232/230/228/226 (M^+). Anal. Calcd: C, 47.2; H, 5.7. Found: C, 47.4; H, 5.7.

Identical treatment of *m*-bromoanisole produced *m*-anisyltrimethylgermanium: 19.3 g (86%); bp 112 °C (33 mm); d^{25} = 1.1426; IR (neat) 3200–2990, 2850, 1650, 1500, 1280, 1235, 1050, 850, 815, 750, 665 cm^{-1}; ^1H NMR (acetone-d_6) δ 0.38 (s, 9 H), 3.46 (s, 3 H), 7.12 (m, 4 H); MS, *m/e* 226/224/222 (M^+). Anal. Calcd: C, 53.4; H, 7.2. Found: C, 53.2; H, 7.2.

Halogenation Experiments. All halogenation reactions were performed at 25 °C in tightly sealed 100-mL glass reaction vessels equipped with magnetic stirrers. The general sequence used for the halogenodegermylation experiments was to place the aryltrimethylgermanium compound (2–3 mmol) into the vessel and add the reaction solvent (10 mL), followed by addition of 1 equiv of halogen (dissolved in the reaction solvent) while stirring. Stock solutions of the halogens were prepared immediately prior to use. Solutions (0.25 M) of bromine, iodine, and iodine monochloride were obtained by dissolving the calculated amount of halogen in the appropriate volume of solvent. Chlorine solutions were prepared by passing dry chlorine gas through the respective solvents. Concentrations from 0.05 to 0.3 M were obtained, as determined by treatment with excess potassium iodide and subsequent titration for iodine.

Following various reaction intervals (1 min, 5 min, 10 min, 30 min, 1 h, 2 h, 4 h, 6 h, 24 h), a 500-μL aliquot was removed with a glass syringe and transferred to aqueous sodium sulfite (10%, 4 mL) to quench the halogenation reaction. The organic products were extracted into dichloromethane (4 mL), and the organic layer was dried with calcium chloride.

Analysis of Reaction Products. The organic reaction products in 100 μL of the organic layer were analyzed by either gas chromatography or high-performance liquid chromatography. GC analyses were performed using a Hewlett-Packard 5880-A series gas chromatograph with integrator. The isomeric chlorinated, brominated, and iodinated analogues of benzene and chlorobenzene were separated using a $^1/_8$ in. × 13 ft column of 6% Bentone-34 and 20% silicon oil DC-200 on 60/80 Chromosorb W-AW-DMCS,[29] while the corresponding halogenated isomers of anisole and fluorobenzene were separated using a $^1/_8$ in. × 13 ft column of 80% Igepal Co-880 on 60/80 Chromosorb W-AW-DMCS.[30] HPLC analyses were performed with a Waters M-45 solvent delivery system with Model U6K injector and Model 450 variable-wavelength detector connected to a Hewlett-Packard 3390-A reporting integrator. The halogenated isomers of phenol were separated on a stationary phase comprised of 0.5 × 50 cm Lichrosorb Si-60 (Merck) and a mobile phase of 1.5% glacial acetic acid in *n*-heptane.[31] The halogenodegermylation yields were calculated from the GC analyses by comparing the gas chromatograph's thermal conductivity detector response for each product with a calibrated mass–TCD response curve prepared for each of the possible halogenated isomers. A similar approach was used with the UV detector (adjusted to 254 nm) in the HPLC analysis of halogenated phenol products. For both GC and HPLC analyses, complete (98%) passage of the injected mass through the respective detecting devices occurred. This was determined by tracer experiments in which ^{36}Cl-, ^{82}Br-, and ^{131}I-labeled arenes were analyzed, the product peaks collected, and their radioactivities compared to that in a standard sample of the injectate.[2,11]

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Registry No. 1, 25920-26-7; 2, 31608-56-7; 3, 1626-00-2; 4, 23781-64-8; 5, 105183-09-3; 3-ClC_6H_4Cl, 541-73-1; 3-ClC_6H_4OMe, 2845-89-8; PhCl, 108-90-7; 4-ClC_6H_4F, 352-33-0; 4-ClC_6H_4OH, 106-48-9; 3-BrC_6H_4Cl, 108-37-2; 3-BrC_6H_4OMe, 2398-37-0; PhBr, 108-86-1; 4-BrC_6H_4F, 460-00-4; 4-BrC_6H_4OH, 106-41-2; 3-IC_6H_4Cl, 625-99-0; 3-IC_6H_4OMe, 766-85-8; PhI, 591-50-4; 4-IC_6H_4F, 352-34-1; 4-IC_6H_4OH, 540-38-5; trimethylgermanium chloride, 1529-47-1.

(29) Knust, E. J. Schüller, M. *J. Chromatogr.* **1975**, *114*, 207.
(30) Vasaros, L.; Machulla, H.-J.; Tornau, W. *J. Chromatogr.* **1971**, *62*, 458.
(31) Petzold, G. *Untersuchungen zur elektrophilen Radiobromierung und -iodierung aromatischer Verbindungen mit N-Halogenverbindungen ohne Trägerzusatz*, JÜL-Report 1810; Kernforschungsanlage Jülich GmbH: Jülich, FRG, 1982.
(32) In this paper the periodic group notation (in parentheses) is in accord with recent actions by IUPAC and ACS nomenclature committees. A and B notation is eliminated because of wide confusion. Groups IA and IIA become groups 1 and 2. The d-transition elements comprise groups 3 through 12, and the p-block elements comprise groups 13 through 18. (Note that the former Roman number designation is preserved in the last digit of the new numbering: e.g., III → 3 and 13.)

p-Nitrobenzoate Esters of Epoxy Alcohols: Convenient Synthons for Water-Soluble Epoxy Alcohols

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The recently developed catalytic modification of the asymmetric epoxidation of allylic alcohols has expanded the synthetic utility of the process.[1] Beyond its obvious economic advantage, the catalytic procedure is especially effective for the synthesis of low molecular weight epoxy alcohols since workup and product isolation are now much simpler and in situ derivatization of the product epoxy alcohols is feasible. Sulfonylation, silylation, and esterification have been achieved in situ, following the catalytic asymmetric epoxidation of low molecular weight primary allylic alcohols (Scheme I).[2]

While the sulfonylation and silylation processes provide derivatives that are synthetically advanced over the parent epoxy alcohols, in situ esterification provides products which, depending on the selected conditions for subsequent reactions, are either functionally equivalent or are advanced with respect to the epoxy alcohols.

The functional equivalency between the epoxy esters and the parent epoxy alcohols is achieved under two sets of reaction conditions where initial ester hydrolysis occurs to liberate the free epoxy alcohols, which, in the presence of a nucleophile, then undergo ring-opening. To ensure this equivalency, the ester hydrolysis should take place much faster than ring-opening so that the free epoxy alcohol is the substrate for all the ring-opening reactions. Hence, the nucleophile can be present at the start of the reaction. Two quite different types of reaction conditions were studied in this effort (Scheme II).

When epoxy esters were treated with benzenethiol or 1-naphthol in a solution of *t*-BuOH and aqueous NaOH, ester hydrolysis occurred, as expected, to release the free epoxy alcohols. Under the aqueous basic conditions, the free 2,3-epoxy alcohols **1** underwent isomerization to 1,2-epoxy 3-ols **2** by virtue of the Payne rearrangement.[3] Nucleophilic ring-opening then took place selectively at the C-1 center of the latter isomers to afford a high proportion of the 2,3-diol products (eq 1).[4] The results with

(1) (a) Hanson, R. M.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 1952. (b) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.
(2) (a) Hanson, R. M.; Ko, S. Y.; Gao, Y.; Masamune, H.; Klunder, J. M.; Sharpless, K. B. *J. Am. Chem. Soc.*, in press. (b) In situ opening of glycidol and 2-methylglycidol has also been achieved. See ref 13 and 5b.
(3) Payne, G. B. *J. Org. Chem.* **1962**, *27*, 3819.

0022-3263/87/1952-0667$01.50/0

Scheme I

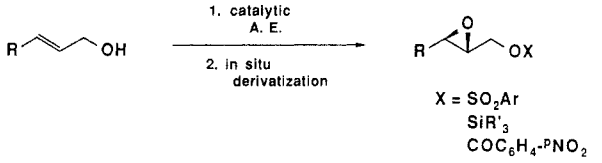
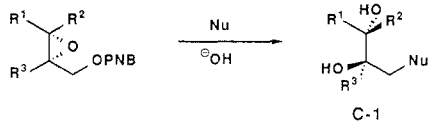


Table I



entry	substrate (PNB)[a]	Nu	yield (%)
1	glycidyl $R^1 = R^2 = R^3 = H$	PhS^-	93
2	glycidyl $R^1 = R^2 = R^3 = H$	ArO^-	54[b]
3	2-methylglycidyl $R^1 = R^2 = H$, $R^3 = Me$	PhS^-	87
4	*trans*-3-methylglycidyl $R^1 = Me$, $R^2 = R^3 = H$	PhS^-	85[c]
5	3,3-dimethylglycidyl $R^1 = R^2 = Me$, $R^3 = H$	PhS^-	70[d]

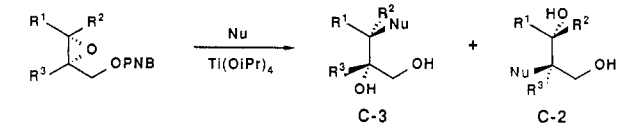
[a] PNB stands for *p*-nitrobenzoate. [b] Reaction was run to completion; no other isolable products observed. [c] A 9.6:4.3:1 mixture of the C-1:C-3:C-2 opened products. [d] A 10:1 mixture of C-1:C-2 opened products.

various epoxy *p*-nitrobenzoate esters in this process are shown in Table I. It is important to note that in the cases of glycidyl and 2-methylglycidyl esters (entries 1–3), the Payne rearrangement is degenerate.[5] Therefore, either direct opening at C-3 or the rearrangement–opening path yield the same product (same enantiomer). In addition, no C-2 opened product was observed.

In the cases of *trans*-3-methylglycidyl and 3,3-dimethylglycidyl *p*-nitrobenzoates (entries 4, 5), the experimental procedures employed here were exactly the same as those reported for the free epoxy alcohols in that the nucleophile was added slowly to the reaction mixture in order to achieve maximum regioselectivity.[4] Although the regioselectivity observed in entry 4 is not high, it should be noted that this ratio is not significantly different from that observed when a closely related free epoxy alcohol was subjected to the same conditions.[4] A more regioselective C-1 opening was observed with 3,3-dimethylglycidyl *p*-nitrobenzoate, due to steric factors disfavoring opening at the C-3 center (entry 5).

The efficacy of these epoxy esters as synthons for the corresponding epoxy alcohols was also realized under the conditions of the Ti-mediated epoxy alcohol opening process.[6] Thus, when epoxy esters were treated with nucleophiles in the presence of $Ti(O\text{-}i\text{-}Pr)_4$, Ti-catalyzed transesterification released the free epoxy alcohols,[7] which then underwent Ti-mediated ring-opening reactions in the same reaction vessel to yield the product diols. Since the Ti-mediated ring-opening reaction does not take place with hydroxyl-protected epoxy alcohols,[6] the results observed in this process with the *p*-nitrobenzoate esters are, again,

Table II



entry	substrate (PNB)[a]	Nu	C-3:C-2	yield (%)
1	glycidyl $R^1 = R^2 = R^3 = H$	PhSH	C-3 only	54[b]
2	glycidyl $R^1 = R^2 = R^3 = H$	$(Bn)_2NH$	C-3 only	88
3	glycidyl $R^1 = R^2 = R^3 = H$	NH_4Br	C-3 only	83
4	2-methylglycidyl $R^1 = R^2 = H$, $R^3 = Me$	PhSH	C-3 only	77
5	*cis*-3-methylglycidyl $R^1 = R^3 = H$, $R^2 = Me$	PhSH	2.3:1	66
6	*trans*-3-methylglycidyl $R^1 = Me$, $R^2 = R^3 = H$	PhSH	1.7:1	63
7	3,3-dimethylglycidyl $R^1 = R^2 = Me$, $R^3 = H$	PhSH	1:1.5	90

[a] PNB stands for *p*-nitrobenzoate. [b] Reaction was run to completion; no other isolable products observed.

expected to be the same as those observed with the free epoxy alcohols (eq 2). Thiophenol, dibenzylamine, and bromide were employed as nucleophiles in this study (Table II). The reactions with glycidyl and 2-methylglycidyl *p*-nitrobenzoates yielded the desired 1,2-diols (C-3 opened products) cleanly since the stereoelectronically favored C-3 centers are also the terminal, sterically favored ones (entries 1–4). Under the same reaction conditions, 3-monosubstituted glycidyl *p*-nitrobenzoates reacted with PhSH to yield mixtures of the C-3 (major) and the C-2 (minor) opened products (entries 5, 6). The reaction with 3,3-dimethylglycidyl *p*-nitrobenzoate showed a predominance of C-2 opening under these conditions (entry 7).

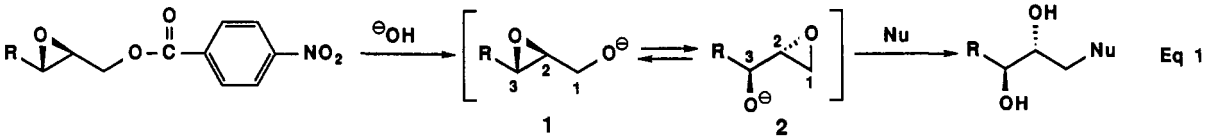
Ring-opening reactions can also be executed without hydrolyzing the ester group, thus providing monoprotected diols (Table III). In most of the cases studied these opening reactions were highly regioselective, giving the 1-(*p*-nitrobenzoyl)oxy 2-ols in good yields. Moreover, in addition to the ease of isolation and the differential protection of the opened products, some of these acid-catalyzed opening reactions are superior to the analogous reactions of the parent epoxy alcohols, since lower regioselectivity as well as decomposition are sometimes observed in the latter reactions.[8]

In the presence of acid catalyst, MeOH, N_3^-, and I^-[9] opened the epoxide ring of glycidyl *p*-nitrobenzoate at the C-3 position (entries 1–3). Ring-opening by CN^- was achieved by Et_2AlCN[10] or acetone cyanohydrin–KCN (entries 4, 5). Benzenethiol in Et_3N or pyridine opened the epoxide ring of glycidyl *p*-nitrobenzoate without attacking the ester group (entries 6, 7). Partial migration of *p*-nitrobenzoyl moiety to the C-2 hydroxyl group was observed in both reactions (C-1:C-2 esters 4:1 in entry 6, 14:1 in entry 7).

Treatment of an acetone solution of glycidyl *p*-nitrobenzoate with a catalytic amount of H_2SO_4 yielded the solketal ester in good yield (entry 8). A loss in optical purity was observed in this reaction, indicating that the opening by acetone was not highly regioselective. Re-

(4) Behrens, C. H.; Ko, S. Y.; Sharpless, K. B.; Walker, F. J. *J. Org. Chem.* **1985**, *50*, 5687.
(5) (a) McClure, D. E.; Engelhardt, E. L.; Mensler, K.; King, S.; Saari, W. S.; Huff, J. R.; Baldwin, J. J. *J. Org. Chem.* **1979**, *44*, 1826. (b) Klunder, J. M.; Ko, S. Y.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 3710.
(6) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557.
(7) Seebach, D.; Hungerbuhler, E.; Maef, R.; Schnurrenberger, P.; Weidmann, B.; Zuger, M. *Synthesis* **1982**, 138.
(8) (a) Biggs, J.; Chapman, N. B.; Wray, V. *J. Chem. Soc. B* **1971**, 66. (b) Behrens, C. H.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 5696.
(9) Cornforth, T. W.; Cornforth, R. H.; Mathew, K. K. *J. Chem. Soc.* **1959**, 112.
(10) (a) Nagata, W.; Yoshioka, M.; Okumura, T. *Tetrahedron Lett.* **1966**, 847. (b) Nagata, W.; Yoshioka, M.; Okumura, T. *J. Chem. Soc. C* **1970**, 2365.

Scheme II



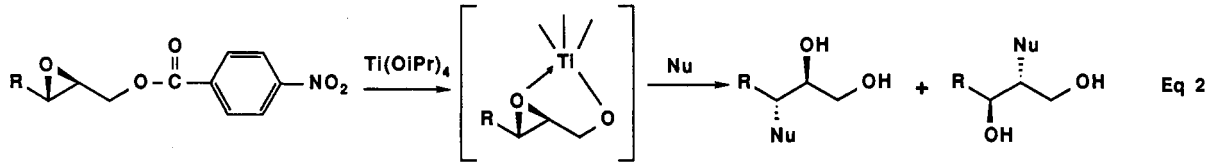
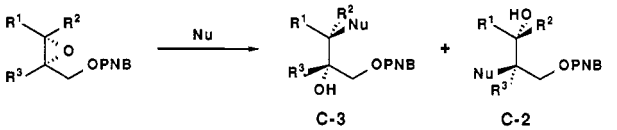


Table III



entry	substrate (PNB)[a]	Nu	conditions	C-3:C-2	yield (%)
1	glycidyl $R^1 = R^2 = R^3 = H$	MeOH	MeOH, H_2SO_4	C-3 only	85
2	$R^1 = R^2 = R^3 = H$	N_3^-	NaN_3, PPTs, DMF	C-3 only	65–88[b]
3	$R^1 = R^2 = R^3 = H$	I^-	NaI, NaOAc, AcOH, $EtCO_2H$	C-3 only	89
4	$R^1 = R^2 = R^3 = H$	CN^-	acetone cyanohydrin, KCN	C-3 only	85
5	$R^1 = R^2 = R^3 = H$	CN^-	Et_2AlCN	C-3 only	71
6	$R^1 = R^2 = R^3 = H$	PhSH	PhSH, Et_3N	C-3 only[b]	100
7	$R^1 = R^2 = R^3 = H$	PhSH	PhSH, pyridine	C-3 only[b]	97
8	$R^1 = R^2 = R^3 = H$	acetone[c]	acetone, H_2SO_4	5.1:1[d,e]	72
				11.3:1[d,f]	67
9	*trans*-3-methylglycidyl $R^1 = Me$, $R^1 = R^3 = H$	MeOH	MeOH, H_2SO_4	5.7:1	65
10	$R^1 = Me$, $R^1 = R^3 = H$	I^-	NaI, NaOAc, AcOH, $EtCO_2H$	C-3 only	95
11	3,3-dimethylglycidyl $R^1 = R^2 = Me$, $R^3 = H$	MeOH	MeOH, H_2SO_4	C-3 only	50
12	$R^1 = R^2 = Me$, $R^3 = H$	I^-	NaI, NaOAc, AcOH, $EtCO_2H$	C-3 only	46

[a] PNB stands for *p*-nitrobenzoate. [b] Partial migration of PNB to the C-2 hydroxyl group was observed. [c] The product in this reaction is solketal *p*-nitrobenzoate. [d] The opening at C-2 yields the enantiomeric product. [e] The reaction was performed at room temperature. [f] The reaction was performed at −20 °C.

gioselectivities of C-3:C-2 = 5.1:1 (at room temperature) and 11.3:1 (at −20 °C) were calculated from the % ee's and absolute configurations of the reactant and the product.[11]

Treatment of a methanol solution of *trans*-3-methylglycidyl *p*-nitrobenzoate with an acid catalyst yielded a 5.7:1 mixture of the C-3 and C-2 opened products (entry 9). The regioselectivity observed in this reaction is higher than that observed from reactions with similar free epoxy alcohols, probably due to the deactivation of the C-2 center by the electronegative ester group.[8b] Ring opening of *trans*-3-methylglycidyl *p*-nitrobenzoate by I^- yielded exclusively the C-3 opened product (entry 10).

The same reactions with 3,3-dimethylglycidyl *p*-nitrobenzoate yielded the C-3 opened products [1-(*p*-nitrobenzoyl)oxy 2-ols] exclusively (entries 11, 12), although some decomposition was observed with this substrate under these acidic conditions.[2]

In summary, epoxy *p*-nitrobenzoate esters are at least as useful as chiral building blocks as their parent epoxy alcohols. Along with convenience in preparation, stability, and improved enantiomeric purity, they are reactive and versatile synthons.

Experimental Section

General. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. High performance liquid chromatography was performed on a Perkin-Elmer Series 2 liquid chromatograph. Flash chromatography was performed on Merck silica gel 60 (230–400 mesh) as described by Still.[12] IR spectra were recorded on a Perkin-Elmer 597 spectrometer. ^1H NMR spectra were recorded on either a Bruker WM-250 (250 MHz) or a Varian XL-300 (300 MHz) spectrometer with tetramethylsilane or deuterated solvents as internal standard. Optical rotations were measured with a Perkin-Elmer Model 241 polarimeter using a 1 cm^3 capacity (1-dm path length) quartz cell. Microanalyses were performed by Robertson Laboratory, Florham Park, NJ.

The epoxy alcohol *p*-nitrobenzoate esters were prepared and characterized as described elsewhere.[2] The esters used in this

(11) The absolute configuration of the product was determined by removing the isopropylidene group (aqueous HOAc, room temperature, overnight) and comparing the optical rotation of the resulting glycerol mono-*p*-nitrobenzoate with that in the literature (ref 14). Although the rotation of the product was lower than that expected from the optical purity of the solketal *p*-nitrobenzoate (measured from the ^1H NMR) and the literature rotation value, it is probably due to the migration of the ester group to the C-3 hydroxyl group under the acidic conditions. Note that this ester migration racemizes the product, and, therefore, lowers the magnitude of the optical rotation, but it cannot change the sign of the rotation.

(12) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

study were optically active unless otherwise noted. The enantiomeric purities were as follows: glycidyl *p*-nitrobenzoate, 92% ee; 2-methylglycidyl, >98% ee; *cis*-3-methylglycidyl, 92% ee; *trans*-3-methylglycidyl, >98% ee; 3,3-dimethylglyicidyl, >98% ee. Benzenethiol and dibenzylamine (Aldrich Chemical Co.) were dried over 3-Å molecular sieves (Pellet form). 1-Naphthol (Aldrich) was sublimed prior to use. 2-propanol and methanol were dried over 3-Å molecular sieves (pellet form). Acetone cyanohydrin (Aldrich) and diethylaluminum cyanide (1.5 M solution in toluene, Alfa Products) were used as received.

Experimental procedures are given below for the reactions of glycidyl *p*-nitrobenzoate. The other reactions were performed in similar ways and details are given in the supplementary material.

Reaction of Glycidyl *p*-Nitrobenzoate with PhSH under Payne Rearrangement Conditions. (2*R*)-Glycidyl *p*-nitrobenzoate (45 mg, 0.2 mmol) was dissolved in *t*-BuOH (2 mL), and PhSH (0.03 mL, 32 mg, 0.3 mmol) and 1 N NaOH (1 mL) were added. The mixture was stirred at room temperature overnight. Dilution with ether (25 mL) was followed by phase separation and the organic layer was dried (Na_2SO_4) and concentrated. Flash chromatography (1:1 hexane–EtOAc) afforded (*S*)-3-(phenylthio)-1,2-propanediol (34 mg, 93%): mp 78–80 °C; $[\alpha]^{25}_D$ +21.8° (*c* 1.06, EtOH). The product was characterized as described elsewhere.[13]

Reaction of Glycidyl *p*-Nitrobenzoate with PhSH in the Presence of Ti(O-*i*-Pr)$_4$. Glycidyl *p*-nitrobenzoate (45 mg, 0.2 mmol, racemic mixture) was dissolved in 2-propanol (2 mL), and PhSH (0.02 mL, 22 mg, 0.2 mmol) and Ti(O-*i*-Pr)$_4$ (0.08 mL, 76 mg, 0.26 mmol) were added. The mixture was stirred at room temperature overnight. Dilution with ether (10 mL) was followed by addition of 10% H_2SO_4 (10 mL). The mixture was stirred for 1 h. The phases were separated, the aqueous layer was extracted with two portions of ether, and the combined organic layers were dried (Na_2SO_4) and purified by flash chromatography (1:1 hexane–EtOAc) to yield 3-(phenylthio)-1,2-propanediol (20 mg, 54%). The product was characterized as described above and elsewhere.[13]

Reaction of Glycidyl *p*-Nitrobenzoate with MeOH in the Presence of Acid Catalyst. Glycidyl *p*-nitrobenzoate (56 mg, 0.25 mmol, racemic mixture) was dissolved in MeOH (5 mL) and a drop of concentrated H_2SO_4 was added. The mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with ether (25 mL) and washed with saturated $NaHCO_3$ solution (10 mL) and with brine (10 mL). The organic layer was dried (Na_2SO_4), concentrated, and chromatographed (2:1 hexane–EtOAc) to afford 3-methoxy-1,2-propanediol 1-*O*-*p*-nitrobenzoate as an oil (54 mg, 85%): ^1H NMR ($CDCl_3$) δ 8.19 (d, J = 9.0 Hz, 2 H), 8.12 (d, J = 8.2 Hz, 2 H), 4.65 (dd, J = 2.4, 9.7 Hz, 1 H), 4.60 (dd, J = 2.6, 10.4 Hz, 1 H), 4.37 (sep, J = 4.9 Hz, 1 H), 3.82 (dd, J = 3.7, 9.3 Hz, 1 H), 3.75 (dd, J = 5.4, 8.6 Hz, 1 H), 3.69 (s, 3 H), 2.99 (d, J = 5.2 Hz, 1 H); IR (neat) 3590, 3120, 3080, 2940, 2850, 1720, 1605, 1525, 1455, 1380, 1355, 1290, 1195, 1120, 1015, 990, 935, 895, 875, 860, 835, 790, 720 cm^{-1}.

Reaction of Glycidyl *p*-Nitrobenzoate with NaN_3 in the Presence of Acid Catalyst. Glycidyl *p*-nitrobenzoate (45 mg, 0.2 mmol, racemic mixture) was dissolved in DMF (5 mL), and NaN_3 (65 mg, 1.0 mmol) and pyridinium tosylate (PPTs, 100 mg, 0.4 mmol) were added. The solution was stirred at room temperature for 7 days. It was diluted with ether (25 mL) and washed with brine. The organic phase was dried (Na_2SO_4), concentrated, and chromatographed (2:1 hexane–EtOAc) to yield 3-azido-1,2-propanediol 1-*O*-*p*-nitrobenzoate as an oil (35 mg, 65%): ^1H NMR ($CDCl_3$) δ 8.21–8.33 (m, 4 H), 4.48 (d, J = 1.1 Hz, 1 H), 4.46 (d, J = 1.7 Hz, 1 H), 4.21 (sextet, J = 5.1 Hz, 1 H), 3.57 (dd, J = 3.8, 12.4 Hz, 1 H), 3.50 (dd, J = 5.6, 12.7 Hz, 1 H), 2.74 (d, J = 5.1 Hz, 1 H); IR (neat) 3440 (br), 3120, 2960, 2870, 2110, 1725, 1610, 1525, 1445, 1410, 1350, 1270, 1130, 1110, 1020, 870, 860, 790, 720 cm^{-1}.

(2*R*)-Glycidyl *p*-nitrobenzoate (223 mg, 1.0 mmol) was dissolved in DMF (10 mL), and NaN_3 (130 mg, 2.0 mmol) and pyridinium tosylate (250 mg, 1 mmol) were added. The solution was heated to ca. 80 °C for 3 h. It was diluted with ether (100 mL) and washed with 10% H_2SO_4, saturated $NaHCO_3$, and then brine. The organic phase was dried (Na_2SO_4), concentrated, and chromatographed (silica gel, 2:1 hexane–EtOAc) to yield an oil (234 mg, 88%). The ^1H NMR indicated that it was a 8:1 mixture of (*R*)-3-azido-1,2-propanediol 1-*O*-*p*-nitrobenzoate and (*R*)-3-azido-1,2-propanediol 2-*O*-*p*-nitrobenzoate. Data for the mixture: ^1H NMR ($CDCl_3$) δ 8.21–8.33 (m, 4 H), 5.32 (quint, J = 5.0 Hz, 0.11 H), 4.48 (d, J = 1.1 Hz, 0.88 H), 4.46 (d, J = 1.7 Hz, 0.88 H), 4.21 (sextet, J = 5.1 Hz, 0.88 H), 3.96 (t, J = 5.2 Hz, 0.22 H), 3.69 (d, J = 5.2 Hz, 0.22 H), 3.57 (dd, J = 3.8, 12.4 Hz, 0.88 H), 3.50 (dd, J = 5.6, 12.7 Hz, 0.88 H), 2.74 (d, J = 5.1 Hz, 0.88 H), 2.12 (t, J = 5.5 Hz, 0.11 H).

The above mixture of the products (84 mg, 0.32 mmol) was dissolved in CH_2Cl_2 (5 mL), and Et_3N (0.1 mL), 4-DMAP (catalytic amount), and *p*-nitrobenzoyl chloride (60 mg, 0.32 mmol) were added. The mixture was stirred at room temperature for 3 h. It was diluted with ether (50 mL) and washed with $NaHCO_3$ and brine. The organic phase was dried (Na_2SO_4), concentrated, and chromatographed (silica gel, hexane–EtOAc 4:1) to give (*R*)-3-azido-1,2-propanediol bis(*p*-nitrobenzoate) as a white solid (94 mg, 71%): mp 100–101.5 °C; $[\alpha]^{25}_D$ +21.1° (*c* 1.13, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.16–8.35 (m, 8 H), 5.63 (quint, J = 6.0 Hz, 1 H), 4.75 (dd, J = 4.7, 14.9 Hz, 1 H), 4.66 (dd, J = 5.6, 14.9 Hz, 1 H), 3.78 (dd, J = 4.1, 12.3 Hz, 1 H), 3.70 (dd, J = 5.2, 12.3 Hz, 1 H); IR (Nujol) 2930, 2860, 2100, 1725, 1605, 1520, 1460, 1380, 1350, 1325, 1265, 1120, 1105 cm^{-1}. Anal. Calcd for $C_{17}H_{13}N_5O_8$ (1,2-bis(*p*-nitrobenzoate)): C, 49.16; H, 3.15; N, 16.86. Found: C, 49.04; H, 3.31; N, 16.57.

Reaction of Glycidyl *p*-Nitrobenzoate with NaI under Cornforth Conditions.[9] A mixture of NaI (1.25 g, 8.3 mmol), NaOAc (126 mg, 1.5 mmol) in acetic acid (2.5 mL), and propionic acid (5 mL) was cooled to −30 °C and (2*R*)-glycidyl *p*-nitrobenzoate (1.15 g, 5 mmol, 92% ee) was added as a solid. The mixture was stirred at −30 to −20 °C for 2 h before being warmed to room temperature. Dilution with ether (100 mL) was followed by washings with saturated $NaHCO_3$, 5% $NaHSO_3$, and brine. The organic phase was dried (Na_2SO_4) and concentrated to give a yellow solid (1.562 g, 89%), which was the pure 3-iodo-1,2-propanediol 1-*O*-*p*-nitrobenzoate. Recrystallization from benzene–hexane afforded 1.326 g (76%) of (*S*)-3-iodo-1,2-propanediol 1-*O*-*p*-nitrobenzoate: mp 82.5–83.5 °C; $[\alpha]^{21}_D$ −4.40° (*c* 2.32, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.32 (d, J = 7.9 Hz, 2 H), 8.24 (d, J = 8.2 Hz, 2 H), 4.52 (d, J = 8.6 Hz, 2 H), 4.04 (sep, J = 5.3 Hz, 1 H), 3.44 (dd, J = 4.9, 10.5 Hz, 1 H), 3.36 (dd, J = 5.6, 10.5 Hz, 1 H), 2.52 (d, J = 5.1 Hz, 1 H); IR (Nujol) 3290, 3200, 2930, 2860, 1715, 1600, 1520, 1460, 1415, 1380, 1350, 1300, 1275, 1250, 1200, 1130, 1100, 1015, 980, 920, 875, 860, 790, 725 cm^{-1}. Anal. Calcd for $C_{10}H_{16}INO_5$: C, 34.20; H, 2.87; N, 3.99. Found: C, 34.40; H, 2.98; N, 3.92.

The iodohydrin (35 mg, 0.1 mmol) was treated with PhSH (11 mg, 0.1 mmol) in *t*-BuOH (2 mL) and 1 N NaOH (0.5 mL). After stirring at room temperature overnight, ether extraction yielded (*S*)-3-(phenylthio)-1,2-propanediol (11 mg, 60%). HPLC analysis (using a Pirkle column, Type 1-A, preparative) of the bis-Mosher ester [(+)-MTPA-Cl, 4-DMAP, Et_3N, CH_2Cl_2] indicated only one diastereomer (i.e., >99% ee).

Reaction of Glycidyl *p*-Nitrobenzoate with Acetone Cyanohydrin. (2*R*)-Glycidyl *p*-nitrobenzoate (223 mg, 1 mmol) was dissolved in acetone cyanohydrin (3 mL) and KCN (13 mg, 0.2 mmol) was added. The mixture was stirred at room temperature overnight. Dilution with ether (100 mL) was followed by washings with 10% H_2SO_4, saturated $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4), concentrated, and chromatographed (2:1 hexane–EtOAc) to give (*R*)-3-cyano-1,2-propanediol 1-*O*-*p*-nitrobenzoate as a yellow oil (212 mg, 85%): ^1H NMR ($CDCl_3$) δ 8.23–8.29 (m, 7 H), 4.55 (dd, J = 4.3, 10.3 Hz, 1 H), 4.37–4.50 (m, 2 H), 3.12 (br, 1 H), 2.80 (dd, J = 4.7, 15.0 Hz, 1 H), 2.72 (dd, J = 7.0, 18.0 Hz, 1 H); IR (neat) 3440, 3105, 3080, 2950, 2870, 2250, 1720, 1605, 1525, 1410, 1350, 1320, 1270, 1180, 1125, 1105, 1015, 875, 855, 785, 770, 750, 720, 710, 700 cm^{-1}.

The above product (113 mg, 0.45 mmol) was dissolved in CH_2Cl_2 (5 mL), and Et_3N (0.1 mL) and *p*-nitrobenzoyl chloride (84 mg, 0.45 mmol) were added. The mixture was stirred at room temperature for 1 h. It was diluted with ether (50 mL) and washed with saturated $NaHCO_3$ and brine. The organic phase was dried (Na_2SO_4), concentrated, and chromatographed (silica gel, hexane–EtOAc 2:1) to yield (*R*)-3-cyano-1,2-propanediol bis(*p*-

(13) Ko, S. Y.; Sharpless, K. B. *J. Org. Chem.*, in press.

nitrobenzoate) as a yellow solid (88 mg, 49%): mp 148–150 °C; $[\alpha]^{25}_D$ −13.6° (c 0.22, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 8.20–8.34 (m, 8 H), 5.67 (quint, J = 5.4 Hz, 1 H), 4.82 (dd, J = 4.4, 12.7 Hz, 1 H), 4.70 (dd, J = 5.6, 12.7 Hz, 1 H), 3.10 (dd, J = 6.0, 16.8 Hz, 1 H), 2.97 (dd, J = 4.8, 16.8 Hz, 1 H): IR (Nujol) 2930, 2860, 1740, 1730, 1610, 1540, 1460, 1415, 1380, 1355, 1280, 1260, 1105, 1095, 1015, 880, 850, 725, 720 cm^{-1}. Anal. Calcd for $C_{18}H_{13}N_3O_8$ (1,2-bis(p-nitrobenzoate)): C, 54.14; H, 3.28; N, 10.52. Found: C, 53.99; H, 3.41; N, 10.40.

Reaction of Glycidyl p-Nitrobenzoate with Et_2AlCN.[10] To a solution of glycidyl p-nitrobenzoate (34 mg, 0.15 mmol, racemic mixture) in toluene (5 mL) was added Et_2AlCN (1.5 M solution in toluene, Alfa, 0.1 mL, 0.15 mmol) at room temperature. After 5 min, the homogeneous yellow solution was diluted with ether (30 mL) and then washed with 10% H_2SO_4, saturated $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4) and concentrated to yield pure 3-cyano-1,2-propanediol 1-O-p-nitrobenzoate (27 mg, 71%). The product was characterized as described above.

Reaction of Glycidyl p-Nitrobenzoate with PhSH in Et_3N. A solution of glycidyl p-nitrobenzoate (56 mg, 0.25 mmol, racemic mixture) and PhSH (56 mg, 0.5 mmol) in Et_3N (3 mL) was stirred at room temperature overnight. It was concentrated and the residue was chromatographed (2:1 hexane–EtOAc) to yield 84 mg (100%) of a 4:1 mixture of 3-(phenylthio)-1,2-propanediol 1-O-p-nitrobenzoate and 3-(phenylthio)-1,2-propanediol 2-O-p-nitrobenzoate as a solid. The product was characterized as described below.

Reaction of Glycidyl p-Nitrobenzoate with PhSH in Pyridine. A solution of glycidyl p-nitrobenzoate (45 mg, 0.2 mmol, racemic mixture) and PhSH (0.04 mL, 44 mg, 0.4 mmol) in pyridine (1 mL) was stirred at room temperature overnight. It was concentrated (0.5 mm at room temperature) and the residue was chromatographed (2:1 hexane–EtOAc) to yield 65 mg (97%) of a yellow solid which was characterized by ^1H NMR as a 14:1 mixture of 3-(phenylthio)-1,2-propanediol 1-O-p-nitrobenzoate and 3-(phenylthio)-1,2-propanediol 2-O-p-nitrobenzoate. Data for the mixture: mp 97.5–100 °C; ^1H NMR ($CDCl_3$) δ 8.19–8.39 (m, 4 H), 7.23–7.47 (m, 5 H), 5.32 (m, 0.07 H), 4.53 (dd, J = 2.6, 9.9 Hz, 0.93 H), 4.43 (dd, J = 5.6, 9.0 Hz, 0.93 H), 4.10 (m, 0.93 H), 4.0 (m, 0.14 H), 3.39 (dd, J = 6.8, 14.3 Hz, 0.07 H), 3.33 (dd, J = 6.4, 14.3 Hz, 0.07 H), 3.24 (dd, J = 4.9, 13.5 Hz, 0.93 H), 3.01 (dd, J = 6.9, 13.5 Hz, 0.93 H), 2.78 (d, J = 3.7 Hz, 0.93 H), 1.93 (br, 0.07). Anal. Calcd for $C_{16}H_{15}NO_5S$: C, 57.65; H, 4.54; N, 4.20. Found: C, 57.59; H, 4.47; N, 4.05.

Reaction of Glycidyl p-Nitrobenzoate with Acetone in the Presence of Acid Catalyst. To a solution of (2R)-glycidyl p-nitrobenzoate (56 mg, 0.25 mmol, 92% ee) in acetone (5 mL) was added a drop of concentrated H_2SO_4, and the solution was stirred at room temperature overnight. The reaction mixture was diluted with ether (30 mL) and washed with saturated $NaHCO_3$ (15 mL). The aqueous layer was extracted with ether (2 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated. Flash chromatography (4:1 hexane–EtOAc) afforded 1,2-O-isopropylideneglycerol p-nitrobenzoate as an oil (54 mg, 76%): ^1H NMR ($CDCl_3$) δ 8.23–8.30 (m, 4 H), 4.47–4.55 (m, 2 H), 4.40 (dd, J = 6.7, 11.3 Hz, 1 H), 4.19 (dd, J = 6.2, 9.0 Hz, 1 H), 3.90 (dd, J = 4.9, 9.0 Hz, 1 H), 1.47 (s, 3 H), 1.41 (s, 3 H); IR (neat) 3110, 3080, 3055, 2990, 2940, 2890, 1720, 1605, 1525, 1450, 1410, 1380, 1370, 1350, 1320, 1275, 1220, 1160, 1120, 1100, 1080, 1055, 1015, 975, 875, 855, 845, 785, 720 cm^{-1}.

The ^1H NMR in the presence of a chiral shift reagent, Eu(hfc)$_3$, indicated that the enantiomeric purity of the product was 62% ee.

The product 1,2-O-isopropylideneglycerol p-nitrobenzoate (45 mg, 0.16 mmol, 62% ee, obtained from above) was treated with 60% aqueous acetic acid (5 mL) at room temperature overnight. Dilution with EtOAc (30 mL) was followed by washing with saturated $NaHCO_3$ (30 mL). The aqueous layer was extracted with EtOAc (2 × 15 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to yield (R)-glycerol mono-p-nitrobenzoate as a yellow solid (34 mg, 88%): mp 77–82 °C; $[\alpha]^{25}_D$ −7.80° (c 1.77, EtOH) [lit.[14] mp 88–89 °C; $[\alpha]^{25}_D$ −17.1° (EtOH)].

(14) Fischer, H. O. L.; Baer, E. *Chem. Rev.* **1941**, *29*, 287.
(15) The R,S assignments are based on the stereochemical consequences of the presumed reaction mechanisms.

(2R)-Glycidyl p-nitrobenzoate (45 mg, 0.2 mmol) was similarly treated with acetone in the presence of concentrated H_2SO_4 catalyst at −20 °C. After 14 days, it was worked up as previously described to afford the (2R)-solketal p-nitrobenzoate (37 mg, 67%). The ^1H NMR in the presence of Eu(hfc)$_3$ indicated that the product was of 77% ee.

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Supplementary Material Available: The experimental procedures and spectroscopic data not described in the Experimental Section (7 pages). Ordering information is given on any current masthead page.

(16) Karpyshev, N. N.; Bushnev, A. S.; Polystyanov, A. E.; Zvonkova, E. N.; Evstigneeva, R. P. *Bioorg. Khim.* **1979**, *5*, 238; *Chem. Abstr.* **1979**, *90*, 167984u.
(17) (a) Kawakami, Y.; Asai, T.; Umeyama, K.; Yamashita, Y. *J. Org. Chem.* **1982**, *47*, 3581. (b) Olah, G. A.; Fung, A. P.; Meidar, D. *Synthesis* **1981**, 280.

Further Studies on Sodium Borohydride–Polyethylene Glycol 400 as a Novel Reducing System

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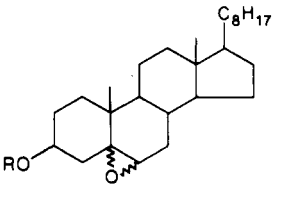
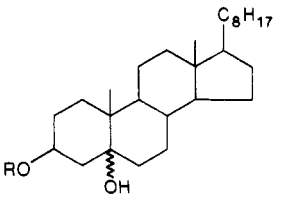
We have previously described the reaction of sodium borohydride with excess PEG (polyethylene glycol) 400 at 80 °C, the ratio 2:1 representing the stoichiometry of the reaction, suggesting that the active species could have the simplified formula $Na[(OCH_2CH_2)_nOH]_2BH_2$ (n = 8,9), $Na(PEG)_2BH_2$, not excluding other reactive species.[1,2] Several substrates were efficiently reduced by using $NaBH_4$ in PEG 400 or 0.5–0.6 M solutions of $Na(PEG)_2BH_2$ in THF.[2] We present now our most recent results of additional studies on $Na(PEG)_2BH_2$ reactivity.

Reduction of Epoxides. Preliminary experiments in THF at 80 °C (ratio of $Na(PEG)_2BH_2$ to epoxide, 3:1) on the epimeric mixture of 5,6-epoxides **1a** prepared from cholesterol acetate were hampered by hydrolysis of the acetate moiety, and yields of the corresponding diol **2a** were 45%. Under the same conditions, reduction of 3β-methoxy-5,6-epoxide **1b** was cleaner and yields of **2b** were 50% along with 50% of unreacted starting material. For



1a, R = $COCH_3$
b, R = CH_3



2a, R = H
b, R = CH_3

further studies, simple epoxides were examined, and we noticed that the best reproducible yields were obtained

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(2) Santaniello, E.; Fiecchi, A.; Manzocchi, A.; Ferraboschi, P. *J. Org. Chem.* **1983**, *48*, 3074.

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