and second, *p,p'*-di-iododiphenyl was treated with monomethylaniline. In both cases, we obtained dimethyldiphenylbenzidine which we could identify with the preparation made by Wieland, for the sample of which we wish to thank Professor Wieland.

It gives me great pleasure to acknowledge the valuable help of Dr. R. Bretagne at the University of Lausanne.

Summary

We have described the preparation of dimethyldiphenyl-*p*-phenylenediamine, and its identity was proved by the fact that we obtained the same compound by three different methods. On oxidation it shows the same characteristics as the corresponding benzidine derivative, dimethyldiphenylbenzidine. We have also carried out two new syntheses of this dimethyldiphenylbenzidine.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE PLAUT RESEARCH LABORATORY OF LEHN AND FINK, INCORPORATED]

FURTHER STUDIES ON THE INTRODUCTION OF ALKYL AND ARYL GROUPS INTO THE NUCLEUS OF POLYPHENOLS

BY EMIL KLARMANN

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The alkyl and aryl substituted derivatives of resorcinol, some of which possess remarkable antiseptic properties, may be obtained by different methods. Thus, benzylresorcinol is prepared either by the direct introduction of the benzyl group into the nucleus of resorcinol or by the reduction of the corresponding *m*-dihydroxybenzophenone. The first way was used by Liebmann[1] who showed that aliphatic alcohols and benzyl alcohols, when heated with resorcinol in the presence of zinc chloride, combine with resorcinol and form the corresponding substitution derivatives. Klarmann[2] effected a substitution of resorcinol by the condensation of benzyl chloride with resorcinol in the presence of aluminum chloride in nitrobenzene solution. It may be mentioned here that Boeseken[3] considers benzyl chloride as unsuitable for the Friedel-Crafts reaction, since it is declared to lead to resinified products. The reduction of the *m*-dihydroxybenzophenone was studied by Hirzel,[4] Dohme[5] and Klarmann.[2] The ketone was obtained by the first two authors by direct condensation of benzoic acid with resorcinol in the presence of zinc chloride, according to

[1] Liebmann, *Ber.*, **14**, 1842 (1881); Ger. pat. 17,311 (1881).

[2] Klarmann, THIS JOURNAL, **48**, 791 (1926).

[3] Boeseken, *Rec. trav. chim.*, **23**, 98 (1904).

[4] Hirzel, Brit. pat. 222,136 (1925).

[5] Dohme, Brit. pat. 223,190 (1925).

Nencki,[6] while the latter used Hoesch's[7] method of condensing benzonitrile with resorcinol. All reductions were carried out according to Clemmensen.[8] The applicability of this method for the reduction of dihydroxyketones was proved by Johnson and Lane.[9]

It has been mentioned in a previous paper that a high germicidal action was shown by 2,4-dihydroxydiphenylmethane and 2,4-dihydroxydiphenylethane. We were interested in finding the maximum germicidal action in this series of dihydroxydiphenyl hydrocarbons and prepared 2,4-dihydroxydiphenylpropane, which shows a phenol coefficient of 31. This suggests that the maximum germicidal strength is shown by 2,4-dihydroxydiphenylethane (Table I). The *m*-dihydroxydiphenylpropane was pre-

TABLE I

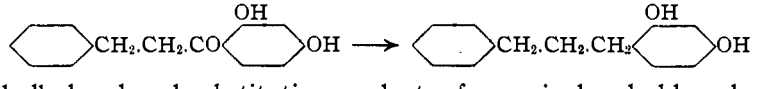
PHENOL COEFFICIENT AND CHEMICAL CONFIGURATION

Resorcinol derivatives				Phloroglucinol derivatives	
Aryl substituent	Ph. coeff.	Alkyl substituent	Ph. coeff.	Substituent	Ph. coeff.
.....	0.3	.....	0.3	.....	$\gg 1$
$C_6H_5CH_2$	23	C_2H_5	1.5[a]	C_6H_{13}	8
$C_6H_5C_2H_4$	41	$(C_2H_5)_2$	10	$(C_2H_5)_3$	2.5
$C_6H_5C_3H_6$	31	C_3H_7	4.3[a]	$C_6H_5CH_2$	7.5
		$(C_3H_7)_2$	18	$C_6H_5C_2H_4$	8
		C_4H_9	8[a]	$C_6H_5C_3H_6$	8.8
		$(C_4H_9)_2$	10		
		C_6H_{13}	45[b]		
		$(C_6H_{13})_2$	21		
		$C_{12}H_{25}$	$\gg 1$		

[a] Johnson and Lane, Ref. 9.

[b] Leonard, Ref. 14.

pared similarly to other compounds of this group by condensation of dihydrocinnamic nitrile with resorcinol and subsequent reduction of the resulting *m*-dihydroxydihydrochalcone. The nitrile was obtained by the action of phosphorus pentoxide on dihydrocinnamamide, the dihydrocinnamoyl chloride having been prepared by the action of thionyl chloride on the free acid.



All alkyl and aryl substitution products of resorcinol and phloroglucinol that were hitherto tested biologically are monosubstituted derivatives. We were interested in the preparation of disubstituted resorcinol and trisubstituted phloroglucinol derivatives in order to see how the introduction

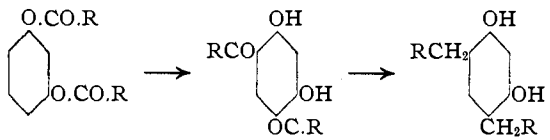
[6] Nencki, *Monatsh.*, **10**, 906 (1889).

[7] Hoesch, *Ber.*, **48**, 1122 (1915).

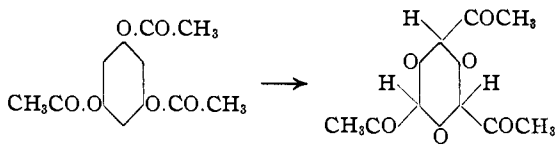
[8] Clemmensen, *Ber.*, **46**, 1837 (1913); **47**, 687 (1914).

[9] (a) Johnson and Lane, THIS JOURNAL, **43**, 348 (1921). (b) Dohme, Cox and Miller, *ibid.*, **48**, 1688 (1926).

of further alkyl groups influences the germicidal action. We availed ourselves of a reaction that was studied first by Doebner,[10] then by Eijkman,[11] who found that diesters of resorcinol undergo a rearrangement with formation of phendiones when heated with zinc chloride. The reduction of the latter, according to Clemmensen, would then lead to dialkyl derivatives of resorcinol.



A similar rearrangement was observed by Heller[12] who regards the reaction product in the case of phloroglucinol as a derivative of triketohexamethylene.



The reduction of this product leads, however, to a trialkyl derivative of phloroglucinol. This fact and Heller's arguments, which permit an explanation different from his, likewise make the phenolic structure appear probable.

In all reductions studied, the end of a reduction was indicated by a practically negative reaction of the alcoholic solution of the product to ferric chloride, while all keto compounds gave a very distinct red coloration with ferric chloride.

We prepared diethyl-, dipropyl-, dibutyl-, dihexyl- and dodecylresorcinol and triethylphloroglucinol. Actually, it is shown in some cases that the phenol coefficient of disubstituted derivatives is several times higher than that of a corresponding monosubstituted compound. In other cases it is lower. Besides, the total weight of side chains may be higher in a disubstituted resorcinol than in a monosubstituted and still a powerful germicidal compound results. Thus dihexylresorcinol shows a phenol coefficient of 21, while dodecylresorcinol is practically inactive. (Table I.)

The dialkyl derivatives of resorcinol were prepared from the corresponding esters and the latter were obtained by heating resorcinol with a small excess of the respective acid chloride. Dodecylresorcinol was prepared by the reduction of lauroresorcinol; the latter results on condensation of resorcinol with lauric acid in the presence of zinc chloride.

[10] Doebner, *Ann.*, **210**, 259 (1881). Nencki and Sieber, *J. prakt. Chem.*, [2] **23**, 149 (1881).

[11] Eijkman, *Chem. Weekblad*, **2**, 59, 79 (1905).

[12] Heller, *Ber.*, **42**, 2736 (1909).

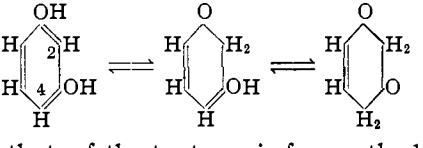
Attempts have also been made to prepare compounds that contain halogen in the side chain. While keto compounds of resorcinol are readily obtained, those of phloroglucinol lead immediately to coumaranone derivatives of the type observed by Sonn,[13] even when the halogen does not stand at the end of the side chain as in Sonn's experiments. The boiling with hydrochloric acid, however, partly eliminates the halogen of the halogen alkylresorcinol derivatives, and products of a changing composition result.

The phenol coefficients were determined according to the method of the Hygienic Laboratory. Since some substances are very difficultly soluble in water, the original emulsion was prepared by adding distilled water to the alcoholic solution of the tested substance. The further dilutions, however, were made with water so that not more than 1% of alcohol was present in the sample on which the final reading was made.

Conclusion

While hexylresorcinol possesses the maximal germicidal action among the mono-alkyl derivatives of resorcinol, according to Johnson and collaborators, and Leonard *m*-dihydroxydiphenylethane seems to be the strongest among the mono-aryl derivatives of resorcinol. Introduction of two alkyl groups into the nucleus of resorcinol in some cases leads to compounds with a stronger germicidal action than that of the mono-alkyl derivatives, while in other cases weaker compounds are obtained. The germicidal strength of phloroglucinol may be similarly increased, all three compounds of the trihydroxydiphenyl hydrocarbon series having approximately the same phenol coefficient while triethylphloroglucinol is weaker than hexylphloroglucinol.[14]

The experiments carried out hitherto allow an explanation for these phenomena to be attempted. We may assume that the antiseptic action of phenols is due to the presence of the hydroxyl groups. On the other hand, it appears from different investigations that a keto structure may be ascribed to many unsubstituted polyphenols.

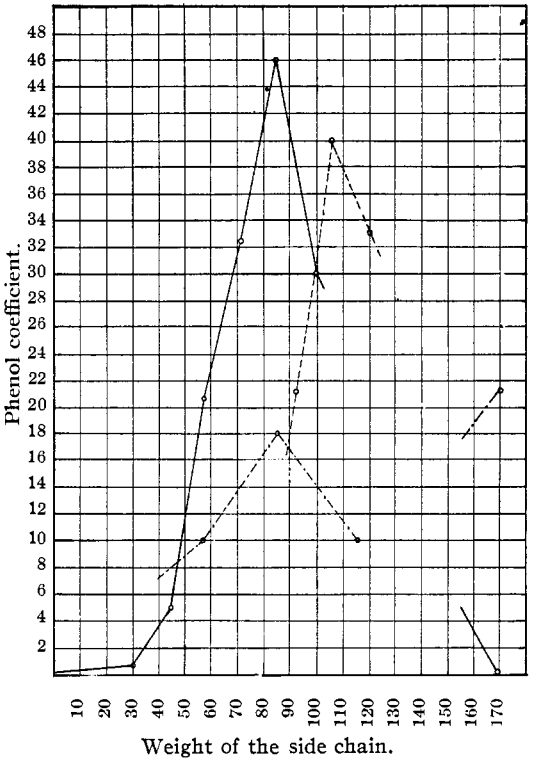


We assume further that, of the tautomeric forms, the keto form does not possess an antiseptic action. It follows from Werner's theory of the changing valence of the carbon atom that the valence with which a radical is attached to a carbon atom varies with various radicals. If we combine this assumption with that of the dynamic keto structure previously men-

[13] Sonn, *Ber.*, **50**, 1262 (1917).

[14] Klarmann and Figdor, THIS JOURNAL, **48**, 803 (1926).

tioned, it follows that the carbon atoms of Positions 2 and 4 will be the less receptive for the hydrogen atom of the hydroxyl groups of Positions 1 and 3, the more their valence is engaged in binding an alkyl group. Thus the shift of the hydrogen atom is made increasingly improbable with the increasing weight of the side chains. This does not mean that the unsubstituted resorcinol is assumed to possess the tautomer keto structure under



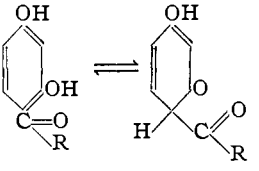
The relationship between the weight of the side chain and the phenol coefficient. ———Full line; alkyl derivatives of resorcinol (Johnson and Lane, Leonard). - - - -Dash line; aryl derivatives of resorcinol. - — - —Dash and dotted line; dialkyl derivatives of resorcinol.

normal conditions, but rather that this configuration may form in the medium in which the processes take place that summarily appear as antiseptic action.

It is perhaps significant in this connection that none of the alkyl and aryl substituted compounds studied gives a pronounced color reaction with ferric chloride, while the unsubstituted resorcinol and phloroglucinol give characteristic colorations. In the case of monosubstituted derivatives

the resemblance of the *ortho* and *para* positions of the hydroxyl groups in relation to the substituting group is to be considered.[14a]

The weakening of the germicidal action on introduction of acyl groups is explainable by considering the possibility of the equilibrium.



In a similar sense the hydroxyl group in *para* position to the keto group might be influenced. The same ideas refer likewise to other phenols. It is, however, not clear why the limit of bactericidal action is reached with a side chain of comparatively few carbon atoms, unless we assume that the solubility in the substance in which the antiseptic action takes place, is entirely changed.

Leonard[15] states that the antiseptic power of mono-alkyl derivatives of resorcinol is due to their ability to lower the surface tension. Therefore the compounds penetrate more easily through the membranes. It is possible that the germicidal action is due to a combination of the physical ability to lower the surface tension with the chemical ability to increase the reactivity of the hydroxyl group as outlined before.

Experimental Part

Preparation of 2',4'-Dihydroxy-α,β-dihydrochalcone, $C_6H_5.CH_2.CH_2.CO.C_6H_3(OH)_2$ **and of 2,4-Dihydroxydiphenylpropane,** $C_6H_5.CH_2.CH_2.CH_2.C_6H_3(OH)_2$.—Forty g. of hydrocinnamic acid and 60 g. of thionyl chloride were heated in a water-bath under a reflux condenser for three hours at 60–70°. The excess of thionyl chloride was removed by evacuation at room temperature. The crude chloride was applied directly for the preparation of the amide.

The hydrocinnamoyl chloride was allowed to drop into a stirred 26% aqueous solution of ammonia which was cooled below 0°. The hydrocinnamamide crystals separated soon and were filtered under suction, washed with water and dried in a vacuum desiccator at room temperature; m. p., 97°; yield, 75%.

Anal. Calcd. for $C_9H_{11}ON$: N, 9.40. Found: 9.26.

The hydrocinnamamide was mixed with phosphorus pentoxide and heated in a vacuum of 65 mm., whereupon the hydrocinnamic nitrile distilled at 170°. This was

[14a] The introduction of one or more halogen atoms into the nucleus of phenol and and related compounds considerably increases their germicidal action, but at the same time reduces their reactivity in the presence of proteins [Bechhold and Ehrlich, *Z. physiol. Chem.*, **47**, 175 (1906).]

This is probably due to the increased electrolytic dissociation of the halogen substituted compound (that is, the more pronounced acid nature of the OH group). In contrast to this phenomenon, it is assumed that in the case of alkyl or aryl substitution the pratically undissociated form of the phenols is to be considered in the keto-enol equilibrium as outlined before.

[15] Leonard and Wood, *J. Am. Med. Assoc.*, **85**, 24, **1855** (1925).

shaken with concd. potassium carbonate solution, filtered, dried with phosphorus pentoxide and redistilled in a vacuum; yield, 40%.

The condensation with resorcinol was carried out in the following way. Twenty-seven g. of the nitrile and 22 g. of resorcinol were dissolved in 100 cc. of dry ether, 6 g. of fused and powdered zinc chloride was added and a current of dry hydrogen chloride was allowed to pass through the mixture for three and one-half hours. The oily residue was allowed to stand in the ice box overnight, then cold hydrochloric acid (1 : 1) was added. On rubbing and shaking, the keto-imido hydrochloride separated in small crystals which were filtered off and washed with ether. By boiling with water for 25 minutes, the 2',4' - dihydroxy - α,β - dihydrochalcone was precipitated. When sufficient water was present, silky needles were obtained. After being washed and dried in air, they melted at 84° (uncorr.); yield, about 50% of the nitrile. It gave a dark red coloration with ferric chloride in alcoholic solution. The substance contains 1 molecule of water of crystallization; the drying of the analysis sample was effected out in a microvacuum desiccator.

All combustions were carried out according to the micro method of Pregl; samples of 3–5 mg. were taken.

Anal. Calcd. for $C_{15}H_{14}O_3.H_2O$: H_2O, 6.92. Found: 6.44.

Calcd. for $C_{15}H_{14}O_3$: C, 74.35; H, 5.82. Found: C, 74.26; H, 5.91.

This compound was reduced with amalgamated zinc and 1: 3 hydrochloric acid in the usual way. The reduction product was shaken out with ether; the ether was evaporated after drying and the residue was allowed to stand with half of its volume of benzene in the ice box overnight. A crystalline mass was formed which was filtered and washed with a mixture of one part of benzene and two parts of petroleum benzine and dried in a vacuum at room temperature; m. p., 70–71° (uncorr.); yield, about 50% of the keto compound. Ferric chloride produces a precipitate after some time; the phenol coefficient is 31.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.91; H, 7.06. Found: C, 79.45; H, 7.41.

Preparation of 2',4',5'-Trihydroxy-α,β-dihydrochalcone, $C_6H_5CH_2.CH_2.CO.C_6H_2(OH)_3$ and of 2,4,6-Trihydroxydiphenylpropane, $C_6H_5.CH_2.CH_2.CH_2.C_6H_2(OH)_3$.—The condensation of hydrocinnamic nitrile with phloroglucinol was carried out in the way that was described before. The weights taken were 13 g. of the nitrile and 12.5 g. of phloroglucinol. The method of isolation was the same; m. p. of the air-dried trihydroxydihydrochalcone, 140° (uncorr.). It gave a red coloration with ferric chloride in alcoholic solution. The compound contains 1 molecule of water of crystallization.

Anal. Calcd. for $C_{15}H_{14}O_4$: C, 69.74; H, 5.46. Found: C, 69.21; H, 5.41.

Calcd. for $C_{15}H_{14}O_4.H_2O$: H_2O, 6.52. Found: 6.83.

The reduction was carried out with amalgamated zinc and 5% hydrochloric acid. The product was isolated with ether, recrystallized from benzene and dried in a vacuum; m. p., 80–81° (uncorr.). On standing, a precipitate with ferric chloride forms; phenol coefficient, 8.8.

Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.77; H, 6.60. Found: C, 73.23; H, 7.05.

Preparation of the Di- and Trisubstituted Phenols

In general the following procedures were used to carry out the three steps in the preparation of the substituted phenol.

Esterification.—The polyphenol was heated under a reflux condenser with a small excess of the acid chloride for two to three hours at 70–75°. The resulting product was shaken with water, extracted with ether and, after evaporation of the latter, subjected to fractional distillation.

Rearrangement.—The rearrangement of the esters was carried out in general by heating to 130° with zinc chloride (previously fused and powdered). This melt was allowed to cool during stirring and addition of methanol. The resulting product, which usually crystallized, was filtered off and recrystallized from an appropriate solvent. The yields were 40–50% based on the ester.

Reduction.—The rearrangement product was reduced by the method of Clemmensen using zinc amalgam and 1:2 or 1:3 hydrochloric acid. The liquefied rearrangement product was reduced during 16 to 24 hours, the reduced compound isolated by means of ether and recrystallized from

TABLE II

EXPERIMENTAL DATA ON THE ALKYL AND ARYL COMPOUNDS

R = Resorcinol derivative. P = Phloroglucinol derivative

		M. p., °C. (uncorr.)	B. p., °C.	*P*, mm. Hg	Analyses C Calcd.	C Found	H Calcd.	H Found
	ESTERS							
R	Dibutyrate		195–200	18	67.19	7.23	66.73	8.03
R	Dicaproate		210–220	12	70.57	8.56	70.32	9.07
	ACYL COMPOUNDS							
R	Diaceto[11]	182						
R	Dipropio[16]	125						
R	Dibutyro	64–65			67.18	7.76	66.46	8.26
R	Dicapro		215–220	6	70.15	8.56	70.19	9.16
R	Lauro	79–80			73.92	9.65	73.50	9.23
						Br		Br
R	α-Bromobutyro	114–115				30.87		29.84
P	Tri-aceto[a]							
	ALKYL COMPOUNDS							
R	Diethyl	71			71.29	8.42	72.38	8.90
R	Dipropyl	59			74.19	9.28	73.35	9.19
R	Dibutyl[c]	.....	194–196	14	75.61	10.0	73.36	11.79
R	Dihexyl		205	7	77.68	10.87	76.96	11.29
R	Dodecyl	65–66			77.86	10.86	77.81	11.12
P	Tri-ethyl[b]	126			68.54	8.54	68.22	8.73

[a] Acetic anhydride and sodium acetate were used to prepare the phloroglucinol triacetate instead of acetyl chloride as suggested by Hlasiwetz [*Ann.*, **119**, 201 (1861)]. The latter method gives poor yields. Ten g. of phloroglucinol, 50 g. of acetic anhydride and 6 g. of sodium acetate were boiled for two hours on a sand-bath. The excess of the acid anhydride was removed with 20 cc. of water; on cooling, the compound crystallized.

[b] The reduction of the triacetophloroglucinol was carried out in amyl alcohol using zinc amalgam and 1 : 5 hydrochloric acid. The mixture was boiled for 24 hours. The compound was isolated from the amyl alcohol layer with 5% sodium hydroxide solution. The sodium hydroxide extract was then acidified, extracted with ether and after evaporation of the latter, recrystallized from a little benzene.

[c] The dibutylresorcinol could not be obtained in crystalline form. The product was purified by vacuum distillation. Judging from the analysis it is not entirely pure.

[16] Wittig, *Ber.*, **59**, 117 (1926).

an appropriate solvent. The yield of the reduction product varied from about 30–60% of the keto compound. The experimental data on the series of compounds prepared by the above method are contained in Table II.

Preparation of 1,3-Dihydroxy-4-laurophenone, $C_6H_3(OH)_2(CO.C_{11}H_{23})$, and of 1,3-Dihydroxy-4-dodecylbenzene (dodecylresorcinol), $C_6H_3(OH)_2.C_{12}H_{25}$.—Twenty-four g. of lauric acid and 10 g. of zinc chloride were heated on a sand-bath until most of the zinc chloride dissolved. The mixture was allowed to cool to 100° and 5 g. of resorcinol was added. Then the flask was heated slowly to 250°. The cooled, solidified mass was remelted, poured into water at 80° and stirred vigorously. The cooled mixture was shaken with ether. The crystalline precipitate of zinc laurate was suspended in the ethereal solution and then filtered off, the ether evaporated and the residue distilled in a vacuum. The fraction distilling at 260–265° (8 mm.) was collected as a heavy, yellow oil that solidified on standing. It was recrystallized thrice from ligroin and formed greasy plates; m. p., 79–80° (uncorr.); yield, 55% of the resorcinol; m. p. of zinc laurate, 129°.

Anal. Calcd. for $C_{18}H_{28}O_3$: C, 73.92; H, 9.65. Found: C, 73.50; H, 9.23.
Calcd. for $C_{12}H_{23}O_2Zn$: Zn, 15.70. Found: 15.44.

Five g. of the keto compound was heated with amalgamated zinc and 1:2 hydrochloric acid for 16 hours under a reflux condenser. A distinct swelling took place and in a short time a jelly-like mass filled a volume of about 300 cc. This voluminous mass falls apart in the cold. Therefore, the heating must be interrupted from time to time. The product was extracted with ether and recrystallized from petroleum benzene; it gave shiny plates; m. p., 65–66°.

Anal. Calcd. for $C_{18}H_{30}O_2$: C, 77.86; H, 10.86. Found: C, 77.81; H, 11.12.

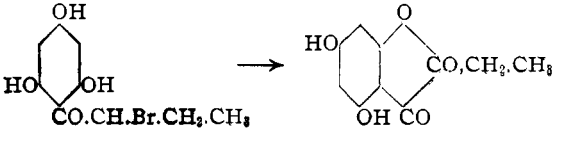
Preparation of 1,3-Dihydroxy-α-bromobutyrophenone-4, $C_6H_2(OH)_2CO.CHBr.CH_2.CH_3$.—The crude product of bromination of butyric acid was kept in a vacuum at room temperature in order to remove the excess of hydrobromic acid and the liquid was then allowed to drop into a cold ammonia solution during stirring, in the shortest time possible. The amide formed was filtered off and washed quickly, dried in a vacuum and distilled with phosphorus pentoxide. The resulting nitrile was purified with potassium carbonate and redistilled.

The condensation, according to Hoesch, was carried out as usual. Equimolecular parts of bromobutyric nitrile and resorcinol were dissolved in ether and a current of dry hydrogen chloride was allowed to pass through the mixture. The keto-imido hydrochloride was isolated and boiled with water for ten minutes. It separated in needles which, after being dried in a vacuum, melted at 114–115° (uncorr.) and gave a red coloration with ferric chloride.

Anal. Calcd. for $C_{10}H_{10}O_3Br$: Br, 30.87. Found: 29.84.

The low bromine content indicates that bromine was split off to a minor extent on boiling with water. No uniform product results when the reduction is attempted.

Preparation of 1-Ethyl-3,5-dihydroxycoumaranone-2.—This compound is obtained when the condensation product of bromobutyric nitrile and phloroglucinol is boiled with water. It probably forms according to the reaction



It is obtained from water in crystalline aggregates; m. p., 165–166° (uncorr.), giving an intense violet coloration with ferric chloride.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 61.84; H, 5.20. Found: C, 61.75; H, 5.76.

Mol. wt. (Rast[17]) Subs., 0.0210 g. in 0.2759 g. of camphor: Δt, 14°. Calcd. for $C_{10}H_{10}O_4$: mol. wt., 194. Found: 222.5.

My thanks are due to Mr. E. Tilly who carried out the determinations of the phenol coefficients according to the method of the Hygienic Laboratory.

Summary

In order to obtain more data on the influence of introduction of aryl and alkyl groups into the nucleus of polyphenols on the germicidal action, a number of new compounds were prepared and their phenol coefficients determined. Methods are given for the preparation of *m*-dihydroxydiphenylpropane, *m*-trihydroxydiphenylpropane, diethyl-, dipropyl-, dibutyl-, dihexyl- and dodecylresorcinol and triethylphloroglucinol and the corresponding mono-, di- and triketo compounds from which they are derived. The antiseptic actions of these compounds and their dependence upon the introduced side chains are discussed and a chemical explanation is attempted. Halogen alkyl compounds could not be obtained since the halogen is either split off when the reduction of the keto compound is attempted or a coumaranone derivative forms when the keto-imide is to be transformed into the ketone.

BLOOMFIELD, NEW JERSEY

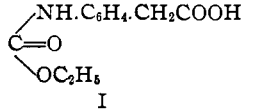
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF SASKATCHEWAN]

STUDIES IN URETHANS. II. ISOMERIC URETHAN DERIVATIVES OF PHENYLACETIC ACID, AND SOME RELATED COMPOUNDS

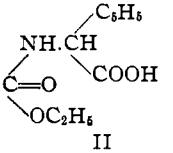
BY S. BASTERFIELD AND HAROLD N. WRIGHT

RECEIVED MAY 20, 1926 PUBLISHED SEPTEMBER 4, 1926

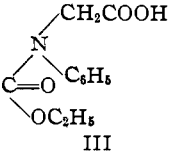
This study was undertaken in order to compare the physiological action of the three isomeric urethans, *p*-carbethoxy-aminophenylacetic acid (I), *dl*-α-carbethoxy-aminophenylacetic acid (II), and N-carbethoxy-phenylglycine (III).



I



II



III

Urethans in general are depressing to the central nervous system, and some of those containing aromatic radicals are antipyretic (for ex-

[17] Rast, *Ber.*, **55**, 1051 (1922).