[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POMONA COLLEGE]

Catalytic Synthesis of Heterocycles.[1] III. Benzofuran

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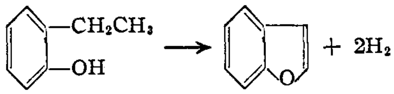
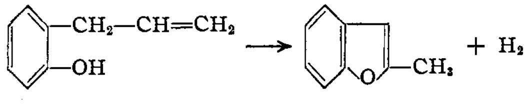
The successful synthesis of thianaphthene from *o*-ethylbenzenethiol[1] suggested the possibility of accomplishing the same type of ring closure with the oxygen analog. This paper discusses the vapor phase catalytic dehydrocyclization of *o*-ethylphenol and *o*-allylphenol to benzofuran and 2-methylbenzofuran according to the equations





Experimental

The apparatus and the technique used for the catalytic reactions have been described previously.[1]

Catalyst Preparations.—The method of preparation for the platinum catalyst has been described.[1] For the preparation of palladium on charcoal,[4] 10 g. of palladium chloride was dissolved in 40 ml. of hot concd. hydrochloric acid. This solution was diluted to 187 ml. with distilled water and 30 g. of activated charcoal added. The mixture was heated to boiling and the charcoal separated by decantation. The catalyst was dried at 115° for two hours. Before using, it was reduced *in situ* with a slow stream of

TABLE I

CONVERSION OF *o*-ALLYLPHENOL TO 2-METHYLBENZOFURAN DISTILLATION

				Alkali insoluble fraction			Alkali soluble fraction	
Allylphenol, g.	Cat.	Temp.[f] °C.	S. V.[g]	Methylbenzofuran,[a] b. p. 190–196°, g.	(730 mm.),[d] %	Benzofuran,[b] b. p. 170–190°, g.	Phenol and Cresol,[c] b. p. 175–200°, g.	Allylphenol, b. p. 200–216° g.
53.5	Pd	525	815	7.9	15.0[e]	2.7	2.9	18.1
49.5	Pd	550	544	14.9	31.0	5.5	3.8	9.8
50.2	Pd	550	773	14.6	29.5	3.2	3.7	9.4
40.0	Pd	550	1568	10.5	26.5	2.8	Trace	9.3
39.8	Pd	575	1470	11.0	28.0	2.2	3.5	9.9
48.9	Pd	600	1208	13.0	27.0	4.6	4.3	6.9
40.2	Pd	625	1407	10.5	26.5	7.4	7.5	0.0
51.1	Pt	550	788	14.4	28.6	6.9	4.7	11.0

[a] Redistillation of 120 g. of this material from several runs through a 20-plate column gave 98 g. of material, b. p. 195–196° (730 mm. cor.), n^{24}_{D} 1.5539. Adams and Rindfusz, THIS JOURNAL, **41**, 655 (1919), report b. p. (744 mm.) 196–197° and n^{22}_{D} 1.555. The material from this batch distillation and from the individual runs formed a picrate m. p. 72–74°. Stoermer and Barthelmer, *Ber.*, **48**, 67 (1915), report m. p. 72–74°. [b] This fraction consisted of mostly benzofuran with some 2-methylbenzofuran. These fractions were refractionated and the benzofuran identified by physical constants and by preparation of picrate. [c] These fractions also lumped together and refractionated and the phenol and *o*-cresol identified by means of the urethan derivatives. [d] The barometer varied on these experiments by ±2 mm.; however, this difference was ignored and the cuts taken at the temperatures listed above. [e] Calculated as per cent. conversion of allylphenol to methylbenzofuran. [f] The temperature of the catalyst varied from this average temperature by ±3 or 4°. [g] The space velocity was calculated as ml. of vapor at s. t. p. per ml. of catalyst per hour.

TABLE II

CONVERSION OF *o*-ETHYLPHENOL TO BENZOFURAN DISTILLATION

				Alkali insoluble fraction				Alkali soluble fraction	
Ethylphenol, g.	Cat.	Temp., °C.[g]	S. V.[g]	Crude benzofuran,[a] b. p. 140–169°, g.	(730 mm.),[d] %	Benzofuran,[b] b. p. 170–172° cor. g.	%	Phenol,[c] b. p. 178–200°, g.	Ethylphenol, b. p. 202–204°, g.
28.2	Pd	600	1702	1.4	5.2[f]	1.1	4.1[f]	6.5	7.8
30.6	Pd	625	1768	1.3	4.4	1.7	5.8	9.6	5.8
26.8	Pd	625	622	3.6	13.9	2.2	8.5	9.8	0.0
54.8	Pd	625	927	1.1	2.1	4.6	8.7	15.6	11.4
51.4	Pd[e]	620	652	2.1	4.2	5.6	11.3	15.2	10.2

[a] This fraction consisted of benzofuran with some unidentified product. [b] The yield of pure benzofuran was somewhat higher than this would indicate because of about 1 to 2 g. holdback of material in the distilling column which contained considerable benzofuran. These fractions when mixed together had n^{24}_{D} 1.5631 and formed a picrate m. p. 102–103°. v. Auwers, *Ann.*, **408**, 271 (1915), reports $n^{22.7}_{\mathrm{D}}$ 1.565. Kramer and Spilker, *Ber.*, **23**, 79 (1890), report b. p. (758 mm.) 170–171° and *ibid.*, 3276, m. p. picrate 102–103°. [c] This fraction consisted of phenol along with some *o*-ethylphenol and probably some *o*-hydroxystyrene. [d] See Table I. [e] Fifteen ml. of catalyst used instead of usual 5 ml. [f] See Table I, *e*. [g] See Table I, *f* and *g*.

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(1) For the preceding papers in this series, see Hansch and Blondon, THIS JOURNAL, **70**, 1561 (1948), and Hansch and Hawthorne, *ibid.*, **70**, 2495 (1948).

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(4) The activated charcoal used in this work was Type B15P, 6-8 mesh, supplied through the courtesy of the Pittsburgh Coke and Chemical Company.

hydrogen saturated with formaldehyde by passing the hydrogen through aqueous 40% formalin. The reduction was carried out for forty-five minutes at 270° and then for forty-five minutes at temperatures slightly above those at which the dehydrogenation run was to be conducted.

Catalytic Synthesis of 2-Methylbenzofuran.—The following is an example of a typical dehydrogenation run for the preparation of 2-methylbenzofuran.

o-Allylphenol[5] (50.2 g.) was processed over 5 ml. of palladium catalyst at a temperature of 550 ± 4° over a period of one hundred thirty minutes. A total of 47.6 g. of condensate was collected and the catalyst tube gained 1.2 g. weight. About 0.3 g. of material remained in the seed system. A total of 3330 ml. of gas was given off during the course of the reaction as measured by a wet test meter. The rate of gas evolution was 40 ml./min. at the end of the first fifteen minutes at which time the catalyst reached a relatively steady activity. This rate gradually fell until it reached a constant value of 16 ml./min. at seventy minutes. This rate then held until the end of the reaction. On longer runs of four hours or more the rate sometimes fell as low as 12 ml./min.

The condensate was made alkaline with 20% sodium hydroxide and the 2-methylbenzofuran extracted with petroleum ether. After drying over sodium sulfate the extract was distilled through a 20-plate, 30″, "spinning band" distilling column. Distillation gave 14.6 g. of 2-methylbenzofuran, b. p. 190–196° (730 mm.), 3.3 g., 170–190° (730 mm.) which was mainly benzofuran, a residue and hold back of 1.7 g. remaining in the distilling flask.

The alkali-soluble portion of the condensate was acidified with hydrochloric acid, extracted with ether, the extract dried over calcium chloride and then distilled. Nine and four-tenths grams of material, mainly *o*-allylphenol, was collected between 200–216° (730 mm.). Three and seven-tenths grams was obtained, boiling at 175–200°, and consisting of a mixture of phenol, *o*-cresol and a trace of *o*-allylphenol.

Tables I and II summarize the results of the run with *o*-allylphenol and *o*-ethylphenol.[6] All of the runs were made and worked up as described above except where indicated.

Discussion

In all of the catalytic runs made in this research using both *o*-ethylphenol and *o*-allylphenol, very little charring occurred on the catalyst or on the quartz chips used as preheater. The catalyst gained 0.6 g. to 1.2 g. depending on the size of the run and the temperature. The condensate was clear and light brown in color.

It should be noted that the catalyst activity as measured by the rate of gas evolution fell off after about the first hour to about 50% of the fifteen minute value. An attempt to use a chromium oxide on alumina catalyst was unsuccessful because of excessive decomposition of the phenols At present work is in progress to find a more stable and more active catalyst. It was discovered that the activated charcoal[4] itself possessed considerable ability to bring about the dehydrocyclization. This may be due to the charcoal itself or possibly to impurities in it.

As noted in Table I, a considerable amount of benzofuran was formed in the preparation of 2-methylbenzofuran. This same phenomenon has been observed in the preliminary investigation of the preparation of other 2-methylbenzofurans and also with the corresponding sulfur analogs.

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Summary

A vapor phase catalytic method for the dehydrogenation of *o*-ethylphenol to benzofuran and *o*-allylphenol to 2-methylbenzofuran is described.

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[5] D. S. Tarbell, "Organic Reactions," John Wiley and Sons Inc., New York, N. Y., 1944, Vol. II, p. 26.

[6] The o-ethylphenol was supplied through the courtesy of Dale Robertson of this Laboratory. It was prepared by vapor-phase alkylation of phenol and had a b. p. of 203.1–205.1° (730 mm. cor.) after two distillations through a 20-plate distilling column.

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE VICK CHEMICAL COMPANY]

Attempted Synthesis of β-2,6-Dihydroxybenzoyl- and β-2,4,6-Trihydroxybenzoylacrylic Acids

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The most active bacteriostatic agent in a series of β-aroyl acrylic acids was β-2,4,6-triethylbenzoylacrylic acid.[2] The preparation of β-2,6-dihydroxy- (I) and β-2,4,6-trihydroxybenzoyl acrylic acid (II) was attempted to determine the effect of ortho hydroxyl groups. The formula chart shows the method used for I.

Condensation of III with diethyl oxalate in the presence of sodium ethoxide gave IV. The crude product was heated under reflux with a mixture of glacial acetic and concentrated hydrochloric acids to give V. This in turn was esterified and hydrogenated to VII.

It had been previously shown that 2-carbethoxy-γ-chromanone was easily converted to β-(*o*-hydroxybenzoyl)-acrylic acid by treatment with dilute alkali. Hence treatment of VII with alkali gave either I or VIII.

It was expected that the reaction between maleic anhydride and phloroglucinol would result in the formation of II and 2-carboxy-5,7-dihydroxy-γ-chromanone (IX), for a similar reaction using

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(2) Cramer, Schroeder, Moran, Nield, Edwards, Jarowski and Puetzer, *J. Am. Pharm. Assoc.*, **37**, 439 (1948)