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

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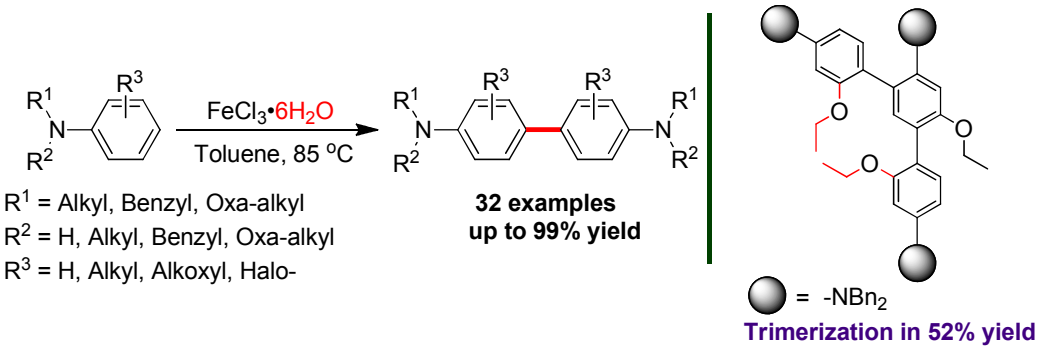


Abstract

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 their applicability in a wide variety of domains. For instance, they 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 by-products.[7] In an important contribution to the field, the group of Cho disclosed that aryl hydrazides with substituent(s) at the *ortho* or *meta* position could suppress the formation of by-products.[8] However, access is limited to *ortho*- and/or *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 oxidant could also be used and 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

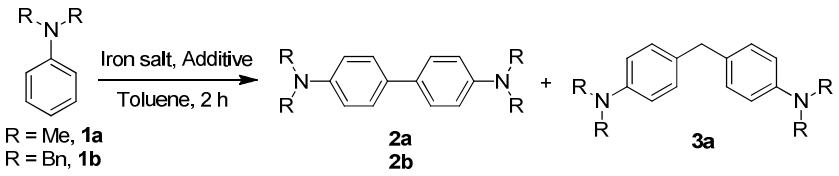
also employed to investigate the transformation of *N,N*-dimethylaniline, which tended to form *N*-methylaniline and 4,4'-methylenebis(*N,N*-dimethylaniline) through iminum cation intermediate.[11] Utilizing anhydrous $FeCl_3/K_2CO_3$, coupling products of naphthylamines were obtained through a possible 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 herein 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, synthetic methodologies based on iron has underwent an explosive growth due to the readily 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** in 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** and under these conditions, benzidine **2a** was obtained in 88% yield (entry 5). The difference between

$FeCl_3·6H_2O$ and $FeCl_3$ prompted us to investigate the effect of water in the system. When 15.0 equiv water was added to anhydrous $FeCl_3$, the coupling reaction proceeded smoothly and **2a** was obtained in 80% yield (entry 6). Subsequently, the amount of $FeCl_3·6H_2O$ was investigated. Addition of 1.0 equiv of $FeCl_3·6H_2O$ led to formation of product **2a** in a very low yield of 2% along with by-product **3a** as the major product while large excess of $FeCl_3·6H_2O$ gave rise selectively to **2a** in unimproved yields (entries 7-9). After screening the temperature, oxidative coupling of **2a** at 85°C using 2.5 equiv of $FeCl_3·6H_2O$ turned out to be the best reaction conditions (entries 5, 10 and 11). In iron(III)-promoted oxidative coupling of naphthylamines, Yang *et al.* reported that reaction was facilitated by 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 by-product **3a** in 68% yield while 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 and 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** in an excellent yield of 96% (entry 14). It is worthwhile noting that reaction of **1b** in the presence of anhydrous $FeCl_3$ or $FeCl_3·6H_2O/K_2CO_3$ afforded only compound **2b** in diminished yield while **3a** was the major compound for the self-coupling of **1a** under indentical conditions (entries 15 and 16).

Table 1. Initial screening results[a]



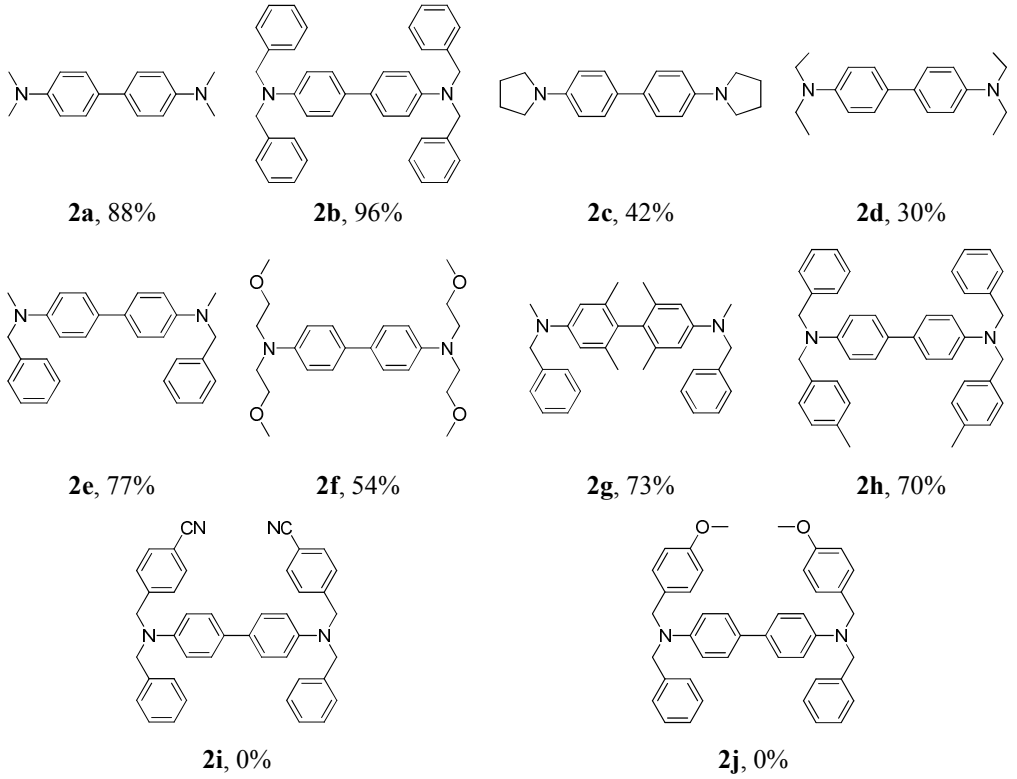
Entry	**1**	Iron salt / Additive (eq)	T °C	Yield %[b]
1	**1a**	$FeCl_2·4H_2O$ (2.5)	85	4
2	**1a**	$Fe_2(SO_4)_3$ (2.5)	85	n.p[c]
3	**1a**	$Fe(NO_3)_3·9H_2O$ (2.5)	85	n.p[c]
4	**1a**	$FeCl_3$ (2.5)	85	28(24)[d]
5	**1a**	**$FeCl_3·6H_2O$ (2.5)**	**85**	**88**
6	**1a**	$FeCl_3$ (2.5) / H_2O (15.0)	85	80
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 parenthesis. [e] Yield of 91% was obtained in distilled toluene under N_2.

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 while *N*-benzyl-*N*-methylanilines underwent self-coupling in good yields. Oxa-alkyl substituted aniline gave the coupling product **2f** in a yield of 54%. The substitution pattern of the benzyl group showed a dramatic influence on the reactivity. Methyl substituent was well-tolerated with the formation of **2h** in 70% yield while starting materials were recovered with methoxy- and cyano-containing substrates.

Table 2. Influence of the nitrogen protecting group[a]



2a, 88% **2b**, 96% **2c**, 42% **2d**, 30%

2e, 77% **2f**, 54% **2g**, 73% **2h**, 70%

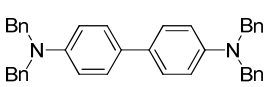
2i, 0% **2j**, 0%

[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.

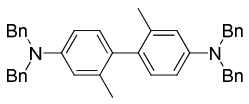
Amongst all the nitrogen protecting group tested, the benzyl group gave the best result. In addition, the benzyl group can be easily introduced and requires mild conditions (H_2, Pd/C) to be cleaved. As a result, the benzyl moiety was selected as a

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

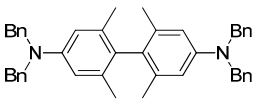
Table 3. Self-coupling reactions of functionalized *N*,*N*-dibenzyl anilines[a]



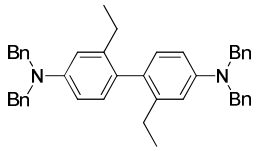
2b, 96%



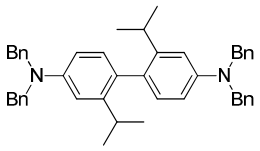
2k, 44%



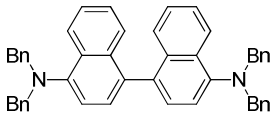
2l, 92%



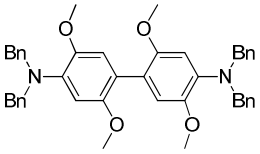
2m, 95%



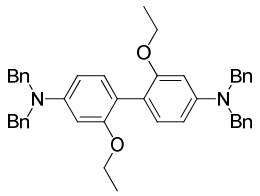
2n, 99%



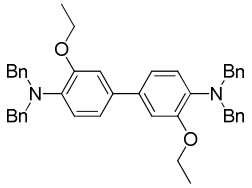
2o, 85%



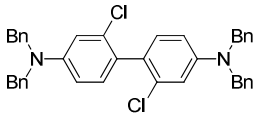
2p, 53%



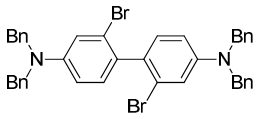
2q, 18%



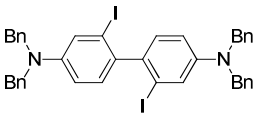
2r, 0%



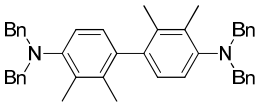
2s, 46%[b]



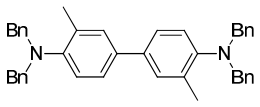
2t, 97%



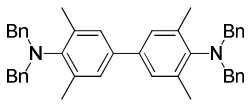
2u, 98%[b]



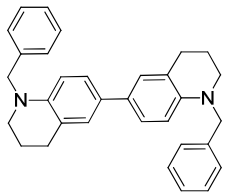
2v, 0%



2w, 0%



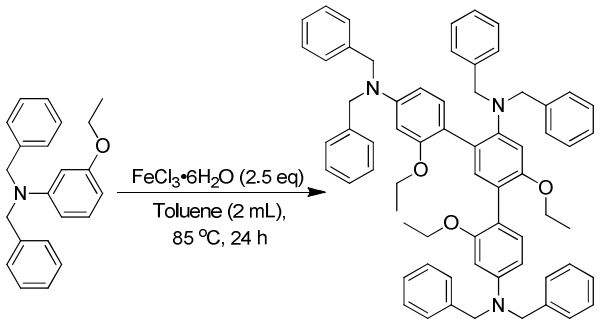
2x, 0%



2y, 61%

[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] 8 h.

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

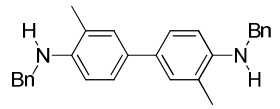


1q **2z**, 52%

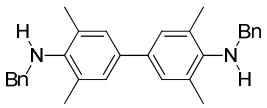
The lack of reactivities in self-coupling of **2r** and **2v**-**x** might be explained by steric repulsions between the *ortho* methyl or alkoxyl group(s) of the benzene ring

and the benzyl 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 oxidised. In this context, we surmised that oxidative coupling of *N*-benzylanilines should be facilitated due to lower steric shielding around the nitrogen. Unlike *N,N*-dibenzyl anilines, *N*-monobenzylanilines underwent self-coupling to provide corresponding benzidines (Table 4). Alkyl substitutions at the *ortho* or *meta* position of the aromatic ring were tolerated, providing desired products in 28% to 86% yields (**4a**-**g**). It is worthwhile noting 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** in moderate yields. Halo-substitutions at the *meta* position of the mother benzene ring could afford coupling product **4j-l** while coupling reaction did not proceed using anilines bearing *ortho* halo-substitutions. Commercially available 1,2,3,4-tetrahydroquinoline gave directly benzidine **4m** in 59% yield.

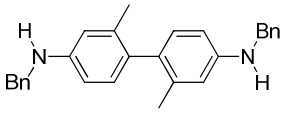
Table 4. Self-coupling reactions of functionalized *N*-benzylanilines[a]



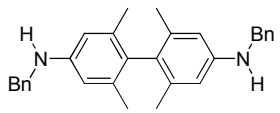
4a, 28%



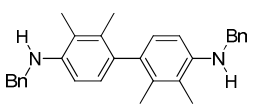
4b, 37%



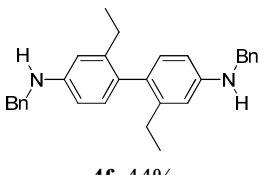
4c, 55%



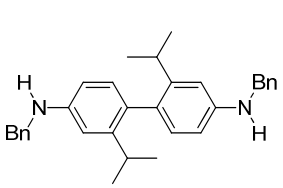
4d, 66%



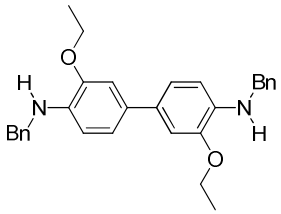
4e, 86%



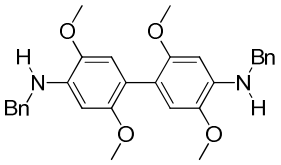
4f, 44%



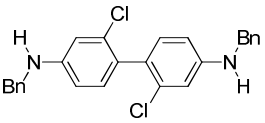
4g, 33%



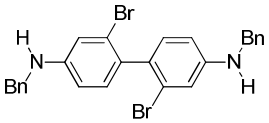
4h, 35%



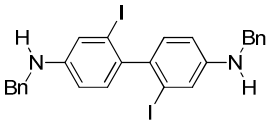
4i, 30%



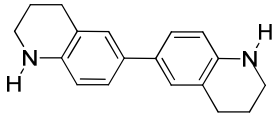
4j, 19%[b]



4k, 42%[b]



4l, 42%[b]

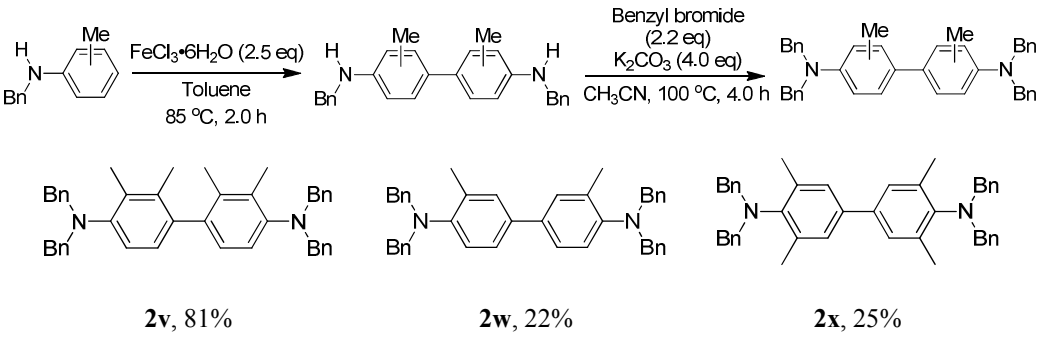


4m, 59%

[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] 8 h.

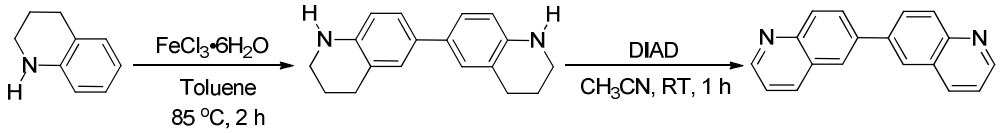
In order to prepare *ortho*-substituted *N*,*N*-dibenzylaninlines **2v-x**, we investigated the synthetic route composed of two steps: 1) self-coupling of *ortho*-methyl substituted *N*-benzylanilines under optimized conditions; and 2) N-benzylation with benzyl bromide (Scheme 2). Following this strategy, benzidines **2v-x** were obtained in moderate-to-good overall yields over the two steps. In addition, the oxidative coupling of *N*-benzyl aniline was applied to the preparation of 6,6'-bisquinoline **5** which was found to be a potential photoactive materials (Scheme 3).[14] Benzidine **4m** was obtained through oxidative coupling of the corresponding aniline and underwent diisopropyl azodicarboxylate (DIAD)-mediated dehydrogenation to afford **5** in 61% yield.[15]

Scheme 2. Synthesis of *o*-methyl substituted benzidines



2v, 81% **2w**, 22% **2x**, 25%

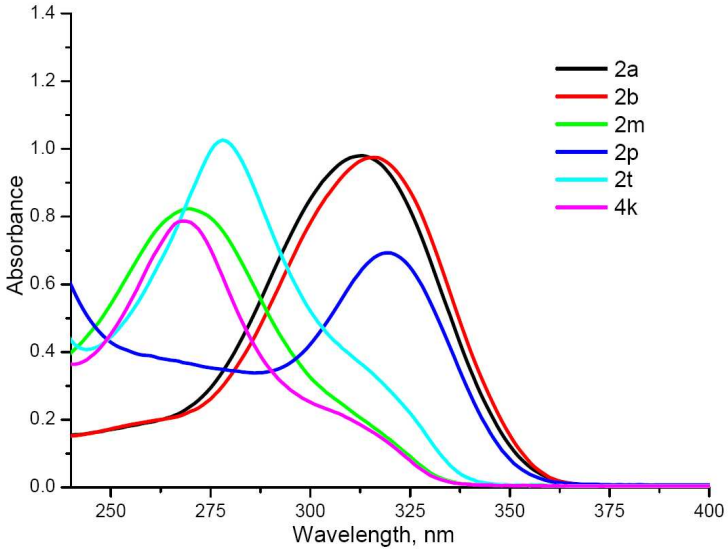
Scheme 3. Synthesis of 6,6'-biquinoline



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

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 dimethyl 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** redshift to 316 and 319 nm, which indicates that π-electrons in **2b** and **2p** are more easily excited to higher anti-bonding 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, which shows that the substitutions on the benzene ring have a stronger impact on the energy gap between the HOMO and the LUMO.

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

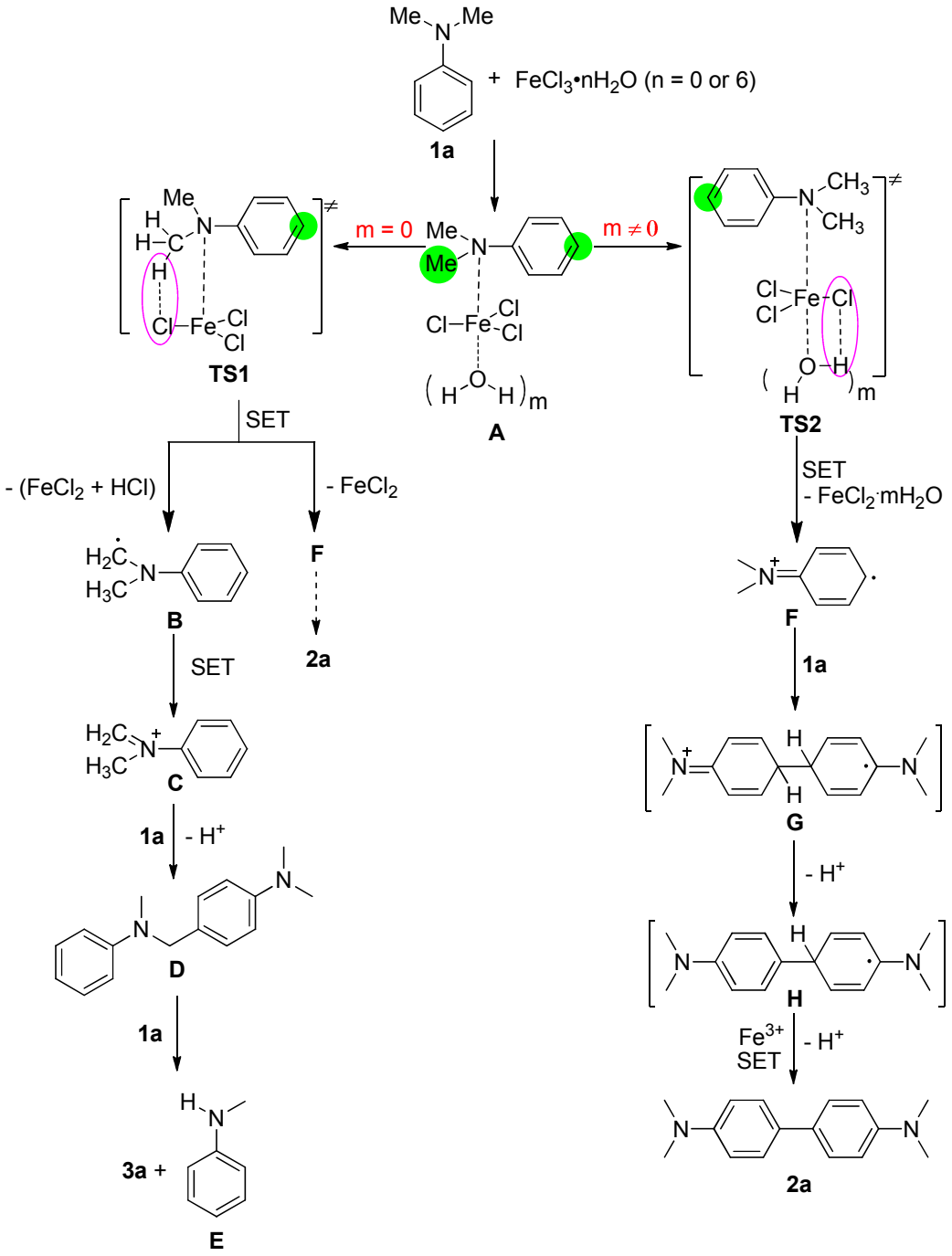


compound	λ_{max}, nm	ϵ, M^{-1} cm^{-1} (log ϵ)
2a	313	39200 (4.59)
2b	316	39000 (4.59)
2m	269	32920 (4.51)
2p	319	27720 (4.44)
2t	278	41040 (4.61)
4k	268	31480 (4.50)

In efforts 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 and under these conditions, the reaction was blocked, contrary to Yang's report,[12] and benzidine **2b** could not be detected by LC-MS. Based on these results, a possible radical mechanism for the oxidative self-coupling reaction was proposed (Figure 2). Anilines **1a** firstly coordinates with Fe^{3+} to generate iron(III) complex **A**, in which methyl group on nitrogen and the *para*-position on aniline are both activated.

With anhydrous $FeCl_3$, radical **B** and **F** are formed from 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 noting that an effective hydrogen bond interaction between chlorine anion and one hydrogen of the methyl group leads to formation of only **3a**. The existence of crystal water decreases the basicity of chlorine anion through hydrogen bonding interaction with water, and suppresses Cl^--assisted deprotonation of the methy group to formation of **3a**. Thus *para*-position on the aniline is relatively more reactive than methyl group. When hydrated $FeCl_2$ 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 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 hydrogen absorption of Cl (Table 1, entries 12 and 13).

Figure 2. Proposed mechanism



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 $FeCl_3 \cdot 6H_2O$ as an oxidant. This methodology was applied to the preparations of

valuable safe staining precursors and 6,6'-biquinoline. Trimeriztion product is obtained by one-step synthesis, which possesses potential application in 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 ^{1}H, 125 MHz for ^{13}C) with deuterated chloroform ($CDCl_3$) as a solvent at 20-25 ^{o}C. ^{1}H 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: To a stirred mixture of $FeCl_3 \cdot 6H_2O$ (270.3 mg, 1.0 mmol) and 2.0 mL toluene was added *N,N*-dimethylaniline **1a** (48.4 mg, 0.4 mmol) at room temperature. The reaction was stirred at 85 ^{o}C for 2 h in 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, 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 silica gel column using 1:80 (*v*/*v*) EtOAc-petroleum ether solution as eluent to afford isolated product **2a**.

Procedure for LC-MS experiments: To a stirred mixture of $FeCl_3 \cdot 6H_2O$ (270.3 mg, 1.0 mmol) and 2.0 mL toluene was added *N,N*-dibenzylaniline (109.3 mg, 0.4 mmol) at room temperature. The reaction was stirred at 85 ^oC for 40 min or 120 min in atmosphere. After it was cooled to room temperature, the reaction mixture was concentrated under reduced pressure to give dark red solid. The solid was dissolved in acetonitrile for LC-MS analysis, the results of which demonstrated that only starting material **1b** and coupling product **2b** was detected after 40 min and only coupling product **2b** was observed after 120 min, respectively. See supporting information for LC-MS spectra.

Procedure for control experiment utilizing 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO): To a stirred mixture of $FeCl_3 \cdot 6H_2O$ (270.3 mg, 1 mmol) in 2.0 mL toluene was added *N,N*-dibenzylaniline **1b** (109.3 mg, 0.4 mmol) and 2,2,6,6-tetramethylpiperidin-1-oxyl (125.0 mg, 0.8 mmol) successively at room temperature. The reaction mixture was stirred at 85 ^oC for 2 h in 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 examined 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 undergo 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 ^{o}C; ^{1}H 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 ^{o}C; ^{1}H 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 ^{o}C; ^{1}H 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 ^{o}C; ^{1}H 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; ^{1}H 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* = 8.5Hz, 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; ^{1}H 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; ^{1}H 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; ^{1}H 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 ^oC; ^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 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.21 (m, 20H), 6.53 (s, 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 ^oC; ^1H 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 ^oC; ^1H 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 ^{o}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 ^{o}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 ^{o}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** of standard condition (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 acetonitrile was stirred at 100 °C for 4 h in atmosphere. After it was cooled to room temperature, the reaction mixture was concentrated under reduced pressure to afford crude product, which was chromatographed on silica gel column using 1:70 (*v*/*v*) EtOAc-petroleum ether solution as eluent to afford product **2v**. Slight 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** of standard condition (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 acetonitrile was stirred at 100 °C for 4 h in atmosphere. After it was cooled to room temperature, the reaction mixture was concentrated under reduced pressure to afford crude product, which was chromatographed on 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** of standard condition (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 acetonitrile was stirred at 100 ^oC for 4 h in atmosphere. After it was cooled to room temperature, the reaction mixture was concentrated under reduced pressure to afford crude product, which was chromatographed on 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 ^oC; ^1H 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): Slight yellow solid; yield 61%, 54.2 mg; mp: 179-180 ^oC; yield 61%, 54.2 mg; ^1H 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 ^oC; ^1H 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): 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 toluene was added *N,N*-dimethylaniline **1a** (48.4 mg, 0.4 mmol) at room temperature. The reaction was stirred at 85 ^{o}C for 2 h in 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, 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 silica gel column using 1:70 (*v*/*v*) EtOAc-petroleum ether solution as eluent to afford isolated product **3a**. white solid; yield 68%, 23.0 mg; mp: 90-91 ^{o}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 ^{o}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): Slight 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):** Slight 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):[15] A solution of isolated **4m** (132 mg, 0.5 mmol) and diisopropyl azodicarboxylate (DIAD; 485.3 mg, 2.4 mmol) in 1.5 mL acetonitrile was stirred at room temperature for 1 h in atmosphere. Then the reaction mixture was concentrated under reduced pressure to afford crude product, which was chromatographed on 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 $C_{18}H_{12}N_2$ $(M+H)^+$ 257.1079, found 257.1068.

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Supporting Information.

Experimental procedures, solvent optimization, X-ray structure of **2y**, LC-MS spectra, ^1H 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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