Convenient Preparation of 1-(*N,N*-Dialkylamino)alkyltributylstannanes from 1-(*N,N*-Dialkylamino)alkylbenzotriazoles

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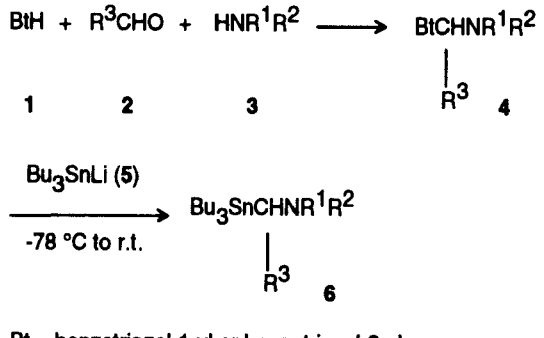
The title compounds have been prepared conveniently and in high yield from 1-(*N,N*-dialkylamino)alkyltributylbenzotriazoles and tributyltinlithium.

1-(*N,N*-Dialkylamino)alkyltributylstannanes are precursors for 1-(*N,N*-dialkylamino)alkylorganolithium reagents[1-2] which are important synthons in organic synthesis. They react with ketones[3-8] and aldehydes[3-8] to give β-amino alcohols, with CO_2 to give α-aminocarboxylic acids,[8] and with alkyl halides to give alkylated amines.[6,8] Four main methods have been reported for the synthesis of 1-(*N,N*-dialkylamino)alkyltributylstannanes: (a), reaction of halomethyltrialkylstannanes with amines or their alkali salts[9] is limited to the synthesis of 1-(*N,N*-dialkylamino)methyltributylstannanes; (b), reactions of trialkylstannyllithium and aminomethyl phenyl sulfides require the use of thiophenol to prepare the aminomethyl phenyl sulfide intermediates;[3,9] (c), reactions of tributyltinmagnesium chloride utilize liquid amino acetals;[3] (d) reaction of tributylstannylmagnesium chloride with immonium salts is the most general method.[5]

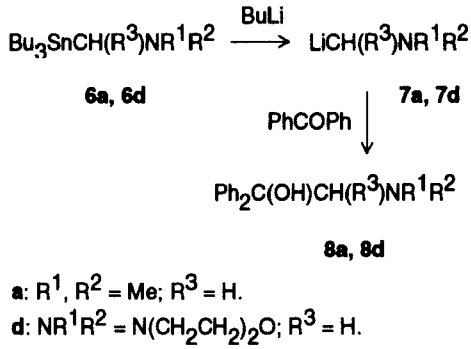


Scheme 1

We now disclose a simple and efficient preparation of α-aminoalkyltrialkylstannanes (Scheme 1) from α-(*N,N*-dialkylamino)alkylbenzotriazole intermediates **4** which are easily prepared from benzotriazole, an aldehyde and the corresponding amine[10-11] (Table 1). The reaction of **4** with tributyltinlithium **(5)**, readily obtained by the lithiation of tributyltin hydride with LDA, gives the corresponding *N,N*-disubstituted α-aminoalkyltributyltin derivatives **6** in high yields (Tables 1 and 2). A new indole-substituted stannane **6i** was also obtained conveniently by the current method in 55% yield.

Compared to methods (c) and (d) described above, which use Grignard reagents and liquid amino acetals or immonium halides to obtain the target compounds **6**, our synthetic route appears to be more convenient, as the intermediates **4** are solid and easy to obtain pure in high yield.

As discussed above, transmetalation of compounds **6** with butyllithium is well known to give very useful aminomethyllithiums **7**; we provide two further examples, the reactions of **7a** and **7d** with benzophenone to afford the corresponding β-amino tertiary alcohols **8a** and **8d**



Scheme 2

In conclusion, a novel procedure for the preparation of 1-(*N,N*-dialkylamino)alkyltributylstannanes has been developed. The starting materials **4** are cheap, easy to handle and are reasonably stable. The workup procedure is very simple, the products are easily purified and yields are good to excellent.

Melting points were determined on a Thomas-Hoover melting point apparatus and were not corrected. ^{13}C and ^{1}H NMR spectra were obtained on a VXR-300 NMR spectrometer in $CDCl_3$ with TMS

Table 1. Preparation of 1-(*N,N*-Dialkylamino)alkylbenzotriazoles **4**[a] and 1-(*N,N*-Dialkylamino)alkyltributylstannanes **6**[b]

Products 4 and 6	NR^1R^2	R^3	Yield of 4 (%)	Yield of 6[c] (%)
a	NMe_2	H	92[12]	75[3]
b	NEt_2	H	91[10]	77[3]
c	$N(i\text{-}Bu)_2$	H	88[13]	73[9]
d	*N*-morpholinyl	H	96[11]	78[16]
e	$N(CH_2Ph)_2$	H	72[10]	76
f	*N*-pyrrolidinyl	H	84[11]	85[1]
g	*N*-piperidyl	H	78[14]	75[3]
h	NMe(*c*-hexyl)	H	76[14]	90[9]
i	*N*-indolyl	H	68[15,d]	55
j	*N*-morpholinyl	Pr	84[10]	89
k	*N*-morpholinyl	*i*-Pr	74[11]	83
l	$N(CH_2Ph)_2$	*i*-Pr	81[10]	74

[a] All compounds **4** were prepared by the literature methods cited, and their mp, ^{1}H or ^{13}C NMR data were in agreement with those reported.

[b] Compounds **6** are all oils. Compounds **6** and **8a, d** gave C, H, N ± 0.036%, except **6a**, N − 0.58; **6c**, H − 0.75%.

[c] References are given as superscripts for those compounds **6** previously reported.

[d] Prepared from indole and 1-chloromethylbenzotriazole.[15]

Table 2. ^1H and ^{13}C NMR Data[a] for Products **6**

Product	^1H NMR δ, J (Hz)	^{13}C NMR δ
a	0.80–1.70 (m, 27H), 2.27 (s, 6H), 2.51 (s, $^2J_{SnH}$ = 12.5, 2H)	9.7, 13.4, 27.1, 28.9, 47.8, 49.0
b	0.80–1.80 (m, 33H), 2.42 (q, J = 7.1, 4H), 2.73 (s, $^2J_{SnH}$ = 9.5, 2H)	10.5, 12.4, 13.6, 27.4, 29.2, 41.5, 51.7
c	0.80–1.80 (m, 41H), 1.95 (d, J = 7.3, 4H), 2.65 (s, $^2J_{SnH}$ = 7.5, 2H)	10.6, 13.7, 20.7, 26.5, 27.5, 29.3, 43.9, 67.8
d	0.80–1.60 (m, 27H), 2.34 (t, J = 4.3, 4H), 2.46 (s, $^2J_{SnH}$ = 12,4, 2H), 3.68 (t, J = 4.3, 4H)	9.9, 13.6, 27.3, 29.1, 46.8, 57.3, 66.9
e	0.80–1.70 (m, 27H), 2.53 (s, $^2J_{SnH}$ = 12.2, 2H), 3.47 (s, 4H), 7.10–7.50 (m, 10H)	9.9, 13.7, 27.4, 29.1, 42.7, 62.4, 126.7, 126.9, 128.3, 128.5
f	0.80–1.60 (m, 27H), 1.83 (m, 4H), 2.52 (m, 4H), 2.61 (s, $^2J_{SnH}$ = 13.7, 2H)	9.9, 13.6, 24.1, 27.3, 28.9, 41.8, 58.2
g	0.80–1.70 (m, 33H), 2.28 (m, 4H), 2.53 (s, $^2J_{SnH}$ = 11.2, 2H)	10.3, 13.7, 23.7, 26.2, 27.4, 29.2, 47.7, 58.2
h	0.80–2.00 (m, 38H), 2.24 (s, 3H), 2.67 (s, $^2J_{SnH}$ = 12.5, 2H)	10.1, 13.6, 25.6, 26.1, 27.4, 27.8, 29.2, 42.3, 42.7, 65.2
i	0.72–1.55 (m, 27H), 3.96 (s, $^2J_{SnH}$ = 10.2, 2H), 6.44 (d, J = 2.8, 1H), 6.96 (d, J = 2.8, 1H), 7.03–7.61 (m, 4H)	9.9, 13.6, 27.6, 28.8, 30.5, 100.3, 109.3, 118.7, 120.7, 120.9, 128.2, 128.4, 136.4
j	0.76–1.90 (m, 34H), 2.27 (m, 2H), 2.51 (m, 2H), 2.82 (q, J = 6.2, CH, 1H), 3.70 (m, 4H)	10.7, 13.7, 13.9, 21.7, 27.6, 29.4, 33.7, 53.4, 61.8, 67.1
k	0.80–1.60 (m, 33H), 2.00 (m, 1H), 2.28 (m, 2H), 2.44 (d, J = 9.9, 1H), 3.68 (m, 4H)	11.8, 13.7, 22.3, 22.6, 27.6, 29.4, 30.7, 53.3, 67.2, 70.9
l	0.78–1.62 (m, 33H), 2.13 (m, 1H), 2.61 (d, J = 10.9, 1H), 3.10 (d, J = 13.4, 2H), 3.88 (d, J = 13.4, 2H), 7.15–7.42 (m, 10H)	12.1, 13.7, 22.2, 22.8, 27.7, 29.5, 30.9, 58.5, 66.7, 126.8, 128.1, 128.9, 140.2

[a] Obtained from solutions in $CDCl_3$ with TMS as the internal reference on a Varian VXR-300 spectrometer.

as the internal standard. Column chromatography was performed on silica gel (230–400 mesh). Elemental analyses were performed at the Chemistry Department, University of Florida. (*N,N*-Dialkylaminomethyl)benzotriazoles **4** were prepared as previously described (Table 1).

1-(*N,N*-Dialkylamino)alkyltributylstannanes 6; General Procedure:
A mixture of dry THF (15 mL) and LDA (10.1 mmol) was cooled to 0 °C under N_2, and $HSnBu_3$ (10 mmol) was added. After stirring at 0 °C for 15 min, the reaction mixture was cooled to − 78 °C, and a solution of 1-(*N,N*-dialkylamino)alkylbenzotriazole (7 mmol) in THF (10–20 mL) was added via a syringe. The mixture was stirred at − 78 °C for 1 h, allowed to warm to r.t. and stirred for 24 h. The mixture was poured into water (50 mL), extracted with Et_2O (2 × 50 mL), washed with water (50 mL), and dried ($MgSO_4$). The solvent was removed under vacuum to give an oily residue which was subjected to column chromatography (silica gel; CH_2Cl_2 or EtOAc) to give **6** as oils.

α-Amino Alcohols 8a and 8d; General Procedure:
To a solution of **7a** or **7d** (2.56 mmol) in THF (10 mL) at − 78 °C under N_2 was added a 2.5 M solution of BuLi in hexane (0.97 mL, 2.43 mmol). After 5 min, a solution of benzophenone (0.36 g, 2 mmol) in THF (3 mL) was added. After stirring at − 78 °C for 15 min, the reaction was quenched by addition of 20% aq NH_4Cl (40 mL). The mixture was extracted with Et_2O (2 × 50 mL), washed with water (50 mL), and dried ($MgSO_4$). The solvent was removed under vacuum to give a residue which was subjected to column chromatography to give **8a** or **8d** as solids.

2-Dimethylamino-1,1-diphenylethanol **(8a)**:
Compound **8a** was prepared by the above general procedure in 71% yield as a solid, mp 45 °C.

^1H NMR: δ = 2.11 (s, 6H), 3.20 (s, 2H), 7.12–7.20 (m, 2H), 7.22–7.30 (m, 4H), 7.45–7.55 (m, 4H).

^{13}C NMR: δ = 47.1, 68.9, 74.2, 125.6, 126.5, 128.1, 147.1.

2-(N-Morpholinyl)-1,1-diphenylethanol **(8d)**:
Compound **8d** was prepared by the above general procedure in 92% yield as a solid, mp 81–82 °C (Lit.[17] 78–79 °C).

^1H NMR: δ = 2.34 (t, J = 4.2, 4H), 3.25 (s, 2H), 3.55 (t, J = 4.2, 4H), 5.16 (s, 1H), 7.10–7.55 (m, 10H).

^{13}C NMR: δ = 54.7, 67.0, 68.2, 74.1, 125.5, 126.6, 128.1, 146.8.

(1) Peterson, D.J. *Organomet. Chem. Rev. A* **1972**, *7*, 295.
(2) Krief, A. *Tetrahedron* **1980**, *36*, 2531.
(3) Quintard, J-P.; Elissondo, B.; Jousseaume, B. *Synthesis* **1984**, 495.
(4) Verlhac, J-B.; Quintard, J-P. *Tetrahedron Lett.* **1986**, *27*, 2361.
(5) Elissondo, B.; Verlhac, J-B.; Quintard, J-P.; Pereyre, M. *J. Organomet. Chem.* **1988**, *339*, 267.
(6) Pearson, W.H.; Lindbeck, A.C. *J. Org. Chem.* **1989**, *54*, 5651.
(7) Pearson, W.H.; Lindbeck, A.C. *J. Am. Chem. Soc.* **1991**, *113*, 8546.
(8) Chong, J.M.; Park, S.B. *J. Org. Chem.* **1992**, *57*, 2220.
(9) Abel, E.W.; Rowley, R.J. *J. Organomet. Chem.* **1975**, *97*, 159.
(10) Katritzky, A.R.; Yannakopoulou, K.; Lue, P.; Rasala, D.; Urogdi, L. *J. Chem. Soc. Perkin Trans. 1* **1989**, 225.
(11) Katritzky, A.R.; Yannakopoulou, K. *Heterocycles* **1989**, *28*, 1121.
(12) Burckhalter, J.H.; Stephens, V.C.; Hall, L.A.R. *J. Am. Chem. Soc.* **1952**, *74*, 3868.
(13) Katritzky, A.R.; Shobana, N.; Harris, P.A. *Organometallics* **1992**, *11*, 1381.
(14) Smith, J.R.L.; Sadd, J.S. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1181.
(15) Katritzky, A.R.; Drewniak-Deyrup, M.; Lan, X.; Brunner, F. *J. Heterocyclic Chem.* **1989**, *26*, 829.
(16) Peterson, D.J. *J. Am. Chem. Soc.* **1971**, *93*, 4027.
(17) Melandri, M.; Buttini, A.; Carminati, G.; Galimberti, P. *Chim. Therap.* **1966**, *4*, 212; *Chem. Abstr.* **1967**, *66*, 2533d.