Catalytic Asymmetric Allylation of Aldehydes†

Gary E. Keck,* Kenneth H. Tarbet, and Leo S. Geraci

Department of Chemistry
University of Utah
Salt Lake City, Utah 84112

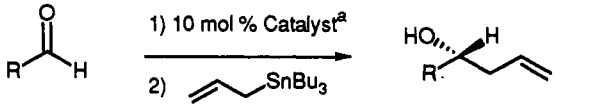
Received June 15, 1993

The Lewis acid-promoted additions of various allylstannanes (and their less reactive silane counterparts) to aldehydes are now well established as powerful synthetic methods. Testament to the utility of such methodology in organic synthesis is the considerable effort expended to date to achieve enantioselectivity in such reactions using "reagent-based" procedures. Considerable progress has been made in this area by Brown,[1] Roush,[2] Corey,[3] and Hafner and Duthaler,[4] among others.[5] Yamamoto[6] and Marshall[7] have also reported examples of asymmetric addition reactions of allylsilanes and allylstannanes, respectively, using Yamamoto's chiral acyloxyborane (CAB) as Lewis acid. However, Marshall reported no examples with the parent allylstannane, and in the one reaction reported by Yamamoto using allyltrimethylsilane (with benzaldehyde), the enantiomeric excess (55%) was somewhat low.

We describe herein two new procedures for the enantioselective allylation of aldehydes which retain the useful characteristics of the original tin- and silicon-based allylations. These processes also possess the desirable feature of being *catalytic* in chiral Lewis acid and employ a chiral ligand which is commercially available as either enantiomer. Moreover, the chiral ligand is easily recovered in high yield and recycled with no decrease in efficiency.

In the first procedure for the catalytic asymmetric allylation (CAA) reaction, the chiral catalyst is prepared by heating a mixture of (*R*)- or (*S*)-binaphthol and titanium tetraisopropoxide (at 1:1 stoichiometry) with powdered 4-Å molecular sieves at reflux in dichloromethane for 1 h (method A).[8] The second procedure (method B) is identical, except that 2:1 BINOL/titanium stoichiometry is used and a catalytic amount of acid (CF_3SO_3H or CF_3CO_2H) is required for best results. Both catalysts are employed at 10 mol % (titanium to aldehyde) as described in the experimental procedures provided. Results obtained for representative achiral aldehydes are summarized in Table I.

Table I



R	method	yield (%)[b]	% ee[c]	configuration
C_6H_5	A	88	95	(*R*)
	B	98	92	(*R*)
c-C_6H_{11}	A	66	94	(*R*)
	B	95	92	(*R*)
(*E*)-C_6H_5CH=CH	A	42	89	(*R*)
	B	78	77	(*R*)
$C_6H_5CH_2CH_2$	A	93	96	ND[e]
	B[d]	98	96	ND
i-C_3H_7	A	89	96	(*R*)
	B	97	87	(*R*)
furyl	A	73	96	ND
	B	97	92	ND

[a] See experimental procedures detailing catalyst preparation according to methods A and B. [b] Isolated yields of the product homoallylic alcohols. [c] Determined by ^{1}H NMR with Eu(hfc)$_3$, except for reactions with 3-phenylpropionaldehyde and isobutyraldehyde, where ^{19}F NMR of the Mosher ester was used. [d] This example used 0.003 equiv of CF_3CO_2H rather than CF_3SO_3H. [e] ND = not determined.

These CAA procedures are the first to achieve high levels of enantioselectivity for the allylation of aldehydes using catalytic quantities of a chiral Lewis acid.[9] The levels of asymmetric induction achieved are quite remarkable for such a simple process. Extensions to more complex stannanes are obvious and are being pursued, as are extensions to enantioselective versions of other Lewis acid-mediated processes. Elucidating the structure of the catalyst–substrate complex responsible for the reaction and the sequence in the catalytic cycle will undoubtedly require considerable effort, particularly since no crystalline materials corresponding to catalyst or catalyst–aldehyde complexes have been obtained to date.[10]

Representative Experimental Procedures. Method A: Preparation of (*R*)-(+)-1-Phenyl-3-buten-1-ol. A mixture of (*R*)-(+)-1,1′-bi-2-naphthol (57.2 mg, 0.199 mmol), 1 M Ti(O-*i*-Pr)$_4$ in CH_2Cl_2 (199 μL, 0.199 mmol), and oven-dried powdered 4-Å sieves (800 mg) in CH_2Cl_2 (4 mL) was heated at reflux for 1 h. The red-brown mixture was cooled to room temperature and benzaldehyde (209 mg, 1.97 mmol) was added. After being stirred for 10 min, the contents were cooled to −78 °C, and allyltri-*n*-butylstannane (726 mg, 2.19 mmol) was added. The reaction was stirred for 10 min and then placed in a −20 °C freezer for 70 h. Saturated $NaHCO_3$ (0.5 mL) was added, and the contents were stirred for 1 h and then poured over Na_2SO_4 and filtered through a plug of Celite. The crude material was purified by flash chromatography, eluting with 19:1 (v/v) hexanes/acetone followed by 17:3 (v/v) hexanes/acetone to give (*R*)-(+)-1-phenyl-3-buten-1-ol as a clear oil (256 mg, 88%). $[\alpha]^{30}_D$ = +45.95 (*c* 7.4, benzene) (lit.[1a] $[\alpha]^{23}_D$ = −44.92 (*c* 7.38, benzene)). The enantiomeric purity was determined to be 95% via ^{1}H NMR using the chiral shift reagent Eu(hfc)$_3$ (0.25 equiv) in $CDCl_3$. The benzylic hydrogen was chosen for this determination relative to (±)-1-phenyl-3-buten-1-ol.

Method B: Preparation of (*R*)-(+)-1-Phenyl-3-buten-1-ol. A mixture of powdered 4-Å molecular sieves (200 mg), (*R*)-(+)-

† Dedicated to Professor E. J. Corey, a true pioneer and inspiring mentor, on the occasion of his 65th birthday.

‡ Portions of this work as well as related results with reagents prepared from BINOL and $TiCl_2$ (O-*i*-Pr)$_2$ have been previously disclosed: Keck, G. E.; Geraci, L. S.; Tarbet, K. H. *Abstracts of Papers*; 205th National Meeting of the American Chemical Society, Denver, CO; American Chemical Society: Washington, DC, March 1993, ORGN 294.

(1) (a) Brown, H. C.; Jadhav, P. K. *J. Am. Chem. Soc.* **1983**, *105*, 2092. (b) Brown, H. C.; Racherla, U. S. *J. Org. Chem.* **1991**, *56*, 401.

(2) (a) Roush, W. R.; Walts, A. E.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8186. (b) Roush, W. R.; Banfi, L. *J. Am. Chem. Soc.* **1988**, *110*, 3979. (c) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Straub, J. A.; Palkowitz, A. D. *J. Org. Chem.* **1990**, *55*, 4117. (d) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 4109.

(3) Corey, E. J.; Yu, C.-M.; Kim, S. S. *J. Am. Chem. Soc.* **1989**, *111*, 5495.

(4) Hafner, A.; Duthaler, R. O.; Marti, R.; Rihs, G.; Rothe-Streit, P.; Schwarzenbach, F. *J. Am. Chem. Soc.* **1992**, *114*, 2321.

(5) (a) Hoffmann, R. W.; Herold, T. *Chem. Ber.* **1981**, *114*, 375. (b) Reetz, M. T.; Zierke, T. *Chem. Ind.* **1988**, 663. (c) Short, R. P.; Masamune, S. *J. Am. Chem. Soc.* **1989**, *111*, 1892. (d) Schmidt, B.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 99.

(6) Furuta, K.; Mouri, M.; Yamamoto, H. *Synlett* **1991**, 561.

(7) Marshall, J. A.; Tang, Y. *Synlett* **1992**, 653.

(8) For previous examples of the use of molecular sieves in reactions of titanium alkoxides, see: (a) Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340. (b) Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1989**, *111*, 1940. (c) Hanson, R. M.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 1922. (d) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

(9) The known Lewis acid-promoted reactions of allylstannanes with achiral Lewis acids such as $TiCl_4$, $SnCl_4$, BF_3·OEt_2, $MgBr_2$, etc. are *stoichiometric* in Lewis acid. Note: (a) Roush, W. R. In *Comprehensive Organic Synthesis;* Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, p 1. (b) Fleming, I. In ref 9a, p 563. (c) Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987; pp 211–230.

(10) A crystal structure and solution NMR data have been reported for materials prepared by mixing (*R*)-BINOL and Ti(O-*i*-Pr)$_4$ at 1:1 stoichiometry. However, neither of the materials prepared as described herein exhibits the same spectral characteristics as those previously reported: Martin, C. A. Ph.D. Thesis, MIT, 1988. We thank Professor Barry Sharpless for sharing these data with us.

0002-7863/93/1515-8467$04.00/0

1,1′ -bi-2-naphthol (26.9 mg, 0.094 mmol), $Ti(O\text{-}i\text{-}Pr)_4$ (13.4 mg, 0.047 mmol), and CF_3SO_3H (0.048 mL of a saturated CH_2Cl_2 solution) in CH_2Cl_2 (2.5 mL) was heated at reflux for 1 h. The red-brown mixture was cooled to room temperature, and benzaldehyde (49.8 mg, 0.470 mmol) was added. The mixture was stirred for 30 min. The mixture was cooled to −78 °C, and allyltri-*n*-butylstannane (466 mg, 1.41 mmol) was added down the inside of the flask. The reaction was stirred for 10 min and then placed in a −20 °C freezer for 70 h. Saturated aqueous $NaHCO_3$ (0.5 mL) and additional CH_2Cl_2 (2 mL) were added. The resultant mixture was washed with brine (2 × 10 mL) and the organic layer dried (Na_2SO_4). The solvents were removed under reduced pressure, and the crude material was purified by flash chromatography, eluting with 19:1 (v/v) hexanes/ethyl acetate, to provide 1-phenyl-3-buten-1-ol as a colorless oil (68.2 mg, 98%, 92% ee). The enantiomeric purity was determined *via* ^1H NMR using the chiral shift reagent $Eu(hfc)_3$ (0.25 equiv) in $CDCl_3$.

Acknowledgment. Financial support of this research by the National Institutes of Health (GM 28961)is gratefully acknowledged.