[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF TEXAS]

The Halogenation of Certain Esters in the Biphenyl Series. I. The Chlorination of 4-Phenylphenyl Acetate[1]

BY CORA MAY SEGURA SAVOY[2] AND JOHN LEO ABERNETHY

A recent review[3] on the relationship of bactericidal activity to structure of substituted phenols suggested the need for a more direct method of preparation of the 4-(4-halophenyl)-phenols. The bactericidal activity of these substances has not been studied. This paper presents a procedure for direct introduction of chlorine into the desired position of the biphenyl nucleus, namely, the 4'-position, when the 4-position contains an acetyloxy group.

It has been shown that bromination of 4-phenylphenylbenzenesulfonate[4] and 4-phenylphenylbenzoate[5] introduces bromine into the 4'-position of the biphenyl nucleus. Hydrolysis of these brominated esters yields 4-(4-bromophenyl)-phenol. On the other hand, bromination of 4-phenylphenyl acetate[6] introduces bromine in an ortho position to the acetyloxy group, and hydrolysis of this ester yields 2-bromo-4-phenylphenol. This difference has been attributed to the difference in sizes of the groups. Thus, the benzenesulfonyloxy and benzoyloxy groups, being much larger than the acetyloxy group, exhibit greater steric hindrance to bromine. Therefore, bromine is shifted to the 4'-position of the biphenyl nucleus in the case of the larger groups, whereas it enters the 3-position in case of the smaller group.

On the basis of these results it was anticipated that chlorination of 4-phenylphenyl acetate would result in an introduction of chlorine in an ortho position to the acetyloxy group. Such was not found to occur. In contrast to bromination, the halogen in this instance entered the 4'-position. This is indeed surprising, if steric hindrance is the predominant factor, in view of the fact that the chlorine atom is considerably smaller than the bromine atom and presumably less steric hindrance should exist to entrance ortho to the acetyloxy group.

4-Phenylphenyl acetate (II) was prepared from 4-phenylphenol (I) by the method of Kaiser.[7] Chlorination of II in the presence of iodine catalyst gave rise to 4-(4-chlorophenyl)-phenylacetate (III). Hydrolysis of this ester took place readily to give a good yield of the desired 4-(4-chlorophenyl)-phenol (IV). That the chlorine had entered the 4'-position was proved by an independent synthesis of IV.

Benzidine (VII) was converted to 4-(4-chlorophenyl)-aniline (VIII), by means of the Sandmeyer reaction, according to the method used by Täubner[8] as modified by van Alphen[9] for the corresponding iodo compound. Diazotization of VIII gave rise to IV. A mixed melting point of the chlorophenylphenol obtained from VII caused no depression. Furthermore, when the chlorophenylphenol obtained from benzidine was acetylated and a mixed melting point was taken with the chlorination product of II, no depression was noted. This is conclusive evidence that chlorination of II resulted in substitution in the 4'-position.

Previous to the independent synthesis of IV from benzidine, it was noted that the melting point (145–146°) of IV was somewhat close to the melting point (133.5–137°) of 4-(4-chlorophenyl)-2,6-dichlorophenol (XI) as obtained by Colbert, Meigs and Mackin.[10] A mixed melting point of these two substances showed them to be different.

During the course of this investigation it was desirable to prepare 2-chloro-4-phenylphenyl acetate (VI) as well as 4-(4-chlorophenyl)-2,6-dichlorophenyl acetate (XII). This was readily accomplished by acetylation of V and XI, respectively, with acetic anhydride and sodium acetate.

Synthesis of 4-(4-chlorophenyl)-phenol leaves only the fluoro compound unsynthesized in this list of 4-(4-halophenyl)-phenols. The corresponding bromo compound has been prepared from 4-phenylphenyl benzenesulfonate[4] and 4-phenylphenylbenzoate[5] as well as from 4-nitro-4'-bromobiphenyl.[11] The iodo compound has been prepared from benzidine.[9]

(1) From a portion of a thesis to be submitted by Mrs. Savoy to the Graduate Faculty of the University of Texas in partial fulfillment of the requirements for the degree of Master of Arts.

(2) Present address: Department of Chemistry. Southwestern Louisiana Institute, Lafayette. Louisiana.

(3) Suter, Chem. Rev., 28, 269 (1941).

(4) Hazlet, THIS JOURNAL, 59, 1087 (1937).

(5) Hazlet, Alliger and Tiede, ibid., 61, 1447 (1939).

(6) Hazlet and Kornberg, ibid., 61, 3037 (1939).

(7) Kaiser, Ann., 257, 95 (1890).

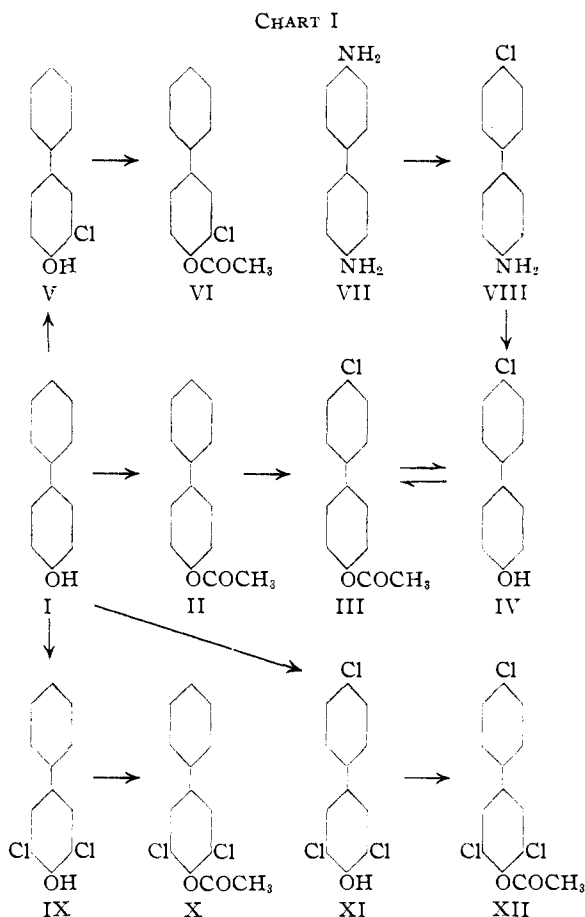(8) Taûbner, Ber., 27, 2627 (1894).

(9) van Alphen, Rec. trav. chim., 50, 1112 (1931).

(10) Colbert, Meigs and Mackin, THIS JOURNAL, 56, 202 (1934)

(11) Bell and Robinson. J. Chem. Soc., 1127 (1927).

The essential reactions of this investigation are correlated in Chart I.

CHART I

Experimental Part

4-(4-Chlorophenyl)-phenyl Acetate (III).—Twenty grams of 4-phenylphenyl acetate, prepared in quantitative yield from 4-phenylphenol,[6] was suspended in 100 cc. of carbon tetrachloride. A trace of iodine was added, and a solution of 7.4 g. (10% excess) of chlorine in 75 cc. of carbon tetrachloride was then added, drop by drop, over a period of two hours. The reaction mixture was stirred during this period and for an additional two hours. When the solvent was removed by distillation under reduced pressure, the crude product crystallized out. After two recrystallizations from methanol, the product, obtained as white plates in 47% yield, melted at 113°. This compound has also been recrystallized from ethanol in approximately the same yield.

An attempt to chlorinate 4-phenylphenyl acetate in sunlight without the use of iodine gave only the original ester.

Anal. Calcd. for $C_{14}H_{11}O_2Cl$: Cl, 14.39. Found: Cl, 14.10, 14.22.

Hydrolysis of 4-(4-Chlorophenyl)-phenyl Acetate.—Five grams of the ester (III) was suspended in a solution of 50 cc. of water, 50 cc. of ethanol, and 5 g. of potassium hydroxide, and refluxed for five minutes; the reaction

mixture was allowed to cool and poured into twice its volume of water. The clear solution obtained was acidified, and the white precipitate which formed was filtered and washed with water. The product, which was obtained in nearly quantitative yield, melted at 145–146°. (This was identified as 4-(4-chlorophenyl)-phenol by synthesis from benzidine.) Acetylation of the 4-(4-chlorophenyl)-phenol obtained by hydrolysis of III gave an ester which melted at 113° and which did not depress the melting point of III.

Anal. Calcd. for $C_{12}H_9OCl$: Cl, 17.34. Found: Cl, 17.11, 17.19.

4-(4-Chlorophenyl)-phenol (IV).—Twelve and one-half grams of benzidine was suspended in a dilute solution of hydrochloric acid, cooled, and allowed to react with a solution containing 10 g. of sodium nitrite. An additional 12.5 g. of benzidine was added to the reaction mixture, and the liquid was kept in the ice-box for three days.[8] A cold solution of 10% cuprous chloride in hydrochloric acid was then added. The mixture was allowed to come to room temperature, after which it was heated at 60° for two hours.

The 4-(4-chlorophenyl)-aniline hydrochloride which separated as a brown solid was filtered and washed with water. This product was suspended in a dilute solution of hydrochloric acid, cooled, and allowed to react with a solution containing 10 g. of sodium nitrite. After two hours, the mixture was heated to 60° and kept at this temperature for one hour. A dark brown tarry material separated; the product was extracted from this tar with boiling water. After three recrystallizations from chloroform and petroleum ether, the purified product (IV), obtained in 4% yield on the basis of the benzidine used, melted at 145.5°. A mixture of this compound and the chlorophenylphenol obtained from the hydrolysis of 4-(4-chlorophenyl)-phenyl acetate melted at 146°. Acetylation of 4-(4-chlorophenyl)-phenol obtained from benzidine gave an ester which, after recrystallization from ethanol, melted at 113° and did not depress the melting point of the ester prepared by the chlorination of II.

Anal. Calcd. for $C_{12}H_9OCl$: Cl, 17.34. Found: Cl, 17.21, 17.30.

2-Chloro-4-phenylphenyl Acetate (VI).—A mixture of three grams of 2-chloro-4-phenylphenol[10] and one-fourth molecular proportion of anhydrous sodium acetate was gently refluxed for ten minutes in an excess of acetic anhydride. The reaction mixture was allowed to cool and poured into five volumes of water. The ester was collected by filtration and twice recrystallized from ethanol. The white needles obtained in 92% yield melted at 68°.

Anal. Calcd. for $C_{12}H_9OCl$: Cl, 14.39. Found: Cl, 14.17, 14.22.

2,6-Dichloro-4-phenylphenyl Acetate (X).—A mixture of three grams of 2,6-dichloro-4-phenylphenol[10] and one-fourth molecular proportion of anhydrous sodium acetate was refluxed gently for ten minutes in an excess of acetic anhydride. The reaction mixture was allowed to cool and poured into five volumes of water. The ester was collected by filtration in quantities representing a quantitative yield. Two recrystallizations from ethanol reduced the yield of 73%. The white rhombic crystals melted at 64°.

Anal. Calcd. for $C_{14}H_{11}O_2Cl$: Cl, 25.24. Found: Cl, 25.08, 25.16.

4-(4-Chlorophenyl)-2,6-dichlorophenol (XI).—The impure 4-(4-chlorophenyl)-2,6-dichlorophenol was prepared according to the method of Colbert, Meigs and Mackin.[10] This was crystallized several times from carbon tetrachloride, thus yielding the pure compound with a constant melting point of 144°. (A 9% yield was obtained.) When a melting point was taken on a mixture of this compound with the chlorophenylphenol obtained from III it was lowered to 120°.

4-(4-Chlorophenyl)-2,6-dichlorophenyl Acetate (XII).—This product was obtained by acetylating 2,6,4'-trichlorophenylphenol in the same manner used to prepare VI and X. After two recrystallizations from ethanol, the product was obtained as white needles which melted at 79.5°, in a yield of 75%.

Anal. Calcd. for $C_{14}H_9O_2Cl_3$: Cl, 33.72. Found: Cl, 33.50, 33.57.

Acknowledgment.—The writers wish to express their appreciation for the helpful suggestions of Mr. Harry Kornberg during the progress of this investigation and for the assistance of Mr. T. R. Thompson in the analyses of the compounds.

Summary

1. Chlorination of 4-phenylphenyl acetate in the presence of iodine catalyst gave rise to 4-(4-chlorophenyl)-phenyl acetate. Hydrolysis of this ester gave a quantitative yield of 4-(4-chlorophenyl)-phenol. Proof of the structure of 4-(4-chlorophenyl)-phenol was given by an independent synthesis of this compound from benzidine.

2. Purification of 4-(4-chlorophenyl)-2,6-dichlorophenol to a constant melting point (144°) was accomplished by several recrystallizations of the impure substance (m. p. 135.5–137°) previously reported. The acetates of 4-(4-chlorophenyl)-phenol, 2-chloro-4-phenylphenol, 2,6-dichloro-4-phenylphenol and 2,6-dichloro-4-(4-chlorophenyl)-phenol were prepared in good yield.

AUSTIN, TEXAS   RECEIVED MAY 5, 1942

A Method for the Synthesis of Certain 2-Substituted Phenanthrenes

BY BYRON RIEGEL, MARVIN H. GOLD[1] AND MICHAEL A. KUBICO

A good general method for the preparation of a number of 2-acyl and amino phenanthrenes was required for the synthesis of polynuclear hydrocarbon derivatives. A few such derivatives have been prepared from phenanthrene, but in low yields because the orientation for substitution is chiefly to the 3-position. Not only are the yields low but the separation is quite often difficult.

By the use of the Friedel–Crafts reaction on phenanthrene a 15% yield of the 2-acetylphenanthrene has been obtained. The major product of this reaction[2] was a 65% yield of the 3-acetylphenanthrene. It is possible to separate readily the 2-acetyl derivative because it has the higher melting point and is less soluble. Using the same method, the 2-propionylphenanthrene could be isolated only in an 8% yield,[3] while with succinic anhydride no 2-succinoylated phenanthrene could be isolated.[4] When there is no particular need for the 3-acylphenanthrenes such reactions constitute an unnecessary waste of laboriously purified phenanthrene.

It has been shown that the 2-position is exclusively involved in the substitution reactions[5] of 9,10-dihydrophenanthrene. The reactions with 9,10-dihydrophenanthrene are not accompanied by the usual resinous products encountered with phenanthrene. We have found that 2-acyl-9,10-dihydrophenanthrenes could be easily dehydrogenated by means of sulfur. Although this method requires three steps in contrast to one step by the older method, they are all readily performed in over-all yields as listed in Table I. The amino

TABLE I

2-Substituted phenanthrene	Over-all yield, %
Acetyl	53
Propionyl	45
Isobutyryl	48
Methoxysuccinyl	70
Amino	25

derivative was made in four steps from phenanthrene, through the 2-amino-9,10-dihydrophe-

(1) Anna Fuller Fund Research Associate.

(2) E. Mosettig and J. van de Kamp, THIS JOURNAL, **52**, 3704 (1930); **54**, 3328 (1932).

(3) W. E. Bachmann and W. S. Struve, *ibid.*, **58**, 1659 (1936).

(4) R. D. Haworth and C. R. Mavin, *J. Chem. Soc.*, 1012 (1933).

(5) A. Burger and E. Mosettig, THIS JOURNAL, **58**, 1857 (1936), **59**, 1302 (1937).