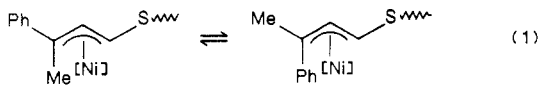

(1)

In summary, we have demonstrated the first regioselective reactions of allylic dithioacetals and its application to facile stereoselective synthesis of silylated dienes. Further extension to other dienes and exploration of **1** is in progress.

Acknowledgment. We thank the Croucher Foundation for generous support. Z.J.N. thanks the Lee Hysan Foundation for a fellowship.

Registry No. **1a**, 70960-88-2; **1b**, 116973-01-4; **1c**, 116973-02-5; **1d**, 116973-03-6; **1e**, 116973-04-7; **1f**, 80400-46-0; (*E*,*E*)-**1g**, 116973-05-8; (*E*,*Z*)-**1g**, 116973-06-9; (*E*,*E*)-**1h**, 116973-07-0; (*E*,*Z*)-**1h**, 116973-08-1; **2a**, 87094-78-8; **2b**, 116972-94-2; **2c**, 116972-95-3; **2d**, 116972-96-4; **2e**, 116972-97-5; **2f**, 116972-98-6; (*E*)-**2g**, 77085-93-9; (*Z*)-**2g**, 77086-06-7; **2h**, 116972-99-7; **2i**, 116973-00-3; **3**, 13170-43-9; (*E*)-$PhCH{=}CHCH(SEt)_2$, 53963-34-1; (*E*)-$PhCH{=}CHCHS\overline{(CH_2)_3}S$, 69178-10-5; $NiCl_2(PPh_3)_2$, 14264-16-5.

Supplementary Material Available: Physical (IR, accurate mass, ^1H and ^{13}C NMR) data for **1a-h** are available (3 pages). Ordering information is given on any current masthead page.

(19) (a) Lee Hysan Foundation Graduate Fellow, 1986-87. (b) On leave from Shanghai Institute of Organic Chemistry, Academia Sinica.

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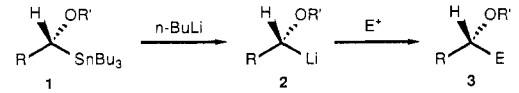
Received August 16, 1988

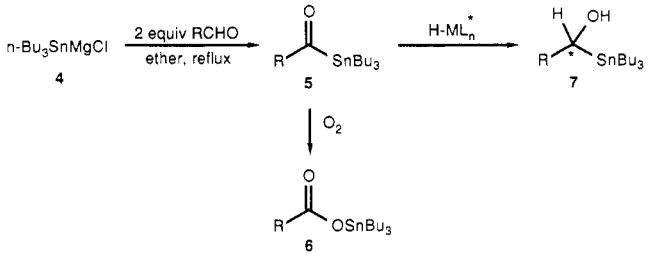
Asymmetric Reduction of Acylstannanes. Preparation of Enantiomerically Enriched α-Alkoxystannanes

Summary: Reduction of acylstannanes (**5**) with BINAL-H reagents affords α-hydroxystannanes in reasonable chemical (45-69%) and consistently good optical (up to 96% ee) yields with predictable stereochemistry.

Sir: α-Alkoxystannanes (**1**) have received considerable recent attention as precursors to α-alkoxyorganolithium reagents (**2**)[1-6] and the corresponding organocopper reagents.[7,8] Tin-lithium exchange occurs readily at low temperatures with retention of configuration to afford configurationally stable α-alkoxyorganolithium reagents.[2] Thus a preparation of enantiomerically pure α-alkoxystannanes would be very desirable as it would constitute an entry into homochiral α-alkoxyorganolithium reagents, species which should be useful as asymmetric building blocks. Previous reports of homochiral α-alkoxystannanes involve chromatographic resolution of diastereomeric derivatives[2,9] and an example of a compound prepared from an α-chloro boronic ester.[10] We report herein that α-alkoxystannanes are readily accessible in good enantiomeric purity by asymmetric reduction of acylstannanes.



Scheme I



As a large number of asymmetric reducing agents have been developed,[11] asymmetric reduction of acylstannanes is a rather obvious approach to homochiral α-alkoxystannanes. However, acylstannanes have been relatively obscure compounds until recently,[12] and little is known about their chemistry other than that they are relatively labile compounds. They were prepared by the reaction of (tributylstannyl)magnesium chloride (1 equiv) with aldehydes (>2 equiv, ether, reflux, Scheme I).[12] Although acyltributylstannanes are sensitive to oxygen (being quantitatively converted to the corresponding crystalline tributyltin carboxylates (**6**) within minutes at room temperature),[13] they may be purified by vacuum distillation and stored under argon in a freezer unchanged for months.

While it had been shown some 20 years ago that $LiAlH_4$ reduction of acetyltriphenylstannane affords 1-(triphenylstannyl)ethanol (unspecified conditions, yield),[14] other reports of the reduction of acylstannanes have not appeared.[15] Preliminary investigations into the feasibility of preparing homochiral α-hydroxystannanes from acylstannanes suggested that the latter compounds are extremely susceptible to reduction. For example, exposure of propanoyltributylstannane to $LiAlH_4$ (1 equiv, ether) or BH_3·THF (1 equiv, THF) at -78 °C for 5 min followed by an aqueous workup gave the expected (racemic) α-hydroxystannane in >95% yield. Hence, we were encouraged

(1) Still, W. C. *J. Am. Chem. Soc.* **1979**, *100*, 1481.
(2) Still, W. C.; Sreekumar, C. *J. Am. Chem. Soc.* **1980**, *102*, 1201.
(3) Sawyer, J. S.; Macdonald, T. L.; McGarvey, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 3376. Sawyer, J. S.; Kucerovy, A.; Macdonald, T. L.; McGarvey, G. J. *J. Am. Chem. Soc.* **1988**, *110*, 842.
(4) McGarvey, G. J.; Kimura, M. *J. Org. Chem.* **1985**, *50*, 4655.
(5) Lesimple, P.; Beau, J.-M.; Sinay, P. *J. Chem. Soc., Chem. Commun.* **1985**, 894.
(6) Duchene, A.; Quintard, J.-P. *J. Chem. Soc., Chem. Commun.* **1987**, 29.
(7) Linderman, R. J.; Godfrey, A. *Tetrahedron Lett.* **1986**, *27*, 4553. Linderman, R. J.; Godfrey, A.; Horne, K. *Tetrahedron Lett.* **1987**, *28*, 3911.
(8) Hutchinson, D. K.; Fuchs, P. L. *J. Am. Chem. Soc.* **1987**, *109*, 4930.
(9) Jephcote, V. J.; Pratt, A. J.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1984**, 800.
(10) Matteson, D. S.; Sarkar, A.; Sadhu, K. M. Poster PS2-36 presented at the 4th IUPAC Symposium on Organometallic Chemistry Directed toward Organic Synthesis, July 26-30, 1987, Vancouver, B.C., Canada.
(11) For recent comparisons of some asymmetric reducing agents, see: Imai, T.; Tamura, T.; Yamamuro, A.; Sato, T.; Wollman, T. A.; Kennedy, R. M.; Masamune, S. *J. Am. Chem. Soc.* **1986**, *108*, 7402. Brown, H. C.; Park, W. S.; Cho, B. T.; Ramachandran, P. V. *J. Org. Chem.* **1987**, *52*, 5406.
(12) Quintard, J.-P.; Elissondo, B.; Mouko Mpegna, D. *J. Organomet. Chem.* **1983**, *251*, 175. Verlhac, J.-B.; Chanson, E.; Jousseaume, B.; Quintard, J.-P. *Tetrahedron Lett.* **1985**, *26*, 6075.
(13) While this work was in progress, similar observations were reported: Kosugi, M.; Naka, H.; Harada, S.; Sano, H.; Migita, T. *Chem. Lett.* **1987**, 1371. Kosugi, M.; Naka, H.; Sano, H.; Migita, T. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3462.
(14) Peddle, G. J. D. *J. Organomet. Chem.* **1966**, *5*, 486.
(15) Very recently, the asymmetric reduction of an acylstannane with (*R*)-BINAL-H was reported: Marshall, J. A.; Gung, W. Y. *Tetrahedron Lett.* **1988**, *29*, 1657. The *S* alcohol was obtained with high enantioselectivity (in agreement with Scheme III).

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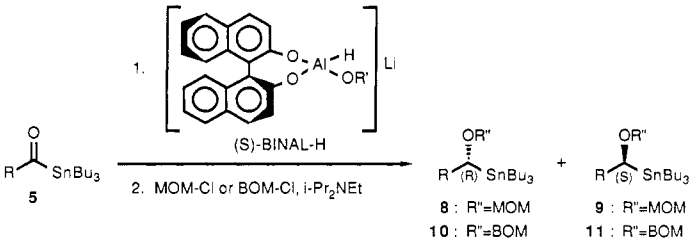
Table I. Asymmetric Reduction of Acylstannanes with (*S*)-BINAL-H[a]



entry	ketone, R	R'-OH, R'	selectivity[b] R:S	selectivity[b] ee, %	rotation[c] $[\alpha]_D$, deg	yield,[d] %
1	**5a**, Me	Me	21:1	91	−32.1*	64
2		Et	32:1	94	−33.1*	58
3		*i*-Pr	21:1	91	−34.6†	54
4	**5b**, Et	Me	20:1	90	−32.5*	60
5		Et	45:1	96	−34.5*	69
6		Et	54:1[e]	96	−34.8*	45
7		*i*-Pr	13:1	85	−36.6†	58
8	**5c**, *i*-Pr	Me	8:1[f]	78	ND[h]	ND
9		Et	14:1[g]	87	ND	ND
10		Et	>50:1[f]	>96	−31.7*	52
11		*i*-Pr	9:1	80	−33.0†	45
12	**5d**, *n*-C_5H_{11}	Me	20:1	90	−28*	68
13		Et	22:1	91	−31.8*	52
14		*i*-Pr	23:1	92	−35.7†	53
15	**5e**, *t*-Bu	*i*-Pr	1:9[i]	80	+11*	55

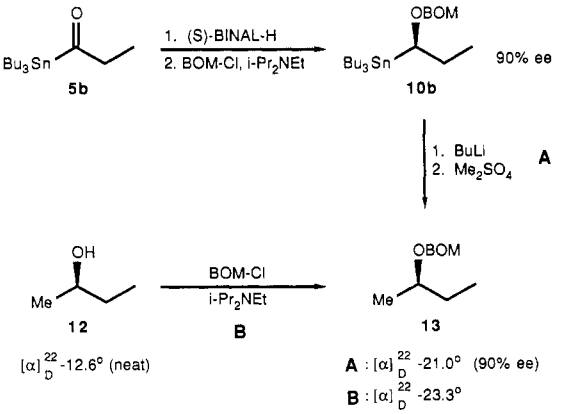
[a] All reactions were carried out at −78 °C for 3 h unless otherwise specified. [b] Determined by ^1H NMR (250 MHz, $CDCl_3$) analysis of the MTPA esters derived from the crude reaction products [(*R*)-(+)-MTPA-Cl, Et_3N, catalytic DMAP, CH_2Cl_2]: Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. [c] Rotations are for the derived methoxymethyl (MOM) (*) or benzyloxymethyl (BOM) (†) ethers (*c* 1.1, $CHCl_3$). [d] Isolated yield of chromatographed (silica gel, 2% ethyl ether–petroleum ether) MOM or BOM ether. The α-hydroxystannanes could not be purified by chromatography on silica gel. [e] Reaction was carried out at −98 °C (N_2, MeOH) for 3 h. [f] Reaction was carried out at −78 °C for 30 h. [g] Reaction was carried out at −45 °C for 5 h. [h] Not done. [i] Reaction was carried out at −78 °C for 60 h.

to examine the reduction of acylstannanes with chiral reducing agents.

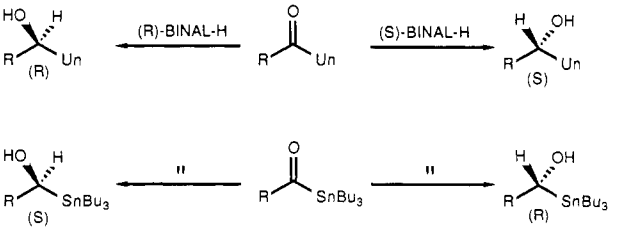
A readily accessible class of chiral reducing agents, which have shown considerable promise for the highly enantioselective reduction of carbonyl compounds, are the 2,2′-dihydroxy-1,1′-binaphthyl-modified lithium aluminum hydride (BINAL-H) reagents.[16,17] Results for the reduction of a number of acylstannanes (**5**, R = Me, Et, *i*-Pr, *n*-C_5H_{11}, *t*-Bu) with various BINAL-H reagents are summarized in Table I. In all cases the relatively unstable alcohol was most conveniently isolated as the MOM or BOM derivative. It is interesting to note that of the three alcohols (MeOH, EtOH, *i*-PrOH) examined as coligands, all gave reasonable optical yields; the ethanol-modified system generally gave the best selectivity.

In contrast to reductions of alkyl aromatic ketones,[16] prolonged reaction times (−100 °C, 3 h → −78 °C, 16 h) are usually not required for the enantioselective reduction of acylstannanes; reactions are typically complete within 3 h at −78 °C. With increasing steric bulk (e.g. entry 10, R = *i*-Pr) the reaction is slower but still shows high enantioselectivity (>95% ee); by comparison, reduction of isobutyrophenone under similar conditions affords the expected carbinol with only 71% ee. Thus the observed enantioselectivity in the reduction of acylstannanes with BINAL-H's seems to be less prone to steric effects than the reduction of alkyl aromatic ketones.

Scheme II



Scheme III



The absolute stereochemistry of the resulting carbinols was established by a transmetalation-trapping sequence, which has been shown to proceed with complete retention of configuration (Scheme II).[2] For example, transmetalation of the reduction product of **5** (*n*-BuLi, DME,

(16) Noyori, R.; Tomino, I.; Tanimoto, Y.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709. Noyori, R.; Tomino, I.; Yamada, M.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6717.

(17) Other reagents that were reported[11] to be particularly effective for aryl alkyl ketones were also tried, but preliminary results were not encouraging. Reduction of **5b** with BH_3–(*S*)-(−)-2-amino-1,1-diphenylbutan-1-ol [Itsuno, S.; Nakano, M.; Miyazaki, K.; Masuda, H.; Ito, K.; Hirao, A.; Nakahama, S. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2039] gave carbinols in a ratio of 1.2:1; $LiAlH_4$–(*S*)-2-(2,6-xylidinomethyl)pyrrolidine [Asami, M.; Mukaiyama, T. *Heterocycles* **1979**, *12*, 499] gave a 3:1 mixture; Ipc_2BCl [Chandrasekharan, J.; Ramachandran, P. V.; Brown, H. C. *J. Org. Chem.* **1985**, *50*, 5448] gave an 8:1 mixture (but reduction of **5c** afforded a 2:1 mixture).

-78 °C) followed by trapping with Me_2SO_4 gave the BOM ether of (*R*)-2-butanol (90% ee). A similar sequence was carried out for the reduction product of **5c**.[18] The absolute stereochemistry of the other carbinols (except **5e**, R = *t*-Bu) produced by (*S*)-BINAL-H is also expected to be *R* based on the similar (same sign and approximate magnitude) rotations of their BOM or MOM ethers.[20] The sense of asymmetric induction is also consistent with Noyori's empirical rule if one considers the tributylstannyl group to be an unsaturated group (Scheme III).[21] As expected, reductions using (*R*)-BINAL-H's gave the (*S*)-carbinols as the major products.

In the case of pivaloyltributylstannane (**5e**, R = *t*-Bu) the reduction proceeded anomalously. With MeOH or EtOH as the coligand, the reduction was exceedingly slow but proceeded more quickly with *i*-PrOH as the coligand (albeit still very slowly, entry 15).[22] Amazingly, reasonable enantioselectivity (80% ee) was observed but in the opposite sense[23] as had been observed for all the other acylstannanes. Presumably this anomalous result is a reflection of the very large steric requirements of a *tert*-butyl group.[25]

A general procedure follows. To a solution of 3.0 mmol of LAH (3.0 mL of a 1 M THF solution) in a total of 9 mL of anhydrous THF at 0 °C under Ar was added slowly a solution of anhydrous EtOH (138 mg, 3 mmol) in 1 mL of THF. After the solution was stirred at room temperature for 20 min, a solution of (*S*)-(-)-1,1′-bi-2-naphthol (859 mg, 3.0 mmol) in 6 mL of THF was added slowly via syringe. The resulting milky mixture was stirred at room temperature for 2 h then cooled to -78 °C. The acylstannane (1.0 mmol) was then added slowly as a solution in 2 mL of THF, and the mixture was stirred at -78 °C for 3 h. The disappearance of the yellow-green color of the acylstannane was a good indication of the progress of the reaction (as monitored by TLC on silica with petroleum ether-ethyl ether, 4:1). The reaction was quenched with 5 mL of saturated aqueous NH_4Cl, and the mixture was diluted with Et_2O (50 mL). The organic layer was washed with water (15 mL) and brine (10 mL), dried ($MgSO_4$), and concentrated. The residue was suspended in petroleum ether (10 mL), and undissolved binaphthol was removed by filtration (and recovered). Concentration of the filtrate afforded the crude alcohol (with nearly quantitative mass balance), which was immediately converted to the MOM (1.5 mmol of MOM-Cl, 2 mmol of *i*-Pr_2NEt, 2 mL of CH_2Cl_2, room temperature, 12 h) or BOM (1.5 mmol of BOM-Cl, 2 mmol of *i*-Pr_2NEt, 2 mL of CH_2Cl_2, room temperature, 12 h) derivative. Standard aqueous workup (Et_2O, $NaHCO_3$) followed by column chromatography on silica gel (2% ethyl ether in petroleum ether) gave the expected compound as a clear colorless oil.

In summary, we have described a general approach to simple alkyl α-alkoxystannanes of good enantiomeric purity and predictable (Scheme III) stereochemistry via reduction of acylstannanes. We anticipate that the availability of enantiomerically enriched α-alkoxystannanes will renew interest in these compounds as reagents for organic synthesis.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada (NSERC) and Research Corporation for financial support.

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(18) Transmetalation of **10c** (96% ee, *n*-BuLi, DME, -78 °C) and reaction with Me_2SO_4 afforded the BOM ether of (*R*)-3-methyl-2-butanol $[\alpha]_D$ -26.2° (*c* 1.5, $CHCl_3$), which had the opposite rotation as the BOM ether of (*S*)-(+)-3-methyl-2-butanol[19] [90% ee $[\alpha]_D$ 25.1° (*c* 1.5, $CHCl_3$)].

(19) Prepared from $LiAlH_4$ opening of the epoxide derived from (*S*)-valine: Koppenhoefer, B.; Schurig, V. *Org. Synth.* **1987**, *66*, 160.

(20) Also, in the ^1H NMR (250 MHz, $CDCl_3$) spectrum of the derived (*R*)-MTPA esters, the methoxy peak of the major diastereomer is consistently the downfield one by ~0.05 ppm.

(21) One might speculate that the similarity between a tributylstannyl group and an unsaturated group is also manifested by their similar effects on the carbonyl stretching frequency in the IR: acetone, 1715 cm^{-1}; acetophenone, 1690 cm^{-1}; acetyltributylstannane (**5a**), 1638 cm^{-1}.

(22) In fact, the reactions with MeOH and EtOH did not proceed at -78 °C. At higher temperatures (-45 °C → 0 °C), some reaction occurred, but the *S* alcohol was formed with only moderate selectivity (1.5-3:1).

(23) That the major isomer produced in this reduction was the *S* isomer was suggested by the rotation (+) of the MOM ether and the relative chemical shifts of the methoxy peaks of the derived (*R*)-MTPA ester (the major peak was upfield). Confirmation was obtained by a transmetalation-trapping sequence as previously described, which gave the BOM ether of (*S*)-(+)-3,3-dimethyl-2-butanol[24] as the major product.

(24) Brown, H. C.; Cho, B. T.; Park, W. S. *J. Org. Chem.* **1988**, *53*, 1231.

(25) A similar reversal of selectivity (from acetophenone to pivalophenone) has been reported for Ipc_2BCl[17] and rationalized on the basis of steric arguments.

Synthesis of (±)-Verrucarol Using a Remarkably Facile Alumina-Catalyzed Intramolecular Diels-Alder Reaction

Summary: The synthesis of the verrucarol skeleton **3** has been achieved in a highly efficient and diastereoselective manner through the intramolecular Diels-Alder reaction of the cyclopentyl C-ring-tethered diene-dienophile **7**. Remarkably, this intramolecular Diels-Alder reaction proceeds readily at room temperature under catalysis by neutral alumina.

Sir: Owing to their unique structures where a number of functional groups are intricately webbed onto a relatively compact sesquiterpene framework, and to their wide-ranging biological activities,[1] the synthesis of the trichothecenes has been extensively scrutinized.[2] Interestingly, most of the successful endeavors involve the biogenetically patterned C_{11}-O_1 or O_1-C_2 bond formation to regio- and stereoselectively construct the B ring of the trichothecene. Surprisingly untested, however, is the seemingly obvious intramolecular Diels-Alder approach to build both A/B rings simultaneously by using the appropriate diene-dienophile precursor based on the disection as illustrated for the archetypical trichothecene verrucarol (**1**) (Scheme I). Herein, we report the highly efficient synthesis of the verrucarol skeleton **3**, the key synthetic intermediate to verrucarol, employing this intramolecular Diels-Alder concept. Furthermore, particular reference is drawn to the unprecedented extent of catalysis exerted by neutral alumina on the reaction.

An earlier model study[3] from these laboratories had revealed the unexpected observation that cycloaddition of **4** proceeds through the transition state **5** in which incipient

(1) For recent reviews, see: *Trichothecenes: Chemical, Biological and Toxicological Aspects*; Ueno, Y., Ed.; Elsevier: Amsterdam, 1983. Tamm, C.; Tori, M. In *Mycotoxin-Production, Isolation, Separation and Purification*; Betina, V., Ed.; Elsevier: Amsterdam, 1984; pp 131-184.

(2) For a recent review on the chemical synthesis of the trichothecenes, see: McDougal, P. G.; Schmuff, N. R. *Prog. Chem. Org. Nat. Prod.* **1985**, *47*, 153.

(3) Koreeda, M.; Leungo, J. I. *J. Org. Chem.* **1984**, *49*, 2079.

0022-3263/88/1953-5586$01.50/0