absorbed 60.0 ml. (S.T.P.) of hydrogen (91% of theory) in 24 minutes.

Ozonization.—A solution of 2 g. of acid III in 100 ml. of redistilled carbon tetrachloride was cooled with an ice–salt cooling mixture while a mixture of oxygen and ozone of unknown concentration was passed through it. After 16 hours it was found that the oxygen–ozone mixture passing through the solution liberated iodine from a potassium iodide solution at the same rate as the oxygen–ozone mixture coming directly from the ozone generator. The carbon tetrachloride solution was then mixed with a 50% solution of acetic acid and zinc dust was added in parts. After the completion of the addition the solution was refluxed for one hour, the organic layer separated and the aqueous layer extracted with several portions of ether which were combined with the carbon tetrachloride solution and dried over magnesium sulfate. The solvents were removed by distillation and the residue treated with 2,4-dinitrophenylhydrazine to yield 0.5 g. of a yellow 2,4-dinitrophenylhydrazone. After two recrystallizations from alcohol it melted at 64–65° and did not depress the melting point of the 2,4-dinitrophenylhydrazone from ethyl *n*-amyl ketone.

Ethyl *n*-amyl ketone was prepared in 77% yields by the method of Newman and Smith.[10] Its 2,4-dinitrophenylhydrazone melted at 64–65°. *Anal.* Calcd. for $C_{14}H_{20}O_4N_4$: C, 54.5; H, 6.5; N, 18.2. Found: C, 54.8; H, 6.3; N, 18.2.

The Reaction of the Addition Product of I to the Acid II with Acetyl Chloride.—A solution of 3.5 g. (0.025 mole) of acid II in dry ether was added to a solution of 0.076 mole of I in ether. The solution was cooled in an ice-bath and 5.9 g. (0.075 mole) of freshly distilled acetyl chloride was added in parts. When the addition was about two thirds completed, the solution turned to a yellowish-green color and separated into two layers. Attempts to crystallize the addition product by cooling to Dry Ice temperature failed. It was therefore refluxed for one hour with a 10% solution of sodium hydroxide, the aqueous solution acidified with hydrochloric acid and extracted with several portions of ether, the ether solution dried with magnesium sulfate, and filtered. The filtrate was distilled at 2-mm. collecting four fractions, up to 107°, 107 to 112°, 112 to 116°, and 116 to 119°. None of the fractions yielded iodoform when treated with a 10% solution of sodium hydroxide and iodine–potassium iodide solution.

[10] M. S. Newman and A. S. Smith, *J. Org. Chem.*, **13**, 592 (1948).

PITTSBURGH, PENNA. RECEIVED AUGUST 3, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLORADO A. AND M. COLLEGE]

The Reaction of *p*-Methoxystyrene Oxide with Phenol[1]

BY CYRUS O. GUSS

RECEIVED DECEMBER 20, 1951

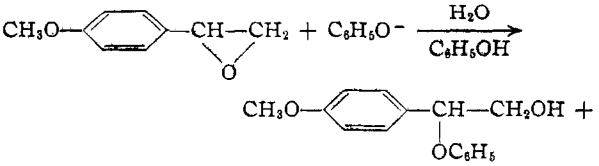
The preparation of *p*-methoxystyrene bromohydrin by solvolysis of *p*-methoxystyrene dibromide provided an easy synthesis of *p*-methoxystyrene oxide. Reaction of the oxide with phenoxide ion gave the primary alcohol, but no secondary alcohol, and products of nuclear alkylation. The acid-catalyzed reaction of the oxide with phenol led almost exclusively to nuclear attack. These results further support the postulate of a unimolecular route to the primary alcohol in the ring-opening reactions of styrene oxides.

The effect of substituents in substituted styrene oxides on the direction of ring opening has been investigated recently[2,3] in order to gain a better understanding of the mechanism of the reaction. Electron-attracting groups, as exemplified by the nitro group, favor the formation of the secondary alcohol in the reaction of the substituted styrene oxide with phenoxide ion, contrary to prediction based on inductive effects by which nitro groups would tend to lower the electron density on the α-carbon atom. On the other hand, if attack at the α-carbon involved a unimolecular ring opening, then the nitro group might well inhibit the formation of the primary alcohol[3] and yet facilitate a bimolecular route to the secondary alcohol.[4] A study of the ring-opening reactions of *p*-methoxystyrene oxide is an obvious source of supplementarily helpful data.

At least one attempt to make *p*-methoxystyrene oxide has been reported.[5] Olefin oxides similarly activated have been found to be rather susceptible to thermal isomerization even when distilled at pressures down to around 1 mm.[6] Therefore, the first objective in the present work was to prepare *p*-methoxystyrene oxide in a sufficiently pure state without distillation or other heat treatment. Ordinarily the conversion of a bromohydrin to the corresponding oxide is rapid and quantitative. With this in mind, pure *p*-methoxystyrene bromohydrin was sought as a desirable precursor.

Among the methods investigated was the solvolysis of *p*-methoxystyrene dibromide to the bromohydrin as reported by Tutin, Caton and Hann.[7] Eventually an acceptable modification of their procedure was developed which led to the bromohydrin in good yield and of analytical purity. The oxide was produced when the solvolysis was conducted in the presence of sodium hydroxide.

The reaction of *p*-methoxystyrene oxide with phenoxide ion was carried out at the same temperature and with the same concentration of components as was used with styrene oxide[8] and the nitrostyrene oxides.[2,3] As shown in the equation



I

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[1] Scientific Series Paper No. 373 of the Experiment Station.

[2] C. O. Guss and H. G. Mautner, *J. Org. Chem.*, **16**, 887 (1951).

[3] C. O. Guss, *ibid.*, in press.

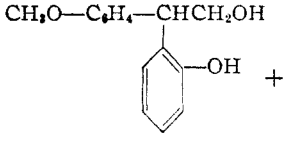
[4] G. Baddeley and G. M. Bennett, *J. Chem. Soc.*, 1819 (1935).

[5] E. D. Bergmann and M. Sulzbacher, *J. Org. Chem.*, **16**, 84 (1951).

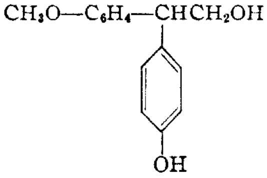
[6] S. Winstein, T. L. Jacobs, R. B. Henderson, J. H. Robson and B. F. Day, *ibid.*, **11**, 157 (1946); G. P. Mueller and R. May, THIS JOURNAL, **71**, 3313 (1949).

[7] F. Tutin, F. W. Caton and A. C. O. Hann, *J. Chem. Soc.*, **95**, 2113 (1909).

[8] C. O. Guss, THIS JOURNAL, **71**, 3460 (1949).

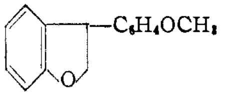


II



III

the primary alcohol-ether and products of nuclear alkylation were isolated. About 70% of the reaction product was alkali insoluble, from which an approximately 45% yield of I was obtained after one recrystallization. None of the isomeric secondary alcohol-ether was evident. The alkali-soluble fraction, presumed to contain II and III,[9] was esterified with phthalic anhydride and then subjected to the conditions used in the intramolecular displacement of carboxylate ion.[10] An alkali-insoluble product was isolated and assigned the structure IV of the dihydrofuran derived from the phenol-alcohol II.



IV

The residue from the isolation of IV was worked up to yield a compound assigned the structure III. Both of the ether-alcohols were synthesized in the proof of the structure of I.

Even when the water in the initial reaction mixture was replaced by dioxane, a change unfavorable to the formation of the primary alcohol,[8,9] the only ether-alcohol isolable was the primary alcohol.

In the acid-catalyzed reaction of *p*-methoxystyrene oxide with excess phenol at 40–45°, a small amount of alkali-insoluble material, neither I nor the isomeric ether-alcohol, was formed. From the major portion of the reaction mixture it was possible to isolate some of the phenol-alcohol III and to obtain evidence for the presence of II. Other products may also have been present.[11]

These results are in accord with the postulate of a unimolecular route to the primary alcohol. Although the postulate of an inductive (I_s) effect only, as applied to styrene oxide in explaining the attack of the nucleophilic agent at the least substituted carbon atom,[12] would lead to the prediction that the primary alcohol ought to be the favored product from *p*-methoxystyrene oxide, it would also require that the primary alcohol ought to be the favored product from the nitrostyrene oxides. Quite the opposite is observed with the latter. Neither is there support for the suggestion that variations in the size of the nucleophilic agent might determine the point of attack,[13] for in the reaction of styrene oxide with phenoxide ion either the primary alcohol or the secondary alcohol can be made the predominant isomer.[9] Moreover, 1,1-diphenylethylene oxide will react with 2-naphthol in basic medium to give the primary alcohol-phenol resulting from the opening of the ring at the α-carbon atom and attachment to the 1-position of the 2-naphthol,[14] while the relatively small methoxide ion attacks styrene oxide predominantly at the β-carbon atom.[15] Actually the process leading to the formation of the primary alcohol does not appear to be very susceptible to steric hindrance, a characteristic of unimolecular reactions involving an intermediate carbonium ion. However, a bimolecular displacement on the α-carbon atom can be considered to be sterically hindered, as indicated, for example, by the reactions of the nitrostyrene oxides.[2,3]

Experimental[16]

***p*-Methoxystyrene Bromohydrin.**—The procedure of Tutin, Caton and Hann[7] was used to prepare *p*-methoxystyrene dibromide from *p*-methoxystyrene[17] except that a chloroform solution of bromine was added to a cooled solution of the olefin in ether. Removal of the solvent under reduced pressure left a quantitative yield of the dibromide, m.p. 78–81°. Although this material was probably pure enough to use, in this study the dibromide was recrystallized once from Skellysolve B to give the pure compound, m.p. 80–81°.[7] Like *p*-methoxybenzyl bromide[18] our *p*-methoxystyrene dibromide showed a tendency to turn slightly purplish on storage. However, another recrystallization, with Nuchar treatment, gave the white needles again.

A number of considerations led to the use of the following procedure as a satisfactory method for the preparation of pure *p*-methoxystyrene bromohydrin. *p*-Methoxystyrene dibromide (8.8 g., 0.03 mole) was dissolved in dioxane (50 cc.) and, with stirring, water (50 cc.) was added in one portion. At room temperature this turbid mixture became clear within 2–3 minutes, and the theoretical amount of bromide ion was released. The change—turbid to clear—was a convenient indicator of the completion of the solvolysis. Dilution to 500 cc. with water and extraction with ether removed the bromohydrin, which was dried over anhydrous sodium sulfate. Evaporation of the ether under reduced pressure left 5.9 g. (87%) of a very pale yellow oil, n^{20}_D 1.5730. This was ***p*-methoxystyrene bromohydrin.**

Anal. Calcd. for $C_9H_{11}O_2Br$: C, 46.77; H, 4.80. Found: C, 47.04; H, 5.03.

The yield was sometimes nearly quantitative, depending on the care taken to avoid loss. Molecular distillation at 10^{-3} mm. raised the refractive index of the bromohydrin so prepared to n^{20}_D 1.5768 and improved the analysis for carbon and hydrogen. After about two weeks at room temperature the *p*-methoxystyrene bromohydrin slowly changed to a mush. The distillation of *p*-methoxystyrene bromohydrin, prepared as herein described or otherwise, at 125–135° (5–6 mm.) caused extensive decomposition to take place. Recrystallization of the solid distillate from ethanol gave leaves, m.p. 54–55°, as reported[19] for 1-bromo-2-(*p*-methoxyphenyl)-ethylene.

Anal. Calcd. for C_9H_9OBr: C, 50.73; H, 4.26. Found: C, 50.74; H, 4.54.

Styrene dibromide was also converted to styrene bromohydrin by a solvolytic reaction.

***p*-Methoxystyrene Oxide.**—The conversion of the isolated *p*-methoxystyrene bromohydrin to *p*-methoxystyrene oxide by dilute sodium hydroxide was, of course, easily accomplished. Generally the bromohydrin was not isolated, however. For example, *p*-methoxystyrene dibromide (8.8 g., 0.03 mole) was dissolved in dioxane (50 cc.) and a solution of sodium hydroxide (2.8 g., 0.07 mole) in water (50 cc.) was added in one portion with stirring at room temperature. The mixture became turbid immediately and warmed slightly. Although the turbidity faded, the mixture did not become clear. All of the bromine was rapidly converted to bromide ion. After 10–15 minutes the mixture was diluted to 500 cc. with water, extracted with ether, and the

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(9) C. O. Guss and H. R. Williams, *J. Org. Chem.*, **16**, 1809 (1951).

(10) C. O. Guss, This Journal, **73**, 608 (1951).

(11) C. O. Guss, H. R. Williams and L. H. Jules, *ibid.*, **73**, 1257 (1951).

(12) R. R. Russell and C. A. VanderWerf, *ibid.*, **69**, 11 (1947).

(13) R. M. Adams and C. A. VanderWerf, *ibid.*, **72**, 4368 (1950).

(14) C. O. Guss and R. Rosenthal, unpublished data.

(15) W. Reeve and I. Christoffel, This Journal, **73**, 1480 (1951).

(16) All temperature measurements are uncorrected.

(17) C. Walling and K. B. Wolfstirn, This Journal, **69**, 852 (1947).

(18) J. W. Baker, *J. Chem. Soc.*, 2631 (1932).

(19) G. Eigel, *Ber.*, **20**, 2527 (1887).

latter solution dried over anhydrous sodium sulfate. Removal of the ether under reduced pressure gave 3.9 g. (86.6%) of *p*-methoxystyrene oxide as a pale yellow oil, $n^{20}D$ 1.5400 ± 0.0025. *p*-Methoxystyrene oxide, as prepared here, melted to a clear liquid at 20 ± 2°. It was not stable, the refractive index and melting point increasing steadily until a solid material, presumably a polymer, resulted. When placed in a refrigerator in the solid state, the deterioration of the oxide may have been delayed, but it was not prevented.

One preparation of the oxide was analyzed after being held for several hours under vacuum to remove the last traces of solvent.

Anal. Calcd. for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 70.89; H, 6.70.

When the oxide was heated with water, with or without the addition of a catalytic amount of hydrochloric acid, the glycol was formed, m.p. 81–82°.[20]

The Reaction of *p*-Methoxystyrene Oxide with Phenoxide Ion.—To freshly prepared *p*-methoxystyrene oxide (3.45 g., 0.023 mole) was added, in one portion, a solution of phenol (6.5 g., 0.069 mole), sodium hydroxide (0.9 g., 0.225 mole) and water (3.5 cc.), which was at the temperature of a boiling water-bath. There appeared to be an immediate exothermic reaction. The one-phase mixture was at once placed in a boiling water-bath for 30 minutes, then poured into iced 4% sodium hydroxide. The insoluble portion was extracted with ether, dried over anhydrous potassium carbonate, and the ether evaporated to give 3.8 g. (67.9%) as a yellow oil that solidified on standing. Recrystallization from heptane was accomplished by allowing a less soluble oil to separate from the hot solution and then cooling the supernatant solution in a separate flask. By repeating this process with the oil, 2.6 g. (46.4%), m.p. 70–72°, of the primary alcohol (I), **2-(4-methoxyphenyl)-2-phenylethanol** was isolated. The analytical sample melted at 71–72°.

Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.76, H, 6.77.

The *p*-nitrobenzoate,[21] from dilute ethanol as faintly yellow needles, melted at 100–101°.

Anal. Calcd. for $C_{22}H_{19}NO_6$: C, 67.17; H, 4.87. Found: C, 66.88; H, 5.14.

In a repetition of this experiment a 70.0% yield of alkali-insoluble material and a 43.3% yield of I was obtained. In both runs the residue from the crystallization of I was a viscous to brittle tan resin. Use of the bromohydrin instead of the oxide gave similar results. When dioxane was used instead of water, the yield of alkali-insoluble material was 51.7% and of I, 36.2%, with no evidence for the presence of the isomeric secondary alcohol.

The alkali-soluble material was isolated by acidification and extraction with ether. To the 5.8 g. of oil obtained in this manner from the run just described in detail was added phthalic anhydride (3.0 g.), dioxane (15 cc.) and pyridine (3 cc.). After 48 hours at room temperature this solution was dissolved in ether, washed with dilute hydrochloric acid and water, and then extracted with four 25-cc. portions of 4% sodium bicarbonate. Sodium hydroxide (1.0 g.) in water (20 cc.) was added to the combined bicarbonate extract, which was then refluxed one-half hour. An insoluble material was isolated as a nearly colorless oil, 0.6 g., which solidified slowly when cooled, m.p. 38–42°. This was purified by recrystallization from ethanol–water to m.p. 45–46°. The assigned structure, **3-(4-methoxyphenyl)-2,3-dihydrobenzofuran** (IV), is based on the mode of formation and the analysis.

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.84; H, 6.42.

Addition of Dry Ice to the alkaline liquid from the hydrolysis and cyclization reaction effected the separation of 0.5 g. of an oil. A solid (III), m.p. 150–151°, was obtained in small amount from this oil by crystallization from benzene–heptane. This material showed no depression in melting point when mixed with the substance of the same melting point isolated from the acid-catalyzed reaction of the oxide with phenol.

The Acid-catalyzed Reaction of *p*-Methoxystyrene Oxide with Phenol.—A mixture of phenol (9.4 g., 0.1 mole) and *p*-toluenesulfonic acid monohydrate (0.1 g.) was held at 40–45° with cooling while *p*-methoxystyrene oxide (3.75 g., 0.025 mole) was added in 15 minutes. The viscous, dark red solution was allowed to stand 15 minutes, then poured into water (150 cc.) containing sodium hydroxide (5 g.). A solid was filtered off, washed and dried; 0.7 g. Recrystallization from heptane gave 0.4 g., m.p. 150–190°. This was apparently a mixture of products from the self-condensation of the oxide, perhaps dimers such as dioxanes[6] or polymerized *p*-methoxyphenylacetaldehyde.

Anal. Calcd. for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 72.11; H, 6.76.

The alkaline filtrate from the isolation of the foregoing was acidified to precipitate a solid, 4.2 g., m.p. 115–140°. This solid (4 g.) in benzene (100 cc.) containing *p*-toluenesulfonic acid monohydrate (0.1 g.) was heated at reflux for 3 hours in order to effect the cyclization of any of the phenol-alcohol (II) to the furan (IV). The reaction mixture, in ether, was then extracted with dilute sodium hydroxide. There was isolated 0.4 g. of alkali-insoluble material, which was probably the furan (IV) although attempts to crystallize the oil failed. The alkali-soluble fraction, 3.2 g., m.p. 130–145°, was recrystallized from benzene–ethanol to yield 1.1 g., m.p. 150–151°, the remainder melting at 135–148°. The material melting at 150–151°, also obtained from the reaction of the oxide with phenoxide ion, was considered to be **2-(4-methoxyphenyl)-2-(4-hydroxyphenyl)-ethanol** (III).

Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.77; H, 6.86.

Preparation of 2-(4-Methoxyphenyl)-2-phenylethanol (I).—Sodium (0.46 g., 0.02 mole) was added to a solution of phenol (3.76 g., 0.04 mole) in dioxane (5 cc.). After all of the sodium had reacted, the solution was heated to the temperature of a boiling water-bath, and to it was added ethyl α-chloro-*p*-methoxyphenylacetate[14] (4.57 g., 0.02 mole) in dioxane (5 cc.). After 3.5 hours the reaction mixture was poured into water and extracted with ether. The material recovered from the ether solution was distilled; 2.45 g., b.p. 190–210° (3 mm.). The impure ester was hydrolyzed in dilute sodium hydroxide and the product recrystallized from heptane to obtain **α-phenoxy-*p*-methoxyphenylacetic acid**, m.p. 108–109°.

Anal. Calcd. for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46. Found: C, 70.07; H, 5.69.

This acid (0.2 g.) in ether was reduced with lithium aluminum hydride in 15 minutes to obtain the alcohol (I), 0.15 g. crude, which, when recrystallized from heptane, melted at 71–72° alone or when mixed with the alcohol (I) from the reaction of *p*-methoxystyrene oxide with phenoxide ion.

Preparation of 1-(4-Methoxyphenyl)-2-phenylethanol.—*p*-Methoxyphenacyl chloride[22] (9.2 g., 0.05 mole) was added to a solution of sodium phenoxide (0.05 mole) in water (25 cc.) and the mixture heated on a water-bath for 30 minutes. The dispersion was cooled and diluted to give a tan solid, 11.0 g., m.p. 45–55°. Two recrystallizations from dilute ethanol (Nuchar) gave white leaves, 4.3 g. (35.5%), m.p. 66–67°. *p*-Anisyl phenoxymethyl ketone has been prepared by Stoermer and Atenstädt[23] by a different method and found to melt at 67°. The oxime, as prepared here, melted at 107–108° (lit.[23] m.p. 105°). A preparation of the **2,4-dinitrophenylhydrazone**[24] gave orange needles, from ethyl acetate, m.p. 178.5–179.5°.

Anal. Calcd. for $C_{21}H_{18}N_4O_6$: C, 59.71; H, 4.29. Found: C, 59.47; H, 4.50.

Reduction of the ketone (2.42 g., 0.01 mole) in isopropyl alcohol (50 cc.) with a 1 molar solution (15 cc.) of aluminum isopropoxide in isopropyl alcohol yielded 2.20 g. (90.9%), m.p. 50–60°. One recrystallization from heptane gave the pure **1-(4-methoxyphenyl)-2-phenylethanol**, m.p. 63.5–64.5°.

Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.92; H, 6.70.

The *p*-nitrobenzoate,[21] from dilute ethanol as faintly yellow needles, melted at 87–88°.

Anal. Calcd. for $C_{22}H_{19}NO_6$: C, 67.17; H, 4.87. Found: C, 67.08; H, 4.99.

Fort Collins, Colorado

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[20] G. Fodor and O. Kovacs, This Journal, **71**, 1045 (1949).

[21] S. M. McElvain, "The Characterization of Organic Compounds," The Macmillan Company, New York, N. Y., 1945, p. 193.

[22] W. J. Hickinbottom, "Reactions of Organic Compounds," Longmans, Green and Co., Inc., New York, N. Y., 1948, p. 65.

[23] R. Stoermer and P. Atenstädt, *Ber.*, **35**, 3560 (1902).

[24] Reference 21, p. 199.