

TABLE I  
OSMOMETRIC DETERMINATION OF MOLECULAR WEIGHTS

	$\lim_{c \rightarrow 0} \pi/c$	$\bar{M}_n$	$\bar{X}$
Bis-methoxymethyl ether of			
Polyvinylhydroquinone	$0.277 \pm 0.004$	$88,300 \pm 1,200$	$390 \pm 6$
3-Polyvinylcatechol	$.057 \pm .004$	$429,000 \pm 29,000$	$1910 \pm 130$
3-Polyvinyl- <i>p,p'</i> -biphenol	$.477 \pm .007$	$51,400 \pm 800$	$171 \pm 3$
Polystyrene IV(3(2-1-49))	$.310 \pm .021$	$79,200 \pm 5,200$	$762 \pm 50$

<sup>a</sup> In atm. cm.<sup>3</sup> g.<sup>-1</sup>.

*Anal.* Calcd. for (C<sub>13</sub>H<sub>20</sub>O<sub>4</sub>)<sub>n</sub>: C, 71.98; H, 6.71. Found: C, 72.00; H, 6.28.

**Polyvinylhydroquinone.**—In about 30 ml. of 10% methanolic hydrochloric acid, obtained by bubbling anhydrous gaseous hydrochloric acid through redistilled C.P. methanol, was dissolved 22.4 mg. (0.1 millimole) of polyvinylhydroquinone bis-methoxymethyl ether. Hydrogen was slowly bubbled through this solution at room temperature for five days. The solvent was then evaporated in a stream of hydrogen and the residue dried for 24 hr. in an Abderhalden apparatus in vacuum (0.1 mm.) over boiling toluene. The vacuum was cut with nitrogen and the flask containing the sample, 13.6 mg. (100% of theory), sealed into a tube filled with pure nitrogen. Because the compound is extremely hygroscopic, good analytical values could only be obtained when the sample was dried again just before analysis and weighed in a special balance under nitrogen atmosphere. *Anal.* Calcd. for (C<sub>9</sub>H<sub>8</sub>O<sub>2</sub>)<sub>n</sub>: C, 70.57; H, 5.92. Found: C, 70.42; H, 6.06.

**3-Polyvinylcatechol.**—3-Polyvinylcatechol bis-methoxymethyl ether, 33.6 mg. (0.15 millimole), was hydrolyzed under identical conditions as the corresponding hydroquinone polymer. *Very careful drying* afforded 20.4 mg. (100%) of 3-polyvinylcatechol. *Anal.* Calcd. for (C<sub>8</sub>H<sub>6</sub>O<sub>2</sub>)<sub>n</sub>: C, 70.57; H, 5.92. Found: C, 70.07; H, 5.76.

**3-Polyvinyl-*p,p'*-biphenol.**—3-Polyvinyl-*p,p'*-biphenol bis-methoxymethyl ether, 30.0 mg. (0.1 millimole), was hydrolyzed under identical conditions as the corresponding hydroquinone polymer. On *very careful drying* 21.2 mg. (100%) of the hydrolyzed polymer was obtained. *Anal.* Calcd. for (C<sub>14</sub>H<sub>12</sub>O<sub>2</sub>)<sub>n</sub>: C, 79.22; H, 5.70. Found: C, 78.90; H, 5.47.

**Osmometric Determination of Molecular Weights.**—The osmotic pressure data were determined at 25.00° by the

static elevation method,<sup>27</sup> using an instrument designed by Zimm and Myerson.<sup>28</sup> Calculation of the data was based<sup>27</sup> on the equation  $\pi/c = RT(1/\bar{M}_n + Bc + \dots)$ , neglecting higher than linear terms;  $\pi$  symbolizes the osmotic pressure,  $c$  the concentration,  $R$  the gas constant,  $T$  the absolute temperature,  $\bar{M}_n$  the number-average molecular weight of the solute and  $B$  the second virial coefficient of the expansion of  $\pi/c$  as a function of  $c$ .

The osmometer was calibrated with a standard sample IV (3(2-1-49)) of polystyrene of the International Union of Pure and Applied Chemistry (courtesy of Professor Raymond M. Fuoss), the number-average molecular weight of which had been determined<sup>29</sup> to be 79,000. In the present calibration a value of  $79,200 \pm 5200$  was obtained. The perfect agreement of these two results is fortuitous, because the validity of the measurements is limited by the estimated error of 5200 or 6.5%.

The osmometric measurements made on polyvinylhydroquinone bis-methoxymethyl ether, 3-polyvinylcatechol bis-methoxymethyl ether and 3-polyvinyl-*p,p'*-biphenol bis-methoxymethyl ether (in toluene solution) are summarized in Table I. The intercept  $RT/\bar{M}_n = \lim_{c \rightarrow 0} \pi/c$  of all three  $\pi/c$  vs.  $c$  plots was determined algebraically by the method of least squares. The corresponding number-average molecular weights,  $\bar{M}_n$ , and number-average degrees of polymerization,  $\bar{X}_n$ , are also listed in Table I.

(27) R. H. Wagner, in A. Weissberger's "Physical Methods of Organic Chemistry," Vol. I, Part I, 2nd ed., Interscience Publishers, Inc., New York, N. Y., 1949, pp. 488-491, 512-514, 517-519 and 532.

(28) B. H. Zimm and I. Myerson, *THIS JOURNAL*, **68**, 911 (1946).

(29) H. P. Frank and H. Mark, *J. Polym. Sci.*, **10**, 139 (1953).

NEW HAVEN, CONNECTICUT

[CONTRIBUTION NO. 1369 FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

## Diastereomeric Tetrahydropyranyl Ethers of Hydroquinone<sup>1a</sup>

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The reaction of hydroquinone with 2,3-dihydropyran is shown to lead to a mixture of *two* diastereomeric bis-2-tetrahydropyranyl ethers, a result not observed by previous workers. The two isomers have been separated, identified and their configurations tentatively assigned on the basis of melting point comparisons. Both form lithium compounds which react with carbon dioxide but not with ethylene oxide; this unreactivity is shown to be due to insolubility of the lithium derivatives.

**Introduction.**—In the formation of 2-tetrahydropyranyl ethers<sup>2,3</sup> an hydroxyl function is added across the double bond of 2,3-dihydropyran, a process which effects the formation of a new asymmetric center; hence, molecules containing an asymmetric carbon atom (*e.g.*, sterols) and molecules permitting the introduction of more than one tetrahydropyran

ring (*e.g.*, dihydric phenols) should yield a mixture of diastereoisomeric (diameric) tetrahydropyranyl ethers. Only one case has been reported in which two isomeric steroidal 2-tetrahydropyranyl ethers have actually been isolated and reasonably well characterized,<sup>4</sup> yet the available experimental evidence and physical data<sup>5</sup> suggest that usually sterols afford *varying* mixtures of two diastereomeric

(1) (a) Abstracted from Part II of the dissertation submitted by Robert Stern in February, 1956, to the Graduate School of Yale University, in partial fulfillment of the requirements for the degree of Doctor of Philosophy. (b) Department of Chemistry, Wesleyan University, Middletown, Conn.

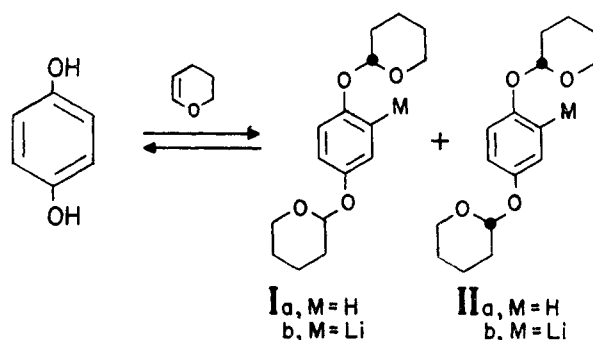
(2) G. F. Woods and D. N. Kramer, *THIS JOURNAL*, **69**, 2246 (1947).

(3) W. E. Parham and E. L. Anderson, *ibid.*, **70**, 4187 (1948).

(4) E. Elisberg, H. Vanderhaeghe and T. F. Gallagher, *ibid.*, **74**, 2814 (1952).

(5) See, for instance: (a) W. G. Dauben and H. L. Bradlow, *ibid.*, **74**, 559 (1952); (b) A. C. Ott, M. F. Murray and R. L. Pederson, *ibid.*, **74**, 1239 (1952); (c) C. W. Greenhalgh, H. B. Henbest and R. R. H. Jones, *J. Chem. Soc.*, 1190 (1951).

ethers. In any event, under reversible conditions, the conformation of a particular sterol may favor thermodynamically the predominant formation of one of the diastereomers. Such an argument, however, could hardly be extended to symmetrical compounds containing two stereochemically equivalent hydroxyl functions at some distance from each other; hence it is surprising that hydroquinone, a dihydric phenol which ought to yield two isomers Ia and IIa, afforded only one bis-2-tetrahydropyranyl ether, m.p. 125–127°, according to Parham and Anderson.<sup>8,6</sup>



#### The Two Diastereomers and Their Configuration.

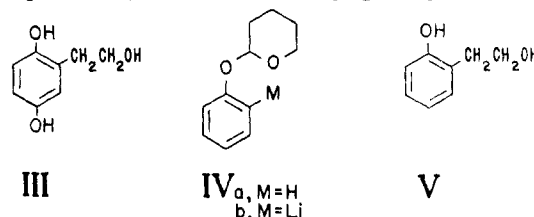
—We repeated Parham and Anderson's preparation, because we needed the bis-2-tetrahydropyranyl ether of hydroquinone for another project.<sup>7</sup> A crude reaction mixture, m.p. 78–122°, was obtained which yielded two substances, one melting at 133.3–134.8° ( $\alpha$ ) and the other at 75.6–77.1° ( $\beta$ ). Separation was achieved by means of a very tedious fractional crystallization, and the two compounds exhibited a depression of the melting point on mixing. It would appear then that the compound reported by Parham and Anderson (m.p. 125–127°) was our  $\alpha$ -modification somewhat contaminated by the low-melting  $\beta$ -form.

Acid hydrolysis of either product afforded hydroquinone but, to our surprise, the solution infrared absorption spectra of the two materials did not differ appreciably. Nevertheless, each compound crystallized unmodified in the presence of seed-crystals of the other, and neither altered its melting point when subjected to sublimation under reduced pressure. In fact, the lithium derivative of each substance on hydrolysis afforded the original material, melting point undepressed. It is therefore clear that the  $\alpha$ - and  $\beta$ -forms do not represent polymorphic modifications of the same compound but have to be considered true *meso* and *racemic* diastereoisomers, as shown in Ia and IIa.

It already has been pointed out elsewhere<sup>8</sup> that with *very few* exceptions a centrosymmetrical *meso* compound containing two identically substituted asymmetric carbon atoms has a higher melting point than the corresponding *racemic* diastere-

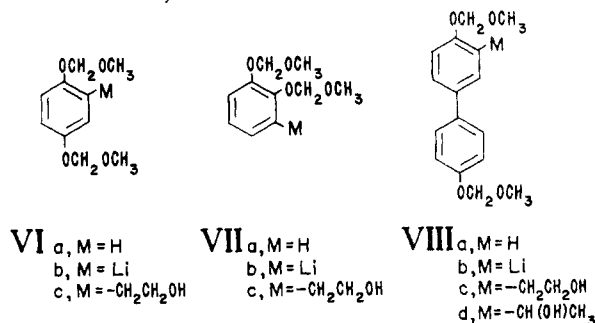
omer.<sup>9</sup> Hence the higher melting  $\alpha$ -(hydroquinone bis-2-tetrahydropyranyl ether) is assigned tentatively the *meso* configuration.

**Preparative Results.**—When *n*-butyllithium was allowed to react with either  $\alpha$ - or  $\beta$ -(hydroquinone bis-2-tetrahydropyranyl ether) the corresponding aromatic lithium compound was obtained; subsequent carbonation by means of solid carbon dioxide and acid hydrolysis of the reaction product afforded in each case 2,5-dihydroxybenzoic (gentisic) acid in 65% yield. This is in agreement with the experience of Parham and Anderson.<sup>8</sup> It was consequently expected that the reaction of  $\alpha$ - or  $\beta$ -(hydroquinone bis-2-tetrahydropyranyl ether) with *n*-butyllithium and ethylene oxide, followed by acid hydrolysis, would afford  $\beta$ -hydroxyethylhydroquinone (III) in reasonably good yields. The



hydrolyzed reaction mixture was analyzed by paper chromatography, because even low concentrations of authentic III could be detected readily by this method in control experiments. However, in none of the attempted syntheses could the presence of III be noticed in paper chromatograms of the hydrolyzed reaction mixtures,<sup>10</sup> and only hydroquinone could be isolated from them.

That the unreactivity of Ib and IIb toward ethylene oxide was not due to steric interference of the tetrahydropyranyl groups was demonstrated by subjecting IVb, the lithium derivative of phenol 2-tetrahydropyranyl ether, to the same reaction conditions.  $\beta$ -(*o*-Hydroxyphenyl)-ethyl alcohol (V) was isolated in very good yields and characterized as the bis-*p*-nitrobenzoate. The mere presence of two acetal groupings  $-\text{O}-\text{CR}_2-\text{O}-$  in the molecule could not be made responsible for the unreactivity of Ib and IIb, because lithium derivatives of other



(9) The melting points of 130 pairs of diastereomers were examined in which the two asymmetric centers are joined directly; exactly 90% of these (117 pairs) had a higher melting *meso* modification. Among the compounds in which the two asymmetric centers are separated by two methylene groups (20 pairs) not a single *meso* form was found that exhibited a lower melting point than its *racemic* isomer.

(10) This reaction was attempted five times using various amounts, sometimes a large excess, of *n*-butyllithium and ethylene oxide. The reaction step involving ethylene oxide was carried out both at room temperature and at 70° in a sealed Parr bomb. In one such experiment *n*-hexane was substituted for ether as solvent.

(6) These authors also prepared the bis-2-tetrahydropyranyl ethers of catechol and resorcinol, both of which should exist in two diastereoisomeric modifications. However, the separation of these isomers would be difficult owing to the fact that they are liquids and that their boiling points should be very similar.

(7) R. Stern, J. English, Jr., and H. G. Cassidy, *THIS JOURNAL*, **79**, 5792 (1957).

(8) R. Stern, Abstracts of Papers, 131st Meeting of the American Chemical Society, Division of Organic Chemistry, April 8, 1957, Miami, Florida, p. 5-O.

diacetals, e.g., VIb or VIIb, have been treated successfully<sup>7</sup> with ethylene oxide to yield the corresponding  $\beta$ -phenethyl alcohols VIc and VIIc. It was clear, however, that the lack of reactivity toward ethylene oxide might have been caused by physical properties of Ib and IIb, and hence we determined their solubilities in ether, along with those of three other organolithium compounds. The results are presented in Table I.

TABLE I  
SOLUBILITY OF LITHIUM DERIVATIVES

Li compound	Mol. wt. <sup>a</sup>	Solubility <sup>b</sup> in ether	Normality of satd. solution
VIb	204.1	39.6	0.20
VIIb	204.1	42.0	.21
Ib or IIb	284.3	5.5	.02
VIIIb	280.2	5.6	.02

<sup>a</sup> Molecular weight of lithium compound. <sup>b</sup> In g./l.

These data indicate that saturated solutions of VIb and VIIb in ether are approximately ten times stronger than those of the hydroquinone bis-2-tetrahydropyranyl ethers, Ib and IIb. The concentration of the latter pair is evidently so low that reaction cannot occur to a significant extent with ethylene oxide, while the success of their reaction with carbon dioxide can be attributed to the massive concentration of that reagent. A similar large excess of ethylene oxide, however, is not permissible because of the competing formation of aromatic polyethylene glycols.

These conclusions are supported by the observation that VIIIb, the lithium derivative of *p,p'*-biphenol bis-methoxymethyl ether, reacts only slightly<sup>7</sup> with ethylene oxide (to afford VIIc, 2.5%)<sup>11</sup> and acetaldehyde (to afford VIIId, 11%). Significantly, VIIIb is only soluble in ether to an extent of 5.6 g./l., and this is similar to the solubility of the equally unreactive hydroquinone derivatives Ib and IIb.

Thus, the usefulness of tetrahydropyranyl ethers as protecting groups for hydroxyl functions in metalation reactions<sup>3</sup> is somewhat limited due to the solubility characteristics of the intermediary organometallic compounds.

**Acknowledgment.**—The financial assistance of the Research Corporation is gratefully acknowledged.

### Experimental<sup>12</sup>

**Separation of *meso*- and *dl*-Hydroquinone Bis-2-tetrahydropyranyl Ether (Ia and IIa).**—To 336.0 g. (4.0 moles) of freshly distilled 2,3-dihydropyran, b.p. 85–86°, containing eight drops of concentrated hydrochloric acid was added slowly and under external cooling 110.1 g. (1.0 mole) of pure hydroquinone. Stirring was continued overnight, 800 ml. of chloroform was added and the solution was washed six times with 10% potassium hydroxide to remove the catalyst and free phenolic compounds. After drying the solution the solvent and the excess dihydropyran was removed by vacuum-distillation at room temperature. The solid residue, 287 g., melted from 78 to 122°. A solution of 144.0 g. of the crude material in boiling *n*-hexane yielded on cooling 77.0 g. of a first fraction, m.p. 95–126°, which on five consecutive crystallizations from the same solvent afforded 46.0 g. of pure  $\alpha$ -isomer as colorless prisms, constant

m.p. 133.3–134.8°. *Anal.* Calcd. for  $C_{16}H_{22}O_4$ : C, 69.04; H, 7.97. Found: C, 69.41; H, 7.73.

It was impossible to obtain the lower melting and highly soluble  $\beta$ -isomer in pure form from the *n*-hexane mother liquors by means of a regular fractional crystallization. After several frustrating attempts a scheme was adopted according to which fractions with sufficiently similar melting points were arbitrarily combined. This reproducible procedure afforded 5.4 g. of the pure  $\beta$ -isomer, after considerable losses in unutilized intermediary fractions; colorless prisms, m.p. 75.6–77.1°. *Anal.* Calcd. for  $C_{16}H_{22}O_4$ : C, 69.04; H, 7.97. Found: C, 69.41; H, 7.91.

A mixture containing equal amounts of the two pure diastereomers melted at 75–118°. Further identification was achieved by hydrolysis to hydroquinone. The  $\beta$ -isomer (1.39 g., 0.005 mole) was dissolved in 30 ml. of ether, and the solution was shaken vigorously with 15% hydrochloric acid. The organic layer afforded on evaporation of the solvent 0.50 g. (91%) of a white crystalline residue. Recrystallization from methanol and benzene yielded 0.45 g. of white needles, m.p. 170°. A mixed melting point with authentic hydroquinone showed no depression.

The solubility properties of the two diastereomers are considerably different. The  $\beta$ -isomer is very soluble in *n*-hexane, benzene, ether and methanol; the  $\alpha$ -isomer dissolves in benzene (56 g./l.) and in methanol, is slightly soluble in ether (20 g./l.) and can be recrystallized from *n*-hexane or 2,2,4-trimethylpentane (8 g./l.).

**2,5-Dihydroxybenzoic (Genticic) Acid from  $\alpha$ -(Hydroquinone Bis-2-tetrahydropyranyl Ether).**—This reaction was carried out under experimental conditions similar to those of Parham and Anderson.<sup>3</sup> Starting with 2.09 g. (0.0075 mole) of  $\alpha$ -(hydroquinone bis-2-tetrahydropyranyl ether), m.p. 133.3–134.8°, and 34.5 ml. (0.022 mole) of 0.65 *N*-butyllithium<sup>13</sup> solution, we obtained 0.75 g. (65%) of gentisic acid, m.p. 193–198°. Microsublimation and crystallization from water afforded the pure compound,<sup>14</sup> m.p. 198°.

**Attempted Reaction of  $\alpha$ -(Hydroquinone Bis-2-tetrahydropyranyl Ether) with *n*-Butyllithium and Ethylene Oxide.**—Lithium-hydrogen exchange was carried out under standard conditions<sup>13</sup> between 63.0 ml. (0.015 mole) of 0.24 *N*-butyllithium solution and 4.17 g. (0.015 mole) of Ia, m.p. 133.3–134.8°, dissolved in 250 ml. of absolute ether. A white precipitate appeared very shortly; refluxing of the suspension was continued for 45 hr. The reaction flask was then fitted with a condenser cooled by solid carbon dioxide and 8.0 g. (0.18 mole) of ethylene oxide, placed into a small flask, was permitted to vaporize into the reaction vessel. After stirring the mixture overnight, it was hydrolyzed with crushed ice; the organic layer afforded a crystalline residue, m.p. 130.3–132.4° weighing 3.8 g. (91% recovery calculated as unchanged Ia). The mixed melting point with authentic starting material was undepressed. The infrared spectrum did not exhibit absorption in the region (2.7–3.0  $\mu$ ) characteristic of oxygen-hydrogen stretching frequency and was perfectly superimposable to that of authentic starting material.

**Attempted Reaction of  $\beta$ -(Hydroquinone Bis-2-tetrahydropyranyl Ether) with *n*-Butyllithium and Ethylene Oxide.**—The experimental conditions were the same as those used in the preceding experiment with Ia. The quantities of materials used were: 5.57 g. (0.02 mole) of IIa, m.p. 75.6–77.1°, dissolved in 100 ml. of anhydrous ether, 21.0 ml. (0.022 mole) of 1.05 *N*-butyllithium solution and 1.07 g. (0.024 mole) of liquid ethylene oxide. The reaction afforded 4.6 g. (83% recovery calculated as unchanged IIa) of yellowish crystals. The infrared spectrum of this material did not exhibit absorption in the region of oxygen-hydrogen stretching frequency (2.7–3.0  $\mu$ ) and was superimposable in all respects to that of authentic starting material.

Two grams of the recovered material was dissolved in 100 ml. of ether, and the solution was shaken vigorously with 20 ml. of 17% hydrochloric acid. The ether phase was washed with saturated sodium chloride solution and the combined aqueous layer in turn extracted with ether. The latter ether extracts were washed several times with saturated sodium chloride solution before adding them to the

(11) This result could not be altered by carrying out the reaction in 1,2-dimethoxyethane.

(12) All melting points were taken in evacuated capillary tubes and are corrected. The boiling points are uncorrected.

(13) H. Gilman and J. W. Morton, Jr., "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 285, 287.

(14) C. Graebe and E. Martz, *Ann.*, **340**, 213 (1905).

main ether phase. The organic layer afforded 0.84 g. of a white crystalline solid in which hydroquinone, but no  $\beta$ -hydroxyethylhydroquinone (III), could be detected by subjecting 20 micrograms to paper chromatography. In control chromatograms one microgram of authentic  $\beta$ -hydroxyethylhydroquinone (III) could be spotted easily when mixed with ten micrograms of reaction product or with nine micrograms of hydroquinone.

Except for development time (26 hr.) and distance (50 cm.) the experimental conditions for these chromatograms were identical to those reported for the model experiment, *i.e.*, the separation of authentic  $\beta$ -hydroxyethylhydroquinone (III), m.p. 76.4–77.6°, and hydroquinone (*vide infra*).

**Separation of Hydroquinone and  $\beta$ -Hydroxyethylhydroquinone (III) by Paper Chromatography.**—*n*-Amyl alcohol and water, 1:1, was used as the developer system.<sup>15</sup> The two solvents were equilibrated at 25°, and the aqueous phase was placed in the chamber to saturate the atmosphere. The organic phase was used as the actual developer.

The one-dimensional descending boundary technique was applied on Whatman No. 1 paper with a developer run of 39 cm. and a development time of 36 hr. The original spots had a diameter of about 2 mm. and contained 5 micrograms ( $5 \times 10^{-6}$  g.) each of hydroquinone and  $\beta$ -hydroxyethylhydroquinone. Visualization was achieved by spraying the developed spots with a 2% aqueous solution of phosphomolybdic acid and exposing the sprayed area to ammonia vapors.<sup>16a</sup> A dark blue color appeared.

Complete separation of the two compounds could be achieved. Hydroquinone  $R_f$ <sup>16</sup> = 0.82;  $\beta$ -hydroxyethylhydroquinone  $R_f$  = 0.75.

**$\beta$ -Hydroxyethylhydroquinone (III).**—A solution of 2.42 g. of  $\beta$ -hydroxyethylhydroquinone bis-methoxymethyl ether<sup>7</sup> (VIc) in 30 ml. of absolute methanol was refluxed on a steam-bath for 3 hr. with 2.42 g. of Amberlite IR-112 cation exchange resin.<sup>17</sup> The cation exchanger was then filtered off, and the solvent was evaporated. A yellow oily residue, 1.5 g. (100% of theory), was obtained; it could not be recrystallized from methanol and benzene and was almost completely insoluble in aliphatic and aromatic hydrocarbons, carbon tetrachloride, chloroform and carbon disulfide. On short path distillation of this material (1.4 g.) the bulk, 1.2 g., went over at 130–150° (1 mm.). There was obtained a very thick and viscous yellow oil<sup>18</sup> which crystallized on standing, m.p. 74–77°. One gram of these impure crystals was added to 250 ml. of boiling pure chloroform; the mixture was refluxed until complete dissolution had been effected and was then filtered. On cooling a few oily droplets appeared on the liquid-glass interface; the solution was transferred into another flask, and a few hours later white, short needles began to form in clusters. Three crops of crystals weighing a total of 0.53 g. were thus obtained, all of them melting at 75–77°, with a small amount of impurity melting at 83°. Two more crystallizations from chloroform afforded pure  $\beta$ -hydroxyethylhydroquinone, m.p. 76.4–77.6°. *Anal.* Calcd. for  $C_8H_{10}O_2$ : C, 62.39; H, 6.54. Found: C, 62.48; H, 6.39.

**$\beta$ -(*o*-Hydroxyphenyl)-ethyl Alcohol (V) from Phenol 2-Tetrahydropyranyl Ether (IVa).**—The synthesis of IVa was carried out with 94.0 g. (1.0 mole) of phenol. After fractionation of the crude product through a two-foot jacketed column packed with helices, there was obtained 116.5 g. (66% yield) of the desired product,<sup>8</sup> b.p. 135° (22 mm.),  $n_D^{20}$  1.5223.

Metallation was effected under standard conditions<sup>13</sup> by adding 340 ml. (0.3 mole) of 0.88 *N* *n*-butyllithium solution to 52.9 g. (0.3 mole) of IVa dissolved in 100 ml. of absolute

ether. A white crystalline precipitate appeared and the suspension was stirred for 26 hr. The reaction flask was equipped then with a condenser for solid carbon dioxide, and ethylene oxide (16.0 g. or 0.36 mole) was permitted to vaporize slowly into the reaction vessel. The mixture was stirred overnight and hydrolyzed. The organic layer afforded 59.0 g. (89% yield) of crude product; it gave a positive alcohol test by the alkali xanthogenate method.<sup>19</sup> When a small portion of it was subjected to distillation at 0.3 mm., decomposition occurred; dihydropyran could be isolated in the pump-trap, and the distillate gave a positive phenol test with ferric chloride.

In order to hydrolyze the tetrahydropyranyl groups, 36.0 g. of the crude reaction product was dissolved in 500 ml. of U.S.P. methanol, 10 ml. of concentrated hydrochloric acid and 40 ml. of distilled water were added, and the solution was refluxed for 90 minutes. The mixture was neutralized approximately to pH 7, and the solvent was evaporated under reduced pressure so as to remove the 5-hydroxypentanal<sup>20</sup> formed during the hydrolysis. Distillation of the residue afforded 17.5 g. of  $\beta$ -(*o*-hydroxyphenyl)-ethyl alcohol (V) boiling at 125–127° (0.5 mm.).<sup>21</sup> A small portion was redistilled through a one-foot jacketed Podbielniak-type column; b.p. 110° (0.55 mm.),  $n_D^{15}$  1.5593.

The bis-*p*-nitrobenzoate was prepared from 1.25 g. (9 millimoles) of V by the usual procedure.<sup>22</sup> Two recrystallizations from acetone and water yielded 1.4 g. of crystals, m.p. 167.8–169.0°. *Anal.* Calcd. for  $C_{22}H_{16}O_8N_2$ : C, 60.55; H, 3.70; N, 6.42. Found: C, 60.58; H, 3.91; N, 6.33.

**Solubility of Phenyllithium Derivatives in Ethyl Ether.**—The solubilities were determined as illustrated here by the following example: Lithium-hydrogen exchange<sup>13</sup> was carried out between 5.57 g. (0.02 mole) of IIa, m.p. 75.6–77.1°, dissolved in 100 ml. of absolute ether, and 21.0 ml. (0.022 mole) of 1.05 *N* *n*-butyllithium solution. After 18 hr. of continuous stirring, the reaction mixture was centrifuged, the yellow ether layer was decanted and the sludge was washed with 20 ml. of absolute cold ether. The combined ether layer, A, and the precipitate, B, were worked up separately.

The ether solution, A, was hydrolyzed with saturated sodium chloride solution and the aqueous phase was extracted with ether. The combined organic layer afforded 0.65 g. (12%) of a yellow oil (corresponding to 0.66 g. of the actual lithium compound) which crystallized partially on standing. Except for a very weak absorption band at 3.0  $\mu$  (oxygen-hydrogen stretching frequency), the infrared spectrum of this compound was identical in all respects with that of the starting material. The reaction had been carried out in a total volume of 120 ml. of ether, and hence the solubility of the lithium compound is, to a first approximation,  $660/120 = 5.50$  g./l. This brings the normality of the solution to  $5.50/284.3 = 0.019$ .

This result was corroborated by working up B, the precipitate from the reaction mixture. On very careful drying<sup>23</sup> 4.9 g. (86%) of the solid lithium compound was obtained; it was taken up in ether and hydrolyzed with saturated sodium chloride solution. The aqueous phase was extracted with ether; the combined organic layer afforded 4.5 g. of crystals. The infrared spectrum of this solid was superimposable on that of the starting material, and no depression of the melting point occurred with authentic IIa. Because we could account for 5.2 g. (93%) out of 5.57 g. of starting material, we estimate the error involved in these determinations as  $\pm 10\%$ . The results of the solubility measurements are summarized in Table I.

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(15) Developer systems that were tried unsuccessfully are: butanol-benzene-water 1:9:10 and 1:19:20; *n*-amyl alcohol-benzene-water 9:1:10, 8:2:10 and 6:4:10.

(16) (a) R. F. Riley, *This Journal*, **72**, 5782 (1950); (b) R. A. Evans, W. H. Parr and W. C. Evans, *Nature*, **164**, 674 (1949).

(17) Rohm and Haas Co., Philadelphia, Penna.

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(19) R. Feigl, "Qualitative Analyse mit Hilfe von Tüpfelreaktionen," 2. Auflage, Akademische Verlagsgesellschaft, Leipzig, 1935, p. 366.

(20) G. Forrest Woods, Jr., "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 470.

(21) R. Stoermer and B. Kahlert, *Ber.*, **34**, 1809 (1901), reported b.p. 177–178° (18 mm.) and 168–169° (12 mm.),  $n_D^{15}$  1.5575.

(22) N. D. Cheronis, "Micro- and Semimicro Methods," Vol. VI of A. Weissberger's "Technique of Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1954, p. 494.

(23) The lithium compound decomposes explosively on standing.