Journal of Organometallic Chemistry, 437 (1992) C19–C22
Elsevier Sequoia S.A., Lausanne
JOM 22883PC

Preliminary communication

Stereoselective opening of chiral α-stannylacetals with organometallic reagents *

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(Received April 6, 1992)

Abstract

α-Tributylstannylacetals derived from 2*R*,3*R*-tartramide or 2*R*,4*R*-pentanediol have been treated with various organometallic reagents to give chiral α-oxygenated organotins. Relatively poor diastereoselectivities were obtained with organoaluminium reagents, but reactions involving RCu or R_2CuLi in the presence of boron trifluoride etherate or allyltributyltin in the presence of $TiCl_2(O^iPr)_2$ gave the desired compounds with diastereoselectivities of > 80/20

Owing to the configurational stability of α-alkoxyalkyl carbanions [1–3], routes to non-racemic chiral α-alkoxyalkyltriorganotins are of much interest because of the ease of transmetallation of such compounds by n-butyllithium in ether, THF, or DME [4]. Furthermore, when the triorganostannyl group is localised on an allylic carbon atom, control of the chemo-, regio- and stereo-selectivity of the reactions involving these α-alkoxyallyltins allows the transfer of the umpoled unit as a d^1 or as a d^3 synthon depending on the experimental conditions [5–9]. In this series non-racemic α-alkoxyallyltins were first exploited by Thomas who obtained α-methyl β-hydroxy-esters with enantiomeric excess of > 90% [7].

These results demonstrate the usefulness of non racemic chiral α-alkoxyorganotins, and synthetic approaches to them have been proposed recently. Most of these involve the enantioselective synthesis of α-hydroxyalkyl (or α-hydroxyallyl) triorganotins by (*R*)- or (*S*)-BINAL-H reduction of the corresponding acyltins and subsequent trapping with chloromethyl ethers. Good yields and enantiomeric excesses of > 95% were obtained by this route [9–11]. An enzymatic resolution of racemic α-stannylalcohols was recently carried out by Chong, but moderate yields

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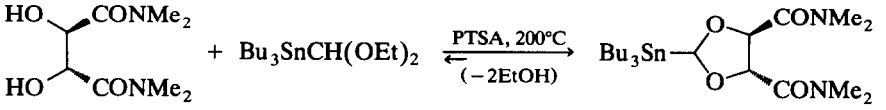
* Dedicated to Professor Alwyn G. Davies in recognition of his exceptional human and scientific qualities.

appear to limit the value of this method in spite of the interesting enantiomeric excess [12].

The fact that organoaluminium bromides have been found to react with α-stannylacetals without transmetallation of the tin–carbon bond [13] suggested a possible route to chiral α-alkoxy (or α-hydroxy) alkyltriorganotins involving reaction of organometallics with chiral α-stannylacetals, especially since non-racemic chiral α-stannylacetals with a C_2 geometry were obtained recently in our group by transacetalisation of the corresponding diols [14], for example:

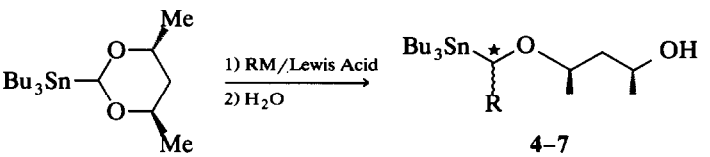


1

1 (yield = 59%; $[\alpha]_D^{24} = -36.7°$, $c = 3.2$, $CHCl_3$)

Similarly, the α-tributylstannyl acetal derived from 2*R*,4*R*-pentanediol (**2**) was obtained in 96% yield via azeotropic distillation in cyclohexane (**2**: $[\alpha]_D^{22} = +15.9°$; $c = 1.35$, $CHCl_3$) [14].

We present here the results of a study of the reactions of various organometallics with α-stannylacetals **1** and mainly **2** with concentration on the chemical yields and the diastereoselectivity in order to evaluate the potential of this reaction, which is depicted in the following equation:



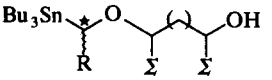
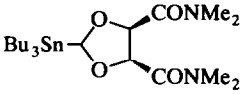
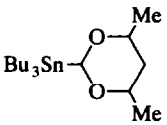
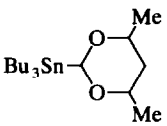
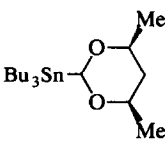
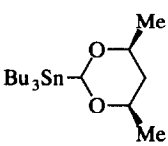
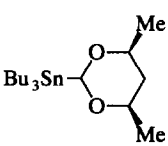
2 **4–7**

The obtained results are reported in Table 1. Good yields were obtained in all cases and except for the reaction involving diethylaluminium chloride (entry 2), diastereoisomeric ratios in the range 4/1 to 13/1 were obtained, the stereoselectivity being higher when the reaction was performed at a lower temperature (*cf.* entries 4 and 5). These results are consistent with the general trends expected on the basis of previous reports relating to non-stannylated 1,3-dioxanes [15–17], and our goal now is to improve the diastereoselectivity of the reaction in the light of the results observed with organic acetals. The absolute configuration of the new asymmetric center should be established firmly by transformation of the adducts into α-stannylalcohols using an oxidation-elimination sequence. In this context it is noteworthy that the reaction of $Me_2AlOC_6F_5$ [18] with α-stannylacetal **2** led directly to the β-alkoxyketone, but unfortunately in this case a hydrogen atom is transferred more easily than a methyl group (H transfer/Me transfer = 97/3), giving mainly the tributylstannylmethanol derivative.

In conclusion, the above results justify a more extensive exploration of this new route to non-racemic chiral α-oxygenated organotin compounds, even though it involves sacrifice of the chiral diol, it would be of considerable value if high diastereomeric excesses could be obtained with α-stannylacetals derived from readily available inexpensive optically active diols.

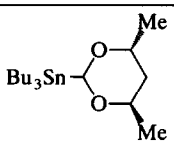
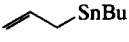
Table 1

Reaction of organometallic reagents with chiral α-stannylacetals

Entry	α-Stannylacetal	Organometallic reagent (RM) experimental conditions [a,b]	Bu_3Sn 		
			No.	Yield [c] (%)	Diastereomeric ratio [d]
1	 **1** (*R*, *R*)	Me_3Al(5 eq), $CHCl_3$, −10°C, 16 h then hydrolysis at r.t.	**3**	86	80/20 [e]
2	 **2** (*R*, *R* + *S*, *S*)	Et_2AlCl (2.2 eq), hexane, −10°C, 4 h then hydrolysis	**4**	90	65/35
3	 **2** (*R*, *R* + *S*, *S*)	MeCu (3 eq)/ $BF_3 \cdot Et_2O$ (3 eq), ether, −78°C, 4 h then hydrolysis	**5**	93	80/20
4	 **2** (*R*, *R*)	Me_2CuLi (3 eq)/ $BF_3 \cdot Et_2O$ (3 eq), ether, −78°C, 4 h then hydrolysis	**5**	97	85/15 [e]
5	 **2** (*R*, *R*)	Me_2CuLi (3 eq)/ $BF_3 \cdot Et_2O$ (3 eq), ether, −100°C, 4 h then hydrolysis	**5**	62	90/10 [e]
6	 **2** (*R*, *R*)	Ph_2CuLi (3 eq)/ $BF_3 \cdot Et_2O$ (3 eq), ether, −78°C, 4 h then hydrolysis	**6**	62	80/20 [e]

Acknowledgments. We are indebted to Chemetall GMBH, Continentale Parker, Schering and Rhône–Poulenc Societies for generous gifts of organometallic starting materials.

Table 1 (continued)

Entry	α-Stannylacetal	Organometallic reagent (RM) experimental conditions [a,b]	Bu_3Sn O ( ) OH (R, Σ, Σ)		
			No.	Yield [c] (%)	Diastereomeric ratio [d]
7	 2 (*R*, *R*)	 $TiCl_2(O^iPr)_2$ (5 eq) CH_2Cl_2, −78°C, 3 h then NaOH (0.1 *N*)	7	95	93/7 [e]

[a] A solution of α-stannylacetal was added to the organometallic reagent mixed with a Lewis acid for entries 1–6. The reaction with allyltributyltin (entry 7) was performed by addition of the acetal to the allyltin before addition of $TiCl_2(O^iPr)_2$. [b] The choice of the experimental conditions took into account previously described procedures involving reactions of organometallics with organic acetals (entry 1 [19], entry 2 [13], entries 3–6 [20], entry 7 [21]). [c] Isolated yields after liquid chromatography. [d] Compounds **3–7** were firmly identified from their physicochemical data (^1H NMR, ^{13}C NMR, IR and MS). The diastereomeric ratios were established by the appropriate methods (^1H NMR, ^{13}C NMR for **3**, ^{13}C NMR and GC-MS for compounds **4–7**). [e] On the basis of the general trends observed for organic acetals, the absolute configuration of the new asymmetric carbon atom is expected to be *R* for compounds **5–7** (entries 4–7) and *S* for compound **3** (entry 1).

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