[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Electronic Effects in the Lithium Borohydride Reduction of Styrene Oxides[1]

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The reduction of *p*-methyl-, *m*-methoxy- and 3,4-dichlorostyrene oxides with lithium borohydride in ether solution afforded products which are 67, 23 and 6% primary alcohol, respectively. These and previous data give a straight-line plot of log % primary alcohol *vs.* σ-, and a ρ-value of -1.6. The preparation of these three oxides is reported.

Previous work[2] on the lithium borohydride reduction of three *p*-substituted styrene oxides and styrene oxide itself, demonstrated that the formation of a primary phenylethanol is favored by an electron-donating *p*-methoxy group, and the formation of a secondary phenylethanol is facilitated by an electron-withdrawing *p*-bromo. The *p*-nitro compound is an exception to the general order of substituent effects.

The substituted styrene oxides with *p*-methyl, *m*-methoxy and 3,4-dichloro substituents have now been reduced with lithium borohydride in ether solution. The composition of each resulting mixture (Table I) has been determined by comparison of the infrared absorption spectrum with spectra of known mixtures of the two pure component alcohols.

TABLE I

LITHIUM BOROHYDRIDE REDUCTION OF SUBSTITUTED STYRENE OXIDES

$Y{-}C_6H_4{-}\underset{\diagdown\,O\,\diagup}{CH{-}CH_2}$ Y =	$Y{-}C_6H_4{-}CH_2{-}CH_2OH$, %	$Y{-}C_6H_4{-}\underset{\overset{\vert}{OH}}{CH}{-}CH_3$, %
p-CH_3O[a]	95	5
p-CH_3	67, 69	33, 31
p-H[a]	26	74
m-CH_3O	23, 23.5	77, 76.5
p-Br[a]	16	84
3,4-Dichloro	5, 6	95, 94
p-NO_2[a]	62	38

[a] Reference 2.

It is interesting that, for the most part, the percentage of primary alcohol present in each reaction mixture can be correlated with the Hammett σ-values[3] of the substituent (Fig. 1). Rho for the reaction is -1.6. A large negative value of ρ, which is somewhat unexpected for an "SN2" reaction, has been rationalized in terms of a mechanism with both "SN1" and "SN2" character.[2] *p*-Nitrostyrene oxide, which is believed to react by a somewhat different mechanism,[2] was omitted in the calculation of ρ. The percentage of primary alcohol obtained from the *p*-H compound is unexpectedly low, probably because of the low concentration of lithium borohydride which was used in that case.[2,4] The ρ-value obtained from the plot of log % primary alcohol *vs.* σ (Fig. 1) is not entirely comparable with ρ-values obtained from the usual plots involving log *k*. If it is assumed that substituents act only at the benzyl carbon atom and leave the other epoxide carbon atom unaffected, it is then possible to calculate the rates of reaction at the benzyl carbon atom of each substituted styrene oxide, relative to styrene oxide. The Hammett equation plot of relative rates obtained in this way (*vs.* σ) is not a straight line. The assumption is, therefore, probably incorrect.

It may be noted that the position of the methoxy group greatly affects the percentage of primary alcohol produced. This group is electron-withdrawing inductively, but strongly electron-donating by conjugation. A methoxy group in the *para* position has a net effect of electron-donation at the side chain, but a *m*-methoxy group withdraws electrons from the side chain because conjugation is not possible. This is reflected in the σ-values[3] of -0.286 and $+0.115$, for the *p*- and *m*-methoxy groups, respectively.

The electronic effects of aryl groups in substituted styrene oxides are probably exercised mainly at the benzyl carbon atom of the epoxide ring. However, the main influence may instead be exercised at the primary carbon atom of the epoxide ring[5] as in the case of styrene, because of the "double bond character" of the strained ring. In the reaction of *p*-methoxystyrene oxide with lithium borohydride,[2] the borohydride ion attacks at the benzyl carbon atom, and a primary alcohol is obtained, whereas, styrene oxide affords mainly a secondary alcohol. The *p*-methoxy group must either increase the rate of reaction at the benzyl carbon atom, or it must decrease the rate at the primary epoxide carbon atom, or both. Further studies designed to resolve this question are in progress in this Laboratory.

Experimental

***m*-Methoxy-α-bromoacetophenone.**—To a solution of 162 g. (1.08 moles) of *m*-methoxyacetophenone[6] in 270 ml. of acetic acid maintained at 15–20°, was added a solution of 55 ml. (1.08 moles) of bromine in 50 ml. of acetic acid. The solvent was then removed by distillation under reduced pressure, and the brown oil was shaken with ice-water which caused solidification. Recrystallization from aqueous ethanol gave 168 g. (68%) of *m*-methoxy-α-bromoacetophenone, m.p. 57.5–59.5°. A better solvent is a mixture of 90% heptane and 10% isopropyl ether, from which the product was obtained in higher purity, m.p. 62–63°.

Anal. Calcd. for $C_9H_9BrO_2$: C, 47.2; H, 4.0. Found: C, 47.6; H, 4.0.

***m*-Methoxystyrene Oxide.**—In 400 ml. of dioxane was dissolved 83.4 g. (0.364 mole) of *m*-methoxy-α-bromoaceto-

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(1) This work was begun at the University of Alabama, University, Alabama.

(2) R. Fuchs and C. A. VanderWerf, THIS JOURNAL, **76**, 1631 (1954).

(3) H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

(4) The decrease in the percentage of primary alcohol formed with decreased concentration of lithium aluminum hydride has been reported in the reduction of 3,4-epoxy-1-butene: R. Fuchs and C. A. VanderWerf, THIS JOURNAL, **74**, 5917 (1952).

(5) A. Feldstein and C. A. VanderWerf, *ibid.*, **76**, 1626 (1954).

(6) E. T. Cobb, *Proc. S. Dakota Acad. Sci.*, **25**, 64 (1945); *C. A.*, **40**, 7180 (1946). *m*-Aminoacetophenone was supplied by the Carbide and Carbon Chemicals Co.

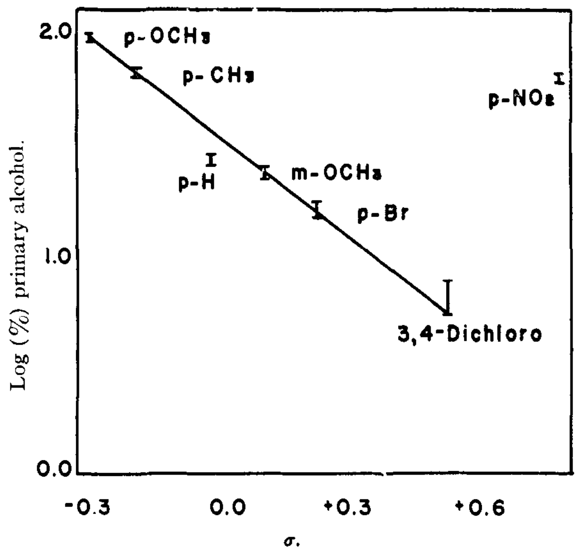

Fig. 1.—Hammett equation plot for the reaction of substituted styrene oxides with lithium borohydride.

phenone, and to this was added a solution of 8.1 g. (0.21 mole) of sodium borohydride in 100 ml. of water. The mixture stood for one hour, and then was decomposed by the addition of dilute sulfuric acid, poured into 2 l. of water, and extracted twice with isopropyl ether. For 15 minutes the extract was stirred vigorously and refluxed with a solution of 25.4 g. (0.45 mole) of potassium hydroxide in 200 ml. of water. The organic layer was separated, washed with water and dried. The product of distillation was 34.6 g. (64%) of *m*-methoxystyrene oxide, b.p. 77° at 1 mm., $n^{26}\text{D}$ 1.5377.

Anal. Calcd. for $C_9H_{10}O_2$: C, 72.0; H, 6.7. Found: C, 71.9; H, 6.8.

Lithium Borohydride Reduction of *m*-Methoxystyrene Oxide.—Lithium borohydride (4.4 g., 0.20 mole) was dissolved in 150 ml. of anhydrous ether. To this was added a solution of 15.0 g. (0.10 mole) of *m*-methoxystyrene oxide in 50 ml. of ether. The mixture was stirred overnight and then decomposed by the addition of water, followed by dilute sulfuric acid. The isopropyl ether extract was washed with dilute sodium carbonate solution, dried, and distilled. The product collected at 90.5–98° at 1 mm. (12.1 g., 80%) was analyzed by comparison with synthetic mixtures of the isomeric alcohols,[7] of the infrared absorption at 920, 1110, 860, 910 and 900 cm.$^{-1}$. This and a duplicate product obtained in 63% yield have the composition indicated in Table I.

***p*-Methylstyrene Oxide.**—*p*-Methyl-α-chloroacetophenone[8] was reduced with sodium borohydride, and the chlorohydrin was treated with base by the procedure used for *m*-methoxy-α-bromoacetophenone. *p*-Methylstyrene oxide[9] (b.p. 51–52° at 1 mm., $n^{26}\text{D}$ 1.5277) was obtained in 67% yield.

Anal. Calcd. for $C_9H_{10}O$: C, 80.6; H, 7.5. Found: C, 80.5; H, 7.5.

The same product was isolated in 81% yield from *p*-methyl-α-bromoacetophenone, obtained by bromination of *p*-methylacetophenone.

Duplicate portions of *p*-methylstyrene oxide were reduced with lithium borohydride in 81% yield by the procedure used for *m*-methoxystyrene oxide. The compositions listed in Table I were established by the use of the absorption bands at 900, 1200 and 1110 cm.$^{-1}$[10]

2-(3,4-Dichlorophenyl)-ethanol.—3,4-Dichlorobenzylmagnesium chloride was prepared from α-3,4-trichlorotoluene, and poured onto Dry Ice. The oil produced by hydrolysis deposited crystals of 3,4-dichlorophenylacetic acid from heptane solution in 35% yield. An ether solution of 26.6 g. (0.13 mole) of the acid was added to a solution of 11.4 g. (0.30 mole) of lithium aluminum hydride in ether, and the mixture was stirred for 5 hours at room temperature before hydrolysis. The oil isolated by extraction was distilled, and 10.7 g. (43%) of product was collected in the range 113–113.5° at 1 mm., $n^{25}\text{D}$ 1.5666.

Anal. Calcd. for $C_8H_8OCl_2$: C, 50.3; H, 4.2. Found: C, 50.8; H, 4.3.

The phenylurethan melted at 90–90.5°.

Anal. Calcd. for $C_{15}H_{13}O_2NCl_2$: C, 58.1; H, 4.2; N, 4.5. Found: C, 58.2; H, 4.3; N, 4.4.

3,4-Dichlorostyrene Oxide.—To a solution of 184.5 g. (0.98 mole) of 3,4-dichloroacetophenone in 500 ml. of dichloromethane was added dropwise 50.3 ml. (157 g., 0.98 mole) of bromine in 50 ml. of dichloromethane. Decolorization of the bromine began almost immediately at room temperature, and the reaction flask was then cooled in ice. After the addition, the solvent was distilled under reduced pressure, and the solid residue was recrystallized from a mixture of 450 ml. of heptane and 125 ml. of isopropyl ether. A yield of 163.5 g. (62%) of 3,4-dichloro-α-bromoacetophenone was obtained, m.p. 54–56.5° (reported[13] 58°). By the procedure used for *m*-methoxy-α-bromoacetophenone, 73.6 g. (64%) of 3,4-dichlorostyrene oxide was obtained, b.p. 87.5–88° at 1 mm., $n^{26}\text{D}$ 1.5688.

Anal. Calcd. for $C_8H_6OCl_2$: C, 50.8; H, 3.2. Found: C, 51.3; H, 3.2.

Duplicate portions of 3,4-dichlorostyrene oxide were reduced in 76 and 88% yields with lithium borohydride by the procedure used for *m*-methoxystyrene oxide. The composition listed in Table I was established by the use of the bands at 860, 1030 and 1040 cm.$^{-1}$[14]

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(7) (a) 1-(*m*-Methoxyphenyl)-ethanol (b) was prepared by sodium borohydride reduction of *m*-methoxyacetophenone. 2-(*m*-Methoxyphenyl)-ethanol (c) was prepared by lithium aluminum hydride reduction of *m*-methoxyphenylacetic acid, (b) A. Klages, *Ber.*, **36**, 3584 (1903); (c) J. B. Shoesmith and R. J. Conner, *J. Chem. Soc.*, 2230 (1927).

(8) A. Collet, *Bull. soc. chim.*, [3] **17**, 507 (1897).

(9) J. J. P. Staudinger and C. A. Brighton, British Patent 586,715; *C. A.*, **42**, 2134 (1948).

(10) 1-(*p*-Tolyl)-ethanol[11] was prepared from *p*-tolyllithium and acetaldehyde. 2-(*p*-Tolyl)-ethanol[12] was prepared from *p*-tolyllithium and ethylene oxide.

(11) M. Sulzbacher and E. Bergmann, *J. Org. Chem.*, **13**, 303 (1948).

(12) I. G. Farbenind. A. G., French Patent 752,478, September 23, 1933; *C. A.*, **28**, 1047 (1934).

(13) M. Jastrzebski and J. Susko, *Roczniki Chem.*, **13**, 293 (1933); *C. A.*, **27**, 4531 (1933).

(14) 1-(3,4-Dichlorophenyl)-ethanol[15] was prepared by sodium borohydride reduction of 3,4-dichloroacetophenone.

(15) C. S. Marvel, C. G. Overberger, R. E. Allen, H. W. Johnston, J. H. Saunders and J. D. Young, THIS JOURNAL, **68**, 861 (1946).