRMS (ESI) calcd for $C_{40}H_{37}N_2$ $(M + H)^+$ 545.2957, found 545.2948.

4,4′-Di(pyrrolidin-1-yl)-1,1′-biphenyl (2c): white solid; yield 42%, 24.6 mg; mp 208 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, J = 7.5 Hz, 4H), 6.61 (d, J = 7.5 Hz, 4H), 3.31 (s, 8H), 2.00 (s, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.7, 129.1, 127.1, 112.1, 47.9, 25.6; HRMS (ESI) calcd for $C_{20}H_{25}N_2$ $(M + H)^+$ 293.2018, found 293.2007.

***N*,*N*,*N*′,*N*′-Tetraethyl-[1,1′-biphenyl]-4,4′-diamine (2d)[9a]:** white solid; yield 30%, 17.8 mg; mp 87−88 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, J = 8.5 Hz, 4H), 6.72 (d, J = 8.0 Hz, 4H), 3.37 (s, 8H), 1.18 (t, J = 7.0 Hz, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.4, 129.0, 127.3, 112.3, 44.6, 12.9; HRMS (ESI) calcd for $C_{20}H_{29}N_2$ $(M + H)^+$ 297.2331, found 297.2327.

***N*⁴,*N*⁴′-Dibenzyl-*N*⁴,*N*⁴′-dimethyl-[1,1′-biphenyl]-4,4′-diamine (2e):** white solid; yield 77%, 60.4 mg; mp 146−147 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, J = 8.5 Hz, 4H), 7.32−7.30 (m, 4H), 7.26−7.24 (m, 6H), 6.78 (d, J = 8.5 Hz, 4H), 4.54 (s, 4H), 3.03 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.5, 139.3, 129.8, 128.7, 127.2, 127.0, 126.9, 112.9, 56.9, 38.8; HRMS (ESI) calcd for $C_{28}H_{29}N_2$ $(M + H)^+$ 393.2331, found 393.2331.

***N*⁴,*N*⁴,*N*⁴′,*N*⁴′-Tetrakis(2-methoxyethyl)-[1,1′-biphenyl]-4,4′-diamine (2f):** white solid; yield 54%, 43.3 mg; mp 49−51 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 8.5 Hz, 4H), 6.75 (d, J = 9.0 Hz, 4H), 3.59−3.56 (m, 16H), 3.37 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.5, 129.4, 127.3, 112.2, 70.3, 59.2, 51.2; HRMS (ESI) calcd for $C_{24}H_{37}N_2O_4$ $(M + H)^+$ 417.2753, found 417.2763.

***N*⁴,*N*⁴′-Dibenzyl-*N*⁴,*N*⁴′,2,2′,6,6′-hexamethyl-[1,1′-biphenyl]-4,4′-diamine (2g):** white solid; yield 73%, 65.5 mg; mp 96−97 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35−7.29 (m, 8H), 7.25−7.24 (m, 2H), 6.55 (s, 4H), 4.51 (s, 4H), 2.96 (s, 6H), 1.87 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.9, 139.9, 137.3, 129.5, 128.6, 127.3, 126.9, 111.8, 57.2, 38.3, 20.8; HRMS (ESI) calcd for $C_{32}H_{37}N_2$ $(M + H)^+$ 449.2957, found 449.2959.

***N*⁴,*N*⁴′-Dibenzyl-*N*⁴,*N*⁴′-bis(4-methylbenzyl)-[1,1′-biphenyl]-4,4′-diamine (2h):** white solid; yield 70%, 80.1 mg; mp 200−201 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37−7.33 (m, 8H), 7.29−7.28 (m, 6H), 7.19−7.15 (m, 8H), 6.78 (d, J = 8.5 Hz, 4H), 4.67 (s, 4H), 4.65 (s, 4H), 2.36 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 138.9, 136.6, 135.7, 129.9, 129.5, 128.8, 127.2, 127.0, 126.9, 112.9, 54.3, 54.2, 21.3; HRMS (ESI) calcd for $C_{42}H_{41}N_2$ $(M + H)^+$ 573.3270, found 573.3271.

***N*,*N*,*N*′,*N*′-Tetrabenzyl-2,2′-dimethyl-[1,1′-biphenyl]-4,4′-diamine (2k):** white solid; yield 44%, 50.4 mg; mp 169−170 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34−7.31 (m, 8H), 7.28−7.23 (m, 12H), 6.90 (d, J = 8.5 Hz, 2H), 6.64 (d, J = 2.5 Hz, 2H), 6.57 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 2H), 4.63 (s, 8H), 1.99 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.4, 139.1, 137.4, 131.1, 130.7, 128.8, 127.0, 127.0, 113.5, 109.9, 54.2, 20.9; HRMS (ESI) calcd for $C_{42}H_{41}N_2$ $(M + H)^+$ 573.3270, found 573.3260.

***N*⁴,*N*⁴,*N*⁴′,*N*⁴′-Tetrabenzyl-2,2′,6,6′-tetramethyl-[1,1′-biphenyl]-4,4′-diamine (2l)[10a]:** white solid; yield 92%, 110.5 mg; mp 189−190 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33−7.21 (m, 20H), 6.53 (s,

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4H), 4.59 (s, 8H), 1.82 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.3, 139.4, 137.2, 129.5, 128.7, 127.2, 126.9, 111.7, 53.9, 20.8; HRMS (ESI) calcd for $C_{44}H_{45}N_2$ $(M + H)^+$ 601.3583, found 601.3565.

$N^4,N^4,N^{4'},N^{4'}$-Tetrabenzyl-2,2′-diethyl-[1,1′-biphenyl]-4,4′-diamine (2m): white solid; yield 95%, 114.0 mg; mp 138−139 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.29 (m, 16H), 7.26−7.23 (m, 4H), 6.89 (d, J = 8.5 Hz, 2H), 6.67 (d, J = 2.0 Hz, 2H), 6.57 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 2H), 4.64 (s, 8H), 2.29 (dq, J_1 = 7.5 Hz, J_2= 2.5 Hz, 4H), 0.92 (t, J = 7.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.7, 143.5, 139.3, 131.4, 129.9, 128.7, 127.1, 127.0, 112.3, 109.9, 54.4, 26.8, 15.5; HRMS (ESI) calcd for $C_{44}H_{45}N_2$ $(M + H)^+$ 601.3583, found 601.3572.

$N^4,N^4,N^{4'},N^{4'}$-Tetrabenzyl-2,2′-diisopropyl-[1,1′-biphenyl]-4,4′-diamine (2n): white solid; yield 99%, 124.5 mg; mp 58−59 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32−7.25 (m, 20H), 6.86 (d, J = 7.5 Hz, 2H), 6.69 (s, 2H), 6.56 (d, J = 7.5 Hz, 2H), 4.64 (s, 8H), 2.72 (quat, J = 6.0 Hz, 1H), 2.71 (quat, J = 6.0 Hz, 1H), 0.95 (d, J = 6.5 Hz, 6H), 0.94 (d, J = 6.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.8, 148.1, 139.3, 131.3, 129.4, 128.7, 127.1, 127.0, 110.0, 109.7, 54.7, 30.0, 24.9, 23.5; HRMS (ESI) calcd for $C_{46}H_{49}N_2$ $(M + H)^+$ 629.3896, found 629.3896.

***N,N,N′,N′*-Tetrabenzyl-[1,1′-binaphthalene]-4,4′-diamine (2o):** white solid; yield 85%, 109.6 mg; mp 170−171 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, J = 8.0 Hz, 2H), 7.53−7.50 (m, 2H), 7.42 (d, J = 8.0 Hz, 2H), 7.34−7.27 (m, 19H), 7.25−7.18 (m, 5H), 7.00 (d, J = 7.5 Hz, 2H), 4.36 (s, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.4, 138.4, 134.6, 134.1, 129.7, 128.8, 128.4, 127.9, 127.5, 127.2, 125.9, 125.5, 124.1, 118.1, 57.3; HRMS (ESI) calcd for $C_{48}H_{41}N_2$ $(M + H)^+$ 645.3270, found 645.3261.

$N^4,N^4,N^{4'},N^{4'}$-Tetrabenzyl-2,2′,5,5′-tetramethoxy-[1,1′-biphenyl]-4,4′-diamine (2p): white solid; yield 53%, 70.5 mg; mp 156−157 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.25 (m, 16H), 7.22−7.18 (m, 4H), 6.85 (s, 2H), 6.45 (s, 2H), 4.30 (s, 8H), 3.85 (s, 6H), 3.51 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.1, 146.7, 139.8, 139.3, 128.6, 128.3, 126.9, 120.4, 116.3, 106.9, 56.8, 56.6, 55.8; HRMS (ESI) calcd for $C_{44}H_{45}N_2O_4$ $(M + H)^+$ 665.3379, found 665.3359.

$N^4,N^4,N^{4'},N^{4'}$-Tetrabenzyl-2,2′-diethoxy-[1,1′-biphenyl]-4,4′-diamine (2q): slightly yellow solid; yield 18%, 22.8 mg; mp 63−64 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32−7.24 (m, 20H), 7.06 (d, J = 8.0 Hz, 2H), 6.36 (d, J = 7.5 Hz, 2H), 6.31 (s, 2H), 4.63 (s, 8H), 3.78 (quat, J = 6.5 Hz, 4H), 1.13 (t, J = 6.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 149.5, 139.2, 132.4, 128.7, 127.0, 127.0, 117.3, 105.0, 98.4, 63.8, 54.6, 14.9; HRMS (ESI) calcd for $C_{44}H_{45}N_2O_2$ $(M + H)^+$ 633.3481, found 633.3470.

$N^4,N^4,N^{4'},N^{4'}$-Tetrabenzyl-2,2′-dichloro-[1,1′-biphenyl]-4,4′-diamine (2s): white solid; yield 46%, 56.1 mg; mp 202−203 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.32 (m, 8H), 7.28−7.24 (m, 12H), 7.03 (d, J = 8.5 Hz, 2H), 6.82 (d, J = 2.5 Hz, 2H), 6.63 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 2H), 4.64 (s, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.7, 138.1, 134.9, 132.5, 128.9, 127.3, 126.8, 126.7, 112.6, 110.7, 54.2; HRMS (ESI) calcd for $C_{40}H_{35}Cl_2N_2$ $(M + H)^+$ 613.2177, found 613.2120.

$N^4,N^4,N^{4'},N^{4'}$-Tetrabenzyl-2,2′-dibromo-[1,1′-biphenyl]-4,4′-diamine (2t): white solid; yield 97%, 136.4 mg; mp 203−204 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35−7.32 (m, 8H), 7.28−7.24 (m, 12H), 7.02 (d, J = 2.5 Hz, 2H), 7.00 (d, J = 8.5 Hz, 2H), 6.66 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 2H), 4.63 (s, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.7, 138.1, 132.3, 130.5, 128.9, 127.3, 126.9, 125.4, 115.6, 111.2, 54.1; HRMS (ESI) calcd for $C_{40}H_{35}Br_2N_2$ $(M + H)^+$ 701.1167, found 701.1217.

$N^4,N^4,N^{4'},N^{4'}$-Tetrabenzyl-2,2′-diiodo-[1,1′-biphenyl]-4,4′-diamine (2u): white solid; yield 98%, 156.0 mg; mp 185−186 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36−7.33 (m, 8H), 7.30 (d, J = 2.5 Hz, 2H), 7.28−7.24 (m, 12H), 6.94 (d, J = 8.5 Hz, 2H), 6.71 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 2H), 4.62 (s, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.5, 138.1, 137.8, 130.9, 128.9, 127.3, 126.9, 121.8, 112.1, 102.5, 54.0; HRMS (ESI) calcd for $C_{40}H_{35}I_2N_2$ $(M + H)^+$ 797.0890, found 797.0878.

$N^4,N^4,N^{4'},N^{4'}$-Tetrabenzyl-2,2′,3,3′-tetramethyl-[1,1′-biphenyl]-4,4′-diamine (2v). A mixture of isolated **4e** (72.3 mg, 0.17 mmol), benzylic bromide (65.0 mg, 0.38 mmol), and K_2CO_3 (95.1 mg, 0.69 mmol) in 2.0 mL of acetonitrile was stirred at 100 °C for 4 h in the atmosphere. After it cooled to room temperature, the reaction mixture was concentrated under reduced pressure to afford crude product, which was chromatographed on a silica gel column using 1:70 (v/v) EtOAc−petroleum ether solution as eluent to afford product **2v**: slightly yellow gum; overall yield 81%, 97.3 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29−7.27 (m, 4H), 7.26−7.23 (m, 13H), 7.22−7.20 (m, 3H), 6.80 (d, J = 3.0 Hz, 4H), 4.06 (s, 8H), 2.42 (s, 6H) 1.94 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.7, 138.7, 138.2, 136.0, 132.3, 129.1, 128.2, 127.1, 127.0, 119.7, 57.2, 17.6, 15.0; HRMS (ESI) calcd for $C_{44}H_{45}N_2$ $(M + H)^+$ 601.3583, found 601.3577.

$N^4,N^4,N^{4'},N^{4'}$-Tetrabenzyl-3,3′-dimethyl-[1,1′-biphenyl]-4,4′-diamine (2w). A mixture of isolated **4a** (22.1 mg, 0.056 mmol), benzylic bromide (21.1 mg, 0.12 mmol), and K_2CO_3 (30.9 mg, 0.22 mmol) in 2.0 mL of acetonitrile was stirred at 100 °C for 4 h in the atmosphere. After it cooled to room temperature, the reaction mixture was concentrated under reduced pressure to afford crude product, which was chromatographed on a silica gel column using 1:70 (v/v) EtOAc−petroleum ether solution as eluent to afford product **2s**: white solid; overall yield 22%, 25.2 mg; mp 145−146 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 1.5 Hz, 2H), 7.28−7.26 (m, 17H), 7.25−7.21 (m, 5H), 6.95 (d, J = 8.5 Hz, 2H), 4.10 (s, 8H), 2.49 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.0, 138.7, 135.9, 134.0, 129.6, 128.9, 128.3, 127.1, 124.5, 122.8, 57.0, 18.9; HRMS (ESI) calcd for $C_{42}H_{41}N_2$ $(M + H)^+$ 573.3270, found 573.3257.

$N^4,N^4,N^{4'},N^{4'}$-Tetrabenzyl-3,3′,5,5′-tetramethyl-[1,1′-biphenyl]-4,4′-diamine (2x). A mixture of isolated **4b** (31.1 mg, 0.074 mmol), benzylic bromide (27.8 mg, 0.16 mmol), and K_2CO_3 (40.9 mg, 0.30 mmol) in 2.0 mL of acetonitrile was stirred at 100 °C for 4 h in the atmosphere. After it was cooled to room temperature, the reaction mixture was concentrated under reduced pressure to afford crude product, which was chromatographed on a silica gel column using 1:70 (v/v) EtOAc−petroleum ether solution as eluent to afford product **2t**: white solid; overall yield 25%, 30.0 mg; mp 94−95 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30−7.27 (m, 8H), 7.25−7.24 (m, 8H), 7.23−7.21 (m, 8H), 4.11 (s, 8H), 2.21 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.4, 139.7, 137.2, 137.1, 129.4, 128.3, 127.7, 127.1, 56.5, 20.2; HRMS (ESI) calcd for $C_{44}H_{45}N_2$ $(M + H)^+$ 601.3583, found 601.3561.

1,1′-Dibenzyl-1,1′,2,2′,3,3′,4,4′-octahydro-6,6′-biquinoline (2y): slightly yellow solid; yield 61%, 54.2 mg; mp 179−180 °C; H NMR (500 MHz, $CDCl_3$) δ 7.33−7.28 (m, 8H), 7.24−7.22 (m, 2H), 7.14−7.12 (m, 4H), 6.52 (d, J = 8.0 Hz, 2H), 4.48 (s, 4H), 3.36 (s, 4H), 2.85 (t, J = 6.0 Hz, 4H), 2.03 (quint, J = 6.0 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.3, 139.3, 129.5, 128.7, 127.2, 126.9, 126.8, 125.1, 122.5, 111.5, 55.5, 50.1, 28.5, 22.7; HRMS (ESI) calcd for $C_{32}H_{33}N_2$ $(M + H)^+$ 445.2643, found 445.2646.

$N^4,N^4,N^{4'},N^{4'},N^{4''},N^{4''}$-Hexabenzyl-2,2″,6′-triethoxy-[1,1′:3′,1″-terphenyl]-4,4′,4″-triamine (2z): white solid; yield 52%, 65.7 mg; mp 60−61 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.27 (m, 16H), 7.25−7.22 (m, 4H), 7.20−7.14 (m, 6H), 7.13−7.11 (m, 5H), 7.08−7.06 (m, 2H), 6.43 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 6.41 (s, 1H), 6.37 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 6.31 (d, J = 2.5 Hz, 1H), 6.29 (d, J = 2.0 Hz, 1H), 4.64 (s, 4H), 4.62 (s, 4H), 3.94 (s, 4H), 3.82 (quat, J = 7.0 Hz, 2H), 3.73 (quat, J = 7.0 Hz, 2H), 3.71 (quat, J = 7.0 Hz, 2H), 1.15 (t, J = 7.0 Hz, 3H), 1.09 (t, J = 7.0 Hz, 3H), 1.03 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 157.2, 155.3, 149.7, 149.2, 139.1, 139.1, 135.8, 132.7, 132.3, 129.1, 128.8, 128.7, 128.0, 127.1, 127.0, 126.6, 126.0, 122.2, 119.8, 117.9, 106.9, 105.4, 105.0, 99.2, 98.2, 64.4, 64.0, 63.6, 56.3, 54.6, 54.5, 15.0, 14.9; HRMS (ESI) calcd for $C_{66}H_{66}N_3O_3$ $(M + H)^+$ 948.5104, found 948.5117.

4,4′-Methylenebis(*N*,*N*-dimethylaniline) (3a). *N*,*N*-Dimethylaniline **1a** (48.4 mg, 0.4 mmol) was added to a stirred mixture of $FeCl_3{\cdot}6H_2O$ (270.3 mg, 1.0 mmol), triethylamine (40.5 mg, 0.4 mmol), and 2.0 mL of toluene at room temperature. The reaction mixture was stirred at 85 °C for 2 h in the atmosphere. After it cooled

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to room temperature, the reaction mixture was quenched by aqueous ammonia solution (mass fraction: 25−28%, 10 mL) and extracted with dichloromethane (10 mL per time) until no product was observed in the extract, as monitored by TLC. The combined extract was washed with water (10 mL × 3) followed by saturated NaCl solution (10 mL × 1). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to give the crude product, which was chromatographed on a silica gel column using 1:70 (v/v) EtOAc−petroleum ether solution as the eluent to afford the isolated product **3a**: white solid; yield 68%, 23.0 mg; mp 90−91 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (d, J = 9.0 Hz, 4H), 6.68 (d, J = 8.5 Hz, 4H), 3.80 (s, 2H), 2.89 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.3, 130.5, 129.6, 113.2, 41.1, 40.1; HRMS (ESI) calcd for $C_{17}H_{23}N_2$ $(M + H)^+$ 255.1861, found 255.1863.

***N*^{4},*N*$^{4'}$-Dibenzyl-3,3′-dimethyl-[1,1′-biphenyl]-4,4′-diamine (4a):** white solid; yield 28%, 22.1 mg; mp 167−168 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43−7.41 (m, 4H), 7.39−7.36 (m, 4H), 7.32−7.28 (m, 6H), 6.66 (d, J = 8.5 Hz, 2H), 4.41 (s, 4H), 3.86 (s, 2H), 2.23 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.8, 139.8, 130.9, 128.8, 128.6, 127.7, 127.4, 125.2, 122.4, 110.5, 48.7, 17.9; HRMS (ESI) calcd for $C_{28}H_{29}N_2$ $(M + H)^+$ 393.2331, found 393.2325.

***N*^{4},*N*$^{4'}$-Dibenzyl-3,3′,5,5′-tetramethyl-[1,1′-biphenyl]-4,4′-diamine (4b):** white solid; yield 37%, 31.1 mg; mp 90−91 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.38 (m, 4H), 7.36−7.33 (m, 4H), 7.30−7.27 (m, 2H), 7.22 (s, 4H), 4.14 (s, 4H), 3.21 (br, 2H), 2.32 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.0, 140.7, 135.1, 130.1, 128.8, 128.2, 127.5, 127.4, 53.2, 18.9; HRMS (ESI) calcd for $C_{30}H_{33}N_2$ $(M + H)^+$ 421.2644, found 421.2642.

***N*^{4},*N*$^{4'}$-Dibenzyl-2,2′-dimethyl-[1,1′-biphenyl]-4,4′-diamine (4c):** white solid; yield 55%, 43.2 mg; mp 144−145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44−7.42 (m, 4H), 7.40−7.37 (m, 4H), 7.32−7.30 (m, 2H), 6.93 (d, J = 8.0 Hz, 2H), 6.58 (d, J = 2.0 Hz, 2H), 6.52 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 2H), 4.36 (s, 4H), 3.95 (s, 2H), 2.03 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.2, 139.8, 137.6, 131.6, 131.1, 128.8, 127.9, 127.4, 114.2, 110.1, 48.8, 20.5; HRMS (ESI) calcd for $C_{28}H_{29}N_2$ $(M + H)^+$ 393.2331, found 393.2332.

***N*^{4},*N*$^{4'}$-Dibenzyl-2,2′,6,6′-tetramethyl-[1,1′-biphenyl]-4,4′-diamine (4d):** white gum; yield 66%, 55.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.39 (m, 4H), 7.36−7.33 (m, 4H), 7.29−7.26 (m, 2H), 6.43 (s, 4H), 4.29 (s, 4H), 3.78 (br, 2H), 1.84 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.9, 139.9, 137.4, 130.2, 128.7, 128.0, 127.4, 112.0, 48.9, 20.4; HRMS (ESI) calcd for $C_{30}H_{33}N_2$ $(M + H)^+$ 421.2644, found 421.2643.

***N*^{4},*N*$^{4'}$-Dibenzyl-2,2′,3,3′-tetramethyl-[1,1′-biphenyl]-4,4′-diamine (4e):** white solid; yield 86%, 72.3 mg; mp 138−140 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44−7.42 (m, 4H), 7.38−7.35 (m, 4H), 7.31−7.26 (m, 2H), 6.89 (d, J = 8.5 Hz, 2H), 6.57 (d, J = 8.5 Hz, 2H), 4.38 (s, 4H), 3.81 (s, 2H), 2.13 (s, 6H), 2.01 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.9, 140.0, 135.4, 133.2, 128.8, 128.4, 128.0, 127.4, 120.4, 107.9, 49.0, 17.7, 13.4; HRMS (ESI) calcd for $C_{30}H_{33}N_2$ $(M + H)^+$ 421.2644, found 421.2636.

***N*^{4},*N*$^{4'}$-Dibenzyl-2,2′-diethyl-[1,1′-biphenyl]-4,4′-diamine (4f):** white gum; yield 44%, 37.0 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46−7.45 (m, 4H), 7.42−7.39 (m, 4H), 7.34−7.32 (m, 2H), 6.96 (d, J = 8.0 Hz, 2H), 6.63 (d, J = 2.5 Hz, 2H), 6.54 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 2H), 4.38 (s, 4H), 3.98 (s, 2H), 2.41−2.33 (m, 4H), 1.06 (t, J = 7.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.4, 143.7, 139.8, 131.5, 130.8, 128.8, 127.9, 127.4, 112.7, 109.9, 48.9, 26.6, 15.3; HRMS (ESI) calcd for $C_{30}H_{33}N_2$ $(M + H)^+$ 421.2644, found 421.2639.

***N*^{4},*N*$^{4'}$-Dibenzyl-2,2′-diisopropyl-[1,1′-biphenyl]-4,4′-diamine (4g):** slightly yellow gum; yield 33%, 29.7 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.41 (m, 4H), 7.37−7.34 (m, 4H), 7.30−7.27 (m, 2H), 6.90 (d, J = 8.0 Hz, 2H), 6.63 (d, J = 2.5 Hz, 2H), 6.48 (dd, J_1 = 8.0 Hz, J_2 = 2.5 Hz, 2H), 4.33 (s, 4H), 3.90 (br, 2H), 2.73 (heptet, J = 7.0 Hz, 2H), 1.09−1.04 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.5, 147.5, 139.8, 131.4, 130.3, 128.8, 128.0, 127.4, 109.8, 49.0, 30.0, 24.9, 23.3; HRMS (ESI) calcd for $C_{32}H_{37}N_2$ $(M + H)^+$ 449.2957, found 449.2960.

***N*^{4},*N*$^{4'}$-Dibenzyl-3,3′-diethoxy-[1,1′-biphenyl]-4,4′-diamine (4h):** light gray solid; yield 35%, 31.6 mg; mp 140−141 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.41 (m, 4H), 7.38−7.35 (m, 4H), 7.30−7.27 (m, 2H), 6.99 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 2H), 6.97 (s, 2H), 6.61 (d, J = 8.0 Hz, 2H), 4.68 (s, 2H), 4.41 (s, 4H), 4.14 (quat, J = 7.0 Hz, 4H), 1.45 (t, J = 7.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.5, 140.0, 137.1, 131.0, 128.7, 127.6, 127.2, 119.3, 110.5, 109.6, 64.1, 48.3, 15.2; HRMS (ESI) calcd for $C_{30}H_{33}N_2O_2$ $(M + H)^+$ 453.2542, found 453.2533.

***N*^{4},*N*$^{4'}$-Dibenzyl-2,2′,5,5′-tetramethoxy-[1,1′-biphenyl]-4,4′-diamine (4i):** white solid; yield 30%, 29.2 mg; mp 179−180 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45−7.43 (m, 4H), 7.39−7.36 (m, 4H), 7.31−7.28 (m, 2H), 6.75 (s, 2H), 6.32 (s, 2H), 4.67 (s, 2H), 4.39 (s, 4H), 3.81 (s, 6H), 3.65 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.0, 140.9, 139.8, 138.1, 128.8, 127.8, 127.3, 115.3, 113.8, 96.9, 56.9, 56.2, 48.5; HRMS (ESI) calcd for $C_{30}H_{33}N_2O_4$ $(M + H)^+$ 485.2440, found 485.2435.

***N*^{4},*N*$^{4'}$-Dibenzyl-2,2′-dichloro-[1,1′-biphenyl]-4,4′-diamine (4j):** slightly yellow solid; yield 19%, 16.0 mg; mp 153−154 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.35 (m, 8H), 7.31−7.28 (m, 2H), 7.04 (d, J = 8.5 Hz, 2H), 6.72 (d, J = 2.5 Hz, 2H), 6.54 (dd, J_1 = 8.0 Hz, J_2 = 2.5 Hz, 2H), 4.32 (s, 4H), 4.13 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.5, 139.0, 134.9, 132.5, 128.9, 127.7, 127.6, 127.5, 112.9, 111.3, 48.4; HRMS (ESI) calcd for $C_{26}H_{23}Cl_2N_2$ $(M + H)^+$ 433.1238, found 433.1239.

***N*^{4},*N*$^{4'}$-Dibenzyl-2,2′-dibromo-[1,1′-biphenyl]-4,4′-diamine (4k):** white solid; yield 42%, 44.0 mg; mp 173−174 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.30 (m, 10H), 7.01 (d, J = 8.5 Hz, 2H), 6.92 (s, 2H), 6.58 (d, J = 8.5 Hz, 2H), 4.32 (s, 4H), 4.10 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.6, 138.9, 132.3, 131.3, 128.9, 127.8, 127.7, 125.3, 115.9, 111.7, 48.4; HRMS (ESI) calcd for $C_{26}H_{23}Br_2N_2$ $(M + H)^+$ 521.0228, found 521.0246.

***N*^{4},*N*$^{4'}$-Dibenzyl-2,2′-diiodo-[1,1′-biphenyl]-4,4′-diamine (4l):** white solid; yield 42%, 52.0 mg; mp 152−153 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.34 (m, 8H), 7.32−7.28 (m, 2H), 7.19 (d, J = 2.5 Hz, 2H), 6.95 (d, J = 8.5 Hz, 2H), 6.61 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 2H), 4.30 (s, 4H), 4.04 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.3, 138.9, 138.6, 130.9, 128.9, 127.8, 127.7, 122.1, 112.5, 102.3, 48.4; HRMS (ESI) calcd for $C_{26}H_{23}I_2N_2$ $(M + H)^+$ 616.9951, found 616.9971.

1,1′,2,2′,3,3′,4,4′-Octahydro-6,6′-biquinoline (4m)[16]: white solid; yield 59%, 31.1 mg; mp 126−127 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, J = 7.5 Hz, 2H), 7.14 (s, 2H), 6.51 (d, J = 7.5 Hz, 2H), 3.80 (s, 2H), 3.32 (s, 4H), 2.82 (s, 4H), 1.98 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4, 130.9, 127.6, 125.0, 121.7, 114.7, 42.3, 27.3, 22.5; HRMS (ESI) calcd for $C_{18}H_{21}N_2$ $(M + H)^+$ 265.1705, found 265.1699.

6,6′-Biquinoline (5)[14a]. A solution of isolated **4m** (132 mg, 0.5 mmol) and diisopropyl azodicarboxylate (DIAD; 485.3 mg, 2.4 mmol) in 1.5 mL of acetonitrile was stirred at room temperature for 1 h in the atmosphere. Then the reaction mixture was concentrated under reduced pressure to afford the crude product, which was chromatographed on a silica gel column using 1:1 (v/v) EtOAc−petroleum ether solution as eluent to give 6,6′-biquinoline **5**: white solid; mp 179−181 °C; yield 61%, 81 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.95 (s, 2H), 8.26−8.23 (m 4H), 8.14−8.10 (m, 4H), 7.47 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.9, 148.0, 138.6, 136.5, 130.4, 129.4, 128.7, 126.3, 121.9; HRMS (ESI) calcd for $C_{18}H_{13}N_2$ $(M + H)^+$ 257.1079, found 257.1068.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures, solvent optimization, X-ray structure of **2y**, LC−MS spectra, and ^{1}H and ^{13}C NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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■ REFERENCES

(1) (a) Feiring, A. E.; Auman, B. C.; Wonchoba, E. R. *Macromolecules* **1993**, *26*, 2779. (b) Chen, R.-F.; Fan, Q.-L.; Zheng, C.; Huang, W. *Org. Lett.* **2006**, *8*, 203.

(2) Vogel, A. I. *Practical Organic Chemistry*, 5th ed.; Longman: London, 1991; p 49.

(3) (a) Holland, V. R.; Saunders, B. C.; Rose, F. L.; Walpole, A. L. *Tetrahedron* **1974**, *30*, 3299. (b) Liu, L.-F.; Zhang, Y.-L.; Qian, X.-H. *Dyes Pigm.* **2004**, *60*, 17.

(4) (a) Bissell, R. A.; Córdova, E.; Kaifer, A. E.; Stoddart, J. F. *Nature* **1994**, *369*, 133. (b) Ballardini, R.; Balzani, V.; Gandolfi, M. T.; Prodi, L.; Venturi, M.; Philip, D.; Ricketts, H. G.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **1993**, *32*, 1301.

(5) (a) Sariciftci, N. S.; Smilowitz, L.; Heeger, A. J.; Wudl, F. *Science* **1992**, *258*, 1474. (b) Johnson, G. E.; McGrane, K. M.; Stolka, M. *Pure Appl. Chem.* **1995**, *67*, 175. (c) Horowitz, G. *Adv. Mater.* **1998**, *10*, 365. (d) O'Brien, D. F.; Burrows, P. E.; Forrest, S. R.; Koene, B. E.; Loy, D. E.; Thompson, M. E. *Adv. Mater.* **1998**, *10*, 1108. (e) Noda, T.; Ogawa, H.; Noma, N.; Shirota, Y. *J. Mater. Chem.* **1999**, *9*, 2177. (f) Goodbrand, H. B.; Hu, N.-X. *J. Org. Chem.* **1999**, *64*, 670. (g) Getautis, V.; Stanisauskaite, A.; Paliulis, O.; Uss, S.; Uss, V. *J. Prakt. Chem.* **2000**, *342*, 58.

(6) Hmadeh, M.; Traboulsi, H.; Elhabiri, M.; Braunstein, P.; Albrecht-Gary, A.; Siri, O. *Tetrahedron* **2008**, *64*, 6522.

(7) (a) Cheng, J.-D.; Shine, H. J. *J. Org. Chem.* **1975**, *40*, 703. (b) Gündüz, T.; Kiliç, E.; Kenar, A.; Öztaş, S. G. *Analyst* **1989**, *114*, 727. (c) Zhu-Ohlbach, Q.; Gleiter, R.; Rominger, F.; Schmidt, H. L.; Reda, T. *Eur. J. Org. Chem.* **1998**, 2409. (d) Buncel, E. *Can. J. Chem.* **2000**, *78*, 1251.

(8) Kang, H.-M.; Lim, Y.-K.; Shin, I.-J.; Kim, H.-Y.; Cho, C.-G. *Org. Lett.* **2006**, *8*, 2047.

(9) (a) Periasamy, M.; Jayakumar, K. N.; Bharathi, P. *J. Org. Chem.* **2000**, *65*, 3548. (b) Xi, C.-J.; Jiang, Y.-F.; Yang, X.-H. *Tetrahedron Lett.* **2005**, *46*, 3909. (c) Jiang, Y.-F.; Xi, C.-J.; Yang, X.-H. *Synlett* **2005**, 1381. (d) Yang, X.-H.; Xi, C.-J.; Jiang, Y.-F. *Synth. Commun.* **2006**, *36*, 2413. (e) Kirchgessner, M.; Sreenath, K.; Gopidas, K. R. *J. Org. Chem.* **2006**, *71*, 9849.

(10) (a) Saitoh, T.; Yoshida, S.; Ichikawa, J. *Org. Lett.* **2004**, *6*, 4563. (b) Saitoh, T.; Yoshida, S.; Ichikawa, J. *J. Org. Chem.* **2006**, *71*, 6414.

(11) (a) Murata, S.; Miura, M.; Nomura, M. *J. Chem. Soc., Chem. Commun.* **1989**, 116. (b) Murata, S.; Miura, M.; Nomura, M. *J. Org. Chem.* **1989**, *54*, 4700.

(12) Li, X.-L.; Huang, J.-H.; Yang, L.-M. *Org. Lett.* **2011**, *13*, 4950.

(13) (a) Bolm, C.; Legros, J.; Paih, J. L.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217. (b) Enthaler, S.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3317. (c) Sarhan, A. A. O.; Bolm, C. *Chem. Soc. Rev.* **2009**, *38*, 2730. (d) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293.

(14) (a) Hu, Y.-Z.; Zhang, G.; Thummel, R. P. *Org. Lett.* **2003**, *5*, 2251. (b) Tonzola, C. J.; Alam, M. M.; Jenekhe, S. A. *Macromolecules* **2005**, *38*, 9539.

(15) Stone, M. T. *Org. Lett.* **2011**, *13*, 2326.

(16) Benincori, T.; Pagani, S. B.; Fusco, R.; Sannicolò, F. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2721.