Highly Coordinated Tin Hydrides: A Novel Synthesis of Tertiary Amines via Hydrostannation of Imines

Takayo Kawakami, Takayuki Sugimoto, Ikuya Shibata,* Akio Baba, Haruo Matsuda,† and Noboru Sonoda

Department of Applied Chemistry, Faculty of Engineering, Osaka University, 2-1 Yamadaoka, Suita, Osaka 565, Japan

Received August 15, 1994®

The highly coordinated tin hydride, Bu_2SnClH–HMPA (**B**), is shown to be an effective agent for the reduction of imines. The subsequent alkylation of the resulting intermediate tin amides permitted the preparation of a series of tertiary amines in a one-pot procedure. The spectral identification of the novel tin hydrides, **B** and Bu_2SnClH–Bu_4NF, was accomplished by ^1H, ^{13}C, and ^{119}Sn NMR and FT-IR studies.

Introduction

The preparation of amines is of interest in synthetic and pharmaceutical chemistry because of the significant role of amines as pharmacophoric groups in biologically active substances, and it is often accomplished by reductive procedures. For the synthesis of tertiary amines, there are two such means: the reduction of amides[1] and the reductive alkylation of amines.[2] However, no direct transformation of imines to tertiary amines *via* hydrometalation has been reported, even though the hydrolysis of similar resulting metal amides to secondary amines is a common procedure[3] due to the ready availability of various types of imines.[4] The reductive alkylation of amines using $NaBH_3CN$ is a notable exception because it includes the reduction of intermediate imino groups.[2b,d,f] However, this method is hardly applicable to the preparation of unsymmetric tertiary amines or to the alkylation of aromatic amines.

Organotin hydrides are good candidates for the one-pot synthesis of tertiary amines from imines,[5] because the intermediate organotin amides arising from the hydrostannation are vulnerable to attack by electrophiles. Unfortunately, tin hydrides ($R_{4-n}SnH_n$ (n = 1, 2)) alone have exhibited relatively low reactivities even in the reductions of carbonyl compounds.[6] Although the activation of tin hydrides with radical initiators is the most common method used,[5b,7] it has been shown that ionic activation[5b,8] is required for the reduction of polar multiple bonds such as imino groups. We have recently developed two types of ionic organotin hydride reagents, namely, highly coordinated tin hydride reagents (Bu_3SnH–Lewis base (Lewis bases; HMPA and Bu_4NX (X = Cl, F, CN)))[6,9,10a] and dibutyltin halide hydrides bearing an electron-withdrawing group (Bu_2SnXH (X = Cl (**A**), F)),[10] with which the chemo- or stereoselective carbonyl reductions have been accomplished. It is expected that highly coordinated tin hydride systems bearing an electron-withdrawing group will act as more effective reagents. In this paper, we discuss the design of effective organotin hydride reagents for the convenient synthesis of secondary and tertiary amines from imines. A novel, highly-coordinated tin hydride complex, Bu_2SnClH–HMPA (**B**), proved to be the most effective reagent for this purpose. The spectral evidence for the formation and structure of highly coordinated organotin hydride complexes is also presented.

† Present address: Department of Applied Chemistry, Osaka Institute of Technology, 5-16-1 Omiya, Asahi, Osaka 535, Japan.

® Abstract published in *Advance ACS Abstracts,* April 15, 1995.

(1) (a) Brown, H. C.; Subba, R. B. C. *J. Am. Chem. Soc.* **1960**, *82*, 681. (b) Brown, H. C.; Heim, P. *J. Am. Chem. Soc.* **1964**, *86*, 3566. (c) Brown, H. C.; Weissman, P. M. *J. Am. Chem. Soc.* **1965**, *87*, 5614. (d) Yoon, N. M.; Brown, H. C. *J. Am. Chem. Soc.* **1968**, *90*, 2927. (e) Brown, H. C.; Heim, P. *J. Org. Chem.* **1973**, *38*, 912. (f) Umino, N.; Iwakuma, T.; Itoh, N. *Tetrahedron Lett.* **1976**, 763.

(2) (a) Clarke, H. T.; Gillespie, H. B.; Weisshaus, S. Z. *J. Am. Chem. Soc.* **1933**, *55*, 4571. (b) Borch, R. F.; Bernstein, M. D.; Durst, H. D. *J. Am. Chem. Soc.* **1971**, *93*, 2897. (c) Gribble, G. W.; Lord P. D.; Skotnicki, J.; Dietz, S. E.; Eaton, J. T.; Johnson, J. L. *J. Am. Chem. Soc.* **1974**, *96*, 7812. (d) Clinton, F. L. *Synthesis* **1975**, 135. (e) Gribble G. W.; Jasinski J. M.; Pellicone, J. T.; Panetta, J. A. *Synthesis* **1978**, 766. (f) Hutchins, R. O.; Natale, N. R. *Org. Prep. Proc. Int.* **1979**, *11*, 201. (g) Abdel-Magid, A. F.; Maryanoff, C. A.; Carson, K. G. *Tetrahedron Lett.* **1990**, *31*, 5595.

(3) (a) Layer. R. W. *Chem. Rev.* **1963**, 489. (b) Neumann, W. P.; Heymann, E. *Liebigs Ann. Chem.* **1965**, *683*, 24. (c) Bumgardner, C. L.; Lawton, E. L.; Carver, J. G. *J. Org. Chem.* **1972**, *37*, 407. (d) Wrobel, J. E.; Ganem, B. *Tetrahedron Lett.* **1981**, *22*, 3447. (e) Benkeser, R. A.; Snyder, D. C. *J. Organomet. Chem.* **1982**, *225*, 107. (f) Yamada, K.; Takeda, M.; Iwakuma, T. *J. Chem. Soc. Perkin Trans. 1* **1983**, 265. (g) Imamoto, T.; Mita, T.; Yokoyama, M. *J. Chem. Soc., Chem. Commun.* **1984**, 163. (h) Hutchins, R. O.; Su, W. Y. *Tetrahedron Lett.* **1984**, *25*, 695. (i) Knorr, R.; Ruf, F.; Högerl, J.; Hilpert, M.; Hassel, P. *Chem. Ber.* **1985**, *118*, 4743. (j) Hutchins, R. O.; Rutledge, M. C. *Tetrahedron Lett.* **1987**, *28*, 5619. (k) Hutchins, R. O.; Magid, A. A.; Stercho, Y. P.; Wambsgans, A. *J. Org. Chem.* **1987**, *52*, 702. (l) Maiti, S. B.; Raychaudhuri, S. R.; Chatterjee, A.; Chakravarty, A. K. *J. Chem. Soc. Perkin Trans. 1* **1988**, 611. (m) Pégorier, L.; Petit Y.; Larchevêque, M. *J. Chem. Soc., Chem. Commun.* **1994**, 633.

(4) Wagner, R. B.; Zook, H. D. *Synthetic Organic Chemistry*; John Wiley & Sons, Inc.: New York, 1953.

(5) (a) Hänssgen, D.; Puff, H.; Beckermann, N. *J. Organomet. Chem.* **1985**, *293*, 191. (b) Pereyre, M.; Quintard, P. J.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987.

(6) (a) Shibata, I.; Yoshida, T.; Baba, A.; Matsuda, H. *Chem. Lett.* **1989**, 619. (b) Shibata, I.; Yoshida, T.; Baba, A.; Matsuda, H. *Chem. Lett.* **1991**, 307.

(7) (a) Neumann, W. P. *Angew. Chem.*, **1963**, 225. (b) Kuivila, H. G. *Adv. Organomet. Chem.* **1964**, *1*, 47. (c) Kuivila, H. G. *Synthesis* **1970**, 499. (d) Fisch, M. H.; Dannenberg, J. J.; Pereyre, M.; Anderson, W. G.; Rens, J.; Grossman, W. E. L. *Tetrahedron* **1984**, *40*, 293. (e) Neumann, W. P. *Synthesis* **1987**, 665. (f) Curran, D. P. *Synthesis* **1988**, 417.

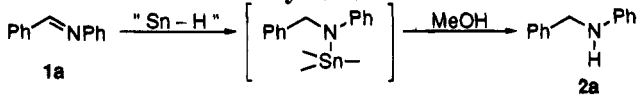
(8) (a) Neumann, W. P.; Heymann, E. *Liebigs Ann. Chem.* **1965**, *683*, 11. (b) Fung, N. Y. M.; Mayo, P.; Schauble, J. H.; Weedon, A. C. *J. Org. Chem.* **1978**, *43*, 3977. (c) Keinan, E.; Gleize, P. A. *Tetrahedron Lett.* **1982**, *23*, 477. (d) Four, P.; Guibé, F. *Tetrahedron Lett.* **1982**, *23*, 1825. (e) Castain, M. D.; Rahm, A. *J. Org. Chem.* **1986**, *51*, 1672. (f) Zhang, H. X.; Guibé, F.; Balavoine, G. *Tetrahedron Lett.* **1988**, *29*, 619. (g) Kikukawa, K.; Umekawa, H.; Wada, F.; Matsuda, T. *Chem. Lett.* **1988**, 881. (h) Cochran, J. C.; Bronk, B. S.; Terrence, K. M.; Phillips, H. K. *Tetrahedron Lett.* **1990**, *31*, 6621. (i) Zhang, H. X.; Guibé, F.; Balavoine, G. *J. Org. Chem.* **1990**, *55*, 1857.

(9) (a) Shibata, I.; Suzuki, T.; Baba, A.; Matsuda, H. *J. Chem. Soc. Chem. Commun.* **1988**, 882. (b) Kawakami, T.; Shibata, I.; Baba, A.; Matsuda, H.; Sonoda, N. *Tetrahedron Lett.* **1994**, *35*, 8625.

(10) (a) Shibata, I.; Yoshida, T.; Kawakami, T.; Baba, A.; Matsuda, H. *J. Org. Chem.* **1992**, *57*, 4049. (b) Kawakami, T.; Shibata, I.; Baba, A.; Matsuda, H. *J. Org. Chem.* **1993**, *58*, 7608.

0022-3263/95/1960-2677$09.00/0

Table 1. Reduction of Aldimine 1a by Tin Hydride Systems[a]



1a 2a

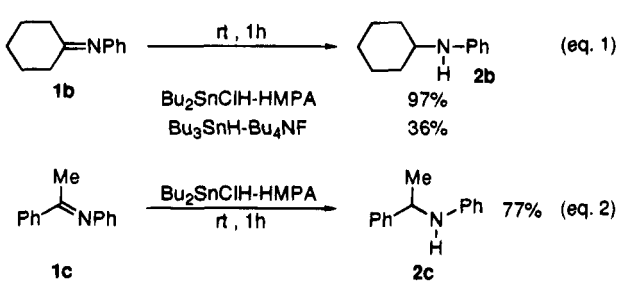
entry	reducing system	conditions	yield (%)[b]
1	$Bu_3SnH-Bu_3PO$[c]	50 °C, 8 h	trace
2	$Bu_3SnH-HMPA$[c]	rt, 4 d	30
3	$Bu_3SnH-Bu_4NCl$	rt, 2 d	29
4	$Bu_3SnH-Bu4NCN$	−15 °C → rt, 3 h	24
5	$Bu_3SnH-Bu_4NF$	rt, 1 h	82
6	Bu_2SnClH (**A**)	rt, 1 h	71
7	Bu_2SnFH	rt, 5 h	70
8	$Bu_2SnClH-Bu_3PO$	rt, 1 h	77
9	$Bu_2SnClH-HMPA$ (**B**)	rt, 1 h	97
10	$Bu_2SnClH-Bu_4NCl$	rt, 1 h	72
11	$Bu_2SnClH-Bu_4NF$	rt, 1 h	41
12	$Bu_2SnFH-HMPA$	rt, 2 h	87

[a] Aldimine **1a** 1 mmol, reducing system 1 mmol, THF 1 mL. Bu_2SnClH and Bu_2SnFH were formed in situ from Bu_2SnH_2 and Bu_2SnX_2 (X = Cl, F). [b] GLC yield. [c] Without solvent.

Results and Discussion

Reduction of Imines. Table 1 outlines the reactivity of Bu_3SnH–Lewis base, Bu_2SnXH and Bu_2SnXH-Lewis base systems (X = Cl, F) for the reduction of N-benzylideneaniline (**1a**) to benzylphenylamine (**2a**). The activity of the Bu_3SnH–Lewis base systems (entries 1–4) was not sufficient for the reduction of **1a** except for the $Bu_3SnH-Bu_4NF$ system (82% yield) (entry 5), although these reagents have been shown to readily reduce carbonyl groups of aldehydes and ketones.[6,9,10] The tin hydrides bearing a halogen group, Bu_2SnClH (**A**) and Bu_2SnFH, furnished **2a** in 71 and 70% yields, respectively, even without any ligands (entries 6 and 7), whereas Bu_2SnH_2 alone yielded none, even after 2 days. These reagents were generated *in situ* by redistribution between Bu_2SnH_2 and Bu_2SnCl_2[11] or Bu_2SnF_2.[12] It is noteworthy that both reagents were effectively activated by the addition of HMPA (entries 9 and 12). In particular, the $Bu_2SnClH-HMPA$ system (**B**) produced **2a** nearly quantitatively (entry 9). We examined the coordination of Bu_4NF to **A** in anticipation of an effective activation comparable to the case of $Bu_3SnH-Bu_4NF$. However, the yield of **2a** diminished to 41% (entry 11), because of the evolution of hydrogen gas from the mixture of imine **1a** and $Bu_2SnClH-Bu_4NF$.

Under similar conditions, system **B** also reduced ketimines **1b** and **1c** to the corresponding bulky secondary amines **2b** and **2c**, respectively, in up to 97% yield (eqs 1 and 2). On the other hand, $Bu_3SnH-Bu_4NF$ again produced a low yield of **2b** (eq 1). Thus, the novel reducing system **B** has proven to be a versatile reagent for the reduction of aldimines and ketimines.



Spectroscopic Data for Bu_2SnClH Systems. The ^1H, ^{13}C, and ^{119}Sn NMR spectral data and the FT-IR data for Bu_2SnClH (**A**), $Bu_2SnClH-HMPA$ (**B**), and $Bu_2SnClH-Bu_4NF$ are summarized in Table 2. Although some spectral studies on **A** have been performed so far,[11b,13] no ^{119}Sn NMR spectral data has been reported. As shown in Figure 1, parts a and b, the peaks at 35.2 ppm and −205.4 ppm in the ^{119}Sn NMR spectra correspond to Bu_2SnCl_2 and Bu_2SnH_2, respectively. The ^{119}Sn NMR spectra indicate the clear formation of **A**, because both of the peaks due to Bu_2SnH_2 and Bu_2SnCl_2 disappeared and a new peak was detected at −18.3 ppm (Figure 1c). The addition of HMPA to **A** caused a large upfield shift of greater than 100 ppm (from −18.3 to −139.3 ppm) (Figure 1d). The addition of HMPA also caused an increase in the values of ^1J (Sn−^{1}H) and ^nJ (Sn−^{13}C) (Table 2). These data strongly suggest the formation of the five-coordinate tin hydride complex **B** as illustrated in Scheme 1.[14] Moreover, the formation of **A** seems to be accelerated by HMPA because of the complete disappearance of the peak due to Bu_2SnH_2 (Figure 1, parts c and d).

Table 2. Spectral Data for Bu_2SnClH and Its Complexes in THF-d_8

	A	B	$Bu_2SnClH-Bu_4NF$
FT-IR (neat)			
ν (Sn−H)	1867.3 cm^{-1}	1861.5 cm^{-1}	1859.6 cm^{-1}
^{119}Sn NMR			
δ (^{119}Sn)	−18.3 ppm	−139.3 ppm	−159.8 ppm, br
^1H NMR			
δ (Sn-^{1}H)	7.19 ppm	7.19 ppm	7.21 ppm
^{13}C NMR			
δ (C_α)	18.7 ppm	22.3 ppm	20.8 ppm
δ (C_β)	28.5 ppm	29.0 ppm	29.3 ppm
δ (C_γ)	26.9 ppm	27.4 ppm	27.9 ppm
δ (C_δ)	13.9 ppm	14.4 ppm	14.5 ppm
^1J (^{119}Sn−^{1}H)	2178 Hz	2389 Hz	2438 Hz
^1J (^{117}Sn−^{1}H)	2081 Hz	2283 Hz	2329 Hz
^1J (Sn−$^{13}C_\alpha$)[a]	451/431 Hz	547/522 Hz	–
^2J (Sn−$^{13}C_\beta$)[b]	30 Hz	31 Hz	28 Hz
^3J (Sn−$^{13}C_\gamma$)	73.5 (75/72)[a] Hz	82[b] Hz	86[b] Hz

[a] ^{119}Sn/^{117}Sn coupling values resolved. [b] Average value; ^{119}Sn/^{117}Sn splitting not resolved.

Further, we confirmed the coordination of the P=O group to the tin atom in complex **B** by FT-IR spectroscopy. With HMPA, it was difficult to distinguish the P = O absorption, hence Bu_3PO was employed. When an equimolar amount of Bu_3PO was added to **A**, a decrease of 32.8 cm^{-1} in the P=O stretching frequency (from 1170.9 cm^{-1} to 1138.1 cm^{-1}) was observed. This decrease

(11) (a) Neumann, W. P.; Pedain, J. *Tetrahedron Lett.* **1964**, 2461. (b) Sawyer, A. K.; Brown, J. E.; Hanson, E. L. *J. Organomet. Chem.* **1965**, *3*, 464. (c) Sawyer, A. K.; George, S. M.; Scofield, R. E. *J. Organomet. Chem.* **1968**, *14*, 213.

(12) The slow redistribution was observed in the progress of the reduction of **1a**.[11b]

(13) (a) Kawakami, K.; Saito, T.; Okawara, R. *J. Organomet. Chem.* **1967**, *8*, 377. (b) Mitchell, T. N. *J. Organomet. Chem.* **1973**, *59*, 189.

(14) (a) Otera, J. *J. Organomet. Chem.* **1981**, *221*, 57. (b) Holecek, J.; Nádvorník, M.; Handlír, K.; Lycka, A. *J. Organomet. Chem.* **1983**, *241*, 177. (c) Nádvorník, M.; Holecek, J.; Handlír, K.; Lycka, A. *J. Organomet. Chem.* **1984**, *275*, 43. (d) Lycka, A.; Holecek, J.; Nádvorník, M.; Handlír, K. *J. Organomet. Chem.* **1985**, *280*, 323. (e) Birchall, T.; Manivannan, V. *J. Chem. Soc. Dalton Trans.* **1985**, 2671. (f) Holecek, J.; Nádvorník, M.; Handlír, K.; Lycka, A. *J. Organomet. Chem.*, **1986**, *315*, 299. (g) Edlund, U.; Arshadi, M.; Johnels, D. *J. Organomet. Chem.*, **1993**, *456*, 57.

(15) (a) Kuivila, H. G.; Dixon, J. E.; Maxfield, P. L.; Scarpa, N. M.; Topka, T. M.; Tsai, K.; Wursthorn, K. R. *J. Organomet. Chem.* **1975**, *86*, 89. (b) Chopa, A. B.; Koll, L. C.; Savini, M. C.; Podestá, J. C.; Neumann, W. P. *Organometallics* **1985**, *4*, 1036. (c) Ayala, A. D.; Giagante, N.; Podestá, J. C.; Neumann, W. P. *J. Organomet. Chem.* **1988**, *340*, 317. (d) Podestá, J. C.; Ayala, A. D.; Chopa, A. B.; Giagante, N. N. *J. Organomet. Chem.* **1989**, *364*, 39.

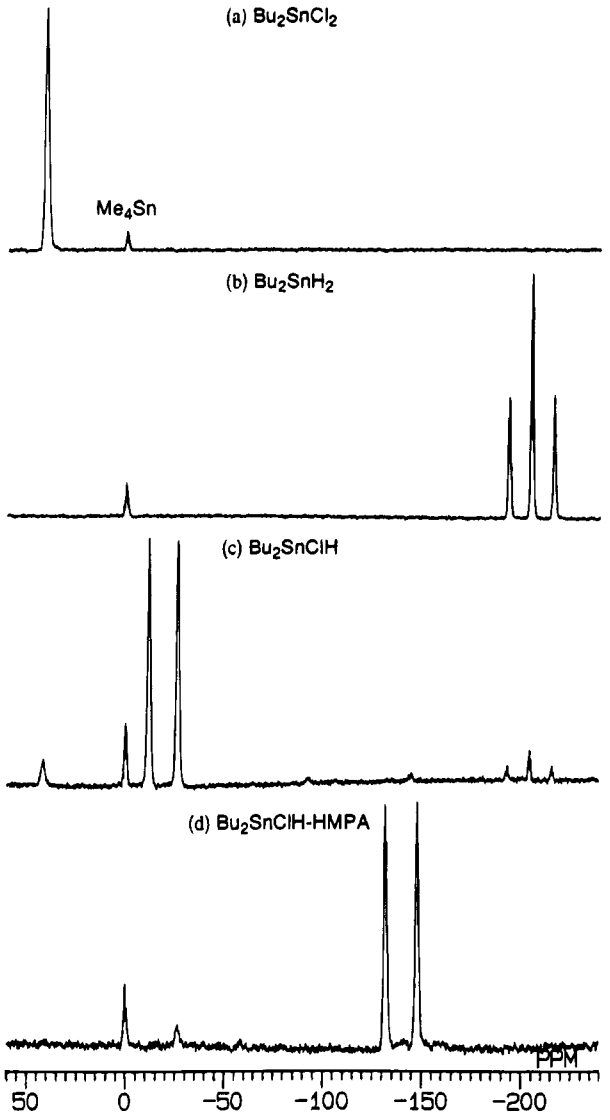
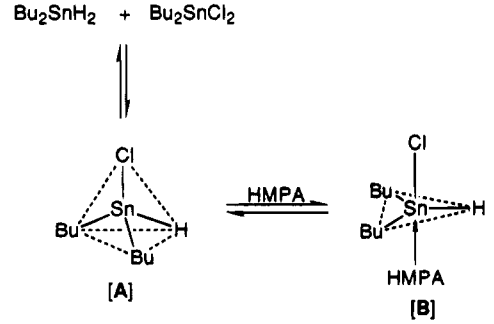


Figure 1. NMR spectra: (a) Bu_2SnCl_2, (b) Bu_2SnH_2, (c) $Bu_2SnCl_2 + Bu_2SnH_2$, (d) $Bu_2SnCl_2 + Bu_2SnH_2 + 2$ HMPa.

Scheme 1



strongly suggests the coordination of the P=O group of Bu_3PO to **A** (Table 3).[15]

The large increase in the values of ^1J (Sn−^{1}H) and ^1J (Sn−^{13}C) upon the addition of HMPA (Table 2) is plausibly due to the rehybridization of the tin orbital from sp^3 to sp^2, given that such an increase is known to correspond to an increase of s-character in the bonds.[14b,e,g] This investigation supposes that the Sn−H and two Sn−C bonds of **B** occupy equatorial positions in a trigonal bipyramidal geometry[14b,16] of **B**. In addition, we presume that the electronegative ligands, Cl and HMPA, occupy

Table 3. FT-IR Data for Bu_2SnClH–Bu_3PO in THF

	ν (P=O), cm^{-1}
Bu_3PO[a]	1170.9
Bu_2SnClH–Bu_3PO[b]	1138.1

[a] Bu_3PO 1.0 mmol, THF 3 mL. [b] Bu_2SnCl_2 0.5 mmol, Bu_2SnH_2 0.5 mmol, Bu_3PO 1.0 mmol, THF 3 mL.

apical positions (Scheme 1).[17] The electron-withdrawing effect of the chlorine atom in **B** seems to be responsible for the high acceptor property of the tin atom as observed for stable complex **B**.[16,17b,18] In contrast, no formation of stable complexes was detected for the Bu_3SnH-Lewis base systems, including Bu_3SnH–Bu_4NF which showed good reducing strength as noted in Table 1.

An X-ray investigation of five-coordinated silicon hydrides, the structures of which are similar to those of the tin hydrides, has demonstrated that the Si−H bond occupies an equatorial position in the trigonal bipyramidal structure.[19] Furthermore, the Si−H bond has been reported to have enhanced reactivity compared to that in the related four-coordinated compounds.[20] Consistent with this is the high reducing ability of the equatorial Sn−H bond in the complex **B**. This idea is also supported by the FT-IR spectra of **B** which show a strong Sn−H stretching absorption at lower frequencies than does that of Bu_2SnClH (Table 2).

The spectral data in Table 2 indicate that the combination of **A** and Bu_4NF forms a complex analogous to **B**. Moreover, the coordinating ability of Bu_4NF is expected to be superior to that of HMPA because of the larger values of ^1J (Sn−^{1}H) and δ(^{119}Sn) of Bu_2SnClH–Bu_4NF compared to those of **B**. These data and the lower Sn−H stretching frequency of Bu_2SnClH–Bu_4NF in the FT-IR spectra support the idea that Bu_2SnClH–Bu_4NF is a more versatile reducing reagent than **B**. Unfortunately, the yield of **2a** in the reduction of **1a** using Bu_2SnClH-Bu_4NF was lower, perhaps because of its instability toward imines; this hydride system partially decomposed into $ClBu_2SnSnBu_2Cl$ upon the addition of **1a**, and evolved hydrogen gas. On the other hand, the poor activity of Bu_2SnClH–Bu_4NCl might also be attributed to the weak coordination of Bu_4NCl to Bu_2SnClH.[21]

Synthesis of Tertiary Amines. The Bu_2SnClH–HMPA system (**B**) stoichiometrically promoted hydrostannation of imine **1a** under mild and neutral conditions, furnishing an adduct with a nucleophilic Sn−N bond. Without isolation of the tin amide **C**, we attempted the subsequent N-benzylation with benzyl bromide (eq 3). The reaction mixture was heated at 60 °C for 3 h giving the corresponding tertiary amine **3a** in 91% yield based on the starting imine **1a**. The high reactivity of **C** can be similarly explained in terms of the activation of the Sn−N bond by coordination with HMPA,[22] as well as the

(16) Barbieri, G.; Taddei, F. *J. Chem. Soc. Perkin Trans. 2*, **1972**, 1327.

(17) (a) McGardy M. M.; Tobias R. S. *J. Am. Chem. Soc.* **1965**, *87*, 1909. (b) Molloy, K. C.; Blunden, S. J.; Hill, R. *J. Chem. Soc. Dalton Trans.* **1988**, 1259.

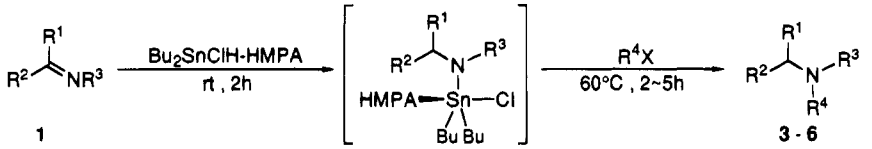
(18) Maddox, M. L.; Flitcroft, N.; Kaesz, H. D. *J. Organomet. Chem.* **1965**, *4*, 50.

(19) Brelière, C.; Carré, F.; Corriu, R. J. P.; Poirier, M.; Royo, G. *Organometallics* **1986**, *5*, 388.

(20) Boyer, J.; Breliere, C.; Corriu, R. J. P.; Kpoton, A.; Poirier, M.; Royo, G. *J. Organomet. Chem.* **1986**, *311*, C39.

(21) Bu_2SnClH–Bu_4NCl (8.00 mmol in 1 mL of THF-d_8): ^{1}H NMR (THF-d_8) δ 7.27 (s, 1H, ^1J(^{119}Sn−^{1}H) = 2295 Hz, ^1J(^{117}Sn−^{1}H) = 2193 Hz, Sn−H); ^{13}C NMR (THF-d_8) δ 14.1, 21.9 (^1J(^{119}Sn−^{13}C$_\alpha$) = 496 Hz, ^1J(^{117}Sn−^{13}C$_\alpha$) = 475 Hz), 27.1 (^3J(^{119}Sn−^{13}C$_\gamma$) = 79 Hz, ^3J(^{117}Sn−^{13}C$_\gamma$) = 72 Hz), 28.8 (^2J(Sn−^{13}C$_\beta$) = 31 Hz); ^{119}Sn NMR (THF-d_8) δ −84.3 (d).

Table 4. Synthesis of Tertiary Amines[a]

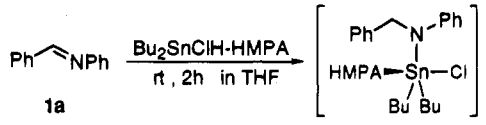


1 C 3 - 6

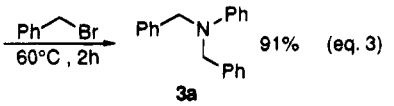
1 \ R^4X	PhCH2Br	MeI	Allyl Br	PhCH=CHCH2Br
PhCH=NPh (1a)	3a, 91%	4a, 96%	5a, 96%	6a, 74%
=NPh (1b)	3b, 93%	4b, 46%	5b, 71%	6b, 56%
PhC(Me)=NPh (1c)	3c, 42%	4c, 40%	5c, 62%	6c, 47%

[a] Imine (**1a–c**) 1 mmol, Bu_2SnClH–HMPA 1 mmol, R^4X 1–3 mmol.

electron-withdrawing effect of the chlorine atom. Although Bu_3SnH–Bu_4NF was expected to furnish the reactive tin amide in the hydrostannation of **1a** (entry 5 in Table 1), the subsequent reaction with benzyl bromide gave **3a** in only 44% yield.



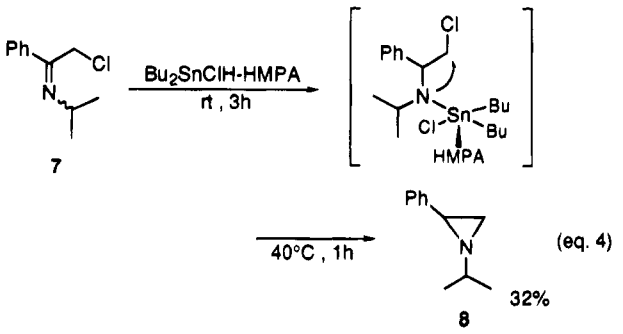
1a C



3a

As shown in Table 4, the corresponding unsymmetrical tertiary amines, **3a–6a**, were obtained in 74–96% yields, as a result of the N-alkylation of **C** with alkyl halides such as allylic bromides and methyl iodide. The presented method was also applied to ketimines, using **1b** and **1c** as starting materials. The yields of bulky tertiary amines **3b–6b** and **3c–6c** were moderate to good (Table 4). Thus, it has been demonstrated that the $BuSn_2ClH$–HMPA complex (**B**) is an excellent reagent for the preparation of various unsymmetric tertiary amines in a one-pot procedure *via* the tandem reactions, hydrostannation, and alkylation.

One of the characteristics of Bu_2SnClH–HMPA is that it promotes an ionic reduction. We have already reported that ionically-activated tin hydrides promoted the chemoselective reduction of carbonyl groups while tolerating the presence of halogens.[9a] We attempted the synthesis of aziridine from α-chloromethyl ketimine **7** (eq 4).[23] As expected, the chemoselective hydrostannation of the imino group of **7** proceeded without radical dechlorination. The subsequent intramolecular nucleophilic reaction took place at 40 °C to produce aziridine **8** in 32% yield.



7 8

Conclusion. A novel, highly-coordinated tin hydride, Bu_2SnClH–HMPA (**B**), effectively reduces imines to the corresponding secondary amines in good yields. Moreover, the resulting tin amides from hydrostannation of imines subsequently react with various alkyl halides to furnish unsymmetrical tertiary amines in a one-pot procedure. The formation and structure of these highly-coordinated tin hydrides were confirmed by ^1H, ^{13}C, and ^{119}Sn NMR and FT-IR spectroscopy. The coordination of HMPA to the tin atom and the electron-withdrawing effect of the chlorine substituent are presumably responsible for the high ionic reactivity of **B** and **C**.

Experimental Section

Analysis. ^1H, ^{13}C, and ^{119}Sn NMR spectra were recorded at 400, 100, and 149 MHz, respectively. Samples for ^1H and ^{13}C NMR spectra of produced amines were examined in $CDCl_3$

(22) (a) Shibata, I.; Nakamura, K.; Baba, A.; Matsuda, H. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 853. (b) Shibata, I.; Toyota, M.; Baba, A.; Matsuda, H. *J. Org. Chem.* **1990**, *55*, 2487. (c) Shibata, I.; Yamasaki, H.; Baba, A.; Matsuda, H. *J. Org. Chem.* **1992**, *57*, 6909. (d) Shibata, I.; Mori, Y.; Yamasaki, H.; Baba, A.; Matsuda, H. *Tetrahedron Lett.* **1993**, *34*, 6567.

(23) Synthesis of aziridine from α-halomethyl ketimines: (a) Kimpe, N.; Verhé, R.; Buyck, L.; Schamp, N. *J. Org. Chem.* **1980**, *45*, 5319. (b) Kimpe, N.; Verhé, R.; Buyck, L.; Schamp, N. *J. Org. Chem.* **1981**, *46*, 2079. (c) Kimpe, N.; Moens, L. *Tetrahedron* **1990**, *46*, 2965.

containing 0.03% (w/v) of TMS. Samples for ^1H, ^{13}C, and ^{119}Sn NMR spectra of tin hydrides were examined in THF-d_8 containing tetramethyltin. GLC analyses were performed with a FFAP or with a OV-1 (2-m × 3-mm glass column). Column chromatography was performed by using Fuji Davison gel FL 100DX. Preparative TLC was carried out on Wakogel B-5F mesh silica gel. Yields were determined by GLC or ^1H NMR using internal standards.

Materials. Tri-*n*-butyltin hydride (Bu_3SnH) and di-*n*-butyltin dihydride (Bu_2SnH_2) were respectively prepared by the reduction of Bu_3SnCl and Bu_2SnCl_2 with $LiAlH_4$.[24] Bu_2SnClH was synthesized by the reaction of Bu_2SnH_2 and Bu_2SnCl_2.[11a] N-Benzylideneaniline (**1a**) was commercially available and used as received. Ketimines **1b** and **1c** were prepared by the azetropic dehydration of ketone and aniline in toluene at reflux temperature.[4] α-Chloromethyl ketimine **7** was synthesized by $TiCl_4$-mediated condensation of 2-chloroacetophenone and isopropylamine.[25] THF was freshly distilled over sodium benzophenone ketyl, and HMPA was distilled from finely powdered CaH_2. All reactions were carried out under dry nitrogen.

***N*-Benzylphenylamine (2a) (Representative Procedure for the Reduction of Imines).** In the case using Bu_3SnH-Bu_4NF, Bu_3SnH (1 mmol) was added to the solution of Bu_4NF (1 mmol) in 1 mL of THF. Aldimine **1a** (1 mmol) was added at rt and the mixture was stirred for 1 h. After quenching the reaction with MeOH (5 mL), volatiles were removed under reduced pressure. The residue was subjected to column chromatography eluting with hexane–EtOAc (9:1) to give almost pure product **2a**. Further purification was performed by TLC eluting with hexane–EtOAc (9:1).

In the case using Bu_2SnClH–HMPA, Bu_2SnCl_2 (0.5 mmol) was added to the solution of Bu_2SnH_2 (0.5 mmol) in 1 mL of THF. The mixture was stirred at rt for 10 min. The FT-IR absorption band at 1836.5 cm^{-1} due to the Sn–H bond of Bu_2SnH_2 was shifted to 1867.3 cm^{-1}, which indicated the formation of Bu_2SnClH. After HMPA (1 mmol) was added, the FT-IR absorption band due to Sn–H shifted to 1861.5 cm^{-1}, which indicated the formation of Bu_2SnClH-HMPA. Aldimine **1a** (1 mmol) was added, and the mixture was stirred at rt for 1 h. After quenching the reaction with MeOH (5 mL), volatiles were removed under reduced pressure. The residue was subjected to column chromatography eluting with hexane–EtOAc (9:1) to give almost pure product **2a**. Further purification was performed by TLC eluting with hexane–EtOAc (9:1): white solid; mp 35.5–37.8 °C (lit.[26] 36–37.2 °C); IR (KBr) 3400, 1320 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.88 (br, 1H), 4.23 (s, 2H), 6.55–7.32 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 48.1, 112.7, 117.4, 127.1, 127.4, 128.5, 129.2, 139.4, 148.1; HRMS calcd for $C_{13}H_{13}N$, 183.1049, found 183.1033.

***N*-Cyclohexylphenylamine (2b):** colorless liquid, purified by TLC with hexane–EtOAc (9:1); IR (neat) 3360, 1310 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08–2.07 (m, 10H), 3.20–3.28 (m, 1H), 3.38 (br, 1H), 6.56–7.17 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 25.0, 25.9, 33.4, 51.6, 113.1, 116.8, 129.2, 147.4; HRMS calcd for $C_{12}H_{17}N$ 175.1362, found 175.1366.

***N*-α-Phenethylphenylamine (2c):** colorless liquid, purified by TLC with hexane–EtOAc (9:1); IR (neat) 3380, 1305 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.48 (d, 3H, J = 6.84 Hz), 3.99 (br, 1H), 4.46 (q, 1H, J = 6.84 Hz), 6.47–7.36 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 25.0, 53.4, 113.2, 117.2, 125.8, 126.8, 128.6, 129.0, 145.2, 147.2; HRMS calcd for $C_{14}H_{15}N$ 197.1206, found 197.1199.

^1H, ^{13}C, and ^{119}Sn NMR Study of $Bu_2SnCl_{2-n}H_n$ (n = 0–2). Chemical shifts for ^1H and ^{119}Sn NMR were measured relative to Me_4Sn. Chemical shifts for ^{13}C NMR was measured relative to THF-d_8.

Bu_2SnCl_2: In a small flask, Bu_2SnCl_2 (4.11 mmol) was kept under dry N_2 in 0.5 mL of THF-d_8 containing tetramethyltin (TMT); 0.8 mL of the solution was transferred to a NMR tube. ^{13}C and ^{119}Sn NMR spectra were recorded at 24 °C; ^{13}C NMR (THF-d_8) δ 13.8, 26.5 ($^3J(^{119}Sn-^{13}C_\gamma)$ = 98 Hz, $^3J(^{117}Sn-^{13}C_\gamma)$ = 95 Hz), 27.6 ($^2J(Sn-^{13}C_\beta)$ = 40 Hz), 28.8 ($^1J(^{119}Sn-^{13}C_\alpha)$ = 518 Hz, $^1J(^{117}Sn-^{13}C_\alpha)$ = 495 Hz); ^{119}Sn NMR (THF-d_8) δ 35.2.

Bu_2SnH_2 (7.91 mmol in 1 mL of THF-d_8): ^1H NMR (THF-d_8) δ 4.47 (m, 1H, $^1J(^{119}Sn-^1H)$ = 1681 Hz, $^1J(^{117}Sn-^1H)$ = 1606 Hz, Sn–H); ^{13}C NMR (THF-d_8) δ 7.6 ($^1J(^{119}Sn-^{13}C_\alpha)$ = 376 Hz, $^1J(^{117}Sn-^{13}C_\alpha)$ = 359 Hz), 14.3, 27.7 ($^3J(Sn-^{13}C_\gamma)$ = 58 Hz), 31.3 ($^2J(Sn-^{13}C_\beta)$ = 24 Hz); ^{119}Sn NMR (THF-d_8) δ −205.4 (t).

Bu_2SnClH (8.00 mmol in 1 mL of THF-d_8): ^1H NMR (THF-d_8) δ 7.19 (m, 1H, $^1J(^{119}Sn-^1H)$ = 2178 Hz, $^1J(^{117}Sn-^1H)$ = 2081 Hz, Sn–H); ^{13}C NMR (THF-d_8) δ 13.9, 18.7 ($^1J(^{119}Sn-^{13}C_\alpha)$ = 451 Hz, $^1J(^{117}Sn-^{13}C_\alpha)$ = 431 Hz), 26.9 ($^3J(^{119}Sn-^{13}C_\gamma)$ = 75 Hz, $^3J(^{117}Sn-^{13}C_\gamma)$ = 72 Hz), 28.5 ($^2J(Sn-^{13}C_\beta)$ = 30 Hz); ^{119}Sn NMR (THF-d_8) δ −18.3 (d).

Bu_2SnClH–HMPA (8.00 mmol in 1 mL of THF-d_8): ^1H NMR (THF-d_8) δ 7.19 (m, 1H, $^1J(^{119}Sn-^1H)$ = 2389 Hz, $^1J(^{117}Sn-^1H)$ = 2283 Hz, Sn–H); ^{13}C NMR (THF-d_8) δ 14.4, 22.3 ($^1J(^{119}Sn-^{13}C_\alpha)$ = 547 Hz, $^1J(^{117}Sn-^{13}C_\alpha)$ = 522 Hz), 27.4 ($^3J(Sn-^{13}C_\gamma)$ = 82 Hz), 29.0 ($^2J(Sn-^{13}C_\beta)$ = 31 Hz); ^{119}Sn NMR (THF-d_8) δ −139.3 (d).

Bu_2SnClH–Bu_4NF (1.11 mmol in 1 mL of THF-d_8): ^1H NMR (THF-d_8) δ 7.21 (s, 1H, $^1J(^{119}Sn-^1H)$ = 2438 Hz, $^1J(^{117}Sn-^1H)$ = 2329 Hz, Sn–H); ^{13}C NMR (THF-d_8) δ 14.5, 20.8, 27.9 ($^3J(Sn-^{13}C_\gamma)$ = 86 Hz), 29.3 ($^2J(Sn-^{13}C_\beta)$ = 28 Hz); ^{119}Sn NMR (THF-d_8) δ −159.8 (br).

***N*,*N*-Dibenzylphenylamine (3a) (Representative Procedure for the Synthesis of Tertiary Amines).** After the reduction of aldimine (**1a**) (1 mmol) by Bu_2SnClH–HMPA as discribed for the synthesis of **2a**, benzyl bromide (1 mmol) was added to the *in situ* formed tin amide intermediate (**C**), and the mixture was stirred at 60 °C for 3 h. After quenching the mixture with MeOH, the solvent was removed under reduced pressure. The residue was subjected to column chromatography eluting with hexane to give a crude product (**3a**). Further purification was performed by TLC eluting with hexane–EtOAc (9:1) and then by Kugelrohr distillation at 150 °C (0.01 mmHg): white solid; mp 65.8–67.2 °C (lit.[27] 67–70 °C); IR (KBr) 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.58 (s, 4H), 6.63–7.28 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 54.1, 112.4, 116.7, 126.6, 126.8, 128.6, 129.2, 138.5, 149.1; HRMS calcd for $C_{20}H_{19}N$ 273.1519, found 273.1519.

***N*-Benzyl-*N*-methylphenylamine (4a):** colorless liquid, purified by Kugelrohr distillation at 200 °C (0.01 mmHg); IR (neat) 1345 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.97 (s, 3H), 4.49 (s, 2H), 6.67–7.30 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 38.4, 56.6, 112.3, 116.5, 126.7, 126.8, 128.5, 129.1, 139.0, 149.7; HRMS calcd for $C_{14}H_{15}N$ 197.1206, found 197.1199.

***N*-Allyl-*N*-benzylphenylamine (5a):** colorless liquid, purified by Kugelrohr distillation at 85 °C (0.01 mmHg); IR (neat) 1360 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.97–3.99 (m, 2H), 4.52 (s, 2H), 5.15–5.21 (m, 2H), 5.81–5.91 (m, 1H), 6.65–7.32 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 53.0, 53.9, 112.4, 116.3, 116.5, 126.6, 126.8, 128.5, 129.1, 133.6, 138.9, 148.9; HRMS calcd for $C_{16}H_{17}N$ 223.1362, found 223.1351.

***N*-Benzyl-*N*-cinnamylphenylamine (6a):** colorless liquid, purified by TLC with hexane–EtOAc (96:4); IR (neat) 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.10 (d, 2H, J = 4.39 Hz), 4.54 (s, 2H), 6.22 (td, 1H, J = 4.39 and 16.11 Hz), 6.47 (d, 1H, J = 16.11 Hz), 6.66–7.30 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 52.4, 53.8, 112.4, 116.6, 125.4, 126.3, 126.6, 126.8, 127.4, 128.5, 128.5, 129.2, 131.3, 136.8, 138.8, 148.9; HRMS calcd for $C_{22}H_{21}N$ 299.1675, found 299.1684.

***N*-Benzyl-*N*-cyclohexylphenylamine (3b):** white solid, purified by TLC with hexane–EtOAc (9:1); mp 65.0–68.8 °C; IR (KBr) 1330 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05–2.03 (m, 10H), 3.73–3.78 (m, 1H), 4.45 (s, 2H), 6.62–7.28 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 25.9, 26.1, 30.4, 49.3, 57.1, 112.8, 116.1, 126.2, 126.3, 128.3, 129.1, 140.9, 149.2; HRMS calcd for $C_{19}H_{23}N$ 265.1832, found 265.1839.

***N*-Cyclohexyl-*N*-methylphenylamine (4b):** colorless liquid, purified by TLC with hexane–EtOAc (9:1); IR (neat) 1300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00–1.78 (m, 10H), 2.68 (s, 3H), 3.45–3.53 (m, 1H), 6.59–7.17 (m, 5H); ^{13}C NMR ($CDCl_3$) δ

(24) Kerk, G. J. M.; Noltes, J. G.; Luijiten, J. G. A. *J. Appl. Chem.* **1957**, *7*, 366.
(25) Kimpe, N.; Cock, W.; Stevens, C. *Tetrahedron* **1992**, *48*, 2739.
(26) Schellenberg, K. A. *J. Org. Chem.* **1963**, *28*, 3259.
(27) Pollak, I. E.; Grillot, G. F. *J. Org. Chem.* **1967**, *32*, 2892.

25.9, 26.1, 29.9, 31.0, 58.0, 113.1, 116.2, 128.9, 150.0; HRMS calcd for $C_{13}H_{19}N$ 189.1519, found 189.1533.

***N*-Allyl-*N*-cyclohexylphenylamine (5b):** colorless liquid, purified by TLC with hexane–EtOAc (9:1); IR (neat) 1345 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05–1.89 (m, 10H), 3.55–3.62 (m, 1H), 3.77–3.80 (m, 2H), 5.06–5.21 (m, 2H), 5.77–5.88 (m, 1H), 6.60–7.19 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 25.9, 26.1, 30.4, 47.6, 56.9, 112.6, 115.0, 115.9, 128.9, 136.8, 148.8; HRMS calcd for $C_{15}H_{20}N$ 215.1675, found 215.1661.

***N*-Cinnamyl-*N*-cyclohexylphenylamine (6b):** colorless liquid, purified by TLC with hexane–EtOAc (10:1); IR (neat) 1335 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09–1.93 (m, 10H), 3.29–3.69 (m, 1H), 3.99 (d, 1H, J = 4.40 Hz), 4.00 (d, 1H, J = 4.88 Hz), 6.25 (ddd, 2H, J = 4.40, 4.88 and 16.11 Hz), 6.53 (d, 1H, J = 16.11 Hz), 6.64–7.35 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 25.9, 26.2, 30.6, 47.4, 57.0, 112.7, 116.0, 126.2, 127.1, 128.5, 128.9, 129.1, 130.0, 137.2, 149.0; HRMS calcd for $C_{21}H_{25}N$ 291.1989, found 291.1987.

***N*-α-Phenethyl-*N*-benzylphenylamine (3c)**: colorless liquid, purified by TLC with hexane–EtOAc (9:1) and by Kugelrohr distillation at 200 °C (0.1 mmHg); IR (neat) 1375 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.55 (d, 3H, J = 6.84 Hz), 4.38–4.50 (m, 2H), 5.24 (q, 1H, J = 6.84 Hz), 6.64–7.30 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 18.7, 50.3, 57.0, 114.1, 117.1, 126.4, 126.4, 126.8, 126.8, 128.3, 128.4, 129.0, 140.0, 142.8, 149.1; HRMS calcd for $C_{21}H_{21}N$ 287.1675, found 287.1655.

***N*-Methyl-*N*-α-phenethylphenylamine (4c)**: colorless liquid, purified by TLC with hexane–EtOAc (9:1); IR (neat) 1365 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.53 (d, 3H, J = 6.84 Hz), 2.66 (s, 3H), 5.11 (q, 1H, J = 6.84 Hz), 6.69–7.31 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 16.3, 31.8, 56.5, 113.0, 116.6, 126.8, 126.9, 128.3, 129.2, 142.8, 150.2; HRMS calcd for $C_{15}H_{17}N$ 211.1362, found 211.1345.

***N*-Allyl-*N*-α-phenethylphenylamine (5c)**: colorless liquid, purified by TLC with hexane–EtOAc (9:1) and Kugelrohr distillation at 120 °C (0.1 mmHg); IR (neat) 1378 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.57 (m, 3H), 3.80–3.82 (m, 2H), 5.05–5.18 (m, 3H), 5.73–5.83 (m, 1H), 6.67–7.30 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 18.5, 49.2, 56.9, 114.1, 116.1, 117.1, 127.2, 127.3, 128.8, 129.4, 136.7, 143.3, 149.4; HRMS calcd for $C_{17}H_{19}N$ 237.1519, found 237.1502.

***N*-Cinnamyl-*N*-α-phenethylphenylamine (6c)**: wax, purified by TLC with hexane–EtOAc (9:1); IR (neat) 1350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.63 (d, 3H, J = 6.84 Hz), 3.99 (d, 2H, J = 4.88 Hz), 5.19 (q, 1H, J = 6.84 Hz), 6.17 (dt, 1H, J = 4.88 and 16.11 Hz) 6.46 (d, 1H, J = 16.11 Hz), 6.69–7.33 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 18.2, 48.5, 56.5, 113.7, 116.9, 126.2, 126.9, 127.0, 127.2, 128.2, 128.5, 128.5, 129.1, 130.6, 137.1, 142.8, 149.1; HRMS calcd for $C_{23}H_{23}N$ 313.1832, found 313.1824.

1-Isopropyl-2-methylaziridine (8): α-Chloromethyl ketimine **7** (1 mmol) was added to the solution of Bu_2SnClH–HMPA (1 mmol) in 1 mL of THF. This mixture was stirred at rt for 3 h and at 40 °C for 1 h. After quenching the reaction with MeOH, volatiles were removed under reduced pressure. The residue was subjected to column chromatography eluting with hexane to give the crude product.[28]

Acknowledgment. This work was financially supported by the JSPS Fellowships for Japanese Junior Scientists and the Grant-in Aid for Scientific Research on Priority Area of Reactive Organometallics No. 05236102 from Ministry of Education, Science and Culture. Thanks are due to Mrs. Y. Miyaji and Mr. H. Moriguchi, Faculty of Engineering, Osaka University, for assistance in obtaining NMR and HRMS spectra.

Supplementary Material Available: Copies of ^1H and ^{13}C NMR spectra of **2–6a**, **2–6b**, **2–6c** (30 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO941408F

(28) Brois, S. J. *Tetrahedron* **1970**, *26*, 227.