Pergamon

Tetrahedron Letters, Vol. 35, No. 45, pp. 8323-8324, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01855-3

Asymmetric Synthesis of Homopropargylic Alcohols from Aldehydes and Allenyltri-*n*-butylstannane

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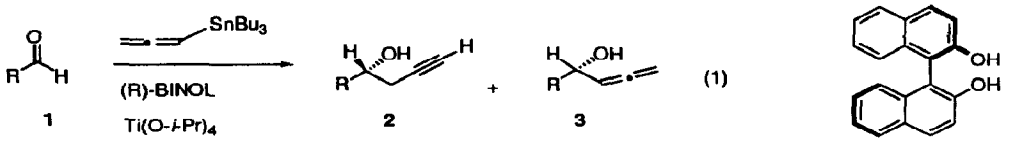
Abstract: The reaction of allenyltri-*n*-butylstannane with aldehydes and a chiral Lewis acid prepared from (R)-BINOL and Ti(O-*i*-Pr)$_4$ gives homopropargylic alcohols with 82 - >99% ee.

Recently we have described effective procedures for the reaction of aldehydes with allyltri-*n*-butylstannane and methallyltri-*n*-butylstannane using catalytic quantities (10 mol percent) of chiral Lewis acids prepared from (R)- or (S)-BINOL and Ti(O-*i*-Pr)$_4$.[1] Tagliavini and Umani-Ronchi have also reported catalytic asymmetric allylations using catalysts prepared from BINOL and $TiCl_2$(O-*i*-Pr)$_2$ according to a similar protocol.[2] In this note we describe the preliminary results of an investigation of these Lewis acids in the reaction of aldehydes with allenylstannane to afford homopropargylic alcohols, as shown in equation 1 below.

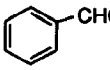
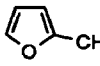
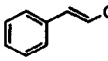
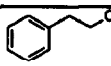
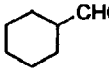


(R)-(+)-1,1'-Bi-2-naphthol

Of the methods which have proven generally useful for the allylation reaction,[1] "method A", utilizing 1:1 BINOL/Ti stoichiometry and molecular sieves for preparation of the chiral Lewis acid,[1a] proved most successful in this instance. Other methods previously described[1] gave very poor conversion to products. Varying amounts of the allenic alcohol **3** were also observed in these reactions. Even under optimal conditions with method A, only low conversions of starting material could be realized with the catalytic quantities of Lewis acid successfully used previously in the allylation reaction. In fact, the isolated yield of the desired product **2** was roughly comparable to the mol percent of Lewis acid utilized in the reaction, always being within a factor of two of the mol percent of titanium tetraisopropoxide employed. These observations suggested an interruption of the catalytic cycle in this case, and the reaction was thus investigated with stoichiometric amounts (100 mol %) and near stoichiometric amounts (50 mol %) of chiral Lewis acid prepared according to "method A." Much better conversions were realized under these conditions, although the yields and enantiomeric excesses were still inferior to those obtainable for reaction of the same substrates with allyl or methallylstannane. As shown in the Table below, very similar results were obtained with 0.50 and 1.0 equivalents of Lewis acid. The ratio of the desired homopropargylic alcohol **2** to allenic alcohol **3** was observed to be substrate dependent under these conditions. Thus, cyclohexanecarboxaldehyde gave significant amounts of allenic alcohol **3** (20% of the product obtained) while only trace amounts, or no detectable amount, were observed with furaldehyde and

cinnamaldehyde, respectively. Benzaldehyde and 3-phenylpropionaldehyde gave intermediate results (7:1 to 23:1 ratio of **2** to **3**), and the ratio was higher using 50 mol % of catalyst in these cases.

Table: Yields and Enantiomeric Excess for Product Alcohols **2**

Aldehyde **1**	Mol % Ti	Reaction Condition	Isolated Yield (%)	% ee (**2**)	**2** : **3**
	50	-20 / 100 h	48	>99	14 : 1
	100	-20 / 100 h	58	95	7:1
	50	-20 / 100 h	50	94	traces of **3**
	100	-20 / 100 h	52	94	traces of **3**
	50	-20 / 72 h	25	82	only **2**
	100	-20 / 72 h	27	82	only **2**
	50	-20 / 72 h	76	95	23 : 1
	100	-20 / 72 h	80	92	11 : 1
	50	-20 / 100 h	64	89	4 : 1
	100	-20 / 100 h	82	89	4 : 1

Although the yields are generally much lower than for the CAA reactions,[1] these reflect primarily the diminished reactivity of allenyltri-*n*-butylstannane as compared to the allyl or methallylstannanes employed earlier. Thus, in all cases examined, unreacted starting material accounted for almost all of the mass balance unaccounted for by conversion to **2** + **3** under the conditions given in the Table.[3,4] Lower reactivity for the allenylstannane (as compared to its allyl counterpart) is not unexpected due to less effective C-Sn hyperconjugation (sp^2 hybridization at carbon) and development of positive charge at an sp (as opposed to sp^2) carbon during the electrophilic addition to the allenyl moiety.

Acknowledgment: This research was assisted financially by the National Institutes of Health.

References

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2. Costa, A. L.; Piazza, M. G.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Am. Chem. Soc.* **1993**, *115*, 7001.
3. (a) The best available enantioselective method for the **1** → **2** transformation is due to Corey: Corey, E. J.; Yu, C.-M.; Lee, D.-H. *J. Am. Chem. Soc.* **1990**, *112*, 878. (b) Allenyltri-*n*-butylstannane was prepared as described by Corey in reference 3a.
4. The catalyst utilized was prepared by heating a CH_2Cl_2 solution of (R)-BINOL (1.0 eq), Ti(O-*i*-Pr)$_4$ (1.0 eq) and 4Å MS at reflux for 1 h. See reference 1a for experimental details.

(*Received in USA* 24 *June* 1994; *revised* 7 *September* 1994; *accepted* 15 *September* 1994)