Rearrangement of Tetramethylethylene Bromohydrin by Chemical Reagents.—Portions of a solution of bromohydrin in absolute ether were treated with aqueous solutions of (1) silver nitrate and (2) sodium thiosulfate and (3) an aqueous suspension of silver oxide. After treatments (1) and (3) gave precipitates of silver bromide, excess sodium chloride solution was added and the precipitates were removed by filtration. In treatment (2) the ether was decanted from the turbid aqueous layer. All three then gave copious precipitates with Nessler's solution. A fourth sample, untreated otherwise, gave no precipitate with this reagent, nor did an aqueous solution of pinacol hydrate, which had been previously treated, as above, with silver nitrate and sodium chloride.

Summary

1. Depending on the reaction conditions, the action of gaseous hydrogen bromide on anhydrous pinacol leads to tetramethylethylene bromohydrin, tetramethylethylene dibromide, pinacol hydrobromide or dipinacol hydrobromide. Pinacol hydrobromide is the intermediate in bromohydrin formation, as well as the postulated intermediate in the hydrobromic acid-catalyzed rearrangement of pinacol to pinacolone.

2. Tetramethylethylene bromohydrin rearranges to pinacolone on heating or on treatment, at room temperature, with halide abstracting reagents. This lends support to the Stieglitz mechanism of the pinacol–pinacolone rearrangement.

CHICAGO, ILLINOIS RECEIVED JULY 13, 1938

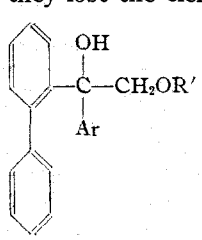
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

Synthesis of Phenanthrene Derivatives. I. 9-Phenyl- and 9-*p*-Tolylphenanthrene

BY CHARLES K. BRADSHER AND ALLAN K. SCHNEIDER

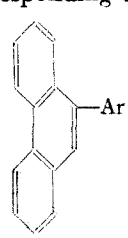
With the exception of the elaborate Pschorr[1] synthesis, all of the methods usually employed for the synthesis of phenanthrene derivatives have a common disadvantage. They involve one step in which hydrophenanthrenes are dehydrogenated at high temperatures by the action of sulfur, selenium or platinum. Frequently a desired phenanthrene derivative is incapable of surviving such a treatment, and it was in the hope of providing a means for the synthesis of such derivatives that this research was undertaken.

A new cyclization reaction has been discovered giving promise of accomplishing this end. When compounds of type I were treated with mineral acids they lost the elements corresponding to one



I

($R' = CH_3$ or C_6H_5)

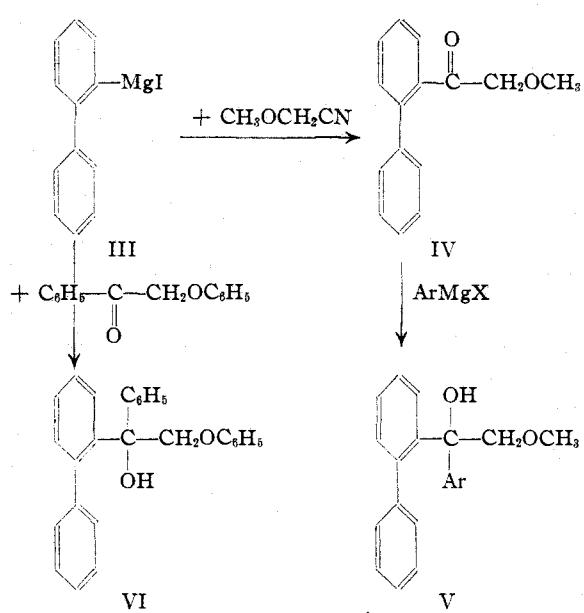


II

molecule of water and one molecule of methyl alcohol or phenol to form the corresponding 9-arylphenanthrene (II).

The carbinols used were prepared by two methods.

(1) Pschorr, *Ber.*, **29**, 496 (1896).



III IV V VI

In the first, 2-xenylmagnesium iodide (III) was treated with methoxyacetonitrile. Upon hydrolysis the reaction product gave 2-(ω-methoxyaceto)-biphenyl (IV). This upon treatment with phenyl- or *p*-tolylmagnesium bromide gave the corresponding carbinol (V).

In the second method, ω-phenoxyacetophenone was treated with 2-xenylmagnesium iodide (III) to form 1-phenyl-1-(2-xenyl)-2-phenoxyethanol-1 (VI).

When treated with concentrated sulfuric acid

the methoxyethanols (V) underwent cyclization to give the corresponding hydrocarbons, 9-phenyl- and 9-*p*-tolylphenanthrene. The phenoxyethanol (VI) lost only the elements of water when treated with concentrated sulfuric acid. The structure of this new compound has not been determined. When VI was refluxed for twenty-two hours with constant-boiling hydrobromic acid, 9-phenylphenanthrene was obtained in good yield. This hydrocarbon has been prepared previously by Koelsch,[2] by Bergmann[3] and by Weizmann.[4] The 9-*p*-tolylphenanthrene is a new hydrocarbon and was found to melt slightly lower than the corresponding phenyl compound.

Further work is in progress on the development of this synthesis.

The authors are indebted to the Monsanto Chemical Company for a gift of 2-aminobiphenyl.

Experimental

2-(ω-Methoxy)-acetobiphenyl (IV).—A Grignard reagent was prepared in an atmosphere of nitrogen by the action of 2.7 g. of magnesium turnings on 28 g. of 2-iodobiphenyl[5] in 100 cc. of anhydrous ether. When the formation of the reagent was complete, about two-thirds of the ether was distilled from the reaction mixture. A solution of 7.1 g. of methoxyacetonitrile[6] in 100 cc. of dry benzene was added and the mixture refluxed for fifteen hours. At the conclusion of this period the magnesium salt was decomposed by the addition of a mixture of ammonium hydroxide and ammonium chloride solution. The ether–benzene layer was separated and extracted with 0.1 *N* hydrochloric acid. Concentrated hydrochloric acid was then added and the mixture refluxed for two hours. The ketone was taken up in ether, dried and distilled. The product was a slightly yellow oil, b. p. 159–162° (4 mm.); yield, 13.3 g. (60%).

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.61; H, 6.24. Found: C, 79.92; H, 6.35.

1-Phenyl-1-(2-biphenyl)-2-methoxyethanol-1 (V).—A solution of 4 g. (0.018 mole) of 2-(ω-methoxy)-acetobiphenyl in 20 cc. of dry ether was added to 0.03 mole of phenylmagnesium bromide and the mixture refluxed for thirty minutes. A solution of ammonium chloride was then added and the ether layer separated and dried. After removal of the ether under reduced pressure there remained about 3 cc. of a red-brown oil. No effort was made to purify this material further.

9-Phenylphenanthrene.—Approximately 0.75 cc. of the above carbinol was dissolved at room temperature in 5 cc. of concentrated sulfuric acid. After thirty minutes the dark brown sirup was poured on 25 g. of ice. The hydrocarbon was extracted with ether and isolated by vacuum sublimation. A small amount of a white substance was obtained which, twice recrystallized, melted at 104–105°.

Anal. Calcd. for $C_{20}H_{14}$: C, 94.49; H, 5.51. Found: C, 94.24; H, 5.59.

The picrate crystallized as orange-red needles, m. p. 114°. It decomposed on attempted recrystallization. Upon decomposition of the picrate in ether with dilute ammonium hydroxide the hydrocarbon was recovered; m. p. 104–105°.

1-*p*-Tolyl-1-(2-biphenyl)-2-methoxyethanol-1 was made in the same manner as the corresponding phenylcarbinol, using *p*-tolylmagnesium bromide. The resulting light brown oil was not purified.

9-*p*-Tolylphenanthrene.—Three cubic centimeters of the oil obtained above was mixed with 8 cc. of concentrated sulfuric acid and allowed to stand for thirty minutes. The remainder of the procedure was identical with that used for the preparation of the phenylphenanthrene. Large, rhombic, transparent crystals were obtained from ether–petroleum ether, m. p. 90–91°.

Anal. Calcd. for $C_{12}H_{16}$: C, 94.03; H, 5.97. Found: C, 94.14; H, 6.06.

A picrate was made in the usual manner. Fine orange-red needles precipitated after an hour in an ice–salt bath. These melted at 126–127°.

1-Phenyl-1-(2-biphenyl)-2-phenoxyethanol-1 (VI).—A Grignard reagent was prepared from 20 g. of 2-iodobiphenyl. To this was added a solution of 15.2 g. of ω-phenoxyacetophenone[7] in 50 cc. of dry benzene. The mixture was refluxed for one hour and then decomposed with a 20% solution of ammonium chloride. After removal of the solvents under reduced pressure the carbinol was crystallized from ether–petroleum ether. Irregular white crystals, m. p. 93–95°, were obtained. The yield was 17.1 g. (65% of the theoretical). An analytical sample prepared by repeated crystallization melted at 94–95°.

Anal. Calcd. for $C_{26}H_{22}O_2$: C, 85.24; H, 6.01. Found: C, 85.06; H, 6.10.

Reaction of VI with Sulfuric Acid.—One gram of the above carbinol was suspended in 7 cc. of concentrated sulfuric acid and the mixture heated at about 100° until the oil formed at first had resolidified. The mixture was poured on ice and the product collected and crystallized from acetic acid as white prisms with m. p. 148–149°. The yield was 0.3 g. Twice recrystallized the product melted at 150–152°.

Anal. Calcd. for $C_{26}H_{20}O$: C, 89.65; H, 5.75. Found: C, 89.54; H, 5.96.

Cyclization of VI with Hydrobromic Acid.—To a boiling solution of 3.4 g. of VI in 20 cc. of acetic acid, 10 cc. of constant boiling hydrobromic acid was added. The mixture was refluxed for twenty hours, poured into water and taken up in ether. The phenol was extracted with dilute alkali and the ethereal solution evaporated. The residue, once recrystallized from ethyl alcohol, melted at 103–104° and was shown to be **9-phenylphenanthrene** by a mixed melting point determination; yield, 2 g. (84%).

(2) Koelsch, THIS JOURNAL, **56**, 480 (1934).
(3) Bergmann and Bergmann, *ibid.*, **59**, 1443 (1937).
(4) Weizmann, Bergmann and Berlin, *ibid.*, **60**, 1331 (1938).
(5) Cook, *J. Chem. Soc.*, 1087 (1930).
(6) Scarrow and Allen, *Org. Syntheses*, **18**, 56 (1938).
(7) Möhlau, *Ber.*, **15**, 2497 (1882).

Summary

Two phenanthrene hydrocarbons, 9-phenyl- and 9-*p*-tolylphenanthrene, have been prepared from 2-iodobiphenyl by a synthesis involving a new type of ring closure.

URBANA, ILLINOIS RECEIVED SEPTEMBER 26, 1938

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

Studies in the Phenanthrene Series. XXII. Derivatives of Dibenzisoquinoline and Naphthisoquinoline[1]

BY ERICH MOSETTIG AND EVERETTE L. MAY[2]

In previous communications from this Laboratory we described the synthesis of a number of hydrogenated and N-methylated benzofuroquinolines[3] and naphthoquinolines,[4] which we hoped might exhibit an analgesic effect because of their superficial structural similarity to morphine. These compounds, however, proved to be either very weak analgesics or were entirely ineffective.[5] Since morphine may be interpreted as an isoquinoline derivative, a higher analgesic effectiveness—within the series of tetracyclic compounds consisting of three isocyclic rings and one nitrogen-containing ring—may be expected of phenanthrene derivatives in which the nitrogen is located in β-position to one of the benzene nuclei, *i. e.*, of compounds that include in their structure the isoquinoline system.

Apparently, the most practicable methods for preparing isoquinoline derivatives are those in which compounds of the general type R—C—C—N— are employed as starting materials. In various attempts to prepare compounds of this type we found that the phenanthrene derivatives $C_{14}H_9$-$CHOCH_3CH_2NH_2$ (IV, V) were relatively easily accessible by the method of Rosenmund,[6] which was later somewhat modified by Mannich and coworkers.[7] We employed in the second step of this preparation—the reduction of the corresponding nitro ether—platinum oxide as catalyst successfully, and alcohol as solvent. Attempts to cyclize the formyl derivatives of IV and V and the benzoyl derivative of V, according to Mannich and coworkers,[7] in order to obtain isoquinoline derivatives, by simultaneous loss of water and methanol, were unsuccessful, in spite of manifold experimental variations in respect to solvent and condensing agent. The resulting reaction mixtures consisted of colored, tarry, or partly charred products.

Equally unsuccessful were the attempts to cyclize the formyl derivatives of the β-phenanthryl ethyl amines VII and VIII to dihydroisoquinoline derivatives by the Bischler–Napieralski method. Also in this series of experiments we employed many variations such as those devised by Pictet, by Decker, and by Späth.[8] After several practically unsuccessful attempts to prepare the ethylamine derivatives (VI, VII, VIII) by the Hofmann or Curtius degradation of β-phenanthrylpropionic acids,[9] we finally obtained these amines, according to the method of Slotta and Szyszka,[10] by electrolytic reduction of the corresponding nitrostyrene derivatives (I, II, III). The 3-derivative (VII) was also prepared by chlorination of 3-(2-amino-1-hydroxyethyl)-phenanthrene and subsequent catalytic dechlorination.

By cyclizing the formaldehyde condensation products of VI and VIII with dilute aqueous hydrochloric acid according to the method of Decker and Becker,[11] we obtained the expected tetrahydroisoquinoline derivatives (IX, X)[12] in satisfactory yields. The cyclization apparently proceeded in both series (2 and 9) only in one di-

(1) The work reported in this paper is part of a unification of effort by a number of agencies having responsibility for the solution of the problem of drug addiction. The organizations taking part are: The Rockefeller Foundation, the National Research Council, the U. S. Public Health Service, the U. S. Bureau of Narcotics, the University of Virginia, and the University of Michigan. Paper XXI. THIS JOURNAL, **60**, 2464 (1938).

(2) Mallinckrodt Research Fellow, 1937–1938, E. R. Squibb and Sons Research Fellow, 1938–.

(3) Mosettig and Robinson, THIS JOURNAL, **57**, 902 (1935).

(4) (a) Mosettig and Krueger, *ibid.*, **58**, 1311 (1936); (b) Continued in "Studies in the Phenanthrene Series, XIX," Mosettig and Krueger, *J. Org. Chem.*, in press.

(5) Eddy, *J. Pharmacol.*, **58**, 159 (1936), and unpublished results.

(6) Rosenmund, *Ber.*, **46**, 1034 (1913).

(7) Mannich and Walther, *Arch. Pharm.*, **265**, 1 (1927); Mannich and Falber, *ibid.*, **267**, 601 (1929).

(8) Bischler and Napieralski, *Ber.*, **26**, 1903 (1893); Pictet and Kay, *ibid.*, **42**, 1973 (1909); Decker, Kropp, Hayer and Becker, *Ann.*, **395**, 299 (1913); Späth, Berger and Kuntara, *Ber.*, **63**, 134 (1930).

(9) See van de Kamp, Burger and Mosettig, THIS JOURNAL, **60**, 1321 (1938).

(10) Slotta and Szyszka, *J. prakt. Chem.*, [2] **137**, 339 (1933).

(11) Decker and Becker, *Ann.*, **395**, 342 (1913).

(12) The orientation, numbering, and names of the heterocyclic compounds included in this paper have been recommended to us by Dr. Capell through the kindness of Dr. Crane. *Cf.* Patterson, THIS JOURNAL, **50**, 3083 (1928).