Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.4; H, 6.0. Found: C, 83.16; H, 6.09.

The third fraction was an amber-colored glass which did not crystallize. Reaction with excess chloroacetic acid in aqueous alkali gave an oily acid which was converted into its insoluble silver salt by adding silver nitrate to an aqueous solution of the ammonium salt.

Anal. Calcd. for $C_{25}H_{20}O_6Ag_2$: Ag, 34.0. Found: Ag, 34.3.

Analysis of the diphenol itself confirmed the formula indicated by the silver salt.

Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.4; H, 6.0. Found: C, 83.3; H, 6.1.

The methyl ether, prepared by alkylation with methyl sulfate in alkali, b. p. 200–210° (3 mm.), reacted with benzene and aluminum chloride upon refluxing. The products were anisole and an oil, b. p. 157–165° (4 mm.), probably an impure 3-phenylindene.

Reaction of 2-Methyl-5*a*,10*b*-dihydro-6-benz[*b*]indeno-[1,2,*d*]-furan with Benzene and Aluminum Chloride.—To 125 cc. of dry benzene was added 7 g. of the ether obtained from *p*-cresol and indene chloride. The solution was cooled, 20 g. of aluminum chloride was added and the mixture was refluxed for three hours. After hydrolysis with cold dilute acid extraction of the benzene layer gave a good yield of *p*-cresol, identified as the benzoate, m. p. 69–70°. Fractionation of the alkali insoluble portion gave 2.1 g. of 3-phenylindene,[12] b. p. 148–150° (3 mm.), $n^{24}D$ 1.6313, d^{27}_4 1.083. Using less than one equivalent of aluminum chloride instead of an excess gave substantially the same results.

In the case of the ether obtained from indene chloride and *p*-chlorophenol an 80–85% yield of *p*-chlorophenol was isolated when either benzene or toluene was used with the aluminum chloride. Phenol and *m*-cresol together with the phenylindene were obtained by treatment of the corresponding ethers with benzene and aluminum chloride.

After refluxing the ether from *p*-chlorophenol with hydriodic acid for thirty hours, or heating with the same reagent in a sealed tube at 225° for four hours most of the starting material was recovered unchanged.

(12) Von Braun, *Ber.*, **62B**, 1059 (1929).

Summary

1. Indene chloride reacts rapidly with phenol and its simple derivatives with loss of two molecules of hydrogen chloride.

2. One of the compounds formed in each case is an ether which is probably a derivative of a benzindenofuran. The major part of the reaction product is, however, phenolic in character.

3. A reaction mechanism is suggested that explains the formation of most of the compounds isolated.

EVANSTON, ILLINOIS RECEIVED APRIL 7, 1938

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Synthesis of 5-Chloro-10-methyl-1,2-benzanthracene and Related Compounds

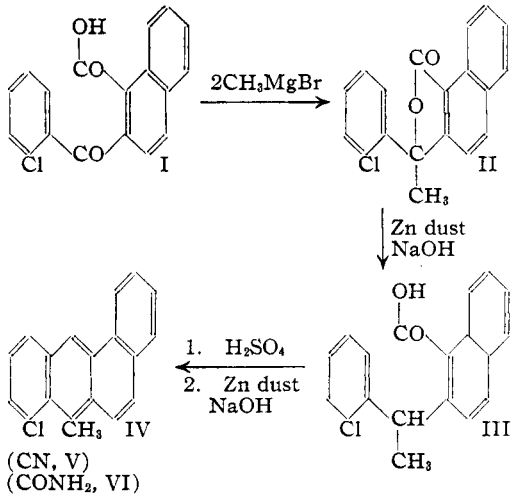
BY MELVIN S. NEWMAN

The synthesis of 7-chloro-10-methyl-1,2-benzanthracene and the corresponding 7-cyano, 7-carboxy, and carbomethoxy derivatives has recently been described.[1] These compounds were prepared in order that a study might be made of the effect of certain functional groups on the carcinogenic activity of 10-methyl-1,2-benzanthracene. It seemed advisable to prepare similar series of compounds in which the functional groups were attached at other positions of the nucleus in order to determine to what extent the positions occupied by the various functional groups affect the carcinogenicity of the resulting compounds. In this report the preparation of 5-chloro- and 5-cyano-10-methyl-1,2-benzanthracene and of the amide of 5-carboxy-10-methyl-1,2-benzanthracene is described.[2]

The method of synthesis was similar to that employed in the case of the isomeric 7-substituted compounds.[1] The Grignard reagent from 1-bromo-2-chlorobenzene (92% yield) was condensed with 1,2-naphthalic anhydride to produce a mixture of keto acids from which only the desired 2-*o*-chlorobenzoyl-1-naphthoic acid was isolated in a pure condition. The structure of this acid was proved by decarboxylation to *o*-chlorophenyl 2-naphthyl ketone. As this ketone proved difficult to crystallize, the comparison with authentic *o*-chlorophenyl 2-naphthyl ketone was effected through the crystalline 2,4-dinitrophenylhydrazone. The rest of the synthesis offered no particular difficulties and the entire scheme is indicated in the chart.

(1) Newman and Orchin, THIS JOURNAL, **60**, 586 (1938).

(2) It was originally intended to complete the series by the synthesis of the corresponding 5-carboxy and 5-carbomethoxy derivatives, but the unexpected difficulty encountered in the hydrolysis of the nitrile, resulting in the formation of the amide, blocked efforts in this direction. Further experiments on hydrolysis of the amide were not made owing to the small amounts of amide available and it did not seem advisable at this time to repeat the entire synthesis in order to complete this part of the program.



A recent report from Dr. Shear states that 5-cyano-10-methyl-1,2-benzanthracene produced tumors in 50% of the mice in three months and in 90% of the mice in four months, whereas 7-cyano-10-methyl-1,2-benzanthracene is much less active, tumors being produced in four of ten mice in eight months. The corresponding chloro derivatives proved inactive except for one tumor from the 7-compound after seven months.

Experimental[3]

2-*o*-Chlorobenzoyl-1-naphthoic Acid, I.—The filtered Grignard reagent (92% by titration) from 21.1 g. (0.11 mole) of 1-bromo-2-chlorobenzene in 100 cc. of ether was added all at once to a well-stirred solution of 19.8 g. (0.1 mole) of 1,2-naphthalic anhydride in 400 cc. of thiophene-free benzene and 100 cc. of ether. A yellow complex separated immediately. After refluxing for one hour the mixture was treated with dilute hydrochloric acid and the reaction products separated into acid and neutral fractions. By fractional crystallization from acetic acid and from alcohol there was obtained 13.3 g. (43%) of the desired keto acid with a melting range of 200.8–202.0°. A sample for analysis, recrystallized from alcohol, melted at 202.0–202.8°.

Anal.[a] Calcd. for $C_{18}H_{11}O_3Cl$: C, 69.57; H, 3.57. Found: C, 69.30; H, 3.74.

Proof of Structure of I.—The keto acid I was decarboxylated[4] and gave a ketone which was difficult to crystallize. The 2,4-dinitrophenylhydrazone was prepared as in a previous case.[1] It formed bright orange needles, m. p. 265.2–266.2°, when crystallized from pyridine–alcohol. The melting point was not depressed when mixed with an authentic sample of the 2,4-dinitrophenylhydrazone of 2-*o*-chlorophenyl 2-naphthyl ketone.

The 2,4-Dinitrophenylhydrazone of *o*-Chlorophenyl 2-Naphthyl Ketone.—The ketone was prepared essentially as before[1] using *o*-chlorophenylmagnesium bromide and 2-naphthonitrile. The 2,4-dinitrophenylhydrazone was prepared and melted, after recrystallization from pyridine–alcohol, at 265.6–266.2°.

Anal.[b] Calcd. for $C_{23}H_{15}O_4N_4Cl$: N, 12.54: Found: N, 12.27.

Lactone of 2-(*o*-Chloro-α-hydroxy-α-methylbenzyl)-1-naphthoic Acid, II.—To a warm solution of 6.21 g. (0.02 mole) of I in 300 cc. of benzene and 100 cc. of ether there was added slowly 20 cc. of 0.214 *M* methylmagnesium bromide in ether. A bright yellow complex separated until about one-half of the reagent had been added. As more was added the reaction mixture took on a greenish tinge and the insoluble complex began to disappear, a clear yellow solution resulting one hour after all of the Grignard reagent had been added. After four hours of refluxing the reaction mixture was decomposed by adding dilute hydrochloric acid and there was obtained from the neutral portion 4.86 g. (79%) of the lactone III, m. p. 120.8–121.4°. A portion for analysis, recrystallized from alcohol, melted at 122.0–122.6°.

Anal.[a] Calcd. for $C_{19}H_{13}O_2Cl$: C, 73.91; H, 4.24. Found: C, 73.51; H, 4.33.

2-(*o*-Chloro-α-methylbenzyl)-1-naphthoic Acid, III.—To a solution of 4.27 g. of the lactone II in 100 cc. of alcohol was added 10 cc. of aqueous 55% sodium hydroxide. The solution was refluxed for twenty-two hours, diluted with 50 cc. of water and the alcohol allowed to distil until copious foaming interfered. Then 10 g. of zinc dust (activated with copper sulfate), 50 cc. of water, and 20 cc. of 55% sodium hydroxide solution were added and the mixture refluxed for twenty-four hours. The zinc was removed by filtration and the crude acid precipitated from the filtrate by acidification. On crystallization from benzene–ligroin, 3.93 g. (91%) of acid melting at 168.0–168.8° was obtained.

Anal.[a] Calcd. for $C_{19}H_{15}O_2Cl$: C, 73.43; H, 4.87. Found: C, 73.14; H, 5.04.

5-Chloro-10-methyl-1,2-benzanthracene, IV.—One and one-half grams of III (finely powdered) was dissolved in 30 cc. of concentrated sulfuric acid at room temperature giving a clear orange solution. After standing for two and one-half hours the solution was poured on ice and the colorless anthrone which separated collected on an iced Büchner funnel and quickly transferred to a flask containing 5 g. of zinc dust (activated with copper sulfate), 100 cc. of water, and 20 cc. of 55% sodium hydroxide. This mixture was refluxed for seven hours. The cooled solution was acidified and the solids collected and dried. By extraction with acetone and benzene crystalline material was obtained. As this product did not have a sharp melting point, the desired 5-chloro-10-methyl-1,2-benzanthracene was isolated as a red picrate, m. p. 141.2–142.2°, in 62% yield. The recrystallized picrate melted at 141.8–142.4°. The final product, IV, freed from picric acid by chromatographic adsorption using activated alumina, crystallized from benzene–alcohol in almost colorless plates, m. p. 133.0–133.4°. When further purified by chromatographic adsorption, a small amount of absolutely colorless material having a brilliant blue-violet fluorescence in ultraviolet light was obtained. This product, which had the same

(3) All melting points corrected. Analyses marked (a) by M. Renoll, (b) by K. Eder, University of Chicago, and (c) by H. S. Clark.

(4) Dougherty, THIS JOURNAL, **50**, 571 (1928).

melting point and mixed melting point, crystallized in long slender needles. On attempted recrystallization from alcohol, the substance invariably came out as slightly yellow plates, characterized by a greenish fluorescence.

Anal.[c] Calcd. for $C_{26}H_{16}O_7N_3Cl$: N, 8.31. Found: N, 8.16. [b] Calcd. for $C_{19}H_{13}Cl$: Cl, 12.81. Found: Cl, 12.60, 12.68.

Two attempts were made to oxidize IV and obtain 5-chloro-1,2-benzanthraquinone. However, only a trace of a yellow crystalline material, m. p. 175–176°, was isolated and analysis showed that this was not the desired compound.

5-Cyano-10-methyl-1,2-benzanthracene, V.—The conversion of IV into a nitrile by heating with cuprous cyanide in pyridine gave variable results. In the best experiment, 0.51 g. of IV, 0.50 g. of cuprous cyanide, and 1 cc. of pyridine were heated in a sealed tube at 260 ± 3° for forty-eight hours. The reaction mixture was worked up as in a similar case.[1] The nitrile V crystallized in shining yellow plates from benzene–alcohol and the yield of material melting at 182.8–183.2° was 0.21 g. or 43%. An additional quantity of V, m. p. 179–181°, raised the yield to 62%.

Anal.[c] Calcd. for $C_{20}H_{13}N$: N, 5.24. Found: N, 5.16.

The Amide of 5-Carboxy-10-methyl-1,2-benzanthracene, VI.—Various attempts at hydrolysis of the nitrile to the acid gave crystalline products obviously impure and melting over a wide range. In the best experiment, 0.229 g. of nitrile was dissolved in 20 cc. of hot acetic acid and 2 cc. of 65% sulfuric acid was added. This solution was refluxed for eleven hours, diluted with hot water, and allowed to stand overnight at 0°. The solids were collected and weighed 0.237 g. The melting point was fairly sharp at 303–305°, uncorr. On recrystallization from dioxane–alcohol or from acetic acid the amide was obtained as fine yellow needles with little loss in weight. The highest melting point was 308–310°, uncorr. Several other runs were made but rarely did the yield exceed 50%.

Anal.[c] Calcd. for $C_{20}H_{15}ON$: C, 84.18; H, 5.30; N, 4.91. Found: C, 84.21; H, 5.12; N, 5.07.

Summary

A rather general method for the synthesis of chloro derivatives of 10-methyl-1,2-benzanthracenes is illustrated by the synthesis of 5-chloro-10-methyl-1,2-benzanthracene. The method involves: reaction of *o*-chlorophenylmagnesium bromide with 1,2-naphthalic anhydride; addition of methylmagnesium bromide to the ketone group of the resulting 2-*o*-chlorobenzoyl-1-naphthoic acid; reduction of the resulting lactone to an acid; and cyclization and reduction to 5-chloro-10-methyl-1,2-benzanthracene. The conversion of this compound into the corresponding 5-cyano compound and into the amide of the 5-carboxy compound is also described.

COLUMBUS, OHIO RECEIVED APRIL 11, 1938

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

Arsenated Derivatives of Mixed Ketones. II. Arsenicals of Peonol

BY C. KENNETH BANKS[1] AND CLIFF S. HAMILTON

In a previous paper[2] it was shown that, although 2,4-dimethoxyacetophenone formed a stable arsonic acid, no stable arsenic derivative of the unmethylated ketone was isolable. In an effort to retain a free hydroxyl group in the molecule, one of the monomethyl ethers of resacetophenone, 2-hydroxy-4-methoxyacetophenone,[3] peonol, was investigated.

Direct arsonation of the ketone with arsenic acid failed to give even a trace of an arsonic acid. In order to introduce the arsono group through the diazo reaction,[4] it was necessary to prepare the amine of the ketone. Adams[5] obtained a mononitropeonol in low yields but did not prove the structure of the compound. Baker[6] prepared the same compound in 60% yields and proved it to be 2-hydroxy-4-methoxy-5-nitroacetophenone. By a modification of the nitration process of Omer and Hamilton,[2] 80% yields of this nitro compound were obtained.

The corresponding amine was also isolated by Adams with difficulty. By using Raney catalyst,[7] nitropeonol was reduced quantitatively to the amine in an acetone solution with molecular hydrogen. After removing the catalyst, the free amine could be isolated by evaporation of the solvent in an inert atmosphere. As the amine was unstable, it was generally isolated as the stable hydrochloride.

Arsonation of the amine hydrochloride proceeded smoothly, giving good yields of 2-hydroxy-4-methoxy-5-arsonoacetophenone. This product was then reduced to 2-methoxy-4-hydroxy-5-

(1) Parke, Davis and Company Fellow.
(2) Omer and Hamilton, THIS JOURNAL, **59**, 642 (1937).
(3) Hoesch, *Ber.*, **48**, 1122 (1915).
(4) Bart, *Ann.*, **429**, 55 (1922).
(5) Adams, THIS JOURNAL, **41**, 247 (1919).
(6) Baker, *J. Chem. Soc.*, 1684 (1934).
(7) Raney, U. S. Patent 1,638,190 (1927).