removal of the solvent, silica gel column chromatography was performed by using hexane–ether. First, a mixture of 49 mg (10%) of **10** and 23 mg (6%) of **11** was eluted and then 416 mg (73%) of **8** was separated. The same reaction was carried out with 775 mg (2.12 mmol) of **2** under reduced pressure (30 mm), using equipment with a trap cooled to −78 °C by dry ice–acetone. After being heated at 150 °C for 3 h, the residue in the flask was chromatographed on silica gel with hexane–ether to afford 404 mg (74%) of **8**, 52 mg (16%) of **10**, and 8 mg (3%) of **11**. From the cooled trap, 220 mg (16%) of DTMSP and 149 mg (65%) of trimethylsilyl chloride were obtained.

Reaction of DTMSP with 10 in the Presence of Benzaldehyde. A mixture of 1.106 g (3.03 mmol) of **2** and 342 mg (3.23 mmol) of benzaldehyde was heated at 150 °C for 2 h. Column chromatography of the residue on silica gel with hexane–ether gave 333 mg (45%) of **8**, 159 mg (34%) of **10**, and 73 mg (20%) of **11**.

Reaction of DTMSP with 10 in the Presence of Benzaldehyde. To a mixture of 495 mg (3.20 mmol) of **10** and 345 mg (3.25 mmol) of benzaldehyde preheated to 150 °C in an oil bath was added dropwise 710 mg (3.38 mmol) of DTMSP. After the mixture was heated for 2 h, the usual workup gave 323 mg (39%) of **8**, 231 mg (46%) of **10**, and 23 mg (6%) of **11**.

Treatment of 3 with 10. A mixture of 1.04 g (3.3 mmol) of **3** and 536 mg (3.47 mmol) of **10** was heated at 150 °C for 2 h. Almost no reaction took place and 756 mg (72%) of **3** and 509 mg (95%) of **10** were recovered by silica gel column chromatography.

Treatment of 1 with TBAF. To a solution of 3.14 g (7.46 mmol) of **1** in 2 mL of dry CH_2Cl_2 was added 2.16 g (8.26 mmol) of TBAF in 6 mL of dry CH_2Cl_2. The solution was stirred at room temperature for 5 min, and 30 mL of water was then added. Extraction was performed with CH_2Cl_2 (3 × 20 mL). The extracts were combined, dried over Na_2SO_4, and concentrated in vacuo, and the residual oil was chromatographed on silica gel with hexane–ether to afford 105 mg (7%) of benzil, 305 mg (19%) of benzoin, and 1.69 g (65%) of **7**:[20] ^1H NMR ($CDCl_3$) δ 1.13 (3 H, t, J_{H-H} = 7.0 Hz, CH_3), 1.30 (3 H, t, J_{H-H} = 7.0 Hz, CH_3), 3.65–4.42 (4 H, m, CH_2), 6.65 (1 H, d, J_{P-H} = 8.0 Hz, CH), 7.44 (8 H, m, aromatic), 7.90 (2 H, m, aromatic); ^{31}P NMR (Et_2O) δ +2.0.

Treatment of 2.72 g (6.46 mmol) of **1** with 371 mg (1.42 mmol) of TBAF in 10 mL of dry CH_2Cl_2 at room temperature for 17 h gave 677 mg (30%) of **7**, and 1.52 g (56%) of **1** was recovered.

Treatment of 2 with TBAF. To a solution of 542 mg (1.49 mmol) of **2** in 1 mL of dry CH_2Cl_2 was added 400 mg (1.53 mmol) of TBAF in 1 mL of dry CH_2Cl_2 at room temperature. After 0.5 h, the mixture was poured into 20 mL of CH_2Cl_2 and 20 mL of water. The organic layer was separated and the aqueous solution further extracted with CH_2Cl_2 (3 × 20 mL). The organic extracts were combined, dried over Na_2SO_4, and concentrated in vacuo, and the residual oil was chromatographed on silica gel to afford 47 ng (20%) of **10**, 147 mg (27%) of **8**, and 161 mg (42%) of **14**: IR (NaCl) 972, 1025, 1100, 1164, 1225, 1256 (P=O), 1391, 1449, 1495, 2900, 2970, 3045 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (3 H, t, J_{H-H} = 7.0 Hz, CH_3), 2.81 (1 H, dd, J_{P-H} = 4.5 Hz, J_{H-H} = 6.0 Hz, one CH_2 of epoxy ring), 3.36 (1 H, dd, J_{P-H} = 4.5 Hz, J_{H-H} = 6.0 Hz, one CH_2 of epoxy ring), 4.05 (4 H, m, CH_2OP), 7.31 (5 H, m, aromatic); ^{31}P δ NMR ($CDCl_3$) −18.0. Anal. Calcd for $C_{12}H_{17}O_4P$: C, 56.25; H, 6.69. Found: C, 56.13; H, 6.66.

When the same reaction was prolonged for 5 h, 49 mg (9%) of **10**, 255 mg (27%) of **8**, and 549 mg (58%) of **14** were obtained from 1.36 g (3.72 mmol) of **2**.

Registry No. **1**, 71292-75-6; **2**, 78610-05-6; **3**, 31675-43-1; (*E*)-**5**, 78610-06-7; (*Z*)-**5**, 78610-07-8; **6**, 16830-69-6; **7**, 3491-28-9; **8**, 1021-45-0; **10**, 532-27-4; **11**, 98-86-2; **14**, 1021-15-4; benzil, 134-81-6; DTMSP, 13716-45-5.

(19) I. P. Gazman and V. A. Kukhtin, *Zh. Obshch. Khim.*, **37**, 881 (1969); *Chem. Abstr.*, **68**, 29361 (1968).
(20) A. N. Pudovik, V. I. Nikitina, and V. V. Evdokimova, *Zh. Obshch. Khim.*, **40**, 290 (1970); *Chem. Abstr.*, **72**, 132871 (1970).

Stereochemical Course of the "Mixed Hydride" (AlD_3 and $AlCl_2H$) Reduction of Optically Active Styrene-2,2-d_2 Oxide[1-3]

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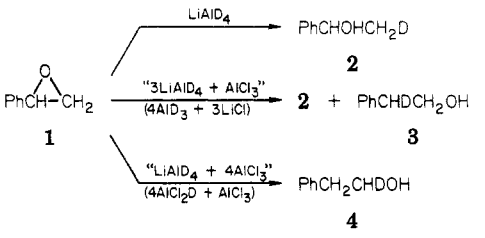
The reduction of (*R*)-(+)-styrene-2,2-d_2 oxide with aluminum deuteride (AlD_3) in diethyl ether at 0 °C gives a nearly equal mixture of (*S*)-(+)-1-phenylethanol-2,2,2-d_3 and (*S*)-(−)-2-phenylethanol-1,1,2-d_3, the latter being formed with almost complete inversion of configuration at the benzylic position (96 ± 2% ee). These results were obtained with AlD_3 generated either from mixtures of $LiAlD_4/AlCl_3$ (3:1) or $LiAlD_4$/100% H_2SO_4 (2:1) and were unaffected by the presence or absence of soluble LiCl. The 1,2 deuteride shift, which accompanies the reduction with $AlCl_2H$, was found to proceed with 62% inversion and 38% retention of configuration at the benzylic position (24% net asymmetric induction). No asymmetric induction at the carbinol position was detected.

Since the pioneering work of Eliel and co-workers,[4,5] the course of the "mixed hydride" (mixtures of $LiAlH_4$ and $AlCl_3$) reduction with ring opening of epoxides has been the subject of several investigations.[6-12] It has been shown that the mechanism of the "mixed hydride" reduction of

Scheme I



(1) Presented at the 180th National Meeting of the American Chemical Society, Las Vegas, Aug 27, 1980, Abstract No. ORGN 192.
(2) Taken in part from the Ph.D. Thesis of J.E.T., University of New Hampshire, Mar 1970.
(3) Presented at the 164th National Meeting of the American Chemical Society, Boston, 1972, Abstract No. ORGN 49. Also see *Chem. Eng. News*, **50**, (Apr 25), 25 (1972).
(4) E. L. Eliel and D. W. Delmonte, *J. Am. Chem. Soc.*, **78**, 3326 (1956); **80**, 1744 (1958).
(5) E. L. Eliel and M. N. Rerick, *J. Am. Chem. Soc.*, **82**, 1362 (1960); **84**, 2356 (1962).

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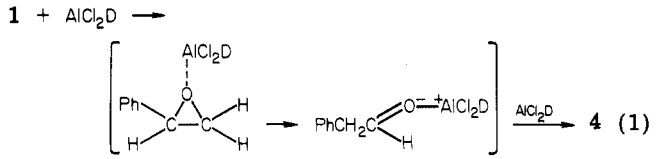
epoxides is more complicated than the corresponding reduction with $LiAlH_4$. Through the use of isotopically labeled reagents, Eliel and co-workers were able to show that different proportions of $LiAlD_4$ and $AlCl_3$ gave rise to different modes of attack on the epoxide. The producst derived from the reduction of styrene oxide by using reagents with these different proportions are summarized in Scheme I. Studies by Ashby and Prather[6] established the composition of the "mixed hydride" reagents to be those indicated in parentheses under the arrows in Scheme I.

While $LiAlD_4$ gives deuteride attack on styrene oxide almost exclusively at the least hindered carbon atom to produce **2**, AlD_3 gives attack on both the benzylic and primary carbon atoms, producing a mixture of **2** and **3**. Reduction with the more Lewis acidic reagent, $AlCl_2D$, proceeds with a 1,2 hydride shift, followed by reduction of the intermediate phenylacetaldehyde to give **4** (eq 1). Reduction of **1** with $AlClD_2$, a reagent with Lewis acidity intermediate between that of AlD_3 and $AlCl_2D$ gives rise to a mixture of **2**–**4**. Coordination may also be with $AlCl_3$.

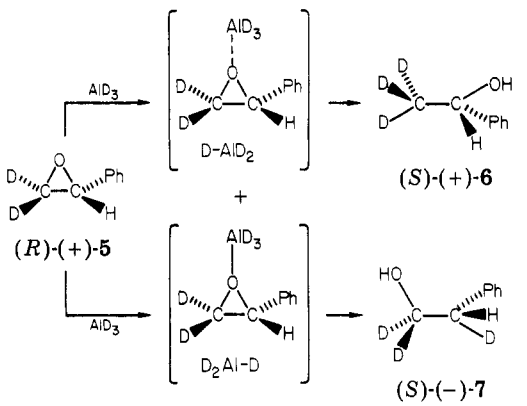


The regio- and stereoselectivity of epoxide ring opening with AlH_3 and $AlCl_2H$ have been determined on several bicyclic and trisubstituted epoxides.[7,11,13,14] Studies by Ashby and Cooke[10] further showed the effects of reagent composition, nature of the halogen, and solvating ligand on the regioselectivity of epoxide reduction. Just recently Sankawa and Sato[12] attempted to determine the stereochemical course of the reduction with these reagents on chiral styrene oxide, a system devoid of major steric and ring-strain considerations. This system was investigated earlier by us[2] but not published, due in part to the nontrivial problem of establishing with certainty the enantiomeric purity and absolute configuration of the product alcohols. Most recently the configurations and enantiomeric purities of these products have been painstakingly determined by Sankawa and Sato through the use of stereospecific enzymatic processes. Since we had discovered a simple method for the direct determination of the enantiomeric purity and absolute configuration of the chiral product 2-phenylethanol-2-*d* (**3**),[15,16] we reinvestigated the course of the reduction of optically active styrene-2,2-d_2 oxide (**5**) with mixed hydride reagents of known composition.[1]

Results and Discussion

(*R*)-(+)-Styrene-2,2-d_2 oxide (**5**) was prepared according to the method of Tömösközi[17] from (*R*)-(−)-mandelic acid. The epoxide was found to be 98% enantiomerically pure by NMR spectroscopy with the use of the chiral shift reagent $Eu(hfbc)_3$.[18] The method of preparation of AlD_3 and $AlCl_2H$ used in these studies was crucial to the reproducibility of the results. If the $LiAlH_4$ and $AlCl_3$ are not mixed in the proper ratio to produce the desired reducing reagent (AlH_3, $AlClH_2$, $AlCl_2H$), then the desired reagent will be contaminated with an unknown amount of $LiAlH_4$, AlH_3, or chloroalanes of undetermined stoichiometry. Since these reagents are known to reduce epoxides by different mechanisms, their presence as impurities will make moot any meaningful stereochemical conclusion on the course of the reduction.

Scheme II

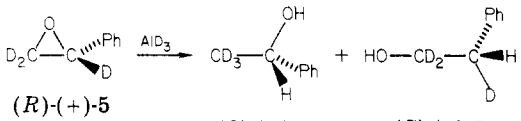


We have found that using standardized solutions of $LiAlD_4$ or $LiAlH_4$ in ether with freshly sublimed $AlCl_3$ produced the best results. Paramount then to the success of generating the desired reagent (AlD_3 or $AlCl_2H$) was the precise determination of the $LiAlH_4$ concentration in ether. A convenient method was found for the determination of *reducing* hydride concentration by reducing an excess of acetophenone and determining (by GC) the amount of 1-phenylethanol produced (see Experimental Section).[19]

Treatment of (*R*)-(+)-styrene-2,2-d_2 oxide (**5**, 98% enantiomerically pure) with excess AlD_3 in ether at 0 °C, prepared from $LiAlD_4$ and $AlCl_3$ (3:1), afforded a nearly equal mixture of (*S*)-(+)-1-phenylethanol-2,2,2-d_3 (**6**) and (*R*)-(+)-2-phenylethanol-1,1,2-d_3 (**7**). Compound **6**, resulting from ring opening by hydride attack at the terminal position, was found to be 98% enantiomerically pure:[16] it is therefore formed by a stereospecific reaction as shown in Scheme II. Determination of the enantiomeric purity of **7** was accomplished[15,16] by NMR spectroscopy with the aid of Whitesides' chiral shift reagent, $Eu(dcm)_3$.[20] Product **7** was found to be 96 ± 2% enantiomerically pure. On the basis of our previous studies,[15,16] and now also on the work of Sankawa and Sato,[12] the absolute configuration of the (−) isomer of **7** is known to be *S*. The fact that (*R*)-styrene-2,2-d_2 oxide (**5**, 98% ee) gives (*S*)-2-phenylethanol-1,1,2-d_3 (**7**, 96% ± 2% ee) means that deuteride attack at the benzylic position occurs with 98% or higher inversion of configuration. This, coupled, with the observation that isotopically normal styrene oxide with AlD_3 gives 2-phenylethanol-2-*d* labeled entirely at the benzylic position, established that this product arises via typical S_N2 stereochemistry. This process may be assisted by

(6) E. C. Ashby and J. Prather, *J. Am. Chem. Soc.*, **88**, 729 (1966).
(7) P. T. Lansbury, D. J. Scharf, and V. A. Pattison, *J. Org. Chem.*, **32**, 1748 (1967).
(8) N. M. Yoon and H. C. Brown, *J. Am. Chem. Soc.*, **90**, 2927 (1968).
(9) E. C. Ashby and B. Cooke, *J. Am. Chem. Soc.*, **90**, 1625 (1968).
(10) B. Cooke, E. C. Ashby, and J. Lott, *J. Org. Chem.*, **33**, 1132 (1968).
(11) E. Laurent and P. Villa, *Bull. Soc. Chim. Fr.*, 249 (1969).
(12) V. Sankawa and T. Sato, *Tetrahedron Letts.*, 981 (1978).
(13) R. Guyon and P. Villa, *Bull. Soc. Chim. Fr.*, 1375 (1972).
(14) R. Guyon and P. Villa, *Bull. Soc. Chim. Fr.*, 2599 (1975).
(15) J. D. Morrison, J. E. Tomaszewski, H. S. Mosher, J. Dale, D. Miller, and R. L. Elsenbaumer, *J. Am. Chem. Soc.*, **99**, 3167 (1977).
(16) R. L. Elsenbaumer and H. S. Mosher, *J. Org. Chem.*, **44**, 600 (1979).
(17) I. Tömösközi, *Tetrahedron*, **19**, 1969 (1963).
(18) R. R. Fraser, M. A. Petit, and J. K. Saunders, *J. Chem. Soc., Chem. Commun.*, 1450 (1971).
(19) We thank Natalie McClure of our laboratories for developing this procedure. See Natalie McClure, Ph.D. Thesis, Stanford University, 1979, for a review of literature procedures on determination of $LiAlH_4$ solution concentrations.
(20) M. D. McCreary, D. W. Lewis, D. L. Wernick, and G. M. Whitesides, *J. Am. Chem. Soc.*, **96**, 1038 (1974).

Table I. Reduction of (*R*)-(+)-Styrene-2,2-d_2 Oxide (5) with AlD_3 in Et_2O at 0 °C



(*R*)-(+)-5 (*S*)-(+)-6 (*S*)-(−)-7

entry	reducing reagent (preparation method)	equiv of reagent	yield,[a] %	% (*S*)-6 (% ee)[b]	% (*S*)-7 (% ee)[b]
1	AlD_3, Et_2O ($3LiAlD_4 + AlCl_3$)	2.24	92	50.5 (97.7)	49.2 (95.4 ± 2)
2	AlD_3, Et_2O ($3LiAlD_4 + AlCl_3$ + dioxane)	2.24	90	49.3 (98)	50.7 (96 ± 2)
3	AlD_3, Et_2O ($LiAlD_2 + 0.5H_2SO_4$)	2.00	93	49.9 (98)	50.1 (96 ± 2)
4	"$3LiAlD_4 + AlCl_3$"[c]	*c*	*c*	13.2 (0)[c]	85.8 (32)[c]

[a] Determined by VPC using 1-octanol as an internal standard; the combined yield of 6 and 7. [b] Enantiomeric excess as determined by NMR using Whitesides chiral shift reagent, $Eu(dcm)_3$.[20] [c] Sankawa and Sato's results,[12] reagent composition uncertain, and solvent, temperature, and yield unreported.

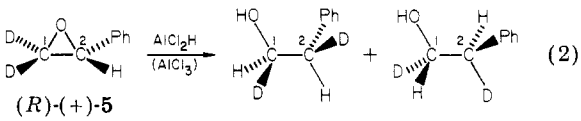
complexation of the AlD_3 or other aluminum species with the epoxide oxygen. Certainly less than 2% can arise via a four-centered retention process (S_Ni) as discussed by Ashby and Prather.[6] This clean inversion was not observed in previously studied more highly substituted epoxides,[4-10] except in the reduction of 1-phenylcyclopentene oxide[7] with excess AlD_3 where a similar result was reported.

It has been postulated[7,21] that the solubilized LiCl generated during the preparation of the reducing agent might play a role in epoxide ring openings. The reduction of **5** was repeated with AlD_3 prepared in different fashions where the amount of soluble LiCl was considerably less. AlD_3, prepared as above but with added dioxane to precipitate LiCl, reduced **5** with results very similar to those obtained when LiCl was present. Preparation of AlD_3 according to Brown[22] by treatment of an ethereal solution of standardized $LiAlD_4$ with 100% H_2SO_4 gave a heavy precipitate of Li_2SO_4. Treatment of **5** with the resulting solution gave results which were very nearly the same as those with AlD_3 made from $LiAlD_4$ and $AlCl_3$. These experiments are summarized in Table I. Clearly, there is no "special" effect on the stereochemical outcome of the reaction due to solubilized LiCl.[9]

Our results and conclusions differ substantially from those recently published by Sankawa and Sato[12] on the reduction of **5** by AlD_3: with properly prepared AlD_3 we find the reaciton with styrene oxide to be highly stereoselective. Two obvious explanations which can reconcile the difference in stereospecificity between their results and ours are the following. The most serious consideration is the purity of the AlD_3 used by Sankawa and Sato. As mentioned above, we found that precisely standardized solutions of $LiAlD_4$ are necessary to obtain consistent results. If an excess of $AlCl_3$ is used inadvertently, it will result in the generation of "mixed hydrides" of the type $AlClD_2$. Their reaction conditions are not published; however, Sankawa and Sato state that these reagents were probably present under the conditions of their study. Indeed, their product ratio of 1-phenyl- to 2-phenylethanol strongly suggests this to be the case (vide infra). A second consideration is the order of addition of the reagents. We have purposely added **5** to at least a twofold excess of AlD_3 to ensure that the reduction was by AlD_3. Adding AlD_3 to the epoxide would generate intermediate reducing species of the type $AlD_n(OR)_{3-n}$ that might possibly have different regio- and stereoselectivities from AlD_3 itself, which could lead to variable stereochemical outcomes.

In addition to the reduction with AlD_3, we determined the stereochemical course of the reduction of **5** with the more Lewis acidic reagent $AlCl_2H/AlCl_3$ ($LiAlH_4/4AlCl_3$). Since the reduction of styrene oxide with this reagent proceeds via a 1,2 hydride shift, reduction of **5** with the isotopically normal $AlCl_2H$ allows the extent and stereospecificity of this shift to be determined. Addition of **5** to a solution of $LiAlH_4/AlCl_3$ ($AlCl_2H/AlCl_3$) in ether at 0 °C afforded 2-phenylethanol-*1,2-*d_2 (**10**) as the major product. Integration of its NMR spectrum showed the ratio of hydrogen (and thus deuterium) at the 1- and 2-positions to be 1.0:1.0. Thus, this reaction proceeded entirely with a 1,2 deuteride shift. It was thought that this reaction might be a stereospecific one; and there is ample precedent for such a process.[23] However, examination of the NMR spectrum of the product in the presence of 1 equiv of $Eu(dcm)_3$ showed it to consist of a 62% to 38% mixture of (2*S*)- to (2*R*)-2-phenylethanol-*1,2-*d_2. In other words, the 1,2 deuteride shift proceeded with 62% inversion and 38% retention of configuration at the benzylic position, giving a net 24% enantiomeric excess. This result again differs from that of Sankawa and Sato,[12] who found no stereochemical selection. This may be the result of some solvent or temperature difference or a greater excess of $AlCl_3$ in their experiments.

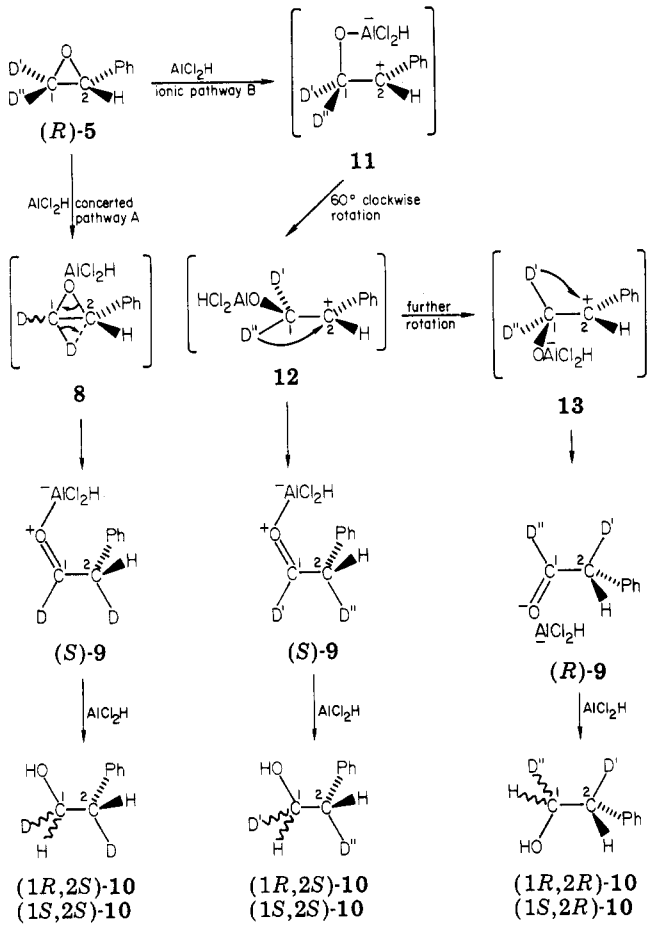
As a consequence of the use of **5** with the 1,1-dideuterio substitutents in this reaction, the product **10** has an additional chiral center at the carbinol carbon; i.e., a mixture of four diastereomers was formed. The extent of asymmetric induction at the carbinol center was determined by the method of Gerlach.[24,25] Conversion of **10** into its camphanate ester and examination by NMR spectroscopy in the presence of $Eu(dpm)_3$ showed the sample to be an equal mixture of *R* and *S* isomers at this position as shown in eq 2.



(*R*)-(+)-5 62% (2*R*)-10 50% (1*R*)-10 38% (2*R*)-10 50% (1*S*)-10 (2)

(21) L. I. Zakharkin and I. M. Khorline, *Izv. Akad. Nauk. SSR, Ser. Khim*, 5, 852 (1965).
(22) H. C. Brown and N. M. Yoon, *J. Am. Chem. Soc.*, 88, 1464 (1966).
(23) For example see J. M. Domagala, R. D. Back, and J. Wemple, *J. Am. Chem. Soc.*, 98, 1975 (1976).
(24) H. Gerlach and B. Zagalak, *J. Chem. Soc., Chem. Commun.*, 274 (1974).
(25) E. Caspi and C. R. Eck, *J. Org. Chem.*, 42, 767 (1977).

Scheme III



Two possible mechanisms for this ring cleavage and reduction of styrene oxide wiith the stronger Lewis acid reagent $AlCl_2H$ are outlined in Scheme III. If the deuteride shift were entirely concerted and via pathway A, then the intermediate aldehyde derivative, **9**, would be enantiomerically pure at the benzylic carbon with inverted configuration. Subsequent reduction of **9** by $AlCl_2H$ would be expected to give products (1*R*,2*S*)-**10** and (1*S*,2*S*)-**10**, with inverted chirality at C-2 and unequal amounts of *R* and *S* stereochemistry at C-1 since one would expect some slight selectivity in the hydride attack on **9**. This scenario was not realized experimentally; 62% *S* (inversion) and 38% *R* (retention) at the benzylic position and a 50:50 *R* to *S* ratio at the carbinol center were actually observed. Therefore, the completely concerted route via pathway A is untenable on the basis of the observed stereochemistry at the benzylic center.

Alternatively, the stereochemical results can be rationalized by stepwise pathway B. Here, carbon–oxygen bond clevage gives the ion pair **11**. Deuteride migration is most probably preceded by some carbon–carbon bond rotation. In accordance with the observation of Blackett,[26] one would expect the direction of this rotation to be influenced by steric interactions. Thus the bulky alkoxy group would rotate preferentially away from the phenyl moiety, giving conformer **12**. Now D″ is favorably aligned for migration to give (*S*)-**9** with inversion of configuration (D″ in (*S*)-**9** assuming the position opposite to that of oxygen at C-2 in **5**). Further rotation around the C–C bond of **12** would give **13** in which D′ is suitably aligned for migration to give (*R*)-**9** with retention of configuration (D′ in (*R*)-**9** assuming a position on the same side as that of oxygen at C-2 in **5**). Although unfavorable, D′ migration might also occur by rotation of the alkoxy group toward the phenyl moiety, thus leading to (*S*)-**9** with inversion of configuration. Since (1*SR*,2*S*)-**10** was formed in excess over (1*SR*,2*R*)-**10** (62:38 ratio), rotational equilibration between **12** and **13** could not be reached before deuteride migration if one assumes that the mechanism proceeds through the stepwise process.

In summary, the reduction of chiral styrene oxide (*R*)-(+)-**5** with AlD_3 in ether gave an unequal mixture of (*S*)-(+)-**6** and (*S*)-**7**, the latter being formed with inversion of configuration in what seems to be a classical S_N2 attack by AlD_3 at the benzylic site. On the other hand, reduction with the more Lewis acidic $AlCl_2H/AlCl_3$ ($4AlCl_3/LiAlH_4$) results in the formation of **10** by a 1,2 hydride shift of low stereospecificity. A stepwise path with the formation of ion pairs probably occurs here; the extent of C–C bond rotation prior to migration probably controls the stereoselectivity.

We believe that the varying results in previous work on epoxide ring openings with the "mixed hydride" reducing agents undoubtedly arose from the failure to obtain the desired reducing reagent uncontaminated with other chloroalumino hydride species.

Experimental Section

NMR spectra were recorded on a Varian Associates XL-100 NMR spectrometer[27] as solutions in $CDCl_3$ with Me_4Si as an internal standard. $Eu(dpm)_3$ and $Eu(hfbc)_3$ were obtained commercially.[28] $Eu(dcm)_3$ was prepared according to the method of Whitesides.[20] (−)-Camphanic acid chloride was obtained as a gift from H. Gerlach.[24] (*R*)-(+)-Styrene-2,2-d_2 oxide was prepared according to the method of Tömösközi;[17] α^{20}_D +31.99° (neat). It was found to be 98% enantiomerically pure by NMR spectroscopy with $Eu(hfbc)_3$.[18] $AlCl_3$ was sublimed and stored under nitrogen. Diethyl ether was distilled from $LiAlH_4$ just prior to use. All reductions were performed under an inert atmosphere. Analyses by VPC were performed on a Hewlett-Packard 5750 gas chromatograph with flame-ionization detection, 6 × 2 mm glass columns, and Carbowax 20 M at 175 °C. Peak areas were determined by electronic integration and suitably corrected for response relative to added 1-octanol. Preparative VPC was performed on a Varian Aerograph A-90P using a 10 × $^1/_2$ in. SS column of Carbowax 20 M.

Preparation and Standardization[19] of a $LiAlD_4$ Solution in Ether. Into a dry 100-mL Airlessware flask fitted with a filtering side arm and reflux condenser were placed 2.5 g of $LiAlD_4$, 0.20 g of LiD,[29] and 45 mL of anhydrous ether, all under N_2. After being stirred at 30 °C for 44 h, the suspension was filtered and the gray solids were washed with ether (2 × 20 mL). Enough ether was added to the filtrate to make the total volume 100 mL. The solution was stored in a sealed container under N_2 until used. The above solution was titrated as follows. Into a dry 8-dram vial fitted with a septum cap and stirring bar were placed 0.242 g of hexamethylbenzene (internal standard), 1.208 g of acetophenone, and 3 mL of ether under N_2. To this at 0 °C was added 1.0 mL of the above $LiAlD_4$ solution. The mixture was warmed to 30 °C for 2 h and then hydrolyzed by the addition of 1.0 mL of H_2O, 4 mL of saturated NH_4Cl, and 0.5 mL of concentrated HCl. The ether layer was then analyzed by VPC (Carbowax 20 M, 155 °C) for 1-phenylethanol and acetophenone content (corrected for response vs. hexamethylbenzene in a control experiment without added $LiAlD_4$). The molarity of $LiAlD_4$ was found to be 0.41 M based on unreacted acetophenone and 0.411 M based on the

(26) B. N. Blackett, J. M. Coxon, M. P. Hartshorn, and K. E. Richards, *Aust. J. Chem.*, **23**, 2077 (1970); *J. Am. Chem. Soc.*, **92**, 2574 (1970).

(27) We acknowledge with thanks National Science Foundation Grant GP 28142 for the NMR instrument used in these studies.

(28) Aldrich Chemical Co.

(29) Lithium deuteride is added as a precaution to convert any aluminum chloride which might be present into lithium aluminum deuteride. LiD by itself under these reaction conditions will not reduce epoxides or carbonyl compounds.

observed 1-phenylethanol produced.

Styrene Oxide Reduction. (1) With AlD_3 Generated from $LiAlD_4$ and $AlCl_3$ (3:1). Into a 25-mL, round-bottomed flask fitted with a septum cap and stir bar was placed sublimed $AlCl_3$ (131 mg, 0.98 mmol) under N_2. To this at 0 °C was added 2.0 mL of ether, and the mixture was stirred until homogeneous. Then, 7.17 mL of 0.41 M $LiAlD_4$ solution (2.94 mmol) was slowly added with stirring. After 30 min at 0 °C a solution of (*R*)-(+)-styrene oxide (1.75 mmol) in 1.0 mL ether was added slowly. After being stirred for 30 min at 0 °C, the reaction mixture was hydrolyzed by the addition of 0.5 mL of H_2O and 2.0 mL of 10% HCl. The ether layer was separated, the aqueous layer was extracted (2 × 10 mL ether), and the combined ether layers were dried ($MgSO_4$). A precisely weighed amount of 1-octanol (internal standard) was added, and the products were analyzed by VPC. A pure sample of **7** was obtained by preparative VPC and analyzed by NMR spectroscopy. When the NMR in the presence of 1 equiv of $Eu(dcm)_3$ was taken, the sample was found to be 97.7 ± 1.5% enantiomerically pure. A sample of (*R*)-**7** prepared by a different route[16] was added to this NMR sample; this gave rise to a new, further downfield, benzylic resonance. Thus, the absolute configuration of **7** obtained in the epoxide reduction is *S*. The results are summarized in Table I.

(2) With AlD_3 Generated from $LiAlD_4$ and $AlCl_3$ (3:1) with Added Dioxane. The procedure above was repeated. Before addition of the epoxide to the reagent, 480 μL of dry dioxane was added. A heavy white precipitate appeared. To the solution was then added a solution of **5** in ether. The products were treated and analyzed as above.

(3) With AlD_3 Generated from $LiAlD_4$ and 100% H_2SO_4. Into a dry, 25-mL, round-bottomed flask fitted with a septum stopper, magnetic stirring bar, and N_2 inlet was placed 8.54 mL of 0.41 M $LiAlD_4$ solution. To this at 0 °C was slowly added 93.2 μL of 100% H_2SO_4. This produced a dense white precipitate. After 40 min at 0 °C, a solution of **5** (1.75 mmol) in 2 mL of anhydrous ether was added. After 30 min at 0 °C no noticeable change occurred, and the reaction was worked up and analyzed as above. The results are summarized in Table I.

(4) With $AlCl_2H$ Generated from $LiAlH_4$ and $AlCl_3$ (1:4) in Ether. Into a 25-mL, round-bottomed flask equipped with a rubber septum, stirring bar, and N_2 inlet was placed 485 mg (3.64 mmol) of $AlCl_3$ and 2.0 mL of anhydrous ether at 0 °C. After all dissolved, 0.70 mL of a 1.29 M $LiAlH_4$ solution (titrated as above) was added slowly. A clear solution resulted even after stirring 40 min at 0 °C. To this was added a solution of **5** (1.75 mmol) in 2.0 mL of anhydrous ether. A white precipitate formed with the addition. After 30 min at 0 °C, 0.5 mL of water followed by 2.0 mL of 10% HCl were added. The layers were separated, the aqueous layer was extracted (ether 2 × 10 mL), and the ether layers were combined and dried over $MgSO_4$. Analysis showed 67% of **10** and 12% of a higher boiling component, and the rest was polymer from styrene oxide. Integration of an NMR spectrum of VPC-purified **10** showed the ratio of benzylic protons to carbinol protons to be 1.0:1.0. In the presence of $Eu(dcm)_3$ the sample was found to be 24 ± 2% ee *S* at the benzylic center.

A second purified sample of **10** (23 mg, 0.185 mmol) was converted into its camphanate ester with (−)-camphanic acid chloride (44 mg, 0.2 mmol) in dry pyridine (300 μL).[24] Examination of the NMR spectrum of the camphanate ester (50 mg) in the presence of $Eu(dpm)_3$ showed two sets of doublets centered at 6.15 and 5.85 ppm.[25] Integration of this region revealed the sample to be a 50:50 (±2%) mixture of diastereomers [(1*R*,2*S*)-**10** and (1*S*,2*S*)-**10**].

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Registry No. **5**, 78638-63-8; **6**, 78638-64-9; **7**, 63423-65-4; (1*R*,2*S*)-**10**, 78684-41-0; (1*S*,2*S*)-**10**, 78684-42-1; (1*R*,2*R*)-**10**, 78684-43-2; (1*S*,2*R*)-**10**, 78684-44-3; AlO_3, 10294-03-8; $AlCl_2H$, 13497-97-7.

Reactions of Oxaphospholenes. 1. Solvolysis and Ring Opening

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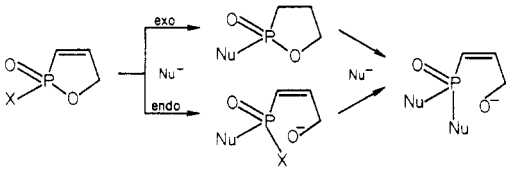
The hydrolysis of 2-methoxy-2-oxo-5,5-dimethyl-1,2-oxaphosphol-3-ene (**3**) in neutral or acidic media gives the corresponding 2-hydroxy derivative (**5**). The reaction is subject to acid catalysis and is also autocatalytic. Potassium hydroxide promoted hydrolysis occurs instantaneously at 25 °C to give the potassium salt of **5** (**13**), while the much slower reaction of **3** with sodium methoxide in methanol provides the sodium salt of **5**. All of these reactions involve alkyl–oxygen cleavage, not attack at phosphorus. When **13** is heated in the presence of excess hydroxide, attack at phosphorus does occur to give the product of endocyclic cleavage, dipotassium (3-hydroxy-3-methyl-1-(*Z*)-butenyl)phosphonate. Similarly, the reaction of 2-chloro-5,5-dimethyl-2-oxo-1,2-oxaphosphol-3-ene with methyllithium gives ring-opened (3-hydroxy-3-methyl-1-(*Z*)-butenyl)dimethylphosphine oxide.

Studies of the hydrolysis of phosphate esters and related compounds have been central in shaping our understanding of nucleophilic substitution at phosphorus.[1] The concept of pseudorotation was refined through this area of research, but the importance of understanding these reactions goes beyond their interest to the physical organic chemist. Indeed, crucially important biochemical processes such as phosphorylation involve just such reactions. For these reasons the area remains an active one today.[2]

Scheme I



Several years ago we discovered[3] a general synthetic entry into a novel family of phosphorus heterocycles,

(1) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70.
(2) See, for example: Gorenstein, D. G.; Rowell, R. *J. Am. Chem. Soc.* **1980**, *102*, 6165 and references therein.
(3) Macomber, R. S. *J. Org. Chem.* **1971**, *36*, 2713. For a leading reference to subsequent work, see: Macomber, R. S.; Krudy, G. A. *Ibid.* **1978**, *43*, 4656.

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