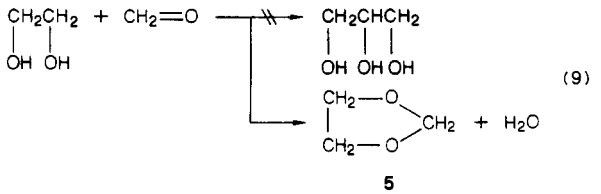
Table II. Reaction of 2,2-Dimethyl-1,3-dioxolane with Formaldehyde in the Presence of UV Light[a]

expt no.	1 (mL)	$(CH_2=O)_x$[b] (g)	formalin (mL)	acetone (mL)	TBPB[b] (g)	conv. 1 (%)	select. 2 (%)	select. EG (%)	select. glycerol (%)
7	3.0	0.3				7.5	70.7	<1	<1
8	3.0	0.3		1.0		8.6	52.3	<1	1.5
9	3.0	0.3			0.05	10.8	58.4	<1	<1
10	3.0		1.0			21.5	52.5	39.7	1.0
11	3.0		1.0	1.0		22.9	46.9	41.3	2.6
12	3.0		1.0		0.05	24.5	39.9	48.0	2.1

[a] Procedure given in Experimental Section. [b] $(CH_2=O)_x$ = paraformaldehyde, TBPB = *tert*-butyl perbenzoate, EG = ethylene glycol.

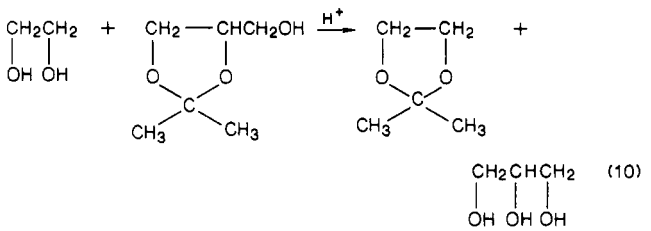
main product from this reaction was 1,3-dioxolane (**5**) (eq 9).



(9)

5

The hydromethyl derivative **2** was used to prepare glycerol and **1** by reaction with ethylene glycol (eq 10). A



(10)

variety of acids and acidic resins could be used for this reaction but phosphoric acid appeared to give the highest yield and purity (80% distilled yield of **1**, 97% purity). Glycerol could also be obtained in high yield. Details may be found in the Experimental Section.

Conclusion

The reaction of **1** with formaldehyde to produce **2** and the reaction of **2** with ethylene glycol to produce **1** and glycerol offers a route to glycerol based on ethylene glycol and formaldehyde. The direct reaction of formaldehyde and ethylene glycol does not produce significant quantities of glycerol.

Experimental Section

Materials. Di-*tert*-butyl peroxide, *tert*-butyl perbenzoate, and paraformaldehyde were obtained from Aldrich Chemical Co. *tert*-Butyl cumyl peroxide was Trigonox T from Noury Chemical. 2,2-Dimethyl-1,3-dioxolane, 2,2-dimethyl-4-(hydroxymethyl)-1,3-dioxolane, and phosphoric acid (85%) were obtained from Alfa Chemicals.

Analytical. ^1H NMR spectra were recorded on a Varian EM-390 spectrometer. The GC/FTIR work was done on a Digilab FTS 15E. Other GC work was done on a Hewlett-Packard 5890 with a 3392A integrator. The column was a 15-m capillary (fused silica) with 5% crosslinked phenyl methyl silicone.

Photochemical Reactor. The photochemical reactor was a RMR 500 Rayonet chamber reactor. A RMA 400 Rayonet merry-go-round was used. Four RPR 2537-Å lamps or four RPR 3500-Å lamps were used.

Procedure (Thermal). 2,2-Dimethyl-1,3-dioxolane, paraformaldehyde, and initiator were charged to a 300-mL stainless steel autoclave equipped with a cooling coil, electric heater, Magne-Drive stirrer, and glass liner. The autoclave was sealed and heated to the desired temperature for the required time. The autoclave was then cooled to ambient temperature and vented slowly, and the liquid was filtered from a small amount of solid and analyzed by GC or GC/FTIR.

Procedure (Photochemical). Pyrex test tubes (100 × 13 mm) equipped with screw caps were charged with 2,2-dimethyl-1,3-dioxolane, paraformaldehyde (or formalin), and initiators (or sensitizers) and then placed in the photochemical reactor for a week. Analysis was by GC or GC/FTIR as above.

Reaction of 2,2-Dimethyl-4-(hydroxymethyl)-1,3-dioxolane with Ethylene Glycol. Best yields of **1** were obtained when the reaction was run in the following manner: Ethylene glycol and 85% H_3PO_4 were charged to a flask equipped with a stirrer, a thermometer, a heating mantle, a small Vigereaux column, and distilling head (water-cooled condenser). The mixture was heated to 100–110 °C and a stream of nitrogen passed over the reaction mixture to aid in the removal of water. After removal of the water, the reaction mixture was cooled to 40–50 °C and 2,2-dimethyl-4-(hydroxymethyl)-1,3-dioxolane added. The mixture was heated over several hours to a pot temperature of 150 °C. Pure (>97%) 2,2-dimethyl-1,3-dioxolane was found to distill at 93–97 °C. Identifiction was by ^1H NMR. Pure glycerol was obtained from the pot residue by vacuum distillation.

An Efficient and Catalytically Enantioselective Route to (*S*)-(−)-Phenyloxirane

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Chiral oxiranes are often useful starting materials in enantiospecific synthesis. We describe herein a practical method for the synthesis of (*S*)-(−)-phenyloxirane (styrene oxide, **1**) which illustrates an approach that is potentially applicable to the enantioselective preparation of numerous chiral 1-substituted oxiranes. A key step in the process is the catalytic reduction of an achiral chloromethyl ketone by means of a chiral oxazaborolidine as catalyst and borane as stoichiometric reductant, a method recently developed in these laboratories.[1,2] This paper describes in detail the preparation of the chiral catalyst starting from proline, the enantioselective catalytic reduction, and the further conversion to epoxide.

N-(Benzyloxycarbonyl)-(*S*)-proline[3] was synthesized from proline by reaction with benzyl chloroformate in aqueous solution at 0–5 °C in 96% yield and esterified in methanol with boron trifluoride etherate as catalyst[4] to give the oily methyl ester in essentially quantitative crude yield. Reaction of this unpurified product with phenylmagnesium chloride in tetrahydrofuran (THF) provided directly (*S*)-(−)-2-(diphenylhydroxymethyl)pyrrolidine (**2**)

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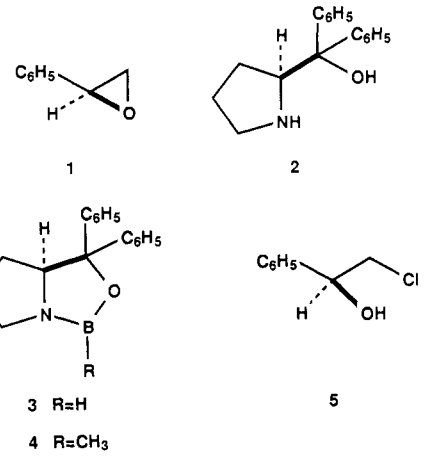
as a crystalline solid, mp 76.5–77.5 °C, in 52% yield and in 99.4% *S* enantiomeric excess. The amino alcohol **2** upon heating in THF solution with 3 equiv of borane at 70–75 °C bath temperature at a small positive pressure (ca. 50 cm of Hg using a U-tube to prevent loss of borane and an inert atmosphere) for 48 h produced the oxazaborolidine derivative **3** after removal of solvent. Although **3** can be purified by sublimation in vacuo, for most synthetic purposes it can be employed as a catalyst directly without further purification. It can be analyzed by ^1H and ^{11}B NMR and by infrared spectroscopy.[1] Reaction of **2** with methylboronic acid[5] in benzene in the presence of 4A molecular sieves at 23 °C for 1.5 h produced the oxazaborolidine derivative **4**,[2] which is also an excellent catalyst for enantioselective reduction of ketones.[2]



α-Chloroacetophenone was reduced by borane (0.6 molar equiv) in the presence of 1 mol % of oxazaborolidine **3** as catalyst in THF at 25 °C under nitrogen to give after isolation and vacuum distillation (*S*)-(+)-α-(chloromethyl)benzenemethanol (**5**) in 97% yield and 96.5% enantiomeric excess. Treatment of chloro alcohol **5** with aqueous sodium hydroxide afforded (*S*)-(−)-phenyloxirane (styrene oxide) (**1**) in 96% yield after vacuum distillation.

The practicality and effectiveness of the chiral oxazaborolidine catalyzed reduction (CBS reduction[2]) can be evaluated from the detailed experimental procedure which follows. It is noteworthy that in each step the isolation of product is simple and that the chiral amino alcohol **2** can be recovered efficiently as the hydrochloride from the CBS reduction.

Experimental Section

***N*-(Benzyloxycarbonyl)-(*S*)-proline.** A 500-mL, three-necked, round-bottomed flash was equipped with two pressure equalizing dropping funnels (50- and 100-mL), a thermometer, and a magnetic stirrer. The flask was charged with 100 mL (0.2 mol) of a 2 M aqueous solution of sodium hydroxide and cooled with an ice–salt bath. To the aqueous solution 23.0 g (0.2 mol) of (*S*)-proline (Aldrich Chem. Co., $[\alpha]_D^{20}$ −84° (water, *c* = 4)) was added with stirring. To the resulting solution maintained at 0 to −5 °C were added dropwise 36.4 mL (40.9 g, 0.24 mol) of benzyl chloroformate (Aldrich) and 70 mL (0.28 mol) of 4 M aqueous solution of sodium hydroxide over 1 h with vigorous stirring. The reaction mixture was stirred for another 1 h at 0 to −5 °C and then washed with ethyl ether (2 × 50 mL). The aqueous solution was acidified to pH 2 (ice bath cooling) by a dropwise addition of 6 M hydrochloric acid and the resulting mixture was saturated with sodium sulfate and extracted with ethyl acetate (3 × 100 mL). The extracts were combined, dried over anhydrous sodium sulfate (2 portions), and evaporated under reduced pressure to give a colorless oil, which was dissolved in 50 mL of ethyl acetate and diluted with 200 mL of petroleum ether. Crystallization of the resulting mixture was induced by cooling and scratching with a glass rod. The crystals were collected by filtration and washed with 20 mL of petroleum ether. After drying in vacuo 47.9 g (0.192 mol) of colorless crystals of *N*-(benzyloxycarbonyl)-(*S*)-proline[3] were obtained, mp 69–74 °C, $[\alpha]_D^{22}$ −39.9° (ethanol, *c* 2.0), 96% yield.

***N*-(Benzyloxycarbonyl)-(*S*)-proline Methyl Ester.** A 1-L, one-necked, round-bottomed flask equipped with a magnetic stirrer and a Liebig condenser fitted with a rubber septum was charged with 33.7 g (0.135 mol) of *N*-(benzyloxycarbonyl)-(*S*)-proline and 400 mL of anhydrous methanol, and the contents were placed under dry nitrogen. After the addition of 24.6 mL (28.4 g, 0.2 mol) of boron trifluoride etherate with stirring, the solution was heated at reflux for 1 h. Solvent was removed under reduced pressure and the residue was vigorously stirred with 200 mL of ice–water and extracted with ethyl acetate (3 × 100 mL). The extracts were combined and successively washed with brine, 1 M aqueous sodium bicarbonate solution, and brine, and dried over anhydrous sodium sulfate. After the removal of the solvent under reduced pressure, the residual colorless oil was dried by twice dissolving in 100 mL of dry toluene and removing solvent under reduced pressure to give 35.9 g of methyl ester as a colorless oil, $[\alpha]_D^{21}$ −53.9° (methanol, *c* 1.0).[4]

(*S*)-(−)-2-(Diphenylhydroxymethyl)pyrrolidine (2). A dry 1-L, three-necked, round-bottomed flask was equipped with a pressure-equalizing 250-mL dropping funnel, a thermometer, a rubber septum, and a large magnetic stirrer. The contents of the flask were placed under nitrogen, and 400 mL (0.8 mol) of phenylmagnesium chloride in THF solution (2 M) was added. A solution of *N*-(benzyloxycarbonyl)-(*S*)-proline methyl ester (23.6 g, 0.1 mol) in 100 mL of dry THF was added to the phenylmagnesium chloride solution over 1 h at 0 to −10 °C with ice–salt bath cooling. After the addition, the cooling bath was removed and the reaction mixture was allowed to warm to room temperature and stirred for 16 h. The reaction mixture was poured with stirring into 300 g of crushed ice and 60 g of ammonium chloride in 100 mL of water. The resulting mixture was concentrated under reduced pressure to remove THF and the resulting aqueous mixture was extracted with ethyl ether. The ethereal extract was washed with brine, dried over anhydrous potassium carbonate, and concentrated in a rotary evaporator to a total volume of 500 mL. Dry hydrogen chloride gas was bubbled into the solution with stirring until the mixture was acidic. The precipitated amine hydrochloride was collected by filtration, washed with ether, and dissolved in 150 mL of hot methanol. To this solution was added 600 mL of ethyl ether, and the resulting mixture was stirred and cooled with an ice bath. The precipitate was filtered, washed with ether, and dried to give 16.7 g of crude product. The hydrochloride was suspended in 300 mL of ether and treated with 60 mL of 2 M sodium hydroxide aqueous solution with vigorous stirring. The resulting mixture was stirred vigorously for 45 min and extracted with ethyl ether. The extracts were washed with brine, dried over anhydrous potassium carbonate, and evaporated under reduced pressure to give a solid, which was recrystallized from methanol (15 mL) and water (3 mL) to give 13.3 g (0.0527 mol, 52.7% yield) of colorless crystals of **2** (50.8% yield based on (*S*)-proline), mp 76.5–77.5 °C, $[\alpha]_D^{24}$ −58.8° (methanol, *c* 3.0), enantiomeric excess 99.4%.[6]

Oxazaborolidine 3. A dry 25-mL, one-necked, round-bottomed flask equipped with a Claisen adapter and a magnetic stirrer was charged with 0.76 g (0.003 mol) of (*S*)-(−)-2-(diphenylhydroxymethyl)pyrrolidine (**2**). The Claisen adapter was fitted with a cold finger condenser and a three-way stopcock, capped by a rubber septum, and also connected to a mercury U-tube bubbler to maintain 500 mm of positive gas pressure. The stopcock was turned to connect only the rubber septum and the

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flask, and the flask was evacuated and flushed with argon (five cycles). Then the stopcock was turned to connect the rubber septum and the mercury bubbler, and the bubbler was flushed with argon. The flask was charged with 8.2 mL (0.009 mol) of borane THF (1.1 M) through the three-way stopcock with a syringe. The stopcock was turned to connect only the flask and the mercury bubbler, and the reaction mixture was heated at 70–75 °C (bath temperature) with gentle stirring for 2 days. The solvent was removed under reduced pressure (exclusion of air) to give 1.21 g of colorless residue, which was dissolved in dry THF (6 mL total volume) to give a 0.5 M solution of catalyst **2**.

Oxazaborolidine 4. A solution of (*S*)-(−)-2-(diphenylhydroxymethyl)pyrrolidine (96 mg, 0.38 mmol) and methylboronic acid (23 mg, 0.38 mmol) in benzene (6 mL) was stirred at room temperature in the presence of powdered molecular sieves (4A type, 0.8 g) for 1.5 h. The reaction mixture was filtered and the residue was washed with benzene (2 mL). Concentration of the combined extracts under vacuum afforded B-methylated oxazaborolidine **4** (95 mg, 0.34 mmol, 94.5% yield).

(*S*)-(+)-α-(Chloromethyl)benzenemethanol. A dry 250-mL, two-necked, round-bottomed flask equipped with a rubber septum, a thermometer, and a magnetic stirrer was flushed with nitrogen and charged with 2 mL (0.001-mol scale) of the above solution of catalyst **3** (0.5 M). To this solution was added 9.1 mL (0.01 mol) of borane–THF (1.1 M) with stirring under nitrogen. A solution of 15.5 g (0.1 mol) of 2-chloroacetophenone in 45.5 mL of THF contained in a syringe and a solution of 45.5 mL (0.05 mol) of borane–THF (1.1 M) were added simultaneously to the THF solution of **3** with stirring at 20–30 °C under nitrogen (addition rate 1 mL/min). The reaction mixture was stirred for 10 min and decomposed by the addition of 14.6 mL (0.36 mol) of methanol with stirring and ice bath cooling over 10 min. To the resulting solution was added 2 mL of dry saturated hydrogen chloride in ether with stirring and ice bath cooling over 5 min. After 30 min at 20 °C the solvent was removed under reduced pressure to give an oily residue. The residue was dissolved in 50 mL of benzene, and the solvent was removed under reduced pressure (twice). To the residue was added 100 mL of ether and the mixture was cooled to 0 °C. Colorless crystals of ((*S*)-(−)-2-(diphenylhydroxymethyl)pyrrolidine hydrochloride) were collected by filtration and converted to amino alcohol **2** (recovery 218 mg, 86.5%). The ether solutions were combined, washed successively with brine, saturated sodium bicarbonate solution, and brine, dried over anhydrous magnesium sulfate, and evaporated under reduced pressure to give after distillation (bp 112-114 °C/6 Torr) 15.2 g (0.0971 mol, 97.1% yield) of chloro alcohol **5** $[\alpha]_D^{24}$ +49.6° (cyclohexane, *c* 2.81), absolute configuration *S*, enantiomeric excess (ee) 96.5%.[1,7]

(*S*)-(−)-Phenyloxirane (1). A 250-mL, one-necked, round-bottomed flask equipped with a pressure-equalizing 10-mL dropping funnel and a magnetic stirrer was charged with 100 mL of a 2 M sodium hydroxide aqueous solution. To the aqueous solution was added dropwise 10 g (0.0647 mol) of (*S*)-(+)-α-(chloromethyl)benzenemethanol over 15 min at 22 °C with stirring. The dropping funnel was rinsed with 2 mL of ether, and the ether solution was added to the reaction mixture. The resulting mixture was stirred vigorously for 1 h at room temperature, saturated with sodium sulfate, and extracted with pentane (3 × 20 mL). The extracts were combined and dried over calcium chloride, and the solvent was removed at atmospheric pressure to give 8.64 g of colorless oil. This oil was distilled in a short-path still to give 7.48 g (0.0623 mol, 96.2% yield) of **1** as a colorless oil, bp 88–89 °C (19 Torr), α_D^{24} −34.9 (neat, *c* 1.0), $[\alpha]_D^{24}$ −33.2° (neat), $[\alpha]_D^{23}$ −44.9° (benzene *c* 1.02), absolute configuration *S*.[1,8–10]

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New Manganese Tetrakis(halogenoaryl)porphyrins Featuring Sterically Hindering Electronegative Substituents: Synthesis of Highly Stable Catalysts in Olefin Epoxidation

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Metal tetraarylporphyrins, especially Mn(III) and Fe(III) complexes, are very efficient catalysts in the oxidation of organic substrates carried out with a variety of oxidants.[1] Among these, the use of NaOCl under phase-transfer conditions aroused a special interest from the preparative point of view.[2] Unfortunately, metal tetraarylporphyrins are easily deactivated in the course of the reactions, mainly by the irreversible formation of μ-oxo dimers[3] and by autocatalytic oxidative demolition.[4] The latter becomes very fast in the oxidation of poorly reactive substrates, as in the epoxidation of α-olefins, or with a deficiency of substrate.[1] Porphyrin stability also depends on the nature of the oxidizing species.[5]

It has been reported that the chemical stability of tetraphenylporphyrin (**1**) is increased by the introduction of sterically hindering[4,6,7] and/or electron-withdrawing groups[4,8] on the phenyl rings. However, the relative importance of these two parameters has never been thoroughly studied and unambiguously established. Only the Mn(III) and Fe(III) complexes of tetrakis(2,6-dichlorophenyl)porphyrin (**2**),[4,5,9] tetrakis(pentafluorophenyl)-porphyrin (**6**),[8,10,11] and tetrakis(2,4,6-triphenylphenyl)-porphyrin[7] were found to be noticeably stable.[12] Furthermore, the claimed stability of some metalloporphyrins often relies upon very particular reaction conditions, such as large substrate/oxidant ratios.[9,11,13]

In order to get a deeper insight into the effects of substituents, we synthesized tetrakis(3,5-dimethyl-2,4,6-trichlorophenyl)- (**3**), tetrakis(3,5-dimethyl-2,4,6-tribromophenyl)- (**4**), and tetrakis(3,5-dichlorophenyl)porphyrin (**5**). These compounds were prepared in 7.4, 2.7, and 5.1% yield, respectively, from the corresponding aldehydes,

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