Monophenyl ether of triethylene glycol[3] was prepared as above using the phenyl ether of diethylene glycol prepared above and a similar ratio of reactants. The yield was 55%; b. p. 135–137° at 2 mm.; $n^{20}D$ 1.5200; d_{20} 1.1132; MR_D calcd. 60.62, found 61.79.

p-X-C_6H_4-OCH_2CH_2OH (X = CH_3, NO_2 Br, OH).—In general 50 g. of the *para*-substituted phenol was dissolved in 250 ml. of absolute alcohol in a 500-ml. three-necked flask fitted with a mechanical stirrer, a condenser with a drying tube and a cork in the third neck. An equivalent quantity of sodium shavings was added. Upon solution of the sodium the mixture was refluxed for an hour to ensure the formation of the sodium salt of the phenol. The cork was replaced by a dropping funnel from which 1.1 equivalents of anhydrous ethylene chlorohydrin was introduced dropwise while the mixture was stirred; when all the halohydrin had been added the solution was refluxed for twelve to twenty-four hours. The precipitate of sodium chloride was filtered off, the filtrate transferred to a Claisen flask, the alcohol removed and the residue distilled under reduced pressure. The distillate usually solidified in the receiver and was recrystallized from methanol or benzene.

***p*-Aminophenyl Ether of Ethylene Glycol.**—A mixture of 5.6 g. (0.0306 mole) of 2-(*p*-nitrophenoxy)-ethanol (see above), 100 ml. of absolute alcohol and 0.050 g. of platinum oxide catalyst was hydrogenated at atmospheric pressure. The reaction took up 2,315 ml. of hydrogen in an hour; calculated 2,410 ml. ($3H_2$ per mole of NO_2). (After the addition of 1400 ml. of hydrogen, the pressure bottle had to be cooled externally.) The catalyst was filtered off and the alcoholic solution concentrated to one half the original volume. The theoretical quantity of hydrogen chloride gas, 1.1 g., was added to the solution whereupon the amine hydrochloride precipitated out. Sufficient absolute alcohol to dissolve the hydrochloride was added and the solution chilled; yield, 5.7 g. of the hydrochloride (calcd. 5.77 g.), m. p. 200–205° dec. The theoretical quantity of ammonia, 4.6 ml. of 28% ammonium hydroxide solution, was added to the hydrochloride followed by 10–20 ml. of distilled water, and the mixture warmed to effect solution. On chilling there was obtained 3.5 g. of a salmon pink, leafy, crystalline solid, m. p. 71–72°; yield 80%.

Summary

Three series of aromatic glycols were prepared and characterized by means of derivatives.

NEW YORK, N. Y. RECEIVED JUNE 1, 1944

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF SCHIEFFELIN & CO.]

Aromatic Glycol Mercurials

BY ANTHONY J. SHUKIS AND RALPH C. TALLMAN

Our study on glycol mercurials[1] has been extended to the series of aromatic glycols described in the preceding paper.[2]

The mercuration of these compounds, the aromatic glycols, afforded an opportunity to introduce a mercury residue either into the ring (see Table I) or the side chain (see Table II) and to study the consequent effect produced on the antibacterial activity. It was desirable to prepare, for each glycol, both the ring mercurial and the corresponding chain substituted mercurial. This plan was followed as far as practicable, being limited by experimental difficulties in certain of the attempted chain mercurations; in these instances, either the glycol was recovered unchanged (no reaction), or the mercurial could not be purified without decomposition.

In general, the mercury residue was introduced into the side chain by the method previously described, namely, the interaction of the glycol with mercuric acetate and ethylene.[1] In those instances where a solid glycol was used the procedure was modified by conducting the reaction above the melting point of the glycol or by using a solvent. Ring mercuration occurred when the aromatic glycol was treated with mercuric acetate in alcohol containing 5% glacial acetic acid. Those aromatic glycols which contain no other substituent in the benzene ring yielded monomercurials. By controlling conditions, either one or two mercury residues could be introduced into compounds where more than one ring substituent was already present.

In the series of ring mercurials, the effect of substituting at the phenyl group (see Table I) was an increase in the antibacterial potency of the compounds. For *para* substituents, this enhancement by the various groups decreases in the following sequence: $NH_2 > NO_2 > OH > Br > CH_3 > H$. The effect of position isomerism, where the group studied was OH, follows the order para > meta > ortho. The monomercurial was more active than the dimercurial of the same compound in this series.

In the chain mercurial series (see Table II) the effect of substituents on the benzene ring was the opposite of that observed with the ring mercurials. The order of decreasing activity found was H > Br > *p*-OH > NO_2 > *o*-OH > CH_3. In regard to position isomerism in the two instances studied the order para > ortho prevailed.

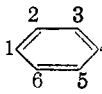
In general, in this investigation, we found that the chain mercurials were more effective bactericides than their ring analogs. The ring mercurials, compounds 4, 7, 9, 13, were less effective than their respective chain analogs, compounds 21, 20, 19, 24 (see Tables I and II, respectively). However, in the pairs of analogs 1–18, and 10–22 the reverse seems true. Attempts to prepare the chain analog of compound 11 met with no success. Should the general pattern be followed, this member, the corresponding chain mercurial, should prove to be an efficient bactericide. Also the attempt to prepare α-chloromercuri-β-phen-

(1) Shukis and Tallman, THIS JOURNAL, **65**, 2365 (1943).

(2) Shukis and Tallman, *ibid.*, **66**, 1461 (1944).

TABLE I

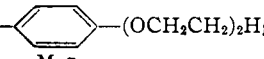
PHYSICAL PROPERTIES, ANALYSES, BACTERIOLOGICAL DATA

Type I:  H at 1–6, unless specified.

No.	1	2	3	4	5	6	M. p., °C., (uncor.)	Hg, Anal., % Calcd.	Found	Bacteri-cidal diln. × 10^{-3}
1	CH_3	HgCl		OCH_2CH_2OH			132	51.82	48.10	0.32
2	CH_3	HgCl		OCH_2CH_2OH		HgCl	218	64.50	64.00	.2
3	OH	OCH_3		$HgOCOCH_3$		$HgOCOCH_3$	154	62.57	63.88	.2
4	OH	OCH_2CH_2OH				HgCl	158	51.56	53.71	.2
5	OH		OCH_2CH_2OH			HgCl	178	51.56	52.11	.3
6	OH	HgCl	OCH_2CH_2OH			HgCl	212	64.36	63.00	.3
7	OH	HgCl		OCH_2CH_2OH			170	51.56	51.25	.5
8	OH	$HgOCOCH_3$		OCH_2CH_2OH		$HgOCOCH_3$	240	59.77	57.58	.2
9	Br	HgCl		OCH_2CH_2OH			185	44.40	44.45	.3
10	NO_2	$HgOCOCH_3$		OCH_2CH_2OH			200	45.42	43.20	1.0
11	NH_2	HgCl		OCH_2CH_2OH			149	51.70	47.45	3.0
12	OCH_2CH_2OH			$HgOCOCH_3$			147	50.57	50.12	0.2
13	OCH_2CH_2OH			HgCl			235	53.76	53.00	.2
14	$(OCH_2CH_2)_2OH$			$HgOCOCH_3$			145	45.50	44.30	.2
15	$(OCH_2CH_2)_2OH$			HgCl			187	49.98	48.60	.2
16	OCH_2CH_2OH		OCH_2CH_2OH	$HgOCOCH_3$		$HgOCOCH_3$	198	56.09	55.28	.5
17	OCH_2CH_2OH	$HgOCOCH_3$		OCH_2CH_2OH	$HgOCOCH_3$		209	56.09	54.70	1.0
	HgCl	....	....	....	...	...	...	...	...	< 0.5

TABLE II

PHYSICAL PROPERTIES, ANALYSES, BACTERIOLOGICAL DATA

Type II: 

No.	X	n	Y	M. p., °C. (uncor.)	Hg, Anal., % Calcd.	Found	Bacteri-cidal diln. × 10^{-3}
18	CH_3	2	Cl	70	48.33	48.10	0.2
19	Br	2	Cl	136	41.80	39.43	1.5
20	OH	2	Cl	65	48.08	46.10	1.0
21	(o-OH)	2	Cl	92	48.08	47.20	0.3
22	NO_2	2	I	165	37.30	37.50	0.4
23	H	2	$OCOCH_3$	oil	47.25	49.12	0.3
24	H	2	Cl	58	50.23	50.06	2.0
25	H	3	$OCOCH_3$	oil	45.05	43.00	0.25
26	H	4	Cl	185	41.00	43.37	0.5
	$HgCl_2$	..	..	..	...	...	<0.5

oxyethane, $C_6H_5OCH_2CH_2HgCl$, by the general scheme outlined below, from phenol, mercuric acetate and ethylene was unsuccessful. This compound should be of interest since it would be the first member of the series (see Table II) in which compound 24, the most effective chain mercurial, is located.

On the basis of this and other studies[1] we feel that the aromatic glycol mercurials hold more promise as a source of efficient bactericides than do the aliphatic glycol mercurials.

In the present investigation the bactericidal activity of the mercurials was differentiated from the bacteriostatic effect by means of the thioglycolate media.[3] The results given are the bactericidal dilutions killing *Staph. aureus* in ten minutes using the thioglycolate media technique. More complete results of the bacteriological study conducted on these compounds will appear elsewhere.

Experimental

Ring Monoacetoxymercurials.—A mixture of 0.1 mole of the glycol, 200 ml. of ethanol, 10 ml. of glacial acetic acid and 0.05 mole of mercuric acetate was allowed to stand at room temperature until the solution was free of Hg^{++} ions. The solution was concentrated by allowing the alcohol to evaporate, the precipitate of the monomercurial filtered off and the filtrate processed for more product. The solid was recrystallized from water or a small volume of ethanol. The yields varied from 60–85%.

Ring Diacetoxymercurials.—A mixture of 0.1 mole of the glycol, 200 ml. of ethanol, 10 ml. of glacial acetic acid and 0.1 mole of mercuric acetate was refluxed until free of Hg^{++} ions; usually two to three hours sufficed. The precipitate of dimercurial was filtered off and recrystallized from ethanol or glacial acetic acid. The filtrate was worked up to yield more product. The yields were 70 to 90%.

Mono- and Dihalomercurials.—A solution of the corresponding mono or diacetoxymercurial in ethanol or glacial acetic acid was poured into a 10–20% aqueous solution of reagent sodium halide. The precipitated halomercurial was filtered off and recrystallized from ethanol or glacial acetic acid. The yields were in the neighborhood of 90–95%. The majority of our compounds were converted to the chloromercurials.

Chain Mercurials (where X is CH_3, Br, NO_2, see Table II).—A mixture of 0.05 mole of the glycol and 0.02–0.03 mole of mercuric acetate was maintained at a temperature of 5–10° above the melting point of the glycol while ethylene was slowly bubbled through the thick mass by means of a narrow inlet tube reaching the bottom of the test-tube. The mass was stirred by means of the inlet tube during the addition of the gas, which was passed through the mixture until no Hg^{++} ions remained. The mass was then dissolved in a small volume of ethanol and poured into an equal volume of 10–20% aqueous solution of reagent grade sodium halide (in general, Cl^-; for no. 22, I^-). The chain halomercurial was filtered off and recrystallized from ethanol. The yields ranged from 20 to 30%.

Chain Mercurials (where X is OH).—In order to avoid ring mercuration, enhanced by the presence of a hydroxyl group in the ring, it was necessary to suspend the glycol in benzene. Ethylene was passed through a suspension of 0.025 mole of the glycol and 0.015 mole of mercuric acetate in 150–175 ml. of benzene until most of the material had dissolved. The solution was filtered and the filtrate evaporated to dryness. The chain acetoxymercurial was converted to the halomercurial as indicated above and then recrystallized from ethanol. The yields were 10–15%.

Chain Mercurials (where X is H and *n* is 2, 3, 4, see Table II).—The method used is that described in an earlier paper[1]; it differs from the above directions in that an excess of the glycol is used as solvent.

(3) Heinemann, *J. Am. Pharm. Assocn., Sci. Ed.*, **32**, 298 (Nov., 1943).

The mercury analyses were carried out according to Rauscher's method as modified by us.[4]

Summary

Several series of aromatic glycol mercurials have been prepared and their bactericidal properties evaluated. An attempt has been made to correlate the antibacterial activity with the structure of the mercurials.

(4) Shukis and Tallman, *Ind. Eng. Chem., Anal. Ed.*, **12**, 123 (1940).

NEW YORK, N. Y. RECEIVED JUNE 1, 1944

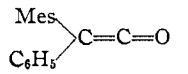
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Vinyl Alcohols. XIII.[1] 1,2-Dimesityl-2-phenylvinyl Alcohol

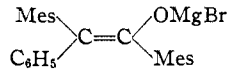
BY REYNOLD C. FUSON, L. J. ARMSTRONG,[2] J. WAYNE KNEISLEY[3] AND W. J. SHENK, JR.

The condensation of diphenylketene[4] and of mesitylketene[5] with Grignard reagents has been shown to yield unstable vinyl alcohols. By proper choice of substituents it appeared possible to synthesize in this way vinyl alcohols which would be stable. This paper reports such a synthesis.

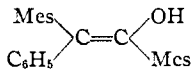
When mesitylphenylketene (I) was treated with mesitylmagnesium bromide the enolate (II) of 1,2-dimesityl-2-phenylvinyl alcohol (III) was formed. Treatment of the reaction mixture with acetyl chloride produced an acetate (m. p. 179.5–180.5°) and with dilute acids the free vinyl alcohol (m. p. 139–140°). A second acetate (m. p. 160–161°), evidently the *cis–trans* isomer of the first, was obtained by treatment of the alcohol with acetic anhydride in the presence of pyridine. Since both acetates yielded the same alcohol when hydrolyzed, it appears that in one of these reactions a change of configuration must have occurred. A similar observation was made by Kohler and Thompson,[6] who obtained the same enol peroxide from the *cis* and *trans* enolates of benzohydrylacetomesitylene. The vinyl alcohol is clearly one of the two possible *cis–trans* isomers corresponding to the two acetates. The other has not yet been found.



I

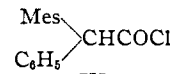


II

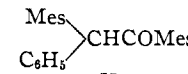


III

Perhaps the most significant observation in this connection was that the product obtained from mesitylphenylacetyl chloride (IV) and mesitylmagnesium bromide was not a vinyl alcohol at all but the corresponding ketone, α-phenyldesoxymesitoin (V). Its properties contrast sharply



IV



V

with those of the enol. Infrared spectra[7] showed absorption maxima at 2.86 and 2.78 μ, confirming the presence of a hydroxyl group in the enol. A maximum at 5.88 μ was observed in the spectrum of the ketone, showing the presence of a carbonyl group.

The ketone, as would be expected, failed to yield an acetate. Under the influence of sodium ethoxide, however, it was isomerized to the enol (III). The production of the ketone in this manner can be explained on the assumption that the Grignard reagent does not add to the carbonyl group of the acid chloride but merely replaces the chloride atom by direct metathesis. The structure of the ketone was confirmed by its synthesis from α-chlorophenacetyl chloride and mesitylene by the Friedel–Crafts method.

Mesitylphenylketene (I) was made first from mesityl phenyl diketone by the general method of Schroeter[8] as modified by Smith and Hoehn.[9] A far better method, however, was developed by which the ketene could be made from mandelic acid and mesitylene. The conversion of mandelic acid to mesitylphenylacetic acid was effected in 61% yield according to a procedure similar to that used by Gyr[10] to prepare phenyl-*p*-tolylacetic acid. The acid chloride, produced by a method developed by Fieser and Fieser,[11] was dehydrochlorinated by heating with pyridine. The yield of ketene, based on the acid, was 78%.

Experimental

Mesityl Phenyl Diketone Monohydrazone.—Twenty cubic centimeters of 85% hydrazine hydrate solution was dropped into a hot solution of 40 g. of mesityl phenyl diketone in 1 liter of methanol. The reaction mixture was heated under reflux for thirty hours and cooled to 0°. The hydrazone, which separated in the form of white needles, was recrystallized from methanol; m. p. 186–188°; yield 5 g.

(1) For the preceding paper of this series see Fuson, Armstrong, Wallace and Kneisley, THIS JOURNAL, **66**, 1274 (1944).

(2) Present address: Rohm and Haas Company, Philadelphia, Pennsylvania.

(3) Present address: Hercules Powder Company, Wilmington, Delaware.

(4) Gilman and Heckert, THIS JOURNAL, **42**, 1010 (1920).

(5) Fuson, Armstrong and Shenk, *ibid.*, **66**, 964 (1944).

(6) Kohler and Thompson, *ibid.*, **59**, 887 (1937).

(7) The authors are indebted to Professor W. H. Rodebush and Mr. Robert Whitney for the measurement and interpretation of the absorption spectra mentioned in this paper.

(8) Schroeter, *Ber.*, **42**, 2346 (1909).

(9) Smith and Hoehn, "Organic Syntheses," **20**, 47 (1940).

(10) Gyr, *Ber.*, **41**, 4321 (1908).

(11) Fieser and Fieser, THIS JOURNAL, **57**, 782 (1935).