Journal of Sulfur Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713926081

Silylation and alkylation of thioamide dianions of *N*-arylmethyl secondary thioamides, and reduction of the resulting thioamides leading to secondary and primary amines

Toshiaki Murai[a]; Tadashi Michigami[a]; Mai Yamaguchi[a]; Noriko Mizuhata[a]
[a] Department of Chemistry, Faculty of Engineering, Gifu University, Gifu, Japan

To cite this Article Murai, Toshiaki , Michigami, Tadashi , Yamaguchi, Mai and Mizuhata, Noriko(2009) 'Silylation and alkylation of thioamide dianions of *N*-arylmethyl secondary thioamides, and reduction of the resulting thioamides leading to secondary and primary amines', Journal of Sulfur Chemistry, 30: 3, 225 — 235
To link to this Article: DOI: 10.1080/17415990902774202
URL: http://dx.doi.org/10.1080/17415990902774202

Journal of Sulfur Chemistry
Vol. 30, Nos. 3–4, June–August 2009, 225–235

Taylor & Francis
Taylor & Francis Group

Silylation and alkylation of thioamide dianions of *N*-arylmethyl secondary thioamides, and reduction of the resulting thioamides leading to secondary and primary amines

Toshiaki Murai*, Tadashi Michigami, Mai Yamaguchi and Noriko Mizuhata

Department of Chemistry, Faculty of Engineering, Gifu University, Yanagido, Gifu 501-1193, Japan

(*Received 23 December 2008; final version received 24 January 2009*)

This paper is dedicated to Professor Juzo Nakayama on the occasion of his 65th birthday and retirement.

N-arylmethyl aromatic thioamides were reacted with *n*-BuLi (2 equivalents), and then treated with silylpropyl chloride and silyl chlorides. As a result, these electrophiles were introduced to the carbon atom adjacent to the nitrogen atom of thioamides via thioamide dianions. The efficiency of the reaction was largely influenced by the substituents on the aromatic ring of thioamides. The reaction of thioamides having pyridyl groups was not always successful and depended on the position of the nitrogen atom of these groups. Reduction of the resulting thioamides with $LiAlH_4$ proceeded smoothly to give the corresponding secondary *N*-1-silylarylmethyl amines in good yields. In contrast, the reduction of thioamides bearing pyridyl groups gave complex mixtures. In these cases, the use of DIBAH successfully gave the desired secondary amines.

Keywords: *N*-arylmethyl aromatic thioamides; BuLi; thioamide dianions; $LiAlH_4$; DIBAH; *N*-1-silylarylmethyl amines

1. Introduction

Thioamides are some of the most readily available and widely used thiocarbonyl compounds. Compared with ordinary amides, which are generally considered to be the least reactive carbonyl compounds in organic chemistry, thioamides are less polar and more reactive. In fact, a wide range of synthetic procedures have been developed over the past 80 years (*1–5*). For example, a three-component coupling reaction of aldehydes, amines, and elemental sulfur, which is called the Willgerodt–Kindler reaction, can provide *N*-secondary and -tertiary thioamides with high efficiency (*6–10*). Many synthetic applications of thioamides have also been reported (*11*). As an example, the treatment of thioamides with bases gives various types of carbanions (*12–21*). During the course of our studies on chalcogenoamides (*22–30*), we also found that the reaction of *N*-benzyl secondary thioamides (**1**) with 2 equivalents of BuLi led to thioamide dianions (**2**) (*31*, *32*)

*Corresponding author. Email: mtoshi@gifu-u.ac.jp

ISSN 1741-5993 print/ISSN 1741-6000 online

DOI: 10.1080/17415990902774202
http://www.informaworld.com

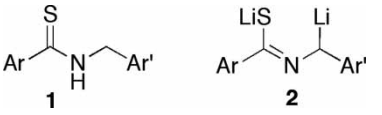
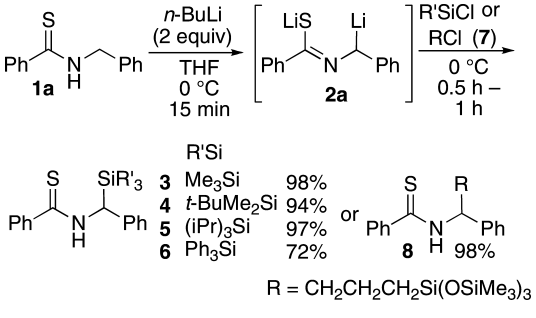


Figure 1. Secondary thioamides and thioamide dianions.

(Figure 1). We report here the alkylation and silylation of (**1**) obtained by the Willgerodt–Kindler reaction, and reduction of the resulting thioamides leading to secondary and primary amines.

2. Results and discussion

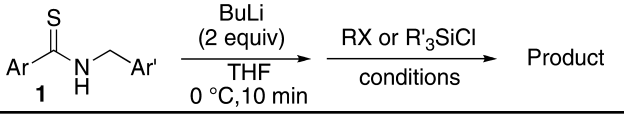
Initially, *N*-benzyl thiobenzamide (**1a**) was treated with *n*-BuLi at 0 °C, and the mixture was stirred at this temperature for 15 min to form thioamide dianion (**2a**) (Scheme 1). Silyl chlorides with various alkyl substituents were then added to (**2a**) at 0 °C to give *N*-1-silylphenylmethyl thiobenzamides (**3**–**6**) within 1 h. *N*-silylmethyl thioamides are precursors of nitrile ylide equivalents (*33, 34*) and are generally prepared by using silylmethylamine as a starting material. In contrast, in the present reaction, electrophilic silylating agents are introduced to the nucleophilic carbon atom adjacent to the nitrogen atom, and this enabled us to develop a facile method for the synthesis of *N*-1-silylarylmethyl thioamides. The efficiency of silylation was dependent on the substituents on the silyl group. The use of *i*-Pr_3SiCl required a longer reaction time. The reaction with Ph_3SiCl gave the product (**6**) in lower yield. Additionally, $(Me_3SiO)_3SiCH_2CH_2CH_2Cl$ (**7**) was used as one of the primary alkyl chlorides. The presumed products can be new types of precursors of amines bearing an oxygen-permeable functional group (*35, 36*). The reaction of the thioamide dianion (**2a**) with (**7**) also proceeded smoothly to give the desired product in 98% yield. This implied the high nucleophilicity of thioamide dianions (**2**), and a $(Me_3SiO)_3Si$ group did not influence the reaction course.

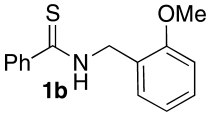
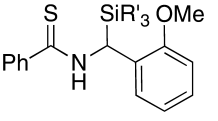
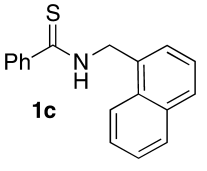
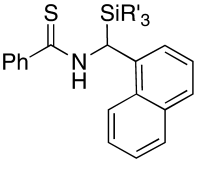
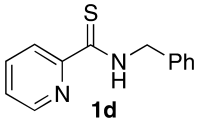
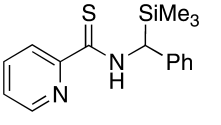
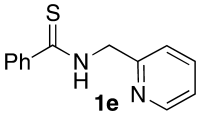
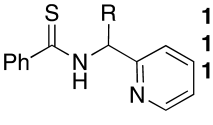
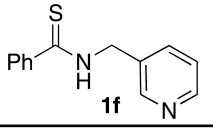
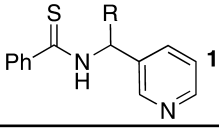


Scheme 1.

Next, a variety of thioamides (**1**) were used as starting materials, and the results are shown in Table 1. In addition to thioamides with methoxyphenyl and naphthyl groups (**1b**) and (**1c**), the reactivities of those having pyridyl groups (**1d**–**1f**) were also tested. The deprotonation of thioamides (**1b**) and (**1c**) took place as with (**1a**) but a slightly longer reaction time was necessary to complete the silylation (entries 1–4). The use of *i*-Pr_3SiCl gave the products (**10**) and (**12**) in moderate yields (entries 2 and 4). *N*-phenylmethyl-2-pyridinecarbothioamide (**1d**) was then reacted with *n*-BuLi (2 equivalents), and to the reaction mixture was added Me_3SiCl (entry 5). However, only a small amount of the desired silylated product (**13**) was confirmed by NMR spectra, and instead a complex mixture that included unreacted starting thioamide (**1d**) was obtained.

Table 1. Alkylation or silylation of thioamide dianions.



Entry	Thioamide **1**	RX or R'_3SiCl	Conditions	Product, yield[a]
1	 **1b**	*t*-$BuMe_2SiCl$	0 °C, 2 h	 **9** 91%
2		$(iPr)_3SiCl$	0 °C, 2 h	**10** 58%
3	 **1c**	*t*-$BuMe_2SiCl$	0 °C, 2 h	 **11** 91%
4		$(iPr)_3SiCl$	0 °C, 2 h	**12** 53%
5	 **1d**	Me_3SiCl	0 °C, 1.5 h	 **13** 7%[b]
6[c]		Me_3SiCl	0 °C, 1.5 h	**13** 99%
7	 **1e**	$Cl(CH_2)_3Si(OSiMe_3)_3$	0 °C, 2 h	 **14** 0%
8		$CH_2{=}CHCH_2Br$	0 °C, 1.5 h	**15** 71%
9		$Cl(CH_2)_3Si(OSiMe_3)_3$	40 °C, 4 h	**14** 72%
10	 **1f**	$Cl(CH_2)_3Si(OSiMe_3)_3$	40 °C, 4 h	 **16** 75%

Notes: [a]Isolated yield. [b]NMR yield.[c]*n*-BuLi (3 equivalents) and Me_3SiCl (2 equivalents) were used.

To enhance the efficiency of the deprotonation of **1d**, *n*-BuLi (3 equivalents) and Me_3SiCl (2 equivalents) were used. As a result, the desired silylated product (**13**) was obtained quantitatively (entry 6). Additionally, the use of Me_3SiCl (3 equivalents) reduced the yield of (**13**) (67%), and disilylated product (**13′**) was also formed in 24% yield (Figure 2). This result has implied in the reaction of (**1d**) and *n*-BuLi, not only thioamide dianion (**2d**) but also thioamide trianion (**2d′**) may be generated. Thioamide dianions were also generated from *N*-(2-pyridylmethyl)- and -(3-pyridylmethyl) benzenecarbothioamide (**1e**) and (**1f**). The reaction mixture of (**1e**) and (**1f**) with *n*-BuLi turned deep purple, which indicated the formation of thioamide dianions (**2**), but the silylation of the reaction mixture of (**1e**) and *n*-BuLi with Me_3SiCl did not take place. To confirm the formation of thioamide dianion from (**1e**), (**7**) was used as an electrophile, but the alkylation was not successful, and a complex mixture was formed (entry 7). Allyl bromide as a more reactive electrophile was then added to the reaction mixture, and in this case allylation at the carbon atom adjacent to the nitrogen atom proceeded smoothly to give thioamide (**15**) in good yield (entry 8). To obtain the silylated product of (**1**) from (**1e**), the use of excess *n*-BuLi and reaction at a higher temperature was attempted but gave only a complex mixture, whereas the alkylation of (**1e**) with (**7**) was successful at a higher temperature to give (**14**). Likewise, alkylation of the thioamide dianion generated from (**1f**) with (**7**) at 40 °C proceeded smoothly to give the product (**16**) in good yield.

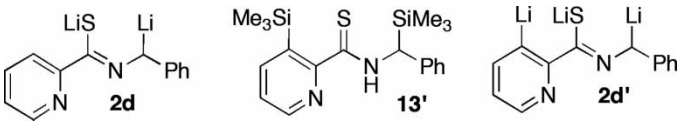
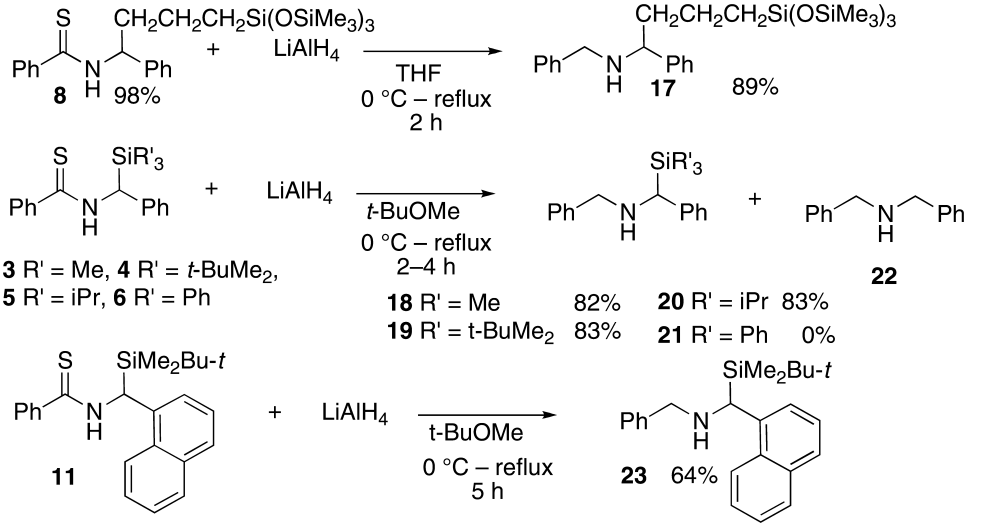


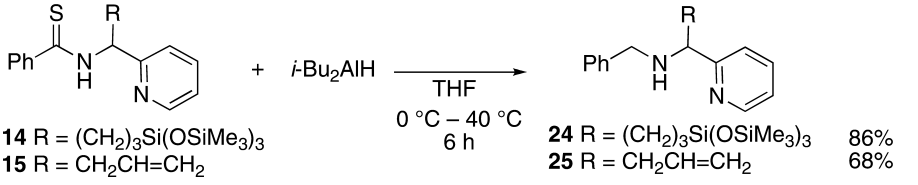
Figure 2. Thioamide dianions, trianions and byproduct.

Reduction of the resulting thioamides was examined to lead to *N*-1-silylarylmethyl amines, which are not readily accessible by known methods (*37–39*). The combination of Et_3OBF_4 and $NaBH_4$ (*40*), Ni_2B (*41*) and $LiAlH_4$ (*32*) are known to reduce thioamides. Initially, the reduction of thioamides (**3**–**6**) and (**8**) with $LiAlH_4$ was carried out (Scheme 2). As exemplified by the reaction of (**8**), the reaction in THF proceeded smoothly to give the corresponding amine (**17**) in high yield. In contrast, in the reduction of (**3**), the use of THF as a solvent gave the corresponding product (**18**), but along with ca. 10% yield of (**22**), which may be the result of the formal substitution reaction at the silicon atom of (**18**) with hydride ion. Et_2O and *t*-BuOMe were then used as solvents. As a result, the selective reduction of (**3**) proceeded in *t*-BuOMe to give (**18**) in 82% yield. The reduction of (**4**), (**5**), and (**11**) with $LiAlH_4$ took place in a similar way to give (**19**), (**20**), and (**23**), respectively, in good yields, whereas the reduction of (**6**) did not give the corresponding product (**20**) but rather gave complex mixtures, including (**22**). In contrast to these results, the reduction with $LiAlH_4$ could not be applied to thioamides bearing a pyridyl group (**13**–**16**). The partial reduction not only of thiocarbonyl groups but also of pyridyl groups took place to form complex mixtures. The reduction with the combination of Et_3OBF_4, $NaBH_4$ and Ni_2B was also attempted. Reduction at room temperature did not occur, and that at higher temperature gave complex mixtures that included the desired products. Thioamides (**14**) and (**15**) were then reacted with DIBAH in THF (Scheme 3). As a result, the reduction at 40 °C proceeded selectively to give the corresponding amines (**24**) and (**25**) (*42*). Nevertheless, *N*-1-silyl-(2-pyridylmethyl) thioamide (**13**) was not selectively reduced with DIBAH.

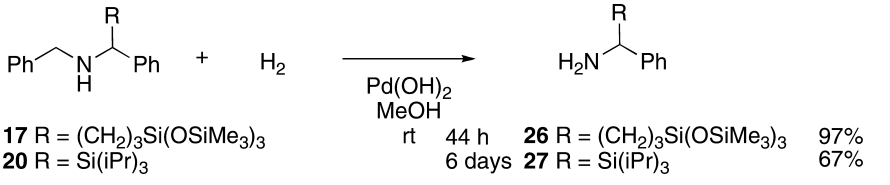


Scheme 2.

Finally, hydrogenolysis of some of the secondary amines obtained in Scheme 2 was carried out to lead to primary amines (Scheme 4). The hydrogenolysis of (**17**) and (**20**) mediated by a stoichiometric amount of $Ph(OH)_2$ proceeded smoothly under a hydrogen atmosphere. Although



Scheme 3.



Scheme 4.

the reaction required a very long reaction time, the debenzylation of (**17**) and (**20**) took place selectively without the elimination of silyl groups, to give the corresponding primary amines (**26**) and (**27**) in good yields.

In summary, a new method for the synthesis of silylated thioamides via thioamide dianions has been demonstrated. The reaction of thioamide dianions derived from secondary *N*-arylmethyl aromatic thioamides with silyl chlorides and silylpropyl chloride was highly efficient, whereas the efficiency and selectivity of the reaction of thioamides bearing pyridyl groups depended on the position of the nitrogen atom of the pyridyl group. To reduce the resulting thioamides, $LiAlH_4$ and DIBAH were used as reducing agents depending on the substituents on the thioamides.

3. Experimental

3.1. *General considerations*

Melting points were measured by a Yanagimoto micro melting point apparatus (uncorrected). IR spectra were obtained on a JASCO FT/IR 410 spectrophotometer. ^{1}H (399.7 MHz) and ^{13}C (100.4 MHz) NMR spectra were measured on a JEOL α-400 spectrometer. The ^{1}H and ^{13}C chemical shifts are reported in δ values with reference to Me_4Si and $CDCl_3$ as internal standards, respectively. All spectra were acquired in the proton-decoupled mode. Mass (MS) and high-resolution mass spectra (HRMS) were measured on a JEOL JMS-700 spectrometer. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University. All the manipulations were carried out under Ar atmosphere.

3.2. *General procedure for the reaction of thioamide dianions with silyl chlorides and alkyl halides*

3.2.1. *N-4-tris(trimethylsiloxy)silyl-1-phenylbutyl benzenecarbothioamide (**8**)*

To a solution of *N*-phenylmethyl benzenecarbothioamide (2.27 g, 10.0 mmol) in THF (10 mL) was added butyllithium (1.6 M solution in hexane, 12.5 mL, 20.0 mmol) at 0 °C under an Ar atmosphere. The mixture was stirred at that temperature for 5 min. After the addition of 3-chloropropyl tris(trimethylsiloxy)silane (4.45 mL, 11.0 mmol), the mixture was stirred at that

temperature for 30 min. The reaction mixture was poured onto water and extracted with Et_2O (20 mL). The organic layer was washed with 2×10 mL of water. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane:AcOEt = 8:1) to give *N*-4-tris(trimethylsiloxy)silyl-1-phenylbutyl benzenecarbothioamide (5.50 g, 9.75 mmol, 98%, Rf = 0.55) as a yellow solid; mp: 66–68 °C; IR (KBr): 2958, 1597, 1514, 1485, 1451, 1374, 1346, 1251, 1205, 1181, 1066, 969, 913, 843, 773, 755, 691, 634, 593, 541, 493, 433 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.05 (s, 27H, $SiCH_3$), 0.45–0.57 (m, 2H, CH_2), 1.31–1.51 (m, 2H, CH_2), 1.92–2.01 (m, 1H, CH_2), 2.09–2.18 (m, 1H, CH_2), 5.74 (q, J = 7.5 Hz, 1H, CH), 7.22–7.43 (m, 8H, Ar), 7.67–7.72 (m, 3H, Ar, NH); ^{13}C NMR ($CDCl_3$): δ 1.7 (t, $^1J_{C-Si}$ = 29.7 Hz, $SiCH_3$), 14.2, 20.2, 38.6 (CH_2), 59.7 (CH), 126.6, 127.0, 127.7, 128.5, 128.8, 130.9, 140.6, 142.4 (Ar), 198.3 (C=S); MS (EI) m/z 564 (M^+); HRMS Calcd for $C_{26}H_{45}NO_3SSi_4$: 563.2197; found: 563.2200.

3.2.2. *N-[phenyl(trimethylsilyl)methyl]benzenecarbothioamide (**3**)*

mp: 89–94 °C (dec); IR (KBr): 3238, 2958, 1598, 1515, 1447, 1354, 1249, 1062, 957, 841, 697, 611, 492 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.15 (s, 9H, CH_3), 5.74 (d, J = 9.0 Hz, 1H), 7.17–7.24 (m, 3H, Ar), 7.35–7.37 (m, 2H, Ar), 7.41–7.51 (m, 3H, Ar), 7.73–7.76 (m, 2H, Ar), 8.00 (d, J = 9.0 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$): δ − 3.10 (CH_3), 53.8 (CH), 126.2, 126.2, 126.6, 128.7, 128.7, 130.9, 139.5, 142.7 (Ar), 198.6 (C=S); MS (EI) m/z 299 (M^+); Anal. Calcd for $C_{17}H_{21}NSSi$: C, 68.17; H, 7.07; N, 4.68; found: C, 68.05; H, 7.12; N, 4.69.

3.2.3. *N-[phenyl(dimethyl(1,1-dimethylethyl)silyl)methylbenzenecarbothioamide (**4**)*

mp: 100–102 °C(dec); IR (KBr): 3375, 2951, 2925, 2853, 1505, 1448, 1357, 1254, 1222, 1065, 953, 844, 700, 646 cm^{-1}; ^1H NMR ($CDCl_3$): δ − 0.10 (s, 3H, CH_3), 0.20 (s, 3H, CH_3), 0.96 (s, 9H, CH_3), 5.83 (d, J = 9.3 Hz, 1H, CH), 7.17–7.21 (m, 3H, Ar), 7.26–7.33 (m, 2H, Ar), 7.38–7.48 (m, 3H, Ar), 7.69–7.71 (m, 2H, Ar), 8.01 (d, J = 9.3 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$) δ − 8.08 (CH_3), −6.59 (CH_3), 17.4 (C), 26.8 (CH_3), 50.8 (CH), 126.2, 126.5, 126.9, 128.6, 128.7, 130.9, 140.3, 142.7 (Ar), 198.4 (C=S); MS (EI) m/z 341 (M^+); Anal. Calcd for $C_{20}H_{27}NSSi$: C, 70.32; H, 7.97; N, 4.10; found: C, 70.20; H, 8.01; N, 4.07.

3.2.4. *N-[phenyl(tris(1-methylethyl)silyl)methyl]benzenecarbothioamide (**5**)*

IR (KBr): 3411, 2945, 2867, 1599, 1483, 1449, 1354, 1064, 882, 772, 696, 587, 559 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.05 (d, J = 7.3 Hz, 9H, CH_3), 1.15 (d, J = 7.3 Hz, 9H, CH_3), 1.26 (sext, J = 7.3 Hz, 3H, C<u>H</u>CH_3), 5.94 (d, J = 9.6 Hz, 1H, C<u>H</u>NH), 7.14–7.18 (m, 3H, Ar), 7.26–7.31 (m, 2H, Ar), 7.36–7.45 (m, 3H, Ar), 7.75 (d, J = 7.3 Hz, 2H, Ar), 8.29 (d, J = 9.6 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 10.9 (CH), 18.4, 18.6 (CH_3), 50.1 (CHNH), 125.9, 126.2, 126.7, 128.3, 128.5, 130.7, 140.2, 142.3 (Ar), 198.5 (C=S); MS (EI) m/z 383 (M^+). HRMS Calcd for $C_{23}H_{33}NSSi$: 383.2103; found: 383.2133.

3.2.5. *N-[phenyl(triphenylsilyl)methyl]benzenecarbothioamide (**6**)*

mp: 135–145 °C (dec); IR (KBr): 3296, 3067, 3010, 1588, 1500, 1485, 1427, 1347, 1119, 1109, 855, 836, 742, 699, 515, 483 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.52 (d, J = 9.3 Hz, 1H, CH), 6.87–6.89 (m, 2H, Ar), 7.13–7.14 (m, 3H, Ar), 7.26–7.51 (m, 14H, Ar), 7.62–7.65 (m, 6H, Ar), 7.98 (d, J = 9.3 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 50.1 (CH), 126.5, 127.6, 128.1, 128.3, 128.5, 130.4,

130.9, 131.2, 135.0, 136.2, 138.4, 142.1 (Ar), 198.8 (C=S); MS (EI) m/z 486 (M^+). Anal. Calcd for $C_{32}H_{27}NSSi$: C, 79.13; H, 5.60; N, 2.88; found: C, 79.23; H, 5.68; N, 2.86.

3.2.6. *N-[2-methoxyphenyl(dimethyl (1,1-dimethylethyl)silyl)methyl]benzenecarbothioamide (**9**)*

mp: 91–96 °C(dec); IR (KBr): 3365, 2929, 2854, 1582, 1504, 1460, 1369, 1239, 1174, 1110, 1019, 951, 803, 750, 663, 627, 466 cm^{-1}; ^1H NMR ($CDCl_3$): δ − 0.30 (s, 3H, CH_3), 0.11 (s, 3H, CH_3), 0.88 (s, 9H, CH_3), 3.78 (s, 3H, OCH_3), 6.00 (d, J = 9.6 Hz, 1H, C<u>H</u>NH), 6.76–6.85 (m, 2H, Ar), 7.08–7.16 (m, 2H, Ar), 7.26–7.35 (m, 3H, Ar), 7.59–7.61 (m, 2H, Ar), 8.69 (d, J = 9.6 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$): δ − 6.74, −6.58 (CH_3), 17.3 (C), 26.5 (CH_3), 49.6 (CHNH), 55.1 (OCH_3), 110.6, 121.2, 126.5, 127.7, 128.1, 128.5, 129.8, 130.5, 142.7, 156.8 (Ar), 195.7 (C=S); MS (EI) m/z 371 (M^+); HRMS Calcd for $C_{21}H_{28}NOSSi$ (M^+−H): 370.1661; found: 370.1636.

3.2.7. *N-[2-methoxyphenyl(tris(1-methylethyl)silyl)methyl]benzenecarbothioamide (**10**)*

mp: 75–85 °C(dec); IR (KBr): 3416, 2941, 2866, 1584, 1485, 1364, 1248, 1111, 1049, 1025, 881, 748, 665, 642, 573 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.965 (d, J = 7.3 Hz, 9H, CH_3), 0.971 (d, J = 7.3 Hz, 9H, CH_3), 1.13 (sept, J = 7.3 Hz, 3H, C<u>H</u>CH_3), 3.75 (s, 3H, OCH_3), 6.12 (d, J = 10.1 Hz, 1H, C<u>H</u>NH), 6.74–6.82 (m, 2H, Ar), 7.05–7.10 (m, 1H, Ar), 7.16–7.18 (m, 1H, Ar), 7.24–7.32 (m, 3H, Ar), 7.61–7.63 (m, 2H, Ar), 8.88 (d, J = 10.1 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 11.6 (CH), 18.6, 18.7 (CH_3), 49.7 (CHNH), 54.8 (OCH_3), 110.6, 120.9, 126.3, 127.6, 127.8, 128.4, 129.9, 130.4, 142.4, 156.7 (Ar), 195.6 (C=S); MS (EI) m/z 413 (M^+); HRMS Calcd for $C_{24}H_{35}NOSSi$: 413.2209; found: 413.2214.

3.2.8. *N-[1-naphthyl(dimethyl (1,1-dimethylethyl)silyl)methyl]benzenecarbothioamide (**11**)*

mp: 179–185 °C(dec); IR (KBr): 3391, 2948, 2855, 1596, 1500, 1446, 1362, 1256, 1179, 1066, 1006, 939, 833, 778, 693, 592, 420 cm^{-1}; ^1H NMR ($CDCl_3$): δ − 0.49 (s, 3H, CH_3), 0.19 (s, 3H, CH_3), 0.98 (s, 9H, CH_3), 6.72 (d, J = 9.3 Hz, 1H, CH), 7.15–7.52 (m, 7H, Ar), 7.63–7.78 (m, 3H, Ar), 7.77 (d, J = 8.8 Hz, 1H, Ar), 8.11 (d, J = 8.8 Hz, 1H, Ar), 8.36 (d, J = 9.3 Hz, 1H, NH); ^{13}C NMR ($CDCl_3$): δ − 8.49, −6.60 (CH_3), 17.6 (C), 26.8 (CH_3), 45.7 (CH), 122.8, 123.8, 125.2, 125.8, 126.1, 126.5, 126.8, 128.7, 128.8, 130.8, 130.9, 133.9, 137.6, 142.6 (Ar), 198.2 (C=S); MS (EI) m/z 391 (M^+); HRMS Calcd for $C_{24}H_{29}NSSi$: 391.1790; found: 391.1784.

3.2.9. *N-[1-naphthyl(tris(1-methylethyl)silyl)methyl]benzenecarbothioamide (**12**)*

IR (KBr): 3413, 3060, 2943, 2866, 1597, 1464, 1364, 1257, 1069, 1009, 882, 801, 782, 770, 676 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.97 (d, J = 7.3 Hz, 9H, CH_3), 1.11 (d, J = 7.3 Hz, 9H, CH_3), 1.28 (sept, J = 7.3 Hz, 3H, CH), 6.85 (d, J = 9.8 Hz, 1H, C<u>H</u>NH), 7.26–7.52 (m, 6H, Ar), 7.57–7.60 (m, 1H, Ar), 7.72–7.74 (m, 3H, Ar), 7.82–7.85 (m, 1H, Ar), 8.40 (d, J = 9.3 Hz, 1H, NH), 8.56 (d, J = 8.8 Hz, 1H, Ar); ^{13}C NMR ($CDCl_3$): δ 11.3 (CH), 18.7, 18.8 (CH_3), 46.2 (CHNH), 124.4, 125.1, 125.8, 125.8, 126.4, 126.4, 127.0, 128.6, 130.8, 131.2, 134.0, 137.8, 142.5 (Ar), 198.0 (C=S); MS (EI) m/z 433 (M^+); HRMS Calcd for $C_{27}H_{35}NSSi$: 433.2259; found: 433.2277.

3.2.10. *N-[phenyl(trimethylsilyl)methyl]-2-pyridinecarbothioamide (**13**)*

mp: 150–160 °C(dec); IR (KBr): 3431, 3268, 2949, 2893, 1584, 1508, 1433, 1366, 1251, 1150, 1063, 959, 854, 720, 623, 507 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.11 (s, 9H, CH_3), 5.74 (d, J = 9.3 Hz,

1H, CH), 7.11–7.39 (m, 5H, Ar), 7.75–7.79 (m, 2H, Ar), 8.50–8.66 (m, 1H, Ar), 8.64–8.66 (m, 1H, Ar), 10.9 (d, $J = 9.3$ Hz, 1H, NH); ^{13}C NMR ($CDCl_3$): δ −3.20 (CH_3), 52.6 (CH), 125.0, 125.8, 125.9, 126.0, 128.5, 137.2, 139.6, 146.9, 151.2 (Ar), 189.2 (C=S); MS (EI) m/z 300 (M^+); Anal. Calcd for $C_{16}H_{20}N_2SSi$: C, 63.95; H, 6.71; N, 9.32; found: C, 63.72; H, 6.86; N, 9.22.

3.2.11. *N-4-tris(trimethylsiloxy)silyl-1-(2-pyridyl)butyl benzenecarbothioamide (**14**)*

^{1}H NMR ($CDCl_3$): δ 0.00 (s, 27H), 0.38–0.45 (m, 2H), 1.22–1.31 (m, 2H), 2.10 (q, $J = 7.5$ Hz, 2H), 5.78 (q, $J = 6.8$ Hz, 1H), 7.21–7.24 (m, 1H), 7.30–7.44 (m, 4H), 7.69 (td, $J = 1.6$, 7.7 Hz, 1H), 7.80–7.82 (m, 2H), 8.54 (d, $J = 4.9$ Hz, 1H), 9.20 (brd, $J = 6.8$ Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 1.4, 1.7, 2.0, 14.2, 19.2, 38.2, 59.7, 122.7, 123.0, 126.8, 128.4, 130.9, 137.1, 141.9, 148.6, 158.5, 197.3; MS (EI) m/z 565 (M^+).

3.2.12. *N-1-(2-pyridyl)-3-butenyl benzenecarbothioamide (**15**)*

mp: 79 °C; IR (KBr): 3179, 2989, 1643, 1593, 1570, 1523, 1449, 1435, 1374, 1285, 1236, 1149, 1099, 1053, 1000, 961, 928, 776, 737, 717, 696, 553, 510 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.91 (q, $J = 6.8$ Hz, 2H), 5.04 (d, $J = 15.6$ Hz, 1H), 5.05 (d, J = 8.7 Hz, 1H), 5.63–5.74 (m, 1H), 5.84 (q, $J = 6.8$ Hz, 1H), 7.22–7.48 (m, 5H), 7.70 (td, $J = 1.6$, 7.8 Hz, 1H), 7.84 (d, $J = 7.8$ Hz, 2H), 8.58 (d, $J = 4.9$ Hz), 9.28 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ 38.9, 59.0, 118.8, 122.5, 122.7, 126.8, 128.4, 130.9, 132.7, 136.8, 141.9, 148.8, 157.7, 197.4; MS (EI) m/z 268 (M^+); Anal. Calcd for $C_{16}H_{16}N_2S$: C, 71.60; H, 6.01; N, 10.44; found: C, 71.40; H, 6.11; N, 10.24.

3.2.13. *N-4-tris(trimethylsiloxy)silyl-1-(3-pyridyl)butyl benzenecarbothioamide (**16**)*

mp: 91 °C; IR (KBr): 3201, 2957, 2360, 1536, 1489, 1449, 1432, 1378, 1360, 1318, 1252, 1194, 1179, 1055, 944, 842, 760, 713, 688, 591, 436 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ −0.04 (s, 27H), 0.42 (t, $J = 6.8$ Hz, 2H), 1.28–1.42 (m, 2H), 1.88–2.07 (m, 2H), 5.65 (q, $J = 7.6$ Hz), 7.16–7.35 (m, 4H), 7.59–7.67 (m, 3H), 8.15 (brd, $J = 7.8$ Hz, 1H), 8.34 (s, 1H), 8.56 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 1.4, 1.7, 2.0, 14.1, 20.3, 38.6, 57.5, 123.7, 126.7, 128.4, 131.1, 135.7, 137.0, 141.8, 147.9, 158.5, 199.0; MS (EI) (m/z) 565 (M^+).

3.3. *General procedure for the reduction of thioamides*

3.3.1. *N-benzyl 4-tris(trimethylsiloxy)silyl-1-phenylbutylamine (**17**)*

In a 200 mL three-necked flask, lithium aluminum hydride (2.43 g, 64.0 mmol) was added to a THF solution (32 mL) of *N*-4-tris(trimethylsiloxy)silyl-1-phenylbutyl benzenecarbothioamide (9.03 g, 16.0 mmol) at 0 °C, and the mixture was heated at reflux for 2 h with stirring. To the reaction mixture was then added water (2.4 mL), 15% NaOH aq (2.4 mL), and water (7.3 mL) at 0 °C. The resulting oil was extracted with Et_2O (20 mL), filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane:AcOEt = 8:1) to give *N*-benzyl 4-tris(trimethylsiloxy)silyl-1-phenylbutylamine (7.64 g, 14.3 mmol, 89%) as a pale yellow oil: IR (neat): 3085, 3063, 3028, 2957, 1494, 1454, 1252, 1179, 1100, 1057, 842, 756, 700, 594, 421 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.00 (s, 27H, $SiCH_3$), 0.28–0.43 (m, 2H, CH_2),1.12–1.32 (m, 2H, CH_2), 1.54–1.74 (m, 3H, CH_2, NH), 3.46–3.61 (m, 3H, CH_2, CH), 7.13–7.34 (m, 10H, Ar); ^{13}C NMR ($CDCl_3$): δ 1.7 ($SiCH_3$), 14.4 (t, $J = 18.3$ Hz, CH_2), 20.3, 41.9 (CH_2), 51.5 (t, $J = 9.0$ Hz, CH_2), 62.5 (CH), 126.8, 126.9, 127.4, 128.2, 128.3, 128.4, 140.8, 144.4 (Ar); MS (EI) m/z 518 (M^+-CH_3, H); HRMS Calcd for $C_{26}H_{47}NO_3Si_4$: 533.2633; found: 533.2601.

3.3.2. *N-[phenyl(dimethyl (1,1-dimethylethyl)silyl)methyl]benzenemethaneamine (**19**)*

IR (KBr): 3061, 3024, 2954, 2855, 1599, 1494, 1453, 1249, 1069, 1028, 833, 759, 701, 572, 514 cm^{-1}; ^1H NMR ($CDCl_3$): δ −0.39 (s, 3H, CH_3), −0.09 (s, 3H, CH_3), 0.78 (s, 9H, CH_3), 3.33 (s, 1H, CH), 3.36 (d, $J = 13.2$ Hz, 1H, CH_2), 3.66 (d, $J = 13.2$ Hz, 1H, CH_2), 7.02–7.20 (m, 10H, Ar); ^{13}C NMR ($CDCl_3$): δ −8.63, −6.76 (CH_3), 17.4 (C), 27.2 (CH_3), 53.0, 53.0 (CHNH, CH_2NH), 125.3, 126.8, 127.3, 128.2, 128.2, 128.5, 140.8, 143.3 (Ar); MS (EI) m/z 311 (M^+); HRMS Calcd for $C_{20}H_{28}NSi$ (M^+−H): 310.1991; found: 310.1971.

3.3.3. *N-[phenyl(tris(1-methylethyl)silyl)methyl]benzenemethaneamine (**20**)*

IR (KBr): 3061, 3025, 2944, 2866, 1599, 1491, 1453, 1259, 1069, 1017, 882, 769, 701, 663, 555, 517 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.91 (d, $J = 7.3$ Hz, 9H, CH_3), 0.93 (d, $J = 7.3$ Hz, 9H, CH_3), 1.04 (sept, $J = 7.3$ Hz, 3H, C<u>H</u>CH_3), 3.35 (d, $J = 13.2$ Hz, 1H, CH_2), 3.55 (s, 1H, CH), 3.69 (d, $J = 13.2$ Hz, 1H, CH_2), 7.06–7.28 (m, 10H, Ar); ^{13}C NMR ($CDCl_3$): δ 10.7 (CH), 18.8, 18.9 (CH_3), 52.9, 53.5 (CH or CH_2), 125.3, 126.7, 127.7, 128.1, 128.2, 128.4, 141.0, 143.5 (Ar); MS (EI) m/z 270 ($M^+-C_5H_{13}$); HRMS Calcd for $C_{23}H_{34}NSi$ (M^+−H): 352.2461; found: 352.2431.

3.3.4. *N-[1-naphthyl(dimethyl (1,1-dimethylethyl)silyl)methyl]benzenemethaneamine (**23**)*

IR (KBr): 3061, 2953, 2926, 2882, 1594, 1463, 1390, 1254, 1080, 1028, 909, 824, 781, 736, 700, 578, 422 cm^{-1}; ^1H NMR ($CDCl_3$): δ −0.53 (s, 3H, CH_3), 0.13 (s, 3H, CH_3), 1.07 (s, 9H, CH_3), 3.56 (d, $J = 13.0$ Hz, 1H, CH_2), 3.83 (d, $J = 13.0$ Hz, 1H, CH_2), 4.52 (s, 1H, CH), 7.27–7.46 (m, 5H, Ar), 7.50–7.61 (m, 3H, Ar), 7.70–7.78 (m, 2H, Ar), 7.91–8.08 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$): δ −9.31, −6.45 (CH_3), 17.6 (C), 19.4 (CH_3), 46.0, 53.1 (CH or CH_2), 122.9, 123.3, 125.1, 125.2, 125.5, 125.7, 126.8, 128.1, 128.6, 128.9, 132.0, 133.9, 139.8, 140.8 (Ar); MS (EI) m/z 361 (M^+); HRMS Calcd for $C_{24}H_{31}NSi$: 361.2226; found: 361.2201.

3.3.5. *N-phenylmethyl 1-4-tris(trimethylsiloxy)silyl-1-2-pyridylbutylamine (**24**)*

IR (neat): 3323, 3064, 3029, 3007, 2957, 2361, 1944, 1589, 1455, 1433, 1252, 1181, 1055, 843, 755, 697, 593 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.05 (s, 27H), 0.35–0.49 (m, 2H), 1.14–1.45 (m, 2H), 1.71–1.87 (m, 2H), 2.37 (brs, 1H), 3.59 (d, $J = 13.2$ Hz, 1H), 3.66 (d, $J = 13.2$ Hz, 1H), 3.76 (t, $J = 7.1$ Hz, 1H), 7.29–7.31 (m, 7H), 7.64 (td, $J = 1.8$, 7.6 Hz), 8.60 (d, $J = 3.9$ Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 1.4, 1.7, 2.0, 14.4, 20.1, 30.9, 40.5, 51.6, 63.4, 121.8, 122.3, 126.8, 128.2, 128.3, 136.1, 140.3, 149.4, 163.6; MS (EI) m/z 534 (M^+).

3.4. *General procedure for the hydrogenation of N-benzyl secondary amines*

3.4.1. *N-4-tris(trimethylsiloxy)silyl-1-phenylbutylamine (**26**)*

In a 200 mL three-necked flask, 20% wt $Pd(OH)_2$ (2.32 g) was added to a MeOH solution (75 mL) of *N*-benzyl 4-tris(trimethylsiloxy)silyl-1-phenylbutylamine (8.01 g, 15.0 mmol), and the mixture was stirred at room temperature for 44 h under a H_2 atmosphere. The reaction mixture was filtered with celite, extracted with MeOH and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (hexane:AcOEt:Et_3N = 3:1:1v%) to give *N*-4-tris(trimethylsiloxy)silyl-1-phenylbutylamine (6.44 g, 14.5 mmol, 97%, Rf = 0.38) as a colorless oil; IR (neat): 3085, 3063, 3028, 2957, 1944, 1604, 1494, 1454, 1411, 1252, 1179, 1059, 844, 757, 700, 593, 552 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.04 (s, 27H, $SiCH_3$), 0.36–0.49 (m, 2H, CH_2),

1.15–1.41 (m, 2H, CH_2), 1.55 (brs, s, 2H, NH_2), 1.59–1.74 (m, 2H, CH_2), 3.85 (t, $J = 7.1$ Hz, 1H, CH), 7.17–7.31 (m, 5H, Ar); ^{13}C NMR ($CDCl_3$): δ 1.7 (t, $^1J_{C-Si} = 30.0$ Hz, $SiCH_3$), 14.3, 20.4, 43.1 (CH_2), 56.1 (CH), 126.3, 126.8, 128.3, 146.6 (Ar); MS (EI) m/z 443 (M^+); HRMS Calcd for $C_{19}H_{41}NO_3Si_4$: 443.2164; found: 443.2182.

3.4.2. *N-[(1,1-dimethylethyl)silyl]benzylamine (27)*

IR (KBr): 3060, 2962, 2866, 1600, 1464, 1413, 1260, 1094, 1018, 882, 800, 701, 584, 550, 515 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.97 (d, $J = 7.3$ Hz, 9H, CH_3), 1.00 (d, $J = 7.3$ Hz, 9H, CH_3), 1.10 (sept, $J = 7.3$ Hz, 3H, CH), 1.45 (br, 2H, NH_2), 3.83 (s, 1H, C<u>H</u>NH_2), 7.06–7.07 (m, 1H, Ar), 7.18–7.24 (m, 4H, Ar); ^{13}C NMR ($CDCl_3$): δ 10.8 (CH), 17.7 (CHNH), 18.9, 18.9 (CH_3), 125.3, 126.6, 128.1, 128.1 (Ar); MS (EI) m/z 263 (M^+); HRMS Calcd for $C_{16}H_{29}NSi$: 263.2069; found: 263.2044.

Acknowledgement

This work was supported in part by a Grant-in-Aid for Scientific Research on Priority Areas (No. 19020020 "Advanced Molecular Transformations of Carbon Resources") from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

References

(1) Moore, A.J. In *Comprehensive Organic Functional Group Transformations II*; Katritzky, A.R., Taylor, R.J.K., Eds.; Pergamon: Amsterdam, 2005; Vol. 5, 519–570.
(2) Murai, T. In *Topics in Current Chemistry*; Kato, S., Ed.; Springer GmbH: Berlin, 2005; Vol. 251, 247–272.
(3) Lebel, H. In *Science of Synthesis*; Charette, A.B., Ed.; Georg Thieme Verlag KG: Stuttgart, 2005; Vol. 22, 141–179.
(4) Koketsu, M; Ishihara, H. *Curr. Org. Chem.* **2007,** *4*, 15–29.
(5) Koketsu, M; Ishihara, H. In *Handbook of Chalcogen Chemistry*; Devillanova, F.A., Ed.; RSC Publishing: Cambridge, 2007; 146–194.
(6) Brown, E.V. *Synthesis* **1975,** 358–375.
(7) Purrello, G. *Heterocycles* **2005,** *65*, 411–449.
(8) Okamoto, K.; Yamamoto, T.; Kanbara, T.; *Synlett* **2007**, 2687–2690.
(9) Fedorovich, I.S.; Ganushchak, N.I.; Karpyak, V.V.; Obushchak, N.D.; Lesyuk, A.I. *Russ. J. Org. Chem.* **2007,** *43*, 1190–1195.
(10) Darabi, R.H. *Monat. Chem.* **2007,** *138*, 61–65.
(11) Metzner, P. In *Topics in Current Chemistry*; Page, P.C.B., Ed.; Springer-Verlag: Berlin, 1999; Vol. 204, 127–181.
(12) Seebach, D.; Lubosch, W.; Enders, D. *Chem. Ber.* **1976,** *109*, 1309–1323.
(13) Lubosch, W.; Seebach, D. *Helv. Chim. Acta* **1980,** *63*, 102–116.
(14) Fitt, J.J.; Gschwend, H.W. *J. Org. Chem.* **1976,** *41*, 4029–4031.
(15) Tamaru, Y.; Kagotani, M.; Furukawa, Y.; Amino, Y.; Yoshida, Z. *Tetrahedron Lett.* **1981,** *22*, 3413–3416.
(16) Creary, X.; Zhu, C. *J. Am. Chem. Soc.* **1995,** *117*, 5859–5860.
(17) Katritzky, A.R.; Denisko, O.; Lang, H. *Tetrahedron* **1995,** *51*, 8703–8710.
(18) Dantale, S.; Reboul, V.; Metzner, P. *Chem. Eur. J.* **2002,** *8*, 632–640.
(19) Ach, D.; Reboul, V.; Metzner, P. *Eur. J. Org. Chem.* **2002,** 2573–2586.
(20) Ach, D.; Reboul, V.; Metzner, P. *Eur. J. Org. Chem.* **2003,** 3398–3406.
(21) Freifeld, I.; Armbrust, H.; Langer, P. *Synthesis* **2006,** 1807–1810.
(22) Murai, T.; Mutoh, Y.; Ohta, Y.; Murakami, M. *J. Am. Chem. Soc.* **2004,** *126*, 5968–5969.
(23) Murai, T.; Toshio, R.; Mutoh, Y. *Tetrahedron* **2006,** *62*, 6312–6320.
(24) Mutoh, Y.; Murai, T.; Yamago, S. *J. Organomet. Chem.* **2007,** *692*, 129–135.
(25) Murai, T.; Asai, F. *J. Am. Chem. Soc.* **2007,** *129*, 780–781.
(26) Shibahara, F.; Suenami, A.; Yoshida, A. *Chem. Commun.* **2007,** 2354–2356.
(27) Murai, T.; Nogawa, S.; Mutoh, Y. *Bull. Soc. Chem. Jpn.* **2007,** *80*, 2220–2225.
(28) Murai, T.; Fukushima, K; Mutoh, Y. *Org. Lett.* **2007,** *9*, 5295–5298.
(29) Shibahara, F.; Yoshida, A.; Murai, T. *Chem. Lett.* **2008,** *37*, 646–647.
(30) Asai, F.; Murai, T. *J. Org. Chem.* **2008,** *73*, 9518–9521.
(31) Murai, T,; Aso, H.; Tatematsu, Y.; Itoh, Y.; Niwa, H.; Kato, S. *J. Org. Chem.* **2003,** *68*, 8514–8519.
(32) Murai, T.; Sano, H.; Kawai, H.; Aso, H.; Shibahara, F. *J. Org. Chem.* **2005,** *70*, 8148–8153.
(33) Komatsu, M.; Kasano, Y.; Yonemori, J.; Oderaotoshi, Y.; Minakata, S. *Chem. Commun.* **2006,** 526–528.
(34) Komatsu, M.; Minakata, S.; Oderaotoshi, Y. *ARKIVOC* **2006,** 370–389.

(35) Nakamura, M.; Kawabe, K.; Yokota, M. JP 11326848, 1999.
(36) Murai, T.; Kato, Y. JP 2007023246, 2007.
(37) Brook, A.G.; Duff, J.M. *J. Am. Chem. Soc.* **1974,** *96,* 4692–4693.
(38) Duff, M.J.; Brook, G.A. *Can. J. Chem.* **1997,** *55,* 2589–2600.
(39) Sieburth, M.S.; O'Hara, K.H.; Chen, Y.; Liu, G. *Org. Lett.* **2003,** *11,* 1859–1861.
(40) Laszlo, E.K.; Jozsef, R.; Laszlo, V.; Istvan, K. *Synlett* **1998,** 1243–1245.
(41) Guziec, F.S., Jr.; Loide, M.W. *Tetrahedron Lett.* **1990,** *31,* 23–26.
(42) Vladimir, V.K.; Juliette, R.C.; Cristian, O.P.; Elena, E.S.; Jairo, R.M.; Carmen, O.; David, M.P.; Juan, J.N.R.; Carlos, F.P.; Susana, M.S.; Alicia, G.B.; Ali, B.; Juan, A.-L. *Arch. Pharm. Chem. Life Sci.* **2005,** *338,* 32–37.