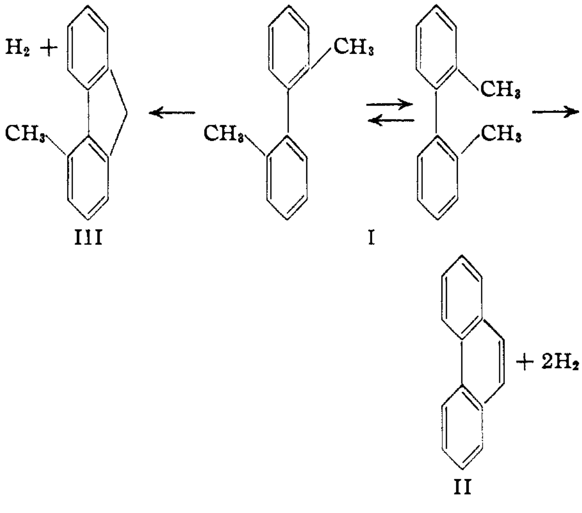
[Contribution from the Central Experiment Station, Bureau of Mines, Pittsburgh, Pennsylvania]

# Aromatic Cyclodehydrogenation. I. 4-Methylfluorene from 2,2'-Dimethylbiphenyl[1]

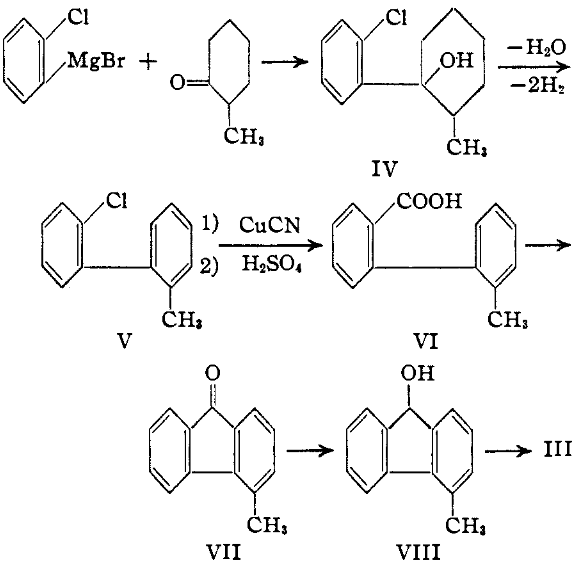
By Milton Orchin[2] and E. Oscar Woolfolk[2]

The products obtained by the hydrogenation or carbonization of coal are, in part, assumed to be present in the original coal structure and to arise from the catalytic or thermal "depolymerization" of coal.[3] We have been interested in the possibility that some of the condensed aromatic nuclei obtained from coal by these processes result from less highly cyclic structures by the thermal or catalytic intramolecular loss of hydrogen. Such transformations might occur by the loss of hydrogen from two suitably situated methyl groups[4] or from a methyl group and an aromatic nucleus. As applied to 2,2'-dimethylbiphenyl, the first compound we have studied, the cyclodehydrogenation could give either phenanthrene, II, or 4-methylfluorene, III.



We have found that when 2,2'-dimethylbiphenyl is passed over palladium charcoal at 450°, 4-methylfluorene, m. p. 71–72°, is produced. Since the properties of our hydrocarbon did not correspond to those reported[5] for 4-methylfluorene, we synthesized this compound by the method shown.

The synthetic 4-methylfluorene was identical with the hydrocarbon obtained from the vapor-phase cyclodehydrogenation of I. The ultraviolet absorption spectrum of III[6] showed maxima at 2660 Å., log $E$ 4.31 and 2960 Å., log $E$ 3.60 and minima at 2340 Å., log $E$ 3.40 and 2940 Å., log $E$ 3.53.



The fact that no phenanthrene was isolated from the cyclodehydrogenation of I is of interest. It has been shown[7] that the methyl groups of I are large enough to restrict somewhat the free rotation of the tolyl groups, but it is not to be expected that such a steric effect would be operative at elevated temperatures. Furthermore, Berger[4c] was able earlier to obtain a 50% yield of phenanthrene by heating 2,2'-dimethylbiphenyl with sulfur. Apparently the products from a dehydrogenation may depend upon whether the operation is in the liquid or vapor phase and whether the reaction is a pyrolysis, a catalytic reaction or a chemical reaction (with or without catalyst) involving an oxidation–reduction process.[8] The cyclodehydrogenation of other biphenyls and binaphthyls is now being studied.

## Experimental[9]

**2,2'-Dimethylbiphenyl, I,** was prepared from *o*-tolylmagnesium bromide according to the directions of Turner.[10] After several purifications by distillation *in vacuo* the compound had a freezing point of 18.3°, $n^{25}_{D}$ 1.5720.

The apparatus used for the cyclodehydrogenation was

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[3] Storch, Fisher, Hawk and Eisner, Bureau of Mines Technical Paper 654 (1943).

[4] Examples of this type of cyclodehydrogenation are contained in the following papers: (a) Meyer and Hofmann, *Monatsh.*, **37**, 712 (1916); (b) Weitzenboch, *ibid.*, **39**, 310 (1918); (c) Berger, *J. prakt. Chem.*, **133**, 339 (1932); (d) Newman, This Journal, **62**, 1683 (1940).

[5] Mascarelli and Angeletti, *Gazz. chim. ital.*, **68**, 29 (1938).

[6] We wish to thank the Coal Research Laboratory of Carnegie Institute of Technology for the generous use of their spectrophotometer.

[7] O'Shaughnessy and Rodebush, This Journal, **62**, 2906 (1940).

[8] Orchin, *ibid.*, **66**, 535 (1944).

[9] All melting points are corrected unless otherwise noted. Analyses by Dr. T. S. Ma, University of Chicago, unless otherwise noted.

[10] Turner, *J. Proc. Royal Soc. N. S. Wales*, **54**, 37 (1920).

constructed as follows. The heating element consisted of an iron pipe about 70 cm. long and 15 mm. inside diameter, covered well with asbestos and wrapped with 24 feet of no. 22 nichrome wire. The windings were covered with asbestos and the pipe placed inside a piece of glass tubing for insulation. The wattage input was controlled by an external resistance. The catalyst tube was made of 14 mm. Pyrex glass and fitted rather snugly into the heating element. The apparatus was mounted in a horizontal position with about a 20-degree downward slope. The sample was placed in a 60-cc. separatory funnel which was connected through a piece of rubber tubing to a vertical 2-mm. capillary tube. The capillary tube was bent at the end and made to extend 2 inches into the catalyst tube by means of an inner seal. A second piece of capillary tubing was sealed to the end of the catalyst tube below the inner seal. A slow stream of dry hydrogen was admitted past a safety trap through this second capillary tube. The hydrogen was kept flowing throughout the entire experiment. The top of the separatory funnel was connected by rubber tubing to the top of an 8-inch long empty vertical glass tube, the bottom of which was connected to a levelling bulb containing mercury. The sample was forced from the separatory funnel through the capillary and into the catalyst tube by means of the air pressure obtained by raising the levelling bulb. The rate of flow was controlled by manipulating the head of mercury and the opening in the stopcock of the funnel. The temperature was determined by calibrating one thermometer placed between the iron pipe and the insulating glass tube against a second thermometer placed inside the empty glass catalyst tube. The catalyst was prepared by shaking 5 g. of 30% palladium charcoal[11] with 9 g. of ignited asbestos and adding glass helices to this mixture. This catalyst was then packed loosely into the catalyst tube. The exit end of the tube was connected to a receiver.[12]

Twelve grams of I was passed over the catalyst bed at a rate of about 5–8 cc. per hour. After all the material was collected in the receiver it was returned to the separatory funnel and the procedure repeated. The material was passed over the catalyst five times. The product (10.5 g. $n^{25}$D 1.5968) was separated by chromatographic adsorption on activated alumina into a fluorescent (in ultraviolet light) and a non-fluorescent fraction. The non-fluorescent fraction (6.5 g.) was unchanged I. The fluorescent fraction gave 100 mg. of high molecular weight colored material, which was not investigated, and 2.75 g. of crystalline 4-methylfluorene, which after repeated crystallization from methanol had a melting point of 70.4–71.2°.

*Anal.* Calcd. for $C_{14}H_{12}$: C, 93.23; H, 6.77. Found: C, 93.02; H, 6.91.

The melting point was not depressed when mixed with synthetic 4-methylfluorene prepared as described below.

**Oxidation of 4-Methylfluorene.**—To 270 mg. of 4-methylfluorene obtained from I there was added 20 cc. of 1% sodium hydroxide solution and 0.7 g. of potassium permanganate. The mixture was stirred and heated at 70–80° for seven hours. A petroleum ether extract of the precipitate was passed over a tower of a mixture prepared from 1 part of activated alumina and 1 part of Super-Cel. The tower was extruded, the yellow layer separated and eluted with benzene. This fraction gave 0.130 g. of 4-methylfluorenone, yellow needles, m. p. 88–89.5°, no depression on admixture of synthetic 4-methylfluorenone prepared as described below. Refluxing III for three and a half hours in an acetic acid solution of sodium dichromate gave no oxidation.

**1-*o*-Chlorophenyl-2-methylcyclohexanol, IV.**—*o*-Chlorophenylmagnesium bromide was prepared from 100 g. of pure *o*-chlorobromobenzene, 13.2 g. magnesium and 350 cc. of dry ether. To this dark-colored Grignard solution there was added dropwise with stirring a solution of 56 g. of freshly distilled *o*-methylcyclohexanone in 100 cc. of dry ether. The solution was refluxed 3.5 hours, and decomposed with ammonium chloride solution. The organic layer gave 57 g. (51%) of crude carbinol, b. p. 119–25° (2–3 mm.). This was not further purified.

**2-Chloro-2′-methyl-3′,4′,5′,6′(or 2′,3′,4′,5′)-tetrahydrobiphenyl.**—A mixture of 56.8 g. of crude carbinol and 75 cc. of 90% formic acid was refluxed three hours. The dehydrated material was separated and distilled. The middle fraction had b. p. 93–94° (2–3 mm.) and weighed 44.4 g. (85%). It was a mobile water-white liquid. The chlorine analysis gave a low value. Fractional distillation *in vacuo* through an 18-inch packed column was ineffective in separating the impurity. A small portion of the material was treated with 2,4-dinitrophenylhydrazine but only unchanged hydrazine precipitated. The filtrate from the hydrazine reaction was passed through a tower of silica gel and the material in the first fractions to come through was recovered for analysis. *Anal.* (Parr bomb by M.O.). Calcd. for $C_{13}H_{15}Cl$: Cl, 17.15. Found: Cl, 17.06; $n^{25}$D 1.5486. No attempt was made to determine the location of the double bond in the olefin. The impurity in the crude material is conceivably the cyclohexylidenecyclohexanone, $C_{14}H_{22}O$, formed by the condensation of 2 moles of *o*-methylcyclohexanone in the manner in which cyclohexanone condenses with itself.[13]

**2-Chloro-2′-methylbiphenyl, V.**—To 10.7 g. of the crude tetrahydro compound above there was added 3.2 g. of sulfur. The mixture was heated at 200–240° for two and one-half hours, during which time 850 cc. of hydrogen sulfide was liberated (31%). The material was distilled at the water pump and 6.8 g. of distillate obtained. The distillate was purified by treatment with alumina and redistilled. The middle fraction, b. p. 103–106° (2–3 mm.), weighed 4.85 g. (46%) and had $n^{25}$D 1.588 and freezing point 17°. *Anal.* Calcd. for $C_{13}H_{11}Cl$: Cl, 17.48; C, 77.04; H, 5.49. Found: Cl, 16.73; C, 77.37; H, 5.45.

**2-Carboxy-2′-methylbiphenyl, VI.**—A mixture of 3.42 g. of V, 10 cc. of pyridine and 2.25 g. of cuprous cyanide was sealed in a glass tube and heated at 270° for fifty-five hours. The nitrile was separated in the usual manner[14] and distilled *in vacuo* to give 2.78 g. of distillate. This was hydrolyzed with sulfuric acid and the product separated into acidic and neutral fractions. The acid fraction gave 1.588 g. (44% on the two steps) of VI, m. p. 98.5–100.5°. The acid was extremely soluble in petroleum ether and methanol. After several recrystallizations from dilute methanol the sample for analysis had melting point 104.4–105.6°. *Anal.* Calcd. for $C_{14}H_{12}O_2$; C, 79.22; H, 5.67; neut. equiv., 212. Found: C, 79.50; H, 6.49; neut. equiv., 212. The benzene solution of the neutral fraction was concentrated and the residue heated *in vacuo* whereupon a few drops of oil distilled (discarded). The undistilled portion on crystallization from alcohol-water gave 0.180 g. of the **amide** of **2-carboxy-2′-methylbiphenyl,** colorless needles, m. p. 105–108°. The sample for analysis melted at 109.8–110.4°. *Anal.* Calcd. for $C_{14}H_{13}ON$; N, 6.33. Found: N, 6.40. The mother liquor gave an additional 0.185 g. of less pure amide.

**4-Methylfluorenone, VII.**—When 0.435 g. of VI was cyclized with sulfuric acid,[15] there was obtained 0.305 g. (77%) of VII, yellow needles, m. p. 90.6–91.4°. *Anal.* Calcd. for $C_{14}H_{10}O$: C, 86.57; H, 5.19. Found: C, 86.26; H, 5.20.

**4-Carboxyfluorenone.**—A mixture of 0.218 g. of VII, 0.36 g. potassium permanganate and 15 cc. of 1.5% sodium hydroxide solution was stirred with heating at 85–90° for eight and a half hours. A pinch of sodium bisulfite was added to destroy the excess permanganate and the mixture filtered. From the precipitate there was isolated 0.120 g. of unchanged VII. Acidification of the filtrate gave about 20 mg. of yellow crystals, m. p. 218–225° uncor. The melting point was not depressed when mixed with a sample of 4-carboxyfluorenone kindly supplied by Professor W. E. Bachmann.

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[11] Zelinsky and Turowa-Pollak, *Ber.*, **58**, 1295 (1925).

[12] We wish to thank Mr. Paul L. Golden for his helpful suggestions regarding the apparatus.

[13] Rapson, *J. Chem. Soc.*, 15 (1941).

[14] Newman and Orchin, THIS JOURNAL, **60**, 586 (1938); **61**, 244 (1939).

[15] Heilbron, Hey and Wilkinson, *J. Chem. Soc.*, 113 (1938).

**4-Methylfluorenol, VIII.**—A mixture of 0.445 g. of VII, 2 g. of zinc dust, 20 cc. of ethanol and 3 cc. of 28% ammonium hydroxide was refluxed for two and a half hours. The hot mixture was filtered and the filtrate poured onto ice. The precipitate, which contained some unchanged ketone, was dried and recrystallized from benzene-petroleum ether. The first crop gave 0.210 g. (47%) of colorless very fine needles, m. p. 160-162.5°, which when recrystallized from benzene had a melting point of 164.0-164.6°. *Anal.* Calcd. for $C_{14}H_{12}O$: C, 85.67; H, 6.16. Found: C, 84.78; H, 6.18. The mother liquor was chromatographed on a 1:1 mixture of alumina and Super-Cel. The yellow band on elution gave 0.085 g. of unchanged ketone, m.p. 90.5-91.5°. Longer refluxing with intermittent addition of ammonium hydroxide did not increase the yield.

**4-Methylfluorene, III.**—Reduction of 0.120 g. of VIII with red phosphorus and iodine[16] gave, after recrystallization from methanol-water, 0.055 g. (50%) of III, m. p. 71.5-72.5°

## Summary

When 2,2′-dimethylbiphenyl is repeatedly passed over a palladium-charcoal catalyst at 450° it is converted to 4-methylfluorene.

The synthesis of 4-methylfluorenone and its reduction to 4-methylfluorene are described.

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[16] Miller and Bachman, THIS JOURNAL, 57, 2448 (1935).

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

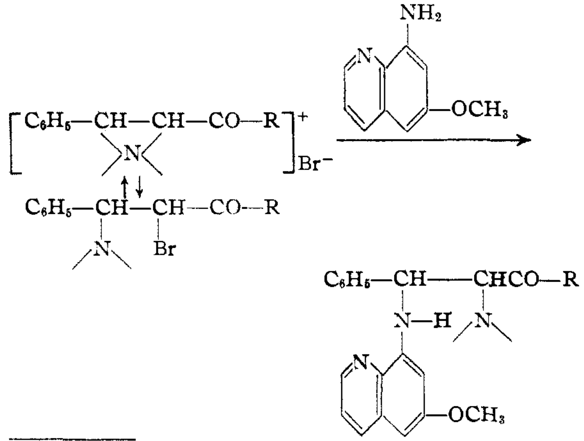
# α,β-Diamino Ketones. III.[1] Reaction of 8-Amino-6-methoxyquinoline with α-Bromo-β-aminoketones

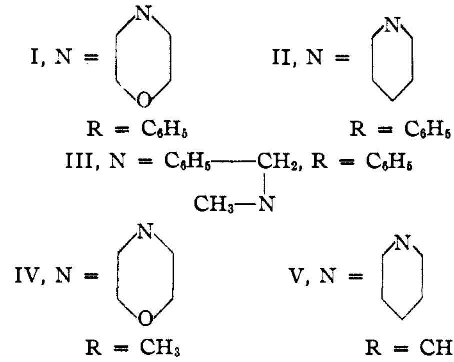
BY NORMAN H. CROMWELL AND HERMAN HOEKSEMA[2]

α-Bromo-β-aminoketones have been found to react readily with various heterocyclic secondary amines but less readily with open chain secondary amines[1] to give mixed diamino ketones. It was also shown that a primary amine might be used in these reactions.[3]

Since certain of the diamino ketones which have resulted from these investigations have shown mild activity as avian antimalarials it seemed important to attempt to introduce the plasmoquin base group into these molecules by treating various α-bromo-β-aminoketones with 8-amino-6-methoxyquinoline,[4] with the hope that such antimalarial activity might be enhanced.

8-Amino-6-methoxyquinoline, which is a relatively weak base, reacted quite readily with a series of α-bromo-β-aminoketones to give good yields of the desired mixed diamino ketones.





Although the entering amino group has always been shown to take the β-position in these molecules, it seemed necessary to prove by hydrolysis that one of these, namely (I), actually had the structure assigned. On acid hydrolysis (I) gave only the expected products, benzaldehyde, 8-amino-6-methoxyquinoline and ω-morpholino-acetophenone, isolated as the oxime.

Plasmoquin base was not strong enough to react with α,β-dibromobenzylacetone or with α-bromobenzalacetone under the usual conditions. In an attempt to convert the keto to a hydroxy group in (V), only non-resolvable oils resulted from catalytic hydrogenation using palladium on charcoal or platinum oxide in glacial acetic acid solutions. These diamino ketones seem quite resistent to reduction by any of the usual methods. Moreover, it was impossible to add the methyl Grignard reagent to (IV) to form the diamino tertiary carbinol, although such additions have been accomplished with certain of the diamino ketones mentioned in previous papers.[5] The carbonyl group seems to be quite hindered in many of these diamino ketones.

Unsuccessful attempts were made to introduce

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[1] Previous paper in series: Cromwell, Caughlan and Gilbert, THIS JOURNAL, 66, 401 (1944).

[2] Parke, Davis and Co. Research Fellow, 1943-1944.

[3] Cromwell, Harris and Cram, THIS JOURNAL, 66, 134 (1944).

[4] A supply of this base was generously furnished for this work by the Parke, Davis and Co. Research Laboratories, Detroit, Michigan.

[5] (a) Cromwell, THIS JOURNAL, 62, 3470 (1940). (b) Unpublished work from this Laboratory.