Selective Transformation of 2,3-Epoxy Alcohols and Related Derivatives. Strategies for Nucleophilic Attack at Carbon-1

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Received July 31, 1984

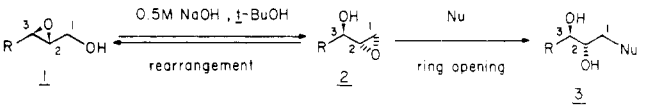
In connection with the continuing recent interest in the stereoselective synthesis of epoxy alcohols, a systematic investigation of the bimolecular nucleophilic ring-opening reactions of acyclic 2,3-epoxy alcohols was undertaken. Strategies for nucleophilic attack at C-1 of a 2,3-epoxy alcohol, each of which depends upon the regioselective ring-opening of a 1,2-epoxy 3-ol, were explored. Under Payne rearrangement conditions, *t*-BuSNa was found to react with 2,3-epoxy alcohols to afford 1-*tert*-butylthio 2,3-diols. These diols can be readily converted to 1,2-epoxy 3-ols via S-alkylation followed by treatment with base. Alternatively, 1,2-epoxy 3-ols can be prepared from 2,3-epoxy alcohols by sulfonylation and acidic hydrolysis followed by ring-closure of the diol sulfonate intermediate. Dialkylamines were also found to react selectively with 2,3-epoxy alcohols under Payne rearrangement conditions to afford 1-amino 2,3-diols.

"If carbonyl compounds have been said to be 'virtually the backbone of organic synthesis', the epoxides correspond to at least 'one of the main muscles'." This sentiment, recently expressed by Seebach,[1] effectively conveys to the reader the importance of epoxides in synthesis. Indeed, the literature confirms that much effort has been expended on the investigation of epoxide chemistry in the past.[1,2] More importantly, it indicates that syntheses of natural products via epoxide-containing intermediates are of great interest.

Epoxides are easily prepared from a variety of compounds. In addition, epoxides are easily opened under a wide range of conditions. One very favorable aspect of epoxide-opening reactions is that they are usually stereospecific, proceeding with inversion of configuration at the site of ring opening via an S_N2 mechanism. For this reason, methods for the highly enantioselective synthesis of epoxides would be quite valuable. Unfortunately, the known enantioselective epoxidations of isolated olefins usually provide only a modest level of asymmetric induction.

In contrast, general methods for the syntheses of enantiomerically pure (homochiral) 2,3-epoxy alcohols are known.[3-5] The regioselective ring-opening reactions of 2,3-epoxy alcohols provide convenient access to useful, highly functionalized homochiral molecules. However, this subject has not been systematically explored in the literature. In principle, there are three reactive sites for nucleophilic substitution in a 2,3-epoxy alcohol corresponding to the carbon backbone of the epoxy alcohol. In this paper, strategies for nucleophilic substitution at C-1 of a 2,3-epoxy alcohol are explored. In the following paper, strategies for nucleophilic substitution at C-3 or C-2 of a 2,3-epoxy alcohol are discussed.

Scheme I. Payne Rearrangement-Opening Reaction



Results and Discussion

Payne Rearrangement–Opening Reactions of 2,3-Epoxy Alcohols with *t*-BuSNa. A subtle latent reactivity at the C-1 position of 2,3-epoxy alcohol 1 can be revealed in one step by means of the Payne rearrangement.[6] The Payne rearrangement of a 2,3-epoxy alcohol is carried out in an aqueous sodium hydroxide solution, usually in the presence of a cosolvent, and involves the equilibration of the epoxy alcohol 1 with the isomeric 1,2-epoxy 3-ol 2 as shown in Scheme I. This epoxide migration reaction was well-known to sugar chemists.[2h,k] However, Payne was the first to publish detailed observations of the epoxide migration reaction in simple acyclic epoxides. He found that the relative proportions of the 2,3- and 1,2-epoxy alcohols at equlibrium are highly substrate dependent. Since the Payne rearrangement usually produces a mixture of epoxy alcohols, it is of limited preparative value per se. For this reason, it was regarded as more of a curiosity than a useful reaction. However, due to the renewed interest in the chemistry of epoxy alcohols, the Payne rearrangement has been reinvestigated.[7,8]

A major advance in the synthetic utility of the Payne rearrangement came with the realization that a nucleophile which is introduced into an equlibrating mixture of epoxy

(1) Seebach, D.; Weidmann, B.; Wilder, L. In "Modern Synthetic Methods 1983"; Scheffold, R., Ed.; Otto Salle Verlag: Frankfurt, 1983; p 323.

(2) The following are reviews concerned with the synthesis and selective transformations of epoxides: (a) Gorzynski-Smith, J. *Synthesis* **1984**, 629. (b) Behrens, C. H.; Sharpless, K. B. *Aldrichimica Acta* **1983**, *16*, 67. (c) Rao, A. S.; Paknikar, S. K.; Kirtane, J. G. *Tetrahedron* **1983**, *39*, 2323. (d) Arata, K.; Tanabe, K. *Catal. Rev.-Sci. Eng.* **1983**, *25*, 365. (e) Sharpless, K. B.; Behrens, C. H.; Katsuki, T.; Lee, A. W. M.; Martin, V. S.; Takatani, M.; Viti, S. M.; Walker, F. J.; Woodard, S. S. *Pure Appl. Chem.* **1983**, *55*, 589. (f) Sharpless, K. B.; Verhoeven, T. R.; *Aldrichimica Acta* **1979**, *12*, 63. (g) Berti, G. In "Topics in Stereochemistry"; Allinger, N. L., Eliel, E. L., Eds.; Interscience Publishers: New York, 1973; Vol. 7, p 93. (h) Buchanan, J. G.; Sable, H. Z. In "Selective Organic Transformations"; Thyagarajan, B. S., Ed.; Wiley: New York, 1972; Vol. 2, p 1. (i) Yandovskii, V. N.; Ershov, B. A. *Russ. Chem. Rev. (Engl. Transl.)* **1972**, *41*, 403. (j) Swern, D. In "Organic Peroxides"; Swern, D., Ed.; Wiley-Interscience: New York, 1971; Vol. 2, Chapter 5. (k) Williamms, N. R. In "Advances in Carbohydrate Chemistry and Biochemistry"; Tipson, R. S., Horton, D., Eds.; Academic Press: New York, 1970; Vol. 25, p 109. (l) Rosowsky, A. In "The Chemistry of Heterocyclic Compounds"; Weissberger, A., Ed.; Interscience: New York; Vol. 19, Part 1, Chapter 1. (m) Parker, R. E.; Isaacs, N. S. *Chem. Rev.* **1959**, *59*, 737. (n) Winstein, S.; Henderson, R. B. In "Heterocyclic Compounds"; Elderfield, R. C., Ed.; Wiley: New York, 1950, Vol. 1, Chapter 1.

(3) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (b) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237. (c) Lu, L. D.-L.; Johnson, R. A.; Finn, M. G.; Sharpless, K. B. *J. Org. Chem.* **1984**, *49*, 728.

(4) (a) Hungerbühler, E.; Seebach, D. *Helv. Chim. Acta* **1981**, *64*, 687. (b) Hungerbühler, E.; Seebach, D.; Wasmuth, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 958.

(5) Ladner, W. E.; Whitesides, G. M. *J. Am. Chem. Soc.* **1984**, *106*, 7250.

(6) Payne, G. B. *J. Org. Chem.* **1962**, *27*, 3819.

(7) Koizumi, N.; Ishiguro, M.; Yasuda, M.; Ikekawa, N. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1401.

(8) Rokach, J.; Lau, C.-K.; Zamboni, R.; Guindon, Y. *Tetrahedron Lett.* **1981**, *22*, 2763.

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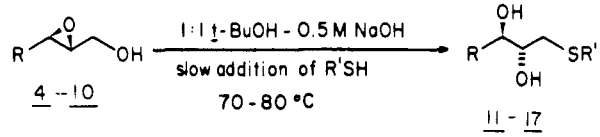
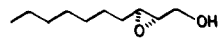
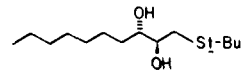
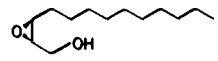
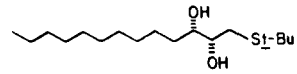
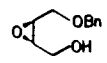
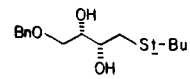
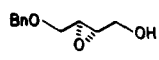
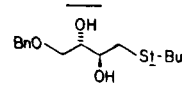
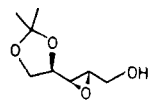
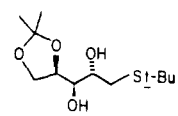
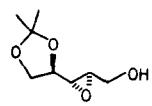
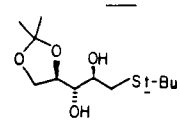
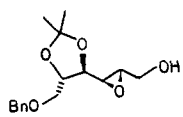
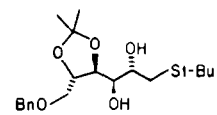
Table I. Payne Rearrangement-Opening Reaction of 2,3-Epoxy Alcohols with *t*-BuSNa



entry	2,3-epoxy alcohol	product	regioselectivity	yield,[d] %
1	 4	 11	(6.7:3.7:1)[a]	47
2	 5	 12	(2:1)[b,c]	65
3	 6	 13	(20:1)[b]	81
4	 7	 14	(20:1)[b]	85
5	 8	 15	(20:1)[b]	88
6	 9	 16	(20:1)[b]	84
7	 10	 17	(15:1)[b]	75

[a] Indicates the ratio of the C-1 to C-3 to C-2 regioisomers. [b] Indicates the ratio of the C-1 product to the combined C-3 and C-2 regioisomers. [c] The major contaminant was the C-3 regioisomer. [d] Indicates the isolated yield of C-1 product.

alcohols may react selectively with one of the epoxy alcohols (see Scheme I). The rate of reaction of **2** with any given nucleophile is expected to be much faster than that of **1** with the same nucleophile because the C-1 position of **2** is much less hindered than either the C-2 or C-3 position of **1**. Therefore, it appeared plausible that **2**, continuously regenerated in situ via the Payne rearrangement of **1**, could be selectively and irreversibly captured by a nucleophile to afford high yields of **3** in a process that is designated as a Payne rearrangement–opening reaction. This reaction was independently conceived and developed by Masamune and Sharpless at MIT[9] and the Ganem group at Cornell.[10]

The Payne rearrangement–opening reaction of a 2,3-epoxy alcohol to afford a 1-thio 2,3-diol is a fairly complex reaction in that the product distribution is affected by several factors including the reaction temperature, sodium hydroxide concentration, and the rate of addition of the thiol. The rate of addition of the thiol is probably the most important concern in these reactions. If the thiol is introduced rapidly the undesired products of the ring opening of **1** at C-3 and C-2 (i.e., 1,2- and 1,3-diols) may be present in the product mixture in greater amounts than when slow addition of the thiol is practiced.

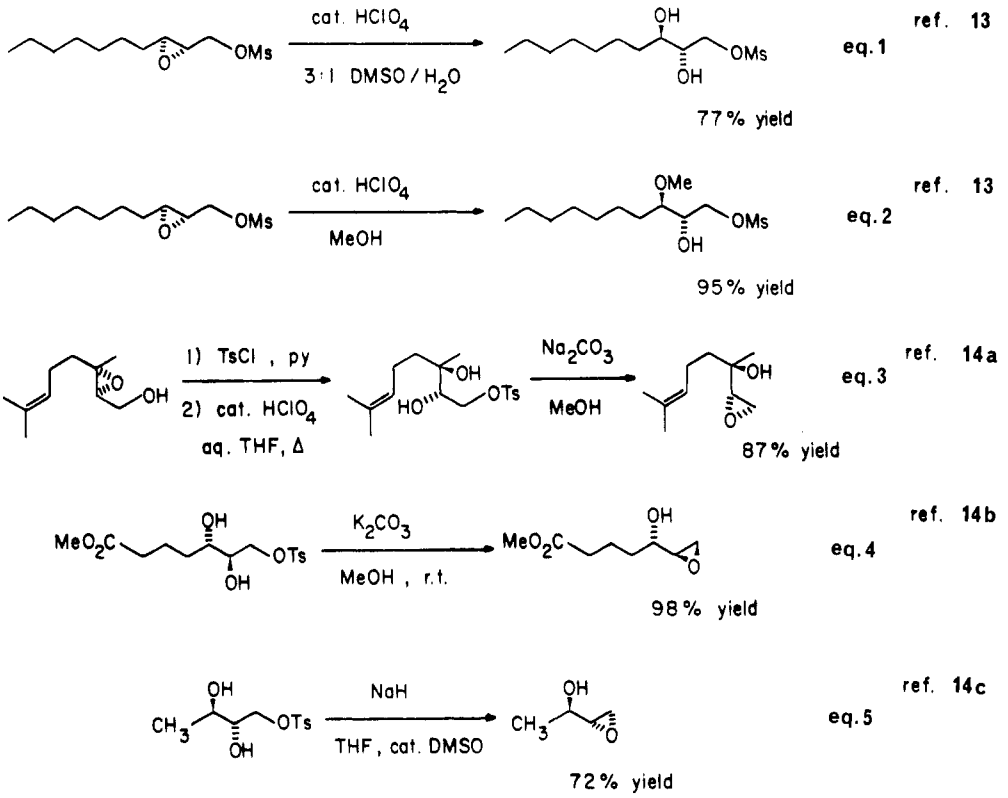
An experimental procedure that was successfully employed by Masamune and Sharpless required that a solution of the epoxy alcohol **1** in a 1:1 *t*-BuOH–0.5 M NaOH mixture be immersed in an oil bath (70–80 °C) and treated with a solution of PhSH in *t*-BuOH (slow addition) over a period of 1–2 h.[9a] Normally, 1.2 equiv of PhSH and 2.5 equiv of NaOH (based on **1**) were employed.

In the present work, this rearrangement–opening procedure was applied to a series of 2,3-epoxy alcohols, and the results are given in Table I. The reaction conditions employed are the same as those previously described with the exception that *t*-BuSH was used in place of PhSH as the nucleophile. It was thought that the greater reactivity of dialkyl sulfides compared to alkyl aryl sulfides with alkylating agents would be useful in the subsequent reactions of the thio diol (vide infra). In addition, it was felt that the greater steric bulk of the *tert*-butyl group relative to the phenyl group might improve (or at least should not diminish) the regioselectivity exhibited for ring opening at C-1.

(9) This new concept was conceived, discovered, and developed in full collaboration with Professor S. Masamune and his group as part of a joint program directed toward the synthesis of polyhydroxylated natural products. (a) Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373. (b) Masamune, S.; Choy, W. *Aldrichimica Acta* **1982**, *15*, 47. (c) Ko, S. Y.; Lee, A. W. M.; Masamune, S.; Reed, III, L. A.; Sharpless, K. B.; Walker, F. J. *Science (Washington, D.C.)* **1983**, *220*, 949.

(10) Wrobel, J. E.; Ganem, B. *J. Org. Chem.* **1983**, *48*, 3761.

Scheme II. Diol Sulfonate Method



From the results in Table I it is apparent that the regioselectivity in the Payne rearrangement–opening reaction depends on the structure of the epoxy alcohol. The regioselectivity is very good with epoxy alcohols **8**–**10** in which ring-opening at the C-3 position is sterically hindered by branching at C-4. Much poorer regioselectivity is found with epoxy alcohols such as **4** and **5** in which there is no branching at C-4. It is interesting to note that the regioselectivity found with **6** and **7** is very good even though there is no branching at C-4 in these cases. Evidently, the benzyloxy group in **6** and **7** serves to suppress the unwanted ring-opening at C-3.[11] Another factor that may affect the regioselectivity is the geometry (i.e., cis or trans) of the epoxy alcohol. It is known from the original work of Payne[6] and a study by Seebach[4a] that the thermodynamic equilibration of a cis-disubstituted 2,3-epoxy alcohol with a *threo*-1,2-epoxy 3-ol via the Payne rearrangement affords approximately a 1:1 mixture of each, whereas a similar equilibration of a trans-disubstituted 2,3-epoxy alcohol with an *erythro*-1,2-epoxy 3-ol leads to about a 9:1 mixture of the respective epoxy alcohols. However, a comparison of entries 1–4 reveals that this effect on the Payne rearrangement equilibrium does not greatly affect the regioselectivity of the Payne rearrangement–opening reaction.

A nucleophile must naturally be stable to the typical reaction conditions (i.e., 0.5 N NaOH at 80 °C) in order to participate effectively in the Payne rearrangement–opening reaction. These criteria are stringent enough to preclude the use of many potentially useful nucleophiles. Furthermore, some reagents that do survive the reaction conditions (e.g., $NaBH_4$) have been found effective only with certain favorable 2,3-epoxy alcohol substrates.[2e] One way to circumvent this problem has been described in the literature.

In this method (Scheme II) the C-1 hydroxyl group of **1** is converted into a good leaving group, usually a mesylate or a tosylate. Under basic conditions, the reaction of a nucleophile with a 2,3-epoxy 1-sulfonate ester normally results in selective displacement of the sulfonate group rather than epoxide opening.[2e,12] However, a 2,3-epoxy 1-sulfonate ester reacts in acidic aqueous media to give a 2,3-diol-1-sulfonate ester, as shown in eq 1–3.[13,14] A careful examination of the products revealed that in each case (eq 1–3) the hydrolysis of the 2,3-epoxy 1-sulfonate ester was regioselective for ring-opening at C-3 and was stereospecific with inversion of configuration at C-3.

The 2,3-diol-1-sulfonate ester can be converted to a 1,2-epoxy 3-ol by treatment with a suitable base such as K_2CO_3 or NaH as illustrated in eq 3–5.[14] With the isolated 1,2-epoxy 3-ol in hand, ring opening at C-1 with almost any nucleophile that is known to open epoxides should present little difficulty. This three-step route to a 1,2-epoxy alcohol from a 2,3-epoxy alcohol, the "diol sulfonate method", affords a convenient and useful alternative to the Payne rearrangement for unveiling the latent reactivity at the C-1 position of a 2,3-epoxy alcohol.

The Payne rearrangement–opening reaction with *t*-BuSNa also offers a solution to the problem of nucleophilic substitution at C-1 of a 2,3-epoxy alcohol with nonsulfur nucleophiles that is similar to the "diol sulfonate method". Since the Payne rearrangement is stereospecific with inversion at C-2, and the ring-opening with *t*-BuSNa is regioselective for C-1, the enantiomeric excess in the 2,3-epoxy alcohol will be completely retained in the product

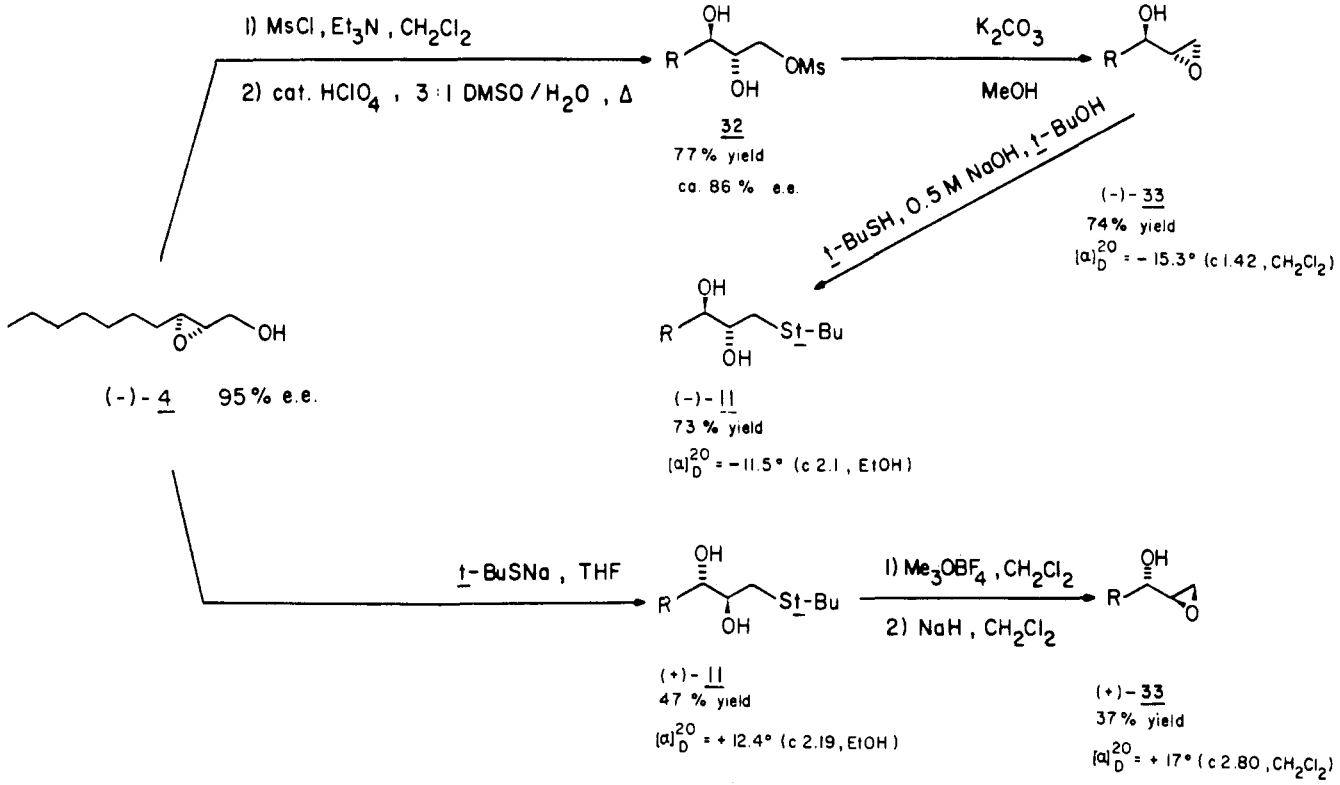
(11) Observations such as these are central to the issue of regioselective ring opening reactions of 2,3-epoxy alcohols at C-2 or C-3 and are dealt with in greater detail in the following paper in this issue.

(12) (a) Mori, K.; Ebata, T. *Tetrahedron Lett.* **1981**, *22*, 4281. (b) Kigoshi, H.; Ojika, M.; Shizuri, Y.; Niwa, H.; Yamada, K. *Tetrahedron Lett.* **1982**, *23*, 5413. (c) Chen, R.; Rowand, D. A. *J. Am. Chem. Soc.* **1980**, *102*, 6609.

(13) We thank Steven M. Viti for performing this experiment.

(14) (a) Morgans, D. J., Jr.; Sharpless, K. B.; Traynor, S. G. *J. Am. Chem. Soc.* **1981**, *103*, 462. (b) Corey, E. J.; Marfat, A.; Goto, G.; Brion, F. *J. Am. Chem. Soc.* **1980**, *102*, 7984. (c) White, J. D.; Kang, M.; Sheldon, B. G. *Tetrahedron Lett.* **1983**, *24*, 4539. (d) See also: Salomon, I.; Reichstein, T. *Helv. Chim. Acta* **1947**, *30*, 1929.

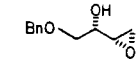
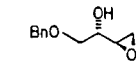
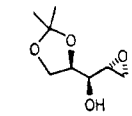
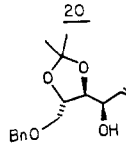
Scheme III. Comparison of the "Diol Sulfonate" and "Diol Sulfide" Methods



2,3-diol. The transformation of a 2,3-diol-1-sulfide to a 1,2-epoxy 3-ol may then be accomplished by the conversion of the C-1 sulfide to a good leaving group (e.g., via S-alkylation) followed by treatment with a suitable base to effect ring-closure.[15] Freshly prepared Me_3OBF_4 was found to be a very effective reagent for S-alkylation.[16] In a typical procedure, a solution of **13** in CH_2Cl_2 was treated with Me_3OBF_4 (added portion-wise as a solid) until complete consumption of **13** was observed by TLC. The reaction mixture (in CH_2Cl_2) was then treated with an excess of a 10% aqueous NaOH solution and stirred vigorously. After 1–2 h, a new product was visible by TLC of an R_f slightly greater than that of **13**. A standard extractive workup afforded the *threo*-1,2-epoxy 3-ol **18** in 88% yield (entry 1, Table II).

The S-alkylation of **14** with Me_3OBF_4 proceeds efficiently as above, but a similar treatment of the sulfonium salt (in CH_2Cl_2) with 10% aqueous NaOH unexpectedly did not provide pure **19** but rather a mixture of **19** and **7**. Evidently the *erythro*-1,2-epoxy 3-ol **19** is so easily rearranged to the *trans*-2,3-epoxy alcohol **7** that it is not stable to contact with aqueous base, even in a heterogeneous medium. Rokach and co-workers have made similar observations.[8] However, treatment of the sulfonium salt with NaH in CH_2Cl_2 afforded pure **19** (entry 2).[17]

Table II. Synthesis of 1,2-Epoxy 3-ols

entry	1-*tert*-butylthio 2,3-diol	reactn conditns	product	yield, %
1	**13**	*a*, *c*	 **18**	88
2	**14**	*a*, *d*	 **18**	89
3	**15**	*b*, *d*	 **19**	65
4	**17**	*b*, *d*	 **20** **21**	72

[a] Me_3OBF_4, CH_2Cl_2, room temperature. [b] Me_3OBF_4, 2,6-*tert*-butylpyridine, CH_2Cl_2, room temperature. [c] 10% aqueous NaOH, CH_2Cl_2, room temperature. [d] NaH, CH_2Cl_2, room temperature.

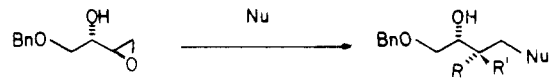
When the *tert*-butylthio diol to be alkylated contains an acid-labile functional group it is advisable to introduce a buffer such as 2,6-di-*tert*-butylpyridine to the reaction mixture. For example, the reaction of **15** or **17** with Me_3OBF_4 alone produces a complex mixture. Presumably acid-catalyzed migration and/or removal of the acetonide protecting groups of **15** or **17** is at least partially responsible for the problem. However, the use of 2–3 equiv of 2,6-di-*tert*-butylpyridine circumvents the problem. Treatment of the sulfonium salts with NaH in CH_2Cl_2 as before affords the 1,2-epoxy 3-ols **20** and **21** (entries 3 and 4) in good yield.

(15) (a) Fujisawa, T.; Sato, T.; Kawara, T.; Ohashi, K. *Tetrahedron Lett.* **1981**, *22*, 4823. (b) Pirkle, W. H.; Rinaldi, P. L. *J. Org. Chem.* **1978**, *43*, 3803. (c) Shanklin, J. R.; Johnson, C. R.; Ollinger, J.; Coates, R. M. *J. Am. Chem. Soc.* **1973**, *95*, 3429. (d) Kano, S.; Yokomatsu, T.; Shibuya, S. *J. Chem. Soc. Chem. Commun.* **1978**, 785. (e) Ikeda, Y.; Furuta, K.; Meguriya, N.; Ikeda, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1982**, *104*, 7663. (f) Townsend, J. M.; Sharpless, K. B. *Tetrahedron Lett.* **1972**, 3313. (g) Johnson, C. R.; Schroeck, C. W.; Shanklin, J. R. *J. Am. Chem. Soc.* **1973**, *95*, 7424. (h) Schauder, J. R.; Krief, A. *Tetrahedron Lett.* **1982**, *23*, 4389. (i) Van Ende, D.; Krief, A. *Tetrahedron Lett.* **1976**, 457.

(16) Curphey, T. J. *Org. Synth.* **1971**, *51*, 142.

(17) The epoxy alcohols **18** and **19** can be purified by flash chromatography, but a significant loss of product is inevitable. These 1,2-epoxy 3-ols are rather easily opened and even undergo partial decomposition during chromatography. It is more convenient to use these compounds directly and then purify the product at a later stage.

Table III. 1,2-Epoxy 3-ol Ring-Opening Reactions



18 - 19 22 - 31

entry	1,2-epoxy 3-ol	reactn conditns	product	yield, %
1	18	*a*	**22**, R = OH; R′ = H; Nu = N_3	83
2	19	*a*	**23**, R = H; R′ = OH; Nu = N_3	93
3	18	*b*	**24**, R = OH; R′ = H; Nu = H	84
4	19	*b*	**25**, R = H; R′ = OH; Nu = H	83
5	18	*c*	**26**, R = OH; R′ = H; Nu = CH_3	76
6	19	*c*	**27**, R = H; R′ = OH; Nu = CH_3	73
7	18	*d*	**28**, R = OH; R′ = H; Nu = $C{\equiv}CCH_2OTHP$	76
8	19	*d*	**29**, R = H; R′ = OH; Nu = $C{\equiv}CCH_2OTHP$	64
9	18	*e*	**30**, R = OH; R′ = H; Nu = CN	89
10	19	*e*	**31**, R = H; R′ = OH; Nu = CN	<50

[a] NaN_3, NH_4Cl, 1:8 H_2O–$CH_3OCH_2CH_2OH$, reflux. [b] $LiAlH_4$, Et_2O, −78 °C. [c] Me_2CuLi, Et_2O, −40 °C. [d] $LiC{\equiv}CCH_2OTHP$, Et_2O, −40 °C. [e] KCN, MeOH, 25 °C.

The utility of the 1,2-epoxy 3-ols available by these methods are highlighted in Table III in which a series of high-yield ring-opening reactions of **18** and **19** are presented. Although NaN_3 is not an effective nucleophile in the rearrangement–opening reaction of either **6** or **7**, it is an excellent nucleophile for the ring-opening of **18** and **19**.[18] Similarly, the reduction of 2,3-epoxy alcohols with $NaBH_4$ under rearrangement–opening conditions often leads to a mixture of diols.[2e] In contrast, $LiAlH_4$ reduces 1,2-epoxy 3-ols cleanly to the corresponding 2,3-diol.[19] The examples in entries 6–10 illustrate that the 1,2-epoxy 3-ol is a useful electrophile in carbon–carbon bond-forming reactions even without prior protection of the free hydroxyl group.[20]

A comparison of this newly developed "diol sulfide method" with the "diol sulfonate method" is presented in Scheme III. It can be seen that they complement each other well. As just described, the diol sulfide route is ideal for the rearrangement of certain types of 2,3-epoxy alcohols to the corresponding 1,2-epoxy 3-ols. The requirements are that the substituents on the 2,3-epoxy alcohol moiety must be inert to both NaOH and *t*-BuSNa at 80 °C and that the 2,3-epoxy alcohol should bear an alkoxy substituent at C-4. The latter requirement ensures a higher regioselectivity for C-1 in the first step of the diol sulfide route.

In contrast to the diol sulfide method, the diol sulfonate method requires that the substituents on the 2,3-epoxy alcohol be resistant to fairly acidic conditions. The success of the diol sulfonate method depends heavily upon high regioselectivity in the hydrolysis of the epoxide. If the hydrolysis is not regioselective a loss of enantiomeric purity will result because in this case the regioisomers are actually enantiomers. Therefore, the 2,3-epoxy alcohol must be free of any steric and/or electronic influences (e.g., an alkoxy substituent at C-4) which disfavor ring-opening at C-3.

A detailed comparison of the diol sulfonate and diol sulfide methods was undertaken with (2*S*,3*S*)-2,3-epoxy-1-decanol (**4**) as the starting epoxy alcohol. Mesylation of (−)-**4** (95% ee) (MsCl, Et_3N, CH_2Cl_2) followed by acid-catalyzed hydrolysis (catalytic $HClO_4$, aqueous Me_2SO, reflux) provides the 1-mesyloxy 2,3-diol **32** in 86% ee.[13] The enantiomeric purity of **32** was assigned by chrial shift reagent ^1H NMR analysis of the diacetate of **32**. The slight loss of enantiomeric purity indicates that the epoxide hydrolysis is not completely regioselective but proceeds with at least 20:1 selectivity.[21] The loss of enantiomeric purity indicates the *magnitude* of the regioselectivity, but it gives no information concerning the *direction* of the regioselectivity. In order to show that ring-opening in this case occurred mainly at C-3, the following experiments were performed. The 1-mesyloxy 2,3-diol **32** was treated with K_2CO_3 in methanol to afford (−)-**33**: $[\alpha]_D^{20}$ −15.3° (*c* 1.42, CH_2Cl_2). Ring-opening of (−)-**33** with *t*-BuSNa in THF leads to (−)-**11**; $[\alpha]_D^{20}$ −11.5° (*c* 2.1, EtOH). Samples of (+)-**11** and (+)-**33** were then prepared from (−)-**4** by the diol sulfide method. The diol sulfide method is not subject to a loss of enantiomeric purity due to a nonregioselective epoxide opening. A nonregioselective opening in this case leads to different compounds (regioisomers rather than enantiomers) which are usually separable by flash chromatography. Another difference between the methods is that they give opposite enantiomers of the 1,2-epoxy 3-ol from the same 2,3-epoxy alcohol. Thus treatment of (−)-**4** with *t*-BuSNa under rearrangement–opening conditions (0.5 N NaOH, *t*-BuOH, 75–80 °C) leads to (+)-**11**; $[\alpha]_D^{20}$ +12.4° (*c* 2.19, EtOH). The opposite and slightly greater specific rotation of (+)-**11** compared to (−)-**11** establishes that the epoxy mesylate was hydrolyzed selectively at C-3 (i.e., C-3:C-2 of 20:1) and confirms that there was a slight loss in enantiomeric purity in the hydrolysis step. Treatment of (+)-**11** with Me_3OBF_4 in CH_2Cl_2 followed by NaH in CH_2Cl_2 affords (+)-**33** $[\alpha]_D^{20}$ +17° (*c* 2.8, CH_2Cl_2) which has an opposite and slightly higher specific rotation than (−)-**33**—further proof that the epoxide hydrolysis in the diol sulfonate method is C-3 selective.

Payne Rearrangement–Opening Reactions of 2,3-Epoxy Alcohols with Amines. Until recently, amines were overlooked as nucleophiles in the Payne rearrangement–opening reaction. Although amines do react with epoxides, they do so rather sluggishly. The usual conditions are to heat an aqueous solution of the epoxide and excess amine for several hours. Accordingly, there was concern that in a rearrangement–opening process the neutral amine would not compete well against the hydroxide anion for the role of nucleophile. However, amines

(18) These azides are convenient precursors to 1-amino 2,3-diols. For example, **22** was reduced (Pd on carbon, 1 atm H_2, CH_3OH, room temperature) and then peracetylated (Ac_2O/py) to provide (2*S*,3*S*)-1-acetamido-4-(benzyloxy)-2,3-butanediol diacetate (**22a**) in 71% yield after chromatography.

(19) This reaction is a good complement to the known methods for the selective reduction of 2,3-epoxy alcohols to 1,3-diols. (a) Minami, N.; Ko, S. S.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 1109. (b) Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Viti, S. M. *J. Org. Chem.* **1982**, *47*, 1378. (c) Finan, J. M.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2719. (d) Viti, S. M. *Tetrahedron Lett.* **1982**, *23*, 4541. (e) Nicolaou, K. C.; Venishi, J. *J. Chem. Soc., Chem. Commun.* **1982**, 1292. (f) Mubarak, A. M.; Brown, D. M. *J. Chem. Soc., Perkin Trans 1* **1982**, 809. (g) Takano, S.; Kasahara, C.; Ogasawara, K. *Chem. Lett.* **1983**, 175.

(20) We first learned of the use of this particular acetylide nucleophile for opening an unprotected 1,2-epoxy 3-ol from Professor J. D. White (M.I.T. Organic Seminar, spring, 1983. See ref 14c). For examples of related reactions, see: (a) Mori, K.; Oda, M.; Matsui, M. *Tetrahedron Lett.* **1976**, 3173. (b) Just, G.; Luthe, C. *Tetrahedron Lett.* **1982**, *23*, 1331. (c) Suzuki, T.; Saimoto, H.; Tomioka, H.; Oshima, K. *Tetrahedron Lett.* **1982**, *23*, 3597. (d) Yamaguchi, M.; Hirao, I. *Tetrahedron Lett.* **1983**, *24*, 391.

(21) The C-3:C-2 ratio for the hydrolysis is calculated (assuming that hydrolysis of the epoxide is stereospecific) from the enantiomeric excess of the starting epoxide (% ee_E) and the enantiomeric excess of the product diol (% ee_D) according to the equation

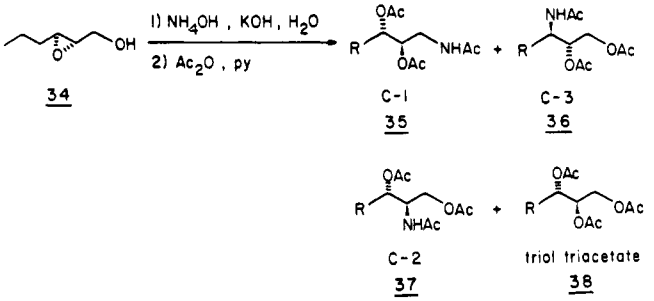
$$\text{C-3:C-2} = (1 + ee_D/ee_E)/(1 - ee_D/ee_E)$$

are stable to the reaction conditions, and the protic solvent system is a favorable one for the reaction of amines with epoxides. They are also inexpensive, readily available, and easy to handle. Therefore, amines were considered to be attractive candidates for use in the rearrangement–opening reaction. A careful search of the literature actually revealed one example of this type of rearrangement–opening process with amines. In 1972, Macchia reported that the reaction of *cis*-2,3-epoxy-2-methyl-3-phenylbutanol with concentrated NH_4OH provided a mixture of the C-1 product (47%) and the C-2 product (42%).[22] The C-1 product was formed in what is clearly a rearrangement–opening process *without* the presence of KOH in the reaction mixture. However, the rearrangement–opening reaction in the absence of hydroxide or a base of similar strength is probably not a general reaction.

The results for the rearrangement–opening reaction of epoxy alcohol **34** with NH_4OH in the presence of KOH are presented in Table IV. The experimental procedure for the ring-opening entailed dissolving **34** in a sufficient quantity of an aqueous NH_4OH–KOH solution to provide ca. 10 equiv of KOH based on **34**. As shown in Table IV the regioselectivity is very poor. The ratio of the desired 1-acetamido-2,3-hexanediol diacetate **35** to the combined regioisomers **36** and **37** and to 1,2,3-hexanetriol triacetate **38** is approximately 1:1:1.[23] The temperature apparently has very little effect on the regioselectivity. This rearrangement–opening process was tested with a variety of epoxy alcohols and amines to get an indication of the scope of the reaction. These results are presented in Table V. The typical overall regioselectivity (i.e., ratio of C-1 product to combined C-2 and C-3 regioisomers) is ca. 2–4:1.[24] An exception is found in **40**, which provides mainly the C-3 product under these reaction conditions (entries 8, 9). However, **40** is a special case because its C-3 position is benzylic, and epoxide ring-opening reactions at benzylic (or allylic) centers of similar epoxides are known to be facile. The original concern that the neutral amine would not compete well against the hydroxide anion for the role of nucleophile has proved to be partly justified, but the problem has been largely overcome by the use of excess amine. In fact, in only one case (entry 4) was any triacetate detected.

Since the rearrangement–opening reaction with amine nucleophiles appears to be generally applicable, a considerable effort was mounted to optimize the reaction conditions. With **34** as a test substrate, the regioselectivity

Table IV. Payne Rearrangement–Opening Reaction of (2*S*,3*S*)-2,3-Epoxy-1-hexanol (34) with Concentrated NH_4OH and KOH



entry	temp, °C	C-1: [(C-3) + (C-2)]: triol triacetate	reactn time, h	combined yield, %
1	reflux	1.0:1.0:1.2	2	89
2	25	1.6:1.2:1.0	85	89
3	0	1.2:1.0:1.1	231[a]	66[a]

[a] The reaction was incomplete at 231 h, but the yield is not corrected for unreacted **34**.

[i.e., C-1:(C-3 + C-2 + triol triacetate)] in the rearrangement–opening reaction was determined (^1H NMR analysis) for the unpurified reaction product as the reaction conditions were systematically varied. From the results of this work, two general procedures emerged as offering the best balance of regioselectivity, reaction time, and yield. A good procedure is to dissolve the epoxy alcohol in a quantity of 1:1 amine–0.5 N KOH sufficient to provide 2.5–8 equiv of KOH (relative to the epoxy alcohol). This solution is then stirred at room temperature or refluxed until the reaction is complete by TLC. An alternative recommended procedure is identical with the first except that the reaction mixture is diluted with an equal volume of cosolvent such as *t*-BuOH or THF. The presence of the cosolvent increases the regioselectivity by a factor of about 2 although this is achieved at the expense of a longer reaction time (ca. 24 h) compared to the same reaction with no cosolvent (2–8 h). From the results of the experiments which were designed to optimize the regioselectivity of the rearrangement–opening reaction, it is evident that the regioselectivty is *not* very sensitive to the concentration of hydroxide (KOH or Me_4NOH) in the reaction mixture or to the reaction temperature, although the rate of the reaction is increased by increasing the concentration of hydroxide[25] and, of course, by increasing the reaction temperature. As expected, the regioselectivity is found to increase as the steric hindrance of the amine increases. Thus, one of the highest regioselectivities observed to date is found in the reaction of **34** with Et_2NH (1:1:2 Et_2NH–0.5 N KOH–THF, 2.8 equiv KOH, 80 °C, 30 h) to afford crude 1-(*N*,*N*-diethylamino)-2,3-hexanediol diacetate with a regioselectivity of 6:1, which could be isolated chromatographically in 57% yield.

A drawback to the Payne rearrangement–opening reaction with amine nucleophiles is that while the regioselectivity and crude yields are acceptable, the isolated yields are lower than expected. A chromatographic separation of the desired 1-amino 2,3-diol diacetate product from the regioisomers was performed in some cases (Table V, entries 3–7) to afford an analytically pure product, but the re-

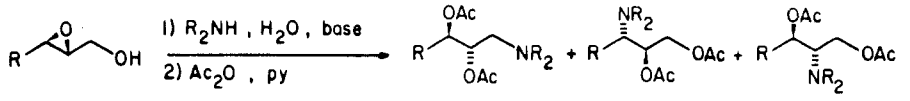
(22) Macchia, B. *Farmaco, Ed. Sci.* **1972**, *27*, 559; *Chem. Abstr.* **1973**, *78*, 42759v.

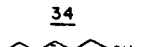
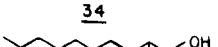
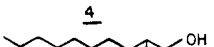
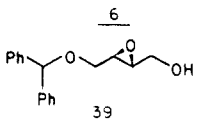
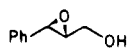
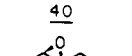
(23) In order to avoid the problems associated with the isolation of the very polar amino diols, the crude reaction mixture was peracetylated to afford the acetamido diol diacetates. This material was analyzed by ^1H NMR to determine the product composition (i.e., regioselectivity). In particular, the diagnostic chemical shift (δ) and multiplicity of the signals in the ^1H NMR spectrum that arise from RR′C*H*OAc (4.9 δ) and RCH_AH_BNHAc (2.0–2.5 δ) were used to assess the regioselectivity in the reaction.

(24) In order to avoid the problems associated with the isolation of the very polar 1-amino 2,3-diol product, the crude reaction mixture was peracetylated to afford the 1-amino 2,3-diol diacetate. The peracetylation procedure requires the prior removal of as much of the starting amine and water as possible. This is conveniently accomplished by concentrating the reaction mixture in vacuo. For this reason (i.e., ease of removal during workup) the volatile, low molecular weight amines are favored. A solution of the peracetylated product in CH_2Cl_2 was washed with water to remove the salts, dried, and concentrated to afford the 1-amino 2,3-diol diacetate (and its regioisomers). This crude material was analyzed by ^1H NMR before purification by flash chromatography. Normally, the regioselectivity in the reaction was assigned on the basis of the diagnostic chemical shift (δ) and multiplicity (d, dd, etc.) of signals in the ^1H NMR spectrum that arise from RR′C*H*OAc (δ 4.9), RCH_AH_BOAc (ca. δ 4.0), $R_2NCHR'R''$ (δ 2.1–2.5), and $R_2NCH_AH_BR'$ (δ 2.1–2.5).

(25) If the concentration of KOH is increased beyond a certain point (e.g., approximately 0.5 N KOH in a 1:1 mixture of Et_2NH–aqueous KOH), a phase separation occurs which retards the rate of reaction. If desired, one can reach higher hydroxide concentrations without phase separation by use of tetraalkylammonium hydroxide.

Table V. Payne Rearrangement–Opening Reaction of 2,3-Epoxy Alcohols with Amines



entry	epoxy alcohol	amine	base[a] (equiv conc)	temp[d]	regioselectivity (C-1:C-3:C-2)	overall regioselectivity [C-1:(C-3 + C-2)]	yield,[b] %
1		Me_2NH	Me_4NOH (6.8, 0.47)	r.t.	15.5:3.7:1.0	3.3:1.0	78
2	34 	Me_2NH	Me_4NOH (16.8, ca. 3)	r.t.	11.1:2.9:1.0	2.8:1.0	94
3	34 	Me_2NH	KOH (13.9, 0.54)	r.t.	10.0:2.8:1.0	2.6:1.0	94 (55)
4	4 	Et_2NH	KOH (7.5, 0.25)	reflux		4.0:1.	87 (63)[c]
5	4 	Me_2NH	KOH (8.5, 0.54)	r.t.	17.7:1.0:5.0	3.0:1.0	89 (41)
6	6 	Et_2NH	KOH (7.7, 0.25)	reflux		6:1	98 (45)
7	6 	Et_2NH	KOH (3.0, 0.25)	reflux		6.5:1.0	84 (64)
8	39 	Et_2NH	KOH (3.3, 0.25)	reflux		1.0.6.0	98
9	40  40	Et_2NH	KOH (1.8, 0.25)	r.t.	1.0:7.0:0	1.0:7.0	96

[a] Equivalents (equiv) are calculated with respect to the epoxy alcohol. Concentration (concn) is the approximate molarity of the base in the reaction mixture. [b] Yield refers to the combined yield of unpurified product. The numbers in parentheses refer to the yield of chromatographically homogeneous C-1 product. [c] In this case a small amount of 1,2,3-decanetriol triacetate was detected. [d] r.t. = room temperature.

covery was not as great as expected on the basis of the yield of unpurified material and the estimated product composition (i.e., regioselectivity). However, this reaction is not without promise, since the lower yield is compensated for by the fact that the 1-amino 2,3-diol diacetate product is prepared in one exceedingly simple step from the 2,3-epoxy alcohol. The reactions are run open to the atmosphere (O_2 is not harmful), and there is no need for slow addition of the nucleophile, both of which are requirements for the corresponding thiolate rearrangement–opening reactions.

In summary, this simple one-step process compares favorably with the alternative approach to the 1-amino 2,3-diol (from the same 2,3-epoxy alcohol) via the diol sulfonate or the diol sulfide methods, both of which would require at least four steps to accomplish the same transformation. Another good feature of this reaction is that it appears to be generally applicable to a variety of epoxy alcohols as shown in Table V. In addition, there is flexibility in the choice of the amine nucleophile to be used, since regioselective opening has now also been observed with *n*-$BuNH_2$, *i*-$PrNH_2$, *t*-$BuNH_2$, diallylamine, and piperidine as the nucleophile.[28]

Experimental Section

Melting points were determined with a Thomas-Hoover capillary melting point apparatus. All melting points are uncorrected. Infrared (IR) spectra were measured with a Perkin-Elmer Model 597 grating infrared spectrophotometer. The 1601-cm^{-1} absorption band of polystyrene film was used to calibrate the chart paper. ^1H NMR spectra were measured with Brucker 250-MHz or 270-MHz spectrometers. The solvent used was $CDCl_3$ unless otherwise noted. Tetramethylsilane (Me_4Si) was used as an internal standard. The chemical shifts are given in δ (ppm) downfield from Me_4Si, and the coupling constants are in hertz. Low-resolution mass spectra (MS) were obtained with a Finnegan MAT 8200 mass spectrometer. Optical rotations were measured with a Perkin-Elmer Model 241 polarimeter with a 1-cm^3 capacity (10-cm path length) quartz cell. Elemental analyses were performed by Robertson Laboratory Inc., Florham Park, NJ.

All oxygen- or water-sensitive reactions were conducted in oven-dried (140 °C) or flame-dried glassware under an atmosphere of dry nitrogen. All commercial chemicals and reagents were used as received. Benzene and methylene chloride (CH_2Cl_2) were distilled from CaH_2; methanol was distilled from magnesium metal; tetrahydrofuran was distilled from sodium benzophenone ketyl. Pyridine and dimethylformamide (DMF) were stored over activated 3-A molecular sieves. Analytical thin-layer chromatography (TLC) was performed with aluminum plates coated with 0.20-mm thickness of Merck silica gel 60 F-254. Flash chroma-

(26) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(27) Micovic, V. M.; Mihailovic, M. L. *J. Org. Chem.* **1953**, *18*, 1190.
(28) Ko, S. Y.; Sharpless, K.B., unpublished results.

tography was performed with Merck silica gel 60 (230–400 mesh) as described by Still.[26]

Reductions with either $LiAlH_4$ or AlH_3 were quenched by the "Fieser workup" according to the following procedure.[27] The reaction mixture from a reaction with n grams of $LiAlH_4$ is treated by successive dropwise addition of n mL of ice-cold water, n mL of an aqueous 15% NaOH solution, and $3n$ mL of ice-cold water. After being stirred for at least 0.5 h, the mixture is filtered through a sintered glass frit. The precipitated aluminum salts are then washed as specified in each particular case.

In general, compounds (e.g., alcohols, diols, amines, etc.) were peracetylated for ^1H NMR analysis according to the following procedure. A 5–10-mL round-bottomed flask is charged with the compound to be peracetylated (0.5–5 mg) and 1.5–3.0 mL of 2:1 pyridine–acetic anhydride. After standing for a period of at least 2 h (but usually overnight) at room temperature, the excess pyridine, acetic anhydride, and acetic acid are removed in vacuo to afford the peracetate.

Representative Experimental Procedures. Payne Rearrangement–Opening Reaction of (2*R*,3*S*)-4-(Benzyloxy)-2,3-epoxy-1-butanol (6) with *t*-BuSH. The solvents required for this reaction (i.e., water and *tert*-butyl alcohol) were deoxygenated prior to use by the rapid passage of nitrogen through the solvent for not less than 30 min. A solution of the epoxy alcohol **6** (0.3017 g, 1.56 mmol) ($[\alpha]^{25}_D$ +23.3° (*c* 1.20, EtOH), lit.[4a] $[\alpha]^{25}_D$ +27° (*c* 1.08, $HCCl_3$)) in 7.8 mL of *tert*-butyl alcohol and 7.8 mL of a 0.5 N aqueous NaOH solution was immersed in a preheated (70 °C) oil bath. The reaction mixture was stirred vigorously as a dropwise addition of a solution of *tert*-butyl mercaptan (0.220 mL, 0.176 g, 1.96 mmol) in 2 mL of *tert*-butyl alcohol was conducted over a period of 40 min. During this time the oil bath temperature rose to 78 °C. Stirring was continued for 20 min after the dropwise addition was complete. The reaction mixture was then cooled to room temperature and neutralized with a saturated aqueous NH_4Cl solution. Sufficient water was added to clarify the aqueous phase, and the phases were then separated. The aqueous phase was extracted 5 times with CH_2Cl_2, and the combined organic phases were washed (saturated aqueous NH_4Cl), dried (Na_2SO_4), concentrated, and dried under high vacuum to afford 0.3996 g (90%) of (2*S*,3*R*)-1-(benzyloxy)-4-(*tert*-butylthio)-2,3-butanediol (**13**) as an oil. This material was purified by flash chromatography to afford 0.2757 g (62%) of **13** as an oil: $[\alpha]^{25}_D$ −10.6° (*c* 1.98, $HCCl_3$); $[\alpha]^{20}_D$ +5.8° (*c* 0.80, EtOH); ^1H NMR ($CDCl_3$) δ 7.25–7.41 (m, 5 H), 4.54, 4.58 (AB, J_{AB} = 12 Hz, 2 H), 3.81 (m, 1 H), 3.64 (m, 2 H), 2.92 (d, J = 4.1 Hz, 1 H), 2.61–2.85 (m, 3 H), 1.32 (s, 9 H); IR (NaCl) 3400 (br), 3090, 3070, 3030, 2960, 2930, 2900, 2870, 1455, 1365, 1100 (br), 740, 700 cm^{-1}. Anal. Calcd for $C_{15}H_{24}O_3S$: C, 63.35; H, 8.51; S, 11.27. Found: C, 63.37; H, 8.31; S, 11.41.

A small sample of **13** was peracetylated in the usual way to afford (2*S*,3*R*)-1-(benzyloxy)-4-(*tert*-butylthio)-2,3-butanediol diacetate as an oil: ^1H NMR ($CDCl_3$) δ 7.25–7.42 (m, 5 H, Ar), 5.39 (m, 1 H), 5.26 (m, 1 H), 4.52, 4.54 (AB, J_{AB} = 13.1 Hz, 2 H), 3.50–3.63 (m, 2 H), 2.72 (d, J = 7.5 Hz, 2 H), 2.10 (s, 3 H), 2.06 (s, 3 H), 1.31 (s, 9 H).

Preparation of (2*S*,3*S*)-1-(Benzyloxy)-3,4-epoxy-2-butanol (18). A solution of (2*S*,3*S*)-1-(benzyloxy)-4-(*tert*-butylthio)-2,3-butanediol (**13**) (0.0823 g, 0.290 mmol) in 3 mL of CH_2Cl_2 was treated with Me_3OBF_4 in several portions until the diol was completely consumed. This process required ca. 0.13 g of Me_3OBF_4 and took about 1 h to complete. The reaction mixture was then treated with 4 mL of a 10% aqueous NaOH solution and stirred for ca. 2.5 h. The reaction mixture was neutralized with saturated aqueous NH_4Cl, and the organic products were extracted from the aqueous phase with CH_2Cl_2. The combined organic portions were dried (Na_2SO_4), concentrated, and dried under high vacuum to afford 0.0494 g (88%) of **18** as an oil. This material was flash chromatographed (1:1 hexane–EtOAc) to afford an analytical sample of **18** as an oil: $[\alpha]^{25}_D$ +12.2° (*c* 3.62, $HCCl_3$), lit.[4b] $[\alpha]^{25}_D$ +13.5° (*c* ca. 1, $HCCl_3$); ^1H NMR ($CDCl_3$) δ 7.25–7.40 (m, 5 H), 4.58 (s, 2 H), 3.75 (m, 1 H), 3.58 (m, 2 H), 3.10 (m, 1 H), 2.76 (m, 2 H), 2.49 (d, J = 6.1 Hz, 1 H); IR (NaCl) 3450 (br), 3070, 3040, 3005, 2920, 2870, 1500, 1465, 1100 (br), 900, 740, 705 cm^{-1}.

A small sample of **18** was peracetylated in the usual way to afford (2*S*,3*S*)-1-(benzyloxy)-3,4-epoxy-2-butanol acetate as an oil: ^1H NMR ($CDCl_3$) δ 7.18–7.43 (m, 5 H), 4.48 (m, 1 H), 4.53, 4.57 (AB, J_{AB} = 12.2 Hz, 2 H), 3.67 (m, 2 H), 3.26 (ddd, J = 2.6, 4.8, 5.7 Hz, 1 H), 2.85 (t, J = 4.5 Hz, 1 H), 2.67 (dd, J = 2.6, 4.1 Hz, 1 H), 2.12 (s, 3 H).

Preparation of (2*S*,3*S*,4*R*,5*R*)-1-(Benzyloxy)-2,3-*O*-isopropylidene-5,6-epoxy-2,3,4-hexanetriol (21). The *tert*-butylthio diol **17** (0.051 g, 0.125 mmol) was *S*-alkylated with Me_3OBF_4 in CH_2Cl_2 in the presence of 0.050 g of 2,6-di-*tert*-butylpyridine and then treated with a slight excess of NaH in CH_2Cl_2 to afford 0.044 g of crude product. This material was purified by chromatography (neutral alumina, activity III, 1:1 hexane–EtOAc) to afford 0.028 g (72%) of (2*S*,3*S*,4*R*,5*R*)-1-(benzyloxy)-2,3-*O*-isopropylidene-5,6-epoxy-2,3,4-hexanetriol (**21**) as an oil: $[\alpha]^{20}_D$ −27.8° (*c* 1.3, EtOH); ^1H NMR ($CDCl_3$) δ 7.28–7.33 (m, 5 H), 4.60 (s, 2 H), 4.19–4.26 (m, 1 H), 3.75–3.88 (m, 2 H), 3.69 (d, J = 4.9 Hz, 2 H), 3.21 (dd, J = 6.3, 3.2 Hz, 1 H), 2.84 (dd, J = 5.6, 3.1 Hz, 1 H), 2.72 (t, J = 4.2 Hz, 1 H), 2.53 (br s, 1 H), 1.43 (s, 6 H).

Reaction of 18 with NaN_3/NH_4Cl. A solution of the epoxy alcohol **18** (0.0172 g, 0.089 mmol) in 1 mL of 8:1 $CH_3OCH_2CH_2OH$–H_2O was refluxed for 5 h with NaN_3 (0.0289 g, 0.44 mmol) and NH_4Cl (0.0189 g, 0.35 mmol). The reaction mixture was cooled to room temperature, concentrated, and passed through a very short silica gel column with EtOAc to afford 0.0198 g (94%) of (2*S*,3*S*)-1-azido-4-(benzyloxy)-2,3-butanediol (**22**) as an oil. This material was purified by flash chromatography (1:1 hexane–EtOAc) to afford **22** as an oil: $[\alpha]^{20}_D$ −1.1° (*c* 1.69, $HCCl_3$); ^1H NMR ($CDCl_3$) δ 7.18–7.45 (m, 5 H), 4.54, 4.58 (AB, J_{AB} = 11.8 Hz, 2 H), 3.75–3.91 (m, 2 H), 3.54–3.69 (m, 2 H), 3.33–3.46 (m, 2 H), 2.80 (d, J = 4.6 Hz, 1 H), 2.61 (d, J = 6.2 Hz, 1 H); IR (NaCl) 3400 (br), 3090, 3070, 3040, 2920, 2870, 2100, 1500, 1455, 1100 (br), 740, 705 cm^{-1}. Anal. Calcd for $C_{11}H_{15}N_3O_3$: C, 55.69; H, 6.37. Found: C, 55.83; H, 6.60.

A small sample of **22** was peracetylated in the usual way to afford (2*S*,3*S*)-1-azido-4-(benzyloxy)-2,3-butanediol diacetate as an oil: ^1H NMR ($CDCl_3$) δ 7.21–7.40 (m, 5 H), 5.22–5.38 (m, 2 H), 4.47, 4.55 (AB, J_{AB} = 12.1 Hz, 2 H), 3.56 (m, 2 H), 3.49 (dd, J = 4.7, 14.2 Hz, 1 H), 3.38 (dd, J = 5.6, 14.2 Hz, 1 H), 2.11 (s, 3 H), 2.10 (s, 3 H).

Preparation of (2*S*,3*S*)-1-Acetamido-4-(benzyloxy)-2,3-butanediol Diacetate (22a). A solution of (2*S*,3*S*)-1-azido-4-(benzyloxy)-2,3-butanediol (**22**) (0.0153 g, 0.065 mmol) in methanol (1 mL) was treated with 0.0210 g of a 5% palladium on carbon catalyst. The reaction vessel was thoroughly flushed with hydrogen, and the reaction mixutre was stirred vigorously for 12 h. A small additional quantity of catalyst was then added, and after reestablishing the hydrogen atmosphere in the reaction vessel, stirring was continued overnight. The crude reaction mixture was then filtered through a pad of Celite (methanol rinse) to remove the catalyst, concentrated to afford a clear colorless oil, and peracetylated in the usual way to afford 0.0209 g (95%) of **22a** as an oil. This product was purified by flash chromatography (EtOAc) to afford 0.0155 g (71%) of **22a** as a solid: mp 83–84 °C; $[\alpha]^{25}_D$ −5.9° (*c* 1.55, EtOH); ^1H NMR ($CDCl_3$) δ 7.24–7.46 (m, 5 H); 5.92 (br m, 1 H), 4.52 (s, 2 H), 3.49–3.66 (m, 3 H), 3.36 (dt, J = 5.0, 14.1 Hz, 1 H), 2.12 (s, 3 H), 2.06 (s, 3 H), 1.97 (s, 3 H); IR (NaCl) 3300 (br), 3070, 3030, 2930, 2870, 1740, 1660, 1550, 1375, 1225, 1050, 740, 705 cm^{-1}. Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15. Found: C, 60.53; H, 7.09; N, 3.92.

Reaction of 19 with $LiAlH_4$. A solution of the epoxy alcohol **19** (0.0319 g, 0.164 mmol) in 2 mL of anhydrous Et_2O was cooled to −78 °C, treated with 1 equiv of a 1 M solution of $LiAlH_4$ in Et_2O (0.040 mL, 0.04 mmol), and stirred for 1.5 h. The reaction mixture was then treated with an additional 2.5 equiv of the $LiAlH_4$ solution (0.100 mL, 0.10 mmol) and warmed to −20 °C. After 2 h the reduction was complete, and the excess $LiAlH_4$ was quenched with a saturated aqueous NH_4Cl solution. Sufficient water was added to clarify the aqueous phase, which was then extracted with Et_2O. The combined organic phases were dried (K_2CO_3), concentrated, and dried under high vacuum to afford 0.0286 g (89%) of (2*S*,3*R*)-1-(benzyloxy)-2,3-butanediol (**25**) as an oil. This material was purified by flash chromatography (1:1 hexane–EtOAc) to afford **25** as an oil: $[\alpha]^{25}_D$ −7.2° (*c* 2.00, EtOH); ^1H NMR ($CDCl_3$) δ 7.25–7.42 (m, 5 H), 4.54 (s, 2 H), 3.89 (m, 1 H), 3.69 (m, 1 H), 3.60 (m, 2 H), 2.87 (d, J = 4.5 Hz, 1 H), 2.49 (d, J = 5.7 Hz, 1 H), 1.17 (d, J = 6.6 Hz, 3 H); IR (NaCl) 3420

(br), 3080, 3060, 3020, 2970, 2910, 2860, 1490, 1450, 1060 (br), 735, 695 cm^{-1}. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.61; H, 8.54.

A small sample of **25** was peracetylated in the usual way to afford (2*S*,3*R*)-1-(benzyloxy)-2,3-butanediol diacetate as an oil: ^1H NMR ($CDCl_3$) δ 7.15–7.40 (m, 5 H), 5.07–5.24 (m, 2 H), 4.50, 4.56 (AB, J_{AB} = 13.0 Hz, 2 H), 3.57 (d, J = 4.1 Hz, 2 H), 2.10 (s, 3 H), 2.00 (s, 3 H), 1.23 (d, J = 6.0 Hz, 3 H).

Reaction of 18 with Me_2CuLi. A 10-mL round-bottomed flask was charged with 0.0733 g (0.385 mmol) of CuI, sealed with a septum, and flushed with nitrogen. Anhydrous Et_2O (2 mL) was introduced via syringe, and the flask was immersed in a slush of Et_2O, CCl_4, and dry ice. This slush was maintained between −40 and −35 °C throughout the course of the reaction. A solution of MeLi (1.4 M in hexane, 0.55 mL, 0.77 mmol) was added with stirring to the CuI to afford an ethereal solution of Me_2CuLi. After allowing the Me_2CuLi to stir for 30 min, the epoxy alcohol **18** (0.0146 g, 0.075 mmol) was added to the reaction mixture, and stirring was continued for an additional 2 h. The reaction mixture was diluted with Et_2O (5 mL) and then quenched with 2 mL of a saturated aqueous NH_4Cl solution, which caused a green solid to precipitate from solution. After stirring the reaction mixture for 2 h in the presence of air, the green precipitate dissolves completely to give a deep blue aqueous layer and a colorless organic layer. The phases were separated, and the aqueous layer was extracted with Et_2O (3×) and EtOAc (3×). The combined organic phases were washed once with a saturated aqueous $NaHCO_3$ solution and once with a saturated aqueous NaCl solution, dried (K_2CO_3), concentrated, and dried under high vacuum to afford 0.0119 g (76%) of (2*S*,3*S*)-1-(benzyloxy)-2,3-pentanediol (**26**) as a solid: mp 52–54 °C; $[\alpha]^{25}_D$ −4.4° (*c* 0.4, EtOH); ^1H NMR ($CDCl_3$) δ 7.25–7.36 (m, 5 H), 4.56, 4.58 (AB, J_{AB} = 12.2 Hz, 2 H), 3.50–3.71 (m, 4 H), 2.59 (br d, J = 3.4 Hz, 1 H), 2.50 (br d, J = 4.4 Hz, 1 H), 1.56 (m, 2 H), 0.97 (t, J = 7.3 Hz, 3 H); IR (NaCl) 3420 (br), 3060, 3030, 2960, 2920, 2870, 1595, 1453, 1100, 735, 700 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.38; H, 8.81.

Reaction of 19 with $LiC{\equiv}CCH_2OTHP$. A 10-mL round-bottomed flask containing THF (2 mL) and a magnetic stirring bar was cooled to −40 °C under a nitrogen atmosphere by immersion in a slush of dry ice, Et_2O, and CCl_4. The chilled THF was charged with 2.2 equiv of 3-[(2′*R**)-2′-(tetrahydropyranyl)-oxy]-1-propyne (0.168 g, 0.120 mmol), and then 2.1 equiv of a 1.7 M solution of CH_3Li in hexane (0.65 mL, 1.1 mmol) was rapidly added to the reaction mixture. This mixture was allowed to stir for 1 h before 1 equiv of the epoxy alcohol **19** (0.0446 g, 0.230 mmol) was added as a solution in 3 mL of THF. The reaction mixture was gradually warmed to room temperature, and stirring was continued overnight at room temperature. The reaction mixture was then quenched with an excess of an aqueous NH_4Cl solution, and a small amount of water was added to dissolve the precipitate. The reaction mixture was extracted with Et_2O (3×), and the combined organic phases were dried (K_2CO_3) and concentrated. This material was purified via flash chromatography (3:1 petroleum ether–EtOAc) to afford 0.0488 g (64%) of (2*S*,3*R*)-1-(benzyloxy)-7-[(2′*R**)-2′-(tetrahydropyranyl)oxy]-5-heptyne-2,3-diol (**29**) as an oil: $[\alpha]^{20}_D$ −5.8° (*c* 3.30, EtOH); ^1H NMR ($CDCl_3$) δ 7.25–7.41 (m, 5 H), 4.80 (t, J = 3.7 Hz, 1 H), 4.57 (s, 2 H), 4.16–4.34 (m, 2 H), 3.75–3.89 (m, 3 H), 3.61–3.72 (m, 2 H), 3.47–3.54 (m, 1 H), 2.77 (d, J = 4.1 Hz, 2 H), 2.57 (m, 2 H), 1.47–1.90 (m, 6 H); IR (NaCl) 3430 (br), 3060, 3030, 2940, 2860, 1495, 1450, 1360, 1115, 1020, 740, 700 cm^{-1}.

A small sample of **29** was peracetylated in the usual way to afford (2*S*,3*R*)-1-(benzyloxy)-7-[(2′*R**)-2′-(tetrahydropyranyl)-oxy]-5-heptyne-2,3-diol diacetate as an oil: ^1H NMR ($CDCl_3$) δ 7.22–7.40 (m, 5 H), 5.19–5.33 (m, 2 H), 4.78 (br m, 1 H), 4.48, 4.56 (AB, J_{AB} = 12.1 Hz, 2 H), 4.12–4.31 (m, 2 H), 3.76–3.87 (m, 1 H), 3.47–3.69 (m, 3 H), 2.52–2.74 (m, 2 H), 2.08 (s, 3 H), 2.02 (s, 3 H), 1.46–1.85 (m, 6 H).

Reaction of 18 with KCN. A solution of the epoxy alcohol **18** (0.0108 g, 0.056 mmol) in 1 mL of methanol was treated with KCN (0.030 g, 0.46 mmol) for 24 h at room temperature. The reaction mixture was concentrated and acidified (1 M HCl). The reaction mixture was extracted with Et_2O, dried (K_2CO_3), and concentrated to afford 0.0110 g (89%) of (3*S*,4*S*)-5-(benzyloxy)-3,4-dihydroxy-1-pentanenitrile (**30**) as an oil: $[\alpha]^{25}_D$ −4.1° (*c* 1.52, EtOH); ^1H NMR ($CDCl_3$) δ 7.24–7.44 (m, 5 H), 4.56, 4.58 (AB, J_{AB} = 12.3 Hz, 2 H), 4.06 (m, 1 H), 3.79 (m, 1 H), 3.67 (m, 2 H), 3.01 (d, J = 5.2 Hz, 1 H), 2.64 (d, J = 6.7 Hz, 2 H), 2.63 (d, J = 7.1 Hz, 1 H); IR (NaCl) 3420 (br), 3090, 3060, 3030, 2920, 2870, 2250, 1680, 1495, 1100 (br), 740, 700 cm^{-1}.

A small sample of **30** was peracetylated in the usual way to afford (3*S*,4*S*)-5-(benzyloxy)-3,4-dihydroxy-1-pentanenitrile diacetate as an oil: ^1H NMR ($CDCl_3$) δ 7.19–7.42 (m, 5 H), 5.33 (m, 1 H), 5.21 (m, 1 H), 4.51 (s, 2 H), 3.57 (m, 2 H), 2.82 (dd, J = 5.5, 17.1 Hz, 1 H), 2.67 (dd, J = 5.5, 17.1 Hz, 1 H), 2.14 (s, 3 H), 2.10 (s, 3 H).

Preparation of (2*S*,3*S*)-1-(Mesyloxy)-2,3-epoxydecane. A solution of (2*S*,3*S*)-2,3-epoxy-1-decanol (**4**) (0.250 g, 1.45 mmol) in 5 mL of dry CH_2Cl_2 at 0 °C was treated with methanesulfonyl chloride (0.250 g, 2.18 mmol) and triethylamine (0.294 g, 2.91 mmol), stirred at 0 °C for 5 min, and then put in a 0 °C refrigerator overnight. The reaction mixture was diluted with 40 mL of diethyl ether and washed with water (3 × 5 mL). The organic phase was dried over $MgSO_4$, filtered, and evaporated to afford 0.300 g of crude product. This material was purified by flash chromatography (3:1 hexane–EtOAc) to afford 0.246 g (73%) of (2*S*,3*S*)-1-(mesyloxy)-2,3-epoxydecane as a waxy solid: ^1H NMR ($CDCl_3$) δ 4.48 (dd, J = 11.4, 3.8 Hz, 1 H), 4.12 (dd, J = 11.4, 6.8 Hz, 1 H), 3.09 (s, 3 H), 3.08 (m, 1 H), 2.91 (m, 1 H), 1.59 (m, 2 H), 1.45 (m, 2 H), 1.29 (br s, 8 H), 0.89 (t, J = 6.8 Hz, 3 H).

Preparation of (2*S*,3*R*)-1-(Mesyloxy)-2,3-decanediol (32). A solution of (2*S*,3*S*)-1-(mesyloxy)-2,3-epoxydecane (0.117 g, 0.47 mmol) in 5 mL of a 60% aqueous Me_2SO solution was treated with 0.01 mL of a 70% $HClO_4$ solution and stirred at room temperature for 20 h. The reaction mixture was diluted with 75 mL of EtOAc and washed with water (3 × 20 mL). The organic phase was dried (Na_2SO_4), concentrated, and dried under vacuum to afford 0.115 g (92%) of (2*S*,3*R*)-1-(mesyloxy)-2,3-decanediol (**32**) as an oil. This material was purified by flash chromatography (2:1 hexane–EtOAc) to afford 0.095 g (75%) of **32** as a white solid: mp 72–74 °C; ^1H NMR ($CDCl_3$) δ 4.39 (m, 2 H), 3.80–3.89 (m, 1 H), 3.68–3.80 (m, 1 H), 3.09 (s, 3 H), 2.65 (d, J = 4.5 Hz, 1 H), 2.00 (d, J = 4.5 Hz, 1 H), 1.21–1.65 (m, 12 H), 0.90 (t, J = 6.6 Hz, 3 H); IR ($HCCl_3$) 3590 (br), 3050, 2960, 2930, 2860, 1460, 1360, 1175, 1075, 960, 825 cm^{-1}.

A small sample of **32** was peracetylated in the usual way to afford (2*S*,3*R*)-1-(mesyloxy)-2,3-decanediol diacetate as an oil: ^1H NMR ($CDCl_3$) δ 5.22 (m, 2 H), 4.36 (m, 2 H), 3.05 (s, 3 H), 2.12 (s, 3 H), 2.10 (s, 3 H), 1.51–1.66 (m, 4 H), 2.15–2.39 (m, 8 H), 0.90 (t, J = 6.6 Hz, 3 H).

Preparation of (2*S*,3*R*)-1-(Mesyloxy)-3-methoxy-2-decanol. A solution of (2*S*,3*S*)-1-(mesyloxy)-2,3-epoxydecane (0.125 g, 0.50 mmol) in 5 mL of anhydrous methanol was treated with 0.01 mL of a 1.4% methanolic $HClO_4$ solution and stirred at room temperature for 3 h. The reaction mixture was treated with 2 mL of a saturated aqueous $NaHCO_3$ solution and then concentrated. The precipitate was redissolved in a minimum amount of water, and the aqueous phase was extracted with diethyl ether. The combined organic phases were dried ($MgSO_4$), concentrated, and dried under high vacuum to afford 0.137 g (97%) of (2*S*,3*R*)-1-(mesyloxy)-3-methoxy-2-decanol as an oil: ^1H NMR ($CDCl_3$) δ 4.30 (m, 2 H), 3.90–4.00 (m, 1 H), 3.35–3.44 (br s, 3 H), 3.20–3.33 (m, 1 H), 3.03–3.12 (br s, 3 H), 2.39 (d, J = 4.2 Hz, 1 H), 1.20–1.71 (m, 12 H), 0.90 (t, J = 6.6 Hz, 3 H); IR (NaCl) 3520 (br), 3030, 2930, 2860, 1790, 1740, 1640, 1460, 1350 (br), 1175, 1100, 960, 830 cm^{-1}.

A small sample of (2*S*,3*R*)-1-(mesyloxy)-3-methoxy-2-decanol was acetylated in the usual way to afford (2*S*,3*R*)-1-(mesyloxy)-3-methoxy-2-decanol acetate as an oil: ^1H NMR ($CDCl_3$) δ 5.09 (m, 1 H), 4.42 (m, 2 H), 3.42 (m, 4 H), 3.05 (s, 3 H), 3.14 (s, 3 H), 1.19–1.55 (m, 12 H), 0.90 (t, J = 6.6 Hz, 3 H).

Preparation of (2*S*,3*R*)-1,2-Epoxy-3-decanol ((−)-33). A solution of the diol mesylate **32** (0.360 g, 1.34 mmol) in 15 mL of anhydrous methanol was treated with 0.360 g of K_2CO_3 and stirred at room temperature for 5 h. The reaction mixture was then concentrated and purified by flash chromatography (neutral alumina, activity II, 5:1 hexane–EtOAc) to afford 0.190 g (77%) of (2*S*,3*R*)-1,2-epoxy-3-decanol ((−)-**33**) as an oil: $[\alpha]^{20}_D$ −15.3° (*c* 1.42, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 3.84 (m, 1 H), 3.03 (m, 1 H), 2.82 (dd, J = 6.4, 1.9 Hz, 1 H), 2.76 (dd, J = 6.4, 3.8 Hz, 1 H), 1.76 (d, J = 3.4 Hz, 1 H), 1.21–1.67 (m, 12 H), 0.90 (t, J = 6.6 Hz,

3 H); IR (NaCl) 3440 (br), 3060, 2960, 2930, 2860, 1470, 1380, 1070, 970, 850 cm^{-1}.

General Procedure for the Workup of the Payne Rearrangement–Opening Reaction of a 2,3-Epoxy Alcohol with an Amine. The reaction mixture is brought to room temperature and concentrated. After all of the volatile amine and most of the water are removed, a semisolid mass remains in the flask. This material is dried under high vacuum and then peracetylated in the usual way. The product thus obtained is taken up in CH_2Cl_2 and a minimum amount of water. The aqueous phase is extracted with CH_2Cl_2, and the combined organic portions are washed with water (1×), dried (Na_2SO_4), concentrated, and dried under high vacuum to constant weight.

Payne Rearrangement–Opening Reaction of (2*R,3*R**)-2,3-Epoxy-1-decanol (4) with Me_2NH/KOH.** The epoxy alcohol **4** (0.0531 g, 0.309 mmol) in 8 mL of a solution prepared by dissolving KOH (0.6 g, 10.7 mmol) in 20 mL of 40% aqueous Me_2NH was stirred at room temperature for 37 h and worked up according to the general procedure to afford 0.0875 g (94%) of a 10:2.8:1.0 mixture of (2*R**,3*S**)-1-(dimethylamino)-2,3-decanediol diacetate (**41a**), (2*R**,3*R**)-3-(dimethylamino)-1,2-decanediol diacetate (**41b**), and (2*R**,3*S**)-2-(dimethylamino)-1,3-decanediol diacetate (**41c**) as an oil. Purification by flash chromatography (4:1 hexane–acetone) affords 0.0507 g (55%) of **41a** and 0.0193 g (21%) of a mixture of **41b** and **41c**.

41a: ^1H NMR ($CDCl_3$) δ 5.16 (m, 1 H), 5.06 (m, 1 H), 2.52 (dd, J = 7.5, 14.9 Hz, 1 H), 2.39 (dd, J = 3.8, 14.9 Hz, 1 H), 2.24 (s, 6 H), 2.07 (s, 3 H), 2.05 (s, 3 H), 1.55 (m, 2 H), 1.28 (br, 10 H), 0.88 (t, J = 5.6 Hz, 3 H); IR (NaCl) 2960, 2940, 2870, 2835, 1745, 1465, 1375, 1250, 1230, 1040, 950, 850 cm^{-1}; mass spectrum, m/e 301 (parent ion). Anal. Calcd for $C_{16}H_{31}NO_4$: C, 63.76; H, 10.37; N, 4.65. Found: C, 63.64; H, 10.38; N, 4.87.

41b and 41c: IR (NaCl) 2960, 2930, 2860, 2800, 1745, 1460, 1375, 1240 (br), 1050, 840 cm^{-1}. Anal. Calcd for $C_{16}H_{31}NO_4$: C, 63.76; H, 10.37; N, 4.65. Found: C, 63.88; H, 10.60; N, 4.35.

Payne Rearrangement–Opening Reaction of (2*S*,3*S*)-2,3-Epoxy-1-hexanol (34) with Me_2NH/Me_4NOH. The epoxy alcohol **34** (0.0866 g, 0.746 mmol) in 4 mL of 40% aqueous Me_2NH was treated with 2.2611 g (12.5 mmol) of $Me_4NOH{\cdot}5H_2O$, stirred at room temperature for 36 h, and then worked up according to the general procedure to afford 0.1140 g (94%) of a 11.1:2.9:1.0 mixture of **42a**, **42b**, and **42c** along with a trace of **38** as an oil.

42a: ^1H NMR ($CDCl_3$) δ 5.04–5.21 (m, 2 H), 2.52 (dd, J = 8.1, 13.1 Hz, 1 H), 2.38 (dd, J = 4.5, 13.1 Hz, 1 H), 2.24 (s, 6 H), 2.07 (s, 3 H), 2.05 (s, 3 H), 1.22–1.71 (m, 4 H), 0.92 (t, 3 H); IR (NaCl) 2970, 2940, 2880, 1740, 1650, 1240, 1030, 840 cm^{-1}.

Payne Rearrangement–Opening Reaction of (2*S*,3*S*)-2,3-Epoxy-1-hexanol (34) with Et_2NH/KOH in THF. The epoxy alcohol **34** (0.083 g, 0.71 mmol) in 16 mL of 1:1:2 Et_2NH–0.5 N KOH–THF was heated to reflux for 20 h and worked up according to the general procedure to afford 0.155 g (80%) of a 6:1 mixture of (2*R*,3*S*)-1-(*N*,*N*-diethylamino)-2,3-hexanediol diacetate (**43**) and the combined regioisomers along with 1,2,3-hexanetriol triacetate (**38**). Flash chromatography (2:1 hexane–EtOAc) afforded 0.110 g (57%) of **43** as an oil: ^1H NMR ($CDCl_3$) δ 5.06–5.20 (m, 2 H), 2.49–2.59 (m, 6 H), 2.06 (s, 3 H), 2.05 (s, 3 H), 1.23–1.66 (m, 4 H), 1.01 (t, J = 7.4 Hz, 6 H), 0.93 (t, J = 7.3 Hz, 3 H).

Acknowledgment. This work was supported by a National Institutes of Health Grant (GM31124). Financial assistance in the form of unrestricted grants from Eli Lilly, Merck, and Exxon Chemicals is sincerely appreciated. C.H.B. thanks the National Science Foundation for a graduate fellowship. We are pleased to acknowledge the very enjoyable and fruitful collaboration with Professor Masamune and his group which led to some of the most important discoveries cited in this paper. We are deeply indebted to Steven M. Viti and Dr. Albert W. M. Lee of our group for their contributions both cited and uncited.

Supplementary Material Available: The experimental procedures and spectroscopic data not described in the Experimental Section (18 pages). Ordering information is given on any current masthead page.

Selective Transformations of 2,3-Epoxy Alcohols and Related Derivatives. Strategies for Nucleophilic Attack at Carbon-3 or Carbon-2

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Received July 31, 1984

The ring-opening reactions of 2,3-epoxy alcohols 1 under nonisomerizing conditions were investigated. There is an inherent tendency for ring-opening at the C-3 position of 1 due to an electronic effect of the C-1 hydroxyl group. Since the hydroxyl group is a relatively weak inductively electron-withdrawing group, C-3 selective ring-opening reactions are observed only with certain simple 2,3-epoxy alcohols. Since an electronic effect of the C-1 hydroxyl group was found to promote ring-opening at the C-3 position of 1, the ring-opening reactions of 2,3-epoxy acetals and 2,3-epoxy amides were also explored, under the assumption that the acetal and amide groups might promote C-3 opening more strongly than the hydroxyl group. As expected, 2,3-epoxy acetals were opened with various nucleophiles exclusively at the C-3 position. However, the ring-opening reactions of 2,3-epoxy amides exhibited variable behavior, affording the C-3 ring-opened products with $Mg(N_3)_2$ and the C-2 ring-opened products with PhSK.

There are three reactive sites for nucleophilic substitution in 2,3-epoxy alcohol 1. Regioselective nucleophilic substitution at the C-1 position is best accomplished by Payne rearrangement–opening, direct displacement on the corresponding epoxy sulfonate, or through conversion to the 1,2-epoxy 3-ol via the "diol sulfonate" or "diol sulfide" methods.[1] Nucleophilic substitution of 1 at the C-2 or C-3 positions is not as straightforward because the ring-opening reactions are not always regioselective. One reliable means of regioselective ring-opening of a 2,3-epoxy alcohol utilizes the C-1 hydroxyl group as a point of attachment for in-

(1) See: Behrens, C. H.; Ko, S. Y.; Sharpless, K. B.; Walker, F. J. *J. Org. Chem.*, preceding paper in this issue and references cited therein.

0022-3263/85/1950-5696$01.50/0