poured onto 100 g. of crushed ice and this acid mixture made slightly basic to phenolphthalein with 5 molar sodium hydroxide. Distillation yielded a fraction (6.4 g.), b.p. 60–97°, which, after drying over calcium chloride, amounted to 4.6 g. The refractive index of this mixture of ethyl acetate and carbon tetrachloride indicated that it contained 3.8 g. of the ester. The same procedure carried out on a known mixture of 5 g. of ethyl acetate and 55 g. of carbon tetrachloride gave a recovery of 3.9 g. of ethyl acetate. On this basis it was concluded that the original 175 g. of the first distillate contained *ca.* 11 g. (29%) of ethyl acetate.

**The Reaction of Oxygen with Phenylketene Dimethylacetal.**—In an apparatus used for hydrogenation at atmospheric pressure, 20.5 g. of phenylketene dimethylacetal was placed under an atmosphere of oxygen. When stirred the ketene acetal began to absorb oxygen and the reaction soon was sufficiently exothermic that the flask had to be cooled with a water-bath occasionally in order to keep the temperature below 60°. At the end of three hours the oxygen absorption had practically stopped; the reaction flask was warmed to 60° and some additional oxygen was absorbed, but after an hour at 60° the rate of absorption of oxygen was negligible. A total of 2240 ml. (740 mm., 28°) of oxygen was absorbed.

The reaction mixture was then heated at 70° under 8 mm. pressure; 4.5 g. (40%) of dimethyl carbonate, m.p. −1°, $n^{25}$D 1.3761 collected in the cold trap. As the temperature was increased, 5.1 g. (38%) of benzaldehyde distilled at 53° (10 mm.); $n^{25}$D 1.5212. The next fraction (4.9 g.) boiled up to 90° (0.4 mm.) and was shown to be a mixture of methyl benzoate and methyl phenylacetate by preparation of the amides after partial separation of the esters by fractional distillation. Finally, 7 g. (37%) of dimethyl $\alpha,\alpha'$-diphenylsuccinate (XIV) was sublimed from the remaining material; only 1.5 g. of a tarry residue remained.

MADISON, WISCONSIN RECEIVED OCTOBER 11, 1951

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[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

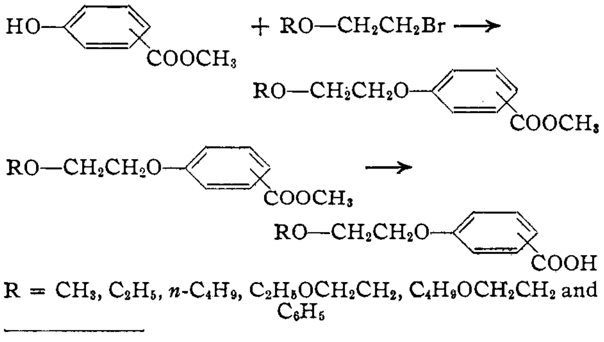
# The Preparation of Some Polyalkoxy Ethers of the Isomeric Hydroxybenzoic Acids[1]

BY R. W. BOST[2] AND MELDRUM B. WINSTEAD, JR.[3]

A number of new compounds have been synthesized in connection with a study of the relationship of position isomerism with surface activity. These compounds are of the type consisting of various polyalkoxy ethers of the isomeric hydroxybenzoic acids, and have been prepared by the Williamson synthesis of mixed ethers.

In connection with the investigation of the relationship of position isomerism with the surface activity of various compounds—a study which has been under observation in this Laboratory for the past ten years—a number of new compounds have been prepared by the present investigators. Due to the availability of various Cellosolves and Carbitols from the Carbide and Carbon Chemicals Corporation, a method was sought which would most conveniently enable one to introduce the polyalkoxy ether linkage into the benzene ring. This was accomplished, first, by converting the various Cellosolves and Carbitols into the corresponding $\beta$-bromoethers by the action of phosphorous tribromide, and, second, by employing the Williamson synthesis of ethers for the reaction between the various $\beta$-bromoethers and the particular substituted phenol desired. The series of reactions followed can be outlined in this manner:

$$3RO—CH_2CH_2OH + PBr_3 \longrightarrow 3RO—CH_2CH_2Br + H_3PO_3$$



$R = CH_3, C_2H_5, n\text{-}C_4H_9, C_2H_5OCH_2CH_2, C_4H_9OCH_2CH_2$ and $C_6H_5$

Of the compounds reported in this article, only one was found to have been previously reported.[4] The phosphorus tribromide employed in this series of reactions, as well as $\beta$-bromoethyl ethyl ether, was obtained in a good degree of purity from Eastman Kodak Company. Methyl cellosolve, butyl cellosolve, ethyl carbitol and butyl carbitol were obtained from Carbide and Carbon Chemicals Corporation and were redistilled before use. $\beta$-Phenoxyethyl bromide was prepared according to the procedure outlined in "Organic Syntheses" for $\gamma$-phenoxypropyl bromide.[5] The procedures involved in the preparation of $\beta$-bromoethyl methyl ether, $\beta$-bromoethyl *n*-butyl ether, 2-(2′-ethoxyethoxy)-ethyl bromide and 2-(2′-butoxyethoxy)-ethyl bromide are described in the experimental section. The yields obtained in these reactions varied from 26% for 2-(2′-ethoxyethoxy)-ethyl bromide and 36% for $\beta$-bromoethyl methyl ether to 52% for $\beta$-bromoethyl *n*-butyl ether and 64% for 2-(2′-butoxyethoxy)-ethyl bromide. In all cases the reaction was considered to involve merely a replacement of the hydroxy group by a bromine atom. However, the reaction appears to be of a more complex nature than one of simple substitution, and this would tend to account in some respects for the low yields obtained in several cases. In connection with this the reader is referred to the work of Gerrard[6] concerning the mechanism of the reaction between hydroxy compounds and phosphorus tribromide.

Methyl *p*-hydroxybenzoate and methyl *m*-hydroxybenzoate were prepared from *p*-hydroxybenzoic acid and *m*-hydroxybenzoic acid, re-

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[1] This paper represents a portion of a thesis submitted by Meldrum B. Winstead, Jr., in partial fulfillment of the requirements for the degree of Doctor of Philosophy, University of North Carolina, June, 1952.

[2] Deceased.

[3] du Pont Fellow in Chemistry, 1951–1952.

[4] W. G. Christiansen and S. E. Harris (to E. R. Squibb and Sons) U. S. 2,404,691, July 23, 1946.

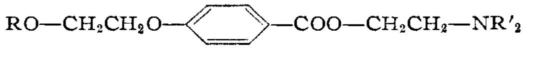
[5] H. Gilman and A. H. Blatt, "Organic Syntheses," Coll. Vol. I 2nd. Edition, 4th Printing, John Wiley and Sons, Inc., New York N. Y., 1947, p. 436 (Note 6).

[6] W. Gerrard, *J. Chem. Soc.*, 848 (1945).

spectively, in good yields according to the procedure described in the literature.[7,8] Methyl salicylate was obtained from Eastman Kodak Company and was dried over Drierite and redistilled before use. The use of the esterified hydroxybenzoic acids was preferred to that of the free acids, because in the subsequent isolation of the methyl polyalkoxybenzoates, any unreacted methyl hydroxybenzoate could be easily removed by washing with dilute sodium hydroxide.

The procedure employed for the preparation of the polyalkoxybenzoic acids described in this report is basically similar to that described for the preparation of *p*-(2-ethoxyethoxy)-benzoic acid.[4] However, various modifications have been introduced for the purpose of improving the applicability as well as the yield of the reaction. In the present investigation no quantitative study was made concerning the connection between the refluxing time of the reaction and the percentage yield obtained. In all cases, however, it was found that in the preparation of the ortho isomers, a longer period of refluxing was required than was necessary for the corresponding meta and para isomers in order to obtain a modest yield of the product. In general, the preparation of the meta isomer required a longer refluxing period than the para isomer. In connection with the use of various solvents for the reaction a study was made concerning the advantages of dioxane over acetone, and it was found that due to the higher reaction temperature that could be maintained by the use of dioxane, the yields were somewhat higher when dioxane was employed as the solvent, particularly in the preparation of the ortho isomers. In addition, the refluxing period was lessened by several hours. Among the observations made in connection with the compounds reported in this article, one is concerned with the melting point of the various isomers. In all cases the melting point of the para isomer was greater than that of the meta isomer, and this, in turn, was greater than that of the ortho isomer. No definite polymorphism was found to occur in the *p*-polyalkoxybenzoic acids prepared in this report.[9]

In view of the relationship of the compounds herein reported to Diethoxin (diethylaminoethyl *p*-ethoxybenzoate hydrochloride), the investigators have undertaken a study of the synthesis and possible local anesthetic activity of esters of the type



where R represents $CH_3$, $C_2H_5$, *n*-$C_4H_9$, $C_2H_5OCH_2$-$CH_2C_4H_9OCH_2CH_2$ and $C_6H_5$ and R′ represents $CH_3$ and $C_2H_5$. The results of this investigation will appear in a future report.

## Experimental[10]

**β-Bromoethyl Methyl Ether (I).**—This compound was prepared by the method of Tallman[11] and, also, by the procedure described by Polomaa and Kenetti for the preparation of various β-bromoethers.[12]

**β-Bromoethyl *n*-Butyl Ether (II).**—This compound was prepared by the method of Polomaa and Kenetti.[12]

**2-(2′-Butoxyethoxy)-ethyl Bromide (III).**—The procedure used for this preparation was a modification of that described by Blicke and Zienty.[13]

Into a 1-l. three-necked flask equipped with a dropping funnel, stirrer and reflux condenser was placed 259.5 g. (1.6 moles) of butyl carbitol. The solution was warmed slightly and 135.4 g. (0.5 mole) of phosphorus tribromide was added slowly through the dropping funnel. The addition of phosphorus tribromide required two hours during which time the reaction mixture became yellowish-orange in color, and fumes of hydrogen bromide were evolved which dissolved in the reaction medium upon cooling slightly. The mixture was cooled, poured into 500 cc. of water, and the crude product settled as an oil. The aqueous solution was separated, thoroughly extracted with ether, and the ether extracts were added to the crude product. The ethereal extract of the product was washed with two 50-cc. portions each of 10% sulfuric acid, 10% sodium carbonate and water. After drying over potassium carbonate overnight the ether was removed and the product was distilled and collected at 111–114° at 13 mm. or at 101–104° at 9 mm. The reported boiling point is 115–118° at 13 mm.; yield 215.2 g. (64%).

**2-(2′-Ethoxyethoxy)-ethyl Bromide (IV).**—This compound was prepared according to the method described by McCusker and Kroeger.[14] It was also prepared by the modified procedure given in the preparation of (III). The product was collected at 97–105° at 33 mm. The reported boiling point is 100–101° at 33 mm. Twenty-six per cent. of the theoretical yield was obtained.

**Preparation of the Polyalkoxybenzoic Acids (Table I).**—The following procedure represents a quite general one that can be used for the preparation of the various polyalkoxybenzoic acids described in this report.

Sixty grams (0.396 mole) of the methyl hydroxybenzoate desired, 0.417 mole of the particular β-bromoether, and 80 g. of anhydrous potassium carbonate were placed in a 500-cc. three-necked flask fitted with a mechanical stirrer and a reflux condenser. Sufficient dioxane (previously dried over sodium and distilled) or C.P. acetone was added to the above mixture until the total volume was approximately 250 cc. The resulting mixture was then refluxed rather vigorously for a considerable period of time, and rapid stirring was maintained in order to reduce the amount of bumping. The mixture was cooled and filtered to remove the insoluble potassium bromide and potassium carbonate, and the clear filtrate was either poured into a liter of water with stirring or else the acetone or dioxane was removed by distillation under reduced pressure. In either case the resulting water-insoluble oil consisted of the methyl ester of the particular polyalkoxybenzoic acid to be prepared. The methyl ester was dissolved in ether, and the aqueous solution was thoroughly extracted with ether to remove all of this ester. The combined ethereal extracts of the methyl ester were washed thoroughly with 10% sodium hydroxide in order to remove any unreacted methyl hydroxybenzoate. Generally, five 50-cc. portions of 10% sodium hydroxide were sufficient to remove the unreacted starting material in the case of the para and meta polyalkoxybenzoic acids, whereas in the case of the ortho polyalkoxybenzoic acids twelve 50-cc. portions of 10% sodium hydroxide were required to remove any unreacted methyl salicylate.

The ether was then removed under diminished pressure and the methyl ester was saponified with 300 cc. of 10% sodium hydroxide containing 0.3 g. of Aerosol OT. Saponification was usually complete within one hour. The alkaline solution was cooled, filtered and extracted with two 75-cc. portions of ether in order to remove any excess β-bromoether, and the ether extracts were discarded. The alkaline solution was acidified with concd. hydrochloric acid with stirring and cooling, and the desired polyalkoxybenzoic acid precipitated either as white or tan crystals or as a yellow oil. If the product was a solid, it was filtered, washed with water, dried over phosphorus pentoxide, and, finally, recrystallized from a suitable solvent until a constant melting point was obtained. Decolorizing charcoal was used when-

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[7] G. H. v. Hoessle, *J. prakt. Chem.*, [2] **49**, 501 (1894).

[8] J. B. Cohen and H. W. Dudley, *J. Chem. Soc.*, **97**, 1742 (1910).

[9] G. M. Bennett and B. Jones, *ibid.*, 420 (1939).

[10] All melting points are corrected. All boiling points are uncorrected.

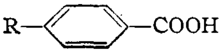
[11] R. C. Tallman, This Journal, **56**, 126 (1934).

[12] M. H. Polomaa and A. Kenetti, *Ber.*, **64B**, 797 (1931).

[13] F. F. Blicke and M. F. Zienty, This Journal, **63**, 2779 (1941).

[14] P. A. McCusker and J. W. Kroeger, *ibid.*, **59**, 213 (1937).

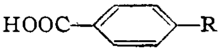
TABLE I

PREPARATION OF 

| Cpd. | R | Reflux time, hours | Crystn. solv. | Yield,[a] % | M.p., °C. | B.p., °C. | Formula | Analyses, % Carbon Calcd. | Carbon Found | Hydrogen Calcd. | Hydrogen Found |
|---|---|---|---|---|---|---|---|---|---|---|---|
| V | *p*-(2-Methoxyethoxy)- | 13 | Benzene[b] | 37 | 152–153 | .............. | $C_{10}H_{12}O_4$ | 61.21 | 61.30 | 6.17 | 6.21 |
| VI | *m*-(2-Methoxyethoxy)- | 27 | Petr. ether (60–90°) | 58 | 81.5–82.5 | .............. | $C_{10}H_{12}O_4$ | 61.21 | 61.31 | 6.17 | 6.36 |
| VII | *o*-(2-Methoxyethoxy)- | 71.5 | ................ | 50 | ........ | 183.5–184 (4 mm.) | $C_{10}H_{12}O_4$ | 61.21 | 60.93 | 6.17 | 6.23 |
| VIII | *p*-(2-Ethoxyethoxy)- | 15 | Benzene[c] | 45 | 134–134.5 | .............. | $C_{11}H_{14}O_4$ | 62.84 | 62.85 | 6.71 | 6.69 |
| IX | *m*-(2-Ethoxyethoxy)- | 21 | Petr. ether (60–90°) | 70 | 77.5–78.5 | .............. | $C_{11}H_{14}O_4$ | 62.84 | 62.87 | 6.71 | 6.70 |
| X | *o*-(2-Ethoxyethoxy)- | 81.5 | ................ | 53 | ........ | 171–172 (2 mm.) | $C_{11}H_{14}O_4$ | 62.84 | 62.79 | 6.71 | 6.95 |
| XI | *p*-(2-Butoxyethoxy)- | 24 | Benzene | 69 | 115.5–116 | .............. | $C_{13}H_{18}O_4$ | 65.51 | 65.46 | 7.60 | 7.79 |
| XII | *m*-(2-Butoxyethoxy)- | 38 | Petr. ether (90–100°) | 61 | 46.5–47 | .............. | $C_{13}H_{18}O_4$ | 65.51 | 65.27 | 7.60 | 7.74 |
| XIII | *o*-(2-Butoxyethoxy)- | 80 | ................ | 51 | ........ | 189–192 (3 mm.) | $C_{13}H_{18}O_4$ | 65.51 | 65.51 | 7.60 | 7.87 |
| XIV | *p*-(2'-Ethoxy-2-ethoxyethoxy)- | 20 | Benzene | 41 | 103.5–104 | .............. | $C_{13}H_{18}O_5$ | 61.38 | 61.12 | 7.12 | 7.19 |
| XV | *m*-(2'-Ethoxy-2-ethoxyethoxy)- | 44.5 | ................ | 71[d] | 38–39 | 206–208 (2.5 mm.) | $C_{13}H_{18}O_5$ | 61.38 | 61.20 | 7.12 | 7.15 |
| XVI | *o*-(2'-Ethoxy-2-ethoxyethoxy)- | 98 | ................ | 22 | ........ | 198–200 (2 mm.) | $C_{13}H_{18}O_5$ | 61.38 | 61.32 | 7.12 | 7.12 |
| XVII | *p*-(2'-Butoxy-2-ethoxyethoxy)- | 18 | Benzene–petr. ether (60–90°) | 53 | 85.5–86.5 | .............. | $C_{15}H_{22}O_5$ | 63.83 | 63.80 | 7.86 | 7.88 |
| XVIII | *m*-(2'-Butoxy-2-ethoxyethoxy)- | 41 | ................ | 62 | ........ | 215–219 (3 mm.) | $C_{15}H_{22}O_5$ | 63.83 | 63.92 | 7.86 | 8.03 |
| XIX | *o*-(2'-Butoxy-2-ethoxyethoxy)- | 100 | ................ | 42 | ........ | 209–212 (2 mm.) | $C_{15}H_{22}O_5$ | 63.83 | 63.85 | 7.86 | 7.89 |
| XXII | *p*-(2-Phenoxyethoxy)- | 22 | Alcohol | 76[e] | 200–200.5 | .............. | $C_{15}H_{14}O_4$ | 69.76 | 69.64 | 5.46 | 5.64 |
| XXIV | *m*-(2-Phenoxyethoxy)- | 35.5 | 80% Alcohol | 55 | 153–154 | .............. | $C_{15}H_{14}O_4$ | 69.76 | 69.79 | 5.46 | 5.64 |
| XXV | *o*-(2-Phenoxyethoxy)- | 90 | Benzene–petr. ether (30–60°) | 65 | 85–86 | .............. | $C_{15}H_{14}O_4$ | 69.76 | 69.80 | 5.46 | 5.69 |

[a] Based on the amount of methyl hydroxybenzoate that reacted unless otherwise noted. [b] Soxhlet extractor used. [c] Aqueous methanol used as crystn. solv. first, followed by benzene. [d] Based on 32 g. (65%) of methyl *m*-(2'-ethoxy-2-ethoxyethoxy)-benzoate, boiling at 183–185° at 6.5 mm. [e] Based on (XXI).

TABLE II

S-BENZYLPSEUDOTHIURONIUM SALTS OF 

| Cpd. No. | R | Crystn. solv. for deriv. | M.p., °C. | Formula of deriv. | Anal. of deriv. Nitrogen, % Calcd. | Found |
|---|---|---|---|---|---|---|
| V | *p*-(2-Methoxyethoxy)- | Dioxane | 143–144 | $C_{18}H_{22}N_2O_4S$ | 7.73 | 7.79 |
| VI | *m*-(2-Methoxyethoxy)- | Dioxane | 134 | $C_{18}H_{22}N_2O_4S$ | 7.73 | 7.72 |
| VII | *o*-(2-Methoxyethoxy)- | Ethyl acetate | 105.5 | $C_{18}H_{22}N_2O_4S$ | 7.73 | 7.69 |
| VIII | *p*-(2-Ethoxyethoxy)- | 95% Alcohol | 155 | $C_{19}H_{24}N_2O_4S$ | 7.44 | 7.35 |
| IX | *m*-(2-Ethoxyethoxy)- | Dioxane | 130 | $C_{19}H_{24}N_2O_4S$ | 7.44 | 7.59 |
| X | *o*-(2-Ethoxyethoxy)- | Ethyl acetate | 126.5 | $C_{19}H_{24}N_2O_4S$ | 7.44 | 7.53 |
| XI | *p*-(2-Butoxyethoxy)- | Dioxane | 142 | $C_{21}H_{28}N_2O_4S$ | 6.92 | 6.91 |
| XII | *m*-(2-Butoxyethoxy)- | Dioxane | 135 | $C_{21}H_{28}N_2O_4S$ | 6.92 | 7.02 |
| XIII | *o*-(2-Butoxyethoxy)- | Ethyl acetate | 114.5 | $C_{21}H_{28}N_2O_4S$ | 6.92 | 7.00 |
| XIV | *p*-(2'-Ethoxy-2-ethoxyethoxy)- | Dioxane | 123 5–124 | $C_{21}H_{28}N_2O_5S$ | 6.66 | 6.85 |
| XV | *m*-(2'-Ethoxy-2-ethoxyethoxy)- | Dioxane | 114 | $C_{21}H_{28}N_2O_5S$ | 6.66 | 6.83 |
| XVI | *o*-(2'-Ethoxy-2-ethoxyethoxy)- | .......... | Oil | | | .. |
| XVII | *p*-(2'-Butoxy-2-ethoxyethoxy)- | Ethyl acetate | 133.5 | $C_{23}H_{32}N_2O_5S$ | 6.24 | 6.13 |
| XVIII | *m*-(2'-Butoxy-2-ethoxyethoxy)- | Ethyl acetate | 124 | $C_{23}H_{32}N_2O_5S$ | 6.24 | 6.25 |
| XIX | *o*-(2'-Butoxy-2-ethoxyethoxy)- | Ethyl acetate | 91–92 | $C_{23}H_{32}N_2O_5S$ | 6.24 | 6.40 |
| XXII | *p*-(2-Phenoxyethoxy)- | Dioxane | 154 | $C_{23}H_{24}N_2O_4S$ | 6.60 | 6.66 |
| XXIV | *m*-(2-Phenoxyethoxy)- | Ethyl acetate | 137 | $C_{23}H_{24}N_2O_4S$ | 6.60 | 6.65 |
| XXV | *o*-(2-Phenoxyethoxy)- | Ethyl acetate | 136–136.5 | $C_{23}H_{24}N_2O_4S$ | 6.60 | 6.68 |

ever necessary. If the polyalkoxybenzoic acid precipitated as an oil, the acid solution containing the product was thoroughly extracted with ether to remove the product, and this ethereal solution was dried over Drierite for twenty-four hours. The ether was removed by distillation under diminished pressure and the desired product was purified by two distillations under diminished pressure, resulting in a practically colorless oil.

**Methyl *p*-(2-Phenoxyethoxy)-benzoate (XX).**—Twenty-nine and one-half grams (0.194 mole) of methyl *p*-hydroxybenzoate, 44 g. (0.219 mole) of β-phenoxyethyl bromide, 35 g. of potassium carbonate and 150 cc. of dioxane were mixed in a 500-cc. three-necked flask. The mixture was stirred and refluxed for 22 hours, an additional 5 g. of β-phenoxyethyl bromide being added after 11 hours of refluxing. The mixture was cooled, poured slowly into 500 cc. of water with stirring, and, after all of the potassium carbonate and potassium bromide had dissolved, the solution was filtered and the product dried. Five grams of (XX) were recrystallized twice from 95% alcohol, m.p. 105–106.5°. The remainder of (XX) was saponified directly to (XXI).

*Anal.* Calcd. for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.55; H, 6.23.

**Sodium *p*-(2-Phenoxyethoxy)-benzoate (XXI).**—The crude product (XX) was dissolved in 300 cc. of hot 95% alcohol, 150 cc. of 10% sodium hydroxide was added slowly, and the solution was refluxed for 2 hours. After 200 cc. of the alcohol had been removed by distillation, the remainder of the solution was chilled, which resulted in the precipitation of (XXI). A portion of (XXI) was recrystallized from a mixture of alcohol and water, and the remainder was converted directly into (XXII) by dissolving it in 1 l. of boiling water with stirring and acidifying with concd. hydrochloric acid.

*Anal.* Calcd. for $C_{15}H_{13}O_4Na$: Na, 8.21. Found: Na, 8.13.

**Methyl *m*-(2-Phenoxyethoxy)-benzoate (XXIII).**—Seventy grams (0.461 mole) of methyl *m*-hydroxybenzoate, 100 g. (0.498 mole) of β-phenoxyethyl bromide, 80 g. of potassium carbonate and 350 cc. of dioxane were mixed in a 1-l. three-necked flask and refluxed with stirring for 35.5 hours. An additional 5 g. of β-phenoxyethyl bromide was added after 13 hours of refluxing had elapsed. The solution was chilled and poured slowly and with stirring into 1200 cc. of cold water. The product precipitated as a yellow oil which solidified upon being chilled overnight. The solution was filtered, and the product, with the exception of a small amount which was reserved for purification and analysis, was saponified directly to (XXIV) using an alcohol-aqueous sodium hydroxide mixture. The product (XXIII), after several recrystallizations from absolute methyl alcohol, melted at 69.5–70.5°.

*Anal.* Calcd. for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.53; H, 6.07.

**S-Benzylpseudothiuronium Salts of Polyalkoxybenzoic Acids (Table II).**—The polyalkoxybenzoic acids were characterized by the formation of the solid S-benzylpseudothiuronium salts. One gram of S-benzylpseudothiuronium chloride was dissolved in 20 cc. of warm absolute alcohol. An equivalent quantity of the organic acid was dissolved in 50 cc. of warm absolute alcohol, and the alcoholic solution was carefully neutralized with either 0.5% aqueous sodium hydroxide or 0.5% alcoholic sodium hydroxide until just pink to phenolphthalein. In a few cases a small amount of water was added to the boiling alcoholic solution in order to keep the sodium salt in solution. The alcoholic solution of S-benzylpseudothiuronium chloride was then added to the alcoholic sodium salt solution of the acid slowly and with shaking. The solution was chilled and the precipitate was filtered and recrystallized. In a number of cases it was necessary to evaporate the solution either to one-third of its original volume or to dryness in a hood in order to obtain the desired derivative.

**Acknowledgment.**—One of us (M.B.W.) wishes to express his appreciation to Dr. Robert L. McKee for his helpful suggestions in the preparation of this paper.

CHAPEL HILL, N. C. RECEIVED OCTOBER 29, 1951

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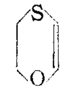
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA]

# Heterocyclic Vinyl Ethers. I. *p*-Oxathiene[1]

BY WILLIAM E. PARHAM, IRVING GORDON AND JEROME D. SWALEN

The synthesis of *p*-oxathiene was achieved by the acid-catalyzed dealkoxylation of 2-methyoxy-*p*-oxathiane. Experimental conditions for the dealkoxylation reaction were established by a preliminary study with a series of 2-tetrahydropyranyl ethers using various acidic catalysts. The mode of addition of unsymmetrical reagents to *p*-oxathiene furnishes direct chemical evidence to indicate that oxygen releases electrons more readily in the direction of its covalent bonds than does sulfur. Other properties of *p*-oxathiene are described.

The heterocyclic vinyl ethers I–IV represent an interesting class of compounds in that a knowledge of their properties might furnish valuable information regarding the relative electronic effects of oxygen and sulfur. This paper is concerned with the synthesis and properties of the first member of this series, *p*-oxathiene (I), prepared in 76% yield by slow distillation of 2-methoxy-1,4-oxathiane (V)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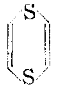
II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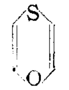
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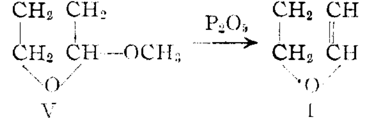
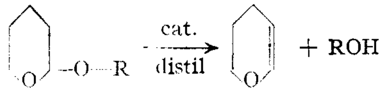
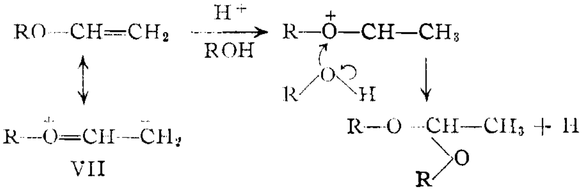

V I

from a small quantity of phosphorus pentoxide. The acetal V was prepared in 72% yield from monothioglycol and dimethyl chloroacetal by a procedure previously described.[2] Previous attempts to dealkoxylate acetals by this procedure have either resulted in failure, or low yields of products.[3] The choice of catalyst and reaction conditions for the dealkoxylation of V was established by a preliminary study with a series of 2-tetrahydropyranyl ethers (VI) using $ZnCl_2$, $P_2O_5$, *p*-$CH_3$–$C_6H_4SO_3H$ and AlCl as catalyst. These experiments are described in the Experimental section of this report. The best results were realized by employing phosphorus pentoxide as a catalyst with acetals whose boiling point was 200° or higher.


VI

R = $C_1$–$C_5$

Acid-catalyzed additions to vinyl ethers takes place[4] essentially as shown in the equations


VII

A study of the mode of addition of unsymmetrical reagents such as methanol and water to *p*-oxathiene would therefore provide data which could be interpreted as a measure of the relative ability of oxygen and sulfur to release electrons in the direction of their covalent bonds (structures Ia and Ib).

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[1] Part of this work was supported by aid received from the research funds of the Graduate School of the University of Minnesota.

[2] W. E. Parham, THIS JOURNAL, **69**, 2449 (1947).

[3] D. B. Killian, G. F. Hennion and J. A. Nieuwland, *ibid.*, **57**, 544 (1935); L. Claisen, *Ber.*, **31**, 1019 (1898).

[4] *Cf.* Hoaglin and Hirsch, THIS JOURNAL, **71**, 3468 (1949), for the mechanism of the acid-catalyzed addition of acetals to vinyl ethers. The β-carbon atom in VII is analogous to the ortho and para positions in anisole.