Summary

The following derivatives of chaulmoogric acid have been prepared: chaulmoogrylcholine iodide, chaulmoogrylcholine chloride, diiodochaulmoogrylcholine iodide, diiodochaulmoogrylcholine chloride, chaulmoogryl *p*-phenetide, chaulmoogryl ethyl-*p*-aminobenzoate, dihydrochaulmoogranilide, dihydrochaulmoogryl *p*-phenetide, and dihydrochaulmoogryl ethyl-*p*-phenetide.

These compounds are of interest as possible antileprotic agents and are under clinical investigation.

Honolulu, Hawaii Received July 2, 1934

[Contribution from the Chemistry Department of the University of Oklahoma]

Derivatives of the Hydroxydiphenyls. II. Nitrogen and Halogen Derivatives of 4-Hydroxydiphenyl[1]

By J. C. Colbert, Wyman Meigs and Arnold H. Stuerke

The Orientation of Chlorine Atoms in Mono- and Dichloro-4-hydroxydiphenyl.—The preparation of mono-, di- and trichloro-4-hydroxydiphenyl was reported in a recent paper[2] from this Laboratory. By analogy with similar work[3] involving bromine derivatives it was held that chlorine probably entered first the *ortho* position to hydroxyl, second the other *ortho* position and lastly the *p'* position. It has now been found possible to obtain partial confirmation of the orientation of the derivatives previously reported by preparing two isomeric dichloromononitro-4-hydroxydiphenyls. Since 5-nitro-4-hydroxydiphenyl upon reduction, acetylation and benzoylation undergoes the rearrangement described by Raiford[4] as being peculiar to *o*-aminophenols, the structure of the mononitro derivative of 4-hydroxydiphenyl may be considered as fixed. 5-Nitro-4-hydroxydiphenyl when completely chlorinated yields a dichloro derivative whose structure, assuming the normal directive influence of the groups already present, must be 5-nitro-3,-4'-dichloro-4-hydroxydiphenyl. The only isomer of this compound obtainable starting with 4-hydroxydiphenyl must be 3,5-dichloro-4'-nitro-4-hydroxydiphenyl. Since this latter compound was prepared by the nitration of dichloro-4-hydroxydiphenyl the chlorine atoms in the dichloro derivative must occupy the two *ortho* positions. Since the same dichloro derivative results either from long chlorination of 4-hydroxydiphenyl or by chlorination of monochloro-4-hydroxydiphenyl, the monochloro-4-hydroxydiphenyl must have chlorine in the 3 position. Upon nitration 3-chloro-4-hydroxydiphenyl yields both mono and dinitro derivatives. The mononitro derivative yields the same dichloro derivative as 5-nitro-4-hydroxydiphenyl when chlorinated and is therefore to be considered 3-chloro-5-nitro-4-hydroxydiphenyl and the dinitro derivative 5,4'-dinitro-3-chloro-4-hydroxydiphenyl. 3-Chloro-5-nitro-4-hydroxydiphenyl may be readily reduced and brominates easily with the formation of 3-chloro-4'-bromo-5-nitro-4-hydroxydiphenyl. This evidence is summarized in Fig. 1.

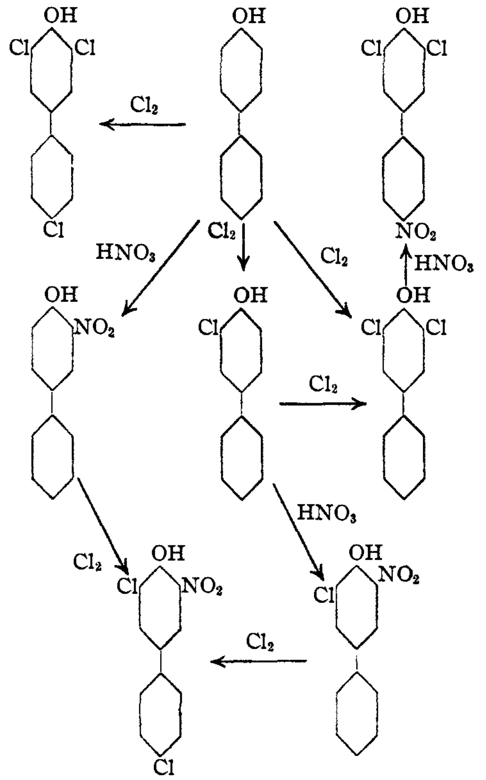

Fig. 1.—Experimental evidence for the orientation of chlorine in mono- and dichloro-4-hydroxydiphenyl.

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[1] The work of Arnold H. Stuerke was financed by means of a C. W. A. grant made to the University for research purposes.

[2] Colbert and others, This Journal, **56**, 202 (1934).

[3] Bell and Robinson, *J. Chem. Soc.*, **130**, 1128 (1927).

[4] Raiford and Colbert, This Journal, **47**, 1127 (1925).

DERIVATIVES OF 4-HYDROXYDIPHENYL

	Name, diphenyl	Reagent and reaction medium	Yield, %	M. p., corr. °C.	Formula	Analytical data, % Nitrogen Calcd.	Nitrogen Found	Halide Calcd.	Halide Found
1	3-Chloro-4-methoxy-	CH_3I–Aq. KOH	37.5	93	$C_6H_5C_6H_3ClOCH_3$	...	...	16.22	15.95
2	3,5-Dichloro-4-methoxy-	CH_3I–Aq. KOH	61.5	54	$C_6H_5C_6H_2Cl_2OCH_3$	...	...	28.03	28.13
3	3-Chloro-5,4′-dinitro-4-hydroxy-	HNO_3–HAc	48.0	subl. 200	$C_6H_4NO_2C_6H_2NO_2ClOH$	9.50	9.10	12.10	12.20
4	3-Chloro-4′-bromo-5-nitro-4-hydroxy-	Br_2–HAc	38.0	193–194	$C_6H_4BrC_6H_2NO_2ClOH$	...	...	35.12	35.78
5	3,5-Dichloro-4′-bromo-4-hydroxy-	Br_2–HAc	63.0	136.5–138	$C_6H_4BrC_6H_2Cl_2OH$	...	...	47.45	46.95
6	3-Chloro-4-hydroxydiphenyl-5-amino hydrochloride	$SnCl_2$, HCl–95% alc.	73.0	180 dec.	$C_6H_5C_6H_2ClNH_2OH$, HCl	...	...	27.71	27.55
7	Dibenzoate of 3-chloro-5-amino-4-hydroxy-	C_6H_5COCl–Pyridine	48.0	181–182	$C_6H_5C_6H_2ClNHCOC_6H_5OCOC_6H_5$	3.27	3.37	8.30	8.73
8	3,4′-Dichloro-4-hydroxydiphenyl-5-amino hydrochloride	$SnCl_2$, HCl–95% alc.	73.0	210 dec.	$C_6H_4ClC_6H_2ClNH_2OH$, HCl	...	...	36.55	36.41
9	Dibenzoate of 3,4′-dichloro-5-amino-4-hydroxy-	C_6H_5COCl–Pyridine	75.0	217–218	$C_6H_4ClC_6H_2ClNHCOC_6H_5OCOC_6H_5$	3.03	3.61	17.51	17.22
10	Benzoate of 5-nitro-4-hydroxy-	C_6H_5COCl–Pyridine	80.0	111	$C_6H_5C_6H_3NO_2OCOC_6H_5$	4.36	4.35	...	...
11	4′-Phenyl-2,4-dinitrodiphenyl ether	KOH, $C_6H_3Cl(NO_2)_2$–Pyridine	96.0	115	$C_6H_5C_6H_4OC_6H_3(NO_2)_2$	8.33	8.12	...	...
12	4′-Phenyl-2,4,6-trinitro-diphenyl ether	Picryl chloride–Pyridine	94.0	224	$C_6H_5C_6H_4OC_6H_2(NO_2)_3$	11.02	11.19	...	...

Polychlorinated Derivatives of 4-Hydroxydiphenyl.—Further investigation of the conditions of formation for trichloro-4-hydroxydiphenyl has led to two results. Chlorination in acetic acid yields mono-, di- or trichloro-derivatives, dependent upon the length of the chlorination process, and not the trichloro alone as was assumed in the first paper of this series.

When chlorination was continued for as long as ten hours a viscous red oil formed which crystallized with difficulty, the first crops of crystals analyzing for seven chlorine atoms and the later crops for five. Analysis and melting point range indicated that our purest preparations of the heptachloro- contained a small percentage of the penta- and the pentachloro- a small quantity of the heptachloro-. Attempts to determine structure by oxidation to a benzoic acid derivative have not been successful; however, further work will be carried out.

Experimental Part

3,4′-Dichloro-5-nitro-4-hydroxydiphenyl.—This compound was prepared both from 5-nitro-4-hydroxydiphenyl and from 3-chloro-5-nitro-4-hydroxydiphenyl.

(1) Three grams of 5-nitro-4-hydroxydiphenyl was dissolved in 30 cc. of glacial acetic acid and chlorine gas passed into the solution for one and one-half hours. The solution, which quickly filled with long yellow needles, was allowed to stand for three hours, cooled in ice and filtered. When recrystallized from carbon tetrachloride and light petroleum ether, a pure compound melting at 190–192° was obtained in 51% yield.

(2) Two grams of 3-chloro-5-nitro-4-hydroxydiphenyl was dissolved in 10 cc. of acetic acid and chlorine gas passed through the solution for two hours, after which the solution stood tightly stoppered for an hour. The excess solvent was evaporated at room temperature to a volume of 3.0 cc. which was cooled in a freezing mixture and filtered. Recrystallization from carbon tetrachloride gave a product melting at 190–191° and in 31% yield. A mixed melting point with the product obtained by the first method gave 191° and identical analyses were obtained from both preparations.

Anal. Calcd. for $C_{12}H_7O_3NCl_2$: Cl, 24.97; N, 4.93. Found: Cl, 24.74; N, 4.26.

3-Chloro-5-nitro-4-hydroxydiphenyl.—Ten grams of 3-chloro-4-hydroxydiphenyl (b. p. 176.6° at 5 mm.) was dissolved in 20 cc. of acetic acid and 10 cc. of acetic acid containing one molar proportion of nitric acid added slowly over a period of several minutes. After standing for three hours, the excess acid was removed under diminished pressure and the remaining solution cooled in a freezing mixture. The crystals were filtered, washed with petroleum ether and recrystallized from 12 cc. of carbon tetrachloride. A 38% yield of thick, yellow, rhombic platelets melting at 89–90° corr. was obtained.

Anal. Calcd. for $C_{12}H_8O_3NCl$: Cl, 14.20; N, 5.61. Found: Cl, 13.70; N, 5.73.

3,5-Dichloro-4′-nitro-4-hydroxydiphenyl.—Two grams of 3,5-dichloro-4-hydroxydiphenyl (b. p. 188.7° at 5 mm.) was dissolved in 10 cc. of acetic acid, and 5 cc. of acetic acid containing one molar proportion of nitric acid was added to the solution over a period of several hours. The long thin needles which formed by the conclusion of the nitration were filtered. Evaporation of the filtrate to dryness even at room temperature left only a tarry mass. Recrystallization of the first crystalline fraction from carbon tetrachloride yielded only 6.5% of the desired product of m. p. 214–215° corr. A mixed melting point with the isomeric phenol of m. p. 191° gave 170°.

Anal. Calcd. for $C_{12}H_7O_3NCl_2$: Cl, 24.97; N, 4.93. Found: Cl, 25.15; N, 5.28.

Chlorination of 4-Hydroxydiphenyl Using Acetic Acid as Solvent.—Chlorine gas was bubbled through solutions of 20-g. portions of 4-hydroxydiphenyl dissolved in 300 cc. of glacial acetic acid. The yields after thirty minutes, one and one-half hours, two and one-half hours, four hours and five hours were, respectively: 95% recovery of starting material, 38% yield of monochloro derivative, 25% yield of dichloro, 10% yield of trichloro and 12.5% yield of trichloro-4-hydroxydiphenyl. It was not found possible to isolate other products than those named.

Ten grams of 4-hydroxydiphenyl was dissolved in 150 cc. of acetic acid and chlorine gas bubbled through the solution for ten hours. A red solution formed and when the evaporation of excess acetic acid was attempted a deep red oil settled to the bottom. After two days evaporation at room temperature well-developed, colorless crystals formed in the oil. When treated with acetone the oil dissolved leaving crystals behind. A second crop of crystals separated from the oil which remained when the acetone was removed from the mother liquor by evaporation. The first and second crystal fractions melted at 142–145°. Soluble in hot acetone, in carbon tetrachloride and in alcohol but insoluble in mineral acids and in alkali with which a black, gummy oil was formed.

Anal. Calcd. for $C_{12}H_3OCl_7$: Cl, 60.36. Found: Cl, 59.43.

Two more crops of crystals separated from the red oil remaining from the preparation already described. The m. p. of the last two fractions was 115–118°. A mixed melting point with the supposed heptachloro derivative gave 115° or a drop of about 30° from the higher melting point. The analysis for chlorine indicated that the pentachloro derivative was contaminated by a small percentage of the heptachloro compound. This substance like the heptachloro is insoluble in alkali.

Anal. Calcd. for $C_{12}H_5OCl_5$: Cl, 51.87. Found: Cl, 52.87.

Derivatives of the Phenols Mentioned in this Paper.—A large number of derivatives of the chloro and nitro phenols already mentioned were obtained in connection with this work. Since the methods used are either self evident or will be found by reference to the preceding paper,[5] this portion of the investigation has been summarized in the table.

Summary

1. The orientation of chlorine atoms in mono and dichloro-4-hydroxydiphenyl has been partially substantiated by the preparation of isomeric dichloronitro derivatives of 4-hydroxydiphenyl.
2. Penta- and heptachloro derivatives of 4-hydroxydiphenyl are described. Investigation into the structure of these polychlorinated hydroxydiphenyls is proceeding in this Laboratory.
3. Numerous new derivatives of 4-hydroxydiphenyl have been reported.

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(5) Colbert and others, THIS JOURNAL, **56**, 202 (1934).

NORMAN, OKLAHOMA RECEIVED JULY 3, 1934

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WASHINGTON UNIVERSITY]

The Photolysis of Halogenated Anthrahydroquinones

BY ALBERT E. GOLDSTEIN WITH JOHN H. GARDNER

It was observed by Weber[1] that when textiles which had been dipped in solutions of the leuco vats of certain halogen-containing anthraquinone and indigoid dyes were exposed to sunlight before oxidation, the resulting dyes were off-color. He regarded this as due to a dehalogenation since the color produced in each case corresponded to that of the corresponding halogen-free dye. Assuming Weber's explanation to be correct, this suggests a method for the removal of halogen from compounds of the anthraquinone series. The results of this investigation show that this method is practical in a number of cases and give some idea of the relation between the position of the halogen and its rate of removal. The compounds studied were 1- and 2-chloro-, 1- and 2-bromo and 1-chloro-4-hydroxyanthraquinone.

Preliminary experiments on solutions of 1-chloroanthrahydroquinone using a small mercury arc lamp with quartz and glass vessels indicated that the effect is due to visible light rather than to ultraviolet. Consequently, the mercury arc was replaced with an Eastman "Floodlight" (500-watt) to provide an intense source of white light. Solutions of the anthrahydroquinones in

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(1) Weber, *Dyestuffs*, **33**, 1 (1933).