$$ \overset{AlH_4^{\ominus}}{\underset{\overset{|}{O}\atop\underset{|}{Li}}{\overset{\oplus}{\bigcirc}=CH-CH-R'}} \longleftrightarrow \overset{AlH_4^{\ominus}}{\oplus\underset{\overset{|}{O}\atop\underset{|}{Li}}{\bigcirc=CH-CH-R'}} \longleftrightarrow \overset{AlH_4^{\ominus}}{\underset{\oplus}{\bigcirc}\underset{\overset{|}{O}\atop\underset{|}{Li}}{=CH-CH-R'}} $$

If R′ is also a phenyl group, a whole series of resonance structures of the type of VIII

$$ \underset{\overset{\cdot\cdot}{Li^+}}{\underset{O}{\bigcirc-\overset{\oplus}{CH}\underset{\diagdown\ \diagup}{}\overset{\ominus}{CH}-\bigcirc}}\overset{AlH_4^{\ominus}}{}\quad VIII $$
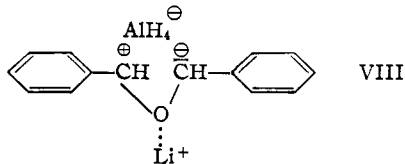
involving no bond between the epoxide carbon atoms, in which the positive and negative charges are diffused over the two phenyl groups, respectively, may also make an important contribution to the transition state. As a result of all these possibilities, it appears that for the reaction of stilbene oxides with lithium aluminum hydride the most important contribution to the transition state may well be made by a whole group of resonance struc-

tures in which a positive charge is diffused over the carbon atom being attacked and the phenyl group attached to it. Now, the effect of a *p*-substituent, which should introduce no steric complication, on the direction of ring opening may perhaps be determined simply on the basis of its stabilization or de-stabilization of the positive charge. An electron-donating group, which would tend to stabilize the positive charge, would promote attack at the carbon to which it is attached, whereas an electron-withdrawing group would have exactly the opposite effect. This is, of course, an example of the negative substituent effect.

Direction of Ring Opening in the Reduction of *p*-Substituted Styrene Oxides with Lithium Borohydride

BY RICHARD FUCHS[1] AND CALVIN A. VANDERWERF

Reduction of *p*-substituted styrene oxides with lithium borohydride in ether solution has been studied in continuation of our evaluation of electronic effects on the direction of S$_N$2 ring opening of unsymmetrical epoxides. Percentage of secondary attack by the borohydride was found to range from less than 16% when the *p*-substituent was the electron-withdrawing –Br to more than 95% when it was the electron releasing –OCH$_3$ group. The –NO$_2$ compound, with 62% of secondary attack, is an exception to this order, which otherwise is the reverse of that considered normal for S$_N$2 reactions. The experimental results are rationalized in terms of Swain's treatment of the substituent effect on the transition state for nucleophilic displacements.

Introduction

It has been fairly generally assumed that the electronic effect of an electron-releasing substituent on the direction of S$_N$2 ring opening in ethylene oxides is to favor attack at the primary carbon atom; conversely, an electron-withdrawing group is assumed to favor attack at the secondary carbon atom. Experimental tests of this assumption have, in most cases, been clouded by the possible interplay of steric factors. Recent studies by Guss[2] on the effect of *p*-substituents on the reported unimolecular ring opening of styrene oxides by sodium phenoxide in excess phenol suggest the desirability of a study on the same series of styrene oxides in an S$_N$2 reaction. Guss found that the percentage of secondary attack for the reaction with sodium phenoxide increased in the *p*-substituent order –NO$_2$ < –H < –OCH$_3$. This order, which corresponds to a negative rho in the Hammett equation,

also has been observed for the rates of solvolysis of the *p*-substituted benzyl chlorides.[3] The opposite substituent effect was noted[3] for the S$_N$2 reaction of the benzyl chlorides with iodide ion in acetone, and it has been commonly inferred[4] for the styrene oxide series under S$_N$2 conditions.

The lithium borohydride reduction is a particularly favorable case for study of the direction of ring opening in *p*-substituted styrene oxides because a change in the ratio of the isomeric alcohols produced can be followed in either direction from the 1:3 primary to secondary alcohol ratio obtained in the case of styrene oxide itself. The products are all known and the composition of the mixture of isomers can be determined by means of fractional distillation, from melting point curves or from infrared absorption.

Results

The relative percentages of secondary alcohols, formed by attack at the primary carbon atom, and of primary alcohols, formed by attack at the sec-
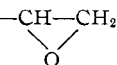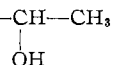
(1) The authors wish to acknowledge their appreciation to the University of Kansas for a fellowship to one of us under which a large part of this work was performed.

(2) (a) C. O. Guss, THIS JOURNAL, **71**, 3460 (1949); (b) *ibid.*, **74**, 2561 (1952); (c) C. O. Guss and H. Mautner, *J. Org. Chem.*, **16**, 887 (1951).

(3) G. M. Bennett and B. Jones, *J. Chem. Soc.*, 1815 (1935).

(4) See, for example, S. J. Cristol and R. F. Helmreich, THIS JOURNAL, **74**, 4083 (1952).

TABLE I

LITHIUM BOROHYDRIDE REDUCTION OF EPOXIDES

$Y-C_6H_4-CH-CH_2\backslash O/$	Rel. % $Y-C_6H_4-CH-CH_3$ OH	Rel. % $Y-C_6H_4-CH_2CH_2OH$	Over-all yield, %
Y = Br–	84	16	66
H–	74	26	100
O₂N–	38	62	64
CH₃O–	5	95	70
CH₃CH₂—CH—CH₂ $\backslash O/$	100% CH₃CH₂CH—CH₃ OH	0% CH₃CH₂CH₂CH₂OH	57

ondary carbon atom, obtained in the lithium borohydride reaction of various p-substituted styrene oxide are shown in Table I.

It is apparent that, excepting the nitro compound, the percentage of secondary attack increases with a decrease in electron-withdrawal power of the p-substituent, ranging from 16% or less for p-bromostyrene oxide to over 95% for p-methoxystyrene oxide. The figures showing 100% primary attack in the case of 1,2-epoxybutane indicate that the usual direction of ring opening observed in typical S$_N$2 reactions prevails for the saturated aliphatic epoxides.

Discussion of Results

It is significant that in the lithium borohydride reductions, the effect of p-substituents in the styrene oxides in directing the attack of the borohydride ion, generally follows the reverse of the usual S$_N$2 substituent order. The exception to the trend by p-nitrostyrene oxide must also be explained, preferably in a way applicable to other known reactions. Classification of these reactions into mechanistic categories is not particularly useful in predicting the direction of ring opening. There are, in fact, numerous borderline cases in which certain of the accepted distinctions between the two classes of reactions disappear. In various so-called S$_N$2 reactions, for example, attack may be observed exclusively at the primary epoxide carbon atom, exclusively at the secondary carbon atom, or at both. Conversely, the knowledge that a reaction is S$_N$2 does not necessarily allow a prediction of the effect of substituents, which may be the same or the opposite of the effect on S$_N$1 reactions. This seeming anomaly can be rationalized in terms of Swain's treatment of the substituent effect in the transition state for nucleophilic displacements.[5] The negative (rho) substituent effect is observed for reactions which are kinetically second order, if in the transition state the ionization of the departing group has proceeded further than the formation of the new bond. In such cases, the positive charge on the central carbon atom is increased in going to the transition state, and the reaction is facilitated by electron donating substituents.

In mono-substituted ethylene oxides of the type R—CH—CH₂ $\backslash O/$, an increase in the positive charge on the secondary carbon is stabilized by conjugation with R or by electron donation by R. In-

creased secondary attack is therefore usually observed under conditions favorable to the negative substituent effect. This electronic influence is superimposed on a steric effect which favors attack at the primary carbon. In p-substituted styrene oxides, Y—C₆H₄—CH–CH₂ $\backslash O/$, the steric effect of Y is slight, however, and the influence of Y on the course of reaction is attributable largely to electronic factors.

A number of factors increase the amount of bond-breaking relative to bond-making in the transition state, and several of these are instrumental in imparting the negative substituent effect to the reactions of the styrene oxide series with lithium borohydride: (a) The ready ionization of the epoxide oxygen, facilitated by ring strain. This factor is exemplified by the preferential reaction of the epoxy group in nucleophilic displacements on epichlorohydrin.[6]

(b) Conjugation with the phenyl group, which stabilizes any increase in positive charge on the secondary carbon, and permits partial ionization of the oxygen in the transition state. For example, styrene oxide is attacked 26% at the secondary carbon by lithium borohydride, whereas 1,2-epoxybutane reacts entirely at the primary position.

(c) Coördination of electrophilic agents at the epoxide oxygen. This decreases the strength of the base being displaced and facilitates bond rupture. The coördinating agent may be a solvating solvent, a proton,[7] or a Lewis acid. Lithium ion may play a minor role in the lithium borohydride reduction of epoxides.[8]

(d) Absence of charge on the nucleophilic reagent or high polarizability of that reagent, which makes possible extensive diffusion of charge in the transition state. These factors reduce bond formation in the transition state. The highly polarizable azide ion, for example, attacks styrene oxide exclusively at the secondary carbon atom,[9] and the uncharged, polarizable base pyridine shows a negative substituent effect for the second-order rates of reaction with the benzyl bromides in acetone[10] and in benzene.[5]

(6) W. Traube and E. Lehmann, Ber. 34, 1971 (1901)

(7) D. Swern, G. N. Billen and H. B. Knight, THIS JOURNAL, 71, 1152 (1949).

(8) For an example of lithium chloride catalysis in another epoxide reaction, see A. M. Eastham, J. Chem. Soc., 1936 (1952).

(9) W. E. McEwen, W. E. Conrad and C. A. VanderWerf, THIS JOURNAL, 74, 1168 (1952).

(10) J. W. Baker and W. S. Nathan, J. Chem. Soc., 519 and 1840 (1935); J. W. Baker, ibid., 1448 (1936).

(5) C. G. Swain and W. P. Langsdorf, Jr., THIS JOURNAL, 73, 2813 (1951).

TABLE II

EFFECT OF ACID CATALYSIS IN REACTIONS OF EPOXIDES WITH SODIUM ALLOXIDE

R—CH—CH2 (O)	Reagent	% R—CH—CH2 (OH, OCH2CH=CH2)	% R—CH—CH2OH (OCH2CH=CH2)
R = -CH3	Sodium alloxide	100	0
-CH2OH	Sodium alloxide	70-75	25-30
-CH3	H+, allyl alcohol	60	40
-CH2OH	H+, allyl alcohol	74	26
-CH2Cl	H+, allyl alcohol	100	0

(e) Conjugative or electron donating properties of the substituent. This has been discussed thoroughly for the benzyl halides.[5] The p-methoxy group can reinforce the phenyl group in stabilizing an increase in positive charge on the secondary carbon, thus favoring bond breaking. When bond-breaking is pre-eminent in the transition state, the negative substituent effect obtains. Powerful electron withdrawal by the p-nitro group, on the other hand, so inhibits bond breaking relative to bond making, that in the transition state the latter has proceeded further than the former and the substituent effect is completely reversed. Thus p-nitrostyrene oxide gives more primary alcohol than styrene oxide itself, because whenever the pre-eminence of bond-making over bond-breaking leads to a positive substituent effect, the nitro group favors reaction at the secondary carbon atom.

A similar reversal in the substituent effect has been demonstrated kinetically in the reaction of pyridine with the monosubstituted ethylene oxides,[11] where the rates are in the order epichlorohydrin > glycidol > ethylene oxide < propylene oxide.

Still another case in which a substituent has reversed the substituent effect is the uncatalyzed hydrolysis of the monosubstituted ethylene oxides,[12] in which the rates follow the order epichlorohydrin > glycidol < ethylene oxide.

Generally several of the above factors must be operative in order that the substituent effect be changed from positive to negative, or that attack on an epoxide be at the secondary position. Strong acid catalysis alone is frequently able to reverse substantially the direction of ring opening and the substituent effect, as shown by the data of Swern, et al.,[7] summarized in Table II.

The increase in secondary attack with acid catalysis compared to base catalysis is clearly demonstrated by the figures for propylene oxide. The concomitant change in the substituent effect from positive (under base catalysis) to negative (under acid catalysis) is evident from a study of the effect of the -CH2OH group relative to that of the -CH3 group under the two conditions. In the base-catalyzed reaction, the effect of -CH2OH relative to -CH3 is to promote secondary attack; in the acid-catalyzed reaction, the relative effect of -CH2OH is to inhibit secondary attack.

It is difficult, at the present time, to assess the relative importance of the individual factors which contribute to the operation of the negative substituent effect in the reaction of the styrene oxide series with lithium borohydride. It is uncertain, in fact, whether the major factor in reversing the usual substituent effect in these cases is the nature of the epoxides studied or the role played by the lithium borohydride. This significant question is being further explored in studies of the reactions of p-substituted styrene oxides with other nucleophilic agents.

Again, in comparison of the present series with analogous reactions involving the other hydrides, the percentage of secondary attack appears to increase with decreasing steric requirement of the nucleophilic reagent. Thus lithium borohydride gives 26% secondary attack on styrene oxide compared to a trace with the larger lithium aluminum hydride.[13]

Experimental

Lithium Borohydride Reduction of Styrene Oxide.—Duplicate 1-mole portions of styrene oxide, reduced by 7.0 g. (125%) of lithium borohydride in anhydrous ether, gave quantitative yields of a mixture of 2-phenylethanol (25, 27%) and 1-phenylethanol (75, 73%), which was separated by fractional distillation. The identity and purity of the alcohols were confirmed by derivatives and by refractive indices.

Lithium Borohydride Reduction of p-Methoxystyrene Oxide.—Twenty-three grams of p-methoxystyrene oxide, prepared by the procedure of Guss[2b] was reduced with 6.0 g. (720%) of lithium borohydride in ether. The product weighed 16.4 g. (70%), distilled at 112–115° at 2.5 mm., and melted at 22.6–23.2°. Synthetic 1-(4-methoxyphenyl)-ethanol, prepared in 71% yield by the lithium borohydride reduction of p-methoxyacetophenone, was a liquid boiling at 109–110° at 2.5 mm. (reported[14] 110° at 13 mm.). Synthetic 2-(4-methoxyphenyl)-ethanol[15] distilled at 115–116° at 2.5 mm. (reported[16] 138–140° at 11 mm.), and melted at 26.2–27.0° (reported[17] 27.5–28°). The phenylurethan, m.p. 127.4–127.9° (reported[18] 123–124°), and the phenylurethan of the epoxide reduction product, m.p. 127.2–127.7°, mixed together, melted at 127.6–127.9°. The melting point curve for synthetic alcohol mixtures indicated that the epoxide reduction product contained less than 5% of the secondary alcohol. The α-naphthylurethan of 2-(4-methoxyphenyl)-ethanol melted at 108.4–108.8°.

Anal. Calcd. for $C_{20}H_{19}O_3N$: C, 74.7; H, 6.0; N, 4.4. Found: C, 74.7; H, 5.9; N, 4.5.

Lithium Borohydride Reduction of p-Bromostyrene Oxide.—1-(4-Bromophenyl)-2-bromoethanol was prepared from 35 g. of p-bromophenacyl bromide in 250 ml. of dioxane by the addition of 3.0 g. (250%) of sodium borohydride in 50 ml. of water with cooling, over a period of 0.5 hour. After 0.5 hour of standing, the mixture was decomposed with 2 N sulfuric acid, poured into water, and extracted with isopropyl ether. The extract was added to a solution of 7.1 g. of potassium hydroxide in 150 ml. of water and the

(11) L. Smith, S. Mattson and S. Anderson, *Kgl. Fysiograf. Sällskap. Lund, Handl.*, **42**, No. 7, 1 (1946); J. Hansson, *Svensk. Kem. Tid.*, **60**, 183 (1948).

(12) J. N. Brönsted, M. Kilpatrick and M. Kilpatrick, THIS JOURNAL, **51**, 428 (1929).

(13) L. W. Trevoy and W. G. Brown, *ibid.*, **71**, 1675 (1949).

(14) H. Stobbe and K. Toepfer, *Ber.*, **57**, 484 (1924).

(15) Prepared according to F. B. LaForge and W. F. Barthel, *J. Org. Chem.*, **9**, 250 (1944).

(16) J. B. Shoesmith and R. J. Connor, *J. Chem. Soc.*, 2230 (1927).

(17) G. M. Bennett and M. M. Hafez, *ibid.*, 652 (1941).

(18) V. Grignard, *Ann. chim. phys.*, [8] **10**, 30 (1907).

resulting mixture was refluxed for 15 minutes with stirring. After dilution with water, separation and drying over anhydrous magnesium sulfate, the product was distilled at 75–76° at 1 mm. (reported[19] 80.5° at 0.8 mm.) yielding 25.1 g. (72%) of colorless p-bromostyrene oxide, m.p. 27.1° (reported[19] 26°).

p-Bromostyrene oxide (26.9 g.) reduced with 3.0 g. (400%) of lithium borohydride, gave an 83% yield of a mixture containing 20.4 g. (91%) of a fraction distilling at 86–92° at 1 mm. [largely 1-(4-bromophenyl)-ethanol[20]] and 2.0 g. (9%) of 2-(4-bromophenyl)-ethanol, b.p. 104° at 1 mm. (reported[21] b.p. 147° at 10 mm., m.p. 36–38°).

The product of a duplicate reduction of p-bromostyrene oxide, obtained in 66% yield, was analyzed by infrared absorption. Comparison of the maxima at 2950, 2930, 1595, 1200, 1110, 900 and 750 waves cm.$^{-1}$ with synthetic mixtures of the two isomeric alcohols, indicated a composition of 84% of the secondary alcohol and 16% of the primary.

1-(4-Bromophenyl)-ethanol (b.p. 98–102.5° at 2 mm.) was prepared independently in 68% yield by sodium borohydride reduction of p-bromoacetophenone in aqueous methanol. The phenylurethan melted at 103.6–104.0° (reported[20] 103–104°). 2-(4-Bromophenyl)-ethanol (b.p. 138° at 9 mm.) was prepared in low yield by the aluminum chloride-catalyzed bromination of 2-phenylethanol. The phenylurethan melted at 127.8–129.0° (reported[21] 126°).

The phenylurethan prepared from the 1-(4-bromophenyl)-ethanol fraction of the p-bromostyrene oxide reduction product melted at 102.1–102.8° and did not depress the m.p. of an authentic sample of the 1-(4-bromophenyl)-ethanol phenylurethan. The urethan prepared from the isomeric fraction melted at 129.2–129.7° and did not depress the m.p. of an authentic sample of the urethan of 2-(4-bromophenyl)-ethanol.

Lithium Borohydride Reduction of p-Nitrostyrene Oxide. —p-Nitrostyrene oxide was prepared from commercial p-nitrophenacyl bromide by the procedure used for p-bromostyrene oxide. The yield of product twice recrystallized from ethanol was 55%; m.p. 84.2–85.4° (reported[26] 85–86°). A solution of 14.8 g. of p-nitrostyrene oxide in ether, reduced by 4.0 g. (800%) of lithium borohydride, gave upon dis-

(19) T. Bergkvist, *Svensk Kem. Tid.*, **59**, 205 (1947); *C. A.*, **42**, 2584 (1948).
(20) R. Quelet, *Bull. soc. chim.*, [4] **45**, 75 (1929), reported b.p. 130° at 12 mm.
(21) T. W. J. Taylor and P. M. Hobson, *J. Chem. Soc.*, 181 (1936).

tillation 9.4 g. (63%) of an oil, b.p. 134–142° at 2 mm., which partially solidified upon standing, and 4.3 g. (29%) of a tarry residue. The mixture was not quantitatively separable by fractional distillation. Infrared analyses of this and a duplicate product fix the composition at 62% 2-(4-nitrophenyl)-ethanol and 38% 1-(4-nitrophenyl)-ethanol, by comparison with synthetic mixtures, of the absorption at 2950, 1200, 1090, 1035, 900 and 840 waves cm.$^{-1}$.

1-(4-Nitrophenyl)-ethanol, prepared independently by the sodium borohydride reduction of p-nitroacetophenone,[22] boiled at 137–138° at 2 mm. (reported[23] 161–163° at 4 mm.). The phenylurethan melted at 97.3–97.6° (reported[24] 205–206°).

Anal. Calcd. for $C_{15}H_{14}O_4N_2$: C, 62.9; H, 4.9; N, 9.8. Found: C, 62.8, 62.6; H, 4.9, 5.1; N, 9.9, 10.1.

The p-nitrobenzoate of 1-(4-nitrophenyl)-ethanol melted at 138.0–138.4° (reported[23] 138°).

2-(4-Nitrophenyl)-ethanol, b.p. 148–149° at 2 mm. (reported[24] 189° at 16 mm.), m.p. 60.7–61.8° (reported[25] 60–61°) was prepared by the method of Ferber.[25] The phenylurethan melted at 132.6–133.0° (reported[24] 127–128°).

1-(4-Nitrophenyl)-ethyl p-nitrobenzoate, m.p. 137.6–138.2°, and the phenylurethan of 2-(4-nitrophenyl)-ethanol, m.p. 130.2–131.0°, prepared from impure samples of the corresponding alcohols obtained by fractional distillation of the reduction mixture from p-nitrostyrene oxide, showed no melting point depressions when mixed with the respective authentic samples.

A mixture containing 62% 2-(4-nitrophenyl)-ethanol and 38% 1-(4-nitrophenyl)-ethanol was treated with lithium borohydride and worked up by the technique employed on the epoxide reduction mixture. The product, once distilled, had the identical composition to the starting mixture. The yield was 61%, with a considerable amount of tarry residue remaining behind.

Lithium Borohydride Reduction of 1,2-Epoxybutane.—A solution of 14.4 g. of 1,2-epoxybutane in ether was reduced by 3.3 g. (300%) of lithium borohydride. Fractional distillation gave 8.5 g. (57%) of 2-butanol, b.p. 98°, n^{20}D 1.3957, with no trace of 1-butanol.

(22) L. Long and H. Troutman, THIS JOURNAL, **71**, 2473 (1949).
(23) A. H. Ford-Moore and H. N. Rydon, *J. Chem. Soc.*, 679 (1946).
(24) J. v. Braun and B. Bartsch, *Ber.*, **46**, 3050 (1913).
(25) E. Ferber, *ibid.*, **62**, 183 (1929).

LAWRENCE, KANSAS

Autocatalysis in Aromatic Alkylations. The Reaction of Phenols with Triphenylmethyl Chloride[1]

BY HAROLD HART AND FRANK A. CASSIS[2]

The kinetic rate curves for the nuclear alkylation of phenol and o-cresol by triphenylmethyl (trityl) chloride in o-dichlorobenzene were S-shaped, typical of an autocatalytic reaction. When the phenol was saturated with hydrogen chloride prior to alkylation, the slow portion of the rate curves was eliminated, and the reaction followed third-order kinetics; *i.e.*, rate = k_3(phenol)(trityl chloride)(hydrogen chloride). The autocatalytic curves were fitted precisely by the expression: rate = k_2(phenol)(trityl chloride) + k_3(phenol)(trityl chloride) (hydrogen chloride). Aryl trityl ethers are rapidly cleaved by hydrogen chloride, and are probably not intermediates in the alkylation. The mechanism of the alkylation and of the catalytic function of the hydrogen chloride are discussed.

The reaction between triphenylmethyl (trityl) chloride and phenols is of interest for several reasons. In particular, it was this reaction, and analogous reactions with methanol, carried out in the presence of pyridine, which supported the postulation of termolecular mechanisms for displacement reactions in non-aqueous solvents.[3] The product of

(1) Presented at the September, 1953, Meeting of the American Chemical Society, Chicago, Ill. Taken in part from the Ph.D. thesis of Frank A. Cassis, Michigan State College, 1953.
(2) Research Corporation Fellow, 1949–1951.
(3) C. G. Swain, THIS JOURNAL, **70**, 1119 (1948).

the reaction was trityl phenyl ether, and the kinetics were third order; first order in trityl halide and second order in phenol. It was of interest to investigate this same reaction in the absence of pyridine, in which case the product is exclusively the p-nuclearly alkylated phenol, rather than the ether.

A previous investigation[4] of the nuclear alkylation of phenol with t-butyl chloride showed that this reaction is polymolecular in phenol when the latter is the solvent. It was in part the purpose of

(4) H. Hart and J. H. Simons, *ibid.*, **71**, 345 (1949).