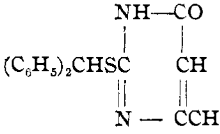
captopyrimidine and 8 grams of chloroacetic acid were dissolved in water and the solution boiled for 5 hours. Mercaptan was evolved immediately on heating. After the reaction was complete the solution was evaporated to dryness and the residue purified by crystallization from alcohol. This pyrimidine separated at once, on cooling, and melted at 236°–237°. The yield was quantitative. It gave no test for sulfur.

2-Diphenylmethylmercapto-4-methyl-6-oxypyrimidine,



.—The bromodiphenylmethane, $(C_6H_5)_2CHBr$, which was used in this experiment, was prepared according to the directions of Friedel and Balsohn.[1] This pyrimidine was obtained by the action of this bromide on the sodium salt of 2-thio-4-methyluracil in alcoholic solution. The yield, however, was small, since most of the bromide was decomposed by the alcohol, on heating, forming the corresponding ether, $(C_6H_5)_2CHOC_2H_5$. The pyrimidine was separated from the recovered 2-thio-4-methyluracil by dissolving in alcohol. It was purified by crystallization from this solvent and it melted at 214°. A nitrogen determination gave:

Calculated for $C_{18}H_{16}ON_2S$: N, 9.0; found: N, 8.7.

NEW HAVEN, CONN.,
June 28, 1913.

[CONTRIBUTIONS FROM THE SHEFFIELD LABORATORY OF YALE UNIVERSITY.]

A NEW METHOD OF SYNTHESIZING THE HIGHER PHENOLS.

BY TREAT B. JOHNSON AND WILLARD W. HODGE.

Received June 11, 1913.

In connection with some work, now in progress, on the antiseptic action of phenols it was necessary to obtain in quantity certain phenols containing long, aliphatic side chains, *viz.*, the higher homologues of the cresols and corresponding derivatives of the dihydroxybenzenes. The lower members of these types of aromatic compounds have been described. On the other hand, we have little knowledge of the higher homologues and no practical method is known by which they can be prepared easily. Regarding their antiseptic properties we have no knowledge. The primary object of the work described in this paper was to develop a new method of introducing alkyl groups into the benzene nucleus of mono- and dihydric phenols.

Ketones in general undergo reduction, under ordinary pressure, with formation of alcohols or pinacones. It has been shown, however, that they can be reduced directly to their corresponding hydrocarbons. The

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[1] *Bull. soc. chim.*, 33, 337.

number of reducing agents, however, which have proved by experience to be of practical utility in effecting this change is comparatively restricted.

Gräbe,[1] in his classical paper entitled "Ueber die Reduction einiger aromatischer Ketone durch Iodwasserstoffsäure und Phosphor," showed that benzophenone and diphenylene ketone, $(C_6H_4)_2.CO$, undergo reduction, when heated with hydriodic acid, forming diphenylmethane and diphenylenemethane, respectively. He also investigated the action of hydriodic acid on dibenzylketone and acetophenone, but observed that the former underwent only partial reduction forming the phosphate of the corresponding alcohol $(C_6H_5CH_2)_2.CHO.PO(OH)_2$, while acetophenone behaved abnormally and was transformed into triphenylbenzene and a hydrocarbon, $C_{16}H_{18}$ (*unsym.*-dibenzylethane). Bogdanowska[2] later reinvestigated the action of reducing agents on dibenzylketone and showed that it undergoes no reduction when digested with zinc in the presence of sulfuric, hydrochloric or acetic acids. The abnormal behavior of acetophenone, when reduced with hydriodic acid, is especially interesting because Claus[3] actually succeeded in reducing the corresponding toluene derivative $CH_3COC_6H_4CH_3$ and higher homologues to hydrocarbons by means of this same reagent. Bargellini and Melacini[4] also used hydriodic acid with success for the complete reduction of the mixed ketones of the naphthalene series $C_{10}H_7COCH_3$, $C_{10}H_7COCH_2CH_3$, etc.

Japp and Klingemann[5] obtained desoxybenzoin by boiling benzyl with hydriodic acid, while Limpricht and Schwanert[6] observed that the same *ortho* diketone is reduced to dibenzyl if heated with hydriodic acid under pressure at 180°. Thörner and Zincke[7] obtained diphenylmethane by heating benzophenone with zinc and sulfuric acid, while Städel[8] accomplished the same result by heating the ketone with zinc dust. Klages and Allendorff[9] made the interesting observation that aromatic ketones also undergo reduction with sodium and alcohol, giving excellent yields of the corresponding hydrocarbons. Attempts, however, to apply this method of reduction to mixed ketones—aromatic-aliphatic—were unsuccessful and only traces of hydrocarbons could be obtained.

Sabatier and Senderens,[10] by application of their catalytic method,

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[1] *Ber.*, **7**, 1624.

[2] *Ibid.*, **25**, 1271.

[3] *J. prakt. Chem.*, **45**, 377.

[4] *Atti R. Accad. dei Lincei Roma*, [5] **17**, II, 26; *Centrbl.*, **2**, 948 (1908).

[5] *J. Chem. Soc. London*, **63**, 770.

[6] *Ann.*, **155**, 61.

[7] *Ber.*, **10**, 1473.

[8] *Ann.*, **194**, 307.

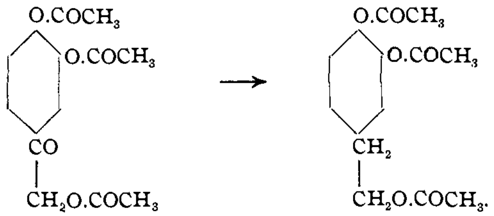
[9] *Ber.*, **31**, 998.

[10] *Compt. rend.*, **137**, 301

were able to reduce aliphatic ketones only to their corresponding alcohols. This was accomplished by passing vapors of these substances, with hydrogen, over reduced nickel at 115°–130°. Later Darzens[1] applied the same method of reduction to mixed ketones, but prepared his reduced nickel under special conditions, and observed that these substances were reduced smoothly to hydrocarbons when heated with hydrogen at 190°–195°. He prepared, for example, ethylbenzene, methylethylbenzene, butylethylbenzene and *n*-butylbenzene by reduction of acetophenone, acetyltoluene, butylacetophenone and benzylacetone, respectively. Leontowitsch[2] observed the formation of dibenzyl when benzoin was heated with hydrogen in contact with nickel at 400°.

The most recent method for the reduction of ketones is that employed by Clemmensen.[3] He digests the ketones with zinc-amalgam and hydrochloric acid, and finds that the mixed ketones as well as the aliphatic are all reduced smoothly to the hydrocarbons. He applied the method successfully in several cases. Whether the method can be applied to aromatic ketones was not determined. Bamberger and Knecht[4] have also recognized the value of zinc-amalgam as a reducing agent and used it with success for the reduction of nitrobenzenes to hydroxylamine compounds.

The hydroxy aromatic ketones $HO.C_6H_4COCH_3$, etc., or their oxygen ethers can be obtained easily in quantity but, so far as the writer is aware, no one has ever shown that they can be converted into alkyl phenols by reduction. The recent work of Voswinkel[5] indicated, however, that such transformations could be effected if the proper reducing agent was employed. This investigator has shown, for example, that the triacetyl derivative of glycollylpyrocatechol (I) is changed smoothly into the corresponding ethane derivative (II) by reduction with zinc dust and glacial acetic acid.



I. II.

On the other hand, an attempt by Dzerzgowski[6] to reduce chloracetylpyrocatechol (III) to the ethane derivative (V) was unsuccessful. He

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[1] *Compt. rend.*, **139**, 868.

[2] *J. Russ. Phys. Chem. Ges.*, **38**, 75; *Centrbl.*, **2**, 86 (1906).

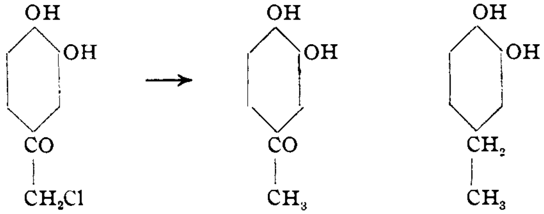
[3] *Orig. Com. 8th Intern. Congr. Appl. Chem.*, **7**, 68–80, September, 1912.

[4] *Ber.*, **29**, 864.

[5] *Ibid.*, **42**, 1651.

[6] *J. Russ. Chem. Soc.*, **25**, 154.

used zinc and hydrochloric acid for reduction and obtained acetylpyrocatechol (IV) as the product of the reaction. There was apparently no evidence of the formation of ethylpyrocatechol (V).


III. IV. V.

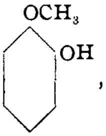
We now find that mixed ketones containing hydroxyl or ether radicals (OCH_3) in the benzene nucleus are reduced smoothly by zinc-amalgam, forming the corresponding alkyl derivatives. We have applied this method of reduction to ten different ketones of this type and in every case the transformation was smooth and the yield of the reduction product was excellent. The number of hydroxyl groups present in the benzene nucleus apparently does not interfere with the course of the reaction. Especially interesting was the behavior of chloracetopyrocatechol, which Dzerzgowski[1] observed to undergo reduction with zinc and hydrochloric acid forming acetylpyrocatechol. When zinc-amalgam is used as the reducing agent the ketone undergoes complete reduction, giving ethyl-

Ketone.		Reduction product.
$CH_3O.C_6H_4COCH_3$ Acetylanisole.	→	$CH_3O.C_6H_4CH_2CH_3$ Ethylanisole.
$C_2H_5O.C_6H_4COCH_3$ Acetylphenetole.	→	$C_2H_5O.C_6H_4CH_2CH_3$ Ethylphenetole.
$C_3H_5OC_6H_4COC_2H_5$ Propionylphenetole.	→	$C_2H_5O.C_6H_4CH_2CH_2CH_3$ Propylphenetole.
$(HO)_2C_6H_3.COCH_2Cl$ Chloracetopyrocatechol.	→	$(HO)_2C_6H_4.CH_2CH_3$ Ethylpyrocatechol.
$(CH_3O)_2C_6H_3COC_2H_5$ Propionylveratrol.	→	$(CH_3O)_2C_6H_3CH_2CH_2CH_3$ Propylveratrol.
$(HO)_2C_6H_3.COCH_3$ Acetylresorcinol.	→	$(HO)_2C_6H_3CH_2CH_3$ Ethylresorcinol.
$(HO)_2C_6H_3COC_2H_5$ Propionylresorcinol.	→	$(HO)_2C_6H_3.CH_2CH_2CH_3$ Propylresorcinol.
$(HO)_2C_6H_3COCH_3$ Acetylhydroquinone.	→	$(HO)_2C_6H_3.CH_2CH_3$ Ethylhydroquinone.
$(HO)_2C_6H_3COC_2H_5$ Propionylhydroquinone.	→	$(HO)_2C_6H_3CH_2CH_2CH_3$ Propylhydroquinone.
$(CH_3O)C_6H_3.COC_2H_5$ Dimethyl ether of propionylhydroquinone.	→	$(CH_3O)_2C_6H_3.CH_2CH_2CH_3$ Dimethyl ether of propylhydroquinone.

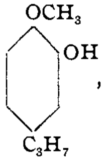
[1] *Loc. cit.*

pyrocatechol (V). For the preparation of an alkyl phenol, therefore, one can start either with the hydroxy ketone or its ether. If the ether is reduced, the resulting alkyl derivative can then be converted into the desired phenol by heating with a halogen acid. The ketones, which we examined and their reduction products, are listed in the preceding table.

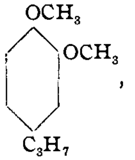
Propylveratrol (VI) is a product of biochemical interest. The monomethylether of propylpyrocatechol (VII), which may be considered as a higher homologue of guaiacol (VIII), is a natural occurring product (*Cörulignol* or *Blauöl*) and was isolated by Pastrovich[1] from beechwood tar oil. It boiled at 240–241° and was transformed into propylpyrocatechol (IX), melting at 56°, when heated with hydrochloric acid. Nencki and Sieber[2] apparently isolated the same monomethyl ether (VII) from pine wood creosote and showed that it is decomposed by heating with potassium hydroxide, giving pyrocatechol. Delange[3] synthesized propylpyrocatechol (IX) and found it to melt at 60°.



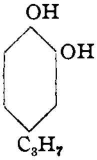
VIII.



VII.



VI.



IX.

The investigation of alkyl phenols will be continued.

Experimental Part.

Methyl Ether of 4-Ethylphenol, $CH_3O.C_6H_4.CH_2CH_3$.—This compound was first prepared by alkylation of the corresponding phenol with methyliodide.[4] It was later synthesized by Klages[5] who states that it boils at 195–197° at ordinary pressure and at 79–80° under 13 mm. pressure. He prepared it by reduction of *p*-vinylanisole with sodium and alcohol. We have obtained the same ether easily and in good yield by reduction of *p*-acetylanisole with zinc-amalgam and hydrochloric acid. The acetylanisole was prepared according to the directions of Gattermann, Ehrhardt and Maisch.[6] Fifty-two grams of the ketone and 115 grams of amalgamated zinc were suspended in 300 cc. of a mixture of two parts of water and one part of concentrated hydrochloric acid, and then digested on a sand bath for 12 hours. We obtained a colorless oil which was insoluble in the acid solution. This was separated by extraction with ether, dried over calcium chloride and purified by fractional distillation.

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[1] *Monats.*, 4, 188.

[2] Beilstein's "Handbuch," Vol. II, p. 969.

[3] *Compt. rend.*, **130**, 659.

[4] Moschner, *Ber.*, **34**, 1262.

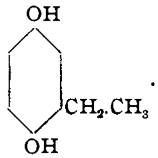
[5] *Ber.*, **36**, 3593.

[6] *Ibid.*, **23**, 1201.

The fraction boiling from 190–215° was saved and redistilled when it practically all boiled at 195–198°. The yield of purified material was 28 grams.

Ethyl Ether of 4-Ethylphenol, $C_2H_5O.C_6H_4.CH_2CH_3$.—This ether has previously been described by Errera,[1] Moschner,[2] and Klages.[2] Errera assigned to it the boiling point of 200°, while Moschner and Klages both observed that their product boiled at 208°. We find that the ether can be prepared easily by reducing *p*-acetylphenetol,[3] $C_2H_5O.C_6H_4.COCH_3$, with zinc-amalgam and hydrochloric acid. From 70 grams of the acetylphenetol we obtained 37 grams of the pure ethyl ether boiling at 208°. The ether was accompanied by an oily, high-boiling impurity, which had no definite boiling point.

Ethyl Ether of 4-Propylphenol, $C_2H_5O.C_6H_4.CH_2.CH_2.CH_3$.—This compound has been described by Klages and was prepared by reduction of *p*-propenyl phenetole, $C_2H_5O.C_6H_4CH : CHCH_3$,[4] with sodium and alcohol. We obtained the same compound easily by reduction of *p*-propionylphenetole with zinc-amalgam and hydrochloric acid. The propionylphenetole was prepared by application of Friedel and Craft's reaction with propionyl chloride and phenetole in petroleum ether solution (Klage's method).[5] The yield was excellent. From 48 grams of the ketone we obtained, by reduction with zinc-amalgam, 34 grams of the above ether, which boiled at 223–230°. Klages[6] has already shown that *p*-propylphenol can be obtained easily by heating its ethers with hydriodic acid at 180°.



Ethyl Hydroquinone, or 1,4-Dihydroxy-2-ethylbenzene, .—Bayrac[7] has described this phenol and prepared it by reduction of ethylquinone with sodium bisulfite. He observed that it melts at 112–113°. We find that it can be prepared easily by reduction of acetylhydroquinone with zinc-amalgam. The acetylhydroquinone was prepared according to the directions of Nencki and Schmid.[8] Three grams of the ketone and 10 grams of amalgamated zinc were suspended in 75 cc. of dilute hydro-

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[1] *Gazz. chim.*, 14, 485.

[2] *Loc. cit.*

[3] Gattermann, Ehrhardt and Maisch, *Loc. cit.;* Boeseken, *Bull. soc. chim.*, [3] 19, 350; Klages, *Loc. cit.*

[4] *Ber.*, 37, 3990.

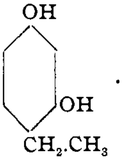
[5] *Ibid.*, 35, 2264.

[6] *Ibid.*, 32, 1437.

[7] *Bull. soc. chim.*, [3] 11, 1130.

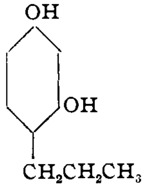
[8] *J. prakt. Chem.*, [2] 23, 547.

chloric acid (1 part of concentrated acid and 2 parts of water) and the mixture digested on a sand bath for 10 hours. The ether was obtained as an oil floating on the acid solution. This was separated from the acid mixture by extraction with ether and then purified by crystallization from hot water. It separated from this solvent in the form of plates or prisms, which melted at 112–113° to a clear oil.. It crystallized from benzene in colorless prisms melting at 113–114°.

Ethyl Resorcinol or 1-Ethyl-2,4-dihydroxybenzene, 

.—This phenol apparently has not been described in the literature. It is formed smoothly by reduction of acetylresorcinol[1] with zinc-amalgam. We obtained from 12 grams of the ketone 11.3 grams of the crude phenol. It was purified by recrystallization from boiling benzene and separated, on cooling, in colorless, prismatic crystals, which melted at 98–99° to a clear oil. The phenol is soluble in water, alcohol, ether and glacial acetic acid. Analysis:

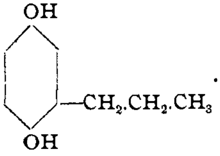
Calculated for $C_8H_{10}O_2$: C, 69.56 H, 7.24.
Found: C, 69.73, 69.42; H, 7.22, 7.14.

Propyl Resorcinol or 1-Propyl-2,4-dihydroxybenzene, 

.—This new phenol was obtained in practically a quantitative yield by reduction of propionylresorcinol[2] with zinc-amalgam and hydrochloric acid. It is soluble in water, alcohol, ether and benzene and crystallizes from benzene in prisms melting at 82–83°. By reduction of 5 grams of the ketone for 10 hours we obtained 4.5 grams of the above phenol.

Calculated for $C_9H_{12}O_2$: C, 71.05; H, 7.89.
Found: C, 70.71; H, 7.96.

Propyl Hydroquinone or 1,4-Dihydroxy-2-propylbenzene,



.—This new phenol was prepared by reduction of propionylhydroquinone[3] with zinc-amalgam. It is very soluble in alcohol,

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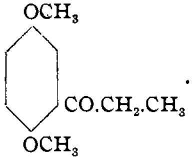
[1] Nencki and Sieber, *J. prakt. Chem.*, [2] 23, 147.

[2] Goldzweig and Kaiser, *J. prakt. Chem.*, [2] 43, 90. Hantzsch, *Ber.*, 39, 3094.

[3] Goldzweig and Kaiser, *Loc. cit.*

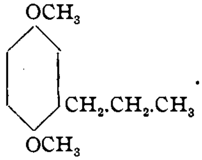
ether, and difficultly soluble in cold benzene, hot water and petroleum ether. It was purified by recrystallization from boiling benzene and separated, on cooling, in clusters of microscopic needles melting at 86° to a clear oil.

Calculated for $C_9H_{12}O_2$: C, 71.05; H, 7.89.
Found: C, 70.82; H, 7.88.



1,4 - Dimethoxy - 2 - propionylbenzene, .—Twenty-nine grams of the dimethyl ether of hydroquinone[1] were dissolved in about 250 cc. of petroleum ether and 36 grams of finely pulverized aluminium chloride suspended in the solution. The flask was then connected with a return condenser, and while warming gently on a steam bath, 24 grams of propionyl chloride were slowly added to the solution. There was an immediate reaction, on adding the acid chloride, and hydrochloric acid gas was evolved. After the final addition of the acid chloride the mixture was then heated almost to the boiling point for 30 hours, in order to complete the reaction. The mixture was then cooled and poured into ice water in order to decompose the double aluminium compound, and the ketone then extracted with ether. After drying over calcium chloride, the ether was then distilled off and the ketone purified by fractional distillation under diminished pressure. We saved the fraction boiling from 165–195° at 13 mm. pressure. This was then redistilled, when we obtained 14 grams of the pure ketone boiling at 167–169° at 13 mm. The oil was light yellow, but assumed a dark color on exposure to the air.

Calculated for $C_{11}H_{14}O_3$: C, 68.04; H, 7.22.
Found: C, 67.93; H, 7.13.



1,4-Dimethoxy-2-propylbenzene, .—This compound has previously been described by Thoms[2] and was prepared by reduction of 1,4-dimethoxy-2-propenylbenzene with sodium and alcohol. We find that it is formed smoothly by reduction of the corresponding ketone, described above, with zinc-amalgam and hydrochloric acid. From 12 grams of the ketone we obtained 6 grams of the propyl derivative boiling at 240–246°. Thoms states that his product boiled at 240° at 760 mm. and at 125° at 20 mm. pressure.

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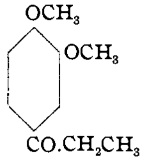
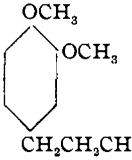
[1] Ullmann, *Ann. Chem.*, **327**, 116.

[2] *Ber.*, **36**, 857.

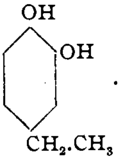


1-Propionyl-3,4-Dimethoxybenzene, —This ketone has been described by Wallach and Pond[1] and also by Hell and Portmann.[2] The latter assigned to it the melting point of 57°, while Wallach and Pond state that their product melted at 62°. They prepared it by the action of sodium alcoholate on the dibromide $(CH_3O)_2.C_6H_3.CHBr.CHBr.CH_3$. We have prepared the ketone by the action of propionyl chloride on veratrol in the presence of aluminium chloride (Friedel and Craft's reaction). The reaction was conducted in petroleum ether solution and the ketone extracted with ether, dried and finally purified by crystallization from ether. It separated in plates melting at 60°. From 38 grams of veratrol we obtained 15 grams of the pure ketone.

Calculated for $C_{11}H_{14}O_3$:	C, 68.04	H, 7.22.
Found:	C, 67.33, 67.9;	H, 7.27, 7.04.



1-Propyl-3,4-dimethoxybenzene, —Ciamician and Silber[3] prepared this compound by reducing the methyl ether of isoeugenol with sodium and alcohol. Their work was later confirmed by Thoms[4] and also by Delange.[5] The same compound is formed smoothly by reduction of the above ketone with zinc-amalgam and hydrochloric acid. From 10 grams of the ketone, after reducing for 10 hours, we obtained 6.0 grams of the dimethyl ether boiling constant at 246–247°.



The Formation of 1-Ethyl-3,4-dihydroxybenzene by Reduction of 1-Chloraceto-3,4-dihydroxybenzene with Zinc-Amalgam, .—This interesting phenol has been described by Delange.[6] Starting with the methylene ether of 1-vinyl-3,4-dihydroxybenzene,[7] $H_2CO_2.C_6H_3CH : CH_2$, he first prepared the corresponding ethyl derivative, $H_2C.O_2.C_6H_3.C_2H_5$,

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[1] *Ber.*, **28**, 2722.

[2] *Ibid.*, **28**, 2092.

[3] *Ibid.*, **23**, 1166.

[4] *Ibid.*, **36**, 860.

[5] *Compt. rend.*, **130**, 659.

[6] *Ibid.*, **138**, 1702.

[7] Klages, *Ber.*, **36**, 3595.

by reduction with sodium and alcohol and then destroyed the ether grouping by treatment with phosphorus pentachloride and water. The phenol was obtained as a solid melting at 39°. The same compound is formed smoothly by reduction of 1-chloroaceto-3,4-dihydroxybenzene[1] with zinc-amalgam and hydrochloric acid. Dzerzgowski[2] has already shown that the chloroketone is reduced to the corresponding ketone, $(HO_2).C_6H_3.COCH_3$, only when treated with zinc and hydrochloric acid.

Twelve grams of the chloroketone and 100 grams of amalgamated zinc were suspended in 200 cc. of hydrochloric acid (2 parts water and 1 part concentrated hydrochloric acid) and the mixture digested on a sand bath for about 22 hours. We obtained a light yellow oil, which was extracted with ether, dried over calcium chloride and finally purified by distillation under diminished pressure. It practically all boiled at 172–175° at 35 mm. and, on cooling, immediately solidified. The phenol gave no test for chlorine, turned brown on standing in the air and melted at 39°. The yield was good.

NEW HAVEN, CONN.

[CONTRIBUTIONS FROM THE SHEFFIELD LABORATORY OF YALE UNIVERSITY.]

THE CATALYTIC ACTION OF ESTERS IN THE CLAISEN CONDENSATION.

BY TREAT B. JOHNSON AND ARTHUR J. HILL.

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The writers communicated to the Eighth International Congress of Applied Chemistry,[3] in September, 1912, an interesting observation that esters have a marked effect on the course of the Claisen condensation. It was shown that the yield of the β-ketone ester was, in some cases, increased by incorporation of another ester, and we published the results of several experiments with ethylphenoxyacetate, which indicated that this was probably due to catalytic action. Since the publication of this original paper we have continued the investigation of this subject and are now able to discuss, in this paper, new data, which still further confirm our original conclusions. We shall also discuss here the role, which the catalyzer possibly plays in these reactions.

Ethyl phenoxyacetate (I) and ethyl naphthoxyacetate (β) (II) both undergo a Claisen condensation in dry ether, and in the presence of metallic sodium, forming the sodium salts of the corresponding β-ketone esters[4] (III), and (IV). The yields obtained, however, are very poor in both

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[1] Dzerzgowski, *J. Russ. Chem. Soc.*, **25**, 154.

[2] *Loc. cit.*

[3] *Original Communications*, **6**, 147.

[4] Johnson and Hill, *Am. Chem. J.*, **48**, 296.