similar reaction, methanolysis was not done but the solids were separated from the supernate and were washed with 4 × 10 mL of pentane to remove any remaining boron species from the zirconium. These washings were combined with the supernate and the solvents were removed under reduced pressure rendering an oil which was distilled using short path distillation to afford 2(*Z*)-4-octenyl-1,3,2-dioxaborazole. Isolated yield: 1.51 g (66%) 2(*Z*)-4-octenyl-1,3,2-dioxaborazole, bp 90–100 °C (0.1 mmHg). Spectroscopic data are in agreement with expected values: ^{1}H NMR ($CDCl_3$) δ 7.11 (m, 4 H), 6.76 (t, 1 H, *J* = 7.3 H), 2.40–2.05 (m, 4 H), 1.50 (m, 4 H), 0.90 (m, 6 H); ^{13}C ($CDCl_3$) δ 149.7, 148.63, 122.30, 112.20, 30.90, 30.47, 23.27, 22.30, 14.02, 13.70; IR (neat) 3063, 2961, 2932, 2873, 1626, 1479, 1414, 1387, 1335, 980, 808, 747 cm^{-1}; EI mass spectrum *m*/*z* (relative intensity) 230 (M^+, 37), 174 (28), 160 (17), 159 (26), 146 (15), 145 (11), 120 (18), 67 (25), 65 (42), 41 (100).

Preparation of 2(*Z*)-2-Hexenyl-1,3,2-dioxaborazole.[24] The preparation was conducted as in the general procedure by adding 5 mmol of the dicyclopentadienyl-2-hexenylzirconium chloride solution to 5 mmol of *B*-bromocatecholborane (0.994 g) in methylene chloride. The same experiment was also conducted using 5 mmol of *B*-chlorocatecholborane (0.769 g) in 5 mL of methylene chloride: ^{11}B NMR (CH_2Cl_2) +31.4 ppm (Br) +31.4 ppm (Cl), after methanolysis +31.3 ppm (Br), +31.7 ppm (Cl) with 63% and 66% conversion of the bromo and chlorocatecholborane, respectively. The remaining material was the methanolyzed starting material. In a similar reaction, methanolysis was not done but the solids were separated from the supernate and were washed with 4 × 10 mL of pentane to remove any remaining boron species from the zirconium. These washings were combined with the supernate and the solvents were removed under reduced pressure rendering an oil which was distilled using short path distillation to afford 2(*Z*)-2-hexenyl-1,3,2-dioxaborazole. Isolated yield: 1.213 g (69%) of 2(*Z*)-2-hexenyl-1,3,2-dioxaborazole, bp 90–100 °C (0.1 mmHg). Spectroscopic data are in agreement with expected values: ^{1}H NMR ($CDCl_3$) δ 7.09 (m, 4 H), 6.75 (tq, 1 H, *J* = 7.3 Hz, *J* = 1.8 Hz), 2.21 (q, 2 H, *J* = 7.1 Hz), 1.88 (s, 3 H), 1.49 (sext, 2 H, *J* = 7.1 Hz), 0.95 (t, 3 H, *J* = 7.3 H); ^{13}C ($CDCl_3$) δ 149.75, 148.57, 122.30, 112.14, 30.95, 21.92, 13.81, 13.38; IR (neat) 3063, 2960, 2932, 2872, 1631, 1475, 1416, 1389, 1331, 956, 814, 741 cm^{-1}; EI mass spectrum *m*/*z* (relative intensity) 202 (M^+, 16), 173 (16), 160 (45), 159 (21), 146 (10), 145 (17), 120 (34), 67 (17), 65 (47), 39 (100).

Preparation of 2(*Z*)-(4-Methyl-2-pentenyl)-1,3,2-dioxaborazole. Following the general procedure for transmetalation, 5 mmol of the dicyclopentadienyl(4-methyl-2-pentenyl)zirconium chloride solution was added to 5 mmol of *B*-bromocatecholborane (0.994 g) in methylene chloride at 0 °C. The same experiment was also conducted using 5 mmol of *B*-chlorocatecholborane (0.769 g) in 5 mL of methylene chloride: ^{11}B NMR (CH_2Cl_2) +31.5 ppm (Br) +31.6 ppm (Cl), after methanolysis +31.7 ppm (Br) 79% conversion, +31.7 ppm (Cl) 76% conversion of starting material. The remaining material was the methanolyzed starting material. In a similar reaction, methanolysis was not done but the solids were separated from the supernate and were washed with 4 × 10 mL of pentane to remove any remaining boron species from the zirconium. These washings were combined with the supernate and the solvents were removed under reduced pressure, rendering an oil which was distilled using short path distillation to afford 2(*Z*)-(4-methyl-2-pentenyl)-1,3,2-dioxaborazole. Isolated yield: 1.006 g (68%) of 2(*Z*)-(4-methyl-2-pentenyl)-1,3,2-dioxaborazole, bp 85–90 °C (0.1 mmHg). Spectroscopic data are in agreement with expected values: ^{1}H NMR ($CDCl_3$) δ 7.08 (m, 4 H), 6.57 (dq, 1 H, *J* = 7.3 Hz, *J* = 1.7 Hz), 2.88–2.70 (m, 1 H), 1.89 (d, 3 H, *J* = 1.7 Hz), 1.03 (d, 6 H, *J* = 6.6 Hz); ^{13}C ($CDCl_3$) δ 156.63, 148.57, 122.30, 112.14, 27.78, 21.98, 13.17; IR (neat) 3064, 2961, 2932, 2873, 1626, 1479, 1418, 1387, 1348, 958, 808, 747 cm^{-1}; EI mass spectrum *m*/*z* (relative intensity) 202 (M^+, 38), 187 (36), 186 (10), 159 (48), 158 (20), 146 (10), 145 (17), 120 (21), 69 (60), 65 (47), 41 (100). Anal. Calcd for $C_{12}H_{15}BO_2$: C, 71.33; H, 7.48. Found: C, 71.28; H, 7.38.

Preparation of (*Z*)-2-Hexenyl-9-BBN.[13] The product was prepared by the addition of 5 mmol of the dicyclopentadienyl-2-hexenylzirconium chloride solution to *B*-bromo-9-BBN in methylene chloride (5 mmol, 5 mL). Because vinyl-9-BBN derivatives are reactive with methanol, the product was analyzed as the pyridine adduct by the addition of 5 mmol of pyridine. Spectroscopic data are in agreement with expected values: ^{11}B NMR (CH_2Cl_2) 0.6 ppm, 71% conversion of starting material with the rest being the pyridine adduct of *B*-bromo-9-BBN.

Preparation of (*Z*)-(4-Methyl-2-pentenyl)-9-BBN.[13] A total of 5 mmol of dicyclopentadienyl-(4-methyl-2-pentenyl)zirconium chloride solution was added to *B*-bromo-9-BBN in methylene chloride (5 mmol, 5 mL). As before, the product was analyzed as the pyridine adduct after addition of 5 mmol of pyridine. Spectroscopic data are in agreement with expected values: ^{11}B NMR (CH_2Cl_2) +0.1 ppm, 84% yield with the other material being the pyridine adduct of *B*-bromo-9-BBN.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by ACS, for support of this research. We thank Dr. Dan Borchardt at the University of California, Riverside for his kind assistance in obtaining the 2D NMR spectra. We also wish to thank Drs. LeRoy Lafferty and Ratnasamy Somanathan for their help in obtaining NMR and mass spectral data.

Supplementary Material Available: The ^{1}H–^{1}H NOSEY and COSY NMR data for 2-hexenyl-, 4-octenyl-, and (4-methyl-2-pentenyl)-1,3,2-dioxaboroazoles and ^{1}H–^{13}C HETCOR NMR data for (4-methyl-2-pentenyl)-1,3,2-dioxaboroazole (13 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(24) Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 5249.

Enantiomerically Pure 2,2′-Oxybis[*N*-(1-phenylethyl)acetamide]. An Especially Effective Chiral Solvating Agent for Determinations of Enantiomer Compositions by NMR Spectroscopy

Branko S. Jursic* and Stanley I. Goldberg

Department of Chemistry, University of New Orleans, New Orleans, Louisiana 70148

Received September 30, 1992

The imposition of a nonracemic influence on an enantiomeric condition changes the latter to diasteromeric states which may display discernably different properties. Thus, determination of the enantiomeric composition of a sample by allowing it to interact with a chiral shift reagent or a chiral solvating agent and measuring the ratio of the resultant diastereomeric NMR signals[1,2] is an application of this principle which should be widely applicable because of its simplicity. In actual practice, however, the method frequently fails because the diastereomeric signals are either insufficiently separated or they are obscured. The solution to these technical problems lies in development of a broad array of chiral solvating agents to cover a sufficiently wide range of applications, and our recent work on the strong solute–solute interactions of chiral carboxamides[3] suggested the possibility of using a solution of an enantiomerically pure carboxamide as a chiral environment into which partially resolved chiral samples may be placed for NMR determinations of their enantiomer compositions. This approach has succeeded, and we describe here the preparation, properties, and use

(1) Parker, D. *Chem. Rev.* **1991**, *91*, 1441–1457.
(2) Pirkle, W. H.; Hoover, D. J. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E. L., Wilen, S. H., Eds.; Wiley: New York, 1982; Vol. 13, pp 263–331.
(3) Jursic, B. S.; Goldberg, S. I. *J. Org. Chem.*, in press.

0022-3263/92/1957-7370$03.00/0

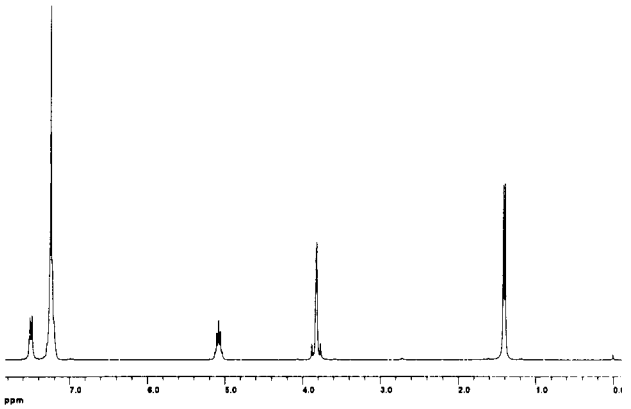
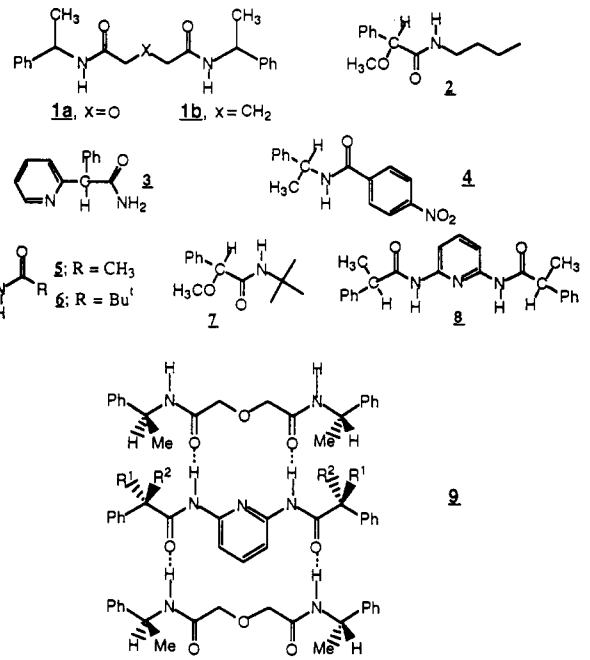


Figure 1. ^1H NMR spectrum of **1a** in $CDCl_3$ solution.

Table I. Diastereomeric ^1H-NMR Signals from Addition of 3–5 mg of Racemic Sample to 0.6–0.8 mL of 1 M Solutions of (*S,S*)-1a in $CDCl_3$

racemic sample	signal	Δδ/ppm (temp./°C)
2	$CH_3O(Ph)CH$–	0.153 (22)
3	$PhCH$–	0.115 (22)
4	CH_3–	0.090 (22)
5	CH_3CO–	0.055 (−55)
6	Bu^t–	0.015 (−55)
7	Bu^t–	0.017 (−55)

of the enantiomerically pure, chloroform-soluble dicarboxamide, **1a**, we developed for this purpose.[4]



Presented in Figure 1 is the ^1H NMR spectrum of **1a**, showing the relatively large regions unoccupied by proton signals owing to **1a** and therefore of potential use for the signals of samples whose enantiomeric composition is to be determined.

In Table I are the diastereomeric ^1H-NMR signal differences (Δδ) generated when small amounts (3–5 mg) of racemic or partially resolved samples of compounds **2–4** were added to 0.6–0.8 mL of a 1 M solution of (*S,S*)-**1a**. We also showed with compound **2** that it was possible to measure the presence of as little as 2% of one enantiomer. The method was extended to enantiomeric amines and

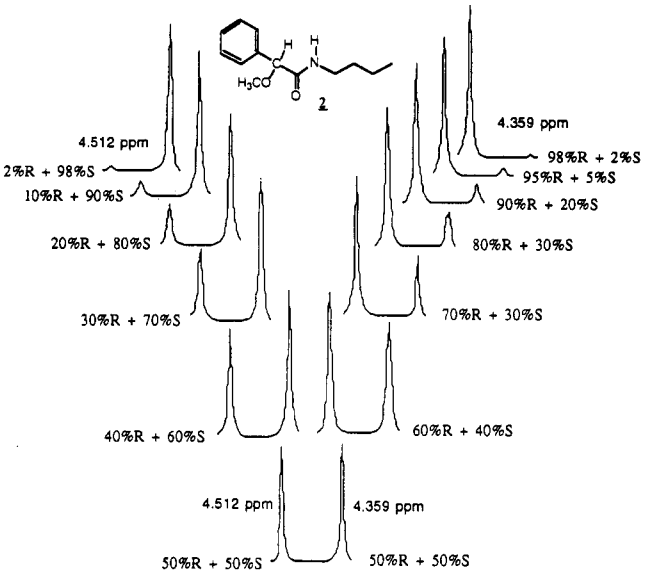


Figure 2. Determination of enantiomeric purity of **2** (5 mg) in a 1 M solution ($CDCl_3$) of (*S,S*)-**1a**.

acids by conversion of each to the amides **5–7**, whose Δδ's, while smaller and had to be observed at lower temperature, were used to measure enantiomer composition.

Finally, the results obtained from the ^1H NMR spectra determined from separate solutions of **1a** and small amounts of the enantiomers of **8** are of interest. Observations are consistent with the presumed presence of a time-averaged trimer, **9**, reminiscent of the β-sheet structure found in peptides.[5]

The benzylic proton in (*R,R*)-**8**, which occurs at δ 6.195 in the absence of (*S,S*)-**1a**, is slightly deshielded (6.136) in the presence of the latter, which is attributed to the benzylic proton being close to the α-hydrogen (**9**, R_1 = H, R_2 = Me). In the diastereomerically related combination (*S,S*)-**8** and (*S,S*)-**1a**), however, the benzylic proton is shifted upfield (6.097) by the deshielding effect of the nearby α-methyl group (**9**, R_1 = Me, R_2 = 2).

These observations suggest the intriguing possibility of an enantiomerically pure, hydrogen-bonded array of **1a** serving as a selective synthesis template for chiral hydrogen-bonding reactants. We are presently studying such processes and will report those results in future accounts of this work.

Experimental Section

General. Melting points are uncorrected. NMR spectra were recorded on a Varian Gemini 300 instrument with a hydrogen probe operating at 300 MHz. The deuterium signal of the solvent ($CDCl_3$) was used as the lock, and tetramethylsilane was the internal reference.

(*S,S*)-(−)-2,2′-Oxybis[*N*-(1-phenylethyl)acetamide] (1a). A THF solution (0.5 L) of diglycolyl chloride (0.413 mol) was added to a cold (5 °C), stirred mixture containing (*S*)-α-methylbenzylamine (0.825 mol), NaOH (0.825 mol), THF (0.3 L), and water (1 L). After it reached room temperature, the mixture was stirred for an additional 0.5 h before the THF was evaporated, leaving white crystals in the aqueous residue. These were dissolved when ethyl acetate (2 L) was added, and the separated organic layer was washed successively with 10% aqueous NaOH (3 × 300 mL), water (3 × 300 mL), 10% aqueous HCl (3 × 300 mL), and water (3 × 300 mL) before it was dried. Evaporation left a white solid which, after recrystallization from ethyl acetate, gave pure (*S,S*)-**1b**: 97% yield; mp 114.8–115.4°; $[\alpha]^{19}_D$ −96.4° (*c* = 1.49, $CHCl_3$); ^1H NMR see Figure 2; ^{13}C NMR 21.6, 48.2, 71.0, 125.9,

(4) We initially prepared and tried enantiomerically pure **1b**, but we switched to **1a** because the latter is much more soluble in chloroform.

(5) Lehninger, A. L. *Principles of Biochemistry*; Worth: New York, 1982; pp 155–156.

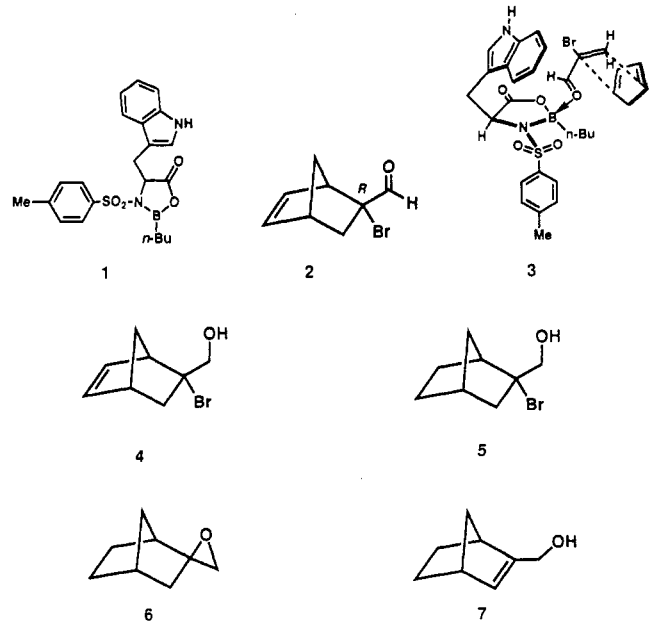
127.3, 128.5, 142.7, 167.7; MS m/z 340 (M^+), 163, 120, 105, 77.

Preparations and characterizations of ***N*-butylmethoxyphenylacetamide (2), *N*-(1-phenylethyl)-4-nitrobenzamide (4), *N*-(1-phenylethyl)acetamide (5),** and ***N*-(1-phenylethyl)-2,2-dimethylpropanamide (6)** are given in ref 3. **2-(2-Pyridyl)propanamide (3)** was provided by Dr. M. Zuanic, Chemica, Inc., Los Angeles, CA 90064.

***N*-(1,1-Dimethylethyl)methoxyphenylacetamide (7)**:[3] mp 94.6–95.4 °C; ^{1}H NMR 1.34 (s, 9 H), 2.16 (s, 3 H), 5.96 (s, 1 H), 7.3–7.4 (m, 5 H); ^{13}C NMR 20.9, 28.4, 51.4, 75.5, 128.5, 128.6, 128.7, 135.3, 167.2, 169.1; MS m/z 249 (M^+), 150, 149, 108, 107, 79, 57.

2,6-Bis[(2-phenylpropanoyl)amino]pyridine (8):[3] mp 186.4–187.8 °C; ^{1}H NMR 2.26 (s, 6 H), 6.20 (s, 2 H), 7.4–7.8 (m, 13 H), 8.45 (s, 2 H); ^{13}C NMR 21.0, 75.7, 110.3, 127.5, 128.9, 129.4, 134.6, 140.8, 148.7, 166.8, 169.9.

Acknowledgment. We are grateful to the Louisiana State Board of Regents for providing an Education Quality Support Fund grant (1990–91 ENH-53) that enabled the purchase of the NMR spectrometer used in this work.



A Simple Enantioselective Synthesis of (1*S*,4*R*)-Bicyclo[2.2.1]hept-2-ene-2-methanol

E. J. Corey* and Charles L. Cywin

Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138

Received August 24, 1992

The power of organic synthesis has been expanded in recent years by advances in catalytic enantioselective reactions mediated by chiral Lewis acids.[1-4] One of the most effective systems is the (*S*)-tryptophan-derived oxazaborolidine **1** which has been shown to be an outstanding catalyst for enantioselective Diels–Alder and Mukaiyama aldol-type reactions.[3,4] For example the Diels–Alder reaction of α-bromoacrolein and cyclopentadiene yields adduct **2** with >200:1 enantioselectivity via the transition-state assembly **3** in which the aldehyde and the Lewis acid form a charge-transfer complex.[3b] This note describes the application of this chemistry to the enantiospecific synthesis of the chiral allylic alcohol **7**,[5] in a formal sense of the Diels–Alder adduct of 2-(hydroxymethyl)cyclopentadiene and ethylene, a reaction for which there is currently no direct enantioselective version.

Reaction of **2** (prepared as described previously[3a]) with 1 molar equiv of sodium borohydride in wet tetrahydrofuran (THF) led to clean reduction of the aldehyde to yield bromo alcohol **4** in 95% yield after recrystallization.[3a,6] Reduction of the double bond was accomplished by hydrogenation, in the presence of palladium on carbon, in ethyl acetate (EtOAc) which afforded, after filtration through silica gel, alcohol **5** as a low-melting solid in 99% yield. The saturated bromo alcohol **5** was then converted to epoxide **6**, in 99% yield, by the action of excess sodium methoxide in methanol (MeOH).[7] Finally, base-catalyzed isomerization to the allylic alcohol **7** with 2 equiv of lithium diethylamide gave, after chromatography, (1*S*,4*R*)-bicyclo[2.2.1]hept-2-ene-2-methanol (**7**) in 93% yield and 87% overall yield from **2**.[8,9]

The versatility and usefulness of the catalyst **1** as an entry to optically pure 2-substituted norbornenes has been demonstrated through a concise and high-yielding conversion of **2** to allylic alcohol **7**. The allylic alcohol **7** and epoxide **6** both represent useful intermediates for further elaboration of these systems. The development of these intermediates into interesting chiral ligands will be the topic of future reports.

Experimental Section

General Methods. Nuclear magnetic resonance spectra were obtained in deuteriochloroform at the frequency indicated. Proton spectra are reported in ppm with chloroform (7.26 ppm) as internal reference. Carbon spectra were referenced to the deuteriochloroform triplet, center peak at 77 ppm. All solvents were distilled prior to use standard purification methods. Mass spectra were determined by the Harvard Chemistry Department Mass Spectrometry Facility.

(1*R*,4*R*,5*R*)-5-Bromobicyclo[2.2.1]hept-2-ene-5-methanol (4). To the aldehyde **2** (4.72 g, 23.4 mmol) in THF (20 mL) was added H_2O (0.5 mL) followed by $NaBH_4$ (0.90 g, 23.8 mmol). After 10 min of stirring the reaction mixture was poured into H_2O (30 mL), extracted with ether (4 × 50 mL), dried over $MgSO_4$, and concentrated to afford alcohol **4** quantitatively. The alcohol was further purified by recrystallization from hexane to afford **4** (4.48 g, 95%) as crystalline solid:[3a] mp 74–76 dec; $[\alpha]^{23}_D$ = +78° (c = 0.96, $CHCl_3$); IR (KBr) 3239, 3069, 2990, 1053, 709 cm^{-1}; ^{13}C NMR

(1) For recent reviews of chiral ligands in asymmetric synthesis: (a) Tomioka, K. *Synthesis* **1990**, 541–549. (b) Kagan, H. B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007–1019.

(2) (a) Corey, E. J.; Ishihara, K. *Tetrahedron Lett.*, in press. (b) Corey, E. J.; Imai, N.; Zhang, H.-Y. *J. Am. Chem. Soc.* **1991**, *113*, 728–729. (c) Corey, E. J.; Matsumura, Y. *Tetrahedron Lett.* **1991**, *32*, 6289–6292. (d) For a review of chiral Lewis acids: Narasaka, K. *Synthesis* **1991**, 1–11.

(3) (a) Corey, E. J.; Loh, T.-P. *J. Am. Chem. Soc.* **1991**, *113*, 8966–8967. (b) Corey, E. J.; Loh, T.-P.; Roper, T. D.; Azimioara, M. D.; Noe, M. C. *J. Am. Chem. Soc.* **1992**, *114*, 8290–8292. (c) Corey, E. J.; Cywin, C. L.; Roper, T. D. *Tetrahedron Lett.*, in press.

(4) For related catalysts see: (a) Parmee, E. R.; Tempkin, O.; Masamune, S. *J. Am. Chem. Soc.* **1991**, *113*, 9365–9366. (b) Takasu, M.; Yamamoto, H. *Synlett* **1990**, 194–196. (c) Sartor, D.; Saffrich, J.; Helmchen, G. *Synlett* **1990**, 197–198. (d) Furuta, K.; Shimizu, S.; Miwa, Y.; Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 1481–1483.

(5) For another recent application of this technology to natural product synthesis see: Marshall, J. A.; Xie, S. *J. Org. Chem.* **1992**, *57*, 2987–2989.

(6) Corey, E. J.; Snider, B. B. *J. Am. Chem. Soc.* **1972**, *94*, 2549–2550.

(7) (a) Krivdin, L. B.; Kas'yan, L. I.; Zinchenko, S. V.; Seferova, M. F.; Porubleva, L. V. *Zh. Org. Khim.* **1990**, *26*, 2482–2489. (b) Bly, R. S.; DuBose, C. M., Jr.; Konizer, G. B. *J. Org. Chem.* **1968**, *33*, 2188–2193.

(8) (a) Crandall, J. K.; Apparu, M. *Org. React. N.Y.* **1983**, *29*, 345–443. (b) Crandall, J. K.; Crawley, L. C. *Organic Synthesis*; Wiley: New York **1988**; Collect. Vol. VI, pp 948–950.

(9) Jefford, C. W.; Wojnarowski, W. *Helv. Chim. Acta* **1970**, *53*, 1194–1202.

0022-3263/92/1957-7372$03.00/0