was poured into ether (50 mL) and washed with water. The organic extracts were washed with 5% HCl (5 × 25 mL), H_2O (2 × 20 mL), saturated $CuSO_4$ (2 × 20 mL), and then brine (2 × 30 mL). Drying (Na_2SO_4) and removal of the solvent gave 3.22 g (79%) of **10** as a yellow oil, which solidified after 2 days at −20 °C. Recrystallization ($MeOH/H_2O$) afforded **10** as a yellow solid: mp 58–60 °C; ^1H NMR ($CDCl_3$) δ 3.99 (s, 3 H), 4.02 (s, 3 H), 7.72 (d, J = 2 Hz, 1 H), 8.08 (d, J = 2 Hz, 1 H), 10.0 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 52.9, 56.7, 114.2, 118.5 (center of triflate quartet), 126.2, 126.3, 135.6, 141.4, 152.6, 163.4, 189.5; IR (neat) 2850, 2750, 1733, 1708 cm^{-1}. Anal. Calcd for $C_{11}H_9F_3SO_7$: C, 38.60; H, 2.63. Found: C, 38.82; H, 2.63.

Methyl 5-Formyl-3-methoxy-2-[(trimethylsilyl)ethynyl]-benzoate (11). A solution of 557 mg (1.62 mmol) of triflate **10** in 5 mL of dry DMF was treated with 0.32 mL (2.3 mmol, 1.5 equiv) of (trimethylsilyl)acetylene, 1.0 mL of dry Et_3N, and 32.4 mg (0.046 mmol) of $(Ph_3P)_2PdCl_2$ and heated at 90 °C for 5 h under N_2. The resulting brown solution was cooled, diluted with 15 mL of H_2O, and extracted with 1:1 ether/petroleum ether (8 × 10 mL). The combined organic extracts were washed with water until neutral, filtered through Florisil, and dried over Na_2SO_4. Evaporation and recrystallization ($CHCl_3$/hexane) left 444 mg (94%) of **11** as a brown solid: ^1H NMR ($CDCl_3$) δ 0.29 (s, 9 H), 3.93 (s, 3 H), 4.00 (s, 3 H), 7.49 (d, J = 1.4 Hz, 1 H), 7.92 (d, J = 1.4 Hz, 1 H), 9.97 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ −0.2, 52.3, 56.5, 97.7, 110.2, 110.8, 118.6, 125.2, 135.5, 135.9, 161.8, 165.9, 190.6; IR (CCl_4) 3311, 2850, 2750, 2153, 1726, 1702 cm^{-1}; HRMS calcd 290.2065, found 290.2098.

Methyl 5-Ethenyl-2-ethynyl-3-methoxybenzoate (4). To a solution of 40.5 mg (0.140 mmol) of aldehyde **11** in 3 mL of dry ether at 0 °C was added 0.15 mL (0.15 mmol) of $(CH_3)_3SiCH_2MgCl$ (1.0 M in ether). The resulting solution was stirred at 0 °C for 1 h and then at 22 °C for 2 h before it was quenched with 5% HCl (1 mL) and extracted with ether (3 × 7 mL). The combined organic solution was washed with H_2O (2 × 5 mL) and then brine, dried (Na_2SO_4), and concentrated to give 47.4 mg (90%) of the (β-hydroxyalkyl)trimethylsilane: ^1H NMR ($CDCl_3$) δ 0.02 (s, 9 H), 0.26 (s, 9 H), 1.19 (t, J = 7 Hz, 2 H), 3.89 ("s", 6 H), 4.83 (t, J = 7 Hz, 1 H), 7.04 (d, J = 1.0 Hz, 1 H), 7.34 (d, J = 1.0, 1 H). The intermediate was dissolved in 1.0 mL of dry THF and added to 2 mL of THF containing 5.0 mg (0.12 mmol) of oil-free KH and 32 mg (0.12 mmol) of 18-crown-6. The reaction mixture was stirred under argon for 1 h, quenched with 3 mL of saturated Na_2CO_3 and 3 mL of MeOH, and diluted with 10 mL of ether. The organic phase was extracted with 3 × 5 mL of saturated Na_2CO_3, 3 × 5 mL of H_2O, and 2 × 5 mL of brine and dried over $MgSO_4$. Flash chromatography (10%, 40% then 75% EtOAc/Hex) left 17.3 mg (67%) of **4**: mp 255 °C; ^1H NMR ($CDCl_3$) δ 3.65 (s, 1 H), 3.93 (s, 3 H), 3.96 (s, 3 H), 5.39 (d, J = 10.9 Hz, 1 H), 5.85 (d, J = 17.6 Hz, 1 H), 6.70 (dd, J = 10.9, 17.6 Hz, 1 H), 7.08 (d, J = 1.4 Hz, 1 H), 7.54 (d, J = 1.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 52.2, 56.3, 77.6, 87.1, 111.1, 116.4, 120.2, 135.0, 135.6, 138.8, 161.8, 166.5; IR (neat) 3310, 1739 cm^{-1}; HRMS calcd 216.0786, found 216.0755.

8-Ethenyl-1,10,12-trimethoxy-6*H*-benzo[*d*]naphtho[1,2-*b*]pyran-6-one (1-*O*-Methyldefucogilvocarcin V, 2a). A 5-mL round-bottom flask was charged with 19.2 mg (88.8 μmol) of acetylene **4**, 20.0 mg (59.2 μmol, 0.67 equiv) of chromium carbene **3a**,[7] and 1.0 mL of heptane and subjected to the freeze–thaw method (3 cycles) back-filling with argon each time. The orange solution was heated to 70 °C for 10 h under argon. Then CH_3CN (4.0 mL) and H_2O (2.0 mL) were added, and the mixture was stirred for 1 h under air and then extracted with ether (3 × 10 mL). The organic phases were combined, washed with H_2O (3 × 5 mL) and brine, and dried over $MgSO_4$. Flash chromatography (10% benzene/ether) gave 10.0 mg (43%) of ester **12** as a yellow oil: ^1H NMR ($CDCl_3$) δ 3.60 (s, 3 H), 3.66 (s, 3 H), 3.81 (s, 3 H), 3.85 (s, 3 H), 5.43 (d, J = 10.9 Hz, 1 H), 5.88 (d, J = 17.6 Hz, 1 H), 6.05 (s, 1 H), 6.42 (d, J = 8.2 Hz, 1 H), 6.57 (d, J = 8.2 Hz, 1 H), 6.66 (t, J = 8.2 Hz, 1 H), 6.80 (dd, J = 10.9, 17.6 Hz, 1 H), 7.00 (m, 2 H), 7.33 (dd, J = 8.2, 0.9 Hz, 1 H); IR (neat) 3400, 1729 cm^{-1}.

To ester **12**, 10.0 mg (0.025 mmol), in 5 mL of dry benzene was added 0.5 mg (2.7 mmol) of *p*-TsOH. The solution was stirred at reflux for 1.5 h. The solvent was removed in vacuo, and the residue was dissolved in CH_2Cl_2, extracted with H_2O (3 × 5 mL), and dried (Na_2SO_4). Flash chromatography (10% benzene/ether) gave 8.6 mg (95%) of **2a** as a yellow solid, mp 243–245 °C dec (lit.[3c] mp 244–247 °C dec), with NMR and IR spectra in agreement with the literature data.[3c]

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Registry No. **1**, 77879-90-4; **2a**, 112374-33-1; **3a**, 27436-99-3; **4**, 131066-92-7; **8**, 3507-08-2; **9**, 3507-09-3; **10**, 131066-90-5; **11**, 131066-91-6; **12**, 131066-93-8.

Supplementary Material Available: ^1H and ^{13}C NMR and infrared spectra for new compounds (structures **9**, **10**, **11**, and **4**) (13 pages). Ordering information is given on any current masthead page.

Quantitative Relationship between Optical Rotation and Conformation

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It has long been known[1] that the magnitude of optical rotation of a chiral aracemic compound depends on temperature, solvent, and concentration. These changes have often been ascribed, qualitatively, to changes in intermolecular association (solute–solute interaction) and in solvation (solute–solvent interaction), especially changes in solute–solute and solute–solvent hydrogen bonding.[1,2] On the other hand, J. H. Brewster recognized, some 30 years ago,[3] that specific (or molar) rotation is crucially dependent on conformation. A salient example is lactic acid, $CH_3CHOHCO_2H$: according to the polarizability of the four substituents at the chiral center (CO_2H, CH_3, OH, H) the *R* acid should be dextrorotatory[3] (as, in fact, are its esters and salts), whereas, actually, it is levorotatory in water. This finding is best interpreted in terms of a cyclic, internally hydrogen-bonded structure.[3]. It is not clear, however, whether hydrogen bonding affects specific rotation (in magnitude and, occasionally, in sign) directly or whether it does so indirectly (by affecting conformation), or both.

Recently[4] we reported large concentration effects on the conformational equilibrium in *cis*-3-hydroxythiane *S*-oxide (**1**, Scheme I[5]). In concentrated solution, this substance is either strongly self-associated through intermolecular

(1) Eliel, E. L. *Stereochemistry of Carbon Compounds*, McGraw-Hill: New York, 1962; p 8.
(2) For a recent example, see: Ko, K.-Y.; Eliel, E. L. *J. Org. Chem. Soc.* **1986**, *51*, 5353.
(3) Brewster, J. H. *J. Am. Chem. Soc.* **1959**, *81*, 5475. See also ref 1, p 406 and Djerassi, C. *Optical Rotatory Dispersion*; McGraw-Hill: New York, 1960; p 125ff.
(4) Eliel, E. L.; Brunet, E. *Tetrahedron Lett.* **1985**, *26*, 3421; *J. Org. Chem.* **1986**, *51*, 677.
(5) The likely absolute configuration of **1** as 1*R*,3*S* has been suggested to the authors by J. H. Brewster, personal communication; cf. ref 3.

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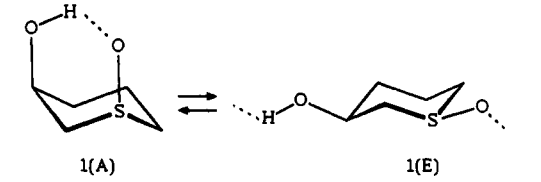
Scheme I



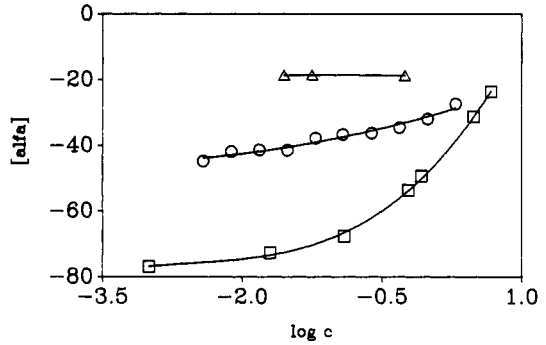


Figure 1. Plot of $[\alpha]^{25}_D$ of compound 1 (Scheme I) vs logarithm of its concentration in methanol (triangles), acetone (circles), and methylene chloride (squares).

hydrogen bonding or (in appropriate solvents) strongly hydrogen bonded to solvent, with the result that the diequatorial conformation (SO and OH equatorial) is preferred because, in this conformation, the bonding groups (SO, OH) are more accessible. In hydrogen bonding solvents, such as methanol, the diequatorial conformation persists on dilution. But in nonbonding solvents, such as methylene chloride, intramolecular hydrogen bonding becomes increasingly important upon dilution and as a result the diaxial conformation (SO and OH axial) becomes preferred (Scheme I) as demonstrated by NMR spectroscopy.[4]

We have now prepared compound 1 in optically active form (61% ee) and have studied its specific rotation as a function of solvent and concentration. The results are summarized in Figure 1.

In methanol-d_4, where the compound is known to exist in the diequatorial form at all concentrations studied, the specific rotation is essentially concentration independent ($[\alpha]^{25}_D$ = −18.7°). The corresponding rotations at the highest attained concentrations in CD_2Cl_2 [−23.7° (4.7 M)] and in acetone [−27.4° (2.0 M)] differ only slightly, suggesting (see below) that the nature of the hydrogen donor—methanol-d_4 or the hydroxyl group of diequatorial **I**—has but a minor effect on the specific rotation.

In contrast, in acetone and in methylene chloride, upon dilution, the specific rotation changes substantially, to final values of −45° and −73.8°, respectively, at the highest dilution attained. In Figure 2 is shown the mole fraction of the diequatorial conformer as a function of the logarithm of concentration in CD_2Cl_2 and in acetone-d_6. In methylene-d_2 chloride a linear plot is obtained, whereas, in acetone-d_6, upon increasing dilution, the mole fraction of the diaxial conformer reaches a limiting value of ca. 57%. Presumably this is indicative of a competition, in dilute solutions, of intramolecular hydrogen bonding of the solute versus hydrogen bonding to solvent acetone acting as an acceptor. (The more important donor bonding to O–S, which occurs in dilute methanol solution, is, of course, not possible in acetone.)

Figure 3 shows that, in methylene chloride, $[\alpha]^{25}_D$ varies linearly with x_E, the mole fraction of the diequatorial conformer. The plot can be expressed as $[\alpha]^{25}_D = -74.9 + 64.3x_E$ (r = 0.998), implying a specific rotation of −74.9°

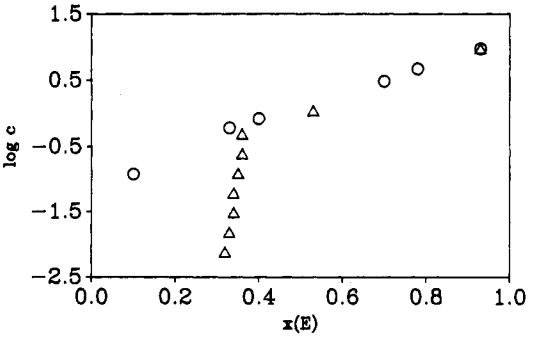


Figure 2. Plot of log c vs the mole fraction of diequatorial conformer [x(E)] of compound 1 (Scheme I) in CD_2Cl_2 (circles) and acetone-d_6 (triangles).

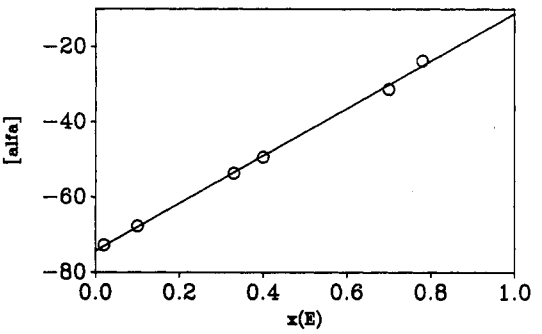


Figure 3. Plot of $[\alpha]^{25}_D$ of compound 1 in methylene chloride vs the mole fraction of its diequatorial conformer (Scheme I).

for conformer A and −10.6° for conformer E. Another way of expressing this result is $[\alpha]^{25}_D = -10.6x_E - 74.9x_A$, implying that the specific rotation is the weighted average of the specific rotation of the diequatorial and that of the diaxial conformer, with the mole fractions of the corresponding conformers as weighting factors. The $[\alpha]_E$ value of −10.6° differs somewhat from the corresponding value in methanol (−18.7°) for the reason mentioned above.

The situation in acetone is considerably more complex. As seen in Figure 2, x_E, the mole fraction of the equatorial isomer, decreases with dilution in about the same fashion as it does in CD_2Cl_2 down to about 0.36 at 0.3 M. At this point, however, further change becomes very slow, the lowest x_E still being 0.32 at 0.0075 M. The rotation also, while rapidly increasing in absolute value with dilution at first, comes to a nearly constant value of $[\alpha]^{25}_D$ = −42° at 0.1 M concentration.

It is very likely that, in acetone, acceptor hydrogen bonding —O—H···O=C plays a significant role. Because of the lower basicity of C=O compared to S—O, this type of hydrogen bonding is less strong than the O–H···O–S hydrogen bonding observed (intermolecularly) in concentrated solution and (to solvent) in dilute methanol solution. A possible explanation is as follows: As the concentration in acetone is decreased, intermolecular hydrogen bonding is replaced by intramolecular hydrogen bonding (concommitant with 1(E) → 1(A) conformational change) down to about 0.2 M. At this concentration the strength of the intramolecular bond in the A conformation and the strength of the solute–solvent hydrogen bond to acetone in the E conformation hold each other in balance, i.e., equilibrium between 1(A) and **I**(E)·acetone is reached. Further dilution then has little effect on x_E or on $[\alpha]^{25}_D$.

The equation $[\alpha]^{25}_D = [\alpha]_E x_E + [\alpha]_A x_A$ is not satisfied for $[\alpha]_A$ = −74.9° (from the results in methylene chloride, vide supra) and any value of $[\alpha]_E$ between −18.7° (the methanol value) and −10.6° (the extrapolated methylene chloride value). Therefore one must assume that either

the value of $[\alpha]_A$ or that of $[\alpha]_E$ or both are different in acetone from the corresponding values in methanol and in methylene chloride, i.e., that there is a substantial intrinsic solvent effect as well as a conformational effect on rotation.

Experimental Section

3-Thianone[4] was enantioselectively oxidized to the corresponding *S*-oxide by Sharpless' reagent.[6] The resulting 3-thianone *S*-oxide, 61% ee (chiral shift reagent) was reduced with sodium borohydride[4] to a mixture of *cis*- and *trans*-3-hydroxythiane *S*-oxide from which the first-eluting cis isomer was obtained by flash chromatography ($CHCl_3$/MeOH, 14:1).

The mole fractions (x_A, x_E) of conformers A and E (Scheme I) in CD_2Cl_2 and CD_3COCD_3 were obtained from the concentration-dependent vicinal H–O–C–H coupling constants (J_{obs}) by using the equation $J_{obs} = J_A x_A + J_E x_E$, where $x_E + x_A = 1$. J_A and J_E were taken from proton NMR spectra of 1 in CD_2Cl_2 and in CD_3COCD_3 at −80 °C at concentrations where both A and E conformers were readily seen: J_A = 9.7 Hz, J_E = 4.8 Hz in CD_2Cl_2; J_A = 9.2 Hz, J_E = 4.2 Hz in CD_3COCD_3. (That x_E = 1.0 at all concentrations in methanol was concluded from the invariance of the coupling constants of the carbinol hydrogen, H(3), which is a near-triplet of triplets with coupling constants of 10.4, 10.0, 3.9, and 3.9 Hz.) $[\alpha]^{25}_D$ was measured at various concentrations; for the plot in Figure 3, the corresponding x_E was obtained from the linear regression of the plot of x_E vs log *c* (Figure 2), r = 0.999.

Acknowledgment. This work was supported by NSF Grant CHE-8703060. E.B. is grateful for a NATO fellowship.

(6) Pitchen, P.; Duñach, E.; Deshmukh, M. N.; Kagan, H. B. *J. Am. Chem. Soc.* **1984**, *106*, 8188.

Reversed Regiochemistry in the Hydroboration of Vinylarenes Catalyzed by Neutral Rhodium Complexes and the Related Asymmetric Version†

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Introduction

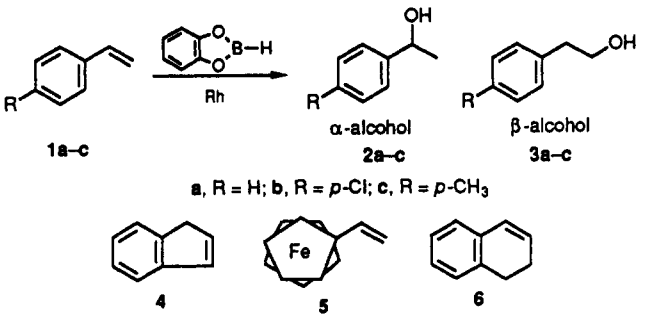
Since its discovery in 1956, the unique olefin hydroboration reaction has became one of the most widely used synthetic reactions.[1] Through the efforts of Brown and co-workers, and many others, the versatility of hydroboration has been repeatedly demonstrated. Thus, many new types of reagents have been introduced, including some which have shown enantioselectivities as high as 100% with certain olefins.[2] When Noth and Mannig[3] reported a catalyzed hydroboration for the first time, a new facet of hydroboration was revealed. The recent reports of Burgess,[4] Hayashi,[5] and Suzuki[6] prompted us to disclose our own results on the catalyzed hydroboration of vinylarenes.[7]

Results and Discussion

In the catalyzed hydroboration of styrenes, Hayashi[5] obtained a very high enantioselectivity with reversed regiochemistry. He claimed that high Markovnikov selectivity was only observed with cationic rhodium complexes

†Dedicated to Prof. Wang Yu on the occasion of his 80th birthday.

Scheme I



and in the presence of tertiary phosphine ligands, whereas Wilkinson's catalyst or $[Rh(COD)_2]BF_4$ without phosphine ligands afforded the anti-Markovnikov products.

Surprisingly, in the present study, in contrast to the results of Hayashi, the α-alcohol was obtained as the major product of the catalyzed hydroboration of styrene with catecholborane (CB) in the presence of Wilkinson's catalyst. The results of catalyzed hydroboration in the presence of Wilkinson's catalyst compared to those of uncatalyzed hydroboration are summarized in Table I.

Substrates 1–6 were all vinylarenes. The catalyzed hydroboration of all these substrates followed a Markovnikov pathway leading to the α-alcohol almost exclusively. This was opposite to that of uncatalyzed hydroboration. In the uncatalyzed reactions, substrates 1–5 showed a high propensity to form β-alcohols. 1,2-Dihydronaphthalene (6) was the only substrate which afforded an α-alcohol as the major product, in the α:β ratio of 90:10. In this case, the catalyzed reaction enhanced the regioselectivity to 98:2 (entry 7). The reversed regiochemistry of all the substrates could further be reinforced by the addition of 4 mol % of a Lewis acid, such as $SnCl_2$, $Ti(OR)_4$, $ZnCl_2$, or BF_3. For example, with styrene, the α:β ratio changed from 90:10 to 98:2, with yields over 90%.

Another neutral rhodium catalyst, $[RhCl(COD)]_2$, was also examined. Without the presence of tertiary phosphine, or in the presence of Lewis acids, the major product was still the β-alcohol. For example, in the presence of $SnCl_2$ the α:β ratio was 33:67. However upon the addition of 2 mol % of triphenylphosphine, the ratio changed to 59:41. With 4 mol % of phosphine, the regiochemistry reversed completely to an α:β ratio of 98:2.

Next, $[RhCl(COD)]_2$, with DIOP or BINAP as chiral

(1) (a) Brewster, J. H. *Aldrichimica Acta* **1987**, *20*(1), 3. (b) Matteson, D. S. *Synthesis* **1986**, 973. (c) Pelter, A.; Smith, K.; Brown, H. C. *Boron Reagents*; Academic: London, 1989.
(2) (a) Madal, A. K.; Jadhav, P. K.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 3543. (b) Brown, H. C.; Jadhav, P. K. *J. Org. Chem.* **1981**, *46*, 5047. (c) Brown, H. C.; Yoon, N. M. *J. Am. Chem. Soc.* **1977**, *99*, 5514. (d) Brown, H. C.; Jadhav, P. K.; Mandal, A. K. *J. Org. Chem.* **1982**, *47*, 5047. (e) Masamune, S.; Kim, B. M.; Peterson, J. S.; Sato, T.; Veenstra, S. J. *J. Am. Chem. Soc.* **1985**, *107*, 4549.
(3) Mannig, D.; Noth. H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878.
(4) (a) Burgess, K.; Ohlmeyer, M. J. *J. Org. Chem.* **1988**, *53*, 5179. (b) Burgess, K.; Ohlmeyer, M. J. *Tetrahedron Lett.* **1989**, *30*, 5857. (c) Burgess, K.; Ohlmeyer, M. J. *Tetrahedron Lett.* **1989**, *30*, 5861.
(5) Hayashi, T.; Matsumoto, Y.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 3426.
(6) Sato, M.; Miyaura, N.; Suzuki, A. *Tetrahedron Lett.* **1990**, *31*, 231.
(7) After submission of this manuscript, a report of mechanistic study of the Rh-catalyzed hydroboration of alkenes appeared (Evans, D. A.; Fu, G. C. *J. Org. Chem.* **1990**, *55*, 2280). It reported that the Rh-catalyzed hydroboration of styrene also gave the α-alcohol as the main product.
(8) Brown, H. C.; Nelson, D. J.; Scouten, C. G. *J. Org. Chem.* **1983**, *48*, 641.
(9) Vishnakarma, L. C.; Fry, A. *J. Org. Chem.* **1980**, *45*, 5306.
(10) Marshall, P. A.; Prager, R. H. *Austr. J. Chem.* **1979**, *32*, 1251.
(11) Losterzo, C.; Ortaggi, G. *J. Organomet. Chem.* **1982**, *234*, C28.
(12) Boaz, N. W. *Tetrahedron Lett.* **1989**, *30*, 2061.
(13) Seebach, D.; Daum, H. *Chem. Ber.* **1974**, *107*, 1748.

0022-3263/91/1956-1670$02.50/0