The Journal of
Organic
Chemistry

VOLUME 56, NUMBER 2 JANUARY 18, 1991

Communications

Diastereoselective Additions of Enantioenriched (γ-Alkoxyallyl)stannanes to α-Alkoxy Aldehydes: A Synthetic Route to Carbohydrates

James A. Marshall* and George P. Luke

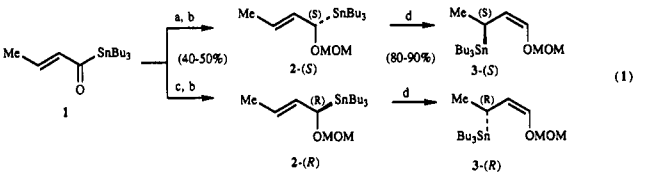
Department of Chemistry, The University of South Carolina, Columbia, South Carolina 29208

Received October 25, 1990

Summary: $BF_3{\cdot}OEt_2$-promoted additions of the (*S*)-(γ-alkoxyallyl)stannane **3**-(*S*) to the (*R*)-α-alkoxy aldehydes **13** and **18** affords the syn adducts **14** and **19** with greater than 90:10 diastereoselectivity. With $MgBr_2$ as the catalyst addition to the (*S*)-α-alkoxy aldehyde **4** is most selective (97:3) with the (*S*)-(γ-alkoxyallyl)stannane **3**-(*S*) whereas BF_3-promoted addition to **4** is most selective (92:8) with the *R* enantiomer **3**-(*R*).

In recent years an increasing recognition of the vital role played by carbohydrates in biologically active natural products has stimulated renewed synthetic interest in simple and complex monosaccharides.[1] Our findings that nonracemic (γ-alkoxyallyl)stannanes undergo stereospecific anti S_E' additions to aldehydes affording monoprotected *syn*-1,2-diol derivatives suggested a possible use for these reagents in carbohydrate synthesis.[2] The present investigation was undertaken to examine matched/mismatched preferences in additions to simple α-alkoxy aldehydes preliminary to more complex applications.

The (γ-alkoxyallyl)stannanes **3**-(*S*) and **3**-(*R*) employed for these studies were prepared by reduction of the acylstannane **1** with (*R*)-(+)- or (*S*)-(−)-BINAL-H followed by treatment of the crude (α-hydroxyallyl)stannanes with MOMCl to give the (α-alkoxyallyl)stannanes **2**-(*S*) and **2**-(*R*) of >95% ee.[3] The expensive (*R*)- and (*S*)-binaphthol ligand can be recovered (~95%) through recrystallization from hexane and reused with no loss of effectiveness.[4] Brief treatment of the (α-alkoxyallyl)stannanes **2**-(*S*) and **2**-(*R*) with $BF_3{\cdot}OEt_2$ at −78 °C afforded the (γ-alkoxyallyl)stannanes **3**-(*S*) and **3**-(*R*) (eq 1). Based on the ee

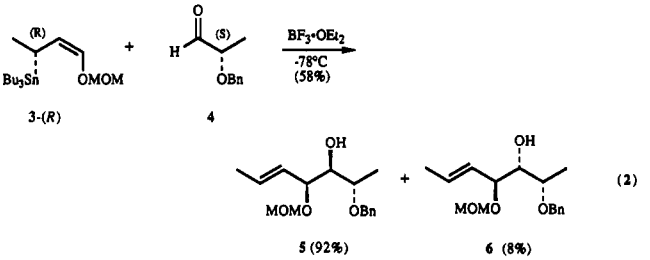


(1)

a) (*R*)-(+)-BINAL-H; b) *i*-Pr_2NEt, MOMCl; c) (*S*)-(-)-BINAL-H; d) $BF_3{\cdot}OEt_2$, -78°C

of products derived from these stannanes, the foregoing rearrangements proceed with essentially complete anti stereospecificity.[3,5]

Addition of stannane **3**-(*R*) to (*S*)-2-(benzyloxy)propanal (**4**)[6] gave the two homoallylic alcohols **5** and **6** as a 92:8 mixture (eq 2).[7] Stannane **3**-(*S*), on the other hand, af-



(2)

(1) Cf.: Danishefsky, S. J.; DeNinno, M. P. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 15. Roush, W. R. In *Trends in Carbohydrate Synthesis*; Horton, D., Hawkins, L. D., McGarvey, G. J., Eds.; ACS Symposium Series 386, Washington, D.C., 1989; pp 242–289.

(2) Marshall, J. A.; Gung, W. Y. *Tetrahedron Lett.* **1989**, *30*, 2183.

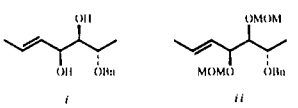
(3) Marshall, J. A.; Gung, W. Y. *Tetrahedron Lett.* **1988**, *29*, 1657. Marshall, J. A.; Gung, W. Y. *Tetrahedron* **1989**, *45*, 1043.

(4) Marshall, J. A.; Welmaker, G.; Gung, B. W. Y. *J. Am. Chem. Soc.*, in press.

(5) Marshall, J. A.; Gung, W. Y. *Tetrahedron Lett.* **1989**, *30*, 7349.

(6) Ireland, R. E.; Thaisrivongs, S.; Dussault, P. H. *J. Am. Chem. Soc.* **1988**, *110*, 5768.

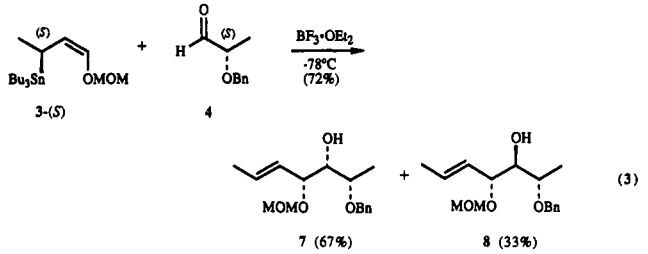
(7) Two other products, diol i and diacetal ii, were also produced in roughly equal amounts as minor products (10–20% yield) from the pairing of **3**-(*R*) and **4**. Comparable byproducts were also observed from the pairing of **3**-(*S*) and **13** (5–10% yield).



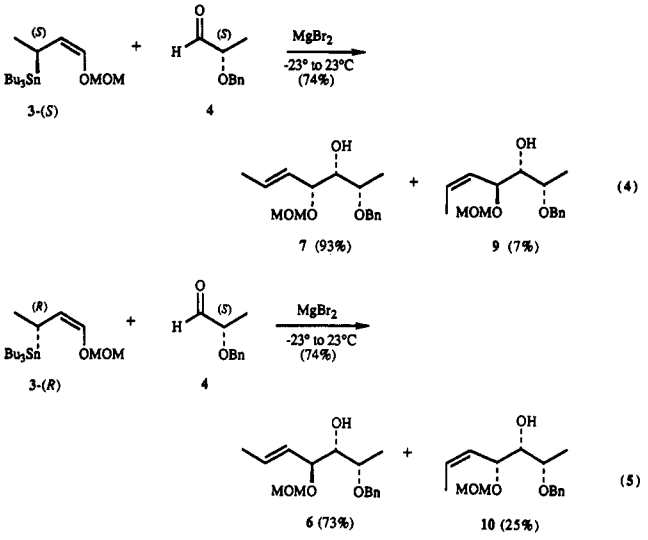
i *ii*

0022-3263/91/1956-0483$02.50/0

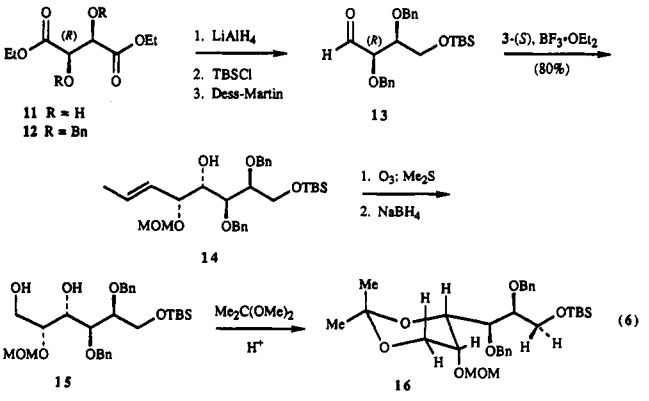
forded a 67:33 mixture of alcohols **7** and **8** upon addition to aldehyde **4** (eq 3). These mixtures were readily analyzed by integration of the ^1H NMR spectra. The stereochemistry of the carbinol center was ascertained from chemical shift differences of the (*S*)- and (*R*)-*O*-methylmandelates.[8]



Addition of the (γ-alkoxyallyl)stannanes **3**-(*S*) and **3**-(*R*) to aldehyde **4** could also be effected with $MgBr_2$ as the catalyst.[9] The reactions were significantly slower than the BF_3 additions and, as expected, the matched/mismatched pairings were reversed. Thus, **3**-(*S*) gave rise to a 93:7 mixture of alcohols **7** and **9**, whereas **3**-(*R*) afforded a 73:25 mixture of alcohols **6** and **10**, along with 2% of alcohol **5** (eqs 4 and 5). The presence of the (*Z*)-olefins **9** and **10** was apparent from the ^1H NMR coupling constants.



As a further extension of this survey we prepared the aldehyde **13** from L-(+)-diethyl tartrate (**11**), as outlined in eq 6. Addition of stannane **3**-(*S*) in the presence of BF_3•OEt_2 afforded alcohol **14** as the sole detectable product. Ozonolysis followed by reduction with $NaBH_4$ yielded



(8) Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. D. *J. Org. Chem.* **1986**, *51*, 2370.

(9) Cf.: Keck, G. E.; Abbott, D. E.; Wiley, M. R. *Tetrahedron Lett.* **1987**, *28*, 139.

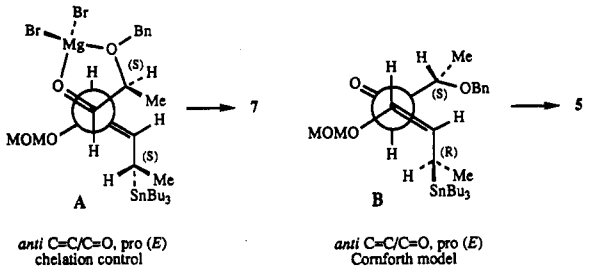
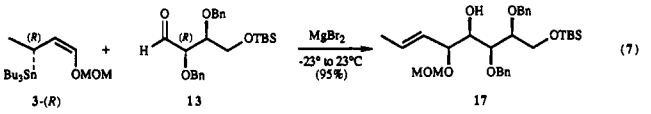


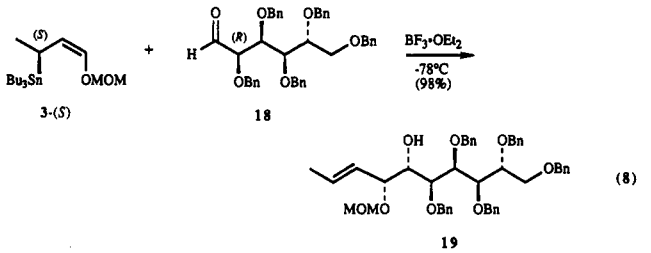
Figure 1. Proposed transition state orientations for matched additions of (γ-alkoxyallyl)stannanes **3**-(*S*) and **3**-(*R*) to α-(benzyloxy) aldehyde **4**.

diol **15**. Support for the relative stereochemistry at C2/C3 was secured from the ^{13}C and ^1H NMR spectra of the acetonide derivative **16**. The ^{13}C spectrum showed methyl peaks at 19.3 and 29.9 ppm as expected for the chair conformation.[10] The bulky side chain is assumed to prefer an equatorial orientation. Two ABX patterns were visible in the ^1H spectrum. Neither showed diaxial coupling. Therefore, the OMOM substituent must be axial and cis to the adjacent side chain as shown.[11]

Several other matched pairings were also examined. Thus, aldehyde **13** afforded alcohol **17** as the only detectable product upon $MgBr_2$-promoted reaction with stannane **3**-(*R*) (eq 7). Finally, BF_3-promoted addition



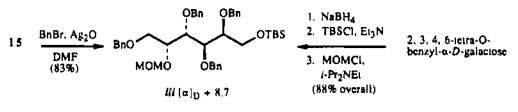
of stannane **3**-(*S*) to pentabenzylglucose (**18**)[12] yielded a single alcohol product **19** (eq 8). The stereochemistry of these latter two products is assigned by analogy.



The stereochemical trends observed in the foregoing addition reactions seem best accommodated by transition states in which the C=O and C=C assume an antiperiplanar relationship as shown in Figure 1.[13] The highly favored anti orientation of the Bu_3Sn grouping[3] and an apparently preferred *E* arrangement of the incipient double bond impose constraints and limit possible transition state orientations. It is assumed that the $MgBr_2$-

(10) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945.

(11) As additional support for the stereochemistry of diol **15** we prepared the tetrabenzyl galactol derivative iii, identical with an authentic sample derived from 2,3,4,6-tetra-*O*-benzyl-α-D-galactose (Austin, P. W.; Hardy, F. E.; Buchanan, J. G.; Baddiley, J. *J. Chem. Soc.* **1965**, 1419).



(12) Pozsgay, V.; Jennings, H. J. *J. Org. Chem.* **1988**, *53*, 4042.

(13) Yamamoto, Y.; Yatagi, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107. A preferred synclinal arrangement of C=C and C=O has been suggested for an intramolecular addition leading to a bicyclo [2.2.2] system. Denmark, S. E.; Weber, E. J. *J. Am. Chem. Soc.* **1984**, *106*, 7970.

promoted additions involve chelation control. The Cornforth model satisfactorily explains the facial selectivity of BF_3-promoted additions.[14]

The present findings are complimentary to previous studies on additions of achiral (γ-alkoxyallyl)stannanes to α-alkoxy aldehydes.[9] The use of stannanes **3**-(*S*) and **3**-(*R*) enable products with a stereochemically defined *E* double bond to be obtained. Further, stereocontrolled hydroxylation of the double bond in these products could lead to ω-deoxy sugars. Studies along these lines will be reported in due course.

Typical Experimental Procedure: (-)-(*E*)-(2*S*,3*R*,4*S*,5*R*)-2,3-Bis(benzyloxy)-1-[(*tert*-butyldimethylsilyl)oxy]-5-(methoxymethoxy)-6-octen-4-ol (14). To a solution of 83.0 mg (0.205 mmol) of stannane **3**-(*S*) and 79.4 mg (0.191 mmol) of aldehyde **13** in 0.5 mL of dry CH_2Cl_2 at -78 °C was added, dropwise, 31 μL (0.248 mmol) of $BF_3{\cdot}Et_2O$. After 40 min at -78 °C, the reaction was quenched with saturated aqueous $NaHCO_3$ and allowed to warm to room temperature. The mixture was then diluted with ether and additional $NaHCO_3$. After the layers were separated, the aqueous layer was reextracted twice with ether. The combined ether extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography on silica gel. Gradient elution from 5 to 10 to 15 to 20% ethyl acetate-hexanes afforded 72.8 mg (72%, 81% based on 8.9 mg of recovered **13**) of alcohol **14**: $[\alpha]_D^{27}$ -38.1° (*c* 1.24, $CHCl_3$); IR (film) ν 3499, 3030, 2929, 1454, 1256, 1095, 1028, 837, 777, 734, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36-7.26 (10 H, m, Ar H), 5.70 (1 H, dq, J = 15.5, 6.4 Hz, H-7), 5.52 (1 H, ddd, J = 15.5, 8.3, 1.5 Hz, H-6), 4.73, 4.54, 4.72, 4.66, 4.63, 4.59 (6 H, AB, J = 6.7, 11.7, 10.4 Hz, OCH_2O, benzylic H's), 4.22 (1 H, d, J = 8.0 Hz, H-5), 3.86-3.76 (5 H, m, H-2,3,4,5), 3.37 (3 H, s, OCH_3), 3.06 (1 H, d, J = 6.3 Hz, OH), 1.69 (3 H, dd, J = 6.3, 1.4 Hz, vinyl CH_3), 0.865 (9 H, s, $SiC(CH_3)_3$), 0.0033 (6 H, s, $Si(CH_3)_2$); EIMS *m/z* (relative intensity) 415 (4), 303 (5), 181 (25), 117 (17), 91 (100). Anal. Calcd for $C_{30}H_{46}O_6Si$: C, 67.89; H, 8.74. Found: C, 67.95; H, 8.75.

Acknowledgment. Support from the National Institutes of Health (Research Grant 2 RO1 GM29475) and the National Science Foundation (Research Grant CHEM 8912745) is gratefully acknowledged.

Supplementary Material Available: ^1H NMR spectra of **5, 6, 7, 8, 10, 13, 14, 15, 16, 17, 19**, and iii and ^{13}C NMR spectrum of **16** (16 pages). Ordering information is given on any current masthead page.

(14) Cornforth, J. W.; Cornforth, R. H.; Mathew, K. K. *J. Chem. Soc.* **1959**, 112.

Resolution, Asymmetric Transformation, and Configuration of Tröger's Base. Application of Tröger's Base as a Chiral Solvating Agent†

Samuel H. Wilen* and Jian Zhong Qi

Department of Chemistry, The City College, City University of New York, New York, New York 10031

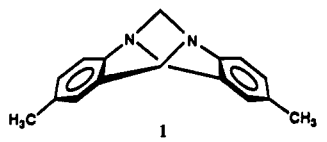
Paul G. Williard

Department of Chemistry, Brown University, Providence, Rhode Island 02912

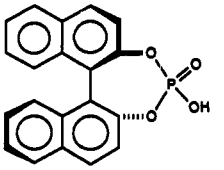
Received October 15, 1990

Summary: Tröger's base, **1**, has been resolved by diastereomeric salt formation with a strongly acidic resolving agent, **2**. The resolution is attended by an asymmetric transformation. Enantiopure **1** acts as a chiral solvating agent toward several secondary and tertiary alcohols. The configuration of **1** has been determined by X-ray crystallography on salt **3** to be (5*S*,11*S*)-(+) which is contrary to that previously established from the circular dichroism spectrum by the method of exciton chirality.

Tröger's base,[1] 2,8-dimethyl-6*H*,12*H*-5,11-methanodibenzo[*b*,*f*][1,5]diazocine (**1**) (TB), is a chiral heterocyclic amine whose chirality is solely due to the presence of two stereogenic nitrogen atoms. The chiral nature of **1** was first recognized by Prelog and Wieland, and this observation was confirmed by optical resolution of the racemate.[2] It is the first chiral tertiary amine devoid of non-nitrogen stereogenic centers to have been resolved.



1



2

† Dedicated to Professor Vladimir Prelog.

Initial efforts to resolve *rac*-**1** with acidic resolving agents, e.g., 10-camphorsulfonic acid, led to the finding that partially resolved samples undergo racemization in acid medium. In order to circumvent the racemization, **1** was subjected to resolution by chromatography on an enantioselective stationary phase (lactose); indeed, **1** is one of the first chiral substances to have been resolved chromatographically.[2] All subsequent reports of resolutions of **1** have been to chromatographic resolutions[3] with the consequence that only small amounts of optically active **1** have been available for study or evaluation of properties. Moreover, it has been asserted that resolution of **1** through formation of diastereomeric salts is not feasible.[4]

There is something of a resurgence of interest in **1** due in large measure to the sharply folded geometry of the molecule, its C_2 symmetry, and its rigidity that makes it

(1) Tröger, J. *J. Prakt. Chem.* **1887**, *36*, 225-245.
(2) Prelog, V.; Wieland, P. *Helv. Chim. Acta* **1944**, *27*, 1127-1134.
(3) E.g.: Hesse, G.; Hargel, R. *Liebigs Ann. Chem.* **1976**, 996-1008. Lindner, K. R.; Mannschreck, A. *J. Chromatogr.* **1980**, *193*, 308-310. Saigo, K.; Chen, Y.; Kubota, N.; Tachibana, K.; Yonezawa, N.; Hasegawa, M. *Chem. Lett.* **1986**, 515-8. Yuki, Y.; Okamoto, I.; Shibata, T.; Nakamura, H. U.S. Patent 4,786,416, Nov. 22, 1988 (to Daicel Chemical Industries); *Chem. Abstr.* **1989**, *111*, 160,330.
(4) (a) Mason, S. F.; Vane, G. W.; Schofield, K.; Wells, R. J.; Whitehurst, J. S. *J. Chem. Soc. B* **1967**, 553-556. (b) Mason, S. F. *Molecular optical activity and the chiral discriminations*; Cambridge Univ. Press: Cambridge, U.K., 1982; p 191.

0022-3263/91/1956-0485$02.50/0