One-Pot Reductive N-Alkylation with Carbonyl Compounds To Give Tertiary Amines via Borane Reduction of Imines

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Dedicated to the hearty memory of the late Professor Yoshihiko Ito of Doshisha University. Deceased on December 23, 2006.

Abstract: One-pot synthesis of tertiary amines via borane-mediated reduction of imines and reductive N-alkylation with carbonyl compounds is described. This protocol's reducing agent is only borane in the reduction of imines, and additional reductant is not necessary in reductive N-alkylation step. When using more than two equivalents of aldehydes, reductive N-alkylation proceeded in good yield.

Key words: reductive N-alkylation, borane reduction, imines, tertiary amines, one-pot reaction

Reductive N-alkylation of primary and secondary amines with carbonyl compounds is a very useful reaction for the synthesis of a variety of amines. Various methods, such as metal hydride reactions[1] and catalytic hydrogenations,[2] have been developed thus far. The use of boron reagents has been especially widely investigated; $NaBH_3CN$,[3] $NaBH(OAc)_3$,[4] $NaBH_4$,[5] and borane complexes[6] have all been used as general reducing agents in this reaction. In many cases, however, these reagents have to be used either under acidic conditions or with molecular sieves and Lewis acids to generate iminium ions. Recently, Suginome et al. reported that aminoborane derivatives react as efficient iminium ion generators.[7] These reagents can be used even in the absence of acid catalysts. In this method, however, reducing agents must be added into the reaction media. Since borane is often used as a reducing agent, reductive N-alkylation of aminoboranes with reducing ability with carbonyl compounds can be performed directly, without the need for externally added reducing agents. Such aminoboranes would seem to be generated in situ by borane reduction of the carbon–nitrogen double bond of imines (Scheme 1).

As a similar concept, Hosomi et al. reported reductive amination using silanes bearing an amino group and a hydride.[8] Although Lewis acids are required when silanes are used as the reducing agent, it was anticipated that activators would be unnecessary in our case because of the nature of the Lewis acidity of boranes. We report herein the one-pot synthesis of tertiary amines from imines via borane reduction and reductive N-alkylation with carbonyl compounds.

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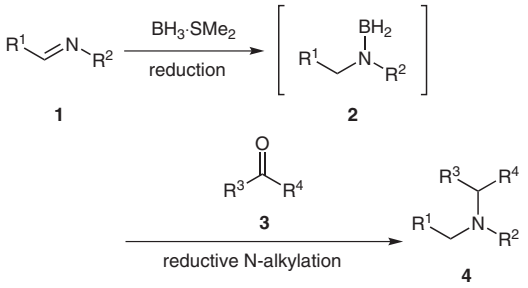
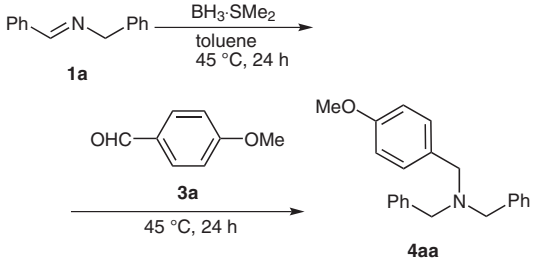


Scheme 1

Initially, the reduction of imine **1a** with 1.25 equivalents of $BH_3{\cdot}SMe_2$ at 45 °C in toluene, followed by reductive N-alkylation reaction with 1.25 equivalents of aldehyde **3a**, afforded the desired tertiary amine **4aa** in only 24% yield based on imine **1a** (Table 1, entry 1). A large amount of 4-methoxybenzyl alcohol was found in the crude mixture. Using 2.5 equivalents of **3a**, the desired product **4aa** was obtained in almost quantitative yield (entry 2). When using $BH_3{\cdot}SMe_2$ and aldehyde **3a** in a 1:2 ratio, good

Table 1 Reductive N-Alkylation with **3a** via Borane Reduction of **1a**[a]



Entry	$BH_3{\cdot}SMe_2$ (equiv)	**3a** (equiv)	Yield (%)[b]
1	1.25	1.25	24
2	1.25	2.5	99
3	1.0	2.0	89
4	1.1	2.2	93
5	1.4	2.9	99

[a] Reaction conditions: (1) imine **1a** (0.7–1.0 mmol), $BH_3{\cdot}SMe_2$ (2 M in toluene, 1.0 mmol), toluene (2.0 mL), 45 °C, 24 h; (2) aldehyde **3a**, toluene (1.0 mL), 45 °C, 24 h.

[b] Based on imine **1a**. Determined by ^1H NMR spectroscopy of the isolated compound after silica gel column chromatography.

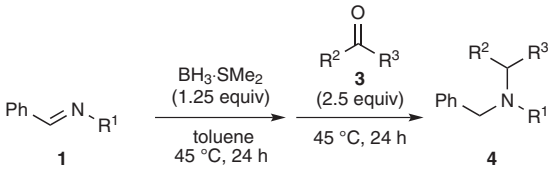
results were obtained (entries 3–5). Especially, in cases where more than 1.25 equivalents of $BH_3{\cdot}SMe_2$ were used, excellent yields were achieved (entries 2 and 5).

The scope of the reaction with carbonyl compounds **3** was next examined (Table 2). Benzaldehyde (**3b**) and its derivatives with electron-withdrawing or electron-donating substituents in the 4-position on the aromatic ring were successful reaction partners (entries 1–6). The introduction of a methoxy substituent in either the 2- or 3-position on the aromatic ring also showed good reactivity (entries 7 and 8). Using the more electron-rich aldehyde **3i** gave reduced yield (entry 9). In the case of substrate **3j**, bearing an acetyl group, amination proceeded only on the aldehyde group, with good yield (entry 10). 2-Pyridinecarboxaldehyde (**3k**) reacted to give a moderate yield of the expected product (entry 11). As with aromatic aldehydes, aliphatic aldehydes **3l** and **3m** were good substrates for this reaction (entries 12 and 13). Less sterically hindered ketones such as acetone (**3n**) and cyclohexanone (**3o**) were converted into the desired products in lower yields (entries 14 and 15). Slightly improved yield was obtained using *N*-methyl imine **1b** (entry 16).

Several imines reacted in the above way with aldehyde **3c**, and the results are presented in Table 3. Using *N*-methyl imine **1b**, an improved yield was observed compared to that using *N*-benzyl imine **1a** (entry 2 vs. entry 1). Compound **1c**, derived from aniline, reacted in good yield (entry 3). Even when using sterically hindered *N*-*tert*-butyl imine **1d**, the reaction proceeded smoothly (entry 4). However, ketimine **1e**, derived from benzophenone, showed low reactivity, and a complex mixture was obtained (entry 5). As these results show, reductive N-alkylation seemed to be affected by steric hindrance on the imine, in other words, on the aminoborane intermediate of the borane reduction.

We presumed that aminoborane **2**, generated by the borane reduction of imine **1**, is the key intermediate in this reaction.[9] Table 1, however, shows that when using approximately one equivalent of aldehyde **3** with respect to **2**, the major product was benzyl alcohol, derived from **3**; in contrast, using more than two equivalents of **3**, the desired reaction proceeded with satisfactory yield. It therefore follows that aminoborane **2**, bearing excess hydride,

Table 2 Reductive N-Alkylation with Carbonyl Compounds[a]

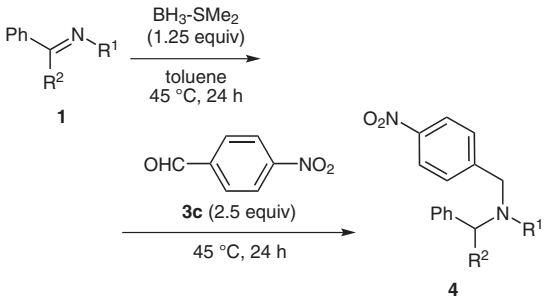


Entry	Imine	Carbonyl compound	R^2	R^3	Product	Yield (%)[b]
1	**1a** (R^1 = Bn)	**3a**	4-$MeOC_6H_4$	H	**4aa**	99
2	**1a**	**3b**	Ph	H	**4ab**	90
3	**1a**	**3c**	4-$O_2NC_6H_4$	H	**4ac**	86
4	**1a**	**3d**	4-NCC_6H_4	H	**4ad**	90
5	**1a**	**3e**	4-FC_6H_4	H	**4ae**	99
6	**1a**	**3f**	4-$F_3CC_6H_4$	H	**4af**	88
7	**1a**	**3g**	2-$MeOC_6H_4$	H	**4ag**	92
8	**1a**	**3h**	3-$MeOC_6H_4$	H	**4ah**	95
9	**1a**	**3i**	2,4,6-$(MeO)_3C_6H_2$	H	**4ai**	73
10	**1a**	**3j**	4-$MeCOC_6H_4$	H	**4aj**	82
11	**1a**	**3k**	2-pyridyl	H	**4ak**	69
12	**1a**	**3l**	cyclohexyl	H	**4al**	98
13	**1a**	**3m**	Et	H	**4am**	88
14	**1a**	**3n**	Me	Me	**4an**	35
15	**1a**	**3o**	$(CH_2)_5$		**4ao**	31
16	**1b** (R^1 = Me)	**3o**	$(CH_2)_5$		**4bo**	47

[a] Reaction conditions: (1) imine **1** (0.8 mmol), $BH_3{\cdot}SMe_2$ (2M in toluene, 1.0 mmol), toluene (2.0 mL), 45 °C, 24 h; (2) compound **3** (2.0 mmol), toluene (1.0 mL), 45 °C, 24 h.

[b] Based on imine **1**. Determined by ^1H NMR spectroscopy of the isolated compound after silica gel column chromatography.

Table 3 Reductive N-Alkylation with **3c** via Borane Reduction of Various Imines[a]



Entry	Substrate	R^1	R^2	Product	Yield (%)[b]
1	**1a**	Bn	H	**4ac**	86
2	**1b**	Me	H	**4bc**	91
3	**1c**	Ph	H	**4cc**	81
4	**1d**	*t*-Bu	H	**4dc**	74
5	**1e**	Ph	Ph	**4ec**	11

[a] Reaction conditions: (1) imine **1** (0.8 mmol), $BH_3{\cdot}SMe_2$ (2M in toluene, 1.0 mmol), toluene (2.0 mL), 45 °C, 24 h; (2) aldehyde **3c** (2.0 mmol), toluene (1.0 mL), 45 °C, 24 h.

[b] Based on imine **1**. Determined by ^{1}H NMR spectroscopy of the isolated compound after silica gel column chromatography.

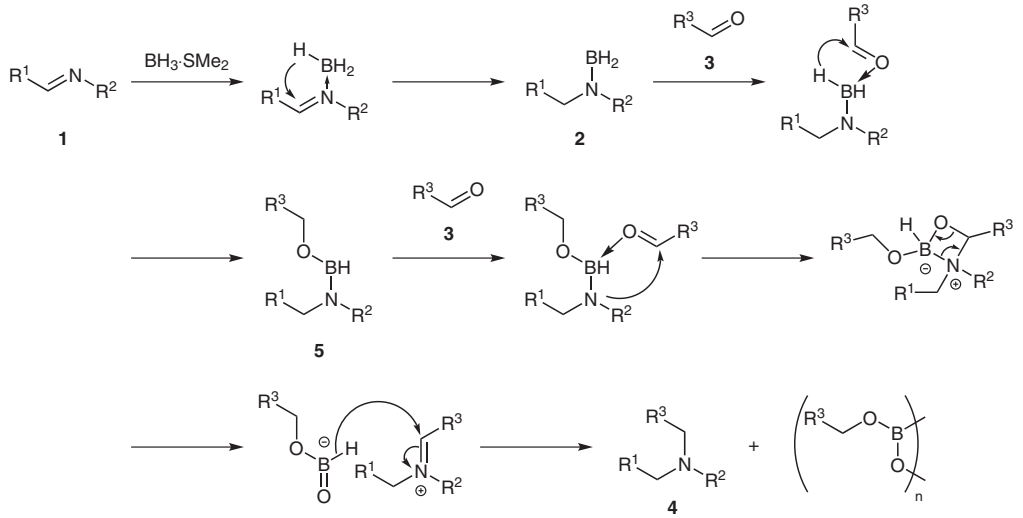
reacted with one equivalent of aldehyde **3** to give the intermediate, such as **5**, followed by reductive N-alkylation with additional aldehyde **3** (Scheme 2). In this reaction mechanism, one hydride of -N-BH_2 in aminoborane **2** is unnecessary in the objective reaction.

Next, the addition of proton sources before reaction with aldehydes (in order to consume excess hydride) was examined (Table 4). In these experiments, an evolution of gas was observed when proton sources were added. When using 1.25 equivalents of 4-methoxybenzaldehyde (**3a**), yields were increased by adding benzyl alcohols **6** (entries 1–3). Using 4-nitrobenzaldehyde (**3c**) as a substrate, however, only the addition of 4-nitorobenzyl alcohol (**6b**) improved the yield (entries 4–6). Notably, other proton sources such as 4-nitrophenol (**7**) and aliphatic alcohol **8** were ineffective (entries 7 and 8).

These results suggest that one hydride in aminoborane **2** is dispensable and that such active species as **5** affect the present reaction. However, we considered that proton sources affect the N–B bond cleavage in addition to the B–H bond consumption. For that reason, although the addition of benzyl alcohols leads to improved yield of the reductive N-alkylation, these results were unsatisfactory compared to using 2.5 equivalents of aldehyde substrate. Based on the above results, we can surmise that aldehydes react with excess hydrides rather than amines of intermediate **2**. After the excess hydrides of intermediate **2** are consumed, the amination of aldehydes proceeds prior to the reduction.

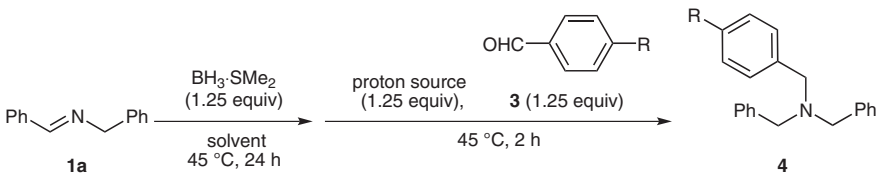
We then conducted a one-pot synthesis of the tertiary amines from the primary amines (Scheme 3). For this reaction, we chose electron-rich aromatic aldehyde **3i** as one of the alkylating agents that showed low reactivity in various reductive N-alkylations.[8] In the presence of molecular sieves, benzylamine (**9**) reacted with benzaldehyde (**3b**) to give imine **1a**. Subsequently, a reduction of derived imine **1a** with $BH_3{\cdot}SMe_2$ was followed by reductive N-alkylation with aldehyde **3i** to obtain the target compound **4ai** in 67% yield based on amine **9** (route 1). This result was comparable to using imine **1a** as a starting material (cf Table 2, entry 9). The reaction proceeded in the same yield when the addition order of aldehydes **3b** and **3i** was reversed (route 2). Imine **1f** was obtained quantitatively since the alcohol derived from **3i** was not observed. These results show that our reductive N-alkylation method includes the synthesis from primary amines in a one-pot reaction.

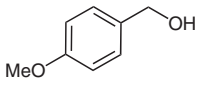
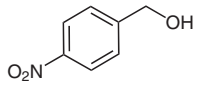
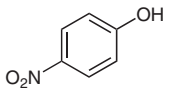
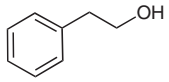
In conclusion, we have demonstrated one-pot reductive N-alkylation with carbonyl compounds via reduction of imines using borane. Although the yields of tertiary



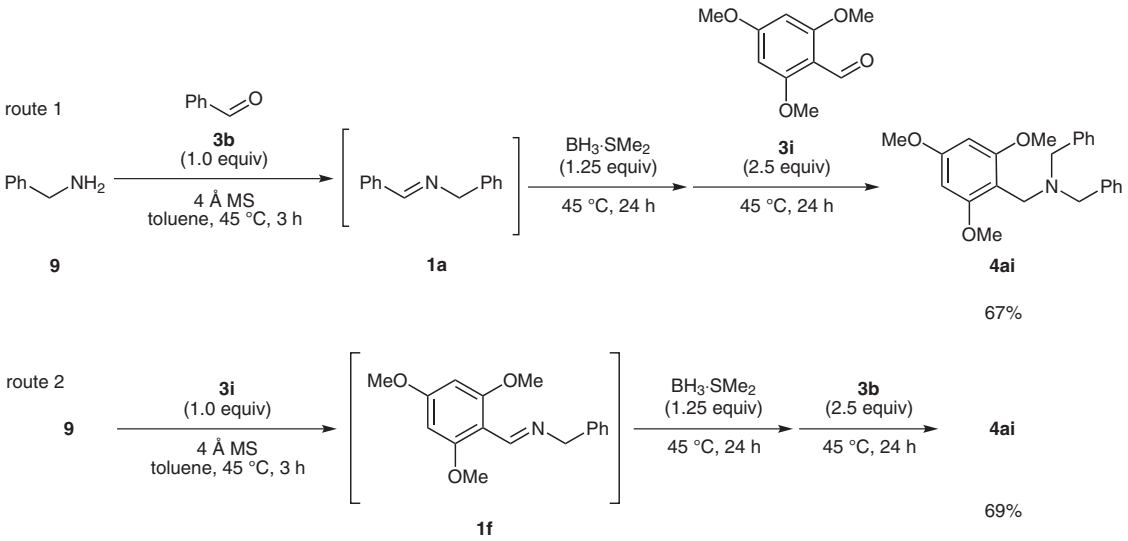
Scheme 2

Table 4 Reductive N-Alkylation with Various Proton Sources[a]



Entry	Aldehyde	Proton source	Solvent	Product	Yield (%)[b]
1[c]	**3a** (R = OMe)	none	toluene	**4aa**	24
2[d]	**3a**	 **6a**	toluene	**4aa**	76
3[e]	**3a**	 **6b**	THF	**4aa**	80
4[c]	**3c** (R = NO_2)	none	toluene	**4ac**	42
5	**3c**	**6a**	THF	**4ac**	48
6	**3c**	**6b**	THF	**4ac**	77
7	**3c**	 **7**	THF	**4ac**	52
8	**3c**	 **8**	THF	**4ac**	54

[a] Reaction conditions: (1) imine **1a** (0.8 mmol), $BH_3{\cdot}SMe_2$ (2 M in toluene, 1.0 mmol), solvent (2.0 mL), 45 °C, 24 h; (2) proton source (1.0 mmol), aldehyde **3** (1.0 mmol), solvent (1.0–2.0 mL), 45 °C, 2 h.
[b] Based on imine **1a**. Determined by ^{1}H NMR spectroscopy of the isolated compound after silica gel column chromatography.
[c] Step 2 reaction time: 24 h.
[d] Step 2 reaction time: 20 h.
[e] Step 2 reaction time: 14 h.



Scheme 3

amines in this reaction were affected by the steric hindrance of substrates, the desired reaction proceeded in good yield when using aldehydes. The present method features two modes of borane reactivity, which acts both in the reduction of imines and in the reductive N-alkylation. We have thus demonstrated the intriguing reactivities of the hydride and the amine of the intermediate derived from the imine by borane reduction.

NMR spectra were measured using a Varian Mercury Plus 300-4N (^{1}H NMR: 300 MHz, ^{13}C NMR: 75 MHz) spectrometer with TMS as an internal standard for ^{1}H NMR and $CDCl_3$ (δ = 77.0 ppm) for ^{13}C NMR and a JEOL JNM-ECA500 (^{11}B NMR: 160.5 MHz) spectrometer with BF_3·OEt_2 as an external standard. IR spectra were measured on a Shimadzu FTIR-8400 spectrometer in the transmission mode or a Horiba FT-710 spectrometer equipped with Dura-Sample IR in the ATR mode. High resolution mass spectra (FAB) were measured using a JEOL JMS-700 with 3-nitrobenzyl alcohol as the matrix and PEG-200 or PEG-600 as the calibration standard. All reactions were performed under an argon atmosphere using standard Schlenk techniques. All solvents were dried by standard methods and distilled under argon.[10] Commercially available compounds were used without further purification.

_N_-Benzhydrylideneaniline (1e)[11]
To a solution of benzophenone (1.82 g, 10 mmol) and activated 4 Å molecular sieves (4.0 g) in toluene (4 mL), aniline (1.12 g, 12 mmol) was added, and the reaction was stirred at r.t. for 4 h. The mixture was then filtered through a Celite pad and the filtrate was concentrated using a rotary evaporator. Recrystallization of the residue from toluene–EtOH gave compound **1e**.

Yield: 1.38 g (54%); yellow crystals; mp 112–114 °C.

^{1}H NMR ($CDCl_3$): δ = 6.69–6.72 (m, 2 H), 6.88–6.93 (m, 1 H), 7.08–7.16 (m, 4 H), 7.20–7.27 (m, 3 H), 7.36–7.49 (m, 3 H), 7.72–7.76 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 120.8, 123.0, 127.8, 128.1, 128.3, 128.4, 129.2, 129.4, 130.6, 136.1, 139.6, 151.1, 168.1.

Tertiary Amines 4 by Reductive N-Alkylation; General Procedure
Under an argon atmosphere, imine **1** (0.8 mmol), BH_3·SMe_2 (2 M in toluene, 1.0 mmol), and toluene (2.0 mL) were added to an 80 mL Schlenk tube. After stirring at 45 °C for 24 h, aldehyde **3** (2.0 mmol) and toluene (1.0 mL) were added to the mixture, which was then allowed to react at 45 °C for 24 h. MeOH (20 mL) was then added to stop the reaction. The solution was concentrated using a rotary evaporator and then separated by silica gel column chromatography (hexane–EtOAc, 20:1) to give products **4**. The yields were determined by ^{1}H NMR analysis of a mixture of the isolated products and anthracene (17.8 mg, 0.1 mmol).

_N_,_N_-Dibenzyl-_N_-(4-methoxybenzyl)amine (4aa)[12]
Yield: 99%; colorless oil.

IR (neat): 3061, 3026, 2930, 2793, 1611, 1583, 1510, 1495, 1454, 1366, 1248, 1036, 737, 698 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.48 (s, 2 H), 3.53 (s, 4 H), 3.77 (s, 3 H), 6.84 (d, J = 8.7 Hz, 2 H), 7.18–7.23 (m, 2 H), 7.27–7.32 (m, 6 H), 7.38 (d, J = 6.9 Hz, 4 H).

^{13}C NMR ($CDCl_3$): δ = 55.3, 57.2, 57.7, 113.5, 126.7, 128.1, 128.6, 129.7, 131.4, 139.6, 158.4.

Tribenzylamine (4ab)[13]
Yield: 90%; white solid; mp 91–93 °C.

IR (ATR): 3062, 3026, 2920, 2802, 1603, 1493, 1446, 1365, 1248, 739, 694 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.55 (s, 6 H), 7.18–7.23 (m, 3 H), 7.28–7.33 (m, 6 H), 7.40 (d, J = 7.2 Hz, 6 H).

^{13}C NMR ($CDCl_3$): δ = 57.9, 126.7, 128.1, 128.6, 139.5.

_N_,_N_-Dibenzyl-_N_-(4-nitrobenzyl)amine (4ac)
Yield: 86%; yellow oil.

IR (neat): 3061, 3028, 2924, 2800, 1599, 1518, 1493, 1454, 1344, 845, 745, 698 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.56 (s, 4 H), 3.63 (s, 2 H), 7.21–7.26 (m, 2 H), 7.30–7.39 (m, 8 H), 7.56 (d, J = 8.4 Hz, 2 H), 8.16 (d, J = 8.4 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 57.3, 58.2, 123.4, 127.1, 128.3, 128.6, 129.1, 138.7, 146.9, 147.7.

HRMS (FAB$^+$): m/z [M + H]$^+$ calcd for $C_{21}H_{21}N_2O_2$: 333.1603; found: 333.1618.

_N_-(4-Cyanobenzyl)-_N_,_N_-dibenzylamine (4ad)
Yield: 90%; light-yellow oil.

IR (neat): 3063, 3028, 2924, 2800, 2228, 1609, 1495, 1454, 1367, 735, 698 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.54 (s, 4 H), 3.58 (s, 2 H), 7.20–7.25 (m, 2 H), 7.28–7.38 (m, 8 H), 7.49 (d, J = 8.4 Hz, 2 H), 7.57 (d, J = 8.4 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 57.5, 58.2, 110.6, 118.9, 127.0, 128.2, 128.6, 129.1, 132.0, 138.8, 145.5.

HRMS (FAB$^+$): m/z [M + H]$^+$ calcd for $C_{22}H_{21}N_2$: 313.1705; found: 313.1689.

_N_,_N_-Dibenzyl-_N_-(4-fluorobenzyl)amine (4ae)
Yield: 99%; white solid; mp 44–46 °C.

IR (KBr): 3061, 3026, 2924, 2800, 1601, 1506, 1493, 1448, 1364 1221, 745, 696 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.49 (s, 2 H), 3.52 (s, 4 H), 6.98 (t, J = 9.0 Hz, 2 H), 7.18–7.24 (m, 2 H), 7.27–7.39 (m, 10 H).

^{13}C NMR ($CDCl_3$): δ = 57.1, 57.8, 114.9 (d, J = 21 Hz), 126.8, 128.1, 128.6, 130.0 (d, J = 8 Hz), 135.1 (d, J = 3 Hz), 139.3, 161.7 (d, J = 242 Hz).

HRMS (FAB$^+$): m/z [M + H]$^+$ calcd for $C_{21}H_{21}FN$: 306.1658; found: 306.1642.

_N_,_N_-Dibenzyl-_N_-(4-trifluoromethylbenzyl)amine (4af)
Yield: 88%; colorless oil.

IR (neat): 3063, 3028, 2926, 2800, 1618, 1585, 1495, 1454, 1367, 1325, 1163, 1103, 1067, 746, 698 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.55 (s, 4 H), 3.58 (s, 2 H), 7.19–7.25 (m, 2 H), 7.28–7.33 (m, 4 H), 7.38 (d, J = 6.9 Hz, 4 H), 7.50 (d, J = 8.4 Hz, 2 H), 7.55 (d, J = 8.4 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 57.5, 58.1, 124.2 (q, J = 270 Hz), 125.1 (q, J = 4 Hz), 127.0, 128.2, 128.6, 128.7, 129.0 (q, J = 32 Hz), 139.0, 143.9.

HRMS (FAB$^+$): m/z [M + H]$^+$ calcd for $C_{22}H_{21}F_3N$: 356.1626; found: 356.1633.

_N_,_N_-Dibenzyl-_N_-(2-methoxybenzyl)amine (4ag)
Yield: 92%; white solid; mp 44–46 °C.

IR (ATR): 3057, 3030, 2906, 2804, 1599, 1587, 1489, 1439, 1377, 1362, 1238, 1026, 737, 696 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.58 (s, 4 H), 3.61 (s, 2 H), 3.78 (s, 3 H), 6.82 (d, *J* = 8.1 Hz, 1 H), 6.95 (t, *J* = 7.5 Hz, 1 H), 7.15–7.22 (m, 3 H), 7.26–7.31 (m, 4 H), 7.41 (d, *J* = 7.2 Hz, 4 H), 7.60 (d, *J* = 7.5 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 51.3, 55.2, 58.3, 110.1, 120.4, 126.6, 127.4, 127.6, 128.0, 128.5, 129.5, 139.9, 157.5.

HRMS (FAB$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{24}NO$: 318.1858; found: 318.1853.

N,N-Dibenzyl-N-(3-methoxybenzyl)amine (4ah)
Yield: 95%; colorless oil.

IR (ATR): 3060, 3026, 2931, 2792, 1601, 1585, 1487, 1452, 1365, 1261, 1049, 739, 694 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.53 (s, 2 H), 3.55 (s, 4 H), 3.80 (s, 3 H), 6.74–6.78 (m, 1 H), 6.96–6.99 (m, 2 H), 7.18–7.23 (m, 3 H), 7.27–7.32 (m, 4 H), 7.39 (d, *J* = 6.9 Hz, 4 H).

^{13}C NMR ($CDCl_3$): δ = 55.2, 57.9, 58.0, 112.0, 114.2, 121.0, 126.7, 128.1, 128.6, 129.0, 139.5, 141.3, 159.5.

HRMS (FAB$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{24}NO$: 318.1858; found: 318.1871.

N,N-Dibenzyl-N-(2,4,6-trimethoxybenzyl)amine (4ai)
Yield: 73%; white solid; mp 84–86 °C.

IR (ATR): 3060, 3022, 2997, 2939, 2833, 2804, 2787, 1604, 1593, 1495, 1460, 1452, 1415, 1367, 742, 694 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.53 (s, 4 H), 3.60 (s, 2 H), 3.74 (s, 6 H), 3.79 (s, 3 H), 6.09 (s, 2 H), 7.13–7.18 (m, 2 H), 7.23–7.27 (m, 4 H), 7.38 (d, *J* = 6.9 Hz, 4 H).

^{13}C NMR ($CDCl_3$): δ = 45.6, 55.3, 55.5, 57.9, 90.4, 108.1, 126.2, 127.6, 128.6, 141.0, 160.1, 160.2.

HRMS (FAB$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{28}NO_3$: 378.2069; found: 378.2058.

N-(4-Acetylbenzyl)-N,N-dibenzylamine (4aj)
Yield: 82%; yellow oil.

IR (ATR): 3060, 3028, 2922, 2796, 1680, 1606, 1493, 1452, 1412, 1356, 1265, 742, 696 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.57 (s, 3 H), 3.55 (s, 4 H), 3.59 (s, 2 H), 7.19–7.25 (m, 2 H), 7.28–7.33 (m, 4 H), 7.38 (d, *J* = 7.2 Hz, 4 H), 7.49 (d, *J* = 8.4 Hz, 2 H), 7.90 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 26.7, 57.6, 58.1, 126.9, 128.2, 128.3, 128.6, 128.6, 135.9, 139.1, 145.5, 197.6.

HRMS (FAB$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{24}NO$: 330.1858; found: 330.1877.

N,N-Dibenzyl-N-(2-pyridylmethyl)amine (4ak)[14]
Yield: 69%; colorless oil.

IR (neat): 3061, 3026, 2924, 2799, 1589, 1570, 1495, 1474, 1454, 1433, 1367, 735, 698 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.61 (s, 4 H), 3.74 (s, 2 H), 7.08–7.12 (m, 1 H), 7.19–7.24 (m, 2 H), 7.28–7.33 (m, 4 H), 7.40 (d, *J* = 7.2 Hz, 4 H), 7.60–7.67 (m, 2 H), 8.48 (d, *J* = 5.1 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 58.2, 59.8, 121.7, 122.5, 126.8, 128.1, 128.6, 136.3, 139.1, 148.6, 160.0.

N,N-Dibenzyl-N-cyclohexylmethylamine (4al)[15]
Yield: 98%; white solid; mp 56–60 °C.

IR (KBr): 3063, 3022, 2916, 2843, 2789, 1601, 1493, 1447, 1366, 743, 735, 698 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.67–0.80 (m, 2 H), 1.01–1.26 (m, 3 H), 1.50–1.68 (m, 4 H), 1.81–1.86 (m, 2 H), 2.18 (d, *J* = 6.9 Hz, 2 H), 3.50 (s, 4 H), 7.17–7.23 (m, 2 H), 7.26–7.31 (m, 4 H), 7.36 (d, *J* = 6.9 Hz, 4 H).

^{13}C NMR ($CDCl_3$): δ = 26.3, 26.9, 31.7, 35.8, 58.8, 60.8, 126.5, 128.0, 128.6, 140.0.

N,N-Dibenzyl-N-propylamine (4am)[16]
Yield: 88%; light-yellow oil.

IR (neat): 3061, 3026, 2932, 2872, 2795, 1601, 1493, 1452, 1366, 743, 696 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.84 (t, *J* = 7.2 Hz, 3 H), 1.52 (sext, *J* = 7.2 Hz, 2 H), 2.36 (t, *J* = 7.2 Hz, 2 H), 3.53 (s, 4 H), 7.15–7.22 (m, 2 H), 7.25–7.30 (m, 4 H), 7.35 (d, *J* = 6.9 Hz, 4 H).

^{13}C NMR ($CDCl_3$): δ = 11.9, 20.3, 55.4, 58.3, 126.6, 128.0, 128.6, 139.9.

N,N-Dibenzyl-N-(1-methylethyl)amine (4an)[17]
Yield: 35%; light-yellow oil.

IR (ATR): 3064, 3024, 2962, 2929, 2827, 2794, 1601, 1493, 1452, 1362, 741, 723, 694 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.05 (d, *J* = 6.6 Hz, 6 H), 2.92 (hept, *J* = 6.6 Hz, 1 H), 3.55 (s, 4 H), 7.16–7.21 (m, 2 H), 7.25–7.30 (m, 4 H), 7.37 (d, *J* = 6.9 Hz, 4 H).

^{13}C NMR ($CDCl_3$): δ = 17.6, 48.1, 53.2, 126.4, 128.0, 128.3, 140.9.

N-Cyclohexyl-N,N-dibenzylamine (4ao)[18]
Yield: 31%; pale-yellow solid; mp 57–58 °C.

IR (ATR): 3064, 3022, 2927, 2852, 2829, 2802, 1603, 1491, 1450, 1375, 741, 731, 696 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.01–1.19 (m, 3 H), 1.25–1.36 (m, 2 H), 1.53–1.59 (m, 1 H), 1.75 (d, *J* = 11.4 Hz, 2 H), 1.88 (d, *J* = 12.6 Hz, 2 H), 2.46 (tt, *J* = 3.3, 11.4 Hz, 1 H), 3.62 (s, 4 H), 7.15–7.20 (m, 2 H), 7.24–7.28 (m, 4 H), 7.36 (d, *J* = 7.2 Hz, 4 H).

^{13}C NMR ($CDCl_3$): δ = 26.2, 26.6, 28.7, 53.8, 57.6, 126.4, 127.9, 128.3, 141.1.

N-Benzyl-N-methyl-N-(4-nitrobenzyl)amine (4bc)[19]
Yield: 91%; light-yellow oil.

IR (neat): 3061, 3028, 2945, 2845, 2789, 1601, 1520, 1495, 1454, 1344, 843, 739, 698 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.19 (s, 3 H), 3.55 (s, 2 H), 3.58 (s, 2 H), 7.22–7.37 (m, 5 H), 7.53 (d, *J* = 8.7 Hz, 2 H), 8.16 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 42.4, 60.9, 62.1, 123.4, 127.1, 128.2, 128.7, 129.1, 138.5, 146.9, 147.3.

N-Benzyl-N-cyclohexyl-N-methylamine (4bo)[13]
Yield: 47%; light-yellow oil.

IR (ATR): 3062, 3026, 2925, 2852, 2783, 1603, 1495, 1450, 1360, 733, 696 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.04–1.36 (m, 5 H), 1.63 (d, *J* = 11.7 Hz, 1 H), 1.78–1.90 (m, 4 H), 2.19 (s, 3 H), 2.39–2.48 (m, 1 H), 3.56 (s, 2 H), 7.18–7.32 (m, 5 H).

^{13}C NMR ($CDCl_3$): δ = 26.1, 26.5, 28.7, 37.7, 57.8, 62.5, 126.5, 128.0, 128.7, 140.2.

N-Benzyl-N-(4-nitrobenzyl)-N-phenylamine (4cc)
Yield: 81%; yellow solid; mp 145–147 °C.

IR (ATR): 3082, 3060, 3030, 2931, 2862, 1597, 1506, 1491, 1450, 1342, 843, 727, 690 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.66 (s, 2 H), 4.69 (s, 2 H), 6.69–6.77 (m, 3 H), 7.15–7.35 (m, 7 H), 7.39 (d, *J* = 8.7 Hz, 2 H), 8.16 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 54.1, 54.7, 112.7, 117.5, 123.8, 126.7, 127.1, 127.3, 128.6, 129.3, 137.8, 146.6, 147.0, 148.4.

HRMS (FAB$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{19}N_2O_2$: 319.1447; found: 319.1438.

***N*-Benzyl-*N*-*tert*-butyl-*N*-(4-nitrobenzyl)amine (4dc)**
Yield: 74%; yellow oil.

IR (neat): 3061, 3024, 2970, 2839, 1597, 1516, 1493, 1342, 1200, 854, 743, 698 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.16 (s, 9 H), 3.72 (s, 2 H), 3.77 (s, 2 H), 7.05–7.18 (m, 3 H), 7.25 (d, *J* = 6.6 Hz, 2 H), 7.34 (d, *J* = 8.7 Hz, 2 H), 7.96 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 27.4, 53.7, 55.1, 55.8, 122.8, 126.5, 127.8, 128.2, 128.6, 141.0, 146.1, 151.3.

HRMS (FAB$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{23}N_2O_2$: 299.1760; found: 299.1754.

***N*-Benzhydryl-*N*-(4-nitrobenzyl)-*N*-phenylamine (4ec)**
Yield: 11%; yellow oil.

IR (ATR): 3059, 3026, 2937, 2852, 1597, 1516, 1500, 1452, 1340, 837, 733, 696 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.68 (s, 2 H), 6.35 (s, 1 H), 6.70–6.78 (m, 3 H), 7.13–7.25 (m, 14 H), 7.94 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 51.7, 67.0, 114.1, 118.1, 123.0, 127.1, 127.4, 128.3, 129.1, 129.2, 139.9, 146.4, 147.4, 148.8.

HRMS (FAB$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{23}N_2O_2$: 395.1760; found: 395.1747.

One-Pot Syntheses of Tertiary Amines 4ai from Benzylamine (9); Representative Procedure (Route 1 in Scheme 3)
Under an argon atmosphere, benzylamine (**9**; 0.8 mmol), benzaldehyde (**3b**; 0.8 mmol), activated 4 Å molecular sieves (0.15 g), and toluene (2.0 mL) were added to an 80 mL Schlenk tube. After stirring at 45 °C for 3 h, $BH_3{\cdot}SMe_2$ (2 M in toluene, 1.0 mmol) was added to the resulting mixture, and then the mixture was reacted at 45 °C for 24 h. After the reaction, aldehyde **3i** (2.0 mmol) and toluene (1.0 mL) were added to the mixture, which was then allowed to react at 45 °C for 24 h. MeOH (20 mL) was then added to stop the reaction and the mixture was filtered through a Celite pad. The filtrate was concentrated using a rotary evaporator and then separated by silica gel column chromatography (hexane–EtOAc, 15:1) to give product **4ai**. The yield was determined by ^{1}H NMR analysis of a mixture of the isolated product and anthracene (17.8 mg, 0.1 mmol).

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