collected (entry 11) or the solvent was evaporated in vacuo. Crude products of entry 9 were fractionated by extraction with ether (40 mL). Concentration of the etheral solution and subsequent crystallization of the residue from petroleum ether gave the imidazoline **10e**. The pyridinium chloride and the cycloadduct **11e**, insoluble in ether, were separated by the above-mentioned aluminum oxide column chromatography (petroleum ether and then ether as eluents).

5-(*tert*-Butylimino)-2-(methylthio)-1,4,4-triphenyl-2-imidazoline (10e): mp 93 °C (EtOH); ^{1}H NMR δ 0.85 (s, 9 H), 2.42 (s, 3 H), 7.2–7.7 (m, 15 H). Anal. Calcd for $C_{26}H_{27}N_3S$: C, 75.54; H, 6.53; N, 10.17; S, 7.75. Found: C, 75.61; H, 6.54; N, 10.29; S, 8.03.

5-Imino-2-(methylthio)-1,4,4-triphenyl-2-imidazoline (11e): mp 138 °C (EtOH); ^{1}H NMR δ 2.54 (s, 3 H), 6.50 (br, 1 H), 7.2–7.6 (m, 15 H). Anal. Calcd for $C_{22}H_{19}N_3S$: C, 73.95; H, 5.32; N, 11.76; S, 8.96. Found: C, 73.77; H, 5.31; N, 11.68; S, 9.04.

1-(2,6-Dimethylphenyl)-4,4-diphenyl-5-imino-2-(methylthio)-2-imidazoline (11g): mp 114 °C (MeOH); IR 1655, 1570 cm^{-1}; ^{1}H NMR δ 2.16 (s, 6 H), 2.57 (s, 3 H), 7.1–7.6 (m, 14 H); MS calcd for $C_{24}H_{23}N_3S$, *m/e* 385.1613 (M$^+$), found 385.1611; *m/e* (relative intensity) 385 (57), 370 (6), 338 (29), 311 (15), 308 (12), 239 (12), 224 (100), 193 (14). Anal. Calcd: C, 74.80; H, 5.97; N, 10.90; S, 8.31. Found: C, 75.00; H, 6.13; N, 10.89; S, 8.48.

Reactions of Diazabutadienes 5 with Isocyanides. General Procedure. A solution of **5e–g** (5 mmol) and *tert*-butyl isocyanide **7** (1 g, 12 mmol) in MeCN (15 mL) was refluxed for several days. Removal of the solvent under reduced pressure gave a brown oil as residue, which was analyzed by ^{1}H NMR. The imidazoline **10g,i** or imidazole **12k** was separated from substantial quantities of unidentified side products by silica gel column chromatography and then fractional crystallization from MeOH. Reactions of **5h** with **7** and **5g,h** with **8** were carried out in the same manner but the resulting solution only afforded a viscous blackish oil whose ^{1}H NMR spectrum showed that starting diazadiene was the main compound.

Isobutene Elimination from 10g. A solution of **10g** (0.44 g, 1 mmol) in Et_2O (30 mL) was treated with dry HCl for 1 min. The precipitated **10g**·HCl was isolated in 94% yield (0.45 g) as a white solid, which was poured into MeCN (15 mL). After being refluxed for 1 h, the suspension was cooled to 20 °C. **11g**·HCl was collected by filtration and dried (0.36 g, 85% yield).

Oxidation of 14l. A solution of **14l** (0.33 g) in $CHCl_3$ (20 mL) was maintained at room temperature for 7 days under aerial oxygen. The reaction mixture was concentrated to a solid material, which was suspended in Et_2O (10 mL) and filtered. Sublimation of this white powder afforded a pure sample of **18**: mp 187 °C; IR 3310, 1635, 1570, 1525 cm^{-1}; ^{1}H NMR δ 1.23 (s, 9 H), 1.36 (d, J = 6 Hz, 6 H), 4.52 (m, 1 H), 5.17 (br, 1 H), 7.2–8.0 (m, 10 H); MS calcd for $C_{22}H_{27}N_3O_2$, *m/e* 365.2103 (M$^+$), found 365.2099; *m/e* (relative intensity) 308 (2), 260 (26), 204 (11), 105 (100). Anal. Calcd: C, 72.32; H, 7.40; N, 11.50. Found: C, 71.71; H, 7.52; N, 12.25.

X-ray Analysis of 11g. Crystal data: orthorhombic $Pna2_1$, a = 15.541 (5), b = 8.908 (2), and c = 15.194 (4) Å, V = 2103.6 (6) Å^3, Z = 4, D_x = 1.22 g cm^{-3}, μ = 1.67 cm^{-1}; 1595 reflections with $I \geq \sigma(I)$ collected with a Enraf-Nonius CAD-4 diffractometer (Mo Kα radiations). The structure was solved by direct methods[24] and the hydrogen atoms were found between 0.37 and 0.16 e Å^{-3}. The best full-matrix refinement gave R = 0.033, R_w = 0.031, S_w = 1.37 (321 variables and 1595 reflections).

X-ray Analysis of 12k. Crystal data: orthorhombic P_{ccn}, a = 11.343 (5), b = 25.390 (5), and c = 13.211 (8) Å, V = 3807 (2) Å^3, Z = 8, D_x = 1.34 g cm^{-3}, μ = 1.69 cm^{-1}, 1374 reflections with $I \geq \sigma(I)$. The structure was solved by direct methods[24] and the hydrogen atoms were found between 0.30 and 0.15 e Å^{-3}. The best full-matrix least-square refinement gave R = 0.056, R_w = 0.056, S_w = 1.29 (261 variables and 1374 reflections). All calculations were performed on a PDP 11/60 Digital computer with the SDP package.[25]

Registry No. 1, 1013-88-3; **2a**, 556-61-6; **2b**, 542-85-8; **2c**, 103-72-0; **3a**, 34979-85-6; **3b**, 118514-70-8; **3c**, 23490-81-5; **4a**, 118514-71-9; **4b**, 118514-72-0; **4c**, 118514-73-1; **4d**, 118514-74-2; **4e**, 118514-75-3; **4f**, 118514-76-4; **4g**, 118514-77-5; **4h**, 118514-78-6; **5a**, 118514-79-7; **5b**, 118514-80-0; **5c**, 118514-81-1; **5e**, 118514-82-2; **5f**, 118514-83-3; **5g**, 118514-84-4; **5h**, 118514-85-5; **6e**, 94518-64-6; **6f**, 94518-60-2; **6g**, 90496-26-7; **6h**, 118514-86-6; **7**, 7188-38-7; **8**, 598-45-8; **9**, 2769-71-3; **10a**, 118514-87-7; **10b**, 118514-88-8; **10c**, 118514-89-9; **10d**, 118514-90-2; **10e**, 118514-91-3; **10f**, 118514-92-4; **10g**, 118514-93-5; **10g**·HCl, 118515-16-5; **10h**, 118514-94-6; **10i**, 118514-95-7; **11a**, 118514-96-8; **11d**, 118514-97-9; **11e**, 52461-01-5; **11g**, 118514-98-0; **11g**·HCl, 118515-17-6; **12i**, 118514-99-1; **12k**, 118515-00-7; **12n**, 118515-01-8; **13b**, 118515-02-9; **13c**, 118515-03-0; **13j**, 118515-04-1; **13l**, 118515-05-2; **13m**, 118515-06-3; **14l**, 118515-07-4; **14m**, 118515-08-5; **12b**, 118515-09-6; **15c**, 118515-10-9; **16e**, 118515-11-0; **16g**, 118515-12-1; **17f**, 118515-13-2; **17h**, 118515-14-3; **18**, 118515-15-4; MeSCl, 5813-48-9.

Supplementary Material Available: Final coordinates and bond geometry tables for **11g** and **12k** (5 pages). Ordering information is given on any current masthead page.

(24) Main, P.; Fiske, S. J.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Woolfson, M. M. MULTAN 80. A system of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data; Universities of York, England and Louvain, Belgium, 1980.

(25) Frenz, B. A. Enraf-Nonius CAD-4 SDP, Real Time System for Current X-ray Data Collection and Crystal Structure Determination in Crystallography; Enraf-Nonius Delpht, 1978.

Preparation of Polymer-Supported (*R*)- and (*S*)-Styrene Oxide

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Polymer-supported (*R*)- and (*S*)-styrene oxide have been prepared via reduction of chloroacetylated styrene–1% divinylbenzene with (–)- and (+)-*B*-chlorodiisopinocampheylborane, respectively, and subsequent base treatment. The ee values for the reductions were estimated to be 85–91% by ^{19}F NMR analyses of diastereomeric MTPA ((*S*)-(–)-α-methoxy-α-(trifluoromethyl)phenylacetic acid) esters of the intermediate chloro alcohols.

Introduction

Polymers containing chiral chelating ligands are receiving increasing attention for use in asymmetric synthesis. Examples include chiral polymer-supported amino alcohols complexed to $LiAlH_4$[1] and to BH_3[2] in asymmetric reductions of ketones, and to Et_2Zn[3] in enantioselective additions to benzaldehyde as well as polymer-bound chiral

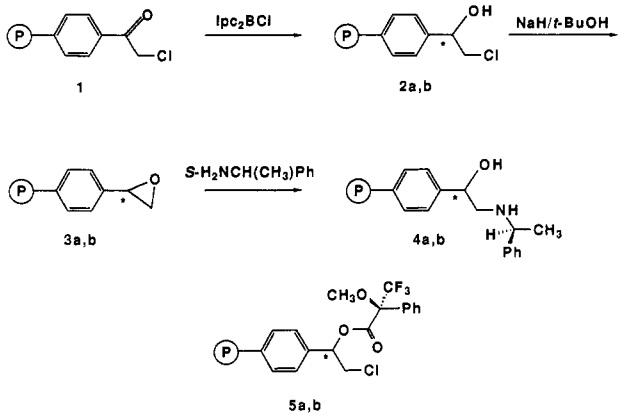
(1) (a) Fréchet, J. M. J.; Bald, E.; Lecavalier, P. *J. Org. Chem.* **1986**, *51*, 3462. (b) Lecavalier, P.; Bald, E.; Jiang, Y.; Fréchet, J. M. J.; Hodge, P. *React. Polym.* **1985**, *3*, 315.

(2) (a) Itsuno, S.; Ito, K.; Hirao, A.; Nakahama, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2887. (b) Itsuno, S.; Nakano, M.; Ito, K.; Hirao, A.; Owa, M.; Kanda, N.; Nakahama, S. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2615.

(3) (a) Itsuno, S.; Fréchet, J. M. J. *J. Org. Chem.* **1987**, *52*, 4140. (b) Soai, K.; Niwa, S.; Watanabe, M. *J. Org. Chem.* **1988**, *53*, 927.

0022-3263/89/1954-1191$01.50/0

Scheme I



phosphines complexed to transition metals for use in catalytic processes such as hydrogenations[4] and hydroformylations.[5]

To date, most asymmetric reactions utilizing polymer-supported reagents have resulted in lower optical yields than the analogous homogeneous reactions, and their use has been justified mainly by their easy handling and ready recovery. However, recent examples have shown that with careful design of the polymeric reagents, properties superior to those shown by analogous monomeric reagents may be achieved.[2-5]

The chiral moiety is usually introduced on the polymer either by copolymerization of a monomer containing the desired chiral functionality and other nonchiral monomers[4-6] or by a substitution reaction on a preformed polymer containing a functional group. The latter method most frequently uses polystyrene–divinylbenzene functionalized with chloromethyl groups and a chiral moiety capable of acting as a nucleophile to displace the chloride ion.[1-3]

An alternative route to chiral polymers consists of chiral modification of a preformed polymer. Few examples of this methodology are known, which may be due to difficulties in analyzing the optical purity of the resulting polymers.[7] We have now been able to prepare the two antipodes of polymeric styrene oxide, previously prepared in racemic form,[8] by chiral reduction of a chloroacetylated styrene–divinylbenzene polymer and subsequent base treatment. The diastereomeric MTPA ((*S*)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetic acid) esters of the intermediate chloro alcohols have been analyzed by ^{19}F and ^{13}C NMR spectroscopy.

The epoxy groups may serve as chiral "handles" for the attachment of a variety of nucleophilic groups,[8] thus allowing the preparation of chiral bifunctional polymers capable of forming five-membered ring chelates with metal ions.

Results and Discussion

Among the preferred reagents for chiral reduction of α-halo ketones,[9] *B*-chlorodiisopinocampheylborane

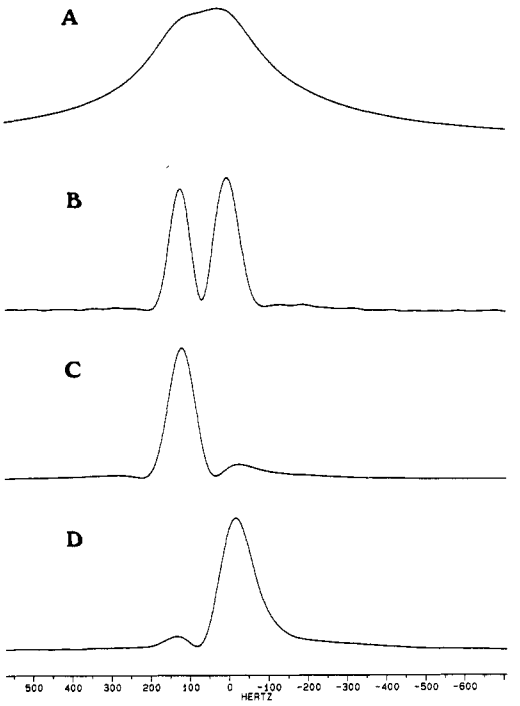


Figure 1. ^{19}F NMR spectra (in C_6D_6) of (A) diastereomeric mixture **4** before data manipulation, (B) **4**, (C) **4a**, and (D) **4b** after data manipulation. The scale has been arbitrarily chosen.

(Ipc_2BCl) was chosen for reduction of the prochiral chloroacetylated polymer due to its high reactivity and high enantioselectivity.[10] Thus, styrene–1% divinylbenzene (SX 1) containing 3.20 mmol of chloroacetyl groups per gram of resin (corresponding to a degree of functionalization, defined as the mole fraction of styrene units being functionalized, of 0.44) was treated with (+)- and (−)-Ipc_2BCl in tetrahydrofuran (THF) to yield polymer-bound chloro alcohols **2a** and **2b**, respectively (Scheme I). The reductions were performed at −33 °C, 0–3 °C, and ambient temperature. The IR spectra of the resulting polymers showed only weak absorptions at 1682 cm^{-1}, indicating essentially complete reduction. In order to determine the extent of reduction, the chloro alcohol obtained by reduction with the (−)-reagent at 0 °C was treated with 3,5-dinitrobenzoyl chloride[11] to yield an ester. Elemental analysis showed that the resin contained 1.88 mmol of 3,5-dinitrobenzoic acid residues per gram. This corresponds to 93% conversion in the reduction reaction, provided the esterification was quantitative.

Treatment of the polymer-bound chloro alcohols **2a** and **2b** with NaH and *t*-BuOH in THF afforded the polymer-bound chiral styrene oxides **3a** and **3b** (Scheme I). Chlorine analyses of resin **3b** prepared via reduction at ambient temperature as well as −33 °C indicate an overall conversion of 98% from **1**, i.e. somewhat higher than that estimated by derivatization of the chloro alcohols. The ^{13}C NMR spectra of the racemic and chiral products were identical.[8]

Reduction of monomeric α-chloroacetophenone using (+)- and (−)-Ipc_2BCl proceeds with excellent asymmetric induction,[9] but the absolute configuration of the chlorohydrins obtained has not been reported. However, according to the proposed mechanism,[12] the absolute con-

(4) Deschenaux, R.; Stille, J. K. *J. Org. Chem.* **1985**, *50*, 2299.
(5) Parrinello, G.; Deschenaux, R.; Stille, J. K. *J. Org. Chem.* **1986**, *51*, 4189.
(6) Villedon-Denaide, F.; Lecavalier, P.; Fréchet, J. M. J. *Polym. Bull.* **1986**, *15*, 491.
(7) (a) Minoura, Y.; Yamaguchi, H. *J. Polym. Sci. A-1* **1968**, *6*, 2013. (b) Masuda, T.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 268. (c) Masuda, T.; Ibuki, H. *Polym. J.* **1980**, *12*, 143. (d) Fréchet, J. M. J.; Amaratunga, W.; Halgas, J. *Nouv. J. Chim.* **1982**, *6*, 609.
(8) Antonsson, T.; Moberg, C. *React. Polym.* **1988**, *8*, 113.
(9) Brown, H. C.; Park, W. S.; Cho, B. T.; Ramachandran, P. V. *J. Org. Chem.* **1987**, *52*, 5406.
(10) Chandrasekharan, J.; Ramachandran, P. V.; Brown, H. C. *J. Org. Chem.* **1985**, *50*, 5446.
(11) Darling, G. D.; Fréchet, J. M. J. *J. Org. Chem.* **1986**, *51*, 2270.

figuration of the product from reaction with the (+)-reagent should have S configuration. Accordingly, we assume that reduction of **1** with this reagent affords a polymeric chloro alcohol with S configuration (**2a**) and, consequently, a styrene oxide with S configuration (**3a**), whereas reduction with the (−)-reagent results in products with opposite absolute configuration.

In order to determine the ee values for the reduction reactions, diastereomeric MTPA ((S)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetic acid) esters[13] of the chloro alcohols were prepared. The ^{19}F NMR signals of the MTPA esters of racemic polymer-bound chloro alcohol (**4**, Figure 1A) were broad with only a hint that there might be two signals due to the two diastereomers before data manipulation. However, separation of the signals could be obtained by application of Gaussian multiplication followed by base-line correction.[14] The relative amounts of the two diastereomeric esters could then be easily determined by integration of the obtained peaks (Figure 1B). In the spectra of esters derived from **2a** and **2b**, the signals for the minor diastereomers were hidden under the wings of those of the major diastereomers. Treating these spectral data in a similar manner as that described above afforded separation of the signals corresponding to the two diastereomers (Figures 1C and 1D). The ee of the reductions could then be calculated and were found to be 85% for the formation of **2a** and, depending on the temperature (−33 °C to ambient temperature), 90–91% for **2b**. The reason for the difference in enantioselectivity between the two reactions is unclear. However, the signal due to the MTPA ester of the presumed R enantiomer was significantly broader in all the samples studied, causing a discrepancy in the expected 1:1 ratio between the esters prepared from racemic chloro alcohol (Figure 1). Correcting for this difference, ee values of 89–90% were obtained for the formation of both **2a** and **2b**. The observed difference in linewidth may be due to a difference in chemical properties or be a result of the mathematical treatment of the spectra.

The ^{13}C NMR signals originating from the methoxy groups of the MTPA esters[13] of racemic polymer-bound chloro alcohol (**4**) were less well resolved and could, even after data manipulation,[14] only be used for a rough estimation of the chiral induction in the formation of **2a** and **2b**.

Polymer-bound amino alcohols can conveniently be prepared from a racemic epoxide and a primary or secondary amine.[8] From the chiral epoxides and chiral amines, polymeric amino alcohols with two chiral centers are therefore accessible. Thus, reaction of **3a** and **3b** with (S)-1-phenylethylamine afforded the polymer-bound diastereomeric amino alcohols **5a** and **5b** (Scheme I) in 72 and 68% yields, respectively. These polymers are light yellow and give rise to significantly broader ^{13}C NMR signals than resins **1**–**4**, probably due to additional cross-linkage of the polymer. Identification of the two diastereomers by NMR was therefore not possible. Since both (S)- and (R)-1-phenylethylamine are commercially available, the new chiral epoxides give access to all four possible stereoisomers of the polymer-bound amino alcohol **5**.

(12) Brown, H. C.; Chandrasekharan, J.; Ramachandran, P. V. *J. Am. Chem. Soc.* **1988**, *110*, 1539.

(13) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(14) Standard Bruker software for the Aspect 3000 was used. Typical parameters used for the Gaussian multiplication of the ^{19}F (^{13}C) spectra were LB −240 (−70) and GB 0.018 (0.07). These values had to be optimized for each spectrum. The spline function was used for baseline correction.

Experimental Section

Materials. The polymer SX 1 was purchased from Bio Rad. Chloroacetylation of this resin was performed as previously described.[15] (+)- and (−)-Ipc_2BCl were purchased from Aldrich and NaH as an 80% suspension in mineral oil from Merck. MTPA was converted to the corresponding acid chloride (MTPA-Cl).[13] Commercially available reagents were used as received. THF was distilled from benzophenone ketyl before use. MeOH was pro analysi grade when used as a reaction medium. CCl_4 and pyridine were distilled from CaH and stored over molecular sieves (4 Å).

^{13}C NMR (100.6 MHz) and ^{19}F NMR (376.5 MHz) spectra were recorded on a Bruker AM 400 instrument. Overnight run, using a pulse width of 3.7 μs (45°) and an aquisition time of 0.33 s without delay between pulses, was required for the ^{13}C NMR spectra. The polymers were swollen in either $CDCl_3$ (δ 77.0 as internal standard) or in C_6D_6 (δ 128 as internal standard). IR spectra (KBr) were recorded on a Perkin-Elmer 1710 FT spectrometer. Elemental analyses were performed by Analytical Laboratories, Engelskirchen, F.R.G.

Polymer-Supported Chloro Alcohols 2a and 2b. A solution of (+)- or (−)-*B*-chlorodiisopinocampheylborane (1.27 g, 3.95 mmol) in 5 mL of THF was added via a syringe to a suspension of chloroacetylated polymer **1** (1.00 g, 3.20 mmol) in 10 mL of THF under nitrogen. The resulting mixture was stirred at ambient temperature, 0–3 °C, or −33 °C for 7 days (using (−)-Ipc_2BCl). Alternatively, the mixture was stirred at −33 °C for 2 days, at 0–3 °C for another 2 days, and finally at ambient temperature for 3 days (using (+)-Ipc_2BCl). In either case, 1 mL of MeOH was then added, and stirring was continued for another 30 min. The polymer was filtered off, washed with THF (3 × 20 mL), MeOH (5 × 20 mL), H_2O (3 × 20 mL), and MeOH (3 × 20 mL), and dried under vacuum at 60 °C overnight to yield 0.95–0.99 g of a light beige polymer. The ^{13}C NMR spectra of **2a** and **2b** were in accordance with that of racemic polymer-bound chloro alcohol.[8] In the IR spectra OH bands appeared at 3425 cm^{-1}.

Polymer-Supported Chloro Alcohol 3,5-Dinitrobenzoic Acid Ester. Polymer-supported chloro alcohol **2b** (209 mg, 0.66 mmol) and 3,5-dinitrobenzoyl chloride (365 mg, 1.59 mmol) were heated in 1.5 mL of CCl_4 and 1 mL of pyridine at 90 °C under nitrogen for 3 h, and the resulting mixture was stirred at ambient temperature overnight. The polymer was filtered off, washed with MeOH (3 × 20 mL), H_2O (3 × 20 mL), and CH_2Cl_2 (3 × 20 mL), and dried under vacuum at 60 °C overnight to yield 315 mg of a reddish brown polymer. IR (KBr): 3096 (Ar H), 1734 (C=O), 1543 and 1343 ($ArNO_2$), 1267 and 1156 (C—O) cm^{-1}. Anal. Found: N, 5.27.

Polymer-Supported Styrene Oxides 3a and 3b. To a suspension of the polymeric chloro alcohol **2b** (300 mg, 0.94 mmol) and NaH (43 mg, 1.43 mmol) in 2 mL of THF was added a solution of *t*-BuOH (70 mg, 0.95 mmol) in 2 mL of THF via a syringe under nitrogen. The reaction mixture was stirred at ambient temperature for 19 h, 1 mL of MeOH was added, and stirring was continued for 30 min. The polymer was filtered off, washed with MeOH (3 × 20 mL), H_2O (3 × 20 mL), CH_2Cl_2 (20 mL), THF (20 mL), and MeOH (3 × 20 mL) and dried under vacuum at 60 °C overnight, yielding 264 mg of a yellow polymer. Resin **3a** was prepared analogously. The ^{13}C NMR spectra of **3a** and **3b** were in agreement with that of racemic polymer-bound epoxide.[8] **3b**: Anal. Found: Cl, 0.32 and 0.34 for polymers reduced at −33 °C and ambient temperature, respectively.

Polymer-Supported Chloro Alcohol MTPA Esters (4). A solution of MTPA-Cl (162 mg, 0.64 mmol) in 1.5 mL of CCl_4 was added under nitrogen to the polymer-supported chloro alcohol **2b** (155 mg, 0.59 mmol) followed by 0.5 mL of pyridine. The reaction mixture was stirred at ambient temperature for 21 h, and the polymer was filtered off, washed with MeOH (2 × 20 mL), MeOH–H_2O (1:1, 3 × 20 mL), CH_2Cl_2 (20 mL), THF (20 mL), and MeOH (3 × 20 mL), and dried under vacuum at 60 °C overnight to yield 236 mg of a yellow polymer (**4b**). Compound **2a** was derivatized analogously. **4a** ^{13}C NMR ($CDCl_3$): δ 45.9 (CH_2Cl), 55.8 (OMe), 77.8 (CHO), 84.5 (quart C), 165.4 (CO). ^{13}C NMR (C_6D_6): δ 46.1 (CH_2Cl), 55.8 (OMe), 77.9 (CHO), 85.0 (quart

(15) Elman, B.; Moberg, C. *J. Organomet. Chem.* **1985**, *294*, 117.

C), 165.7 (CO). **4b** ^{13}C NMR ($CDCl_3$): δ 45.9 (CH_2Cl), 55.4 (OMe), 84.8 (quart C), 165.6 (CO). ^{13}C NMR (C_6D_6): δ 46.0 (CH_2Cl), 55.5 (OMe), 77.4 (CHO), 85.5 (quart C), 165.9 (CO).

Polymer-Supported Amino Alcohols 5. The polymer-supported epoxide **3b** (248 mg, 0.87 mmol) and (*S*)-1-phenylethylamine (333 mg, 2.75 mmol) were reacted in 2 mL of refluxing MeOH under nitrogen for 96 h. The polymer was filtered off, washed with MeOH (3 × 20 mL), CH_2Cl_2 (2 × 20 mL), THF (20 mL), and MeOH (3 × 20 mL), and dried under vacuum at 60 °C overnight to yield 289 mg of a yellow polymer (**5b**). Similar treatment of **3a** yielded amino alcohol **5a**. The ^{13}C NMR spectra of **5a** and **5b** were in agreement with that of the amino alcohol prepared from (*S*)-1-phenylethylamine and racemic polymer-bound styrene oxide.[8] Anal. Found: N, 2.71 and 2.60 for polymers prepared from **3a** and **3b**, respectively.

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Effect of Temperature on Borane Reduction of Representative Malonic Acids

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The controlled reaction of phenylmalonic acid (**1a**) with borane–THF at appropriate temperature makes available (phenylmalonyldioxy)borane [**2a**, $PhCH(CO_2)_2BH$], which has been characterized. Reduction of **2a** or of the corresponding acid **1a** proceeds at 0 °C at the same rate. The reaction, however, is incomplete, showing only 33% product formed in 4 h. Diethylmalonic acid (**1b**), which possesses no α-hydrogen, and the (diethylmalonyldioxy)borane (**2b**) are reduced at the same rate to the corresponding cyclic dialkoxyborane **5b**. These results suggest that the reduction proceeds through intermediate formation of **2**. The rates of the borane reduction for a series of malonic acids (**1a–h**) have been systematically studied and compared at 0 °C and at −20 °C. The reductions of aromatic substituted malonic acids (**1f–h**) are quite sluggish with substantial (46–72%) α-metalation occurring at 0 °C. Aliphatic alkylmalonic acids (**1d–e**) are reduced in 24 h with 34–40% of α-metalation. At −20 °C, most malonic acids are completely reduced in times ranging from 24 h for aliphatic (**1c–e**) to 3 days for aromatic (**1f–h**) compounds, with only 2–24% α-metalation. The reduction of **1a** requires −30 °C for 6 days to avoid α-metalation. The reduction of **1b** at either 0 °C or −20 °C is completed in 8 h. At an appropriate lower temperature the reduction successfully competes with the α-metalation.

Previously, Brown and co-workers described the remarkable ease with which carboxylic acids, both aliphatic and aromatic, are reduced by borane.[1-3] They have also established the details of the borane reduction mechanism, which proceeds through a mono(acyloxy)borane intermediate, formed either directly from the carboxylic acid and borane or by a redistribution reaction of bis(acyloxy)borane with borane.[4]

$$RCOOH + BH_3\text{–}THF \rightarrow RCH_2OH + ...$$

R = alkyl or aryl

Recently, we found the reduction of phenylmalonic acid (**1a**) by borane–THF to be unusually slow.[5] The reaction proceeded sluggishly at 0 °C, requiring 16 h to yield only 35% of 2-phenyl-1,3-propanediol, along with unreacted starting material.[5] Moreover, the yield was not enhanced by the use of borane dimethyl sulfide,[6,7] which led to only 23% of the product. Subsequently an initial systematic study was made of the approximate rates and stoichiometries of the reaction of **1a** with borane–THF.[8] We have continued to study the reduction and have extended our study to a set of representative malonic acids. The results of these investigations are reported in the present paper.

Table I. Reduction of Carboxylic Acids with Borane–THF in Tetrahydrofuran at 0 °C[a]

carboxylic acid	time, h	H_2 evolved, mmol/mmol of FG	total H^- consumed, mmol/mmol of FG	H^- used for reduction, mmol/mmol of FG
benzoic	0.25	1.00	1.08	0.08
	1.0	1.00	1.98	0.98
	3.0	1.00	2.46	1.46
	12.0	1.00	2.95	1.95
	24.0	1.00	3.00	2.00
phenylacetic	0.25	1.09	3.09	2.00
	0.5	1.09	3.09	2.00
	1.0	1.09	3.09	2.00

[a] 0.25 M in functional group (FG) in substrate in 1.0 M in hydride in BH_3–THF unless otherwise indicated.

Results and Discussion

Procedure for Rate and Stoichiometry Studies. The reaction mixtures were 0.33 M in BH_3 and 0.25 M in the functional group (FG) in substrate in THF as solvent. The

(1) Brown, H. C.; Heim, P.; Yoon, N. M. *J. Am. Chem. Soc.* **1970**, *92*, 1637.
(2) Yoon, N. M.; Park, C. S.; Brown, H. C.; Krishnamurthy, S.; Stocky, T. P. *J. Org. Chem.* **1973**, *38*, 2786.
(3) Lane, C. F. *Chem. Rev.* **1976**, *76*, 773.
(4) Brown, H. C.; Stocky, T. P. *J. Am. Chem. Soc.* **1977**, *99*, 8218.
(5) Choi, Y. M.; Kucharczyk, N.; Sofia, R. D., *J. Labeled Compd. Radiopharm.* **1986**, *23*, 545.
(6) Krishnamurthy, S.; Thompson, K. L. *J. Chem. Ed.* **1977**, *54*, 778.
(7) Brown, H. C.; Choi, Y. M. *Synthesis* **1981**, 439.
(8) Choi, Y. M.; Emblidge, R. W.; Kucharczyk, N.; Sofia, R. D. *J. Org. Chem.* **1987**, *52*, 3925.

0022-3263/89/1954-1194$01.50/0