Oxidative Coupling of Benzylamines into *N*-Benzylbenzaldimines with Mn(II)/*tert*-BuOOH

Sung Soo Kim,*,† Santosh S. Thakur,‡ Ji Young Song, and Keun-Hyeung Lee

*Department of Chemistry, Inha University, Incheon 402-751, Korea. *E-mail: sungsoo@inha.ac.kr*
Received January 10, 2005

Key Words : Benzylamines, *N*-Benzylbenzaldimine, Electron transfer, Deprotonation, Oxidation

3-Methyllumiflavin promotes conversion of $C_6H_5CH_2$-NH_2 to *N*-benzylbenzaldimine **4** under acid catalyzed thermal conditions.[1] Aerobic oxidative dehydrogenation of $C_6H_5CH_2NH_2$ is catalyzed by molybdenium-vanadium salt to yield **4**.[2] Clay-catalyzed reaction of benzylamine is suggested to involve $C_6H_5CH{=}NH_2$ that react another $C_6H_5CH_2NH_2$ for the formation of **4**.[3] Polypyrrole catalyst is effective in the dehydrogenation of $C_6H_5CH_2NH_2$ with O_2 to make **4**.[4] The same reaction is also catalyzed by a aniline trimer.[5] Monoamine oxidases catalyze the oxidation of primary amines to give iminium cation that is hydrolyzed to form the aldehydes.[6,7] Mn(III) ions are known to catalyse various oxidative free radical reactions.[8] We'd like to herein report the oxidative coupling of benzylamines utilizing Mn(II)/*tert*–BuOOH.

Benzylamine was oxidized under various conditions to determine the role of each component for the reaction (Table 1). Entry 2 indicates the importance of the catalyst. The oxidation does not occur in the absence of oxidant, *tert*-butylhydroperoxide (TBHP) (entry 3).

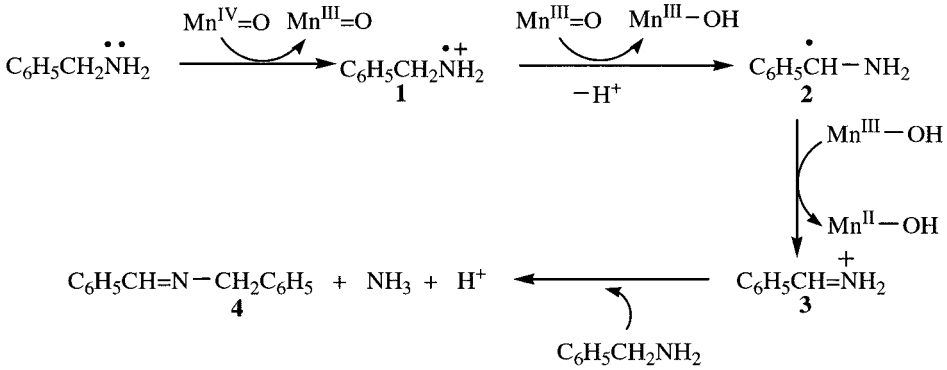
Variously substituted benzylamines undergo coupling reaction to give *N*-benzylbenzaldimines by the catalysis of $Mn^{IV}{=}O$ that is formed from Mn^{II}/*tert*-BuOOH. The reaction takes place within 3-4 h to give the desired product in 93% yield (Table 2). Mn(II) ion may make a complex with TBHP to give $Mn^{IV}{=}O$ that may provoke electron transfer from $C_6H_5CH_2NH_2$ forming aminium radical cation, $C_6H_5CH_2\overset{+\bullet}{N}H_2$ **1**. The intermediate **1** becomes acidic enough to expel benzylic proton to produce $C_6H_5\overset{\bullet}{C}H\text{-}\overset{\bullet\bullet}{N}H_2$ **2** that is oxidized by Mn(III) with formation of $C_6H_5CH{=}\overset{+}{N}H_2$ **3**. C_6H_5CHO might result from hydrolysis of **3**. However, control experiment under the condition of entry 1 of Table 1 at room temperature shows no trace of benzaldehyde (aldehydic proton: δ = 10 ppm) but indicates instead gradual increase of benzylic CH_2 of **4** (chemical shift: δ = 4.84 ppm) with reaction time of 5, 10, 15, 30 min, and 1 h, respectively. This

Table 1. Oxidative Coupling of Benzylamine under Diverse Reaction Conditions

$$C_6H_4CH_2\text{-}NH_2 \xrightarrow[\text{r.t., 3.5 h}]{CH_3CN\ (1\ mL)} C_6H_5CH{=}N\text{-}CH_2C_6H_5$$

Entry	Substrate (mmol)	$MnSO_4$ (mmol)	TBHP (mmol)	Yield (%)
1	1	0.05	1	93
2	1	–	1	0.4
3	1	0.05	–	0

$$Mn^{II} + \textit{tert}\text{-BuOOH} \longrightarrow Mn^{IV}{=}O + \textit{tert}\text{-BuOH}$$



Scheme 1

†This article was written during the sabbatical leave of absence.

‡Dr. Thakur was a visiting scholar from Shree Shankaracharya College of Engineering & Technology on a grant from BK21 (2001).

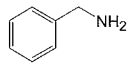
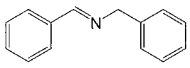
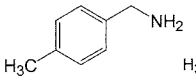
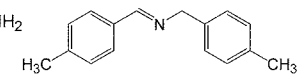
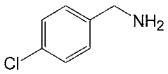
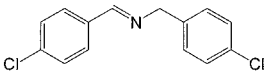
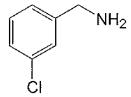
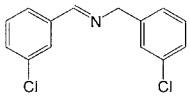
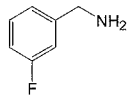
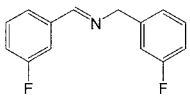
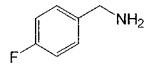
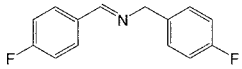
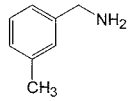
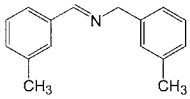
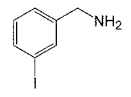
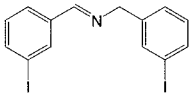
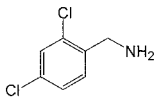
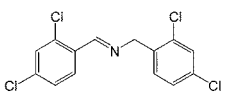
clearly tells hydrolysis of **3** does not occur at all. Accordingly, **3** reacts with $C_6H_5CH_2NH_2$ to yield a complex that fragments to give **4**, NH_3, and proton (Scheme 1 and Table 2).

Neucleophilic addition of $C_6H_5CH_2NH_2$ to benzylidenemalonitriles in CH_3CN is known to occur.[9] α-Methylbenzylamine shows extremely slow reactivity towards the oxidation due to the steric effect of α-methyl group. Cyclohexylamine and *n*-heptylamine do not produce the oxidative products. This could be ascribed to stronger bond dissociation energy of α-C-H that prevents abstraction of proton from **1**. $C_6H_5CH_2OH$ can hardly undergo oxidation because stronger oxidation potential may prohibit formation of **1**.

The reaction mechanism may involve oxo-manganese complex (Mn^{IV}=O) which results in electron transfer followed by deprotonation, oxidation, and coupling with extrusion of NH_3. The oxidation potential of $C_6H_5CH_2NH_2$ is quite important in determining the reactivity because $C_6H_5CH_2OH$ is not oxidized under the same condition. The oxidation is influenced by steric hindrance and α-C-H bond strength. Substituent effect can be profound enough to delay the reaction in case of *o,p*-dichlorobenzylamine. The featured catalytic salt $MnSO_4$ is cheap, readily available, and relatively nontoxic.

Table 2. Oxidative Coupling of Benzylamines by $MnSO_4$/TBHP[a]

$$YC_6H_4CH_2{-}NH_2 \xrightarrow[CH_3CN,\ r.t.]{MnSO_4,\ TBHP} YC_6H_4CH{=}N{-}CH_2C_6H_4Y$$

Entry	Substrate	Product	Time (h)	Yield[b] (%)
1			3.5	93
2			3.5	93
3			4.0	95
4			4.0	99
5			3.5	97
6			3.5	96
7			3.5	94
8			4.5	95
9			12	99

[a]Reaction performed in the presence of benzylamine derivatives (1 mmol), TBHP (1 mmol), and $MnSO_4$ (0.05 mmol) in CH_3CN (1 mL). [b]Isolated yield.

Experimental Section

Oxidative Coupling of Benzylamines Catalyzed by $MnSO_4$. $MnSO_4$ (0.05 mmol) and substrate (1 mmol) were dissolved in CH_3CN (1 mL) at r.t. *tert*–BuOOH (1 mmol) was mixed with the solution and the reaction was stirred for time based upon substrates nature. The reaction mixture was then subject to Silica gel column chromatography using ethyl acetate as an eluent. The ^{1}H NMR, ^{13}C NMR, and GC-MS spectra are cited below.

Control Experiment for Oxidation of Benzylamine. Benzylamine (5 mmol), *tert*–BuOOH (5 mmol), and $MnSO_4$ (0.25 mmol) in CH_3CN (5 mL) were reacted in the same manner of the foregoing coupling reactions. An aliquot of reaction mixture was withdrawn periodically for the NMR analysis to detect the formation of C_6H_5CHO (δ = 10 ppm) and **4** (δ = 4.84 ppm).

***N*-Benzylbenzaldimine.** ^{1}H NMR ($CDCl_3$, 200 MHz): δ 4.88 (s, 2H), 7.40-7.49 (m, 8H), 7.83-7.85 (d, 2H), 8.45 (s, 1H). ^{13}C NMR ($CDCl_3$, 200 MHz): δ 64.9 (CH_2 aliphatic 1C), 126.8-136.6 (CH benzene 10C), 136.1 (C=N-C benzene 1C), 139.2 (C benzene 1C), 164.8 (C from N-imine 1C). MS (EI, 70 eV) *m/z* 194 ($M^{\cdot+}$), 117, 104, 91.

***N*-(4-Methylbenzyl) 4-methylbenzaldimine.** ^{1}H NMR ($CDCl_3$, 200 MHz): δ2.32 (s, 3H), 2.36 (s, 3H), 4.75 (s, 2H), 7.15-7.21 (m, 6H), 7.63-7.67 (d, 2H), 8.32 (s, 1H). ^{13}C NMR ($CDCl_3$, 200 MHz): δ 20.9 (CH_3 aliphatic 1C), 21.3 (N=C-CH_3 aliphatic 1C), 64.6 (CH_2 aliphatic 1C), 127.8-129.2 (CH benzene 8C), 133.6 (C=N-C benzene 1C), 136.3 (C benzene 2C), 140.8 (C benzene 1C), 161.5 (C from N-imine 1C). MS (EI, 70 eV) *m/z* 223 ($M^{\cdot+}$), 208, 131, 105.

***N*-(4-Chlorobenzyl) 4-chlorobenzaldimine.** ^{1}H NMR ($CDCl_3$, 200 MHz): δ4.74 (s, 2H), 7.26-7.67 (m, 6H), 7.68-7.71 (d, 2H), 8.30 (s, 1H). ^{13}C NMR ($CDCl_3$, 200 MHz): δ 64.0 (CH_2 aliphatic 1C), 128.5-129.3 (CH benzene 8C), 132.7 (C benzene 1C), 134.3 (C=N-C benzene 1C), 136.7 (C benzene 1C), 137.5 (C benzene 1C), 160.7 (C from N-imine 1C). MS (EI, 70 eV) *m/z* 263 ($M^{\cdot+}$), 225, 151, 125, 89.

***N*-(3-Chlorobenzyl) 3-chlorobenzaldimine.** ^{1}H NMR ($CDCl_3$, 200 MHz): δ4.75 (s, 2H), 7.23-7.62 (m, 6H), 7.78-7.79 (d, 1H), 8.29-8.30 (d, 1H), 8.30 (s, 1H). ^{13}C NMR ($CDCl_3$, 200 MHz): δ64.1 (CH_2 aliphatic 1C), 125.9-130.8 (CH benzene 8C), 134.3 (C benzene 1C), 134.8 (C benzene 1C), 137.6 (C=N-C benzene 1C), 141.0 (C benzene 1C), 160.7 (C from N-imine 1C). MS (EI, 70 eV) *m/z* 263 ($M^{\cdot+}$), 228, 151, 25, 89.

***N*-(3-Fluorobenzyl) 3-fluorobenzaldimine.** ^{1}H NMR ($CDCl_3$, 200 MHz): δ4.79 (s, 2H), 6.94-7.57 (m, 8H), 8.38

(s, 1H). ^{13}C NMR ($CDCl_3$, 200 MHz): δ64.1 (CH_2 aliphatic 1C), 113.7-130.1 (CH benzene 8C), 138.1 (C=N-C benzene 1C), 160.9 (C benzene 1C), 161.7 (C benzene 1C), 161.7 (C benzene 1C), 164.2 (C from N-imine 1C). MS (EI, 70 eV) *m/z* 231 ($M^{\cdot+}$), 201, 135, 122, 109.

***N*-(4-Fluorobenzyl) 4-fluorobenzaldimine.** ^{1}H NMR ($CDCl_3$, 200 MHz): δ4.49 (s, 2H), 6.94-7.76 (m, 6H), 7.78-7.79 (d, 2H), 8.33 (s, 1H). ^{13}C NMR ($CDCl_3$, 200 MHz): δ 64.0 (CH_2 aliphatic 1C), 115.1 (CH benzene 8C), 132.2 (C=N-C benzene 1C), 134.9 (C benzene 1C), 161.7 (C benzene 1C), 163.1 (C from N-imine 1C), 165.5 (C benzene 1C). MS (EI, 70 eV) *m/z* 231 ($M^{\cdot+}$), 212, 137, 122, 109.

***N*-(3-Methylbenzyl) 3-methylbenzaldimine.** ^{1}H NMR ($CDCl_3$, 200 MHz): δ2.33 (s, 3H), 2.36 (s, 3H), 4.76 (s, 2H), 7.13-7.63 (m, 8H), 8.33 (s, 1H). ^{13}C NMR ($CDCl_3$, 200 MHz): δ21.5 (N=C-CH_3 aliphatic 1C), 21.6 (CH_3 aliphatic 1C), 65.3 (CH_2 aliphatic 1C), 125.3-131.8 (CH benzene 8C), 136.3 (C=N-C benzene 1C), 138.3 (C benzene 2C), 139.4 (C benzene 1C), 162.4 (C from N-imine 1C). MS (EI, 70 eV) *m/z* 223 ($M^{\cdot+}$), 208, 131, 118, 105, 91, 77.

***N*-(3-Iodobenzyl) 3-iodobenzaldimine.** ^{1}H NMR ($CDCl_3$, 200 MHz): δ4.72 (s, 2H), 7.02-7.71 (m, 6H), 7.72-7.75 (d, 1H), 8.13-8.14 (d, 1H), 8.24 (s, 1H). ^{13}C NMR ($CDCl_3$, 200 MHz): δ 64.4 (CH_2 aliphatic 1C), 94.9 (C benzene 1C), 94.9 (C benzene 1C), 126.5-138.6, 143.3 (CH benzene 8C), 139.9 (C=N-C benzene 1C), 141.5 (C benzene 1C), 161.0 (C from N-imine 1C). MS (EI, 70 eV) *m/z* 447 ($M^{\cdot+}$), 320, 244, 217, 165, 90.

***N*-(2,4-Dichlorobenzyl) 2,4-dichlorobenzaldimine.** ^{1}H NMR ($CDCl_3$, 200 MHz): d 4.85 (s, 2H), 7.19-7.34 (m, 5H), 8.01-8.06 (d, 1H), 8.77 (s, 1H). ^{13}C NMR ($CDCl_3$, 200 MHz): δ61.4 (CH_2 aliphatic 1C), 127.1-133.4 (CH benzene 8C), 133.9 (C=N-C benzene 1C), 135.3 (C benzene 1C), 135.8 (C benzene 1C), 137.3 (C benzene 1C), δ158.7 (C from N-imine 1C). MS (EI, 70 eV) *m/z* 333 ($M^{\cdot+}$), 185, 159, 123, 89.

Acknowledgements. The authors warmly thank the Inha University for the financial support (INHA-2005).

References

1. Kim, J. M.; Bogadan, M. A.; Mariano, P. S. *J. Am. Chem. Soc.* **1993**, *115*, 10591.
2. Neumann, R.; Levin, M. *J. Org. Chem.* **1991**, *56*, 5707.
3. Bank, S.; Jewett, R. *Tetrahedron Lett.* **1991**, *32*, 303.
4. Higuchi, M.; Ikeda, I.; Hirao, T. *J. Org. Chem.* **1997**, *62*, 1072.
5. Hirao, T.; Fukuhara, S. *J. Org. Chem.* **1998**, *63*, 7534.
6. (a) Silverman, R. B. *Acc. Chem. Res.* **1995**, *28*, 335. (b) Silverman, R. B.; Wang, X. *J. Org. Chem.* **1998**, *63*, 7357.
7. Miller, J. R.; Edmondson, D. E. *Biochemistry* **1999**, *38*, 13670.
8. Snider, B. B. *Chem. Rev.* **1996**, *96*, 339.
9. Oh, H. K.; Yang, J. H.; Lee, H. W.; Lee, I. *J. Org. Chem.* **2000**, *65*, 2188.