LETTERS

First Enantioselective Protonation of Prochiral Allyltrimethyltins Using Lewis Acid Assisted Chiral Brønsted Acids

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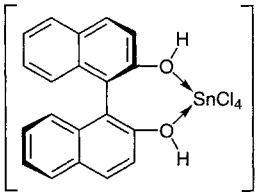
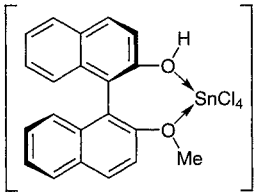
Abstract: The LBA which is prepared from tin tetrachloride and optically active binaphthol or its monomethyl ether is a highly effective reagent for the enantioselective protonation of prochiral allyltrimethyltins. The absolute stereochemical selectivity is quite different from that in the protonation of silyl enol ethers which we reported earlier.

Enantioselective protonation of prochiral allyl anion derivatives is a very simple and attractive route for the preparation of optically active olefins. One example has been reported of enantioselective reduction of allylic esters with formic acid catalyzed by palladium-MOP complexes.[1] The acid-promoted hydrolysis of allyltins or allylsilanes is an interesting alternative which has not yet been investigated with regard to enantioselectivity. Allyltrialkyltin, a synthetic equivalent of allyl anion, is more reactive than the corresponding allylsilane and can be isolated. Recent findings in our laboratory have shown that Lewis acid assisted chiral Brønsted acids (LBA) **1** and **2** are highly effective proton donors for the enantioselective protonation of silyl enol ethers derived from 2-arylcycloalkanones and 2-arylalkanoic acids.[2,3] Herein we report that the enantioselective protonation of allyltrimethyltins with stoichiometric amounts of LBA gives optically active olefins.[4]



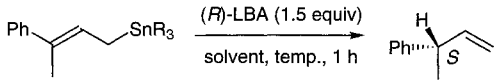
LBA 1



LBA 2

(*E*)-3-Phenyl-2-butenyltrialkyltin derived from racemic 3-phenyl-1-butene[4,5] was chosen for the initial optimization study because it could be prepared as a single (*E*)-isomer, and steric or stereoelectronic interaction between the phenyl group and the naphthyl moiety of LBA was expected with the protonation of allyltrialkyltins as well as silyl enol ethers.[3] The experimental results are summarized in Table 1. In the presence of 1.5 equivalent amounts of (*R*)-LBA **1** in toluene, the protonation of (*E*)-3-phenyl-2-butenyltrimethyltin (**3**) proceeded rapidly at -78 °C to form (*S*)-3-phenyl-1-butene with good enantioselectivity and complete γ-regioselectivity (entry 3). This result suggests that the protonation occurs with allylic rearrangement according to the S_E2' mechanism.[6] The enantioselectivity was increased to 89% ee by lowering the reaction temperature to -90 °C in dichloromethane (entries 1 and 2),[7] and was dramatically decreased by using sterically bulky *Sn*-substituents (entries 4 and 5). This latter tendency is interesting in that the enantioselectivity is independent of the steric features of the trialkylsilyl substituents in the protonation of silyl enol ethers with LBA.[2b,3b] In the above protonation, a proton of (*R*)-LBA approaches the *si*-face of the γ-olefinic carbon of (*E*)-3-phenyl-2-butenyltrialkyltin, while it approaches the opposite enantioface in the protonation of the analogous ketene bis(trimethylsilyl) acetal derived from 2-phenylpropionic acid.[2b,3]

Table 1. Enantioselective Protonation of (*E*)-3-phenyl-2-butenyltrialkyltin with (*R*)-LBAs.[a]



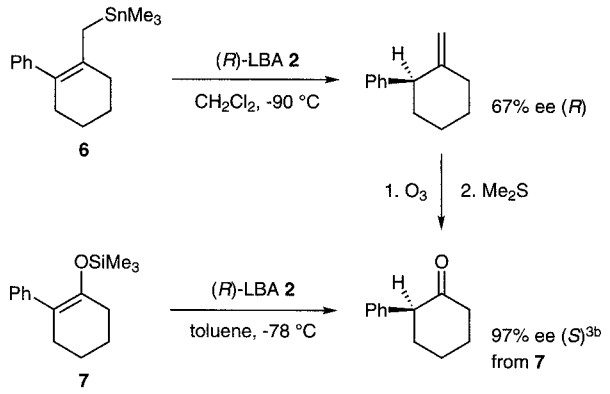
3: R=Me; **4**: R=Bu; **5**: R=Ph >95% conversion

entry	allyltin	(*R*)-LBA	temp. (°C)	solvent	ee (%) of olefin[b]
1	**3**	**2**	-90	CH_2Cl_2	89
2	**3**	**1**	-90	CH_2Cl_2	87
3	**3**	**1**	-78	toluene	71
4	**4**	**1**	-78	toluene	42
5	**5**	**1**	-44	toluene	15

[a] The reaction was carried out using 1.5 equiv of (*R*)-binaphthol or its monomethyl ether and 1.5 equiv of tin tetrachloride. [b] The ee and the absolute configuration were determined by conversion to 3-phenylbutanol with hydroboration [9-BBN (2.5 equiv), THF, 0 °C to ambient temperature], HPLC analysis [Daicel OD-H, hexane/*i*-PrOH=40:1, flow rate=1.0 mL/min: t_R=17.8 min for (*R*)-3-phenyl-1-butanol, t_R=21.0 min for (*S*)-enantiomer], and rotational correlation; see reference 8.

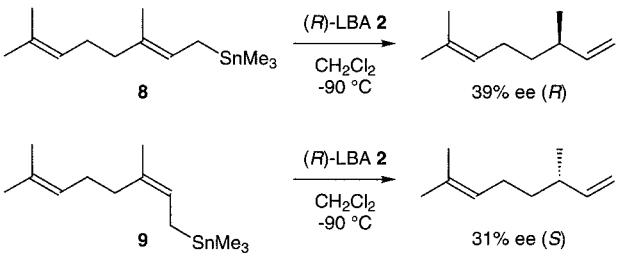
Therefore, we turned our attention to the absolute stereochemical selectivity of the protonation of (*Z*)-allyltrimethyltins with (*R*)-LBA. 1-(Trimethylstannyl)methyl-2-phenylcyclohexene (**6**)[9] as a (*Z*)-allyltrimethyltin was examined under the above optimum conditions (Table 1, entry 1). The enantioselectivity and absolute stereochemistry of the resulting 2-phenyl-1-methylenecyclohexane were determined by HPLC analysis[10] of the ketone formed upon ozonolysis (Scheme 1).[3] Although the observed enantioselectivity was moderate, the absolute stereochemical selectivity was analogous to that in the protonation of silyl enol ether **7**.

Next, we explored the possibility of nonconjugated γ-disubstituted allyltrimethyltins as applicable substrates. Unfortunately, the protonations of geranyltrimethyltin (**8**)[11] and neryltrimethyltin (**9**)[11] with (*R*)-LBA **2** provided 3,7-dimethyl-1,6-octadiene with low enantioselectivities.[12] The absolute stereochemical selectivity showed the same tendency as that in the protonation of γ-phenylallyltrimethyltins **3** and **6**: (*R*)- and (*S*)-olefins were preferentially obtained from **8** and **9**, respectively. The nature of the γ-



Scheme 1

aryl substituent of allyltrimethyltins appears to play a significant role in attaining a higher enantioselectivity.



The (*E*)/(*Z*)-substrate-dependent absolute stereochemistry and the steric influence of *Sn*-substituents on the enantioselectivity observed in these reactions suggest that the mechanism is essentially different from that of silyl enol ethers. Although the detailed stereochemical course is not ascertained, it is possible that the protonation may occur *via* a two chlorine-bridged intermediate between allyltrimethyltin and LBA.[6,13] Keck *et al.* have reported that the transmetalation between allyltributyltin and only free $SnCl_4$ (not complexed with aldehydes) proceeds even at -90 °C.[14a] The tin compounds with a less substituted allyl group immediately and cleanly give the corresponding allyltrichlorotins *via* transmetallation through S_E2' pathway,[14b] while γ-disubstituted ones give precipitates.[14b] Although the precipitates have not been characterized well, they form probably by cationic polymerization as is the case with olefins.[14b] In fact, the protonation proceeds by adding the prochiral allyltrialkyltins to a solution of LBA. Although we still could not exclude a possibility that the protonation proceeds *via* transmetalation, this is rather unlikely by the above reasons.

In conclusion, this paper describes the first example of the enantioselective protonation of allyltrimethyltins. LBAs **1** and **2**, which are available in either enantiomeric form, can be used in 1.5 equivalent amounts to promote the formation of olefins with moderate to high enantioselectivity, in good yield and with a predictable absolute configuration. In addition, the commercially available chiral binaphthol can be recovered efficiently for reuse. We believe that the methodology described herein will prove to have many applications and further improvements are likely.

The following experimental procedure illustrates the details of LBA preparation and protonation.

The enantioselective protonation of **3** with (*R*)-LBA **2**. A heat gun-dried 25-mL Schlenk flask containing the monomethyl ether of (*R*)-binaphthol (225 mg, 0.75 mmol) was evacuated and purged with argon five times and then charged with dry dichloromethane (12 mL, distilled from CaH_2). To the colorless solution was added dropwise a solution of tin tetrachloride (0.75 mL, 0.75 mmol, 1.0 *M*) in dichloromethane at ambient temperature. After 5 min, the slightly yellow solution was cooled to -90 °C, and a solution of freshly prepared **3** (147 mg, 0.5 mmol) in dry dichloromethane (1 mL) was added dropwise along the wall of the flask over 10 min. After being stirred for 1 h at -90 °C, the reaction was quenched with ice-brine, warmed to room temperature, extracted with hexane, dried over $MgSO_4$, filtered, and concentrated to give the crude product. Purification of the crude olefin by silica gel chromatography (hexane alone) provided the corresponding pure product (66 mg, >95% yield).

References and Notes

1. (a) Hayashi, T.; Iwamura, H.; Naito, M.; Matsumoto, Y.; Uozumi, Y. *J. Am. Chem. Soc.* **1994**, *116*, 775. (b) Hayashi, T.; Iwamura, H.; Uozumi, Y.; Matsumoto, Y.; Ozawa, F. *Synthesis* **1994**, 526.
2. For recent reviews of enantioselective protonations, see: (a) Fehr, C. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2566. (b) Yanagisawa, A.; Ishihara, K.; Yamamoto, H. *Synlett* **1997**, in press.
3. (a) Ishihara, K.; Kaneeda, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 11179. (b) Ishihara, K.; Nakamura, S.; Yamamoto, H. *Croat. Chem. Acta* **1996**, *69*, 513. (c) Ishihara, K.; Nakamura, S.; Kaneeda, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1996**, *118*, 12854.
4. Unfortunately, no enantioselectivity was observed in the protonation of (*E*)-3-phenyl-2-propenyltrimethylsilane with (*R*)-LBA **1** in dichloromethane (14 °C, 12 h).
5. Preparation of (*E*)-3-phenyl-2-butenyltrialkyltin, see: Tsuji, Y.; Suzuki, T.; Watanabe, Y.; Takegami, Y. *Polymer J.* **1981**, *13*, 1099.
6. Pereyre, M.; Quintard, J.-P.; Rahm, A. "Tin in Organic Synthesis"; Butterworth & Co., Ltd. (Publishers): London, 1987; pp 131-134.
7. Dichloromethane was used as a solvent to increase the solubility of LBA at -90 °C.
8. Hayashi, T.; Konishi, M.; Fukushima, M.; Mise, T.; Kagotani, M.; Tajika, M.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 180.
9. Compound **6** was prepared from 2-phenyl-1-methylenecyclohexane by deprotonation (superbasic butyl lithium/potassium *tert*-butoxide mixture (2 equiv) in THF at -78 °C for 1 h) and subsequent stannylation (trimethyltin chloride (2.2 equiv) at -78 °C; warmed to room temperature for 1 h), see: (a) Schlosser, M.; Strunk, S. *Tetrahedron Lett.* **1984**, *25*, 741. (b) Schlosser, M.; Choi, J. H.; Takagishi, S. *Tetrahedron* **1990**, *46*, 5633.
10. Daicel OD-H column, hexane-*i*-PrOH=200 : 1, flow rate=1 mL/min) t_R=17.4 min for (*S*)-(-)-enantiomer (major product), t_R=20.2 min for (*R*)-(+)-enantiomer (minor product).
11. For preparation of **8** and **9**, see: Weigand, S.; Brückner, R. *Synthesis* **1996**, 475.
12. The enantioselectivity and absolute configuration of 3,7-dimethyl-1,6-octadiene were determined by GC analysis (PEG) of the acetal formed upon hydroboration [9-BBN (1.2 equiv) in THF at 0 °C; warmed to room temperature for 3 h], Swern oxidation [$(COCl)_2$ (1.2 equiv) and DMSO (2.4 equiv) in dichloromethane at -60 °C for 15 min; Et_3N (5 equiv) at -60 °C for 5 min; warmed to room temperature for 30 min], and acetalization of (2*R*,4*R*)-2,4-pentanediol and the resulting citronellal [cat. TsOH and $HC(OEt)_3$ (1.2 equiv) in benzene at room temperature for 1.5 h]: GC (90 °C) t_R=45.3 min for the acetal derived from (*R*)-3,7-dimethyl-1,6-octadiene, t_R=46.9 min for the acetal derived from (*S*)-enantiomer, see: Fujiwara, J.; Fukutani, Y.; Hasegawa, M.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1984**, *106*, 5004.

13. The stereochemistry of the cleavage has been investigated by Kitching *et al.* for trifluoroacetolysis. The reaction occurs mainly by an *anti* S_E' mechanism when steric factors and conformational mobility are both minimized. However, several examples of a *syn* S_E' mechanism have been reported, see: Young, D.; Kitching, W. *J. Organometal. Chem.* **1983**, *247*, C5. (b) Kuo, C. H.; Patchett, A. A.; Wendler, N. L. *J. Org. Chem.* **1983**, *48*, 1991. (c) Jones, M.; Kitching, W. *Aust. J. Chem.* **1984**, *37*, 1863.

14. (a) Keck, G. E.; Andrus, M. B.; Castellino, S. *J. Am. Chem. Soc.* **1989**, *111*, 8136. (b) Naruta, Y.; Nishigaichi, Y.; Maruyama, K. *Tetrahedron* **1989**, *45*, 1067.