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Syntheses and reactions of optically active α-aminoallenylstannanes and α-aminopropargylboranes*

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Abstract: An efficient synthesis of α-aminoallenylstannane from propargyloxazolidinone has been developed. It undergoes reaction with aldehydes to give homopropargylic alcohols with high syn selectivity. Epoxides undergo a similar reaction preceded by rearrangement to the aldehyde. These alcohols were used in the synthesis of β-amino acids, azasugars, and deoxyaminohexoses. Imines underwent reaction with this stannane to give 1,2-diamines. The related propargylborane reacts with aldehydes to produce allenyl carbinols. The $Co_2(CO)_6$ complexes of propargyloxazolidinones were developed as an α-aminopropargyl cation equivalent.

Keywords: α-aminoallenylstannanes; α-aminopropargylboranes; homopropargylic; rearrangement; oxazolidinones.

INTRODUCTION

Propargyl and allenyl organometallics have a rich reaction chemistry with electrophiles, complicated by their ready interconversion. Regardless of which class of organometallic nucleophile is used, propargyl, allenyl or both kinds of products may be obtained, the regiochemistry depending on the metal, the electrophile, additives, and functionality resident on either reaction partner (Scheme 1) [1]. In spite of this complexity, these organometallic species have found broad application in organic synthesis. Induction of asymmetry into the reaction of propargyl- and allenylstannanes with aldehydes has been achieved by the use of Ti(O-*i*Pr)$_4$/BINOL [2], chiral Lewis acids [3], and most extensively via chiral allenylstannanes, primarily due to the work of Marshall [4]. These reactions are thought to proceed by an S_E2' mechanism, and with high absolute stereoselectivity, the sense of which is dependent on both the substrate and the Lewis acid used. Double diastereoselectivity is observed with chiral α-alkoxy aldehydes, with the syn/anti ratio being dependent on the Lewis acid as well as the absolute configuration of the allene.

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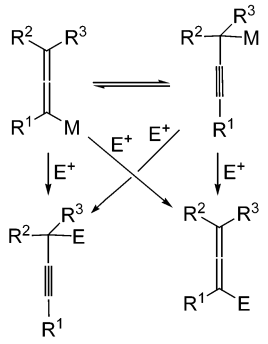
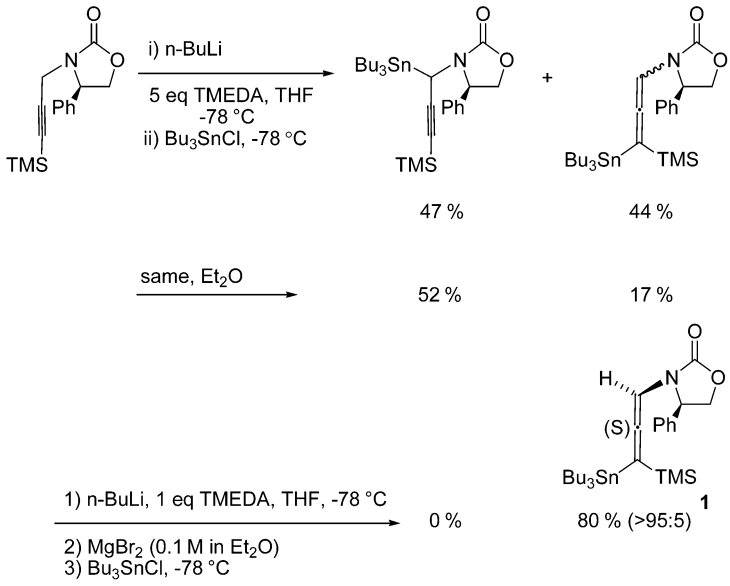


Scheme 1 Reactivity patterns of allenyl and propargyl organometallics.

RESULTS AND DISCUSSION

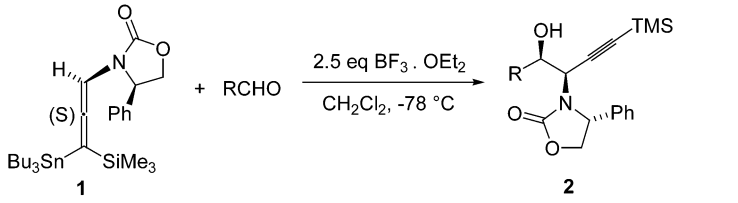
Based on a long-standing group interest in Fischer carbene complex chemistry [5], Peter Ranslow [6] sought to synthesize optically active propargylstannanes containing a chiral α-oxazolidinone group via the reaction of tributyltin hydride with the appropriate alkynyl carbene complex [7]. Although the desired compound could be obtained in this manner, the yields were low and variable, due to instability of the intermediated oxazolidinone-carbene complex. A more conventional approach to the desired α-oxazalidinonyl propargylstannanes via α-metallation [8] of the propargyl oxazolidinone could never be optimized to produce this α-oxazolidinonyl propargylstannane. However, these studies resulted in the highly stereoselective production of the related allenylstannane (Scheme 2). Given the relative inaccessibility and instability of the desired propargylstannanes, reactions of the corresponding optically active allenylstannanes were next addressed [6].



Scheme 2 Attempted alternative approach to propargylstannanes.

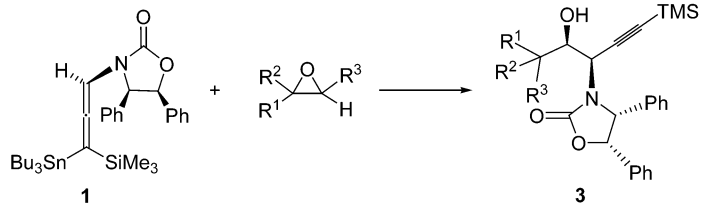
A range of aldehydes underwent reaction with allenylstannane **1** to produce homopropargyl alcohols **2** with high syn selectivity (Scheme 3). Aromatic, aliphatic, and α,β-unsaturated aldehydes all

underwent reaction in high yield and with high syn selectivity. The reaction was relatively insensitive to α-chirality in the aldehyde, again proceeding with high syn selectivity regardless of the stereochemistry of the aldehyde.



Scheme 3 Reaction of α-aminoallenylstannanes **1**.

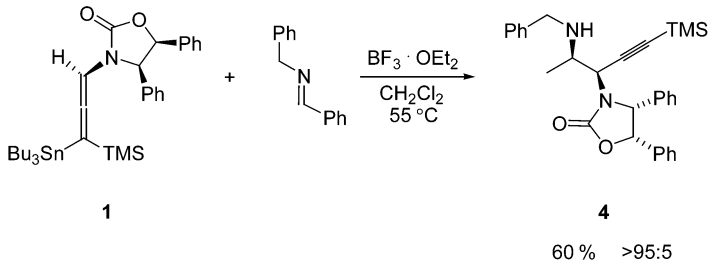
Extension of this chemistry to epoxide substrates produced unexpected results [9]. Products resulting from attack at either terminus of the epoxide were not obtained. Rather, the epoxide apparently underwent Lewis-acid-catalyzed rearrangement to an aldehyde via hydride or alkyl migration [10], followed by alkylation of the aldehyde (Scheme 4). Epoxides having a carbocation-stabilizing group at one terminus and a migrating hydride, phenyl, or alkyl chain underwent efficient reaction. β-Methyl styrene oxide underwent preferential hydride (vs. methyl) migration, producing unreactive 1-phenylpropane-2-one.



R^1	R^2	R^3	Yield, %	dr(*syn/anti*)
Ph	H	H	79	>95:5
Ph	H	Ph	74	94:6
Ph	Me	H	79	>95:5
	H	H	66	>95:5
—$(CH_2)_5$—		H	70	>95:5
Ph	—$(CH_2)_4$—		73	>95:5
Me	H	H	tr.	
H	—$(CH_2)_4$—		0	
H	—$(CH_2)_3$—		0	
Ph	—$(CH_2)_3$—		0	

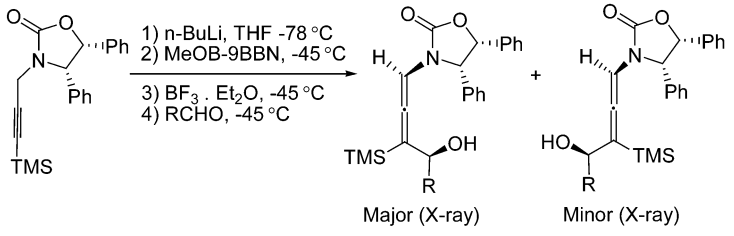
Scheme 4 Reaction of α-aminoallenylstannane **1** with epoxides.

Preliminary experiments indicate that imines can be made to react with allenylstannane **1** with high diastereoselectivity to produce syn diamino compounds (Scheme 5). However, the scope and limitations of this chemistry have not yet been developed.



Scheme 5 Reaction of imines with α-aminoallenylstannanes **1**.

Although the allenylstannane chemistry was effective in a range of applications, the toxicity of tin and the difficulty in removal of tin residue from products led us to attempt similar chemistry utilizing allenylborane reagents [11], previously reported to react with aldehydes to produce homopropargylic alcohols with high diastereoselectivity [12]. In situ generation of the borane by lithiation of the propargyl oxazolidinone followed by BF_3·OEt-assisted reaction with aldehydes produced *allenyl*-carbinols rather than the expected homopropargyl alcohols (Scheme 6). This suggests that the reaction proceeded via the propargylborane, rather than the allenylborane [13]. Although the diastereoselectivity was lower than that observed with the stannanes, the diastereoisomers were easily separated [14,15].

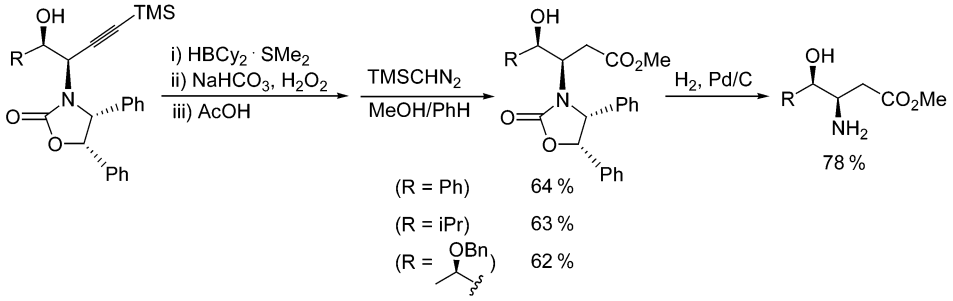


R	dr	Yield (%)	R	dr	Yield (%)
Ph	82:18	87	OBn	88:12	81
i-Pr	77:23	87			
C_5H_{11}	84:16	65	O	83:17	61
	83:17	72			
	83:17	86			
OBn	88:12	79			

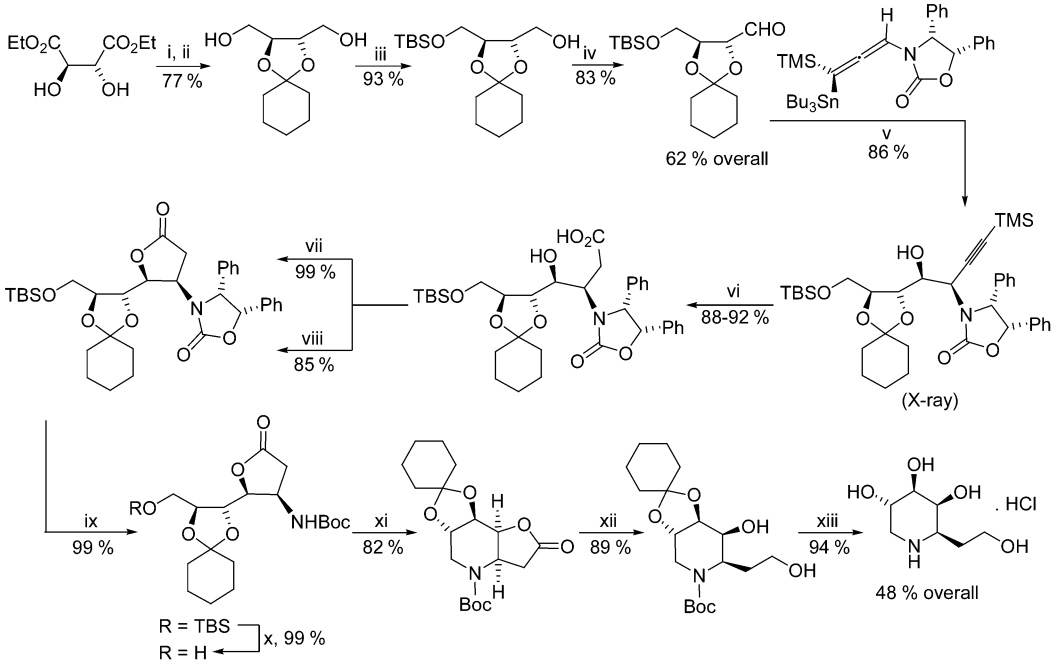
Scheme 6 Reaction of propargylboranes with aldehydes.

The above chemistry produces highly functionalized, optically active compounds of potential utility in the synthesis of biologically active organic compounds. For example, the homopropargyl alcohols from Schemes 3 and 4 can be easily converted into β-amino-γ-hydroxyacids (Scheme 7) [6]. This chem-

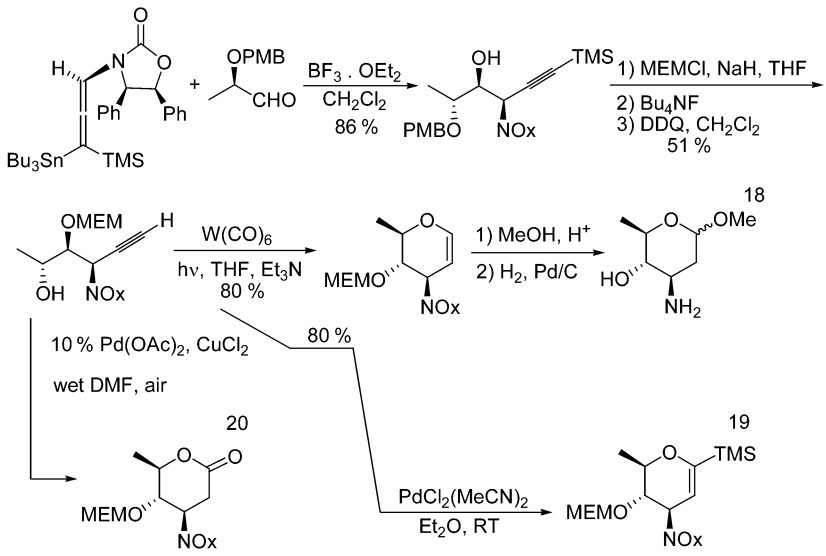
istry was used in an efficient total synthesis of 1-deoxy-D-galactohomonojirimycin (Scheme 8) [16], and a range of deoxyaminohexose derivatives (Scheme 9) [17].



Scheme 7 Conversion to amino acids

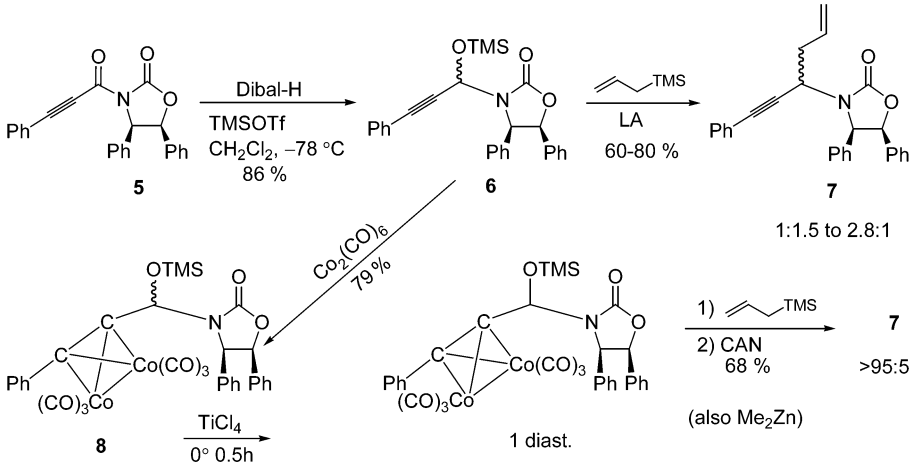


Scheme 8 Synthesis of 1-deoxy-D-galactohomonojirimycin [16]. Reagents and conditions: (i) cyclohexanone, PhH, TsOH, rfx; (ii) $LiAlH_4$, THF, rfx; (iii) NaH, TBSCl, THF, 25 °C; (iv) Dess–Martin periodanane, CH_2Cl_2, 25 °C; (v) $BF_3{\cdot}OEt_2$, CH_2Cl_2, –70 °C; (vi) Cy_2BH, THF, 0→ 25 °C, and then H_2O_2, aq $NaHCO_3$, 0→ 25 °C; (vii) Mukaiyama reagent, Et_3N, CH_2Cl_2, 25 °C; (viii) DEAD, Ph_3P, THF, –20→ +25 °C; (ix) 80 psi H_2, catalyst $Pd(OH)_2$, Boc_2O, THF, 25 °C; (x) HF·Py, MeCN, 25 °C; (xi) DEAD, Ph_3P, THF, –20→ +25 °C; (xii) $LiAlH_4$, THF, –20 °C; (xiii) HCl/MeOH, 25 °C.



Scheme 9 Deoxyaminohexoses, glycals, silylglycals.

All of the above chemistry involved propargyl and allenyl organometallics which are *nucleophilic*. Preliminary studies to prepare *electrophilic* propargyl cation equivalents have been initiated [21]. Reduction of optically active amide **5** followed by silylation gave propargylic aminal **6** as a mixture of diastereoisomers (Scheme 10). Reaction with allylsilane and a variety of Lewis acids gave allylated product **7**, but with very low diastereoselectivity. Complexation of alkynes to dicobalt octacarbonyl greatly stabilizes propargyl cations and can influence the stereochemistry of reaction at the propargylic position [22]. Treatment of the cobalt complex of **6** with titanium tetrachloride equilibrated the mixture of diastereoisomers to a single one, reaction of which with allylsilane gave a single diastereoisomer of **7** after decomplexation with ceric ammonium nitrate. Dimethyl zinc underwent reaction with similar diastereoselectivity and yield. Extension of this chemistry to a wider range of nucleophiles is under current study.



Scheme 10 Development of a propargyl cation equivalent.

SUMMARY

In summary, optically active, functionalized allenylstannanes and propargylboranes have been developed as useful reagents for the synthesis of highly functionalized optically active homopropargyl alcohols and amines, as well as allenyl carbinols. These compounds are useful starting materials for the synthesis of several classes of biologically active compounds. Cobalt-stabilized propargyl cation chemistry is being developed as an electrophilic analog of nucleophilic tin and boron reagents discussed above.

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