

# A one-pot synthesis of *N*-alkylaminobenzenes from nitroaromatics: reduction followed by reductive amination using $B_{10}H_{14}$

Jong Woo Bae, Young Jin Cho, Seung Hwan Lee, Choon-Ock Maing Yoon and Cheol Min Yoon\*

Department of Life Science & Biotechnology, Graduate School of Biotechnology, Korea University, Seoul, South Korea. E-mail: cmyoon@tiger.korea.ac.kr; Fax: +82-2-3290-3433

Received (in Corvallis, OR, USA) 27th June 2000, Accepted 27th July 2000

First published as an Advance Article on the web 14th September 2000

*N*-Alkylaminobenzenes were prepared in a simple and efficient one-pot synthesis by reduction of nitrobenzenes followed by reductive amination with decaborane ( $B_{10}H_{14}$ ) in the presence of 10% Pd/C.

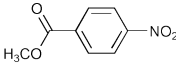
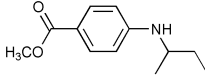
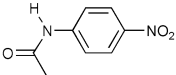
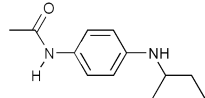
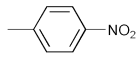
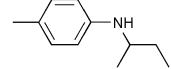
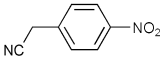
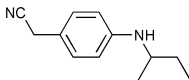
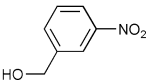
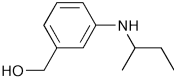
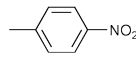
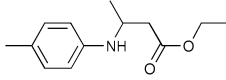
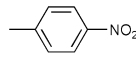
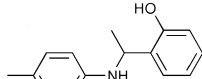
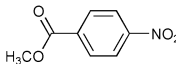
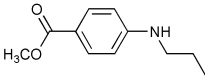
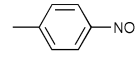
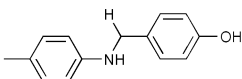
Consecutive reactions<sup>1</sup> have received much attention because they give complex molecules efficiently from simple starting materials. In the first step of these reactions, the functional group necessary for the following transformation is formed. An ideal place for such consecutive reactions is in one-pot synthesis, in which all these processes occur consecutively by successive addition of reagents, without isolation of intermediates. Well known examples of one-pot processes are

multicomponent condensations<sup>2</sup> and palladium-catalyzed reactions,<sup>3</sup> which are known to be useful owing to mild reaction conditions and stability against other functional groups.

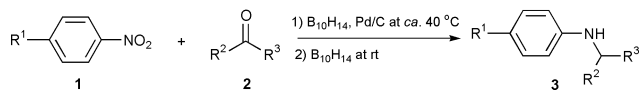
Aromatic amines are important intermediates for dyes and agricultural and pharmaceutical chemicals. One popular method for the preparation of these amines is the reduction of nitroaromatics using various reagents and conditions.<sup>4,5</sup> One of the methods for the synthesis of secondary amines is the reductive amination of primary amines with carbonyls using a variety of reducing reagents.<sup>6</sup>

In the course of our work using decaborane as a mild and stable reducing agent,<sup>7</sup> we found that the reduction of

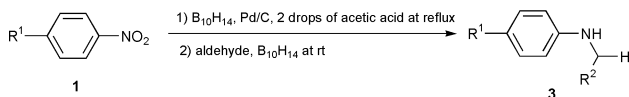
**Table 1** Synthesis of *N*-alkylaminobenzenes

Entry	Nitroaromatics (1)	Carbonyls (2) <sup>a</sup>	Time/h	Product (3) <sup>b</sup>	Yield <sup>c</sup> (%)
1		Butan-2-one	0.5 (ca. 40 °C) 2 (rt)		93
2		Butan-2-one	0.5 (ca. 40 °C) 2 (rt)		91
3		Butan-2-one	1.5 (ca. 40 °C) 2 (rt)		92
4		Butan-2-one	2.5 (ca. 40 °C) 2 (rt)		88
5		Butan-2-one	3 (ca. 40 °C) 2 (rt)		89
6		Ethyl acetoacetate	1.5 (ca. 40 °C) 2 (rt)		92
7		2-Hydroxyacetophenone	1.5 (ca. 40 °C) 10 (rt)		84
8		Propanal	0.5 (reflux) 2 (rt)		91
9		4-Hydroxybenzaldehyde	1.5 (reflux) 2 (rt)		90

<sup>a</sup> 1.1 equiv. of carbonyls (of nitroaromatics) was used in all cases. <sup>b</sup> All products are known compounds and gave spectra (GC-MS, <sup>1</sup>H NMR, IR) consistent with the assigned structures. <sup>c</sup> Isolated yields.



Scheme 1



Scheme 2

nitroaromatics using a decaborane–Pd/C system followed by reductive amination with carbonyls using decaborane gave a one-pot synthesis of *N*-alkylaminoaromatics in high isolated yield. To the best of our knowledge, this is the first example of a one-pot preparation of *N*-alkylaminoaromatics from nitroaromatics.

Decaborane was added in two batches in all of the examples.<sup>8</sup> 30 mol% of decaborane ( $B_{10}H_{14}$ ) was added for the reduction of the nitro group in the first batch, and 20 or 30 mol%<sup>9</sup> was used for reductive amination in the second batch. When a ketone was used for the reductive amination (entries 1–7, Table 1), it was added to the reaction solution at the beginning of the reaction (Scheme 1). The reactions proceeded smoothly at 40 °C without addition of acetic acid. However, when aldehydes were used (entries 8 and 9, Table 1), they were added after the completion<sup>10</sup> of the nitro-group reduction to prevent reductive etherification<sup>11</sup> (Scheme 2). Under these conditions, the reactions were complete in several hours and gave the corresponding secondary amines chemoselectively and in high yields. Other functional groups such as esters (entries 1, 6 and 8), amides (entry 2), nitriles (entry 4) and hydroxy groups (entry 5) were intact under the reaction conditions.<sup>†</sup>

In conclusion, nitroaromatics were converted into *N*-alkylaminoaromatics in a single-pot synthesis using decaborane as a reducing agent in the presence of Pd/C in methanol. The reaction is efficient and chemoselective. Investigations of the scope of this one-pot synthesis are currently underway.

The authors wish to acknowledge the financial support of the Korea Research Foundation made in 2000.

## Notes and references

<sup>†</sup> Representative experimental procedures: Ketone (entry 3). To a solution of 4-nitrotoluene (50 mg, 0.364 mmol) in methanol (5 ml) was added butan-

2-one (28.9 mg, 0.401 mmol), decaborane (13.4 mg, 0.109 mmol) and 10% Pd/C (15 mg). The resulting solution was stirred at ca. 40 °C under nitrogen for 1.5 h. The mixture was then cooled to rt and decaborane (8.9 mg, 0.073 mmol) was added to the mixture. The resulting solution was stirred at rt under nitrogen for 2 h. The mixture was concentrated under reduced pressure, chromatographed on a short pad of silica gel using a solution of ethyl acetate and *n*-hexane (1 : 8) and concentrated to give the product amine as a pale pink syrup. *Aldehyde* (entry 8). To a solution of methyl 4-nitrobenzoate (50 mg, 0.276 mmol) in methanol (5 ml) was added two drops of acetic acid, decaborane (10 mg, 0.083 mmol) and 10% Pd/C (15 mg). The resulting solution was heated to reflux under nitrogen for 0.5 h and the mixture was cooled to rt. Propanal (17 mg, 0.303 mmol) and decaborane (6.7 mg, 0.052 mmol) were then added to the reaction mixture. The solution was stirred at rt under nitrogen for 2 h. The mixture was concentrated under reduced pressure, chromatographed on a short pad of silica gel using a solution of ethyl acetate and *n*-hexane (1 : 8), and concentrated to give the amine as a white solid.

- L. F. Tietze and U. Beifuss, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 131; L. F. Tietze, *Chem. Rev.*, 1996, **96**, 115.
- Multicomponent Reactions in Organic Chemistry*, I. Ugi, A. Domling and W. Horl, *Endeavour*, 1994, **18**, 115.
- S. Brase and A. de Meijere, in *Metal-catalyzed Cross-coupling Reactions*, ed. F. Diederich and P. J. Stang, Wiley-VCH, Weinheim, 1998, p. 99; A. de Meijere and F. E. Meyer, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 2379; T. J. J. Muller, M. Ansorge and S. Aktah, *Angew. Chem., Int. Ed.*, 2000, **39**, 1253.
- G. Mestoni, A. Camus and G. Zassinovich, in *Aspects of Homogeneous Catalysis*, ed. R. Ugo, Reidel, Dordrecht, 1981, Vol. 4, pp. 71–80.
- G. Sauve and V. S. Rao, *Comprehensive Organic Functional Group Transformations*, ed. A. R. Katritzky, O. Meth-Cohn and C. W. Rees, Pergamon Press, Oxford, 1995, Vol. 2, pp. 737–817.
- W. S. Emerson, *Org. React.*, 1948, **4**, 174; M. V. Klyuev and M. L. Khidekel, *Russ. Chem. Rev.*, 1980, **49**, 14; R. Hutchins and N. R. Natale, *Org. Prep. Proced. Int.*, 1979, **11**, 201; M. D. Bomann, I. C. Guch and M. DiMare, *J. Org. Chem.*, 1995, **60**, 5995; N. M. Yoon, E. G. Kim, H. S. Son and J. Choi, *Synth. Commun.*, 1993, **23**, 1595; J. Brussee, R. A. T. M. van Benthem, C. G. Kruse and A. van der Gen, *Tetrahedron: Asymmetry*, 1990, **1**, 163; A. F. Abdel-Magid, K. G. Carson, B. D. Harris, C. A. Maryanoff and R. D. Shah, *J. Org. Chem.*, 1996, **61**, 3849; B. C. Ranu, A. Majee and A. Sakar, *J. Org. Chem.*, 1998, **63**, 370.
- J. W. Bae, S. H. Lee, Y. J. Cho and C. M. Yoon, *J. Chem. Soc., Perkin I*, 2000, 145.
- The addition of 50 or 60 mol% decaborane in one batch at the beginning of the reaction resulted in incomplete reaction.
- In some cases (entries 1, 2 and 7), the reductive amination was slow with 20 mol% of decaborane. In these instances, 30 mol% of decaborane was added.
- The completion of the reduction of the nitro group was followed by TLC using a solution of ethyl acetate and *n*-hexane (1 : 4).
- S. H. Lee, Y. J. Park and C. M. Yoon, *Tetrahedron Lett.*, 1999, **40**, 6049.