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The Effect of Protecting Groups on Tin-Lithium Exchange in α-Alkoxyalkyltrimethylstannanes

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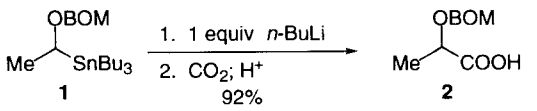
Abstract

MOM-protected α-hydroxytrimethylstannanes do not undergo tin-lithium exchange cleanly as their tributyl-counterparts do. Other protecting groups (*e.g. N,N*-diethylcarbamate) allow for clean transmetalation to occur presumably due to the formation of a more stable α-alkoxyorganolithium species.
Keywords: lithium and compounds; protecting groups; tin and compounds; transmetalation

Since Still introduced the use of α-alkoxyorganostannanes as precursors of α-alkoxyorganolithiums by tin-lithium exchange [1,2], this chemistry has been exploited in a variety of applications [3]. It is significant that essentially all of the transmetalation chemistry of α-alkoxyorganostannanes reported thus far has been with tri-*n*-butylstannanes. The popularity of tributylstannyl groups is to be expected since they are most readily available and were the original group used by Still. However, there are advantages in using other trialkylstannyl groups, particularly trimethylstannyl groups; advantages include spectral simplicity and the formation of an easily removed volatile by-product (Me_4Sn, bp 77 °C) [4]. In fact, trimethylstannyl groups have been widely used in other aspects of organotin chemistry including Stille couplings [5], reactions of vinylstannanes [6] and stannylcuprates [7]. α-Alkoxytrimethylstannanes could be valuable as synthetic intermediates, particularly since enantiomerically-enriched (>98% ee) α-hydroxytrimethylstannanes (but not tributylstannanes) may be efficiently prepared by kinetic resolution using porcine pancreas lipase (PPL) as an acylation catalyst [8]. Unfortunately, there is evidence that α-alkoxyorganotrimethylstannanes do not undergo transmetalations as well as their tributyl analogues [8,9]. The contrast between the following reactions [8,10] is illustrative:



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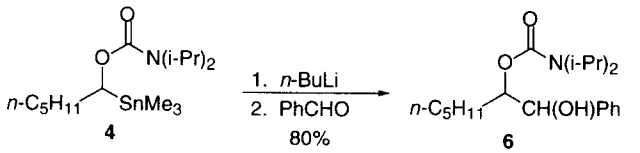
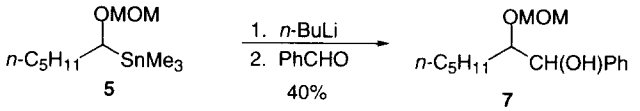
Thus, while tributylstannane **1** underwent quantitative transmetalation with 1 equiv of *n*-BuLi to provide an α-alkoxyorganolithium species which could be trapped in 92% yield with CO_2, the trimethylstannane **3** required 10 equiv of *n*-BuLi in order to generate reasonable amounts of α-alkoxyorganolithium and still only provided a 58% yield of the same trapped product. Hence, it is not too surprising that there has been a noticeable lack of synthetic applications reported for α-alkoxyorganotrimethylstannanes [11]. We report herein our efforts to fill this void.

It is likely that the difference in transmetalation chemistry of **1** and **3** is due to the difference in stabilities of organolithiums involved. In fact, McGarvey has shown that the stability of organolithiums decreases in the order: R^1OCH_2Li > $R^1OCH(R^2)Li$ > MeLi > $R^1OCR^2R^3Li$ > *n*-BuLi > *c*-HexLi (R^1 = MOM) [9]; the trends within these rankings are easily rationalized by invoking stabilization of the organolithium by alkoxy substituents and destabilization by alkyl groups. Based on these rankings, treatment of organostannane **3** with BuLi should provide organolithium BOMOCH(Me)Li selectively rather than MeLi; however, our results suggest that this selectivity must be rather modest. It might then be expected that if the α-alkoxyorganolithium is rendered more stable than MeLi by judicious use of protecting groups, trimethylstannyl groups could be used in the transmetalation chemistry of α-alkoxystannanes. We now report that this is, in fact, the case.

Carbamate protecting groups were chosen for initial study since they are well-known to be effective for the stabilization of organolithiums [12]. The carbamate **4** (*i*-Pr_2NCOCl, Et_3N, 34% yield) and MOM derivative **5** (MOMCl, *i*-Pr_2NEt, 78% yield) were easily prepared from the corresponding hydroxystannane. As expected, transmetalation/trapping (*n*-BuLi; PhCHO) of **5** proceeded in only mediocre (40%) yield; in contrast, analogous treatment of carbamate **4** gave the expected adduct **6** in much higher yield (eq 3,4).



(3)

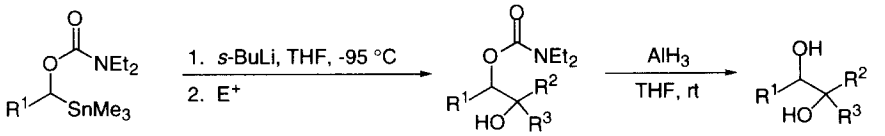


(4)

Insight into the difference in bahaviour between these compounds was gained by analysis of the crude reaction mixtures by GC-MS. In the case of MOM derivative **5**, the reaction mixture contained the expected adducts **7** (as a 1:1 mixture of diastereomers) and significant amounts of starting material **5** along with derivatives of **5** where the methyl groups were replaced by butyl groups (i.e. $C_5H_{11}CH(OMOM)SnMe_{(3-x)}Bu_x$, x = 1, 2, 3) as well as 1-phenylethanol. The formation of this complex mixture is consistent with our hypothesis that, in the transmetalation of MOM protected trimethylalkoxyorganostannanes, formation of the expected alkoxyorganolithium is competitive with formation of methyllithium. This strongly suggests that these two organolithium species are comparable in stability. With the carbamate **4**, no 1-phenylethanol was detected and only traces of a compound where one methyl group was replaced by a butyl group was observed (with no dibutyl or tributyl analogs). Our rationale for this difference is that the carbamate group stabilizes the alkoxyorganolithium more than the MOM group does and thus formation of MeLi is now no longer a serious competitive pathway.

The *N,N*-diisopropylcarbamate group proved to be useful for transmetalation chemistry but could be obtained in only mediocre (<35%) yields from the hydroxystannanes. Therefore, another carbamate group was sought. The *N,N*-diethylcarbamate group was chosen for further study since these derivatives could be prepared (RCHO + Me_3SnLi, then *p*-$NO_2C_6H_4OC(O)Cl$, pyr; Et_2NH) in much higher yields (57-83% from aldehydes). A number of compounds were prepared and their transmetalation chemistry was investigated (Table). Best results were obtained using *s*-BuLi at low temperatures (-95 °C); with *n*-BuLi, some attack by the alkyllithium on the carbonyl group was observed while at higher temperatures (-78 °C) some 1,2-migration to form hydroxyamides was detected (compare entries 5 and 6). Even with an aliphatic aldehyde, a good yield of the expected adduct was obtained (entry 10). Lower yields were observed (a) with stannane **8a** (R^1 = Me), likely because of problems associated with the isolation of the polar water-soluble products, and (b) with cyclohexanone as the electrophile, likely because of competing enolization. In general, however, good yields of adducts were obtained. Furthermore, these adducts could be smoothly transformed to the diols by reduction with AlH_3 (2 eq, THF, rt, 15 min) [13]; $LiAlH_4$ could also be used but reactions were slower.

Table. Reactions of Organolithiums derived from Transmetalation of Stannanes **8**[a]



8 **9** **10**

Entry	Stannane	R^1	E^+	R^2	R^3	**9** (yield)[b]	**10** (yield)[b]
1	**8a**	Me	benzaldehyde	Ph	H	**9a** (60)	nd[c]
2			tolualdehyde	4-$CH_3C_6H_4$	H	**9b** (72)	nd[c]
3	**8b**	*n*-C_5H_{11}	benzaldehyde	Ph	H	**9c** (79)	**10c** (80)
4			*p*-anisaldehyde	4-$CH_3OC_6H_4$	H	**9d** (75)	**10d** (83)
5	**8c**	*i*-Pr	benzaldehyde	Ph	H	**9e** (85)	**10e** (79)
6			benzaldehyde	Ph	H	**9e** (62)[d]	—
7			1-naphthaldehyde	1-naphthyl	H	**9f** (84)	**10f** (91)
8			piperonal	piperonyl	H	**9g** (88)	**10g** (84)
9			cyclohexanone	$-(CH_2)_5-$		**9h** (63)	**10h** (69)
10			hexanal	*n*-C_5H_{11}	H	**9i** (81)	nd[c]
11	**8d**	*c*-C_6H_{11}	benzaldehyde	Ph	H	**9j** (83)	**10j** (82)
12			tolualdehyde	4-$CH_3C_6H_4$	H	**9k** (76)	**10k** (80)

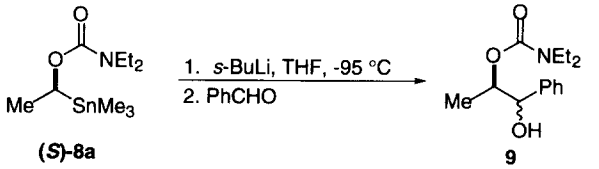
a All new compounds exhibited satisfactory IR, ^1H NMR, ^{13}C NMR, mass spectra and combustion analysis

b Isolated yields of chromatographically-pure products (1:1 mixture of diastereomers except **9h**).

c not done.

d transmetalation using *n*-BuLi, THF, -78 °C.

We also investigated the configurational stability of the carbamate-protected α-alkoxyorganolithium derived from stannane **8a** (eq 5). Stannane **8a** was easily prepared in high enantiomeric purity (>95% ee) from the kinetically-resolved hydroxystannane [8]. Transmetalation of **8a** (*s*-BuLi, THF, -95 °C) and treatment of the resulting organolithium with PhCHO gave alcohol **9a** (as a 1:1 mixture of diastereomers) with no detectable racemization (HPLC).



(*S*)-**8a** **9** (5)

In summary, we have shown that trimethylstannanes bearing an acetal protecting group (*e.g.* MOM, which have traditionally been used with analogous tributylstannanes) are not well suited for the preparation of α-alkoxyorganolithiums. When a carbamate protecting group is used, transmetalation to the corresponding α-alkoxyorganolithium is a facile process; this organolithium may be trapped with electrophiles such as aldehydes in high yields. These findings should increase the synthetic utility of α-alkoxyorganostannanes.

Acknowledgements

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References and Notes

[1] Still WC. J. Am. Chem. Soc. 1978;100:1481-1487.
[2] Still WC, Sreekumar C. J. Am. Chem. Soc. 1980;102:1201-1202.
[3] For recent examples, see: (a) Linderman RJ, Cusack KP, Jaber MR. Tetrahedron Lett. 1996;37:6649-6652. (b) Ye J, Bhatt RK, Falck JR. Tetrahedron Lett. 1993;34:8007-8010. (c) Gilbert P, Lewis ML, Quayle P, Zhao Y, Mills K. Tetrahedron Lett. 1996;37:9115-9118. (d) Bhatt RK, Ye J, Falck JR. Tetrahedron Lett. 1996;37:3811-3814. (e) Kaufman TS. Synlett. 1997:1377-1378.
[4] Trimethylstannanes may provide more selective reactions than tributylstannanes: Ishihara K, Ishida Y, Nakamura S, Yamamoto H. Synlett. 1997:758-759. However, these advantages must be weighed against higher costs and toxicity: Neumann WP. The organic chemistry of tin. London: John Wiley, 1970:230-237.
[5] See, for example: Stille JK. Angew. Chem. Int. Ed. Engl. 1986;25:508-524.
[6] (a) Piers E, McEachern EJ, Romero MA. J. Org. Chem. 1997;62:6034-6040 and references cited therein. (b) Pereira OZ, Chan TH. J. Org. Chem. 1996;61:5406-5413. (c) Niestroj M, Neumann WP, Mitchell TN. J. Organomet. Chem. 1996;519:45-68. (d) Cliff MD, Pyne SG. Tetrahedron Lett. 1995;36:763-766.
[7] Lipshutz BH, Sharma S, Reuter DC. Tetrahedron Lett. 1990;31:7253-7256.
[8] Chong JM, Mar EK. Tetrahedron Lett. 1991;32:5683-5686.
[9] It has been reported that 2-trimethylstannyltetrahydrofuran and 2-trimethylstannyltetrahydropyran do not form the expected alkoxylithiums as well as the corresponding tributylstannanes: Sawyer JS, Kucerovy A, Macdonald TL, McGarvey GJ. J. Am. Chem. Soc. 1988;110:842-853. However, no problems with transmetalation of the acetal $MeCH(OMOM)SnMe_3$ were reported.
[10] Chan PCM, Chong JM. Tetrahedron Lett. 1990;31:1985-1988.
[11] There are scattered examples of such compounds where the alkoxy carbon is unsubstituted, *i.e.* $ROCH_2SnMe_3$. See, for example: Taylor OJ, Wardell JL. J. Chem. Res. (S). 1989:98-99. Eguchi S, Ebihara K, Morisaki M. Chem. Pharm. Bull. 1988;36:4638-4639. Also, zirconocene (α-trimethylstannyl alkoxide) complexes have been reported: Askham FR, Carroll KM. J. Org. Chem. 1993;58:7328-7329.
[12] Carstens A, Hoppe D. Tetrahedron 1994;50:6097-6108.
[13] Burchat AF, Chong JM, Nielsen N. J. Org. Chem. 1996;61:7627-7630.