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Remarkably efficient oxidative coupling of *N*,*N*-dialkylarylamines in water mediated by cerium(IV) ammonium nitrate

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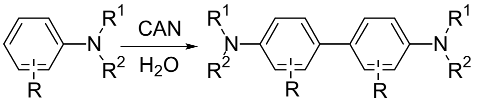
Abstract—A highly effective, economical, and environmentally friendly method using of CAN as oxidant and water as solvent for oxidative coupling of *N*,*N*-dialkylarylamines was reported.

N,*N*,*N*′,*N*′-tetraalkylbenzidine derivatives have received growing interest in their tunable electric conductivity, which admits to diverse applications such as organic light-emitting diodes,[1] organic field-effect transistors,[2] organic solar cells,[3] and organic photoconductors.[4] Oxidative coupling of aniline derivatives provides an efficient access to benzidine derivatives. Although several methods for the coupling reaction have been reported, most of them are low yielding processes.[5–7] Recently, $TiCl_4$-mediated oxidative coupling appeared to be the most practical method for benzidines,[8] despite the requirement of a large excess of starting anilines and utilization of dichloromethane as solvent. More recently, an alternative coupling of *N*,*N*-dialkylanilines in higher yield has been developed by using organic oxidant such as 1,8-bis(diphenyl-methylium)-naphthalenediyl dications.[9] However, to get such organic oxidant could be troublesome.

In light of the current interest to develop more efficient and environmentally friendly methods for chemical syntheses, the use of water as the solvent clearly has both economical and environmental advantages because it is inexpensive, abundant, nontoxic, and readily separated from organic compounds.[10] Accordingly, it is highly desirable to develop a direct oxidative coupling of aniline derivatives in water by using a readily available, water-soluble oxidant.

Cerium(IV) ammonium nitrate (CAN) has emerged as a versatile one-electron oxidant for carbon–carbon bond formation reactions.[11] The advantages of good solubility in water, low cost, low toxicity, commercial available, easy handling, and profound reactivity give rise to the possibility for development of more practical reactions in aqueous medium. To the best of our knowledge, CAN-mediated oxidative coupling of aniline derivatives is rather rare.[12] Herein, we would like to report a remarkable efficient coupling of *N*,*N*-dialkylaniline in water mediated by CAN (Scheme 1).



Scheme 1.

CAN is well known as one electron-transfer oxidant and theoretically one equivalent of CAN is required for mediating this coupling reaction. At first, we tested the coupling of *N*,*N*-diethylaniline **1a** in water using 1 equiv of CAN. However, nearly half of the *N*,*N*-dialkylaniline remained after quenched by an aqueous solution of K_2CO_3. When the amount of CAN was increased to 1.5 equiv, some *N*,*N*-diethylaniline still remained even after two days. The best yield of the coupling product was obtained when the *N*,*N*-diethylaniline:CAN was 1:2 ratio at room temperature for 2 h (Scheme 2).[13] *N*,*N*,*N*′,*N*′-Tetraethylbenzidine **2a** was obtained in 81% isolated yield with excellent regioselectivity. It is noteworthy that neither product nor remaining

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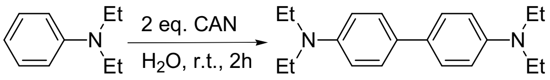


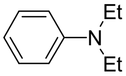
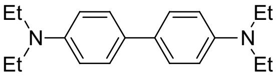
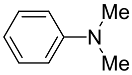
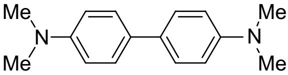
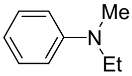
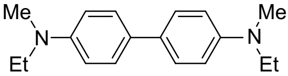
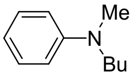
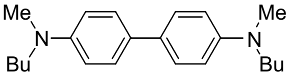
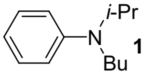
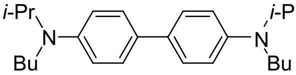
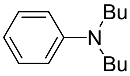
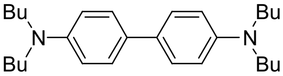
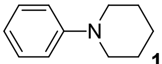
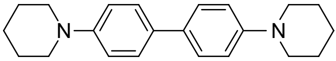
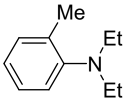
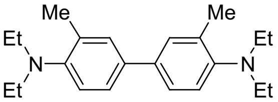
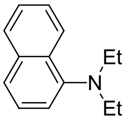
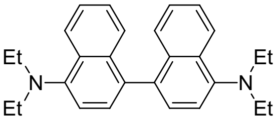
Scheme 2.

N,*N*-diethylaniline was observed without quenching the reaction mixture with aq K_2CO_3 solution. This phenomenon implies that product and starting material coordinate to CAN. In other words, 2 equiv of CAN is required to achieve the reaction.

The transformation was found to be general for various aniline derivatives under the optimized condition. Representative examples are shown in Table 1. In most cases, the reaction gave high regioselectivity to *para*-coupled bisaniline with exceptions of entries 2 and 4. In the cases of entry 2 and entry 4, small amount of *ortho–para*-coupled bisanilines was isolated in 10% and 6% yields, respectively. The use of *N*,*N*-dibutylaniline **1f** diminished the yield of product **2f**. In this case, the reaction gave a polymer-like mixture after the addition of *N*,*N*-dibutylaniline **1f** in 5 min and it made further stirring become impossible. The scope of this method could be extended to the substituted *N*,*N*-dialkylaniline. When *ortho*-methyl substituted *N*,*N*-diethylaniline **1h** was treated, *para*-coupled benzidine was exclusively formed in good yield (Table 1, entry 9), while *N*-dealkylation reaction occurred in the reported method using $TiCl_4$.[8] The reaction of diethyl-naphthalen-1-yl-amine **1i** also gave naphthidines **2i** in good yields.

A mechanistic rationale for this coupling reaction is presented in Scheme 3. Firstly, the *N*,*N*-dialkylaniline **1** is coordinated to CAN to form complex **3**, which undergoes oxidative electron transfer with second CAN to afford the radical cation **4**. Secondly, 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. This is consistent with the fact that 2 equiv of CAN is required for efficient reaction. It is noteworthy that no other reduction product was observed from radical cation **4** abstracting H from water in the experiment, so we

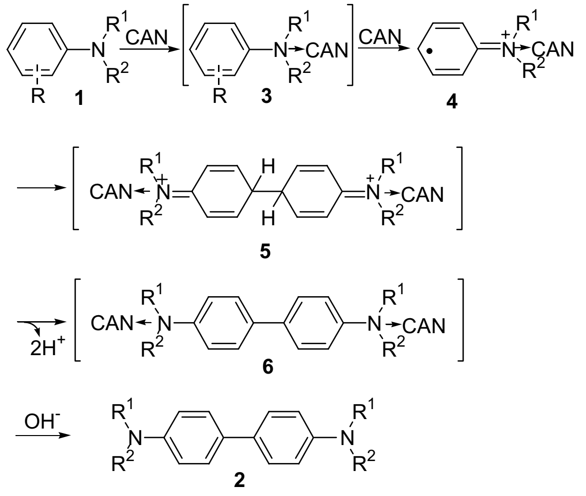
Table 1. The reaction of *N*,*N*-dialkylarylamines with CAN in water[a]

Entry	Substrate	Time (h)	Product[b]	Yield (%)[c]
1	 **1a**	2	 **2a**	81
2	 **1b**	2	 **2b**	81
3	 **1c**	2	 **2c**	71
4	 **1d**	2	 **2d**	78
5	 **1e**	2	 **2e**	85
6	 **1f**	0.25	 **2f**	53
7	 **1g**	2	 **2g**	72
8	 **1h**	2	 **2h**	73
9	 **1i**	2	 **2i**	62

[a] Conditions: *N*,*N*-dialkylarylamines (1 equiv), CAN (2 equiv), room temperature.

[b] The products were identified using ^1H NMR, ^{13}C NMR, mass spectra analysis, and comparison with reported data.

[c] Isolated yield.



Scheme 3.

excluded the possibility that the radical intermediate **4** abstracts H from water, which would lead to a relatively unstable ·OH radical.

In summary, a method using CAN as oxidant and water as solvent for oxidative coupling of *N*,*N*-dialkylarylamines was developed. This method has several advantages, including easy handling, high efficiency, low cost, and friendly to the environment. The synthetic applications of this reaction are currently under investigation.

Acknowledgements

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References and notes

1. (a) Johnson, G. E.; McGrane, K. M.; Stolka, M. *Pure Appl. Chem.* **1995**, *67*, 175–182; (b) Noda, T.; Ogawa, H.; Noma, N.; Shirota, Y. *J. Mater. Chem.* **1999**, *9*, 2177–2181.
2. Horowitz, G. *Adv. Mater.* **1998**, *10*, 365–377.
3. Cariciftci, N. S.; Smilowitz, L.; Heeger, A. J.; Wudl, F. *Science* **1992**, *258*, 1474–1476.
4. (a) Getautis, V.; Stanisauskaite, A.; Paliulis, O.; Uss, S.; Uss, V. *J. Prakt. Chem.* **2000**, *342*, 58–62; (b) Goodbrand, H. C.; Hu, N.-H. *J. Org. Chem.* **1999**, *64*, 670–674; (c) O'Brien, D. F.; Burrows, P. E.; Forrest, S. R.; Koene, B. E.; Loy, D. E.; Thompson, M. E. *Adv. Mater.* **1998**, *10*, 1108–1112.
5. (a) Vettorazzi, N.; Fernandez, H.; Silber, J. J.; Sereno, L. *Electrochim. Acta* **1990**, *35*, 1081–1088; (b) Mizoguchi, T.; Adams, R. N. *J. Am. Chem. Soc.* **1962**, *84*, 2058–2061.
6. Carrick, W. L.; Karapinka, G. L.; Kwiatkowski, G. T. *J. Org. Chem.* **1969**, *34*, 2388–2392.
7. López-cortés, J. G.; Penieres-Carrillo, G.; Ortega-Alfaro, M. C.; Gutiérrez-Pérez, R.; Toscano, R. A.; Alvarez-Toledano, C. *Can. J. Chem.* **2000**, *78*, 1299–1304.
8. Periasamy, M.; Jayakumar, K. N.; Bharathi, P. *J. Org. Chem.* **2000**, *65*, 3548–3550.
9. Saitoh, T.; Yoshida, S.; Ichikawa, J. *Org. Lett.* **2004**, *6*, 4563–4565.
10. (a) Li, C. J.; Chan, T. H. *Organic Reactions in Aqueous Media*; John Wiley & Sons: New York, 1997; (b) Anastas, P. T.; Warner, J. C. *Green Chemsitry: Theory and Practice*; Oxford University Press: Oxford, 1998; (c) Lindström, U. M. *Chem. Rev.* **2002**, *102*, 2751–2772; (d) Lubineau, A; Augé, J. In *Topics in Current Chemistry*; Springer: Berlin, Heidelberg, 1999; Vol. 206, p 1.
11. For reviews on CAN-mediated reactions see: (a) Ho, T. L *Synthesis* **1973**, 354–374; (b) Ho, T. L. *Organic Synthesis by Oxidation with Metal Compounds*; Plenum: New York, 1986; (c) Imamoto, T. *Lanthanide Reagents in Organic Synthesis*; Academic: London, 1994, p 119; (d) Nair, V.; Mathew, J.; Prabhakaran *J. Chem. Soc. Rev.* **1997**, 127–132; (e) Hwu, J. R.; King, K.-Y. *Curr. Sci.* **2001**, *8*, 1043–1053; (f) Nair, V.; Panicker, S. B.; Nair, L. G.; George, T. G.; Augustine, A. *Synlett* **2003**, 156–165; (g) Nair, V.; Balagopal, L.; Rajan, R.; Mathew, J. *Acc. Chem. Res.* **2004**, *37*, 21–30.
12. Galliani, G.; Rindene, B.; Scolastico, C. *Synth. Commun.* **1975**, *5*, 319–323.
13. Representative procedure for the reaction of *N*,*N*-dialkylarylamines. Oxidative coupling of *N*,*N*-diethylaniline. In deionized H_2O (3 mL), CAN (1.098 g, 2 mmol) and *N*,*N*-diethylaniline (160 μL, 1 mmol) were added in turn at room temperature. The reaction mixture was stirred for 2 h. The reaction mixture was quenched by aq K_2CO_3 solution and the organic residue was extracted with CH_2Cl_2. The combined extract was dried over anhydrous $MgSO_4$. The solvent was removed and the residue was chromatographed on an Al_2O_3 gel column. *N*,*N*,*N*′,*N*′-Tetraethylbenzidine **2a**[8] was isolated (120 mg, 81%) as white solid using 1:50 EtOAc/petroleum mixture as eluent. ^{1}H NMR ($CDCl_3$) δ 7.40 (4H, d, $J = 8.6$ Hz), 6.71 (4H, d, $J = 8.6$ Hz), 3.35 (8H, q, $J = 7.2$ Hz), 1.15 (12H, t, $J = 7.2$ Hz); ^{13}C NMR ($CDCl_3$) δ 146.2, 128.8, 127.0, 112.1, 44.4, 12.6; ESI-MS: 297($M+H^+$).