salt by means of sodium carbonate and evaporating to crystallization. It is of a light yellow color and very soluble in water.

Sulfur found, 9.64% and 9.75%, respectively. Theory, 9.66%.

The compound seemed to be very hard to oxidize, even for a sulfur compound, requiring two full days' heating with fuming nitric acid under pressure at a high heat.

2-Nitro-4'-methyl phenyl ether sulfonchloride ($NO_2.CH_3.C_{12}H_7.SO_2Cl$) was prepared by treating the sodium sulfonate with an excess of phosphorus pentachloride. The two substances were powdered, mixed thoroughly, shaken to insure complete mixing, when an action took place accompanied by a marked rise of temperature, the mixture assuming a semipasty condition. Ice water was then poured into the flask and allowed to remain several hours with occasional shaking. The sulfonchloride remained in the bottom of the flask in the form of solid granules and was separated by filtration with suction. The substance is very stable towards water and alcohol. The substance is soluble in alcohol, benzene, and other organic solvents. It crystallizes from alcohol in light yellow plates which melt at 69° (uncor.).

VERMILLION, S. DAK.

[CONTRIBUTIONS FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

PHENOLS III. THE PREPARATION OF SOME NEW SUBSTITUTED CRESOLS.[1]

BY ARTHUR J. HILL AND LOUIS E. GRAF.

Received June 8, 1915.

The work recorded in this paper is a continuation of an investigation on phenols and related compounds which was begun by Johnson and Hodge[2] in 1913. It is the third paper on this subject and is devoted to the synthesis and description of some new derivatives of *p*-cresol.

Our knowledge regarding the alkyl derivatives of the three isomeric cresols is somewhat limited. While several have been described in the literature, in many cases, however, the position occupied by the substituent alkyl group is held as uncertain.

Only two propyl cresols have been described. One of these, 2-hydroxy-4-propyl-1-methylbenzene, was synthesized by Bayrac,[3] who obtained it by alkali fusion of 1-methyl-4-propyl-benzenesulfonic acid. The other, 3-hydroxy-?-normal propyl-1-methylbenzene, was prepared by Mazzara[4]

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[1] The experimental work described in this paper was done by Mr. Louis E. Graf in candidacy for the Degree of Master of Science in the Sheffield Scientific School of Yale University.

[2] THIS JOURNAL, **35**, 1014 (1913).

[3] *Bull. soc. chim.*, [3] **13**, 896 (1895).

[4] *Gazz. chim. ital.*, **12**, 167 (1882).

through the interaction of normal propyl alcohol, *m* cresol and anhydrous magnesium chloride at 200°. In this connection, mention should also be made of Klages'[1] synthesis of the methyl ether of 2-propyl-4-methylphenol (I) which he obtained by the reduction of either 4-methyl-2-propenyl-phenol methyl ether (II) or 1-methoxy-4-methyl-2-propylol benzene (III). A synthesis of the free phenol is now recorded in this paper.

Our information concerning the ethyl substituted cresols is more conflicting than that of the propyl derivatives. Clemmenson[2] has reduced 3-methyl-4-hydroxy-acetophenone (IV) to 2-methyl-4-ethylphenol (V) by means of zinc-amalgam and hydrochloric acid and characterizes his compound as "das Phenol das bisher noch nicht dargestellt worden war." There is a possibility, however, that this statement is not wholly correct. For example, Bayer & Co.[3] have shown that 2-hydroxy-?-ethyl-1-methylbenzene could be synthesized by the interaction of *o*-cresol with ethyl alcohol at 180° in the presence of anhydrous zinc chloride. The boiling point of their product is stated as 220°; that of Clemmenson's is 224° at 740 mm., thus indicating that the two products are possibly identical.

There are also two other ethyl cresols which should be mentioned. These are the so-called "α-" and "β-"phenol derivatives of *p*-ethylmethylbenzene, which Bayrac[4] synthesized by fusion of the corresponding "α-" and "β-"sulfonic acids with alkali.

(α-phenol derivative)-?-hydroxy-4-ethyl-1-methylbenzene. B. p. 222.5–226.5°.

(β-phenol derivative)-?-hydroxy-4-ethyl-1-methylbenzene. B. p. 219.8–220.8°.

The sulfonic acids were isolated by Bayrac in the form of their corresponding barium salts, from the reaction product, resulting from the sulfonation of *p*-ethyl-methylbenzene. He did not prove their constitution. Only a small difference in the physical properties of his barium salts was the basis for Bayrac's assumption that he had actually obtained two different sulfonic acids. Neither did he establish the constitution of his "α-" and "β-"phenols, which in physical properties differed from each other only as regards a few degrees in boiling point.

So far as the writers have been able to ascertain, no ethyl or propyl *p*-cresols are listed either in Beilstein's Handbuch, or Richter's "Lexikon der Kohlenstoff verbindungen." We have now synthesized two such representatives of the *p*-cresol series, namely, 2-ethyl-4-methylphenol (VII) and 2-propyl-4-methylphenol (IX) by the action of zinc-amalgam

[1] *Ber.*, **37**, 3994 (1904).

[2] *Ibid.*, **47**, 51 (1914).

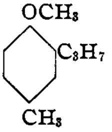
[3] D. R. P. 61575.

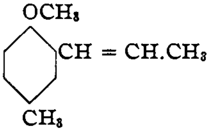
[4] *Bull. soc. chim.*, [3] **13**, 892 (1895).

and hydrochloric acid on 2-hydroxy-5-methyl-acetophenone (VI) and 2-hydroxy-5-methyl-propiophenone (VIII), respectively.

These ketones have been previously synthesized by Betteridge[1] and Auwers[2] by the action of aluminium chloride and acetyl and propionyl chlorides, respectively, upon the methyl ether of *p*-cresol in carbon bisulfide solution. We prepared these same ketones, modifying the above procedure to the extent of using petroleum ether as a solvent instead of carbon bisulfide. The physical properties of our compounds were in agreement with those of the ketones described by Betteridge and Auwers.

Of interest regarding the acylation of the *p*-cresol ethers was the fact that Betteridge, using propionyl chloride and aluminium chloride in carbon bisulfide solution, obtained from the ethyl ether of *p*-cresol, the ethyl ether of propionyl-*p*-cresol. The latter he was obliged to demethyl-


(I).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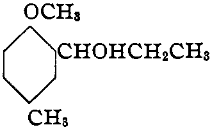
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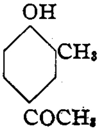
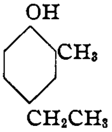
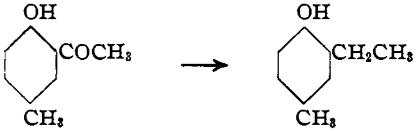
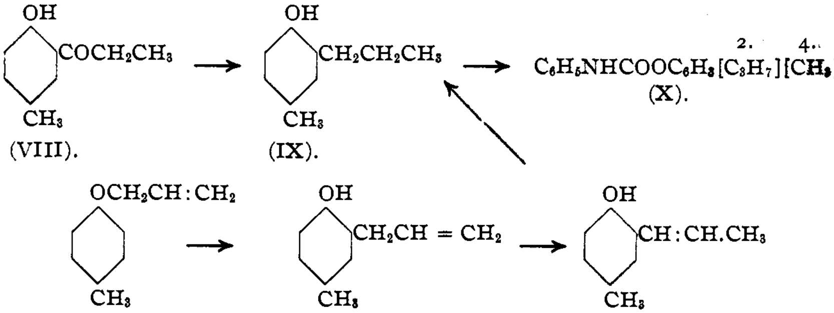

(IV).

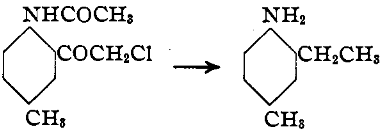

(V).

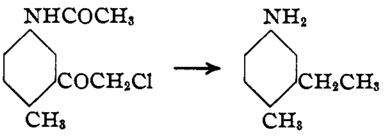

(VI). (VII).


(VIII). (IX).

$C_6H_5NHCOOC_6H_3\overset{2.}{[C_3H_7]}\overset{4.}{[CH_3]}$
(X).

(XI). (XII). (XIII).


(XIV). (XV).


(XVI). (XVII).

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[1] Diss., Breslau, **1898**.

[2] *Ber.*, **36**, 3891 (1903); **47**, 3318 (1914); *Ann.*, **364**, 164 (1908).

ate according to Gattermann's[1] aluminium chloride method in order to obtain his phenol. We found that on applying the Friedel-Craft reaction in petroleum-ether solution, that demethylation took place during the course of the reaction. We investigated both the methyl and ethyl ethers of *p*-cresol in the reaction with acetyl chloride, and observed both demethylation and de-ethylation to occur. In fact, Auwers[2] stated in a later paper that acetyl *p*-cresol could be directly obtained from the methyl ether of *p*-cresol with acetyl chloride. The conversion of a phenolic ether into the free phenol is not uncommon under the above-described conditions, although it has been our experience that this reaction is not so liable to occur in petroleum-ether solution.

In order to establish with certainty the position which the acyl groups occupy when substituting in *p*-cresol we proceeded as follows:

p-Cresol was first converted into its allyl ether (XI) and the latter in accordance with Claisen's[3] recent method then rearranged into 2-allyl-4-methylphenol (XII) by the application of heat. The allyl derivative was then rearranged into its corresponding propenyl derivative (XIII) by heating with aqueous alkali. We observed that 2-propenyl-4-methylphenol (XIII) would easily reduce to 2-propyl-4-methylphenol (IX) with metallic sodium and alcohol. The product thus obtained *was identical with the product resulting from the reduction of 2-hydroxy-5-methyl-acetophenone (VIII) with zinc-amalgam and hydrochloric acid.* In sharp contrast to the behavior of 2-propenyl-4-methylphenol (XIII) was the resistance of 2-allyl-4-methylphenol (XII) to reduction with sodium and alcohol. In fact, we were unable to accomplish a reduction of this compound with zinc-amalgam, or even hydriodic acid and phosphorus. This behavior is quite in accord with the previously observed resistance of *allyl*-substituted phenols to reduction. In fact, Klages states[4] in his article entitled, "Ueber das Dihydro Anethol," that—

> "es bleibt die Frage offen, ob allgemein in Benzol-derivaten die Gruppe $CH = CH - CH_3$ reduzirbar ist, und sich in dieser Hinsicht anders verhält als die Gruppe $CH_2CH = CH_2$."

The reduction products of both 2-propenyl-4-methylphenol (XIII) and 2-hydroxy-5-methyl-propiophenone (VIII) condense with phenyl isocyanate giving the same product, namely, the phenyl urethane of 2-hydroxy-5-methyl-acetophenone (X). *The propionyl group in 2-hydroxy-5-methyl-propiophenone is then in the ortho position in respect to the hydroxyl group.*

Reasoning from analogy we may then assume the structure of 2-hydroxy-

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[1] *Ber.*, **25**, 3531 (1892).

[2] *Ann.*, **364**, 164 (1908).

[3] *Ibid.*, **401**, 44 (1913).

[4] *Ber.*, **32**, 1436 (1899).

5-methyl-acetophenone (VI) which was smoothly reduced to 2-ethyl-4-methylphenol (VII).

As a further extension of the application of zinc-amalgam as a reducing agent, it has been of interest to us, in the light of future investigations, to ascertain the reducibility of amido phenyl ketones. We were successful in reducing 3-acetylamido-6-methyl-chloroacetophenone (XVI) and 2-acetylamido-5-methyl-chloroacetophenone (XIV) to 3-ethyl-4-methylaniline (XVII) and 2-ethyl-4-methylaniline (XV), respectively. We definitely established by these reductions the constitution of the above chloroacetophenones described by Kunckell[1] since 2-ethyl-4-methylaniline (XV) has been described by Willgerodt and Brandt[2] and its constitution established by these same investigators.

The writers wish to acknowledge their indebtedness to Prof. Treat B. Johnson, at whose suggestion these experiments were undertaken.

Experimental Part.

2-Hydroxy-5-methyl-acetophenone, VI. — Thirty-five cc. of acetyl chloride were slowly added to a solution of 30 g. of the methyl ether of *p*-cresol in 200 cc. of dry petroleum ether. Twenty-five grams of aluminium chloride were added as a catalyst. The mixture was then heated for 30 hours on a steam bath. At this time evolution of hydrochloric acid gas had practically ceased. The petroleum ether was then carefully decanted from a dark-colored residue, and the latter poured into ice water, acidulated with hydrochloric acid, in order to decompose the double aluminium compound. The solution was extracted with ether, and the resulting ethereal solution of the phenol carefully washed with sodium carbonate and water, and then dried over calcium chloride. The phenol was distilled at ordinary pressure, sixteen grams being obtained from the fraction boiling at 237–247°. The melting point was 49°. The phenol is quite soluble in the ordinary solvents and crystallizes from 80% alcohol in light yellow needles melting at 50°. Betteridge[3] states that the melting point of his *o*-acetyl-*p*-cresol was 50°.

Calcd. for $C_9H_{10}O_2$: C, 72; H, 6.66; found: C, 71.7; H, 7.10.

2-Ethyl-4-methylphenol, VII.—Thirty-seven grams of 2-hydroxy-5-methyl acetophenone were suspended in 300 cc. of hydrochloric acid with 120 g. of zinc-amalgam. The mixture was then boiled 18 hours on a sand bath. The acid solution was extracted with ether, and the ethereal solution of the phenol dried over calcium chloride. After removal of the ether, the phenol was then purified by fractional distillation at ordinary pressure. Fifteen grams of a heavy oil were obtained boiling at 216–218°

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[1] *Ber.*, **33**, 2646 (1900).

[2] *J. prakt. Chem.*, [2] **69**, 436 (1904).

[3] *Loc. cit.*

The oil was light yellow, but assumed a much darker color on exposure to the air.

Calc. for $C_9H_{12}O$: C, 79.41; H, 8.82; found: C, 79.72; H, 8.76.

Phenyl Urethane of 2-Ethyl-4-methylphenol, $C_6H_5NHCOOC_6H_3\text{-}\overset{2}{(C_2H_5)}\overset{4}{(CH_3)}$.—An intimate mixture of 5 g. of 2-ethyl-4-methylphenol, 2.5 g. of phenyl isocyanate, and a small quantity of aluminium chloride (as a catalyst) were heated for 16 hours in a brine bath. Anhydrous conditions were maintained throughout the heating period by the use of calcium chloride tubes. The semisolid product was finally extracted with ether from the suspended aluminium chloride. After evaporation of the ether, the dark-colored residue was purified by several crystallizations from alcohol. The pure urethane crystallized from this solvent in colorless square plates, which melted at 101°. It was soluble in benzene, alcohol, and ether, but difficultly soluble in petroleum ether. Yield, 2. g.

Calc. for $C_{16}H_{17}O_2N$: N, 5.49; found: N, 5.66, 5.26.

2-Hydroxy-5-methylpropiophenone, VIII.—Sixty-five grams of the methyl ether of *p*-cresol were dissolved in 250 cc. of petroleum ether and 72 g. of aluminium chloride suspended in the solution. The flask was then connected to a return condenser and 55 g. of propionyl chloride slowly added. The solution was heated for 30 hours in a water bath, when the petroleum ether was decanted as in the preparation of 2-hydroxy-5-methyl-acetophenone and the residue disintegrated by pouring into ice-cold hydrochloric acid. After extraction with ether, and drying over calcium chloride the phenol was subjected to distillation under diminished pressure. Twenty-five grams of 2-hydroxy-5-methyl-acetophenone (b. p. 153_{40}—m. p. 2°) were thus obtained. The physical characteristics of this compound agree with those of Betteridge's so-called *o*-propionyl-*p*-cresol. It gave a positive test with Millon's reagent.

2-Propyl-4-methylphenol, IX.—This compound was prepared by the reduction of 2-hydroxy-5-methyl-propiophenone in accordance with the following procedure: Thirty-two grams of 2-hydroxy-5-methyl-propiophenone were digested for 18 hours with 150 g. of zinc-amalgam and 250 cc. of hydrochloric acid. After the usual extraction with ether and drying over calcium chloride, the reduced product was distilled under diminished pressure. The fraction boiling at $128\text{–}130_{27}$ analyzed for 2-propyl-4-methylphenol. The phenol is light yellow in color. It showed no tendency to crystallize even upon long standing in a freezing mixture. Yield, 19 g.

Calc. for $C_{10}H_{14}O$: C, 80; H, 9.33; found: C, 79.6; H, 9.21.

This compound was also obtained by the reduction of 2-propenyl-4-methylphenol (XIII). The synthesis of the latter as well as the corresponding 2-allyl-4-methylphenol has been fully described by Claisen.[1]

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[1] *Loc. cit.*

We were unable to accomplish the reduction of the allyl derivative with any of the following reducing agents:

1. Zinc-amalgam in hydrochloric acid.
2. Hydriodic acid and phosphorus.
3. Sodium or sodium-amalgam in alcohol.

The reduction of 2-propenyl-4-methylphenol was carried out as follows: Thirty-eight grams of metallic sodium were slowly added to a boiling solution of 33 g. of 2-propenyl-4-methylphenol in 300 cc. of absolute alcohol. After the sodium had completely dissolved, the alcohol was distilled off, and the residue after solution in water was acidified with dilute sulfuric acid. The separated oil was extracted with ether and dried over fused sodium sulfate. Upon distillation under diminished pressure 26 g. of a light yellow oil were obtained boiling at 130° at 25 mm. pressure. This oil analyzed for 2-propyl-4-methylphenol. However, to prove with certainty that it was identical with our previously prepared 2-propyl-4-methylphenol, we converted it into its urethane. We again obtained the urethane of 2-propyl-4-methylphenol, which melted unchanged at 99° with the urethane obtained from the reduction product of 2-hydroxy-5-methyl-propiophenone.

Calc. for $C_{17}H_{19}O_2N$: N, 5.20; found: N, 5.12, 5.09.

Phenylurethane of 2-Propyl-4-methylphenol, $C_6H_5NHCOOC_6H_3\underset{2}{(C_3H_7)}\underset{4}{(CH_3)}$.—Five grams of 2-propyl-4-methylphenol, 2.5 g. of phenyl isocyanate and 0.2 g. of aluminium chloride were heated for 12 hours under carefully maintained anhydrous conditions. The resulting semi-solid mass was extracted with ether. After evaporation of the ether, a solid remained which was triturated with ligroin to remove resinous matter and then purified by several crystallizations from alcohol. The pure urethane crystallizes in small needles which melt at 99°. It is soluble in alcohol, ether and benzene, but difficultly soluble in ligroin.

Calc. for $C_{17}H_{19}O_2N$: N, 5.20; found: N, 5.38.

Phenylurethane of 2-Allyl-4-methylphenol, $C_6H_5NHCOOC_6H_3\overset{2}{(C_3H_5)}\overset{4}{(CH_3)}$.—This new urethane was prepared by heating an intimate mixture of 2 g. of 2-allyl-4-methylphenol, 1.6 g. of phenyl isocyamate and 0.3 g. of aluminium chloride at 104° for 14 hours. The reaction product was dissolved in hot alcohol. Upon cooling the solution, the urethane separated in thin needles melting at 68°. It is very soluble in alcohol, petroleum ether and benzene. The yield was excellent.

Calc. for $C_{17}H_{17}O_2N$: N, 5.24; found: N, 5.30, 5.28.

3-Ethyl-4-methylaniline, XVII.—Nineteen grams of 3-acetylamido-6-methyl-chloroacetophenone were digested with 70 g. of zinc-amalgam and 300 cc. of hydrochloric acid for 16 hours. After filtering from zinc-amalgam and mercury, the solution was made distinctly alkaline with ammonium hydroxide and then extracted with ether. This ether solution was dried over sodium sulfate and after removing the ether in the usual manner the base was distilled. Since 2-ethyl-4-methylaniline is not stable, we immediately converted the base into its sulfuric acid salt by solution in equal volumes of dilute sulfuric acid and 50% alcohol. A crystalline product separated upon standing. This product was crystallized twice from dilute alcohol, out of which it separated in characteristic plates melting approximately at 178°. It is soluble in alcohol and ether. Yield, 4 g.

Calc. for $(C_9H_{13}N)_2H_2SO_4$: N, 7.609; found: 7.506, 7.72.

2-Ethyl-4-methylaniline, XIV.—This compound was previously synthesized by Willgerodt and Brandt[1] by the action of molecular quantities of *p*-toluidine, ethyl alcohol and zinc-chloride at 280°. The writers obtained this same amine by the reduction of 2-acetylamido-5-methyl-chloroacetophenone with zinc-amalgam and hydrochloric acid. The procedure followed in this reduction was similar to that employed in the reduction of 3-acetylamido-6-methyl-chloroacetophenone. The product of the reaction was an oil which distilled at 217–220°. Willgerodt and Brandt assign a boiling point of 218–220° to their compound. Owing to the instability of the base, it was converted into its sulfuric acid salt by solution in 50% alcohol and sulfuric acid. The salt soon separated in characteristic platy crystals melting at 241°. The physical and chemical properties of this sulfate are entirely in accord with those of the sulfate described by Willgerodt and Brandt.

Calc. for $(C_9H_{13}N)_2H_2SO_4$: N, 7.608; found: N, 7.60, 7.55.

NEW HAVEN, CONN.

[CONTRIBUTIONS FROM THE SHEFFIELD CHEMICAL LABORATORY OF YALE UNIVERSITY.]

RESEARCHES ON HYDANTOINS. XXXI. A NEW SYNTHESIS OF *o*-TYROSINE.[2]

BY TREAT B. JOHNSON AND WALTER M. SCOTT.

Received June 8, 1915.

It has already been demonstrated that the *hydantoin-method* of synthesizing α-amino acids is one of quite general application. In fact, the results obtained thus far, and discussed in previous papers from this laboratory, show that the methylene radical of the polypeptide grouping—NH.CH₂.CO—in a hydantoin is as reactive towards the aldehyde group as is the same combination in the hippuric acid molecule $C_6H_5CONHCH_2$-

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[1] *J. prakt. Chem.*, [2] 69, 436 (1904).

[2] Part of a dissertation presented by Mr. Walter Moody Scott to the Faculty of the Graduate School of Yale University, 1915, in Candidacy for the Degree of Doctor of Philosophy.