[CONTRIBUTION FROM THE CHEMICAL DEPARTMENT OF THE GENERAL ELECTRIC COMPANY]

DERIVATIVES OF *o*- AND *p*-(α-PHENYLETHYL)PHENOL

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Due to the availability and the low cost of the raw materials, the α-phenylethylphenols and their derivatives seem to offer a wide field of applications.

The reaction between phenol and styrene in acid medium was investigated by Koenigs (1, 2), as early as 1890–1891. He reported the preparation and the structure proof of the reaction products of phenol and styrene, which consisted of a mixture of *o*- and *p*-(α-phenylethyl)phenol. Niederl and co-workers (3, 4, 5), brought forward considerable evidence for the mechanism of this reaction. The reaction presumably proceeds through addition of the acid, usually sulfuric acid, to the ethylenic double bond. The addition compound then reacts with the phenol to form the phenyl ether which on rearrangement yields the phenylethylphenol.

Recently (6, 7, 8, 9), several patents appeared, describing methods for the preparation of α-phenylethylphenols as well as variations in the nature of the phenol and the unsaturated hydrocarbon. However, very little is known of the derivatives of *o*- and *p*-(α-phenylethyl)phenol.

The esters of *o*- and *p*-(α-phenylethyl)phenol, with exception of the acetates, were prepared by extending the method of Cherry (10), using acetic anhydride as a dehydrating agent. The acetates were prepared by refluxing the α-phenylethylphenols with acetic anhydride in the presence of a small amount of anhydrous sodium carbonate.

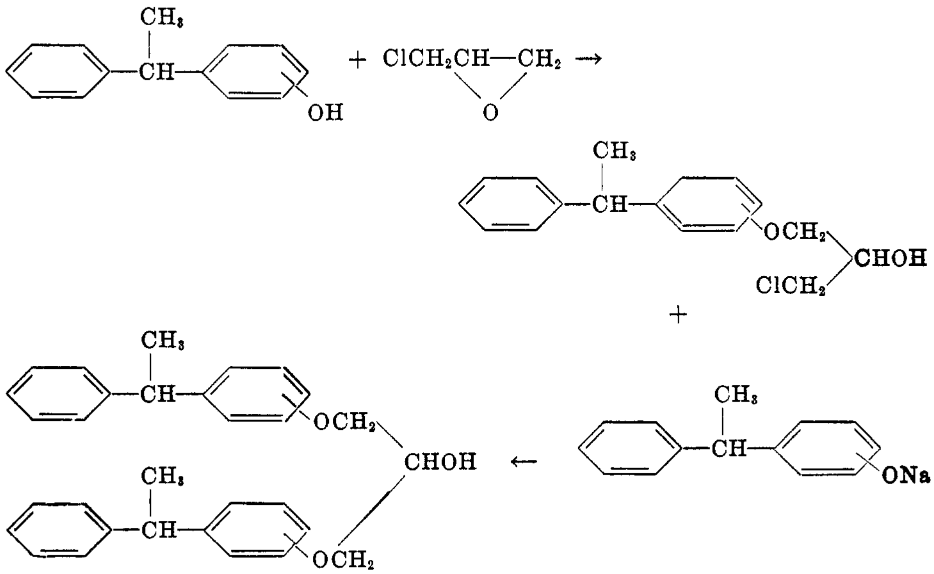
Alkylation of the α-phenylethylphenols was effected by reacting them with the corresponding alkyl bromides in the presence of anhydrous potassium carbonate and acetone as solvent.

The reaction of the α-phenylethylphenols with epichlorohydrin lent itself conveniently to the preparation of the 1,3-substituted glycerol ethers. Using two moles of α-phenylethylphenol to one mole of epichlorohydrin and working in an alkaline medium, the formation of the glycid ether was partly suppressed in favor of the 1,3-substituted glycerol ether. Based on the analogy of the reaction of phenol with epichlorohydrin (11), the reaction presumably proceeds in the following steps, see page 588.

The β-ethanol ethers were prepared by using ethylene oxide in the presence of sodium hydroxide as catalyst.

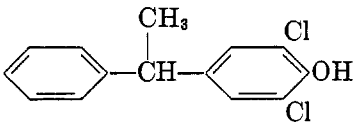
The phenoxyacetic acids were made using the method described by Pokorny (12). These substances appear to be of interest due to their relationship to well-known plant growth substances.

In view of the ever increasing use of chlorinated phenol derivatives as fungicides, growth substances, etc., it was found of interest to prepare the chlorinated *o*- and *p*-(α-phenylethyl)phenols and some of their derivatives. The chlorination

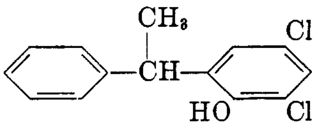


was carried out in carbon tetrachloride as solvent and led to the di-substitution products as could be expected under the conditions of the experiments.

The p-(α-phenylethyl)phenol yielded 2,6-dichloro-4-(α-phenylethyl)phenol (I) and the o-(α-phenylethyl)phenol gave 2,4-dichloro-6-(α-phenylethyl)phenol (II).



(I)



(II)

Esters and ethers of these chlorinated products were made in an analogous fashion to that of the unsubstituted α-phenylethyl phenols.

EXPERIMENTAL

The *o- and p-(α-phenylethyl)phenols* used were prepared in this laboratory by the following procedure. Phenol and styrene were reacted in a mole ratio of 4:1 in the presence of sulfuric acid (0.74% of total weight). The styrene was added dropwise to the phenol with stirring in order to avoid polymerization. The mixture was refluxed for four hours. The acid was then neutralized with sodium carbonate solution. The precipitate, consisting of sodium sulfate and sodium carbonate, was filtered off and the water and excess phenol were distilled off. The residual mixture of the o- and p-(α-phenylethyl)phenol was separated by distillation in a Stedman column. The o-isomer distilled at 300–302° at 742.2 mm. and the p-isomer at 315–316° at 742.2 mm. The total yield was 75–85%, the p-isomer constituting 59–60% and the o-isomer 40–41%.

Procedure for esterification of o- and p-(α-phenylethyl)phenol. A round-bottom flask was fitted with a six-ball Snyder column, at the top of which was mounted a still-head with a side-arm fitted with a stopcock. The still-head was connected to a reflux condenser and thermometer, and the side-arm to a downward condenser, provided with an adapter and receiving flask at its end. In the reaction flask was placed: 1 mole of o- or p-(α-phenylethyl)phenol, 1 mole of a monocarboxylic acid (½ mol for dicarboxylic acids), and 1 mole of acetic anhydride. The mixture was refluxed for a period of time ranging from ½–2 hours (the latter being the case for dicarboxylic acids). The stopcock on the side-arm of the still-head was then opened and the acetic acid distilled off. The residual material was washed with dilute sodium hydroxide to remove any starting materials and was extracted with ether. The ether extract was dried over sodium sulfate. The solvent was removed and the residual product purified either by recrystallization or by a vacuum-distillation.

The *acetates* of *o*- and *p*-(α-phenylethyl)phenol were prepared in the following way: In a 500-cc. round-bottom flask was placed: 100 g. of *o*- or *p*-(α-phenylethyl)phenol, 300 cc. of acetic anhydride, and 10 g. of anhydrous sodium carbonate. The mixture was refluxed for a period of time ranging from 1½ to 5½ hours. The excess acetic anhydride and the acetic acid were distilled off and residual liquid vacuum-distilled.

p-(α-Phenylethyl)phenyl acetate. Colorless liquid, distilling at 186–189° at 6 mm. Yield: 88%.

Anal. Calc'd for $C_{16}H_{16}O_2$: C, 80.0; H, 6.65.
Found: C, 79.87; H, 6.43.

o-(α-Phenylethyl)phenyl acetate. Colorless liquid, distilling at 148° at 2.2 mm. Yield: 82%.

Anal. Calc'd for $C_{16}H_{16}O_2$: C, 80.0; H, 6.65.
Found: C, 80.08; H, 6.64.

p-(α-Phenylethyl)phenyl propionate. Colorless liquid, distilling at 198–204° at 7 mm. Yield: 93%.

Anal. Calc'd for $C_{17}H_{18}O_2$: C, 80.3; H, 7.08.
Found: C, 80.43; H, 6.99.

o-(α-Phenylethyl)phenyl propionate. Colorless liquid, distilling at 136–139° at 1.2 mm. Yield: 88%.

Anal. Calc'd for $C_{17}H_{18}O_2$: C, 80.3; H, 7.08.
Found: C, 80.44; H, 6.80.

p-(α-Phenylethyl)phenyl butyrate. Colorless liquid, distilling at 159° at 1.1 mm. Yield: 91%.

Anal. Calc'd for $C_{16}H_{20}O_2$: C, 80.6; H, 7.4.
Found: C, 80.49; H, 7.54.

o-(α-Phenylethyl)phenyl butyrate. Colorless liquid, distilling at 140° at 0.6 mm. Yield: 88%.

Anal. Calc'd for $C_{18}H_{20}O_2$: C, 80.6; H, 7.4.
Found: C, 80.95; H, 6.9.

p-(α-Phenylethyl)phenyl crotonate. Colorless liquid, distilling at 185–188° at 1.8 mm. Yield: 67%.

Anal. Calc'd for $C_{18}H_{18}O_2$: C, 81.2; H, 6.77.
Found: C, 80.6; H, 6.62.

o-(α-Phenylethyl)phenol crotonate. Colorless liquid, distilling at 142–146° at 1.4 mm. Yield: 63%.

Anal. Calc'd for $C_{18}H_{18}O_2$: C, 81.20; H, 6.77.
Found: C, 81.48; H, 7.02.

Bis-o-(α-phenylethyl)phenyl adipate. Colorless liquid, distilling at 128° at 1.3 mm. Yield: 30%.

Anal. Calc'd for $C_{34}H_{34}O_4$: C, 80.6; H, 6.7.
Found: C, 80.2; H, 6.7.

Bis-p-(α-phenylethyl)phenyl adipate. Colorless liquid, distilling at 165° at 3.0 mm. Yield: 29%.

Anal. Calc'd for $C_{34}H_{34}O_4$: C, 80.6; H, 6.7.
Found: C, 81.0; H, 6.9.

Bis-p-(α-phenylethyl)phenyl sebacate. Colorless liquid, distilling at 150–154° at 1.3 mm. Yield: 36%.

Anal. Calc'd for $C_{38}H_{42}O_4$: C, 81.1; H, 7.4.
Found: C, 81.4; H, 6.8.

Bis-o-(α-phenylethyl)phenyl sebacate. Colorless liquid, distilling at 125–127° at 0.7–0.8 mm. Yield: 32%.

Anal. Calc'd for $C_{38}H_{42}O_4$: C, 81.1; H, 7.4.
Found: C, 81.23; H, 6.7.

Procedure for the preparation of alkyl ethers of o- and p-(α-phenylethyl)phenol. In a round-bottom flask was placed: 1 mole of *o*- or *p*-(α-phenylethyl)phenol, 1 mole of alkyl bromide, 1 mole of anhydrous potassium carbonate, and 5 moles of acetone. The mixture was refluxed for 3½ hours. The white precipitate, consisting of potassium bromide, was filtered off. The filtrate was freed from solvent and washed with dilute sodium hydroxide solution and water to remove any starting materials. It was then extracted with ether and the ether extract dried over sodium sulfate. The solvent was distilled off and the product purified by a vacuum-distillation.

p-(α-Phenylethyl)phenyl n-propyl ether. Colorless liquid, distilling at 189–190° at 6 mm. Yield: 45%.

Anal. Calc'd for $C_{17}H_{20}O$: C, 85.0; H, 8.3.
Found: C, 84.85; H, 8.49.

o-(α-Phenylethyl)phenyl n-propyl ether. Colorless liquid, distilling at 157–160° at 4 mm. Yield: 30%.

Anal. Calc'd for $C_{17}H_{20}O$: C, 85.0; H, 8.3.
Found: C, 85.06; H, 8.03.

p-(α-Phenylethyl)phenyl n-butyl ether. Colorless liquid, distilling at 192–197° at 6 mm. Yield: 45%.

Anal. Calc'd for $C_{18}H_{22}O$: C, 85.0; H, 8.65.
Found: C, 84.87; H, 8.41.

o-(α-Phenylethyl)phenyl n-butyl ether. Colorless liquid, distilling at 160° at 3 mm. Yield: 30%.

Anal. Calc'd for $C_{18}H_{22}O$: C, 85.0; H, 8.65.
Found: C, 85.05; H, 8.80.

Procedure for the preparation of the glycerol diethers of o- and p-(α-phenylethyl)phenol. In a 500-cc. round-bottom flask was placed: 50 g. of *o*- or *p*-(α-phenylethyl)phenol, 10.6 g. of sodium hydroxide in 100 cc. of water, and 11.7 g. of epichlorohydrin. The mixture was refluxed for five hours. Afterwards it was washed with a dilute sodium hydroxide solution and extracted with ether. The ether extract was dried over sodium sulfate. After filtering the solvent was removed and the product was distilled *in vacuo*.

1,3-Bis-[p-(α-phenylethyl)phenoxy]propanol-2. Light yellow oil, distilling at 164–166° at 3 mm. Yield: 20%.

Anal. Calc'd for $C_{31}H_{32}O_3$: C, 84.16; H, 7.23.
Found: C, 84.06; H, 7.14.

1,3-Bis[o-(α-phenylethyl)phenoxy]propanol-2. Light yellow oil, distilling at 142–144° at 2.6 mm. Yield: 20%.

Anal. Calc'd for $C_{31}H_{32}O_3$: C, 84.16; H, 7.23.
Found: C, 83.74; H, 7.21.

Procedure for the preparation of β-ethanol ethers of o- and p-(α-phenylethyl)phenol. In a pressure-bottle was placed: 0.1 mole of *o*- or *p*-(α-phenylethyl)phenol, 0.025 mole of sodium hydroxide, 25 cc. of water, and 0.1 mole of ethylene oxide. The bottle was placed in a thermostatically-controlled water-bath overnight at 40°. A shaking device provided agitation. Two layers formed. The organic layer was separated and fractionally distilled.

2-(α-Phenylethyl)phenoxyethanol-2. Colorless cubes from ligroin, m.p. 83° (uncorr.); b.p. 175° at 0.3 mm. Yield: 66%.

Anal. Calc'd for $C_{16}H_{18}O_2$: C, 79.3; H, 7.45.
Found: C, 79.1; H, 7.50.

4-(α-Phenylethyl)phenoxyethanol-2. Colorless liquid, distilling at 175° at 0.6 mm. Yield: 64%.

Anal. Calc'd for $C_{16}H_{18}O_2$: C, 79.3; H, 7.45.
Found: C, 79.1; H, 7.50.

Procedure for the preparation of o- and p-(α-phenylethyl)phenoxyacetic acids. In a beaker was placed: 0.2 mole of *o*- or *p*-(α-phenylethyl)phenol, 0.2 mole of monochloroacetic acid, 0.21 mole of sodium hydroxide, and 75 cc. of water. The mixture was concentrated on the steam-bath. It was then dissolved in 400 cc. of hot water. After cooling it was made acid to litmus and extracted with ether. The ether extract was dried over sodium sulfate, the solvent was evaporated, and the residual liquid fractionally-distilled.

2-(α-Phenylethyl)phenoxyacetic acid. Colorless prisms from benzene, m.p. 135° (uncorr.). Yield: 48%.

Anal. Calc'd for $C_{16}H_{16}O_3$: C, 75.0; H, 6.3.
Found: C, 75.2; H, 6.4.

4-(α-Phenylethyl)phenoxyacetic acid. Colorless plates from ligroin, m.p. 100° (uncorr.). Yield: 51%.

Anal. Calc'd for $C_{16}H_{16}O_3$: C, 75.0; H, 6.3.
Found: C, 75.1; H, 6.4.

Procedure for the chlorination of o- and p-(α-phenylethyl)phenol. In a 3-l. three-necked flask, equipped with stirrer, gas inlet tube, and outlet tube, was placed 100 g. of *o*- or *p*-(α-phenylethyl)phenol and 500 cc. of carbon tetrachloride. The reaction flask was immersed in a cold-water bath. A stream of chlorine gas was passed through the solution at a fairly rapid rate for three hours. The solvent was then evaporated and the residual liquid distilled *in vacuo*.

2,6-Dichloro-4-(α-phenylethyl)phenol. Light yellow oil, distilling at 196–202° at 6 mm. Yield: 50%.

Anal. Calc'd for $C_{14}H_{12}Cl_2O$: Cl, 26.59. Found: Cl, 26.53.

2,4-Dichloro-6-(α-phenylethyl)phenol. Light yellow oil, distilling at 174–175° at 3.2 mm. Yield: 53%.

Anal. Calc'd for $C_{14}H_{12}Cl_2O$: Cl, 26.59. Found: Cl, 26.28.

2,4-Dichloro-6-(α-phenylethyl)phenyl allyl ether was prepared in the following way: In a 500-cc. three-necked flask, equipped with stirrer, reflux condenser, and dropping-funnel, was placed 27.4 g. of 2,4-dichloro-6-(α-phenylethyl)phenol together with a solution of 4.6 g. of sodium hydroxide in 50 cc. of water and 50 cc. of methanol. Then 13.7 g. of allyl bromide was added gradually through the dropping-funnel. The reaction mixture was stirred for 40 minutes more. The oily product was washed with a dilute sodium hydroxide solution, extracted with ether, and the extract was dried over sodium sulfate. The solvent was removed and the remainder of the liquid was distilled *in vacuo*. Rejecting the forerun, the product distilled at 158–162° at 1.2 mm. as a light yellow liquid. Yield: 50%.

Anal. Calc'd for $C_{17}H_{16}Cl_2O$: C, 66.45; H, 5.2.
Found: C, 66.71; H, 5.33.

The esters of the chlorinated o- and p-(α-phenylethyl)phenols were prepared in the same manner as described for the unsubstituted phenylethylphenols.

2,6-Dichloro-4-(α-phenylethyl)phenyl acetate. Light yellow liquid, distilling at 140–144° at 1.6 mm. Yield: 51%.

Anal. Calc'd for $C_{16}H_{15}Cl_2O_2$: Cl, 22.75. Found: Cl, 22.63.

2,4-Dichloro-6-(α-phenylethyl)phenyl acetate. Colorless prisms from alcohol, m.p. 74.5–75.5° (uncorr.). Yield: 60%.

Anal. Calc'd for $C_{16}H_{15}Cl_2O_2$: C, 62.1; H, 4.52.
Found: C, 61.96; H, 4.35.

2,4-Dichloro-6-(α-phenylethyl)phenyl propionate. Colorless oil, distilling at 180–182° at 1.7 mm. Yield: 40%.

Anal. Calc'd for $C_{17}H_{16}Cl_2O_2$: C, 63.4; H, 4.65.
Found: C, 63.80; H, 4.65.

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SUMMARY

1. A series of new aliphatic esters, ethers, alcohol-ethers, and oxyacetic acids of *o*- and *p*-(α-phenylethyl)phenol was prepared and characterized.

2. The glycerol diethers of *o*- and *p*-(α-phenylethyl)phenol were prepared conveniently by the reaction with epichlorohydrin.

3. The chlorination of *o*- and *p*-(α-phenylethyl)phenol in carbon tetrachloride as solvent, yielded the corresponding dichloro compounds.

4. Esters and ethers of these dichloro compounds were prepared.

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