Elimination *vs.* substitution in the reaction of 3-stannyl esters and 3-stannyl nitriles with sodium *tert*-butoxide in DMSO

Alicia B. Chopa,* Gustavo F. Silbestri, Mercedes A. Badajoz, and Ana P. Murray

INIQO, Departamento de Química, Universidad Nacional del Sur, Avenida Alem 1253, 8000 Bahía Blanca, Argentina
E-mail: abchopa@uns.edu.ar

Dedicated to Professor Edmundo A. Rúveda on his 70th birthday and to Professor Roberto A. Rossi on his 60th birthday

(received 29 Aug 03; accepted 08 Oct 03; published on the web 10 Oct 03)

Abstract

The reaction of 3-stannyl propanoates and 3-stannyl propanonitriles with sodium *tert*-butoxide in DMSO leads to elimination and/or substitution products. The composition of the product mixture depends on the nature of the ligands attached to tin and also on the nature of the functional group (COOMe or CN). Stereochemical results suggest that the elimination reactions proceed through an $(E1cB)_R$ mechanism.

Keywords: Organotin, substitution reaction, $(E1cB)_R$

Introduction

In previous investigations [1] we have reported that the reaction of a series of *threo*-3-(triorganostannyl)nitriles with sodium *tert*-butoxide in *t*-BuOH led to Z/E mixtures of α-methylene nitriles in different yields under appropriate conditions.

Recently [2] we have found that a series of 3-(triorganostannyl)ketones, under similar conditions, afforded elimination and/or substitution products. The elimination reaction exhibited features characteristic of a $(E1cB)_R$ mechanism. Our results indicated that the elimination/substitution ratios obtained were dependent upon the nature of the ligands attached to the tin atom. Thus, while substrates containing better nucleofuges such as Cl_3Sn, Ph_2BrSn and Ph_3Sn led exclusively to elimination products, substrates supporting a poor nucleofuge such as Me_3Sn led to a mixture of elimination/substitution products or to exclusively substitution products which are dependent on the temperature. We have also found that a phenyl group attached to C-2, due to stabilization of the intermediate anion, increased the elimination/substitution ratio in a substrate that contained a poor nucleofuge such as Me_3Sn.

 ©ARKAT USA, Inc

A change from *t*-BuOH to dimethyl sulfoxide (DMSO) caused a very dramatic acceleration of either the elimination or substitution reactions. Under these conditions there were exclusive reactions depending only on the nature of the ligands attached to tin.

Taking into account our results we considered that it would be of interest to investigate the reactivity of comparable 3-(triorganostannyl)nitriles and 3-(triorganostannyl)esters under similar conditions. These reactions could be of interest not only from a mechanistic point of view but also as a synthetic tool. We wish to report the results obtained in the reaction of a series of methyl 3-(triorganostannyl)propanoates and 3-(triorganostannyl)propanonitriles with sodium *tert*-butoxide in DMSO.

Results and Discussion

The reactions were carried out with substrates supporting two chiral centres because we could ascertain at the same time the course and stereochemistry of the reaction by using individual diastereomers as starting material and determining isomeric compositions of the products.

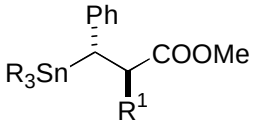
The results obtained indicate that in the studied reactions the stannyl group can depart in a nucleofugal sense as well as an electrofugal sense, leading to elimination or substitution products, respectively.

Thus, the reaction of methyl *erythro*-2,3-diphenyl-3-(triphenylstannyl)propanoate (**1**) with sodium *tert*-butoxide in DMSO, led (15 min) to a mixture of methyl (E)-2,3-diphenyl propenoate (**2**, 36%) and (E)-2,3-diphenyl propenoic acid (**3**, 56%) (Table 1, entry 1).

On the other hand, under similar conditions, methyl *erythro*-2-methyl-3-phenyl-3-(triphenylstannyl)propanoate (**4**) led to a mixture of methyl (E)-2-methyl-3-phenyl propenoate (**5**, 5%) and (E)-2-methyl-3-phenyl propenoic acid (**6**, 46%). The yields were increased to 15 and 77% respectively after 60 min of reaction (Table 1, entries 3 and 4). It should be noted that the amount of acids **3** and **6** progressively increased with time at the expense of esters **2** and **5** respectively, and after 2 hs. **3** and **6** were the only products (Table 1, entries 2 and 5).

Similar reactions were carried out with 3-(trialkylstannyl)esters such as methyl *erythro*-2,3-diphenyl-3-(trimethylstannyl)propanoate (**7**), methyl *erythro*-2,3-diphenyl-3-(tributylstannyl) propanoate (**8**) and methyl *erythro*-2-methyl-3-phenyl-3-(tributylstannyl)propanoate (**9**). These substrates led (2 min) to the corresponding hydrodestannylated products. It is to note that meanwhile **7** gave a mixture of methyl 2,3-diphenyl propanoate (**10**, 37 %) and 2,3-diphenyl propanoic acid (**11**, 41 %), the 3-(tributylstannyl) derivative **8** afforded pure acid **11** (80 %). On the other hand, in the reaction carried out with ester **9** it was detected 2-methyl-3-phenyl propanoic acid (**12**, 73 %) together with the corresponding *tert*-butyl ester **13** in 17 % yield [3] (Table 1, entries 6-8).

Table 1. Reaction of *erythro*-3-stannyl esters with sodium *tert*-butoxide in DMSO[a]



Entry	Compd.	R_3Sn	R^1	Time, min	%Elimination[b,c]	%Substitution[b,d]
1	**1**	Ph_3Sn	Ph	15	92 [36(**2**)/56(**3**)]	0
2	**1**	Ph_3Sn	Ph	120	94 [0/94(**3**)]	0
3	**4**	Ph_3Sn	Me	15	51 [5(**5**)/46(**6**)]	0
4	**4**	Ph_3Sn	Me	60	92 [15(**5**)/77(**6**)]	0
5	**4**	Ph_3Sn	Me	120	91 [0/91(**6**)]	0
6	**7**	Me_3Sn	Ph	2	0	78 [37(**10**)/41(**11**)]
7	**8**	Bu_3Sn	Ph	2	0	80 [0/80(**11**)]
8	**9**	Bu_3Sn	Me	2	0	73 [0/73(**12**)][e]
9	**14**	Bu_2ClSn	Ph	5	91 [0/91(**3**)]	0
10	**15**	Bu_2ClSn	Me	5	93 [0/93(**6**)]	0

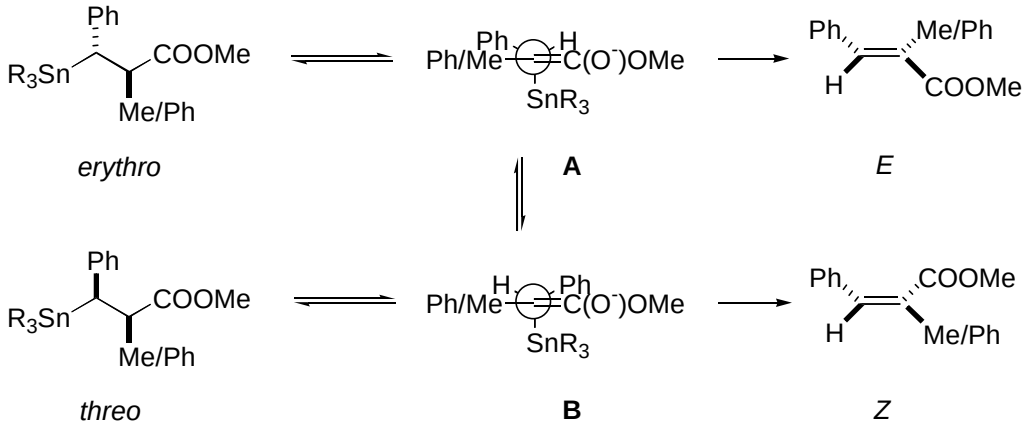
[a] Substrate/base 1/1.1, r.t. [b] Ester and acid yields between brackets. [c] *Threo* isomers led to lower yields. [d] *Threo* isomers led to similar yields. [e] Together with 17% of **13**.

We have also found that there is a fast reaction between dibutylchlorostannyl derivatives **14** and **15** and sodium *tert*-butoxide. The analysis of the product mixtures obtained showed that these reactions led (5 min) to the corresponding (E)-propenoic acids **3** and **6** in 91 % and 93 % yield, respectively (Table1, entries 9 and 10).

The results obtained indicate that the *tert*-butoxide anion reacts with these substrates in a similar way as with 3-stannyl ketones.[2] The hydrodestannylated products obtained could be explained as the result of a nucleophilic attack of the *tert*-butoxide anion at the tin atom.[4] It should be noted that high yields of acids are formed in the reactions carried out with tributyltin derivatives **8** and **9**. Probably, the tin oxide generated in the reaction accelerates the hydrolysis of the ester group leading to high yields of the corresponding acids in very short times. [5]

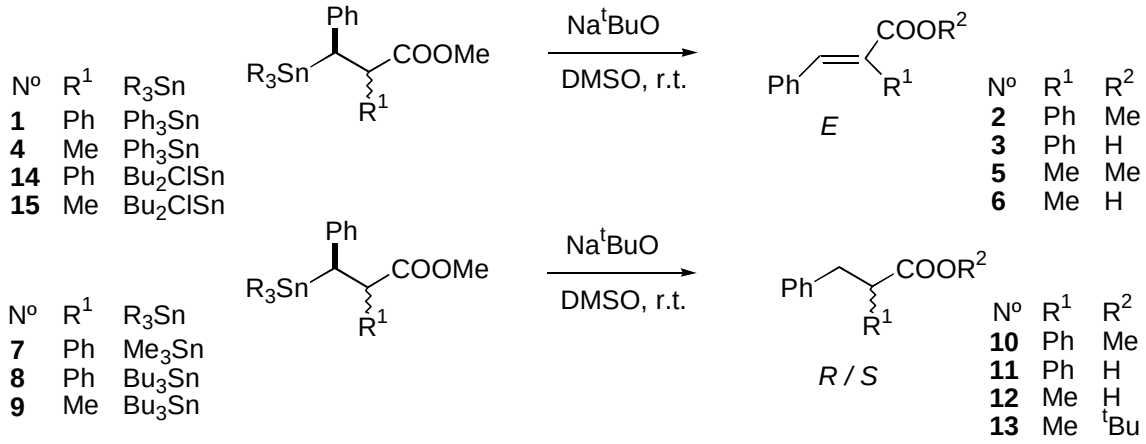
On the other hand, the formation of olefins should be due to an elimination reaction where the *tert*-butoxide anion acts as a base abstracting the proton from C-2 and the organotin anion acts as a nucleofuge. The stereochemical results summarized in Table 1 show that there is complete stereoconvergence in the elimination reaction leading always to the olefin E, independently of the starting substrate configuration. It should be mentioned that *threo* esters always led to lower olefin yields than their *erythro* isomers in the same reaction time. When these reactions were quenched at shorter times (5 min) it was observed that olefins E were formed together with a mixture of isomeric starting material. All these observations support an $(E1cB)_R$ mechanism as represented in Scheme 1. The stereoselectivity of the elimination reaction implies that conformation **A** is preferred instead of **B**. On these grounds it may be assumed that

for these compounds the interaction between 3-Ph and COOMe is energetically less favourable than that between Me/Ph and Ph/Ph, in spite of their A-values.[6] These stereochemical results agreed with those reported by Cabaleiro,[7] related with the debromination of methyl 2,3-diaryl propanoates.



Scheme 1

As shown in Scheme 2, the observed product distribution is strongly dependent on the nature of the ligands attached to the tin atom. Meanwhile 3-(triphenyl) and 3-(dibutylchlorostannyl)esters **1**, **4**, **14** and **15** led, exclusively, to olefins, 3-(trimethyl) and 3-(tributylstannyl)esters **7**, **8** and **9** afforded only substitution products. Changes in the substituent on C-2 have no detectable effect on the product mixtures.



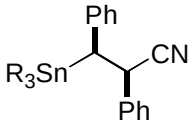
Scheme 2

The results summarized in Table 2 and in Scheme 3 show that in the reactions carried out between 3-(triorganostannyl)propanenitriles and sodium *tert*-butoxide in DMSO the substitution

reaction competes efficiently with the elimination reaction even with substrates containing good nucleofuges such as Ph_3Sn and Bu_2ClSn. Thus, both *threo* 2,3-diphenyl-3-(triphenylstannyl) propanenitrile (**16**) and *threo* 2,3-diphenyl-3-(dibutylchlorostannyl)propanenitrile (**17**) led (3 h) to a mixture of 2,3-diphenyl propenenitrile (**18**, Z/E, 90/10) and 2,3-diphenyl propanenitrile (**19**). Attempts to increase olefin yields by increasing the temperature led to an increase in the amount of **19** (Table 2, entries 1-5).

A similar reaction carried out with 3-(trialkylstannyl)nitriles **20** and **21** afforded (10 min) quantitative yields of **19** (Table 2, entries 6 and 7).

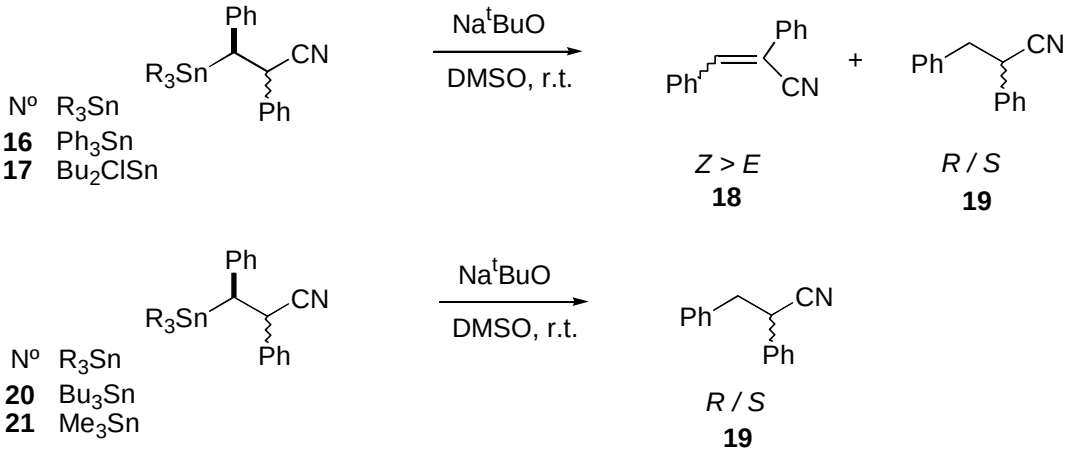
Table 2. Reaction of *threo*-3-stannyl nitriles with sodium *tert*-butoxide in DMSO[a]



Entry	Compd.	R_3Sn	Time, min	%Elimination[b] (Z/E) **18**	%Substitution[c] **19**
1	**16**	Ph_3Sn	180	48 (90/10)	50
2	**16**	Ph_3Sn	10[d]	24 (60/40)	75
3	**17**	Bu_2ClSn	180	39 (90/10)	54
4	**17**	Bu_2ClSn	10[d]	18 (56/44)	76
5	**17**	Bu_2ClSn	10[e]	16 (50/50)	77
6	**20**	Bu_3Sn	10	0	100
7	**21**	Me_3Sn	10	0	98

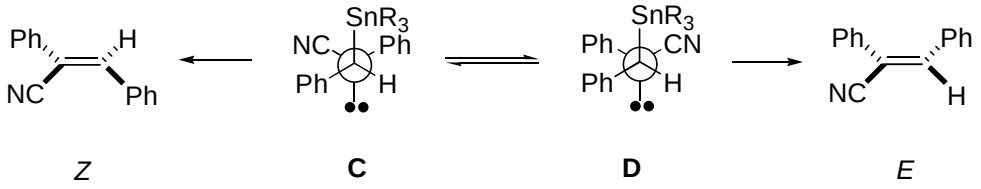
[a] Substrate/base 1/1.1, r.t. unless otherwise stated. [b] *Erythro* isomers led to lower yields. [c] *Erythro* isomers led to similar yields. [d] 65°C. [e] 100°C.

We assumed that with 3-stannyl nitriles as substrates, the substitution reaction is probably preferred over the elimination reaction because the elimination mechanism is slowed by the less acidic character of the hydrogen on C-2.[8]



Scheme 3

Although similar stereochemical results were obtained with the *erythro* nitriles, they always led to lower olefin yields than their *threo* isomers. The diastereoselectivity of the elimination reaction could be explained on the basis of the stability of the carbanion intermediate. Considering steric effects [6] the lowest energy conformation should be conformation **C** (Scheme 4).



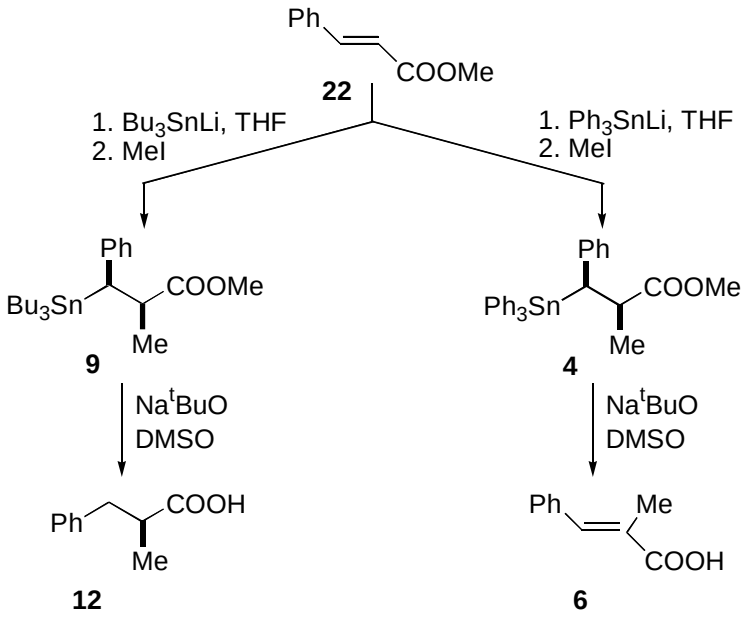
Scheme 4

In summary, the results obtained from the present study confirm that the stannyl group in 3-stannyl esters and in 3-stannyl nitriles as well as in 3-stannyl ketones can be electrofugal or nucleofugal in favorable circumstances. We found that all the substrates studied led exclusively to the corresponding substitution product when a trialkylstannyl group (Me_3Sn, Bu_3Sn) is attached to C-3. On the other hand, the elimination reaction is exclusive with 3-stannyl esters and 3-stannyl ketones[2] containing good nucleofuges (Ph_3Sn, Bu_2ClSn, Ph_2BrSn, Cl_3Sn) but not with comparable 3-stannyl nitriles. The latter substrates, even at higher temperatures, always led to mixtures of elimination/substitution products.

These reactions would have a potential synthetic utility. For example, the reaction of methyl (E)-3-phenyl propenoate (**22**) with triphenyl- or tributylstannyl lithium in THF and quenching the intermediate carbanions with methyl iodide led to the corresponding adducts **4** and **9** in 85% and 65% yield, respectively.[9] The reaction of **4** and **9** with sodium *tert*-butoxide in DMSO led to

eliminations product **6** and to substitution product **12** in high yields, respectively (Table 1, entries 5 and 8). Thus, it is possible, through a simple two step synthesis, to obtain compounds **6** and **12** from ester **22** as is shown in Scheme 5.

Further work is in progress to study the scope of these reactions.



Scheme 5

Experimental Section

General Procedures. The reactions were performed under nitrogen or argon. DMSO was dried under standard methods. Sodium *tert*-butoxide was sublimated periodically and kept under argon atmosphere. 3-Stannyl esters and 3-stannyl nitriles were synthesized according to previously reported procedures.[10] The reactions were monitored by TLC, and quantified by GC and on isolated pure product. The measurements were carried out with either a 10% SE-30 (Chrom W 60/80, 6 ft x 1/8 in., SS) or a 3% SE-30 (Chrom W 60/80, 3 ft x 1/8 in., SS) column.

The reactions were performed following the same procedure in all cases. One experiment is described in detail to illustrate the method used.

Reaction of methyl *erythro*-2,3-diphenyl-3-(triphenylstannyl)propenoate (1) with Na *t*-BuO in DMSO. The reaction was carried out in a two-necked, 10 mL, round bottom flask equipped with a nitrogen (argon) inlet, a magnetic stirrer and septums. To a solution of 46.0 mg (0.482 mmol) of Na*t*-BuO in 2.8 mL of DMSO was added, by syringe, a solution of **1** (211 mg, 0.402 mmol) in 2.8 mL of DMSO. After keeping the reaction mixture under stirring for 15 min at room

temperature it was quenched by adding water and extracted with ether (phase 1). The aqueous alkaline phase was acidified and extracted with ether (phase 2). The ester **2,** extracted from phase 1, was quantified by GC using the external standard method. The acid **3**, extracted from phase 2 was quantified by weighting. Both products were compared with authentic samples prepared by known procedures.

Acknowledgements

This work was partially supported by the Universidad Nacional del Sur and Fundación Antorchas. CONICET is thanked for a research fellowship to G.F.S.

References

* Member of CIC.

1. Podestá, J.C.; Chopa, A.B.; Ayala, A.D.; Koll, L.C. *J. Chem. Soc. Perkin Trans.2* **1993**, 2323.
2. Chopa, A.B.; Murray, A.P. *Organometallics* **2001**, *20*, 1476.
3. We could not explain the formation of compound **13**.
4. Farah, D.; Karol, T.; Kuivila, H. *Organometallics* **1985**, *4*, 662, and references therein
5. Salomon, C.J.; Mata, E.G.; Mascaretti, O.A. *Tetrahedron* **1993**, *49*, 3691.
6. The A value of the different groups are: Ph (2.8 kcal/mol); Me (1.74 kcal/mol); COOMe (1.27 kcal/mol); CN (0.2 kcal/mol): Eliel, E.L.; Wilen, S. H. *Stereochemistry of Organic Compounds*, John Wiley & Sons: USA, 1994, p 696.
7. Badajoz, M.A.; Montani, R.S.; Cabaleiro, M.C. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1717.
8. March, J. *Advanced Organic Chemistry,* John Wiley & Sons: USA, 1992, p 250.
9. We followed the procedure reported by: McGarvey, G.J.; Williams, J.M. *J. Am. Chem. Soc.* **1985**, *107*, 1435.
10. (a) Podestá, J.C.; Chopa, A.B.; Ayala, A.D. *J. Organometal. Chem.* **1981**, *212*, 163. b) Podestá, J.C.; Chopa, A.B. *J. Organometal. Chem.* **1982**, *229*, 223. (c) Chopa, A.B.; Koll, L.C.; Podestá, J.C.; Neumann, W.P. *Organometallics* **1985**, *4*, 1036.