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Oxidative Coupling Reaction of N,N-Dialkylanilines with Cerium(IV) Ammonium Nitrate in the Solid State

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Oxidative Coupling Reaction of *N*,*N*-Dialkylanilines with Cerium(IV) Ammonium Nitrate in the Solid State

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Abstract: Oxidative coupling reactions of *N*,*N*-dialkylanilines with cerium(IV) ammonium nitrate can be achieved by grinding at room temperature in the absence of solvents.

Keywords: Grinding, *N*,*N*-dialkylarylamine, oxidative coupling, solid state

N,*N*,*N*′,*N*′-Tetraalkylbenzidine derivatives have received much attention for their tunable electric conductivity, which has the potential to be utilized in industrial fields such as organic light-emitting diodes,[1] organic field-effect transistors,[2] organic solar cells,[3] and organic photoconductors.[4] Oxidative coupling of *N*,*N*-dialkylanilines provides an efficient access to such products, but most known methods for such reactions are either low yielding[5–7] or not very regioselective. Some newly reported methods seem to be more practical, such as $TiCl_4$-mediated oxidative coupling[8] and 1,8-bis(diphenylmethylium)naphthalenediyl dications,[9] but the former requires a large excess of substrates and dichloromethane as solvent and the organic oxidant for the latter is troublesome to get.

With increasing public concern about environmental degradation, one of the challenges for chemists is to come up with new approaches that are less

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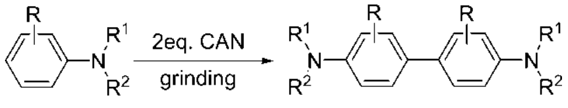
hazardous to human health and the environment.[10] The solvents used in organic synthesis are high on the list of environmental pollutants, because they are employed in large amounts and usually are volatile liquids. To be environmentally friendly, we are interested in seeking new processes involving solvent-free reactions for organic reactions, although the solvent-free method has been utilized in a wide range of reactions recently.[11–14] In our previous work, we developed a cerium(IV) ammonium nitrate (CAN)-mediated oxidative coupling of *N*,*N*-dialkylanilines using water as solvent,[15] which was efficient, economical, and environmentally friendly. During the course of our study, we found oxidative coupling reactions of *N*,*N*-dialkylanilines with CAN can be achieved by grinding at room temperature in the absence of solvents.

By milling constantly with a mortar and pestle, this method was found to be significantly faster than traditional methods based on solvent[12–14] and much easier to carry out. When *N*,*N*-dialkylanilines were tried with this method (Scheme 1), similar conclusions, such as faster proceeding, easier handling, and higher regioselectivity, were demonstrated by our study.

At the very beginning, experiments were made to test the proper amount of CAN, and in accordance with the aqueous system we reported,[15] 2 equiv of CAN seems to be the most proper (Table 1). When 1 equiv of CAN was added to 1 mmol of substrate and ground constantly with a mortar and pestle for 15 min, most substrate still remained. When the amount of CAN changed from 2 equiv to 5 equiv, only the yield mildly differed. When *N*,*N*-diethylaniline **1a** was used in these testing reactions, *para*-position coupling happened and *N*,*N*,*N*′,*N*′-tetraethylbenzidine **2a** was the main isolated product in 58% yield with excellent regioselectivity.

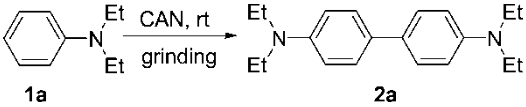
The ratio of 1 : 2 of substrate to CAN for oxidative *p,p*-coupling was found to be general for other *N*,*N*-dialkylanilines, and some examples are shown in Table 2. In most cases, the reaction gave high regioselectivity for *p*,*p*-coupling products, with the only exception of 3,5-dimethyl-*N*,*N*-diethylaniline **1d**, which gave *o*,*p*-coupled product **2d** in 80% yield. 1-Phenylpiperidine **1j** showed low yield of **2j** in 28% probably because the ring on the **N** atom make the proceeding of the reaction harder. Reactions of other substrates were similar to **1a**.

As for the mechanism of this reaction, we hold the radical cation procedure, which we reported in our previous work,[15] as presented in Scheme 2. First, the *N*,*N*-dialkylaniline **1** is coordinated to CAN to form



Scheme 1.

Table 1. Effect of amount of CAN on the oxidative coupling reaction of *N*,*N*-dialkylaniline



Entry	CAN (eq)	Time (min)	Yield (%)[a]
1	1	5	Trace
2	1	15	Trace
3	2	5	Trace
4	2	10	35
5	2	15	58
6	2	20	58
7	3	15	46
8	4	15	42
9	5	15	44

[a] Isolated yield based on the amount of *N*,*N*-dialkylaniline.

complex **3**, which undergoes oxidative electron transfer with second CAN to afford the radical cation **4**. Second, the radical cation **4** directly dimerizes to give diiminium ions intermediate **5**, which is converted to dimer **6** after deprotonation. Finally, product **2** forms after the workup procedure.

In conclusion, we have found a highly regioselective, fast, and environmentally friendly oxidative coupling reaction of *N*,*N*-dialkylanilines with cerium(IV) ammonium nitrate (CAN) in the absence of solvent.

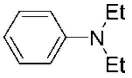
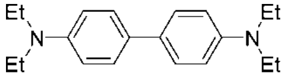
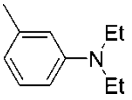
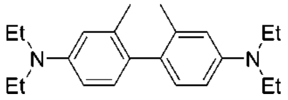
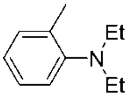
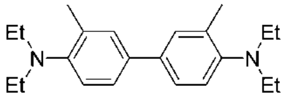
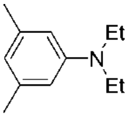
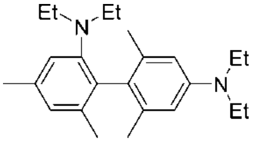
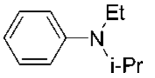
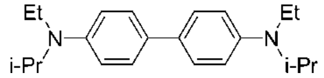
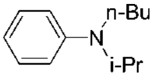
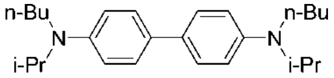
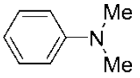
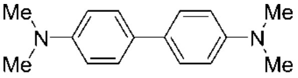
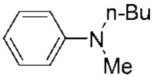
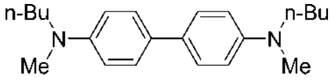
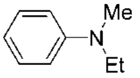
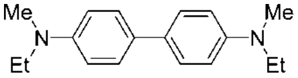
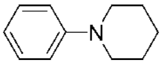
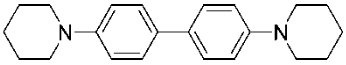
EXPERIMENTAL

Representative Procedure

N,*N*-Diethylaniline **1a** (1 mmol, 159 μL) and CAN (2 eq, 1.096 g) were mixed together in a mortar, and the mixture was constantly milled with a pestle. Ten to fifteen minutes later, the reaction mixture was quenched with an aqueous solution of K_2CO_3, followed by extraction of the organic phase with ethyl acetate. Then the solvent was evaporated under reduced pressure, and the residue was purified by chromatography on neutral Al_2O_3 column using 1:100 EtOAc/petroleum mixture as eluent.

Structures of the final products were comfirmed by ^1H NMR (300 MHz) and ^{13}C NMR (300 MHz) in deuterated chloroform. Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane. Proton and carbon spectra were typically obtained at room temperature. ESI-MS data were used to strengthen our results.

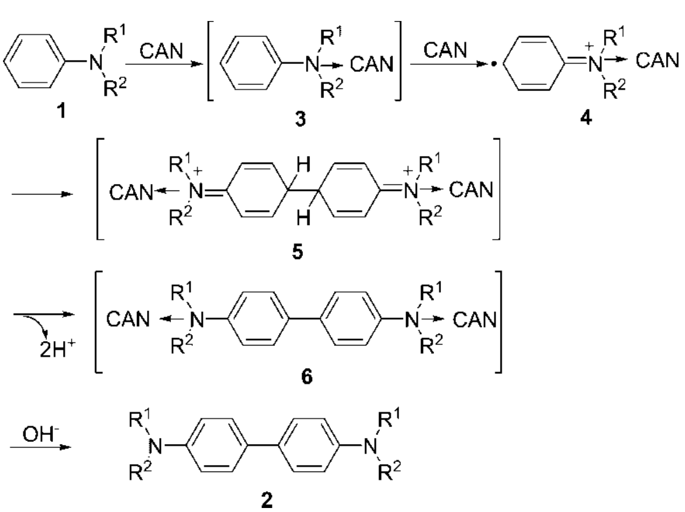
Table 2. Oxidative coupling of *N*,*N*-dialkylanilines with CAN in solid state

Entry	Substrate		Product		Yield (%)[a]
1		**1a**		**2a**	58
2		**1b**		**2b**	78
3		**1c**		**2c**	48
4		**1d**		**2d**	80
5		**1e**		**2e**	77
6		**1f**		**2f**	54
7		**1g**		**2g**	43
8		**1h**		**2h**	49
9		**1i**		**2i**	46
10		**1j**		**2j**	28[b]

[a] Isolated yield based on substrate.
[b] Substrate **1j** remained.

Data

***N*,*N*,*N*′,*N*′-Tetraethylbiphenyl-4,4′-diamine (2a):**[8] yellow solid (58%). ^{1}H NMR (CDCl$_3$) δ 7.40 (d, $J = 8.6$ Hz, 4H), 6.72 (d, $J = 8.6$ Hz, 4H), 3.35



Scheme 2.

(q, $J = 6.9$ Hz, 8H), 1.17 (t, $J = 6.9$ Hz, 12H); ^{13}C NMR ($CDCl_3$) δ 146.4, 128.9, 127.2, 112.3, 44.5, 12.8. ESI-MS: 297 ($M + H^+$).

***N*,*N*,*N*′,*N*′-Tetraethyl-2,2′-dimethylbiphenyl-4,4′-diamine (2b):** light yellow liquid (78%). ^{1}H NMR ($CDCl_3$) δ 6.87 (d, $J = 8.3$ Hz, 2H), 6.46 (m, 4H), 3.26 (q, $J = 7.2$ Hz, 8H), 1.98 (s, 6H), 1.09 (t, $J = 7.2$ Hz, 12H); ^{13}C NMR ($CDCl_3$) δ 146.8, 137.4, 131.2, 129.5, 112.9, 109.2, 44.4, 20.9, 12.9. ESI-MS: 325 ($M + H^+$). HRMS: calcd. for $C_{22}H_{32}N_2$ 324.2565; found 324.2568.

***N*,*N*,*N*′,*N*′-Tetraethyl-3,3′-dimethylbiphenyl-4,4′-diamine (2c):** light yellow liquid (48%). ^{1}H NMR ($CDCl_3$) δ 7.40 (m, 4H), 7.08 (d, $J = 8.3$ Hz, 2H), 3.02 (q, $J = 7.2$ Hz, 8H), 2.35 (s, 6H), 1.00 (t, $J = 7.2$ Hz, 12H); ^{13}C NMR ($CDCl_3$) δ 148.8, 135.9, 135.4, 129.4, 124.5, 122.4, 47.7, 18.7, 12.7. ESI-MS: 325 ($M + H^+$). HRMS: calcd. for $C_{22}H_{32}N_2$ 324.2565; found 324.2563.

***N*,*N*,*N*′,*N*′-Tetraethyl-2′,4,6,6′-tetramethylbiphenyl-2,4′-diamine (2d):** colorless liquid (80%). ^{1}H NMR ($CDCl_3$) δ 6.46 (s, H), 6.31 (s, 3H), 3.31 (m, 8H), 2.26 (s, 9H), 1.89 (s, 3H), 1.15 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 148.0, 146.5, 138.7, 137.1, 128.4, 117.5, 111.1, 109.8, 44.3, 44.2, 21.9, 20.8, 12.9, 12.7. ESI-MS: 353 ($M + H^+$). HRMS: calcd. for $C_{24}H_{36}N_2$ 352.2878; found 352.2875.

***N*,*N*′-Diethyl-*N*,*N*′-diisopropylbiphenyl-4,4′-diamine (2e):** colorless liquid (77%). ^{1}H NMR ($CDCl_3$) δ 7.20 (m, 4H), 6.72 (m, 4H), 4.02 (m, 2H), 3.22 (m, 4H), 1.15 (m, 18H); ^{13}C NMR ($CDCl_3$) δ 148.6, 129.2, 115.8, 112.9, 48.2, 38.0, 20.1, 15.1. ESI-MS: 325 ($M + H^+$). HRMS: calcd. for $C_{22}H_{32}N_2$ 324.2565; found 324.2566.

***N*,*N′*-Dibutyl-*N*,*N′*-diisopropylbiphenyl-4,4′-diamine (2f):**[16] yellow solid (54%). ^{1}H NMR ($CDCl_3$) δ 7.34 (d, $J = 8.9$ Hz, 4H), 6.68 (d, $J = 8.9$ Hz, 4H), 3.98 (m, 2H), 3.04 (m, 4H), 1.49 (m, 4H), 1.32 (m, 4H), 1.27 (m, 12H), 0.88 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 146.6, 128.5, 126.3, 112.8, 18.0, 43.2, 31.0, 19.9, 19.5, 13.4. ESI-MS: 381 ($M + H^+$).

***N,N,N′,N′*-Tetramethylbiphenyl-4,4′-diamine (2 g):**[8] yellow solid (43%). ^{1}H NMR ($CDCl_3$): δ 7.45 (d, $J = 8.4$ Hz, 4H), 6.80 (d, $J = 8.4$ Hz, 4H), 2.97 (s, 12H); ^{13}C NMR ($CDCl_3$): δ 149.4, 130.0, 127.0, 113.2, 40.8. ESI-MS: 241 ($M + H^+$).

***N*,*N′*-Dibutyl-*N*,*N′*-dimethylbiphenyl-4,4′-diamine (2 h):**[16] yellow solid (49%). ^{1}H NMR ($CDCl_3$): δ 7.42 (d, $J = 8.9$ Hz, 4 H), 6.72 (d, $J = 8.9$ Hz, 4 H), 3.30 (br, 4 H), 2.93 (s, 6 H), 1.52–1.58 (m, 4 H), 1.29–1.38 (m, 4 H), 0.94 (t, $J = 7.2$ Hz, 6 H). ^{13}C NMR ($CDCl_3$): δ 147.8, 129.1, 126.9, 112.4, 52.6, 38.4, 28.9, 20.4, 14.0. ESI-MS: 325 ($M + H^+$).

***N*,*N′*-Diethyl-*N*,*N′*-dimethylbiphenyl-4,4′-diamine (2i):**[8] yellow solid (46%). ^{1}H NMR ($CDCl_3$): δ 7.61 (m, 4H), 6.92 (m, 4H), 3.58 (q, $J = 7.2$ Hz, 4H), 3.06 (s, 6H), 1.27 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR ($CDCl_3$): δ 147.8, 129.49, 127.1, 112.9, 47.0, 37.6, 11.4. ESI-MS: 269 ($M + H^+$).

4,4′-Di(piperidin-1-yl)biphenyl (2j):[8] yellow solid (28%). ^{1}H NMR ($CDCl_3$): δ 7.51 (m, 4H), 7.13 (m, 4H), 3.24 (s, 8H), 1.70 (m, 12H); ^{13}C NMR ($CDCl_3$): δ 150.8, 132.0, 127.0, 116.8, 50.8, 25.9, 24.4. ESI-MS: 321 ($M + H^+$).

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