of the 2.15 g. of the crude mixture of acetate was accomplished by employing 5 g. of potassium hydroxide in 25 ml. of water. Work-up and distillation yielded 483 mg. b.p. 72–80° (21 mm.). The infrared showed bands at 2.82, 2.95, 6.85, 6.90 in addition to several bands in the 9.0–11.0-μ region. Gas-liquid chromatography on a 5% erythritol on Celite column produced three peaks identical with 1-methylcyclohexanol (14%), *cis*-2-methylcyclohexanol (27%), and *trans*-2-methylcyclohexanol (59%).

Norcarane and Acetic Acid.—A sealed tube containing 1.9 g. of norcarane and 10 ml. of glacial acetic acid remained in a constant temperature bath for 1 week at 46.5°. Work-up in the usual manner furnished an oil which by gas-liquid chromatographic analysis on an 11-ft. 4% squalene on firebrick column showed only the presence of norcarane.

Gas-Liquid Chromatographic Analyses and Infrared Spectra.—A Baird double beam infrared spectrophotometer was employed to determine the infrared spectra. The gas-liquid chromatographic analyses were carried out with an instrument constructed in these laboratories. The instrument contained a Gow-Mac thermal conductivity cell. Helium was employed as the mobile phase.

Acknowledgment.—The work described above was supported by a Frederick Gardner Cottrell Grant-in-Aid. The author wishes to thank Mr. L. S. Forney for the preparation of norcarane.

A Dihydroresorcinol Derivative[1]

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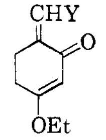
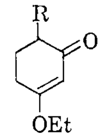
Received January 15, 1962

As a result of our need for 6-hydroxymethylene-3-ethoxycyclohex-2-enone (Ia) the formylation of the dihydroresorcinol derivative, 3-ethoxycyclohex-2-enone(IIa), was investigated. Reaction between the latter, ethyl formate, and sodium ethoxide in benzene yielded a single, crystalline $C_9H_{12}O_3$ compound. Its spectral properties, its alcohol solution giving a positive ferric chloride test, and its conversion to a copper chelate revealed the product to be a readily enolizable substance. It could be transformed into an enol acetate with acetic anhydride and pyridine and into an enol ether by base-induced reaction with isopropyl iodide. While *a priori* the formyl group could have entered the dihydroresorcinol nucleus at C-2,-4, or -6, the preliminary evidence favored C-6 as its site of attachment. Nevertheless, a search for more rigorous data was undertaken.

Catalytic hydrogenation of the formylation product yielded a dihydro derivative whose ultraviolet spectrum was identical with that of dihydroresorcinol ethyl ether(IIa). Thus the formyl (or hydroxymethylene) group had been reduced to a hydroxymethyl function whose position was limited to C-4 or -6 (IIb), since at C-2 it would have been expected to alter the nuclear chromophore.



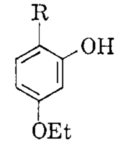
Ia. Y = OH
b. Y = O—*i*-Pro
c. Y = OAc
d. Y = H



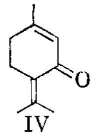
IIa. R = H
b. R = CH_2OH
c. R = CH_2OAc

Catalytic hydrogenation of the enol acetate of the formylation product yielded a mixture from which a crystalline $C_9H_{12}O_2$ compound was isolated. Its spectral properties showed it to be an aromatic substance. On the assumption of its being 4-ethoxy-2-hydroxytoluene(IIIa) this compound was synthesized. Diazoethane treatment of β-resorcylaldehyde yielded 4-ethoxysalicylaldehyde(IIIb). Reduction of the latter with zinc and acetic acid afforded the cresol IIIa, identical in all respects with the product of hydrogenation of the enol acetate of the formylation product. These results establish firmly the C-6 attachment of the carboxaldehyde (or hydroxymethylene) function in the initial formylation product. They further suggest that the latter's enol ether, enol acetate, and dihydro derivative are represented by Ib, Ic, and IIb, respectively.

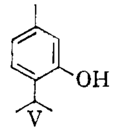
IIIa. R = CH_3
b R = CHO
c. R = CN



The unusual transformation of Ic into IIIa under hydrogenation conditions proceeds most probably *via* Id, produced either by direct hydrogenolysis of Ic or by the latter's hydrogenation to IIc and catalyst-induced β-elimination of acetate to Id.[3] The extraordinary isomerization of an alkylidenecyclohexenone(Id) into a phenol(IIIa) finds precedence in the recent conversion of piperitenone(IV) into thymol(V) under hydrogenation conditions.[4]



IV



V

As an alternate route from the aldehyde IIIb to the cresol IIIa, the Wolff-Kishner reduction of the former's semicarbazone had been examined briefly. This reaction yielded a mixture of prod-

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[1] Financial support for this work by Ciba Pharmaceutical Products Inc., Summit, N. J., hereby is gratefully acknowledged.

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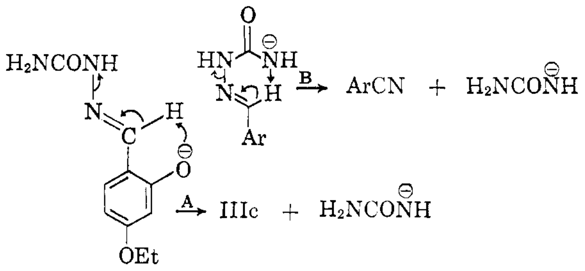
[3] *Cf.* E. Wenkert, A. K. Bose, and T. L. Reid, *J. Am. Chem. Soc.*, **75**, 5514 (1953).

[4] E. D. Bergmann and P. Bracha, *J. Org. Chem.*, **24**, 994 (1959).

ucts from which the desired phenol and, more interesting, the nitrile IIIc (characterized as its acetate) could be isolated. The latter's identity was established by the synthesis of its acetate through the treatment of the aldoxime (of IIIb) with acetic anhydride. The unusual base-induced nitrile production is rationalized most readily on the basis of mechanisms A or B.[5]



Experimental

6-Hydroxymethylene-3-ethoxycyclohex-2-enone(Ia) and Its Derivatives.—A mixture of dry sodium ethoxide, from 4.6 g. of sodium, 13.4 g. of ethyl formate, and 12.9 g. of 3-ethoxycyclohex-2-enone(IIa) [b.p. 61–64°/0.1 mm.; spectra: ultraviolet (EtOH), λ_{max} 249 mμ (log ϵ 4.27); infrared (CH-Cl_3), 6.09(s) and 6.24(s)μ][6] in 100 ml. of anhydrous benzene was left standing at room temperature under nitrogen for 22 hr. The reaction mixture then was stirred with cold water and extracted with 5% sodium hydroxide solution. Addition of solid carbon dioxide to the aqueous extract led to a precipitate which was filtered and washed with water. Crystallization of the colorless solid, 8.0 g., m.p. 93°, from aqueous ethanol yielded crystalline Ia, m.p. 93–93.5°; spectra: ultraviolet (EtOH), λ_{max} 256 mμ (log ϵ 4.05) and 295 mμ (log ϵ 3.93), λ_{min} 225 mμ (log ϵ 3.48) and 276 mμ (log ϵ 3.81); infrared ($CHCl_3$), 3.70(vw), 5.70(w), 6.09(s), and 6.24(s) μ; copper chelate, m.p. 185–187°; semicarbazone, m.p. 203–204°.

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.30; H, 7.19. Found: C, 64.28; H, 7.12.

A mixture of 5.0 g. of Ia, 6.4 g. of isopropyl iodide, and 6.2 g. of anhydrous potassium carbonate in 40 ml. of anhydrous acetone was refluxed under nitrogen for 30 hr. After removal of the solvent and addition of cold water the mixture was extracted with ether. The extract was washed with cold 5% sodium hydroxide solution, with water and with saturated brine solution. The ether solution then was dried over anhydrous potassium carbonate and evaporated under vacuum. Crystallization of the solid residue, 4.5 g., m.p. 58–61°, from petroleum ether yielded crystalline 6-isopropoxymethylene-3-ethoxycyclohex-2-enone(Ib), m.p. 62.5–63.5°; ultraviolet spectrum (EtOH), λ_{max} 292 mμ (log ϵ 4.21), $\lambda_{shoulder}$ 263 mμ (log ϵ 4.06), λ_{min} 229 mμ (log ϵ 3.28).

Anal. Calcd. for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.94; H, 8.73.

A solution of 2.0 g. of Ia and 4 ml. of acetic anhydride in 10 ml. of pyridine was refluxed under nitrogen for 10 min., cooled, and poured onto 40 ml. of ice water. The solid, 1.8 g., was filtered and washed with cold 2% hydrochloric acid solution and with water. Crystallization from aqueous alcohol gave long colorless needles of 6-acetoxymethylene-3-ethoxycyclohex-2-enone(Ic), m.p. 88–89°; spectra: ultraviolet (EtOH), λ_{max} 279 mμ (log ϵ 4.30), λ_{min} 226 mμ(log ϵ 2.19); infrared ($CHCl_3$), 5.66(s), 5.98(s) and 6.24(s) μ.

Anal. Calcd. for $C_{11}H_{14}O_4$: C, 62.90; H, 6.72. Found: C, 62.80; H, 6.73.

6-Hydroxymethyl-3-ethoxycyclohex-2-enone (IIb).—A mixture of 500 mg. of Ia and 50 mg. of 5% palladium-charcoal in 20 ml. of ethyl acetate was hydrogenated at atmospheric pressure and room temperature. After hydrogen uptake had ceased, the catalyst was filtered and the solvent removed under vacuum. Chromatography of the residue on a silica column and elution with 4:1 petroleum ether–ether yielded 200 mg. of a solid, m.p. 71–73°. Crystallization of the latter from petroleum ether–ether gave crystalline IIb, m.p. 72.5–73°; spectra: ultraviolet (EtOH), λ_{max} 250 mμ (log ϵ 4.18); infrared ($CHCl_3$), 2.80(w), 2.88(w), 2.93(w), 6.09(s) and 6.24(s) μ.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.55; H, 8.45.

4-Ethoxy-2-hydroxytoluene (IIIa).—A mixture of 700 mg. of Ic and 100 mg. of 5% palladium-charcoal in 25 ml. of ethyl acetate was hydrogenated at atmospheric pressure and room temperature. After a work-up identical with the above and elution with 19:1 petroleum ether–ether 190 mg. of a solid product was obtained. Crystallization of the latter from benzene yielded colorless needles of IIIa, m.p. 47–48°; infrared spectrum ($CHCl_3$), 2.77(m), 3.00(w), 6.15 (s), and 6.26(s) μ.

Anal. Calcd. for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 71.40; H, 8.13.

A 20% excess of ethereal diazoethane solution was added to 3.0 g. of β-resorcyaldehyde in 100 ml. of ether and the mixture was left standing for 1 hr. Upon solvent removal under reduced pressure the residue was chromatographed on silica. The 1:1 petroleum ether–ether eluates were concentrated and the resulting oil exposed to short-path distillation. This led to 2.5 g. of 4-ethoxysalicylaldehyde (IIIb), m.p. 34°; ultraviolet spectrum (EtOH), λ_{max} 230 mμ (log ϵ 4.17), 278 mμ (log ϵ 4.31) and 319 mμ (log ϵ 3.92), λ_{min} 247 mμ (log ϵ 2.75) and 303 mμ log ϵ 3.90); oxime, m.p. 87–88°.

Anal. Calcd. for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 65.18; H, 6.10.

Zinc dust, 50 g., was added in 10-g. portions at 10-min. intervals to a stirring solution of 700 mg. of 4-ethoxysalicylaldehyde (IIIb) in 50 ml. of glacial acetic acid. After filtration the residue was washed with hot water and ethyl acetate. The combined filtrates were brought to pH 6, the organic phase dried over magnesium sulfate, and its solvent removed under vacuum. Silica chromatography of the residue and elution with 19:1 petroleum ether–ether yielded 105 mg. of starting aldehyde, while elution with a 9:1 solvent mixture afforded 365 mg. of 4-ethoxy-2-hydroxytoluene (IIIa), m.p., m.m.p. 46–47°; spectra identical with those of the above sample.

4-Ethoxysalicylonitrile Acetate.—Crystallization of the semicarbazone of 4-ethoxysalicylaldehyde(IIIb) from ethyl acetate–dimethylformamide produced platelets, m.p. 208-209°; ultraviolet spectrum (EtOH), λ_{max} 232 mμ (log ϵ 4.14), 288 mμ (log ϵ 4.25) and 317 mμ (log ϵ 4.29).

Anal. Calcd. for $C_{10}H_{13}O_3N_3$: C, 53.80; H, 5.87; N, 18.83. Found: C, 53.79; H, 6.11; N, 18.89.

A mixture of 620 mg. of the semicarbazone and 1.5 g. of powdered potassium hydroxide in 10 ml. of ethylene glycol was kept at 180° until the escaping gases no longer turned red litmus blue and then was heated at 210° for 2 hr. Upon cooling 100 mg. of cold water was added and the resulting solution extracted with cold 10% hydrochloric acid solution, with chloroform and with ethyl acetate. After drying of the combined organic solutions over magnesium sulfate, the solvent was removed under vacuum. Silica chromatography of the residue and elution with 4:1 petroleum ether–ether yielded 8 mg. of a solid, m.p. 46–47°, identical in all respects with the phenol IIIa. Elution with ether and ether-methanol gave two unidentified oils, 55 mg. and 38 mg., respectively.

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(5) B may be the preferred pathway since aldehyde semicarbazones having no neighboring, potentially reaction-facilitating group have been shown previously to produce nitriles in low yields in attempted Wolff-Kishner reductions (E. Wenkert and J. W. Chamberlin, unpublished results).

(6) E. G. Meek, J. H. Turnbull, and W. Wilson, *J. Chem. Soc.*, 811 (1953).

TABLE I

2-FUROATES OF 4-PHENYLPHENOL AND BROMO-4-PHENYLPHENOLS

Phenol Used[a]	Yield, %	M.P., °C.[b]	Formula	Bromine, % Calcd.	Bromine, % Found
4-Phenyl-	85.1	125–126	$C_{17}H_{12}O_3$	..	..
4-(4-Bromophenyl)-	88.9	153–154	$C_{17}H_{11}O_3Br$	23.3	23.7
2,6-Dibromo-4-phenyl-	85.5	152–153	$C_{17}H_{10}O_3Br_2$	37.9	37.9
2-Bromo-4-(4-bromophenyl)-	93.5	127–128	$C_{17}H_{10}O_3Br_2$	37.9	38.2
2,6-Dibromo-4-(4-bromophenyl)-	87.9	186.5–187.5	$C_{17}H_9O_3Br_3$	47.9	48.2

[a] The bromo-4-phenylphenols were prepared by recorded methods. [b] The esters were purified by crystallization from ethanol.

Further elution with methanol led to 25 mg. of an oil with an intense nitrile infrared absorption peak. It was acetylated by standard means and the product chromatographed on silica. This produced crystalline 4-ethoxysalicylonitrile acetate, m.p. 72.5–73.5°; spectra: ultraviolet (EtOH), $\lambda_{\max}$ 250 mμ (log ϵ 4.20) and 283 mμ (log ϵ 3.17), $\lambda_{\min}$ 226 mμ (log ϵ 3.74) and 280 mμ (log ϵ 3.09); infrared ($CHCl_3$), 4.48(s), 5.63(s), 6.20(s), and 6.35(m) μ.

Anal. Calcd. for $C_{11}H_{11}O_3N$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.64; H, 5.53; N, 6.67.

A solution of 100 mg. of 4-ethoxysalicylaldoxime and 0.5 ml. of acetic anhydride was refluxed for 2 hr. and then poured onto 5 ml. of ice water. The resulting precipitate was filtered, crystallized from aqueous ethanol, and chromatographed on silica. Elution with 9:1 petroleum ether–ether led to a crystalline solid, m.p., m.m.p. 72–73.5°, identical in all respects with the above sample of 4-ethoxysalicylonitrile acetate.

The Bromination of 4-Phenylphenyl 2-Furoate

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Received January 16, 1962

A number of esters of the phenylphenols have been brominated previously, and the results of these studies have been reported.[1] In this investigation, an acyl group of different type than those involved in previous studies has been used, *viz.*, the furoyl group. The results are different. Bromination occurred in the acyl portion of the molecule rather than in the biphenyl group, and 4-phenylphenyl 5-bromo-2-furoate was formed. Such is in agreement with reports by Gilman[2] that the furan ring undergoes substitution reactions more readily than the benzene ring.

Reaction products were identified by mixed melting point procedures.

A number of related esters have been prepared.

Experimental

2-Furoates of 4-Phenylphenol and Bromo-4-phenylphenols.—4-Phenylphenol (40 g., 0.235 mole) was dissolved in 30 ml. of pyridine and 60 ml. of *p*-dioxane; the solution was cooled to 5°, and 36.8 g. (0.282 mole) of 2-furoyl chloride was added in small portions. The mixture was heated at 70° for 1 hr. and then cooled; 400 ml. of water was added, and the solution was acidified with dilute hydrochloric acid. The crude product was obtained in nearly quantitative yield; purification was effected by crystallizations from ethanol, m.p. 125–126°.

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.3; H, 4.55. Found: C, 77.4; H, 4.61.

Several 2-furoic acid esters of bromo-4-phenylphenols were prepared by similar procedures. The results are shown in Table I.

5-Bromo-2-furoic Acid.—Except that only a small excess of bromine was used, this compound was prepared in 64% yield by the method of Whittaker,[3] m.p. 187–187.5°.

5-Bromo-2-furoyl Chloride.—5-Bromo-2-furoic acid (3 g., 0.0157 mole) was treated with thionyl chloride (12 g., 0.101 mole) and a drop of pyridine. The mixture was refluxed on a steam bath for 6 hr., the excess thionyl chloride was removed by distillation, and the acid chloride—the residue—was used without purification.

4-Phenylphenyl 5-Bromo-2-furoate.—To the crude 5-bromo-2-furoyl chloride (*ca.* 0.0157 mole) were added 2 ml. of pyridine, 7 ml.of *p*-dioxane, and 2.67 g. (0.0157 mole) of 4-phenylphenol. The mixture was heated for 1 hr. on a steam bath, cooled, and diluted with 40 ml. of water; the odor of pyridine was discharged by the addition of dilute hydrochloric acid. The solid product was leached with hot water and then with 5% sodium carbonate solution and washed with hot water. Crystallizations from ethanol gave 2.2 g. (0.00641 mole, 40.8% yield) of 4-phenylphenyl 5-bromo-2-furoate, m.p. 152–153°.

Anal. Calcd. for $C_{17}H_{11}O_3Br$: Br, 23.3. Found: Br, 23.9.

Bromination of 4-Phenylphenyl 2-Furoate.—The ester (10 g., 0.0379 mole) was suspended in 30 ml. of glacial acetic acid, which had been heated to 115°. A trace of iron powder was introduced, and 6 g. (0.0375 mole) of bromine dissolved in 10 ml. of glacial acetic acid was added. The temperature of the mixture was maintained at 100° for 50 min.

The mixture was cooled to room temperature, and the precipitated solid (6 g.) was collected by filtration, m.p. 130–139°. Crystallizations from propanol gave 4.8 g. (0.014 mole, 37.3% yield) of 4-phenylphenyl 5-bromo-2-furoate, m.p. 149–150.5°.

The acidic solution was diluted with 250 ml. of water and neutralized with sodium carbonate solution; the precipitated solid (6.1 g.) was collected by filtration, m.p. 107–117°. Several crystallizations from ethanol gave 3.9 g. (0.0148 mole, 39.5% yield) of 4-phenylphenyl 2-furoate, m.p. 123–124°.

Hydrolysis of 4-Phenylphenyl 5-Bromo-2-furoate.—A

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(1) S. E. Hazlet and L. C. Hensley, *J. Am. Chem. Soc.*, **69**, 708 (1947) and earlier papers.

(2) See, for example: H. Gilman and E. B. Towne, *Rec. trav. chim.*, **51**, 1054 (1932); H. Gilman and N. O. Calloway, *J. Am. Chem. Soc.*, **55**, 4197 (1933); and H. Gilman and R. V. Young, *ibid.*, **56**, 464 (1934).

(3) R. M. Whittaker, *Rec. trav. chim.*, **52**, 352 (1933).