# Reaction of *N,N*-Dimethyl-*N*-[(trialkylstannyl)methyl]benzylammonium Iodides with Organolithium Compounds

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Although ammonium or sulfonium ylide intermediates are usually generated by the α-deprotonation of tetraorganoammonium or triorganosulfonium salts with a strong base, the reaction products are often complex mixtures because of the simultaneous formation of multiple ylides.[1] On the other hand, the fluoride ion-induced desilylation of [1-(trimethylsilyl)alkyl]ammonium or -sulfonium salts is a good technique for ylide formation because a single ylide is quantitatively formed at room temperature.[2−4] Under these nonbasic conditions, however, the isomerization of benzylammonium *N*-alkylides sometimes stops at [2,3] sigmatropic migration, especially when producing bicyclic conjugated triene compounds (*isotoluenes*).[5] In such cases, the addition of a strongly basic amine (e.g., DBU) to the reaction mixtures is required for the aromatization of isotoluenes to Sommelet−Hauser rearrangement products.[6]

When *N*-[1-(trialkylstannyl)alkyl]benzylammonium salts are subjected to base-induced destannylation,[7] benzylammonium *N*-alkylides might be formed regioselectively under basic conditions. Recently, Gawley et al. reported the first example of ylide rearrangement in the reaction of *N,N*-diallyl-2-(tributylstannyl)pyrrolidinium bromide with butyllithium.[8] We examined the reaction of *N*-[(trialkylstannyl)methyl]benzylammonium salts with organolithium compounds.

*N,N*-Dimethyl-*N*-[(trimethylstannyl)methyl]benzylammonium iodide (**2a**) and an *N*-[(tributylstannyl)methyl] analogue (**2b**) were prepared by reacting of *N*-methylbenzylamine (**1**) with (iodomethyl)trialkyltins followed by iodomethane (Scheme 1).

Treatment of a THF solution of **2b** with butyllithium (1 mole equiv) at −78 °C gave a mixture of *N,N*-dimethyl-2-methylbenzylamine **3** (Sommelet-Hauser rearrangement product) and *N,N*-dimethyl-2-[(tributylstannyl)-methyl]benzylamine (**4b**) (total yield 63%, ratio of **3** to **4b** = 66:34) (Table 1, entry 5). Compound **4b** may be formed by an intramolecular [1,4] stannyl migration in isotoluene **9b**, which is a [2,3] sigmatropic migration product of ylide **8b**. We observed a similar migration of triorganosilyl groups in the reaction of *N,N*-dimethyl-*N*-[(triorganosilyl)methyl]benzylammonium halides with butyllithium[9] and in the formation of (3-furylmethyl)- and (3-thienylmethyl)ammonium methylides.[10] Thus, two ylides **5** and **8** are competitively formed by the nucleophilic attack of butyl anion to the tin and to a hydrogen of the $N^+CH_2Sn$ group (Scheme 2).

To obtain higher selectivity, we tested various bases and trialkylstannyl groups (Table 1). Although the highest ratio of **3** was obtained with methylmagnesium bromide, the yield in this case was low (entry 8).

**Scheme 1**

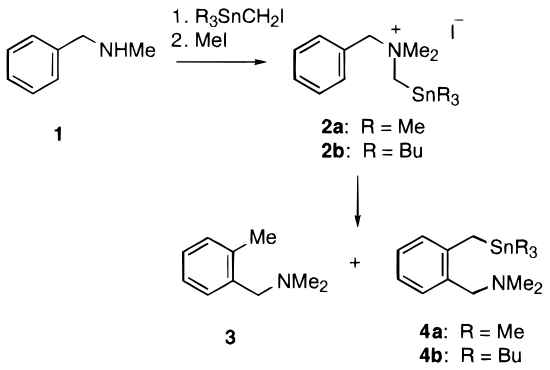


**Table 1. Reaction of *N,N*-Dimethyl-*N*-[(trialkylstannyl)methyl]benzylammonium Iodides 2a,b with Base in THF at −78 °C**

| entry | salt | R | base | total yield of **3** and **4**, % | product ratio[a] **3** | **4** |
|---|---|---|---|---|---|---|
| 1 | **2a** | Me | MeLi | 60 | 60 | 40 |
| 2 | **2a** | Me | BuLi | 59 | 56 | 44 |
| 3 | **2a** | Me | PhLi | 63 | 52 | 48 |
| 4 | **2b** | Bu | MeLi | 41 | 78 | 22 |
| 5 | **2b** | Bu | BuLi | 63 | 66 | 34 |
| 6 | **2b** | Bu | *t*-BuLi | 14 | 48 | 52 |
| 7 | **2b** | Bu | PhLi | 61 | 82 | 18 |
| 8 | **2b** | Bu | MeMgBr | 33 | 98 | 2 |
| 9 | **2b** | Bu | LDA | 72 | 8 | 92 |

[a] The ratio was determined by GC analysis.

**Scheme 2**

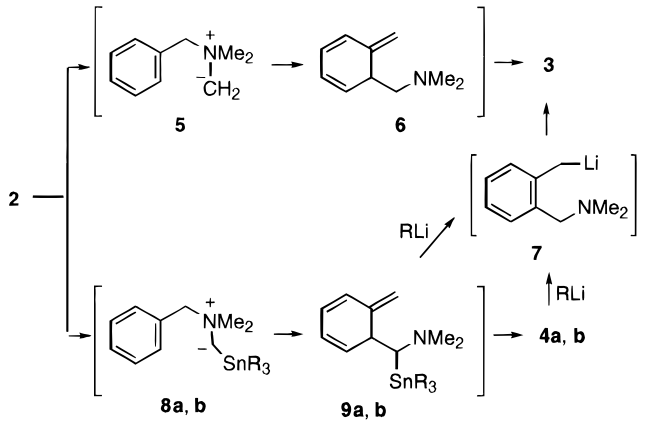


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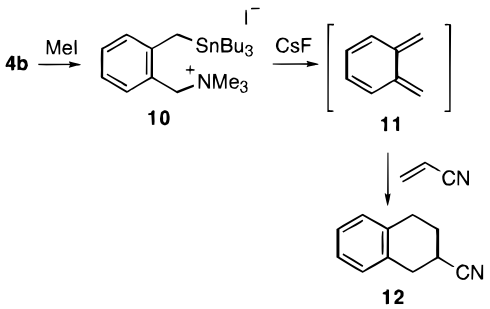
**Table 2. Reaction of 2b with BuLi**

| entry | BuLi mol equiv | solvent | reaction temp, °C | total yield, % | product ratio[a] 3 | 4b |
|---|---|---|---|---|---|---|
| 1 | 1.0 | THF | −78 | 63 | 66 | 34 |
| 2 | 1.0 | THF | 0 | 85 | 22 | 78 |
| 3 | 1.5 | THF | −78 | 65 | 100 | 0 |
| 4 | 1.0 | THF/TMEDA[b] | −78 | 51 | 23 | 77 |
| 5 | 1.0 | THF/HMPA[b] | −78 | 60 | 48 | 52 |
| 6 | 1.0 | DME | −60 | 71 | 10 | 90 |
| 7 | 1.0 | DME | 0 | 85 | 13 | 87 |
| 8 | 1.5 | DME | −60 | 73 | 47 | 53 |
| 9 | 2.0 | DME | −60 | 63 | 100 | 0 |
| 10 | 1.0 | $Et_2O$ | −78 | 50 | 16 | 84 |
| 11 | 1.0 | $Et_2O$ | 0 | 69 | 27 | 73 |
| 12 | 1.5 | $Et_2O$ | −78 | 71 | 27 | 73 |
| 13 | 2.0 | $Et_2O$ | −78 | 61 | 88 | 12 |

[a] The ratio was determined by GC analysis. [b] TMEDA or HMPA (1.0 mol equiv) was added.

**Scheme 3**




Phenyllithium gave a better yield, but a byproduct, tributylphenyltin, caused problems in GC analysis because of insufficient separation among the products (entry 7). *tert*-Butyllithium gave a mixture with many byproducts (entry 6), while the selective generation of **4** was achieved using LDA (entry 9).

When DME or ether was used as the solvent or when 1 mol equiv of TMEDA or HMPA was added to THF, the percentage of **3** was reduced (Table 2, entries 1, 4−6, 10). A reaction temperature of 0 °C gave a lower yield of **3** in THF, but a slightly increased yield in DME and ether (entries 2, 7, 11). Thus, selective formation was difficult under these conditions. However, the use of an excess of butyllithium (1.5 mol equiv in THF or 2.0 mol in DME) gave **3** selectively (entries 3, 9). This selectivity results in the conversion of **4b** or **9b** to **3** by destannylation with excess butyllithium via **7**. The main path may be from **9b** to **3** because the change from **4b** to **3** with butyllithium was slow at −78 °C. More butyllithium was required in DME than in THF for this selective formation because more **4b** was formed in DME (compare entries 1 and 6). Excess butyllithium had much less of an effect (entries 12, 13).

Ito et al. reported that *N*,*N*,*N*-trimethyl-2-[(trimethylsilyl)methyl]benzylammonium halides are a good source of *o*-quinodimethane.[11] When **4b** was quaternized with iodomethane to **10** and then treated with CsF in the presence of acrylonitrile, 1,2,3,4-tetrahydro-2-naphthalenecarbonitrile (**12**) was obtained in 74% yield. Amine **4** is also available as an *o*-quinodimethane precursor.

## Experimental Section

**General.** All reactions were carried out in $N_2$. THF and diethyl ether were distilled from sodium and benzophenone. DME was distilled from $LiAlH_4$. DMF was distilled under reduced pressure from BaO. HMPA was dried by distillation from sodium under reduced pressure, and TMEDA was dried by distillation from $CaH_2$. CsF was dried over $P_2O_5$ at 180 °C under reduced pressure. Mass spectra were obtained using EI ionization. GC analyses were performed using a 2-m, 5% SE-30 on a Uniport HP column. Aluminum oxide (Merck, 70−230 mesh) was used for column chromatography. All melting points and boiling points are uncorrected.

*N*-[(Trimethylstannyl)methyl]- and *N*-[(tributylstannyl)methyl-*N*-methylbenzylamines: A solution *N*-methylbenzylamine (**1**) (4.5 g, 37.0 mmol) and (iodomethyl)tributyltin[12] (8.0 g, 18.5 mmol) or (iodomethyl)trimethyltin[10b] (5.6 g, 18.5 mmol) in THF (20 mL) was stirred at rt for 24 h. Deposited white crystals were filtered and washed with ether (150 mL). The filtrate and washings were combined and washed with water (100 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was distilled under reduced pressure.

***N*-Methyl-*N*-[(trimethylstannyl)methyl]benzylamine:** yield 4.8 g (87%); bp 84−86 °C (0.9 mmHg); IR (film) 2770, 1450, 1120, 760, 740, 700, 520 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 0.16 (t, $J$ = 26.2 Hz, 9 H), 2.21 (s, 3 H), 2.55 (t, $J$ = 12.6 Hz, 2 H), 3.43 (s, 2 H), 7.22−7.37 (m, 5 H). Anal. Calcd for $C_{12}H_{21}NSn$: C, 48.37; H, 7.10; N, 4.70. Found: C, 48.13; H, 7.06; N, 4.66.

***N*-Methyl-*N*-[(tributylstannyl)methyl]benzylamine:**[13] yield 6.0 g (77%); bp 131−140 °C (0.3 mmHg).

**Quaternization of the Amines.** A solution of *N*-methyl-*N*-[(trialkylstannyl)methyl]benzylamine (16.8 mmol) and iodomethane (3.8 g, 26.4 mmol) in THF (15 mL) was stirred at rt for 1 h. The solvent was removed, and the residue was recrystallized from a mixture of acetone and hexane.

***N*,*N*-Dimethyl-*N*-[(trimethylstannyl)methyl]benzylammonium Iodide (2a):** yield 6.8 g (92%); mp 169−170 °C; IR (Nujol) 1380, 870, 780, 730, 540 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 0.42 (t, $J$ = 27.8 Hz, 9 H), 3.31 (s, 6 H), 3.56 (t, $J$ = 14.1 Hz, 2 H), 5.05 (s, 2 H), 7.43−7.51 (m, 3 H), 7.67−7.69 (m, 2 H). Anal. Calcd for $C_{13}H_{24}INSn$: C, 35.49; H, 5.50; N, 3.18. Found: C, 35.52; H, 5.50; N, 3.23.

***N*,*N*-Dimethyl-*N*-[(tributylstannyl)methyl]benzylammonium Iodide (2b):** yield 7.6 g (80%); mp 97−98 °C; IR (Nujol) 1380, 880, 730, 710, 670 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$ 0.87−0.93 (m, 9 H), 1.08−1.14 (m, 6 H), 1.28−1.59 (m, 12 H), 3.29 (s, 6 H), 3.40 (t, $J$ = 12.2 Hz, 2 H), 5.04 (s, 2 H), 7.43−7.70 (m, 5 H). Anal. Calcd for $C_{22}H_{42}INSn$: C, 46.67; H, 7.48; N, 2.47. Found: C, 46.51; H, 7.33; N, 2.69.

**Reaction of 2a,b with Base.** Ammonium salt **2** (1 mmol) was placed in a 20-mL flask equipped with a septum, thermometer, and magnetic stirrer. The apparatus was dried under reduced pressure and was flushed with $N_2$. A solvent (5 mL) was added to the flask by syringe, and the mixture was cooled at the temperature indicated in Tables 1 and 2. To the solution was added one of the following bases (1 mmol): MeLi (1.0 M in $Et_2O$), BuLi (1.52 M in hexane), *tert*-BuLi (1.7 M in pentane), PhLi (1.8 M in cyclohexane/$Et_2O$, 7:3), methylmagnesium bromide (0.92 M in THF), or LDA (1 M in THF). The mixture was stirred 1 h and then poured into water (20 mL) and extracted with ether (3 × 20 mL). The ether layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was chromatographed on an aluminum oxide column (ether/hexane, 1:10) to yield *N*,*N*-dimethyl-2-methylbenzylamine (**3**) and *N*,*N*-dimethyl-2-[(trimethylstannyl)methyl]benzylamine (**4a**) or *N*,*N*-dimethyl-2-[(tributylstannyl)methyl]benzylamine (**4b**). The yields and ratios were determined by comparison of the integrated values of GC analyses (5% SE-30) of the ethereal extract using an internal standard (octadecane, 127 mg, 0.5 mmol). The results are listed in Table 1.

**4a**: bp 98 °C (0.8 mmHg); IR (film) 2820, 2760, 1490, 1460, 1020, 760, 520 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$ 0.00 (t, $J$ = 26.6 Hz, 9 H) , 2.19 (s, 6 H), 2.41 (t, $J$ = 32.9 Hz, 2 H), 3.26 (s, 2 H), 6.89−6.99 (m, 2 H), 7.07−7.12 (m, 2 H); $m/z$ 298 (81, $M^+$ − 14), 294 (34), 165 (31), 146 (75), 105 (100). Anal. Calcd for $C_{13}H_{23}NSn$: C, 50.04; H, 7.43; N, 4.49. Found: C, 49.89; H, 7.39 ; N, 4.52.

**4b**: bp 155 °C (0.7 mmHg); IR (film) 2950, 2920, 1460, 1120, 750 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$ 0.74−0.89 (m, 15 H),

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1.20−1.46 (m, 12 H), 2.22 (s, 6 H), 2.41 (t, $J$ = 29.7 Hz, 2 H), 3.27 (s, 2 H), 6.88−7.13 (m, 4 H). $m/z$ 382 (100, $M^+ - 56$), 235 (29), 179 (46), 105 (53). Anal. Calcd for $C_{22}H_{41}NSn$: C, 60.29; H, 9.43; N, 3.20. Found: C, 60.10; H, 9.54; N, 3.07.

**Reaction of 2b with Cesium Fluoride.** Salt **2b** (566 mg, 1 mmol) was placed in a 20-mL flask equipped with a septum, thermometer, and a test tube which was connected with the flask by a short bent glass tube. CsF (456 mg, 3 mmol) was placed in the test tube. The apparatus was dried under reduced pressure and was flushed with $N_2$. DMF (5 mL) was added to the flask, and CsF was added from the test tube. The mixture was stirred for 24 h at rt, poured into water (10 mL), and extracted with ether (3 × 20 mL). The ethereal extract was washed with water (2 × 50 mL), dried, and concentrated under reduced pressure to give **3** (67 mg, 45%).

**Reaction of 4b with Butyllithium.** To a solution of **4b** (437 mg, 1 mmol) in THF (5 mL) was added butyllithium (1.52 M in hexane, 1 mmol) at −70 °C, The mixture was stirred for 1 h, poured into water (20 mL), and extracted with ether (3 × 20 mL). The extract was analyzed on a GC using the internal standard (octadecane). The products were a mixture of **3** and **4b** (81%, 32:68).

***N,N,N*-Trimethyl-2-[(tributylstannyl)methyl]benzylammonium Iodide (10).** A solution of **4b** (5.5 g, 12.5 mmol) and iodomethane (3.5 g, 24.6 mmol) in THF (15 mL) was stirred for 4 h at rt. The solvent was removed, and the residue was recrystallized from a mixture of acetone and hexane to give **10** (5.7 g, 79%): mp 109−110 °C; IR (Nujol) 1600, 1380, 1190, 880, 770 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$ 0.81−0.93 (m, 15 H), 1.17−1.44 (m, 12 H), 2.48 (t, $J$ = 27.5 Hz, 2 H), 3.47 (s, 9 H), 4.70 (s, 2 H), 7.07−7.12 (m, 2 H), 7.29−7.34 (m, 1 H), 7.49−7.51 (m, 1 H). Anal. Calcd for $C_{23}H_{44}INSn$: C, 47.61; H, 7.64; N, 2.41. Found: C, 47.47; H, 7.38; N, 2.45.

**Reaction of 10 with Cesium Fluoride in the Presence of Acrylonitrile.** In a manner similar to that described for the reaction of **2b** with CsF, **10** (580 mg, 1 mmol) was placed in a 20-mL flask. DMF (5 mL) and acrylonitrile (159 mg, 3 mmol) were added to the flask and then CsF was added. The mixture was stirred for 24 h at rt and poured into water (20 mL). Fluorotributyltin precipitated was filtered and washed with ether (60 mL). The filtrate and washings were combined and washed with water (3 × 50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was distilled by a Kugelrohr distillation apparatus at 140 °C (2 mmHg) to give 1,2,3,4-tetrahydro-2-naphthalenecarbonitrile[11] (**12**). Yield 116 mg (74%); mp 53−55 °C.

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# *Additions and Corrections*

Vol. 60, 1995

**Donald J. Gallagher, Shengde Wu, Nikola A. Nikolic, and Peter Beak*.** Chiral Organolithium Complexes: The Effect of Ligand Structure on the Enantioselective Deprotonation of Boc-Pyrrolidine.

Page 8153, right column. In the experimental procedure reported for the synthesis of compound **36**, the reagents for the Wolff−Kishner reaction were accidently omitted. The first sentence of the second paragraph of the procedure should read "The yellow oil obtained in the previous step, anhydrous hydrazine (0.704 g, 21.9 mmol), and potassium *tert*-butoxide (1.21 g, 10.8 mmol) were dissolved in BuOH (15 mL) and heated to 180 °C in a sealed glass tube for 12 h."

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Vol. 61, 1996

**Mahendra D. Chordia and David G. I. Kingston*.** Synthesis and Biological Evaluation of 2-*epi*-Paclitaxel.

Page 800, column 2, fifth line of experimental procedure for **2′-(*tert*-Butyldimethylsilyl)-2-debenzoyl-7-(triethylsilyl)paclitaxel (3).** The volume of benzyltrimethylammonium hydroxide should be 100 $\mu$L.

JO964005J

S0022-3263(96)04005-4

**Charles S. Swindell,* Madhavi C. Chandler, Julia M. Heerding, Peter G. Klimko, Leera T. Rahman, J. Venkat Raman, and Hemalatha Venkataraman.** Taxane Synthesis through Intramolecular Pinacol Coupling at C-1−C-2. Construction and Oxidative Transformations of a C-Aromatic Taxane Diene.

Page 1101, footnote 1. The following preliminary report of a total synthesis of taxol regrettably was omitted: Masters, J. J.; Link, J. T.; Snyder, L. B.; Young, W. B.; Danishefsky, S. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1723−1726. [Subsequently: Danishefsky, S. J.; Masters, J. J.; Young, W. B.; Link, J. T.; Snyder, L. B.; Magee, T. V.; Jung, D. K.; Isaacs, R. C. A.; Bornmann, W. G.; Alaimo, C. A.; Coburn, C. A.; Di Grandi, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 2843−2859.]

JO9640074

S0022-3263(96)04007-8

**Charles S. Swindell* and Weiming Fan.** Taxane Synthesis through Intramolecular Pinacol Coupling at C-1−C-2. Highly Oxygenated C-Aromatic Taxanes.

Page 1109, footnote 2. The following preliminary report of a total synthesis of taxol regrettably was omitted: Masters, J. J.; Link, J. T.; Snyder, L. B.; Young, W. B.; Danishefsky, S. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1723−1726. [Subsequently: Danishefsky, S. J.; Masters, J. J.; Young, W. B.; Link, J. T.; Snyder, L. B.; Magee, T. V.; Jung, D. K.; Isaacs, R. C. A.; Bornmann, W. G.; Alaimo, C. A.; Coburn, C. A.; Di Grandi, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 2843−2859.]

JO964008W

S0022-3263(96)04008-X

**Ravi S. Garigipati, Bruce Adams, Jerry L. Adams, and Susanta K. Sarkar*.** Use of Spin Echo Magic Angle Spinning $^1H$ NMR in Reaction Monitoring in Combinatorial Organic Synthesis.

Page 2911. The correct affiliations for Dr. Bruce Adams and Dr. Susanta K. Sarkar are as follows. Dr. Bruce Adams: Varian Instruments, 25 Hanover Road, Florham Park, New Jersey 07932. Dr. Susanta K. Sarkar: Department of Physical and Structural Chemistry, SmithKline Beecham Pharmaceuticals, 709 Swedeland Road, King of Prussia, Pennsylvania 19406.

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S0022-3263(96)04011-X