Nucleophilicity vs Basicity in the Reaction of Sodium *tert*-Butoxide with *β*-Stannyl Ketones

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Summary: The reaction of 3-stannyl-1,2,3-triphenyl- and 3-stannyl-1,3-diphenyl-2-methylpropanones with sodium tert-butoxide in either t-BuOH or dimethyl sulfoxide (DMSO) as solvent leads to elimination and/or substitution products. The composition of the product mixtures depends essentially on the nature of the ligands attached to the tin atom, on the solvent, and also on the nature of the substituent on C-2. Thus, β-(triphenyl), β-(bromodiphenyl), and β-(trichlorostannyl) ketones undergo an exclusive elimination reaction leading to an unsaturated ketone in good to high yields (72%−96%) both in t-BuOH and in DMSO. In the latter the reactions lead to higher yields in shorter times. On the other hand, β-(trimethylstannyl) ketones lead to mixtures of olefins and substitution products in t-BuOH and exclusively to substitution products in DMSO (96%−98%). Stereochemical results suggest that the elimination reactions proceed through an $(E1cB)_R$ mechanism.

Introduction

In previous investigations[1] we have found that a series of *threo*-*β*-(triorganostannyl)nitriles led to *Z*/*E* mixtures of α-methylene nitriles in different yields upon treatment with lithium diisopropylamide (LDA) in tetrahydrofurane (THF) or sodium *tert*-butoxide in *tert*-butyl alcohol (*t*-BuOH) under the appropriate conditions.

As far as we know, in the chemical literature there are few references to elimination reactions of organotin compounds via carbanions, and these are restricted to *β*-(trichlorostannyl) ketones and aldehydes.[2]

Therefore, we considered that it would be of interest to study the reactivity of *β*-stannyl ketones under base conditions. Now, we wish to report the results obtained in the reaction of 3-stannyl-1,2,3-triphenyl- and 3-stannyl-1,3-diphenyl-2-methylpropanones with sodium *tert*-butoxide in both *t*-BuOH and dimethyl sulfoxide (DMSO) as solvents.

Results and Discussion

The reactions were carried out with α,*β*-disubstituted-*β*-stannyl ketones because we could ascertain at the same time the course and stereochemistry of the reaction by using individual diastereomers as substrates and examining isomeric compositions of the products.

The results 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 *erythro*-1,3-diphenyl-2-methyl-3-(triphenylstannyl)propanone (**1**) with sodium *tert*-butoxide in *t*-BuOH led (3 h) to a mixture of 1,3-diphenyl-2-methylpropenone (**2**) (41%; *Z*/*E* 8/92) and the isomerized starting substrate (*erythro*/*threo* 30/70). The olefin yield increased to 72% after a 24 h reaction time (Table 1, entries 1 and 2).

On the other hand, under similar conditions, *erythro*-1,3-diphenyl-2-methyl-3-(trimethylstannyl)propanone (**3**) led (3 h) to a mixture of **2** (34%; *Z*/*E* 30/70) and 1,3-diphenyl-2-methylpropanone (**4**) (57%),[3] together with a little amount of isomerized starting adduct (*erythro*/*threo* 15/85) (Table 1, entry 3).

Attempts to increase the olefin yield by increasing either the temperature or the ratio base/substrate (3/1) led to mixtures of undesirable secondary products starting from **1** and to an increase in the amount of **4** (85%) starting from **3** (Table 1, entry 4).

Similar reactions were carried out with *erythro*-1,3-diphenyl-2-methyl-3-(bromodiphenylstannyl)propanone (**5**)[4] and with *erythro*-1,3-diphenyl-2-methyl-3-(trichlorostannyl)propanone (**6**).[5] These substrates led to higher yields of elimination product in shorter times. Thus, ketones **5** (3 h, 30 °C) and **6** (2 h, 30 °C) led to **2** in 88% (*Z*/*E* 4/96) and 93% (*Z*/*E* 6/94) yield, respectively (Table 1, entries 5 and 6). It should be noted that no substitution product was detected.

The substantial amounts of **4** found in the reaction of **3** could be explained as the result of a nucleophilic attack of the *tert*-butoxide anion at the tin atom.[6] On the other hand, the formation of **2** is probably due to an elimination reaction where the *tert*-butoxide anion acts as a base abstracting the proton from C-2 and the R_3Sn anion acts as a nucleofuge. To obtain direct evidence for the existence of organotin anions, we carried out the reaction between **3** and sodium *tert*-butoxide in *t*-BuOH in the presence of an equimolecular amount of allyl bromide. Triphenylallyltin was formed in 37% yield.

All these observations suggest that the *tert*-butoxide anion could react with these substrates as a base by

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(1) Podestá, J. C.; Chopa, A. B.; Ayala, A. D.; Koll, L. C. *J. Chem. Soc., Perkin Trans. 2* **1993,** 2323

(2) Nakahira, H.; Ryu, I.; Ikebe, M.; Oku, Y.; Ogawa, A.; Kambe, N.; Sonoda N.; Murai, S. *J. Org. Chem.* **1992,** *57,* 17

(3) Quantified by GC by comparing with an authentic sample.

(4) Synthesized by electrophilic cleavage of one phenyl group in **1** by bromine. Chopa, A. B.; Koll, L. C.; Podestá J. C.; Mitchell, T. N. *J. Organomet.Chem.* **1989,** *376,* 283.

(5) Synthesized by hydrotrichlorostannation of the appropriate olefin. Chopa A. B.; Murray, A. P. *Main Group Metal Chem.* **1998,** *21,* 347.

(6) There are many examples in the literature about the susceptibility of organostannanes to nucleophilic attack at the tin atom. Farah, D.; Karol T.; Kuivila, H. *Organometallics,* **1985,** *4,* 662, and references therein.

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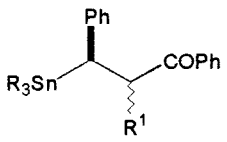
Table 1. Reaction of β-Stannyl Ketones with Sodium *tert*-Butoxide in *t*-BuOH[a]

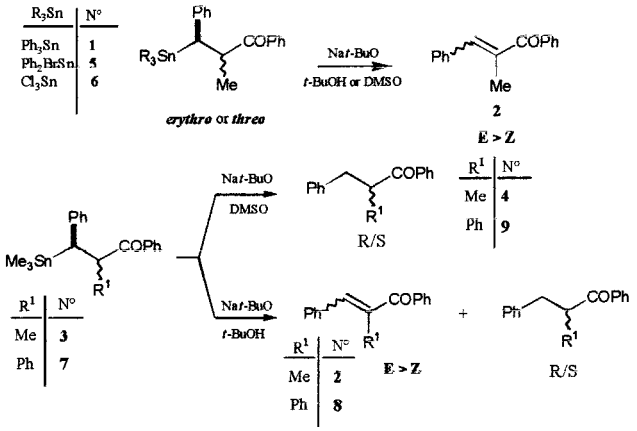


R_3Sn	R^1	N°
Ph_3Sn	Me	**1**
Me_3Sn	Me	**3**
Ph_2BrSn	Me	**5**
Cl_3Sn	Me	**6**
Me_3Sn	Ph	**7**

entry	compound	time, h (*T*, °C)	% elimination[b,c] (*Z*/*E*)	% reduction[c]
1	**1**	3 (30)[d]	41 (8/92)	0
2	**1**	24 (30)[d]	72 (9/91)	0
3	**3**	3 (30)[d]	34 (30/70)	57
4	**3**	3 (65)	0	85
5	**5**	3 (30)	88 (4/96)	0
6	**6**	2 (30)	93 (6/94)	0
7	**7**	3 (30)[d]	47 (30/70)	12

[a] Substrate/base 1/1.1. Similar results were obtained from *erythro* and *threo* isomers. [b] Isomerized starting material was detected. [c] Quantified by GC. [d] First 10 min of reaction at 65 °C.

Scheme 1



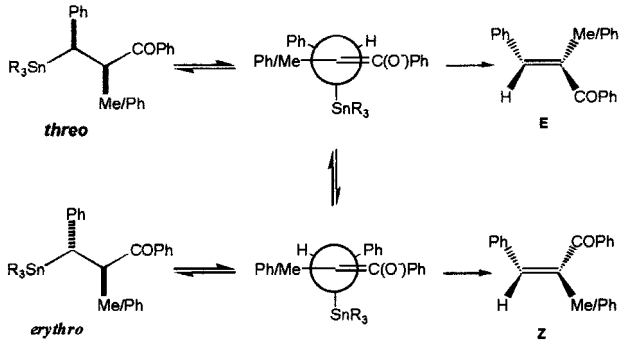
proton abstraction or as a nucleophile by attack to the tin atom. Moreover, the results indicate that the nature of the ligands attached to the tin atom plays an important role in the reactivity of these β-stannyl ketones toward sodium *tert*-butoxide in *t*-BuOH (Scheme 1).

The course followed by the reaction could be explained in part as a consequence of the nucleofugal character of organotin moieties. When $R_3Sn = Me_3Sn$ (ketone **3**) the substitution reaction is probably preferred over the elimination reaction not only because nucleophilic attack at the tin atom is faster but also because the elimination mechanism is slowed by the poor nucleofugal ability of the Me_3Sn anion (electronic effects of methyl group desestabilize the negative charge supported by tin).

On the other hand, due to the extra stabilization of the negative charge supported by the tin atom, the nucleofugal character of Ph_3Sn, Ph_2BrSn, and Cl_3Sn anions would be better than that of the Me_3Sn anion, thus favoring the elimination reaction (ketones **1**, **5**, and **6**).

To reverse the substitution/elimination ratio observed with ketone **3**, we carried out a reaction with a substrate containing a phenyl instead of a methyl group on C-2. We assumed that due to the stabilization of the intermediate anion by resonance, the elimination reaction would be faster than the substitution reaction. As expected, the reaction with *erythro*-1,2,3-triphenyl-3-(trimethylstannyl)propanone (**7**) afforded (3 h) a higher amount of olefin **8** (47%; *Z*/*E* 30/70) compared with the substitution product **9** (12%) (Table 1, entry 7) (Scheme 1). This result suggests that the product mixture of the reaction is also dependent to some degree on the nature of the substituent on C-2.

Scheme 2



It should be noted that similar results were obtained in all cases starting from the *threo*-isomers.

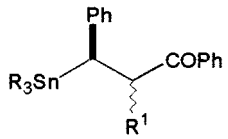
The analysis of the stereochemical results summarized in Table 1 gave valuable information about the elimination mechanism involved in these reactions. In general it has been observed that elimination products were formed together with a mixture of isomeric starting substrates and that the diastereomeric ratios in the product mixtures were identical independently of the starting substrate configuration. Also, product analysis showed that one diastereomer or mixtures of diastereomers with a relatively high predominance of one of them were always obtained; so these reactions are stereoselective but certainly not stereospecific. Additional checks confirmed that *Z* and *E* olefins undergo no isomerization under the reaction conditions. All these observations provide strong evidence for an $(E1cB)_R$ mechanism initiated by proton abstraction by the *tert*-butoxide ion, as represented in Scheme 2.

The intermediate enolate ion returns to starting material faster than it forms products, so the first step is reversible and the second step is slow. The anionic intermediate has a lifetime long enough to undergo stereochemical equilibration before losing the stannyl anion to form the elimination product. The E1cB mechanism is also supported by the effect of organotin moieties attached to C-3 and of substituents attached to C-2 on the elimination/substitution ratio. Thus, better nucleofuges such as Cl_3Sn, Ph_2BrSn, and Ph_3Sn lead exclusively to elimination products.[7] Furthermore, a phenyl group attached to C-2 increases the elimination/substitution ratio in a substrate that contains a poor nucleofuge such as Me_3Sn (ketone **7**).

Taking into account the obtained results, we considered that a change from a protic solvent such as *tert*-butyl alcohol to a dipolar aprotic solvent such as DMSO would cause an acceleration of the elimination reaction which depends on proton abstraction from the C−H

(7) It is known that $(E1cB)_R$ should have considerable leaving groups effects. Saunders W. H.; Cockerill, A. F. *Mechanisms of Elimination Reactions*; J. Wiley & Sons: New York, 1973.

Table 2. Reaction of β-Stannyl Ketones with Sodium *tert*-Butoxide in DMSO[a]



R_3Sn	R^1	N°
Ph_3Sn	Me	**1**
Me_3Sn	Me	**3**
Ph_2BrSn	Me	**5**
Cl_3Sn	Me	**6**
Me_3Sn	Ph	**7**

entry	compound	time, min (*T*, °C)	% elimination[b,c] (*Z*/*E*)	% reduction[c]
1	**1**	15 (65)	86 (19/81)	0
2	**5**	10 (25)	94 (0/100)	0
3	**6**	10 (25)	96 (0/100)	0
4	**3**	10 (25)	0	98
5	**7**	10 (25)	0	96

[a] Substrate/base 1/1.1. Similar results were obtained from *erythro* and *threo* isomers. [b] Isomerized starting material was detected. [c] Quantified by GC.

bond,[8] leading to higher yields of olefins even with ketone **3**. Thus, we carried out a series of reactions of ketones **1**, **3**, and **5**−**7** with sodium *tert*-butoxide in DMSO as solvent.

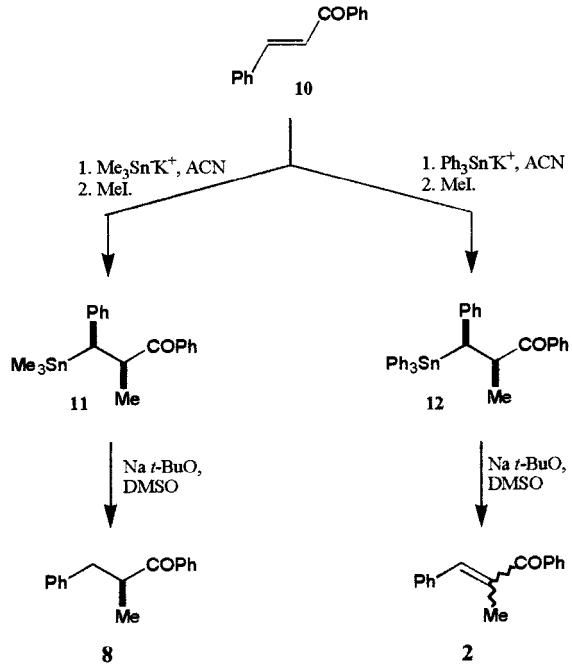
The results summarized in Table 2 show that when these reactions were carried out in DMSO, the yields were raised and the reaction times shortened. Moreover, elimination or substitution were exclusive reactions depending on the nature of the ligands attached to the tin atom, as shown in Scheme 1. It should be noted that changes in the substituent on C-2 has no detectable effect on the product mixtures. Meanwhile β-(triphenyl), β-(bromodiphenyl), and β-(trichlorostannyl) ketones (**1**, **5**, and **6**) led exclusively to olefin **2** (entries 1−3); both β-(trimethylstannyl) ketones (**3** and **7**) led just to substitution products **4** and **9** (entries 4, 5). In all cases the yields were very high and no significant side reactions were detected. The stereochemical results of the elimination reaction support again an $(E1cB)_R$ mechanism.

The experimental results suggest that in DMSO the *tert*-butoxide anion is extremely reactive toward the studied ketones. A change from *t*-BuOH to DMSO caused a very dramatic acceleration of either elimination or substitution reaction.

In conclusion, this study clearly indicates that the stannyl group in these β-stannyl ketones can be nucleofugal or electrofugal in favorable circumstances. The composition of the product mixtures depends essentially on the nature of the ligands attached to the tin atom, on the solvent, and also on the nature of the substituent on C-2. The elimination reaction is stereoselective but not stereospecific, and the stereochemical results suggest an $(E1cB)_R$ mechanism.

These reactions would have a potential synthetic utility as is shown in Scheme 3. The reaction of (*E*)-1,3-diphenylpropenone (**10**) with trimethyl- or triphenylstannyl potassium in acetonitrile (ACN) and quenching the intermediate enolates with methyl iodide led in nearly quantitative yields to the corresponding adducts

Scheme 3



11 and **12**.[9] The reaction of **11** and **12** with sodium *tert*-butoxide in DMSO led to **8** and **2** in 93% and 86% yields, respectively. Therefore, ketones **8** and **2** were synthesized, in high overall yields, from ketone **10** through a simple two-step synthesis.

The knowledge of the mechanism of these reactions would be of value in selecting parameters for synthesis involving specific pairs of reactants. Further work is in progress to study the scope of these reactions.

Experimental Section

General Procedures. The reactions were performed under nitrogen, and solvents were dried by standard methods. Sodium *tert*-butoxide was sublimated periodically and kept under nitrogen atmosphere. β-Stannyl ketones were synthesized according to previously reported procedures.[4,5,9] The reactions were monitored and quantified by GC. The measurements were carried out with either a 10% SE-30 (Chrom W 60/80, 6 ft × 1/8 in., SS) or a 3% SE-30 (Chrom W 60/80, 3 ft × 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 *erythro*-1,3-Diphenyl-2-methyl-3-(triphenylstannyl)propanone (1) with Na *t*-BuO in DMSO. The reaction was carried out in a two-necked, 10 mL, round-bottomed flask equipped with a nitrogen inlet, a magnetic stirrer, and septums. To a solution of 23.5 mg (0.245 mmol) of Na *t*-BuO in 1.4 mL of DMSO was added, by syringe, a solution of **1** (128 mg, 0.225 mmol) in 1.4 mL of DMSO. After keeping the reaction mixture for 15 min at 65 °C it was quenched by adding 5 mL of water and extracted with ether. The products were quantified by GC using the external standard method and compared with authentic samples prepared by known procedures.

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(8) *tert*-Butoxide in DMSO has been shown to be many orders of magnitude stronger than *tert*-butoxide in conventional solvents. Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; VCH: New York, 1988.

(9) Chopa, A. B.; Murray A. P.; Lockhart, M. T. *J. Organomet.Chem.* **1999**, *585*, 35.