Reaction between Vicinal Diols and Hydrogen Bromide in Acetic Acid; Synthesis of Chiral Propylene Oxide

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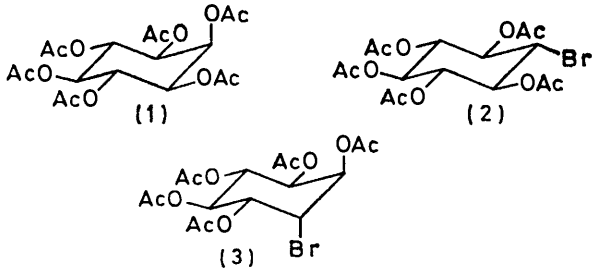
Several vicinal diols react rapidly with 6M-hydrogen bromide in acetic acid to afford vicinal acetoxy-bromides in excellent yield. The mechanism, scope, and limitations of this reaction have been explored. Its mechanism involves monoacetylation of the diol, cyclisation to a 1,3-dioxolan-2-ylium ion, and capture of this intermediate by bromide ion. This has been established by kinetic studies, determination of substrate stereospecificity, and observation of intermediate 1,3-dioxolan-2-ylium ions by n.m.r. spectroscopy. The preparative value of the reaction is illustrated by its application in a simple three-stage synthesis of optically pure (*S*)-propylene oxide from readily available (*S*)-ethyl lactate.

It has been reported that *cis*-cyclodecane-1,2-diol reacts with hydrogen bromide in refluxing acetic acid to yield 1-acetoxy-2-bromocyclodecane [1] (stereochemistry undefined) and that treatment of *myo*-inositol hexa-acetate (1) with this reagent gives a mixture of the bromo-penta-acetates (2) and (probably) (±) (3).[2] Perhaps the



vigour of the experimental conditions apparently required for these reactions and the lack of understanding of their mechanism discouraged further development of this method for preparing acetoxy-bromides.† We have found that the reaction between vicinal diols and hydrogen bromide–acetic acid (HBA) is, in many cases, a general stereospecific reaction of such diols which gives excellent yields of vicinal acetoxy-bromides at 37°. In this paper we define the mechanism of this reaction and describe some synthetic applications.

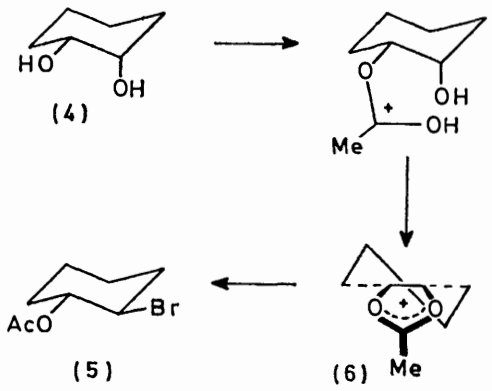
Mechanism.—The characteristics of the reaction between vicinal diols and HBA are clearly demonstrated by use of *cis*- and *trans*-cyclohexane-1,2-diol as substrates. On exposure to HBA (3 mol. equiv. of HBr per mol. equiv. of diol) at 37°, the *trans*-diol is converted into *trans*-1,2-diacetoxycyclohexane, which is stable under these conditions for at least 7 days. Under the same conditions the *cis*-diol (4) disappears (half-life *ca.* 7 min) to give *trans*-1-acetoxy-2-bromocyclohexane (5) (half-time for appearance *ca.* 12 min). The exclusive *trans*-stereochemistry of this product was shown by its reaction with potassium hydroxide in methanol to give a high yield of 1,2-epoxycyclohexane, but no trace of cyclohexanone (g.l.c. analysis). Samples from the reaction mixture of *cis*-cyclohexane-1,2-diol with HBA at 37° were subjected to an aqueous work-up, followed by g.l.c. analysis, and revealed *cis*-2-acetoxycyclohexanol to be

† *Added in proof.* McGhie and his co-workers (F. J. Julietti, J. F. McGhie, B. L. Rao, W. A. Ross, and W. A. Cramp, *J. Chem Soc.*, 1960, 4514 and later papers), following earlier observations (especially A. Albitzky, *J. prakt. Chem.*, 1903, **67**, 289), have used the reaction between vicinal diols and hydrogen bromide–acetic acid *at room temperature* to prepare acetoxy-bromides derived from long-chain fatty acids. These materials were not isolated but were converted by basic treatment into epoxy-acids. The overall stereospecificity of the process was established and agrees with that found in the present work.

[1] A. T. Blomquist, R. E. Burge, and A. C. Sucsy, *J. Amer. Chem. Soc.*, 1952, **74**, 3636.

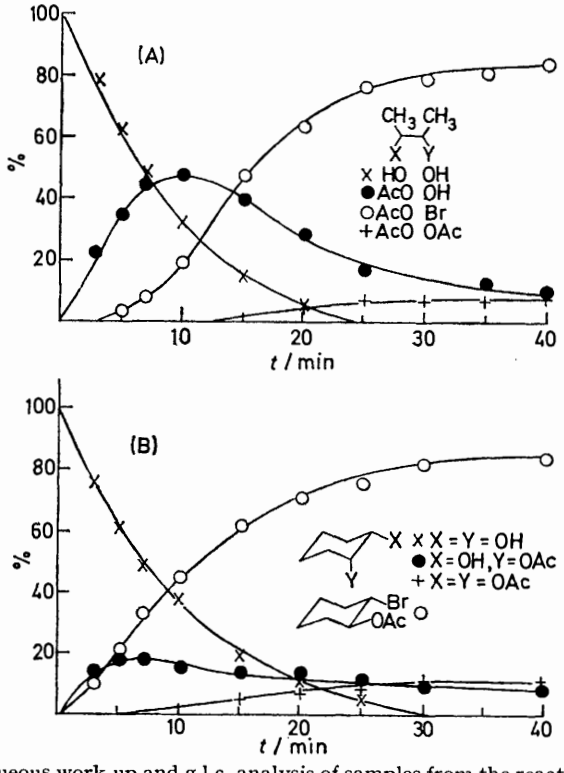
[2] G. E. McCasland and E. C. Horswill, *J. Amer. Chem. Soc.*, 1953, **75**, 4020.

an apparent intermediate (see Figure). However, signals from *cis*-2-acetoxycyclohexanol are not evident in n.m.r. spectra of the reaction mixture taken at intervals.



SCHEME 1

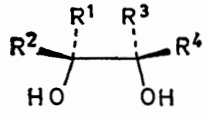
Signals which do appear, at τ 4·08 and 7·10, and then disappear, are consistent [3] with those of the methine protons and methyl protons, respectively, of the 2-methyl-(*cis*-4,5-tetramethylene)-1,3-dioxolan-2-ylium ion



Aqueous work-up and g.l.c. analysis of samples from the reactions at 37° of 3 mol. equiv. of HBr–acetic acid with (A) butane-2,3-diol and (B) *cis*-cyclohexane-1,2-diol

(6), which in the analysis mentioned is quenched by water to yield *cis*-2-acetoxycyclohexanol. In the presence of bromide ions the intermediate (6) is captured by S_N2 attack to give compound (5). (These are known reactions of isolated 1,3-dioxolan-2-ylium ions.[3,4]) The mechanism of conversion of the *cis*-diol (4) into the *trans*-acetoxy-bromide (5) is therefore formulated as shown in Scheme 1. The key step is cyclisation of protonated *cis*-2-acetoxycyclohexanol to the 2-methyl-(*cis*-4,5-tetramethylene)-1,3-dioxolan-2-ylium ion (6). In general, this can only occur readily when a hydroxy-group and protonated acetoxy-group are proximate, and formation of the planar five-membered ring of the 1,3-dioxolan-2-ylium ion is not impeded by other conformational demands within this species. The latter point explains the failure of *trans*-cyclohexane-1,2-diol to yield a 2-methyl-(*trans*-4,5-tetramethylene)-1,3-dioxolan-2-ylium ion and derived acetoxy-bromide. The contrasting behaviour of *cis*- and *trans*-cyclohexane-1,2-diols towards HBA is analogous to the widely differing propensity of various carbohydrates to form a cyclic carbonate on treatment with phosgene.[5]

Our observations extend those of Winstein,[6] who found that *cis*-1,2-diacetoxycyclohexane, but not the corresponding *trans*-isomer, gave *trans*-2-chlorocyclohexanol among other products, on treatment with hot aqueous hydrochloric acid. This was formulated as proceeding *via* monodeacetylation, cyclisation to the 1,3-dioxolan-2-ylium ion (6), capture by chloride ion, and finally deacetylation. Formation of the ion (6) in this manner was called ' front-side participation,' in contrast to the well known routes to ion (6) *via* back-side participation of a neighbouring acetoxy-group. Pedersen [7] has shown that whilst *trans*-1,2-diacetoxycyclohexane is stable to liquid hydrogen fluoride, the corresponding *cis*-isomer is converted into the ion (6). He has further demonstrated that hydrogen fluoride catalyses the reaction between carboxylic acids and vicinal diols producing 1,3-dioxolan-2-ylium ions.[8] Since fluoride ion in a protic medium is a weaker nucleophile than bromide ion,[9] 1,3-dioxolan-2-ylium ions persist in the presence of hydrogen fluoride but react further with hydrogen bromide.



(7) $R^1 = R^2 = R^3 = R^4 = H$
(8) $R^1 = R^2 = R^3 = H$, $R^4 = Me$
(9) $R^1 = R^3 = H$, $R^2 = R^4 = Me$
(10) $R^1 = R^4 = H$, $R^2 = R^3 = Me$
(11) $R^1 = R^2 = R^3 = H$, $R^4 = Ph$
(12) $R^1 = R^3 = H$, $R^2 = CH_3[CH_2]_7$, $R^4 = [CH_2]_7{\cdot}CO_2H$

The acyclic diols (7)—(12) all react readily with HBA to give vicinal acetoxy-bromides. In the Table, kinetic data for the reactions of several diols are compared with

[3] C. B. Anderson, E. C. Friedrich, and S. Winstein, *Tetrahedron Letters*, 1963, 2037.
[4] C. U. Pittman, S. P. McManus, and J. W. Larsen, *Chem. Rev.*, 1972, **72**, 357.
[5] L. Hough, J. E. Priddle, and R. S. Theobald, *Adv. Carbohydrate Chem.*, 1960, **15**, 91.
[6] R. Boschan and S. Winstein, *J. Amer. Chem. Soc.*, 1956, **78**, 4921.
[7] C. Pedersen, *Tetrahedron Letters*, 1967, 511.
[8] I. Lundt and C. Pedersen, *Acta Chem. Scand.*, 1972, **26**, 1938.
[9] A. J. Parker, *Quart. Rev.*, 1962, 163.

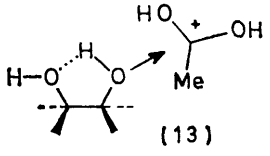
kinetic data for the reactions of some alcohols with HBA. Monitoring reactions by n.m.r. spectroscopy shows that acetylation of these alcohols is followed by

TABLE *

Substrate	$t_{\frac{1}{2}}$ Ac	$t_{\frac{1}{2}}$ Br
Butan-1-ol	2·4	870
Butan-2-ol	29·0	204
Cyclohexanol	38·6	234
Ethane-1,2-diol	Indeterminate	$\ll 3$
Propane-1,2-diol	Indeterminate	< 3
Butane-2,3-diol	6·6	16·3
trans-Cyclohexane-1,2-diol	5·2	$\gg 7$ days (see text)
cis-Cyclohexane-1,2-diol	6·8	11·5
cis-1,2-Diacetoxycyclohexane		366
cis-1,2-Diacetoxycyclohexane ($+\frac{1}{2}H_2O$)		330

* Data for reactions with 3 mol. equiv. HBr–acetic acid at 37°; $t_{\frac{1}{2}}$ is the time (min) required to generate 50% of the theoretical yield of monoacetate (Ac) or acetoxy-bromide (Br). The use of less than 3 mol. equiv. HBr–acetic acid gave slower and incomplete reactions: for example, with 1 mol. equiv. of HBr–acetic acid propane-1,2-diol gave after 30 min 53% acetoxy-bromide, 26% 1-acetoxy-propan-2-ol, and 21% 1,2-diacetoxypropane, whereas the reaction with 3 mol. equiv. gave nearly 100% acetoxy-bromide after 8 min.

production of the bromide. In the case of butane-2,3-diol * and presumably other diols (see later), the reaction progresses through monoacetylation to a 1,3-dioxolan-2-ylium ion and on to acetoxy-bromide. 2,4,5-Trimethyl-1,3-dioxolan-2-ylium ions were observed directly by n.m.r. spectroscopy and their combined concentration was periodically determined by an aqueous work-up of samples and estimation by g.l.c. analysis of the derived 2-acetoxybutan-3-ol (see Figure). As expected, treatment of isolated 2-acetoxybutan-3-ol with HBA leads to acetoxy-bromide even more rapidly than the reaction with the parent diol. Since 2-acetoxybutan-3-ol is not observed spectroscopically (n.m.r.) in the reaction starting from butane-2,3-diol, the rate of appearance of 2,4,5-trimethyl-1,3-dioxolan-2-ylium ions corresponds to the rate of monoacetylation of the diol. It is notable that, with every vicinal diol investigated, the rate of its mono-acetylation is appreciably greater than the rate of acetylation of a comparable alcohol. The half-times for acetylation of cyclohexanol and monoacetylation of *cis*- and *trans*-cyclohexane-1,2-diol

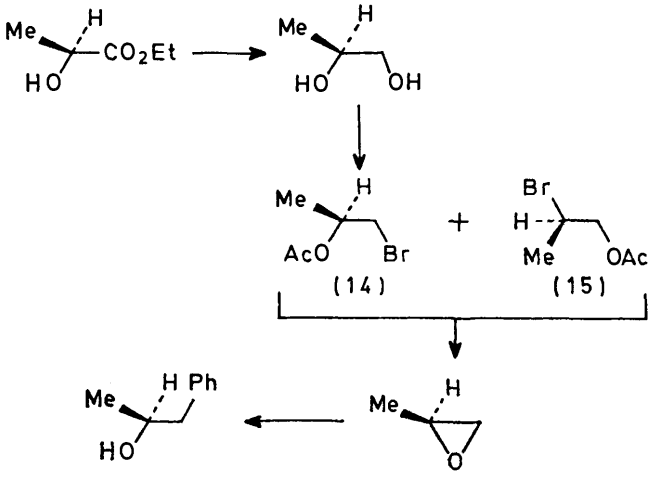


(13)

are 39, 7, and 5 min, respectively. For comparison, the value for cyclohexanol should be halved because of a statistical factor with the diols. This rate enhancement may be due to intramolecular catalysis of acetylation [see (13)] occurring with the diols. Previous studies [10] of related phenomena have given inconclusive results and the point requires further investigation.

Since the reaction between butan-2-ol and HBA leading to bromide is faster than that with butan-1-ol, the former probably proceeds with at least partial S_N1 character, whilst the latter goes *via* S_N2 displacement of a protonated acetoxy-group by bromide ion. That each of these reactions is much slower than the reactions of vicinal diols (see Table) further demonstrates the fundamental difference in mechanism between the reactions of alcohols and diols with HBA.

The reaction between propane-1,2-diol and HBA is regioselective, giving 94% of 2-acetoxy-1-bromopropane and 6% of 1-acetoxy-2-bromopropane. In this case the reaction is also stereospecific: treatment of the mixture of acetoxy-bromides [*i.e.* (*S*)-2-acetoxy-1-bromopropane



SCHEME 2

(14) and (*R*)-1-acetoxy-2-bromopropane (15) obtained from (+)-(*S*)-propane-1,2-diol] with potassium pentylate gave (+)-(*S*)-propylene oxide having optical rotations in a variety of solvents comparable with the best literature values.[11] Furthermore, the (−)-(*S*)-1-phenylpropan-2-ol obtained from treating this epoxide with phenyllithium has optical rotations in several solvents which are numerically nearly identical with those measured for the (*R*)- and (*S*)-isomers prepared by a classical resolution of (*RS*)-1-phenylpropan-2-ol.[12] The sequence of reactions from (+)-(*S*)-propane-1,2-diol is summarised in Scheme 2. It is anticipated that the reaction between HBA and other vicinal diols possessing primary or secondary alcohol functions and alkyl substituents will also be stereospecific.†

* A mixture of diastereomers [mainly (±)-isomer] was used (see next footnote).

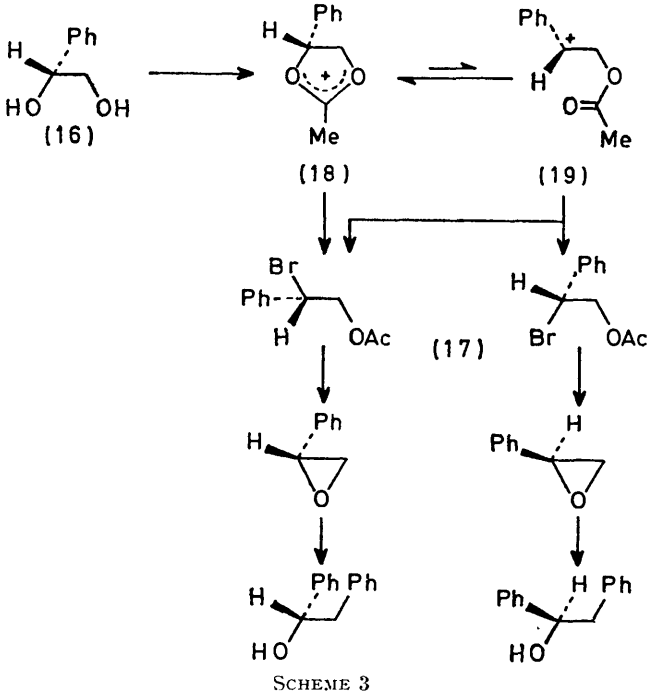
† We have recently shown that *meso*-butane-2,3-diol (99·8% pure) gives *meso*-2,3-epoxybutane (>99% pure) and (±)-butane-2,3-diol (94·4% containing 5·6% *meso*-isomer) gives (±)-2,3-epoxybutane (94 ± 2%) using the method described for the conversion of propane-1,2-diol into propylene oxide. (We thank Mr. L. Carr for these experiments and Bayer for gifts of the butane-2,3-diols.)

[10] K. W. Buck, J. M. Duxbury, A. B. Foster, A. R. Perry, and J. M. Webber, *Carbohydrate Res.*, 1966, **2**, 122.

[11] Y. Kumata, J. Furukawa, and T. Fueno, *Bull. Chem. Soc. Japan*, 1970, **43**, 3920.

[12] (*a*) J. Kenyon, H. Phillips, and V. P. Pittman, *J. Chem. Soc.*, 1935, 1072; (*b*) R. H. Pickard and J. Kenyon, *ibid.*, 1914, **105**, 1124.

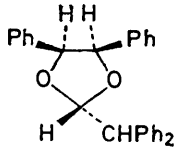
The reaction between (−)-(*R*)-1-phenylethane-1,2-diol (16) and HBA is regiospecific giving (+)-2-acetoxy-1-bromo-1-phenylethane (17), but the (+)-styrene oxide derived by treatment of this acetoxy-bromide with base is only 88% optically pure [predominantly (*R*)-isomer]. This value was checked by treating the styrene oxide with phenyl-lithium, which gave 1,2-diphenylethanol of 88% optical purity. The intermediate 2-methyl-4-phenyl-1,3-dioxolan-2-ylium ion (18) suffers preferential attack at C-4 by bromide ion. This behaviour is analogous to the predominant mode of ring opening of styrene oxide observed in the presence of acids [13] and to the direction of addition of acetyl hypobromite to styrene [14] (giving 2-acetoxy-1-bromo-2-phenylethane). In each case, at the transition state for attack by the anion, there may be appreciable positive character at the benzylic carbon atom. The observed loss of optical integrity may be due to partial racemisation of (18) *via*



SCHEME 3

an acyclic benzylic cation (19). The chemistry based on 1-phenylethane-1,2-diol is summarised in Scheme 3.

When *meso*-1,2-diphenylethane-1,2-diol was exposed to HBA, the reaction mixture solidified after 2 min and gave 30% of the dioxolan (20) and polymeric products, but no acetoxy-bromide (n.m.r. analysis). Compound (20) arises *via* a pinacol-type rearrangement at the expense of formation of acetoxy-bromide and has been reported [15] as a product from treating *meso*-1,2-diphenylethane-1,2-diol with sulphuric acid or 'phosphorus pentoxide.'



(20)

Synthetic Applications.—With respect to the synthesis of acetoxy-bromides from vicinal diols the described reaction is more convenient than the two-step procedures published recently.[16,17] It will be of interest to determine whether these methods are successful * where our procedure fails, for although 1,3-dioxolan-2-ylium ions are also involved as intermediates, these species are generated in a different manner. Where our reaction is stereospecific the way is opened to the convenient preparation of a variety of derived chiral molecules, since many chiral vicinal diols are readily available (*e.g.* by reduction of chiral α-hydroxy-acids). We have used the reaction as a route to chiral alkylcobaloximes [18] (*i.e.* with a chiral alkyl group) and epoxides.† Treatment of the mixture of acetoxy-bromides (see Scheme 2) from (+)-(*S*)-propane-1,2-diol [readily prepared by reduction of commercial (−)-(*S*)-ethyl lactate] with 1 equiv. of potassium pentylate in pentyl alcohol gave 85% of analytically and optically pure (+)-(*S*)-propylene oxide, distilled directly from the reaction mixture. This method of preparation of chiral propylene oxide is far superior to that described in the literature [19] and should also be applicable to the (*R*)-isomer.

We have investigated the reaction between (+)-(*S*)-propylene oxide and organolithium reagents as a potential convenient route to certain chiral alcohols. The reaction with methyl-lithium gave only a low yield of butan-2-ol, accompanied by other, unidentified products. However, with phenyl-lithium, (+)-(*S*)-1-phenylpropan-2-ol was obtained in nearly quantitative yield.

We are exploring the possibility of using the described reaction of diols in a simple sequence for inverting the configuration of an alkene. In principle, the sequence in Scheme 4 can be visualised [20] and we have accomplished an undistinguished conversion of oleic acid into elaidic acid in this manner. The outstanding unsolved problem concerns the last step, since conversion of such acetoxy-bromides into alkenes by treatment with zinc or iodide

* *Added in proof.* M. S. Newman and C. H. Chen (*J. Org. Chem.*, 1973, **38**, 1173) have prepared optically pure styrene oxide by their method.

† *Added in proof.* J. F. McGhie, W. A. Ross, J. W. Spence, and F. J. James, *Chem. Ind.*, 1971, 1074, have also used the reaction between HBA and vicinal diols to give a chiral epoxide.

[13] E. L. Eliel in 'Steric Effects in Organic Chemistry,' ed. M. S. Newman, Wiley, London, 1956, p. 106.

[14] H. Haubenstock and C. VanderWerf, *J. Org. Chem.*, 1964, **29**, 2993.

[15] W. Madelung and M. E. Oberwegner, *Annalen*, 1936, **526**, 226.

[16] A. Rieche, E. Schmitz, W. Schade, and E. Beyer, *Chem. Ber.*, 1961, **94**, 2926; S. Hanessian and N. R. Plessas, *J. Org. Chem.*, 1969, **34**, 1035, 1045, 1053.

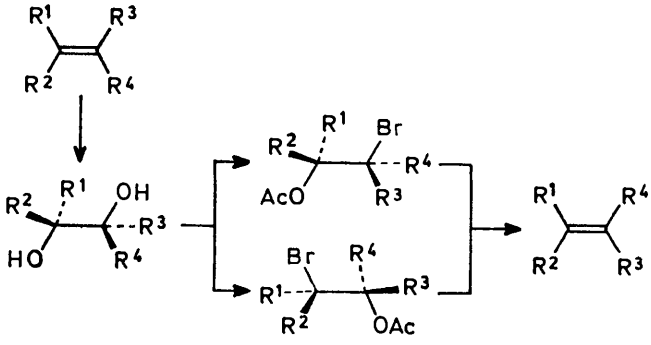
[17] M. S. Newman and C. H. Chen, *J. Amer. Chem. Soc.*, 1972, **94**, 2149.

[18] B. T. Golding and S. Sakrikar, *J.C.S. Chem. Comm.*, 1972, 1183.

[19] P. A. Levine and A. Walti, *J. Biol. Chem.*, 1926, **68**, 415.

[20] This is similar to the method of D. E. Ames and R. E. Bowman, *J. Chem. Soc.*, 1951, 1079, for converting vicinal diols stereospecifically into alkenes.

ions occurs non-stereospecifically.[21] It should be mentioned in this context that Blomquist[1] has reported the formation of pure *trans*-cyclodecene from treating his 1-acetoxy-2-bromocyclodecane with zinc. Since special



SCHEME 4

conformational factors may be at work here, the reactions of medium-sized ring vicinal diols with HBA and the chemistry of the derived acetoxy-bromides should be investigated systematically.

EXPERIMENTAL

Starting Materials and Standard Samples.—The commercial saturated solution of hydrogen bromide in acetic acid was supplied as 48% w/v, *d ca.* 1·4 g ml^{-1}, and was kept in the refrigerator. Titrations at three-monthly intervals showed this material to contain reproducibly 4·2 mmol HBr per g of solution.

Butan-1-ol, butan-2-ol, cyclohexanol, ethane-1,2-diol, (±)-propane-1,2-diol, and butane-2,3-diol [mixture of diastereomers, mainly (±)-isomer] were obtained commercially and redistilled once before use.

Acetates of alcohols and diacetates of diols were obtained by addition of a drop of conc. sulphuric acid to a mixture of the alcohol or diol with a slight excess of acetic anhydride. After 2 h at room temperature, the mixture was quenched with water, neutralised with solid sodium carbonate, and extracted with ether. The extract was dried and evaporated to give a product of high purity which was distilled. 2-Acetoxybutan-3-ol was prepared by the same procedure from butane-2,3-diol and 1 mol. equiv. of acetic anhydride. The resulting mixture of diol, monoacetate, and diacetate was separated by preparative g.l.c. (20 ft E301; 150°). *cis*- and *trans*-Cyclohexane-1,2-diol and *meso*-1,2-diphenylethane-1,2-diol were prepared as described (refs. 22—24, respectively). The *cis*-cyclohexane-1,2-diol was best purified from adipic acid formed through overoxidation by sublimation (100—111° and 11 mmHg) and recrystallisation from ethyl acetate (yield 20%; m.p. 98°). Epoxycyclohexane was obtained in 72% crude yield from cyclohexene and a slight excess of *m*-chloroperbenzoic acid and was used as such for a standard comparison.

Kinetic Experiments (*see Table*).—(a) *Following experiments by n.m.r. spectroscopy.* Experiments were run on *ca.* 0·5—1·0 mmol scale in n.m.r. sample tubes at the temperature of the preheater (37°). For liquid substrates, a suitable volume of HBr–acetic acid was transferred to the stoppered n.m.r. tube and weighed. The calculated amount of substrate was added from a microsyringe, the reactants were mixed at room temperature, and the sample tube was placed in the preheater or probe of the spectrometer (Perkin-Elmer R12). For crystalline diols, the compound was weighed in the n.m.r. tube and then the calculated amount of HBr–acetic acid was weighed directly into the tube.

No special procedures were used for rigorous exclusion of moisture, but operations were performed as quickly as possible without undue exposure of the reagents to the atmosphere. The reactants were not accurately thermostatted before mixing. Since mixing of alcohols and diols, particularly the latter, is slightly exothermic on the scale involved here, this may bring the temperature up to about 37° from room temperature, and could be a source of inaccuracy in subsequent kinetic measurements. However, no irregularities were observed in graphical plots (see Figure).

(b) *Analysis of samples by g.l.c. and n.m.r.* Reactions set up as in (a) were run in stoppered sample vials in a constant temperature bath at 37° on *ca.* 5 mmol scale. Samples containing *ca.* 0·5 mmol of substrate (*ca.* 0·25 ml for reactions with 3 mol. equiv. of HBr–acetic acid) were withdrawn at intervals and transferred into cold water (5 ml). The mixtures were neutralised with solid sodium carbonate and extracted with ether (4 × 10 ml). The extracts were combined, dried, and evaporated. It was important to neutralise the quenched sample as soon as possible as the aqueous acidic medium was efficient at acetate hydrolysis. Ethane- and propane-1,2-diol are not extracted completely from water by ether, but the other diols and products were extracted satisfactorily by this procedure.

In g.l.c. analyses 6 ft E301 and Carbowax columns were used to check both product identities and quantitative analyses by n.m.r. spectroscopy. The reaction mixtures from butane-2,3-diol and *cis*-cyclohexane-1,2-diol could not be satisfactorily analysed by n.m.r. spectroscopy because of variability and obscuring of the OH resonances. The graphs of the Figure were drawn from g.l.c. results (6 ft E301; 130°). Calibration with pure materials showed that in both series, peak areas had to be multiplied by 2·4, 1·0, 1·0, and 0·67 for diol, monoacetate, acetoxy-bromide, and diacetate respectively to convert to molar ratios. Slight variations in running conditions sometimes caused acetoxy-bromides to give multiplet humps on g.l.c. analysis owing to decomposition.

Preparative Procedures

Chiral Propylene Oxide.—(−)-(*S*)-Ethyl lactate is readily available in kilogram quantities from Fluka A.G. and was used as supplied. A redistilled sample had $[\alpha]_D^{26}$ −13·9° (neat), d^{26} 1·044; a sample prepared from (+)-(*S*)-lactic acid (Sigma) by refluxing with excess of ethanol and a catalytic amount of concentrated sulphuric acid and subsequent azeotropic distillation had $[\alpha]_D^{26}$ −14·6° (neat). The literature shows a wide range of values for the optical rotation of ethyl lactate, probably owing to the presence of impurities having high rotations; *e.g.* the dimer, 2,5-dimethyl-1,4-dioxan-3,6-dione, has $[\alpha]_D$ −298° (*c* 1·17 in benzene).[25]

[21] H. O. House and R. S. Ro, *J. Amer. Chem. Soc.*, 1958, **80**, 182.
[22] M. Mugdan and D. P. Young, *J. Chem. Soc.*, 1949, 2988.
[23] A. Roebuck and H. Adkins, *Org. Synth.*, 1955, Coll. Vol. III, 217.
[24] L. F. Fieser, *J. Chem. Educ.*, 1954, **31**, 291.
[25] E. Jungfleisch and M. Godchot, *Compt. rend.*, 1907, **141**, 111.

(+)-(S)-*Propane*-1,2-*diol*.—(−)-(*S*)-Ethyl lactate (33 g, 0·28 mol) in dry ether (150 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (10·8 g, 0·284 mol) in dry ether (200 ml) under nitrogen at such a rate as to maintain steady reflux (*ca.* 30 min). The mixture was stirred at room temperature for 3 h, then a slight excess of water (25 ml) was added carefully, and stirring was continued for a further 1·5 h. The mixture was filtered, and the solid washed well with ether and dichloromethane. The filtrate was dried and evaporated to give the product (5 g, 23%). 2N-Sulphuric acid was added to the solid until the milky suspension was just acidic, and this was then subjected to continuous extraction with twice the volume of dichloromethane (*ca.* 150 ml). After 117 h this gave a combined yield of 17·2 g (81%) of g.l.c.-pure material, which was distilled at 93° and 18 mmHg (yield 15·0 g, 71%); α_D^{25} +16·28° (neat); $[\alpha]_D^{20}$ +20·7° (*c* 7·5 in H_2O) [highest literature value for optical rotation, for (−)-(*R*)-isomer from yeast reductase reduction of hydroxyacetone: [26] α_D^{26} −15·9° (neat)].

Acetoxybromopropanes.—Hydrogen bromide–acetic acid (71 g, 0·3 mol) was added to (+)-(*S*)-propane-1,2-diol (7·6 g, 0·1 mol) with stirring and ice-cooling during *ca.* 5 min. After stirring at room temperature for 30 min, water (200 ml) was added, and the mixture was neutralised with solid sodium carbonate. The neutral solution was extracted with ether (3 × 150 ml), and the extracts were combined, dried, and evaporated. The residue (18 g) was 94% pure by g.l.c. (6 ft E301; 100°), and was distilled; the major fraction, b.p. 57° at 11 mmHg (16·0 g, 89%), was pure by g.l.c.; d^{26} 1·429 g ml^{-1}, n_D^{20} 1·4481, α_D^{26} −9·46° (neat), $[\alpha]_D^{23}$ −13·55° (*c* 5·8 in $CHCl_3$); τ (CCl_4) 4·98 (1H, m), 6·57 (2H, d), and 8·66 (3H, d) due to 2-acetoxy-1-bromopropane (94% by integration) and 5·82 (3H) and 8·30 (3H, d) due to 1-acetoxy-2-bromopropane (6%).

(−)-(S)-1,2-*Epoxypropane*.—0·86N-Potassium pentyloxide in pentyl alcohol (59·1 ml, 50 mmol) was added dropwise to a stirred solution of the redistilled mixture of acetoxybromopropanes (9·05 g, 50 mmol) in pentyl alcohol (20 ml) at room temperature during *ca.* 20 min. Potassium bromide was precipitated after addition of the first few drops, and when addition was complete, the mixture was warmed to about 100°. The epoxypropane was distilled out through a 10 cm Vigreux column with efficiently cooled condenser and receiver giving the product (2·47 g, 85%), b.p. 35°, pure by g.l.c. (6 ft E301; 50°), which showed the absence of any pentyl alcohol.

Solvent	Concn.	$[\alpha]_D^{22}$ (°)	Lit.[11] $[\alpha]_D^{20}$ (°) (*c* 5)
$CHCl_3$	5·04	−8·21	+8·5
CCl_4	5·83	−18·55	+18·7
Et_2O	5·69	−16·6	+17·0
EtOH	5·61	−8·56	+7·9
None			+12·53 [for (+)-(*R*)-isomer]

(+)-(S)-1-*Phenylpropan*-2-*ol*.—(−)-(*S*)-1,2-Epoxypropane (3·37 ml, 50 mmol) was added dropwise to a stirred, ice-cooled ethereal 1·0N-solution of phenyl-lithium (50 ml, 50 mmol) under nitrogen at such a rate that reaction was just detectable (*ca.* 40 min required for the addition). Stirring was continued at room temperature. In one run the mixture rapidly became cloudy and almost set solid; in another run this did not occur until 2 h after addition was complete. After 4 h water (25 ml) was added to dissolve the solid, the ether layer was removed, and the aqueous solution was extracted with two more portions (50 ml) of ether. The combined extracts were washed once with a little water, dried, and evaporated. The residue (7·0 g) was distilled at 103—104° and 17 mmHg to give (+)-(*S*)-phenylpropan-2-ol (6·1 g, 88%), pure by g.l.c. (6 ft E301; 130°), n_D^{27} 1·5181 (lit.,[12a] n_D^{20} 1·5190), τ ($CDCl_3$) 2·72 (5H, s), 6·02 (1H, s), 7·31 (2H, d, *J* 6·5 Hz), 8·01 (1H, s), and 8·82 (3H, d, *J* 6·0 Hz) (Found: C, 79·05; H, 8·8. Calc. for $C_9H_{12}O$: C, 79·35; H, 8·9%). The highest literature $[\alpha]_D$ value is for the (−)-(*R*)-isomer.[12a] The values for the (+)-(*S*)-isomer given are derived by appropriate correction of values given by the same author [12b] for a sample having a rotation of slightly lower magnitude {$[\alpha]_D^{20}$ +26·24° (neat)}.

Solvent	Concn.	$[\alpha]_D^{25}$ (°)	Lit. $[\alpha]_D^{25}$ (°)	$[\alpha]_D^{20}$ (°)
None		+25·6	−27·70	
Et_2O	5·12	+20·5	−20·20	
EtOH	4·55	+16·5		+17·0
$CHCl_3$	4·76	+39·2		+41·2

Reaction of propylene oxide with ethereal methyl-lithium under a variety of conditions gave complex product mixtures containing only *ca.* 20% of the expected butan-2-ol.

(+)-(R)-*Styrene Oxide*.—(−)-(R)-1-*Phenylethane*-1,2-*diol*. (−)-(*R*)-Mandelic acid {Koch–Light; $[\alpha]_D^{26}$ −157·0° (*c* 3·15 in H_2O) [lit.,[27] $[\alpha]_D^{18}$ +157·5° (*c* 3·5 in H_2O) for (+)-(*S*)-isomer]} (7·6 g, 50 mmol) dissolved in dry ether (150 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (2·0 g, 53 mmol) in dry ether (50 ml) under nitrogen. The mixture was refluxed under nitrogen for 4 h; then water (4·5 ml) was added carefully, and stirring was continued for 30 min. The mixture was filtered, the filter pad washed through well with ether, and the filtrate dried and evaporated to give (−)-(*R*)-1-phenylethane-1,2-diol (3·0 g, 43%). The residue from filtration was made acid with 2N-sulphuric acid, and the milky suspension was extracted with ether (4 × 75 ml). The combined extracts were dried and evaporated to give pure (−)-(*R*)-mandelic acid (4·5 g, 57%) that was recycled in a second reduction. The (−)-(*R*)-1-phenylethane-1,2-diol, recrystallised once from benzene–petroleum, had m.p. 65° (lit.,[28] 65—66°), $[\alpha]_D^{26}$ −40·4° (*c* 3·34 in H_2O) {lit.,[28] $[\alpha]_D^{20}$ +40·6° (*c* 3·23 in H_2O) for (+)-(*S*)-isomer}.

(+)-(S)-2-*Acetoxy*-1-*bromo*-1-*phenylethane*. Cold HBr–acetic acid (12·4 g, 52·2 mmol) was added dropwise to (−)-(*R*)-1-phenylethane-1,2-diol (2·4 g, 17·4 mmol) during *ca.* 5 min, and the mixture was stirred at room temperature for 40 min. Water (25 ml) was added, and the solution was neutralised with sodium carbonate and extracted with ether (3 × 30 ml). The combined extracts were dried and evaporated to give (+)-(*S*)-2-acetoxy-1-bromo-1-phenylethane (3·93 g, 93%), d^{25} 1·415 g ml^{-1}, $[\alpha]_D^{25}$ +93·5° (*c* 5·63 in CCl_4), τ (CCl_4) 2·72 (5H, s), 4·98 (1H, dd, *J* 6·7 and 7·0 Hz), and 5·56 (2H, d). This product was not distilled. The isomeric homogeneity was established by comparison of the n.m.r. spectrum (absence of PhC*H*·OAc resonance) with that of 1,2-diacetoxy-1-phenylethane.

(+)-*Styrene oxide* [*principally* (R)-*isomer*]. 3·43N-Potassium hydroxide in methanol (6·34 ml, 21·7 mmol) was

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[28] L. Arpesella, A. LaManna, and M. Grassi, *Gazzetta*, 1955, **85**, 1354.

added dropwise to a stirred solution of (+)-(*S*)-2-acetoxy-1-bromo-1-phenylethane (5·3 g, 21·7 mmol) in methanol (5 ml) at room temperature. After stirring for 30 min, the precipitated potassium bromide was dissolved with water (20 ml), and the mixture was extracted with ether (4 × 25 ml). The combined extracts were washed once with a little water, dried, and evaporated. The residue (2·3 g, 89%) was pure styrene oxide (by g.l.c.; 6 ft E301; 130°), and was distilled at 83—84° and 17 mmHg (yield 2·03 g, 79%), $[\alpha]_D^{26}$ +27·3° (neat). {The highest value in the literature is $[\alpha]_D$ +35·2° (neat),[29] according to which the above material is 88·8% optically pure.}

(+)-1,2-*Diphenylethanol* [*principally* (R)-*isomer*]. 0·54M-Phenyl-lithium in ether (3·71 ml, 2 mmol) was added dropwise to a stirred solution of the (+)-styrene oxide (0·24 g, 2 mmol) in dry ether (2 ml) under nitrogen, with ice cooling. After 4 h stirring at room temperature, water (6 ml) was added, the ether layer was removed, and the aqueous solution was extracted with ether (3 × 15 ml). The extracts were dried and evaporated to give material (0·37 g) that was chromatographed on a short silica gel column. Benzene eluted *trans*-stilbene (17 mg) (identified by comparison of its n.m.r. spectrum with that of authentic material), and 5% ethyl acetate–benzene eluted (+)-1,2-diphenylethanol (70 mg), m.p. 58°, pure by t.l.c. ($CHCl_3$), and 105 mg of slightly less pure material. The pure fraction had $[\alpha]_D^{25}$ +40·7° (*c* 4·73 in EtOH). {The highest value in the literature[30] is $[\alpha]_D^{25}$ +52·8° (*c* 5 in EtOH), according to which the optical purity of the above material is 88·5%.} Low temperature recrystallisation from ether–petroleum gave needles, m.p. 63°, $[\alpha]_D^{21}$ +40·8° (*c* 4·5 in EtOH) (lit.,[30] m.p. 67°), τ (CCl_4) 2·87 (5H, s), 2·95 (5H, s), 5·40 (1H, t, *J* 7 Hz), 7·12 (2H, d, *J* 7 Hz), and 7·62 (1H, s).

Conversion of Oleic into Elaidic Acid.—Commercial oleic acid (*cis*-octadec-9-enoic acid), containing at most 83% of oleic acid (by g.l.c. of the methyl ester) was converted as described[31] by hydrogen peroxide in formic acid into *threo*-9,10-dihydroxyoctadecanoic acid, m.p. 92·5—93·5°, in 20% yield, based on pure starting material, after six recrystallisations from ethanol.

erythro-9(10)-*Acetoxy*-10(9)-*bromo-octadecanoic acid.* *threo*-9,10-Dihydroxyoctadecanoic acid (1·58 g, 5 mmol) was treated with cold HBr–acetic acid (3·57 g, 15 mmol) and the mixture was stirred at room temperature overnight. Water (5 ml) was added, and the aqueous layer was decanted from the oily product. This was repeated five times, and the product was then dried at 0·05 mmHg for 3 h to give 1·93 g (91%) of an oil, pure by t.l.c. (5% MeOH–$CHCl_3$), ν_{max} (film) 3400—3200m, 1741s, and 1711s cm^{-1}.

[29] C. R. Johnson and C. W. Schroeck, *J. Amer. Chem. Soc.*, 1971, **93**, 5303.

cis- *and* trans-*Octadec-9-enoic acids.* The total *erythro*-acetoxybromo-octadecanoic acid product (1·93 g) was dissolved in ethanol (20 ml) and refluxed for 1 h with zinc dust (0·65 g, 10 mmol). Water (100 ml) was added to the cooled mixture after decantation from the zinc residues, and the white crystalline solid was filtered off (yield 1·2 g, 85% based on diol), m.p. 38°. The i.r. spectrum of this material showed complete absence of the acetoxy carbonyl band at 1741 cm^{-1}. T.l.c. on 10% silver nitrate impregnated silica gel failed to resolve the mixture in a variety of solvents (*e.g.* 5% MeOH–$CHCl_3$, EtOAc). Three recrystallisations from ethanol gave 0·17 g (12%) of m.p. 44°, 0·22 g of m.p. 40°, and 0·6 g of oily residues [lit.,[32] m.p. of oleic acid (*cis*) 16°; m.p. of elaidic acid (*trans*) 44—45°].

Reaction of meso-1,2-*Diphenylethane*-1,2-*diol with Hydrogen Bromide–Acetic Acid.*—The diol (187 mg, 0·874 mmol) was treated with HBr–acetic acid (0·625 g, 2·62 mmol). At 37° the solid had all dissolved after 45 s, but after 2 min the mixture set to a white solid. After 10 min at 37°, water was added and the mixture was neutralised and extracted with dichloromethane, leaving voluminous white material soluble in neither solvent. The dichloromethane extract was evaporated and shown to contain a mixture of many products by n.m.r. spectroscopy and t.l.c. (variety of solvents), although the presence of *cis*-4,5-diphenyl-2-diphenylmethyl-1,3-dioxolan (20) in about 30% of the total was detected by comparison of the n.m.r. spectrum with that of an authentic sample, and its presence was verified on t.l.c. (R_F 0·7 in EtOAc–benzene, 1 : 1).

Conversion of trans-1-*Acetoxy*-2-*bromocyclohexane into* 1,2-*Epoxycyclohexane.*—The crude acetoxy-bromide (76 mg, 0·346 mmol) was dissolved in dry methanol (0·4 ml) and 2·93N-potassium hydroxide in methanol (236 μl, 0·692 mmol) was added dropwise from a microsyringe with shaking. Potassium bromide was precipitated after the addition of the first two drops. When addition was complete g.l.c. analyses (6 ft E301 at 100° and at 130°) showed only methanol and 1,2-epoxycyclohexane, with no cyclohexanone or acetoxy-bromide; these observations were confirmed by co-injections.

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